

[0003] The large majority of patients having B cell malignancies, including non-Hodgkin's lymphoma (NHL) and multiple myeloma (MM), are significant contributors to cancer mortality. The response of B cell malignancies to various forms of treatment is mixed. Traditional methods of treating B cell malignancies, including chemotherapy and radiotherapy, have limited utility due to toxic side effects. Immunotherapy with anti-CD19, anti-CD20, anti-CD22, anti-CD23, anti-CD52, anti-CD80, and anti-HLA-DR therapeutic antibodies have provided limited success, due in part to poor pharmacokinetic profiles, rapid elimination of antibodies by serum proteases and filtration at the glomerulus, and limited penetration into the tumor site and expression levels of the target antigen on cancer cells. Attempts to use genetically modified cells expressing chimeric antigen receptors (CARs) have also met with limited success. In addition, the therapeutic efficacy of a given antigen binding domain used in a CAR is unpredictable: if the antigen binding domain binds too strongly, the CAR T cells induce massive cytokine release resulting in a potentially fatal immune reaction deemed a "cytokine storm," and if the antigen binding domain binds too weakly, the CAR T cells do not display sufficient therapeutic efficacy in clearing cancer cells.

2. ~~BRIEF~~ SUMMARY

[0004] The present disclosure generally provides improved methods of treating B-cell-related diseases, e.g, multiple myeloma.

[0005] In one ~~aspect~~example, provided herein is a method of treating a disease caused by B Cell Maturation Agent (BCMA) expressing cells in a subject in need thereof, comprising: determining a first level of soluble BCMA (sBCMA) in a tissue sample from the subject; administering to the subject immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA CAR T cells), and then determining a second level of soluble BCMA in a tissue sample from the subject wherein, if said second level of sBCMA is greater than 30% of said first level of sBCMA, the subject is subsequently provided a non-CAR T cell therapy to treat said disease. Also provided herein is a method of treating a disease caused by B Cell Maturation Agent (BCMA) expressing cells in a subject in need thereof, comprising: (a) determining a first level of soluble BCMA (sBCMA) in a tissue sample from the subject; (b) administering to the subject immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA CAR T cells); and (c) determining that a second level of soluble BCMA in a tissue sample from the subject is greater than 30% of said first level, and on the basis of the

determination in step c, subsequently providing a non-CAR T cell therapy to the subject. In a specific embodimentexample of either of the above embodimentexamples, if said second level of sBCMA is greater than 40% of said first level, the subject is provided a non-CAR T cell therapy to treat said disease. In another specific embodimentexample, said second level of sBCMA is determined at 25-35 days after said administering. In another specific embodimentexample, said second level of sBCMA is determined at 28-31 days after said administering. In more specific embodimentexamples, the subject is provided a non-CAR T cell therapy within three months, two months, or one month after said determining a second level of sBCMA. In specific embodimentexamples, the immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA CAR T cells) are idecabtagene vicleucel cells. In particular embodimentexamples, the disease is multiple myeloma, e.g., relapsed and refractory multiple myeloma.

[0005a] In one aspect, the present disclosure refers to immune cells expressing a chimeric antigen receptor (CAR) directed to B cell maturation antigen (BCMA) for use in treating a disease caused by BCMA expressing cells in a subject in need thereof, wherein: a. a first level of soluble BCMA (sBCMA) in a tissue sample from the subject is to be determined; b. immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA are to be administered to the subject, and c. a second level of sBCMA in a tissue sample from the subject is to be determined and wherein, if said second level of sBCMA is greater than 30% of said first level of sBCMA, the subject is to be subsequently provided a non-CAR therapy to treat said disease.

[0005b] In one aspect, the present disclosure refers to use of immune cells expressing a chimeric antigen receptor (CAR) directed to B cell maturation antigen (BCMA) in the manufacture of a medicament for treating a disease caused by BCMA expressing cells in a subject in need thereof, wherein: a. a first level of soluble BCMA (sBCMA) in a tissue sample from the subject is to be determined; b. immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA are to be administered to the subject, and c. a second level of sBCMA in a tissue sample from the subject is to be determined and wherein, if said second level of sBCMA is greater than 30% of said first level of sBCMA, the subject is to be subsequently provided a non-CAR therapy to treat said disease.

[0006] In another aspectexample, provided herein is a method of treating a disease caused by B Cell Maturation Agent (BCMA) expressing cells, comprising administering to a patient diagnosed with said disease a non-CAR T cell therapy, wherein the patient has previously been administered immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA CAR T cells) and wherein a tissue sample from the patient subsequent to said administration contained a level of soluble BCMA (sBCMA) greater than 30% of a level of sBCMA found in a tissue sample obtained from the patient prior to said administration. In specific embodimentexamples, the immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA CAR T cells) are idecabtagene vicleucel cells. In particular embodimentexamples, the disease is multiple myeloma, e.g., relapsed and refractory multiple myeloma.

[0007] In another aspectexample, provided herein is a method of determining whether a patient diagnosed with a disease caused by B Cell Maturation Agent (BCMA) expressing cells should be administered a non-CAR T cell therapy after treatment with immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA CAR T cells), comprising determining a level of soluble BCMA (sBCMA) in a tissue sample from the patient, wherein the patient has previously been administered the immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA CAR T cells), and wherein if the level of sBCMA in the tissue sample is greater than 20%, 25%, 30%, 35%, 40%, 45% or 50% of a level of sBCMA found in a tissue sample obtained from the patient prior to said administration, then the patient is a candidate for the non-CAR T cell therapy. In a specific embodimentexample, the method further

comprises administering the non-CAR T cell therapy to the candidate for the non-CAR T cell therapy. In specific embodiment examples, the immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA CAR T cells) are idecabtagene vicleucel cells. In particular embodiment examples, the disease is multiple myeloma, e.g., relapsed and refractory multiple myeloma.

[0007a] In one aspect, the present disclosure refers to a non-CAR therapy for use in treating a disease caused by B cell maturation antigen (BCMA) expressing cells, wherein a non-chimeric antigen receptor (CAR) therapy is to be administered to a patient diagnosed with said disease, wherein the patient has previously been administered immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA and wherein a tissue sample from the patient subsequent to said administration contained a level of soluble BCMA (sBCMA) greater than 30% of a level of sBCMA found in a tissue sample obtained from the patient prior to said administration.

[0007b] In one aspect, the present disclosure refers to use of a non-CAR therapy in the manufacture of a medicament for treating a disease caused by B cell maturation antigen (BCMA) expressing cells, wherein the non-chimeric antigen receptor (CAR) therapy is to be administered to a patient diagnosed with said disease, wherein the patient has previously been administered immune cells expressing a CAR directed to BCMA and wherein a tissue sample from the patient subsequent to said administration contained a level of sBCMA greater than 30% of a level of soluble BCMA (sBCMA) found in a tissue sample obtained from the patient prior to said administration.

[0007c] In one aspect, the present disclosure refers to a non-CAR cell therapy for use in treating a disease caused by B cell maturation antigen (BCMA) expressing cells, wherein the patient has been treated with immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA, wherein a level of soluble BCMA (sBCMA) in a tissue sample from the patient is to be determined, wherein the patient has previously been administered the immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA, and wherein if the level of sBCMA in the tissue sample is greater than 30% of a level of sBCMA found in a tissue sample obtained from the patient prior to said administration, then the patient is a candidate for the non-CAR therapy, and the non-CAR therapy is to be administered to the candidate for the non-CAR therapy.

[0007d] In one aspect, the present disclosure refers to use of a non-CAR therapy in the manufacture of a medicament for treating a disease caused by B cell maturation antigen (BCMA) expressing cells, wherein the patient has been treated with immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA, wherein a level of soluble BCMA (sBCMA) in a tissue sample from the patient is to be determined, wherein the patient has previously been administered the immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA, and wherein if the level of sBCMA in the tissue sample is greater than 30% of a level of sBCMA found in a tissue sample obtained from the patient prior to said administration, then the patient is a candidate for the non-CAR therapy, and the non-CAR therapy is to be administered to the candidate for the non-CAR therapy.

[0008] In another [aspectexample](#), provided herein is a method of determining whether a patient diagnosed with a disease caused by B Cell Maturation Agent (BCMA) expressing cells should be administered a non-CAR T cell therapy after treatment with immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA CAR T cells), comprising determining a level of soluble BCMA (sBCMA) in a tissue sample from the patient, wherein the patient has previously been administered the immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA CAR T cells), and wherein if the level of sBCMA in the tissue sample is greater than 30% of a level of sBCMA found in a tissue sample obtained from the patient prior to said administration, then the patient is a candidate for the non-CAR T cell therapy. In a specific [embodimentexample](#), the method further comprises administering the non-CAR T cell therapy to the candidate for the non-CAR T cell therapy. In specific [embodimentexamples](#), the immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA CAR T cells) are idecabtagene vicleucel cells. In particular [embodimentexamples](#), the disease is multiple myeloma, e.g., relapsed and refractory multiple myeloma.

[0009] In particular [embodimentexamples](#), wherein if the level of sBCMA in the tissue sample is greater than about 20%, 25%, 30%, 35%, 40%, 45% or 50% of a level of sBCMA found in a tissue sample obtained from the patient prior to said administration, then the patient is a candidate for the non-CAR T cell therapy. Optionally, the method may further comprises administering the non-CAR T cell therapy to the candidate for the non-CAR T cell therapy.

[0010] In another [embodimentexample](#) provided herein is a method of treating a disease caused by B Cell Maturation Agent (BCMA) expressing cells in a subject in need thereof, comprising: administering to the subject immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA CAR T cells), and determining a level of soluble BCMA (sBCMA) in a tissue sample from the subject; wherein, if said level of sBCMA is greater than 4000 ng/L, the subject is subsequently provided a non-CAR T cell therapy to treat said disease. In a specific [embodimentexample](#), said level of sBCMA is determined at 50-70 days after said administering. In another specific [embodimentexample](#), said level of sBCMA is determined at 55-65 days after said

administering. In another specific embodimentexample, said of sBCMA is determined at 58-62 days after said administering. In a specific embodimentexample of the preceding embodimentexamples, the subject is provided said non-CAR T cell therapy within three months, two months, or one month after said determining a level of sBCMA. In specific embodimentexamples, the immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA CAR T cells) are idecabtagene vicleucel cells. In particular embodimentexample, the disease is multiple myeloma, e.g., relapsed and refractory multiple myeloma.

[0010a] In one aspect, the present disclosure refers to immune cells expressing a chimeric antigen receptor (CAR) directed to B cell maturation antigen (BCMA) for use in treating a disease caused by BCMA expressing cells in a subject in need thereof, wherein: a. immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA are to be administered to the subject, and b. a level of soluble BCMA (sBCMA) in a tissue sample from the subject is to be determined wherein, if said level of sBCMA is greater than 4000 ng/L, the subject is to be subsequently provided a non-CAR therapy to treat said disease.

[0010b] In one aspect, the present disclosure refers to use of immune cells expressing a chimeric antigen receptor (CAR) directed to B cell maturation antigen (BCMA) in the manufacture of a medicament for treating a disease caused by BCMA expressing cells in a subject in need thereof, wherein: a. immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA is to be administered to the subject, and b. a level of soluble BCMA (sBCMA) in a tissue sample from the subject is to be determined wherein, if said level of sBCMA is greater than 4000 ng/L, the subject is to be subsequently provided a non-CAR therapy to treat said disease.

[0011] In another embodimentexample, provided herein is a method of treating a disease caused by B Cell Maturation Agent (BCMA) expressing cells in a subject in need thereof, comprising: determining a first level of interleukin-6 (IL-6), tumor necrosis factor alpha (TNF α) or both in a tissue sample from the subject; administering to the subject immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA CAR T cells), and subsequently determining a second level of IL-6, TNF α or both in a tissue sample from the subject; wherein, if said second level of IL-6, TNF α or both is not greater than said first level of IL-6, TNF α or both, respectively, then the subject is subsequently provided a non-CAR T cell therapy to treat said disease. In a specific embodimentexample, said first level is determined on the day of said

administering to the subject said immune cells expressing a CAR directed to BCMA, and said second level is determined 1-4 days after said administering. In another specific

embodimentexample, said second level is determined two days after said administering. In specific embodimentexamples, the immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA CAR T cells) are idecabtagene vicleucel cells. In particular embodimentexamples, the disease is multiple myeloma, e.g., relapsed and refractory multiple myeloma.

[0011a] In one aspect, the present disclosure refers to immune cells expressing a chimeric antigen receptor (CAR) directed to B cell maturation antigen (BCMA) for use in treating a disease caused by BCMA expressing cells in a subject in need thereof, wherein: a. a first level of interleukin-6 (IL-6), tumor necrosis factor alpha (TNF α) or both in a tissue sample from the subject is to be determined; b. immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA are to be administered to the subject, and c. a second level of IL-6, TNF α or both in a tissue sample from the subject is to be subsequently determined; wherein, if said second level of IL-6 is not greater than first level of IL-6, said second level of TNF α is not greater than said first level of TNF α or both are not greater than said first levels, then the subject is to be subsequently provided a non-CAR therapy to treat said disease.

[0011b] In one aspect, the present disclosure refers to use of immune cells expressing a chimeric antigen receptor (CAR) directed to B cell maturation antigen (BCMA) in the manufacture of a medicament for treating a disease caused by BCMA expressing cells in a subject in need thereof, wherein: a. a first level of interleukin-6 (IL-6), tumor necrosis factor alpha (TNF α) or both in a tissue sample from the subject is to be determined; b. immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA is to be administered to the subject, and c. a second level of IL-6, TNF α or both in a tissue sample from the subject is to be subsequently determined; wherein, if said second level of IL-6 is not greater than first level of IL-6, said second level of TNF α is not greater than said first level of TNF α , or both are not greater than said first levels, then the subject is to be subsequently provided a non-CAR therapy to treat said disease.

[0012] In another aspectexample, provided herein is a method of treating a disease caused by B Cell Maturation Agent (BCMA)-expressing cells in a subject in need thereof, comprising: administering to the subject immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA CAR T cells), and determining a level of ferritin in a tissue sample from the subject; wherein, if said level of ferritin is greater than 1500 picomoles per liter, the subject is subsequently provided a therapy to treat cytokine release syndrome (CRS). In certain embodimentexamples, said determining is performed within 0-4 days prior to said administering. In a specific embodimentexample, said determining is performed on the same day as said administering. In another specific embodimentexample, said therapy to treat CRS is first provided to said subject 0-5 days

after said administering. In specific embodimentexamples, the immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA CAR T cells) are idecabtagene vicleucel cells. In particular embodimentexamples, the disease is multiple myeloma, e.g., relapsed and refractory multiple myeloma.

[0012a] In one aspect, the present disclosure refers to immune cells expressing a chimeric antigen receptor (CAR) directed to B cell maturation antigen (BCMA) for use in treating a disease caused by BCMA expressing cells in a subject in need thereof, wherein: a. immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA are to be administered to the subject, and b. a level of ferritin in a tissue sample from the subject is to be determined; wherein, if said level of ferritin is greater than 1500 picomoles per liter, the subject is subsequently provided a therapy to treat cytokine release syndrome (CRS).

[0012b] In one aspect, the present disclosure refers to use of immune cells expressing a chimeric antigen receptor (CAR) directed to B cell maturation antigen (BCMA) in the manufacture of a medicament for treating a disease caused by BCMA expressing cells in a subject in need thereof, wherein: a. immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA are to be administered to the subject, and b. a level of ferritin in a tissue sample from the subject is to be determined; wherein, if said level of ferritin is greater than 1500 picomoles per liter, the subject is subsequently provided a therapy to treat cytokine release syndrome (CRS).

[0013] In another aspectexample, provided herein is a method of treating a disease caused by B Cell Maturation Agent (BCMA) expressing cells in a subject in need thereof, comprising: (a) determining a first level of soluble BCMA (sBCMA) and/or a first level of interleukin-6 (IL-6), tumor necrosis factor alpha (TNF α), or both in a tissue sample from the subject; (b) administering to the subject immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA CAR T cells), and (c) determining a second level of sBCMA and/or a second level of interleukin-6 (IL-6), tumor necrosis factor alpha (TNF α), or both in a tissue sample from the subject wherein, if said second level of sBCMA is greater than 20%, 25%, 30%, 35%, 40%, 45% or 50% of said first level of sBCMA and/or if said second level of IL-6, TNF α or both is not greater than said first level of IL-6, TNF α or both, the subject is subsequently provided a non-CAR T cell therapy to treat said disease. In certain embodimentexamples, if said second level of IL-6, TNF α or both is not greater than about 80%, 90%, 95%, 100%, 110%, 120%, or 150% of said first level of IL-6, TNF α or both, the subject is subsequently provided a non-CAR T cell therapy to treat said disease. In specific embodimentexamples, the immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA CAR T cells) are idecabtagene vicleucel cells. In particular embodimentexamples, the disease is multiple myeloma, e.g., relapsed and refractory multiple myeloma.

[0014] In another aspectexample, provided herein is a method of treating a disease caused by B Cell Maturation Agent (BCMA) expressing cells in a subject in need thereof, comprising: (a) determining a first level of soluble BCMA (sBCMA) and/or a first level of interleukin-6 (IL-6), tumor necrosis factor alpha (TNF α), or both in a tissue sample from the subject; (b) administering to the subject immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA CAR T cells), and (c) determining a second level of sBCMA and/or a second level of interleukin-6 (IL-6), tumor necrosis factor alpha (TNF α), or both in a tissue sample from the subject wherein, if said second level of sBCMA is greater than 30% of said first level of sBCMA and/or if said second level of IL-6, TNF α or both is not greater than said first level of IL-6, TNF α or both, the subject is subsequently provided a non-CAR T cell therapy to treat said

disease. In certain embodiment examples, if said second level of IL-6, TNF α or both is not greater than about 80%, 90%, 95%, 100%, 110%, 120%, or 150% of said first level of IL-6, TNF α or both, the subject is subsequently provided a non-CAR T cell therapy to treat said disease. In specific embodiment examples, the immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA CAR T cells) are idecabtagene vicleucel cells. In particular embodiment examples, the disease is multiple myeloma, e.g., relapsed and refractory multiple myeloma.

[0014a] In one aspect, the present disclosure refers to immune cells expressing a chimeric antigen receptor (CAR) directed to B cell maturation antigen (BCMA) for use in treating a disease caused by BCMA expressing cells in a subject in need thereof, wherein: a. a first level of soluble BCMA (sBCMA) and/or a first level of interleukin-6 (IL-6), tumor necrosis factor alpha (TNF α), or both in a tissue sample from the subject is to be determined; b. immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA are to be administered to the subject, and c. a second level of sBCMA and/or a second level of interleukin-6 (IL-6), tumor necrosis factor alpha (TNF α), or both in a tissue sample from the subject is to be determined wherein, if said second level of sBCMA is greater than 30% of said first level of sBCMA and/or if said second level of IL-6 is not greater than said first level of IL-6, said second level of TNF α is not greater than said first level of TNF α or both are not greater than said first levels, the subject is to be subsequently provided a non-CAR therapy to treat said disease.

[0014b] In one aspect, the present disclosure refers to use of immune cells expressing a chimeric antigen receptor (CAR) directed to B cell maturation antigen (BCMA) in the manufacture of a medicament for treating a disease caused by BCMA expressing cells in a subject in need thereof, wherein: a. a first level of soluble BCMA (sBCMA) and/or a first level of interleukin-6 (IL-6), tumor necrosis factor alpha (TNF α), or both in a tissue sample from the subject is to be determined; b. immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA are to be administered to the subject, and c. a second level of sBCMA and/or a second level of interleukin-6 (IL-6), tumor necrosis factor alpha (TNF α), or both in a tissue sample from the subject is to be determined wherein, if said second level of sBCMA is greater than 30% of said first level of sBCMA and/or if said second level of IL-6 is not greater than said first level of IL-6, said second level of TNF α is not greater than said first level of TNF α or both are not greater than said first levels, the subject is to be subsequently provided a non-CAR therapy to treat said disease.

[0014c] In one aspect, the present disclosure refers to a non-CAR therapy for use in treating a disease caused by B cell maturation antigen (BCMA) expressing cells, wherein a non-chimeric antigen receptor (CAR) therapy is to be administered to a patient diagnosed with said disease, wherein the patient has previously been administered immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA and wherein a tissue sample from the patient subsequent to said administration contained (i) a level of soluble BCMA (sBCMA) greater than 30% of a level of sBCMA found in a tissue sample obtained from the patient prior to said

administration and/or (ii) a level of IL-6, TNF α or both not greater than a level of IL-6, TNF α or both found in a tissue sample obtained from the patient prior to said administration.

[0014d] In one aspect, the present disclosure refers to use of a non-CAR therapy in the manufacture of a medicament for treating a disease caused by B cell maturation antigen (BCMA) expressing cells, wherein the non-CAR therapy is to be administered to a patient diagnosed with said disease, wherein the patient has previously been administered immune cells expressing a CAR directed to BCMA and wherein a tissue sample from the patient subsequent to said administration contained (i) a level of soluble BCMA (sBCMA) greater than 30% of a level of sBCMA found in a tissue sample obtained from the patient prior to said administration and/or (ii) a level of IL-6, TNF α or both not greater than a level of IL-6, TNF α or both found in a tissue sample obtained from the patient prior to said administration.

[0015] In certain embodimentexamples, if i) said second level of sBCMA is greater than about 20%, 25%, 30%, 35%, 40%, 45% or 50% of said first level of sBCMA, and ii) if said second level of IL-6, TNF α or both is not about 10%, 15%, 20%, 25%, 30%, 35%, 40% 45% or 50% greater than said first level of IL-6, TNF α or both, the subject is subsequently provided a non-CAR T cell therapy to treat said disease. In specific embodimentexamples, the immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA CAR T cells) are idecabtagene vicleucel cells. In particular embodimentexamples, the disease is multiple myeloma, e.g., relapsed and refractory multiple myeloma.

[0016] In another aspectexample, provided herein is a method of treating a disease caused by B Cell Maturation Agent (BCMA) expressing cells in a subject in need thereof, comprising: (a) determining a first level of soluble BCMA (sBCMA) and/or a first level of interleukin-6 (IL-6), tumor necrosis factor alpha (TNF α), or both in a tissue sample from the subject; (b) administering to the subject immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA CAR T cells), (c) determining that a second level of sBCMA in a tissue sample from the subject is greater than 20%, 25%, 30%, 35%, 40%, 45% or 50% of said first level of sBCMA and/or a second level of IL-6, TNF α or both is not greater than said first level of IL-6, TNF α or both, and (d) on the basis of the determination in step c, subsequently providing a non-CAR T cell therapy to the subject. In specific embodimentexamples, the immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA CAR T cells) are idecabtagene vicleucel cells. In particular embodimentexamples, the disease is multiple myeloma, e.g., relapsed and refractory multiple myeloma.

[0017] In another aspectexample, provided herein is a method of treating a disease caused by B Cell Maturation Agent (BCMA) expressing cells in a subject in need thereof, comprising: (a) determining a first level of soluble BCMA (sBCMA) and/or a first level of interleukin-6 (IL-6), tumor necrosis factor alpha (TNF α), or both in a tissue sample from the subject; (b)

administering to the subject immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA CAR T cells), (c) determining that a second level of sBCMA in a tissue sample from the subject is greater than 30% of said first level of sBCMA and/or a second level of IL-6, TNF α or both is not greater than said first level of IL-6, TNF α or both, and (d) on the basis of the determination in step c, subsequently providing a non-CAR T cell therapy to the subject. In specific [embodimentexamples](#), the immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA CAR T cells) are idecabtagene vicleucel cells. In particular [embodimentexample](#), the disease is multiple myeloma, e.g., relapsed and refractory multiple myeloma.

[0018] In certain [embodimentexamples](#) the method comprises: (c) determining that a second level of IL-6, TNF α or both is not greater than about 80%, 90%, 95%, 100%, 110%, 120%, or 150% of said first level of IL-6, TNF α or both, and (d) on the basis of the determination in step (c), subsequently providing a non-CAR T cell therapy to the subject. In specific [embodimentexamples](#), the immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA CAR T cells) are idecabtagene vicleucel cells. In particular [embodimentexamples](#), the disease is multiple myeloma, e.g., relapsed and refractory multiple myeloma.

[0019] In certain [embodimentexamples](#) the method comprises: (c) determining that a second level of sBCMA is greater than about 20%, 25%, 30%, 35%, 40%, 45% or 50% of said first level of sBCMA, and determining that a second level of IL-6, TNF α or both is not greater than about 80%, 90%, 95%, 100%, 110%, 120%, or 150% of said first level of IL-6, TNF α or both, and (d) on the basis of the determination in step (c), subsequently providing a non-CAR T cell therapy to the subject. In specific [embodimentexamples](#), the immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA CAR T cells) are idecabtagene vicleucel cells. In particular [embodimentexamples](#), the disease is multiple myeloma, e.g., relapsed and refractory multiple myeloma.

[0020] In another [aspectexample](#), provided herein is a method of treating a disease caused by B Cell Maturation Agent (BCMA) expressing cells, comprising administering to a patient diagnosed with said disease a non-CAR T cell therapy, wherein the patient has previously been administered immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA CAR T cells) and wherein a tissue sample from the patient subsequent to said administration contained (i) a level of soluble BCMA (sBCMA) greater than 30% of a level of sBCMA found in a tissue sample obtained from the patient prior to said administration and/or (ii) a level of IL-6, TNF α or both not greater than a level of IL-6, TNF α or both found in a tissue

sample obtained from the patient prior to said administration. In specific [embodimentexamples](#), the immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA CAR T cells) are idecabtagene vicleucel cells. In particular [embodimentexamples](#), the disease is multiple myeloma, e.g., relapsed and refractory multiple myeloma.

[0021] In certain [embodimentexamples](#) the method comprises administering to the patient a non-CAR T cell therapy, wherein a tissue sample from the patient subsequent to said administration contained (i) a level of soluble BCMA (sBCMA) greater than about 20%, 25%, 30%, 35%, 40%, 45% or 50% of said first of sBCMA found in a tissue sample obtained from the patient prior to said administration and/or (ii) a level of IL-6, TNF α or both not greater than about 20%, 25%, 30%, 35%, 40%, 45% or 50% of a level of IL-6, TNF α or both found in a tissue sample obtained from the patient prior to said administration. In specific [embodimentexamples](#), the immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA CAR T cells) are idecabtagene vicleucel cells. In particular [embodimentexamples](#), the disease is multiple myeloma, e.g., relapsed and refractory multiple myeloma.

[0022] In another [aspectexample](#), provided herein is a method of determining whether a patient diagnosed with a disease caused by B Cell Maturation Agent (BCMA) expressing cells should be administered a non-CAR T cell therapy after treatment with immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA CAR T cells), comprising determining a level of soluble BCMA (sBCMA) and/or a level of IL-6, TNF α or both in a tissue sample from the patient, wherein the patient has previously been administered the immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA CAR T cells), and wherein if (i) the level of sBCMA in the tissue sample is greater than 20%, 25%, 30%, 35%, 40%, 45% or 50% of a level of sBCMA found in a tissue sample obtained from the patient prior to said administration and/or (ii) the level of IL-6, TNF α or both is not greater than a level of IL-6, TNF α or both found in a tissue sample obtained from the patient prior to said administration, then the patient is a candidate for the non-CAR T cell therapy. In a specific [embodimentexample](#), the method further comprises administering the non-CAR T cell therapy to the candidate for the non-CAR T cell therapy. In specific [embodimentexamples](#), the immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA CAR T cells) are idecabtagene vicleucel cells. In particular [embodimentexample](#), the disease is multiple myeloma, e.g., relapsed and refractory multiple myeloma.

[0022a] In one aspect, the present disclosure refers to a non-CAR therapy for use in a method of treating a disease caused by B cell maturation antigen (BCMA) expressing cells, wherein the patient has been treated with immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA, wherein a level of soluble BCMA (sBCMA) and/or a level of IL-6, TNF α or both in a tissue sample from the patient is to be determined, wherein the patient has previously been administered the immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA, and wherein if (i) the level of sBCMA in the tissue sample is greater than 30% of a level of sBCMA found in a tissue sample obtained from the patient prior to said administration and/or (ii) the level of IL-6, TNF α or both is not greater than a level of IL-6, TNF α or both found in a tissue sample obtained from the patient prior to said administration, then the patient is a candidate for the non-CAR therapy, and the non-CAR therapy is to be administered to the candidate for the non-CAR therapy.

[0022b] In one aspect, the present disclosure refers to use of a non-CAR therapy for use in the manufacture of a medicament for treating a disease caused by B cell maturation antigen (BCMA) expressing cells, wherein the patient has been treated with immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA, wherein a level of soluble BCMA (sBCMA) and/or a level of IL-6, TNF α or both in a tissue sample from the patient is to be determined, wherein the patient has previously been administered the immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA, and wherein if (i) the level of sBCMA in the tissue sample is greater than 30% of a level of sBCMA found in a tissue sample obtained from the patient prior to said administration and/or (ii) the level of IL-6, TNF α or both is not greater than a level of IL-6, TNF α or both found in a tissue sample obtained from the patient prior to said administration, then the patient is a candidate for the non-CAR therapy, and the non-CAR therapy is to be administered to the candidate for the non-CAR therapy.

[0023] In another ~~aspect~~example, provided herein is a method of determining whether a patient diagnosed with a disease caused by B Cell Maturation Agent (BCMA) expressing cells should be administered a non-CAR T cell therapy after treatment with immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA CAR T cells), comprising determining a level of soluble BCMA (sBCMA) and/or a level of IL-6, TNF α or both in a tissue sample from the patient, wherein the patient has previously been administered the immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA CAR T cells), and wherein if (i) the

level of sBCMA in the tissue sample is greater than 30% of a level of sBCMA found in a tissue sample obtained from the patient prior to said administration and/or (ii) the level of IL-6, TNF α or both is not greater than a level of IL-6, TNF α or both found in a tissue sample obtained from the patient prior to said administration, then the patient is a candidate for the non-CAR T cell therapy. In a specific [embodimentexample](#), the method further comprises administering the non-CAR T cell therapy to the candidate for the non-CAR T cell therapy. In specific [embodimentexamples](#), the immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA CAR T cells) are idecabtagene vicleucel cells. In particular [embodimentexamples](#), the disease is multiple myeloma, e.g., relapsed and refractory multiple myeloma.

[0024] In certain [embodimentexamples](#) of the method, if (i) the level of sBCMA in the tissue sample is greater than about 20%, 25%, 30%, 35%, 40%, 45% or 50% of a level of sBCMA found in a tissue sample obtained from the patient prior to said administration and/or (ii) the level of IL-6, TNF α or both is not greater than about 20%, 25%, 30%, 35%, 40%, 45% or 50% of a level of IL-6, TNF α or both found in a tissue sample obtained from the patient prior to said administration, then the patient is a candidate for the non-CAR T cell therapy. In a specific [embodimentexample](#), the method further comprises administering the non-CAR T cell therapy to the candidate for the non-CAR T cell therapy. In specific [embodimentexamples](#), the immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA CAR T cells) are idecabtagene vicleucel cells. In particular [embodimentexamples](#), the disease is multiple myeloma, e.g., relapsed and refractory multiple myeloma.

[0025] In a specific [embodimentexamples](#) of any of the above [aspectexamples](#) or [embodimentexamples](#), said tissue sample is blood, plasma or serum. In another specific [embodimentexamples](#) of any of the above [aspectexamples](#) or [embodimentexamples](#), said disease caused by BCMA-expressing cells is multiple myeloma, chronic lymphocytic leukemia, or a non-Hodgkins lymphoma (e.g., Burkitt's lymphoma, chronic

lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL), diffuse large B cell lymphoma, follicular lymphoma, immunoblastic large cell lymphoma, precursor B-lymphoblastic lymphoma, and mantle cell lymphoma). In specific [embodimentexamples](#), the disease is multiple myeloma, *e.g.*, high-risk multiple myeloma or relapsed and refractory multiple myeloma. In other specific [embodimentexamples](#), the high risk multiple myeloma is R-ISS stage III disease and/or a disease characterized by early relapse (*e.g.*, progressive disease within 12 months since the date of last treatment regimen, such as last treatment regimen with a proteasome inhibitor, an immunomodulatory agent and/or dexamethasone). In specific [embodimentexamples](#), said disease caused by BCMA-expressing cells is a non-Hodgkins lymphoma, and wherein the non-Hodgkins lymphoma is selected from the group consisting of: Burkitt's lymphoma, chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL), diffuse large B cell lymphoma, follicular lymphoma, immunoblastic large cell lymphoma, precursor B-lymphoblastic lymphoma, and mantle cell lymphoma. In one [embodimentexample](#), before the administration of the T cells expressing a chimeric antigen receptor (CAR) directed to B Cell Maturation Antigen (BCMA), the subject having a tumor has been assessed for expression of BCMA by the tumor.

[0026] In specific [embodimentexamples](#) of any of the above [aspectexamples-or-embodiments](#), the immune cells are T cells, *e.g.*, CD4⁺ T cells, CD8⁺ T cells or cytotoxic T lymphocytes (CTLs), T killer cells, or natural killer (NK) cells. In another specific [embodimentexample](#) [specific-embodiment](#), the immune cells are administered in a dosage of from 150 x 10⁶ cells to 450 x 10⁶ cells.

[0027] In a specific [embodimentexample](#) of any of the above [embodimentexamples](#), the non-CAR T cell therapy comprises a proteasome inhibitor, lenalidomide, pomalidomide, thalidomide, bortezomib, dexamethasone, cyclophosphamide, doxorubicin, carfilzomib, ixazomib, cisplatin, doxorubicin, etoposide, an anti-CD38 antibody panobinostat, or elotuzumab. In more specific [embodimentexamples](#), before said administering said subject has received one or more lines of prior therapy comprising: daratumumab, pomalidomide, and dexamethasone (DPd); daratumumab, bortezomib, and dexamethasone (DVd); ixazomib, lenalidomide, and dexamethasone (IRd); daratumumab, lenalidomide and dexamethasone; bortezomib, lenalidomide and dexamethasone (RVd); bortezomib, cyclophosphamide and dexamethasone (BCd); bortezomib, doxorubicin and dexamethasone; carfilzomib, lenalidomide and dexamethasone (CRd); bortezomib and dexamethasone; bortezomib, thalidomide and dexamethasone; lenalidomide and dexamethasone; dexamethasone, thalidomide, cisplatin, doxorubicin, cyclophosphamide, etoposide and

bortezomib (VTD-PACE); lenalidomide and low-dose dexamethasone; bortezomib, cyclophosphamide and dexamethasone; carfilzomib and dexamethasone; lenalidomide alone; bortezomib alone; daratumumab alone; elotuzumab, lenalidomide, and dexamethasone; elotuzumab, lenalidomide and dexamethasone; bendamustine, bortezomib and dexamethasone; bendamustine, lenalidomide, and dexamethasone; pomalidomide and dexamethasone; pomalidomide, bortezomib and dexamethasone; pomalidomide, carfilzomib and dexamethasone; bortezomib and liposomal doxorubicin; cyclophosphamide, lenalidomide, and dexamethasone; elotuzumab, bortezomib and dexamethasone; ixazomib and dexamethasone; panobinostat, bortezomib and dexamethasone; panobinostat and carfilzomib; or pomalidomide, cyclophosphamide and dexamethasone; or any one of the other therapeutic agents listed in Section 5.9, below. In a more specific embodimentexample, the patient has not received said non-CAR T cell therapy prior to administration of CAR T cells.

[0028] In another specific embodimentexample of any of the above aspectexamples or embodiments, before said administering said subject has received three or more lines of prior therapy, or one or more lines of prior therapy. In more specific embodimentexamples, said lines of prior therapy comprise a proteasome inhibitor, lenalidomide, pomalidomide, thalidomide, bortezomib, dexamethasone, cyclophosphamide, doxorubicin, carfilzomib, ixazomib, cisplatin, doxorubicin, etoposide, an anti-CD38 antibody panobinostat, or elotuzumab. In more specific embodimentexamples, before said administering said subject has received one or more lines of prior therapy comprising: daratumumab, pomalidomide, and dexamethasone (DPd); daratumumab, bortezomib, and dexamethasone (DVd); ixazomib, lenalidomide, and dexamethasone (IRd); daratumumab, lenalidomide and dexamethasone; bortezomib, lenalidomide and dexamethasone (RVd); bortezomib, cyclophosphamide and dexamethasone (BCd); bortezomib, doxorubicin and dexamethasone; carfilzomib, lenalidomide and dexamethasone (CRd); bortezomib and dexamethasone; bortezomib, thalidomide and dexamethasone; lenalidomide and dexamethasone; dexamethasone, thalidomide, cisplatin, doxorubicin, cyclophosphamide, etoposide and bortezomib (VTD-PACE); lenalidomide and low-dose dexamethasone; bortezomib, cyclophosphamide and dexamethasone; carfilzomib and dexamethasone; lenalidomide alone; bortezomib alone; daratumumab alone; elotuzumab, lenalidomide, and dexamethasone; elotuzumab, lenalidomide and dexamethasone; bendamustine, bortezomib and dexamethasone; bendamustine, lenalidomide, and dexamethasone; pomalidomide and dexamethasone;

pomalidomide, bortezomib and dexamethasone; pomalidomide, carfilzomib and dexamethasone; bortezomib and liposomal doxorubicin; cyclophosphamide, lenalidomide, and dexamethasone; elotuzumab, bortezomib and dexamethasone; ixazomib and dexamethasone; panobinostat, bortezomib and dexamethasone; panobinostat and carfilzomib; or pomalidomide, cyclophosphamide and dexamethasone. In various more specific [embodimentexamples](#), said subject has received two, three, four, five, six, seven or more of said lines of prior therapy; no more than three of said lines of prior therapy; no more than two of said lines of prior therapy; or no more than one of said lines of prior therapy.

[0029] In specific [embodimentexamples](#) of any of the above [aspectexamples](#) or [embodiments](#), the immune cells are administered at a dose ranging from 150×10^6 cells to 450×10^6 cells, 300×10^6 cells to 600×10^6 cells, 350×10^6 cells to 600×10^6 cells, 350×10^6 cells to 550×10^6 cells, 400×10^6 cells to 600×10^6 cells, 150×10^6 cells to 300×10^6 cells, or 400×10^6 cells to 500×10^6 cells. In some [embodimentexamples](#), the immune cells are administered at a dose of about 150×10^6 cells, about 200×10^6 cells, about 250×10^6 cells, about 300×10^6 cells, about 350×10^6 cells, about 400×10^6 cells, about 450×10^6 cells, about 500×10^6 cells, or about 550×10^6 cells. In one [embodimentexample](#), the immune cells are administered at a dose of about 450×10^6 cells. In some [embodimentexamples](#), the subject is administered one infusion of the immune cells expressing a chimeric antigen receptor (CAR) directed to B Cell Maturation Antigen (BCMA). In some [embodimentexamples](#), the administration of the immune cells expressing a CAR directed to BCMA is repeated (e.g., a second dose of immune cells is administered to the subject).

[0030] In specific [embodimentexamples](#) of any of the [embodimentexamples](#) described herein, the immune cells expressing a CAR directed to BCMA are administered in a dosage of from about 150×10^6 cells to about 300×10^6 cells. In specific [embodimentexamples](#) of any of the [embodimentexamples](#) described herein, the immune cells expressing a CAR directed to BCMA are administered in a dosage of from about 350×10^6 cells to about 550×10^6 cells. In specific [embodimentexamples](#) of any of the [embodimentexamples](#) described herein, the immune cells expressing a CAR directed to BCMA are administered in a dosage of from about 400×10^6 cells to about 500×10^6 cells. In specific [embodimentexamples](#) of any of the [embodimentexamples](#) described herein, the immune cells expressing a CAR directed to BCMA are administered in a dosage of from about 150×10^6 cells to about 250×10^6 cells. In specific [embodimentexamples](#) of any of the [embodimentexamples](#) described herein, the immune cells expressing a CAR directed to BCMA are administered in a dosage of from about 300×10^6 cells

administered in a dosage of from about 250×10^6 cells to about 350×10^6 cells. In specific [embodimentexamples](#) of any of the [embodimentexamples](#) described herein, the immune cells expressing a CAR directed to BCMA are administered in a dosage of about 450×10^6 cells. In specific [embodimentexamples](#) of any of the [embodimentexamples](#) described herein, the immune cells are T cells (e.g., autologous T cells). In specific [embodimentexamples](#) of any of the [embodimentexamples](#) described herein, the subjects being treated undergo a leukapheresis procedure to collect autologous immune cells for the manufacture of the immune cells expressing a CAR directed to BCMA prior to their administration to the subject. In specific [embodimentexamples](#) of any of the [embodimentexamples](#) described herein, the immune cells (e.g., T cells) are administered by an intravenous infusion.

[0031] In specific [embodimentexamples](#) of any of the [aspectexamples-or-embodiments](#) disclosed herein, before administration of immune cells expressing a CAR directed to BCMA, the subject being treated is administered a lymphodepleting (LD) chemotherapy. In specific [embodimentexamples](#), LD chemotherapy comprises fludarabine and/or cyclophosphamide. In specific [embodimentexamples](#), LD chemotherapy comprises fludarabine (e.g., about 30 mg/m^2 for intravenous administration) and cyclophosphamide (e.g., about 300 mg/m^2 for intravenous administration) for a duration of 1, 2, 3, 4, 5, 6, or 7 days (e.g., 3 days). In other specific [embodimentexamples](#), LD chemotherapy comprises any of the chemotherapeutic agents described in Section 5.9. In specific [embodimentexamples](#), the subject is administered immune cells expressing a chimeric antigen receptor (CAR) directed to B Cell Maturation Antigen (BCMA) 1, 2, 3, 4, 5, 6, or 7 days after the administration of the LD chemotherapy (e.g., 2 or 3 days after the administration of the LD chemotherapy). In specific [embodimentexamples](#), the subject has not received any therapy prior to the initiation of the LD chemotherapy for at least or more than 1 week, at least or more than 2 weeks (at least or more than 14 days), at least or more than 3 weeks, at least or more than 4 weeks, at least or more than 5 weeks, or at least or more than 6 weeks. In specific [embodimentexamples](#) of any of the [embodimentexamples](#) disclosed herein, before administration of immune cells expressing a chimeric antigen receptor (CAR) directed to B Cell Maturation Antigen (BCMA), the subject being treated has received only a single prior treatment regimen.

[0032] For any of the above [embodimentexamples](#), the subject undergoes apheresis to collect and isolate said immune cells, e.g., T cells. In a specific [embodimentexample](#) of any of the above [embodimentexamples](#), said subject exhibits at the time of said apheresis: M-protein (serum protein electrophoresis [sPEP] or urine protein electrophoresis [uPEP]): sPEP $\geq 0.5 \text{ g/dL}$ or uPEP $\geq 200 \text{ mg/24 hours}$; light chain

multiple myeloma without measurable disease in the serum or urine, with serum immunoglobulin free light chain ≥ 10 mg/dL and abnormal serum immunoglobulin kappa lambda free light chain ratio; and/or Eastern Cooperative Oncology Group (ECOG) performance status ≤ 1 . In a more specific [embodimentexample](#), said subject at the time of apheresis additionally: has received at least three of said lines of prior treatment, including prior treatment with a proteasome inhibitor, an immunomodulatory agent (lenalidomide or pomalidomide) and an anti-CD38 antibody; has undergone at least 2 consecutive cycles of treatment for each of said at least three lines of prior treatment, unless progressive disease was the best response to a line of treatment; has evidence of progressive disease on or within 60 days of the most recent line of prior treatment; and/or has achieved a response (minimal response or better) to at least one of said prior lines of treatment. In a specific [embodimentexample](#) of any of the above [embodimentexamples](#), said subject exhibits at the time of said administration: M-protein (serum protein electrophoresis [sPEP] or urine protein electrophoresis [uPEP]): sPEP ≥ 0.5 g/dL or uPEP ≥ 200 mg/24 hours; light chain multiple myeloma without measurable disease in the serum or urine, with serum immunoglobulin free light chain ≥ 10 mg/dL and abnormal serum immunoglobulin kappa lambda free light chain ratio; and/or Eastern Cooperative Oncology Group (ECOG) performance status ≤ 1 . In another more specific [embodimentexample](#), said subject additionally: has received only one prior anti-myeloma treatment regimen; has the following high risk factors: R-ISS stage III, and early relapse, defined as (i) if the subject has undergone induction plus a stem cell transplant, progressive disease (PD) less than 12 months since date of first transplant; or (ii) if the subject has received only induction, PD < 12 months since date of last treatment regimen which must contain at minimum, a proteasome inhibitor, an immunomodulatory agent and dexamethasone.

[0033] In a specific [embodimentexample](#) of any of any of the above [aspectexamples](#) or [embodimentexamples](#), said CAR comprises an antibody or antibody fragment that targets BCMA. In a more specific [embodimentexample](#), said CAR comprises a single chain Fv antibody fragment (scFv). In a more specific [embodimentexample](#), said CAR comprises a BCMA02 scFv. In a specific [embodimentexample](#) of any of the above [aspectexamples](#)-or [embodiments](#), said immune cells are idecabtagene vicleucel cells. In one [embodimentexample](#), the chimeric antigen receptor comprises a murine single chain Fv antibody fragment that targets BCMA, *e.g.*, human BCMA. In one [embodimentexample](#), the chimeric antigen receptor comprises a murine anti-BCMA scFv that binds a BCMA polypeptide, *e.g.*, a human BCMA polypeptide, a hinge domain comprising a CD8 α polypeptide, a CD8 α transmembrane domain, a CD137 (4-

1BB) intracellular co-stimulatory signaling domain, and a CD3 ζ primary signaling domain. In one [embodimentexample](#), the chimeric antigen receptor comprises a murine scFv that targets BCMA, *e.g.*, human BCMA, wherein the scFv is that of anti-BCMA02 CAR of SEQ ID NO: 9. In one [embodimentexample](#), the chimeric antigen receptor is or comprises SEQ ID NO: 9. In a more specific [embodimentexample](#) of any [embodimentexample](#) herein, said immune cells are idecabtagene vicleucel cells. In one [embodimentexample](#), the immune cells comprise a chimeric antigen receptor which comprises a murine single chain Fv antibody fragment that targets BCMA, *e.g.*, human BCMA. In one [embodimentexample](#), the immune cells comprise a chimeric antigen receptor which comprises a murine anti-BCMA scFv that binds a BCMA polypeptide, *e.g.*, human BCMA, a hinge domain comprising a CD8 α polypeptide, a CD8 α transmembrane domain, a CD137 (4-1BB) intracellular co-stimulatory signaling domain, and a CD3 ζ primary signaling domain. In one [embodimentexample](#), the immune cells comprise a chimeric antigen receptor which is or comprises SEQ ID NO: 9.

[0034] In one [aspectexample](#), provided herein is a method of treating a disease caused by B Cell Maturation Agent (BCMA) expressing cells in a subject in need thereof, comprising: (a) determining a first level of soluble BCMA (sBCMA) and/or a first level of interleukin-6 (IL-6), tumor necrosis factor alpha (TNF α), or both in a tissue sample from the subject; (b) administering to the subject immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA CAR T cells), and (c) determining a second level of sBCMA and/or a second level of interleukin-6 (IL-6), tumor necrosis factor alpha (TNF α), or both in a tissue sample from the subject wherein, if said second level of sBCMA is greater than 30% of said first level of sBCMA and/or if said second level of IL-6, TNF α or both is not greater than said first level of IL-6, TNF α or both, the subject is subsequently provided a non-CAR T cell therapy to treat said disease.

[0035] In another [aspectexample](#), provided herein is a method of treating a disease caused by B Cell Maturation Agent (BCMA) expressing cells in a subject in need thereof, comprising: (a) determining a first level of soluble BCMA (sBCMA) and/or a first level of interleukin-6 (IL-6), tumor necrosis factor alpha (TNF α), or both in a tissue sample from the subject; (b) administering to the subject immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA CAR T cells), (c) determining that a second level of sBCMA in a tissue sample from the subject is greater than 30% of said first level of sBCMA and/or a second level of IL-6, TNF α or both is not greater than said first level of IL-6, TNF α or both, and (d) on the

basis of the determination in step c, subsequently providing a non-CAR T cell therapy to the subject. In specific [embodimentexamples](#), the immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA CAR T cells) are idecabtagene vicleucel cells. In particular [embodimentexamples](#), the disease is multiple myeloma, e.g., relapsed and refractory multiple myeloma.

[0036] In another [aspectexample](#), provided herein is a method of treating a disease caused by B Cell Maturation Agent (BCMA) expressing cells, comprising administering to a patient diagnosed with said disease a non-CAR T cell therapy, wherein the patient has previously been administered immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA CAR T cells) and wherein a tissue sample from the patient subsequent to said administration contained (i) a level of soluble BCMA (sBCMA) greater than 30% of a level of sBCMA found in a tissue sample obtained from the patient prior to said administration and/or (ii) a level of IL-6, TNF α or both not greater than a level of IL-6, TNF α or both found in a tissue sample obtained from the patient prior to said administration. In specific [embodimentexamples](#), the immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA CAR T cells) are idecabtagene vicleucel cells. In particular [embodimentexamples](#), the disease is multiple myeloma, e.g., relapsed and refractory multiple myeloma.

[0037] In another [aspectexample](#), provided herein is a method of determining whether a patient diagnosed with a disease caused by B Cell Maturation Agent (BCMA) expressing cells should be administered a non-CAR T cell therapy after treatment with immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA CAR T cells), comprising determining a level of soluble BCMA (sBCMA) and/or a level of IL-6, TNF α or both in a tissue sample from the patient, wherein the patient has previously been administered the immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA CAR T cells), and wherein if (i) the level of sBCMA in the tissue sample is greater than 30% of a level of sBCMA found in a tissue sample obtained from the patient prior to said administration and/or (ii) the level of IL-6, TNF α or both is not greater than a level of IL-6, TNF α or both found in a tissue sample obtained from the patient prior to said administration, then the patient is a candidate for the non-CAR T cell therapy. In a specific [embodimentexample](#), the method further comprises administering the non-CAR T cell therapy to the candidate for the non-CAR T cell therapy. In specific [embodimentexamples](#), the immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA CAR T

cells) are idecabtagene vicleucel cells. In particular [embodimentexamples](#), the disease is multiple myeloma, e.g., relapsed and refractory multiple myeloma.

[0038] In another [aspectexample](#), provided herein is a method of treating a disease caused by B Cell Maturation Agent (BCMA) expressing cells in a subject in need thereof, comprising: (a) determining a first level of soluble BCMA (sBCMA) in a tissue sample from the subject; (b) administering to the subject immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA CAR T cells), and (c) determining a second level of sBCMA in a tissue sample from the subject wherein, if said second level of sBCMA is greater than 30% of said first level of sBCMA, the subject is subsequently administered lenalidomide to treat said disease. In a specific [embodimentexample](#), the lenalidomide is administered at a dosage of about 2.5 mg, 5 mg, 10 mg, 15 mg, 20 mg, or 25 mg. In another specific [embodimentexample](#), the lenalidomide is administered at a dosage of about 25 mg daily orally on days 1-21 of a 28-day cycle. In specific [embodimentexamples](#), the immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA CAR T cells) are idecabtagene vicleucel cells. In particular [embodimentexamples](#), the disease is multiple myeloma, e.g., relapsed and refractory multiple myeloma.

[0038a] In one aspect, the present disclosure refers to immune cells expressing a chimeric antigen receptor (CAR) directed to B cell maturation antigen (BCMA) for use in treating a disease caused by BCMA expressing cells in a subject in need thereof, wherein: a. a first level of soluble BCMA (sBCMA) in a tissue sample from the subject is to be determined; b. immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA is to be administered to the subject, and c. a second level of sBCMA in a tissue sample from the subject is to be determined wherein, if said second level of sBCMA is greater than 30% of said first level of sBCMA, the subject is to be subsequently administered lenalidomide to treat said disease.

[0039b] In one aspect, the present disclosure refers to use of immune cells expressing a chimeric antigen receptor (CAR) directed to B cell maturation antigen (BCMA) in the manufacture of a medicament for treating a disease caused by BCMA expressing cells in a subject in need thereof, wherein: a. a first level of soluble BCMA (sBCMA) in a tissue sample from the subject is to be determined; b. immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA are to be administered to the subject, and c. a second level of sBCMA in a tissue sample from the subject is to be determined wherein, if said second level of sBCMA is greater than 30% of said first level of sBCMA, the subject is to be subsequently administered lenalidomide to treat said disease.

[0039] In a specific [embodimentexample](#) of the preceding [embodimentexamples](#), the disease is Multiple Myeloma (MM). In particular [embodimentexamples](#), the disease is relapsed and refractory multiple myeloma.

[0040] In another [aspectexample](#), provided herein is a method of treating a disease caused by B Cell Maturation Agent (BCMA) expressing cells in a subject in need thereof, comprising: (a) determining a first level of soluble BCMA (sBCMA) in a tissue sample from the subject; (b) administering to the subject immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA CAR T cells), and (c) determining a second level of sBCMA in a tissue sample from the subject wherein, if said second level of sBCMA is greater than 30% of said first level of sBCMA, the subject is subsequently administered pomalidomide to treat said disease. In a specific [embodimentexample](#), the pomalidomide is administered at a dosage of about 1 mg, 2 mg, 3 mg, or 4 mg once daily. In another specific [embodimentexample](#), the pomalidomide is administered at a dosage of about 4 mg per day taken orally on days 1-21 of repeated 28-day cycles until disease progression. In specific [embodimentexamples](#), the immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA CAR T cells) are idecabtagene vicleucel cells. In a specific

embodimentexample, the disease is Multiple Myeloma (MM). In particular embodimentexamples, the disease is relapsed and refractory multiple myeloma.

[0040a] In one aspect, the present disclosure refers to immune cells expressing a chimeric antigen receptor (CAR) directed to B cell maturation antigen (BCMA) for use in treating a disease caused by BCMA expressing cells in a subject in need thereof, wherein: a. a first level of soluble BCMA (sBCMA) in a tissue sample from the subject is to be determined; b. immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA are to be administered to the subject, and c. a second level of sBCMA in a tissue sample from the subject is to be determined wherein, if said second level of sBCMA is greater than 30% of said first level of sBCMA, the subject is to be subsequently administered pomalidomide to treat said disease.

[0040b] In one aspect, the present disclosure refers to use of immune cells expressing a chimeric antigen receptor (CAR) directed to B cell maturation antigen (BCMA) in the manufacture of a medicament for treating a disease caused by BCMA expressing cells in a subject in need thereof, wherein: a. a first level of soluble BCMA (sBCMA) in a tissue sample from the subject is to be determined; b. immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA are to be administered to the subject, and c. a second level of sBCMA in a tissue sample from the subject is to be determined wherein, if said second level of sBCMA is greater than 30% of said first level of sBCMA, the subject is to be subsequently administered pomalidomide to treat said disease.

[0041] In another aspectexample, provided herein is a method of treating a disease caused by B Cell Maturation Agent (BCMA) expressing cells in a subject in need thereof, comprising: (a) determining a first level of soluble BCMA (sBCMA) in a tissue sample from the subject; (b) administering to the subject immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA CAR T cells), and (c) determining a second level of sBCMA in a tissue sample from the subject wherein, if said second level of sBCMA is greater than 30% of said first level of sBCMA, the subject is subsequently administered CC-220 to treat said disease. In a specific embodimentexample, the CC-220 is administered at a dosage of about 0.15 mg, 0.3 mg, 0.45 mg, 0.6 mg, 0.75 mg, 0.9 mg, 1.0 mg, 1.1 mg, or 1.2 mg. In a specific embodimentexample, the CC-220 is administered orally at a dosage of about 0.15 mg, 0.3 mg, 0.45 mg, 0.6 mg, 0.75 mg, 0.9 mg, 1.0 mg, 1.1 mg, or 1.2 mg daily on days 1-21 of a 28-day cycle. In specific embodimentexamples, the immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA CAR T cells) are idecabtagene vicleucel cells. In a

specific embodimentexample, the disease is Multiple Myeloma (MM). In particular

embodimentexamples, the disease is relapsed and refractory multiple myeloma.

[0041a] In one aspect, the present disclosure refers to immune cells expressing a chimeric antigen receptor (CAR) directed to B cell maturation antigen (BCMA) for use in treating a disease caused by BCMA expressing cells in a subject in need thereof, wherein: a. a first level of soluble BCMA (sBCMA) in a tissue sample from the subject is to be determined; b. immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA are to be administered to the subject, and c. a second level of sBCMA in a tissue sample from the subject is to be determined wherein, if said second level of sBCMA is greater than 30% of said first level of sBCMA, the subject is to be subsequently administered CC-220 to treat said disease.

[0041b] In one aspect, the present disclosure refers to use of immune cells expressing a chimeric antigen receptor (CAR) directed to B cell maturation antigen (BCMA) in the manufacture of a medicament for treating a disease caused by BCMA expressing cells in a subject in need thereof, wherein: a. a first level of soluble BCMA (sBCMA) in a tissue sample from the subject is to be determined; b. immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA are to be administered to the subject, and c. a second level of sBCMA in a tissue sample from the subject is to be determined wherein, if said second level of sBCMA is greater than 30% of said first level of sBCMA, the subject is to be subsequently administered CC-220 to treat said disease.

[0042] In another aspectexample, provided herein is a method of treating a disease caused by B Cell Maturation Agent (BCMA) expressing cells in a subject in need thereof, comprising: (a) determining a first level of soluble BCMA (sBCMA) in a tissue sample from the subject; (b) administering to the subject immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA CAR T cells), and (c) determining a second level of sBCMA in a tissue sample from the subject wherein, if said second level of sBCMA is greater than 30% of said first level of sBCMA, the subject is subsequently administered CC-220 and dexamethasone to treat said disease. In a specific embodimentexample, the CC-220 is administered at a dosage of about 0.15 mg, 0.3 mg, 0.45 mg, 0.6 mg, 0.75 mg, 0.9 mg, 1.0 mg, 1.1 mg, or 1.2 mg. In a specific embodimentexample, the dexamethasone is administered at a dosage of about 20 mg, 25 mg, 30 mg, 35 mg, 40 mg, 45 mg, 50 mg, 55 mg, or 60 mg. In a specific embodimentexample, the CC-220 is administered orally at a dosage of about 0.15 mg, 0.3 mg, 0.45 mg, 0.6 mg, 0.75 mg, 0.9 mg, 1.0 mg, 1.1 mg, or 1.2 mg daily on days 1-21 of a 28-day cycle. In a specific embodimentexample, the dexamethasone is administered orally at a dosage of about 20 mg, 25 mg, 30 mg, 35 mg, 40 mg,

45 mg, 50 mg, 55 mg, or 60 mg on days 1, 8, 15, and 22 of a 28-day cycle. In specific embodimentexamples, the immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA CAR T cells) are idecabtagene vicleucel cells. In a specific embodimentexample, the disease is Multiple Myeloma (MM). In particular embodimentexamples, the disease is relapsed and refractory multiple myeloma.

[0042a] In one aspect, the present disclosure refers to immune cells expressing a chimeric antigen receptor (CAR) directed to B cell maturation antigen (BCMA) for use in treating a disease caused by BCMA expressing cells in a subject in need thereof, wherein: a. a first level of soluble BCMA (sBCMA) in a tissue sample from the subject is to be determined; b. immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA are to be administered, and c. a second level of sBCMA in a tissue sample from the subject is to be determined wherein, if said second level of sBCMA is greater than 30% of said first level of sBCMA, the subject is to be subsequently administered CC-220 and dexamethasone to treat said disease.

[0042b] In one aspect, the present disclosure refers to use of immune cells expressing a chimeric antigen receptor (CAR) directed to B cell maturation antigen (BCMA) in the manufacture of a medicament for treating a disease caused by BCMA expressing cells in a subject in need thereof, wherein: a. a first level of soluble BCMA (sBCMA) in a tissue sample from the subject is to be determined; b. immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA are to be administered, and c. a second level of sBCMA in a tissue sample from the subject is to be determined wherein, if said second level of sBCMA is greater than 30% of said first level of sBCMA, the subject is to be subsequently administered CC-220 and dexamethasone to treat said disease.

[0043] In one aspectexample, provided herein is a method of treating a disease caused by B Cell Maturation Agent (BCMA) expressing cells in a subject in need thereof, comprising: (a) determining a first level of soluble BCMA (sBCMA) in a tissue sample from the subject; (b) administering to the subject a first BCMA-based treatment modality comprising immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA CAR T cells), and (c) determining a second level of sBCMA in a tissue sample from the subject, wherein, if said second level of sBCMA is greater than 30% of said first level of sBCMA, the subject is subsequently provided a second BCMA-based treatment modality to treat said disease, wherein the first BCMA-based treatment modality and the second BCMA-based treatment modality are different BCMA-based treatment modalities. In specific embodimentexamples, the first BCMA-based treatment modality comprising immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA CAR T cells) are idecabtagene vicleucel cells. In particular embodimentexamples, the disease is multiple myeloma, e.g., relapsed and refractory multiple myeloma.

[0043a] In one aspect, the present disclosure refers to immune cells expressing a chimeric antigen receptor (CAR) directed to B cell maturation antigen (BCMA) for use in treating a disease caused by BCMA expressing cells in a subject in need thereof, wherein: a. a first level of soluble BCMA (sBCMA) in a tissue sample from the subject is to be determined; b. a first

BCMA-based treatment modality comprising immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA is to be administered to the subject, and c. a second level of sBCMA in a tissue sample from the subject is to be determined wherein, if said second level of sBCMA is greater than 30% of said first level of sBCMA, the subject is subsequently provided a second BCMA-based treatment modality to treat said disease; and wherein the first BCMA-based treatment modality and the second BCMA-based treatment modality are different BCMA-based treatment modalities.

[0043b] In one aspect, the present disclosure refers to use of immune cells expressing a chimeric antigen receptor (CAR) directed to B cell maturation antigen (BCMA) in the manufacture of a medicament for treating a disease caused by BCMA expressing cells in a subject in need thereof, wherein: a. a first level of soluble BCMA (sBCMA) in a tissue sample from the subject is to be determined; b. a first BCMA-based treatment modality comprising immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA is to be administered to the subject, and c. a second level of sBCMA in a tissue sample from the subject is to be determined wherein, if said second level of sBCMA is greater than 30% of said first level of sBCMA, the subject is to be subsequently provided a second BCMA-based treatment modality to treat said disease; and wherein the first BCMA-based treatment modality and the second BCMA-based treatment modality are different BCMA-based treatment modalities.

[0044] Also provided herein is a method of treating a disease caused by B Cell Maturation Agent (BCMA) expressing cells in a subject in need thereof, comprising: (a) determining a first level of soluble BCMA (sBCMA) in a tissue sample from the subject; (b) administering to the subject a first BCMA-based treatment modality comprising immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA CAR T cells), (c) determining that a second level of sBCMA in a tissue sample from the subject is greater than 30% of said first level of sBCMA, and (d) on the basis of the determination in step c, subsequently providing a second BCMA-based treatment modality to the subject, wherein the first BCMA-based treatment modality and the second BCMA-based treatment modality are different BCMA-based treatment modalities. In specific embodiment examples, the first BCMA-based treatment modality comprising immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA CAR T cells) are idecabtagene vicleucel cells. In particular embodiment examples, the disease is multiple myeloma, e.g., relapsed and refractory multiple myeloma.

[0045] In a specific [embodimentexample](#) of the above [embodimentexamples](#), if said second level of sBCMA is greater than 40% of said first level of sBCMA, the subject is provided a second BCMA-based treatment modality to treat said disease. In another specific [embodimentexample](#), said second level of sBCMA is determined at 25-35 days after said administering. In another specific [embodimentexample](#), said second level of sBCMA is determined at 28-31 days after said administering. In other specific [embodimentexamples](#), the subject is provided a second BCMA-based treatment modality within three months, two months, or one month after said determining the second level of sBCMA. In specific [embodimentexamples](#), the first BCMA-based treatment modality comprising immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA CAR T cells) are idecabtagene vicleucel cells. In particular [embodimentexamples](#), the disease is multiple myeloma, e.g., relapsed and refractory multiple myeloma.

[0046] In another [aspectexample](#), provided herein is a method of treating a disease caused by B Cell Maturation Agent (BCMA) expressing cells, comprising administering to a patient diagnosed with said disease a second BCMA-based treatment modality, wherein the patient has previously been administered a first BCMA-based treatment modality comprising immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA CAR T cells), wherein the first BCMA-based treatment modality and the second BCMA-based treatment modality are different BCMA-based treatment modalities, and wherein a tissue sample from the patient subsequent to said administration contained a level of soluble BCMA (sBCMA) greater than 30% of a level of sBCMA found in a tissue sample obtained from the patient prior to said administration. In specific [embodimentexamples](#), the first BCMA-based treatment modality comprising immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA CAR T cells) are idecabtagene vicleucel cells. In particular [embodimentexamples](#), the disease is multiple myeloma, e.g., relapsed and refractory multiple myeloma.

[0046a] In one aspect, the present disclosure refers to a non-CAR therapy for use in treating a disease caused by B cell maturation antigen (BCMA) expressing cells, wherein a second BCMA-based treatment modality is to be administered to a patient diagnosed with said disease, wherein the patient has previously been administered a first BCMA-based treatment modality comprising immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA, wherein the first BCMA-based treatment modality and the second BCMA-based treatment modality are different BCMA-based treatment modalities; and wherein a tissue sample from the patient subsequent to said administration contained a level of soluble BCMA (sBCMA) greater than 30% of a level of sBCMA found in a tissue sample obtained from the patient prior to said administration.

[0046b] In one aspect, the present disclosure refers to use of a non-CAR therapy in the manufacture of a medicament for treating a disease caused by B cell maturation antigen (BCMA) expressing cells, wherein a second BCMA-based treatment modality is to be administered to a patient diagnosed with said disease, wherein the patient has previously been administered a first BCMA-based treatment modality comprising immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA, wherein the first BCMA-based treatment modality and the second BCMA-based treatment modality are different BCMA-based treatment modalities; and wherein a tissue sample from the patient subsequent to said administration contained a level of soluble BCMA (sBCMA) greater than 30% of a level of sBCMA found in a tissue sample obtained from the patient prior to said administration.

[0047] In another [aspectexample](#), provided herein is a method of determining whether a patient diagnosed with a disease caused by B Cell Maturation Agent (BCMA) expressing cells should be administered a second BCMA-based treatment modality after treatment with a first BCMA-based treatment modality comprising immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA CAR T cells), wherein the first BCMA-based treatment modality and the second BCMA-based treatment modality are different BCMA-based treatment modalities, comprising determining a level of soluble BCMA (sBCMA) in a tissue sample from

the patient, wherein the patient has previously been administered the first BCMA-based treatment modality comprising immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA CAR T cells), and wherein if the level of sBCMA in the tissue sample is greater than 20%, 25%, 30%, 35%, 40%, 45% or 50% of a level of sBCMA found in a tissue sample obtained from the patient prior to said administration, then the patient is a candidate for the second BCMA-based treatment modality. In a specific [embodimentexample](#), the method further comprises administering the second BCMA-based treatment modality to the candidate for the second BCMA-based treatment modality. In specific [embodimentexamples](#), the first BCMA-based treatment modality comprising immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA CAR T cells) are idecabtagene vicleucel cells. In particular [embodimentexamples](#), the disease is multiple myeloma, e.g., relapsed and refractory multiple myeloma.

[0048] In another [aspectexample](#), provided herein is a method of determining whether a patient diagnosed with a disease caused by B Cell Maturation Agent (BCMA) expressing cells should be administered a second BCMA-based treatment modality after treatment with a first BCMA-based treatment modality comprising immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA CAR T cells), wherein the first BCMA-based treatment modality and the second BCMA-based treatment modality are different BCMA-based treatment modalities, comprising determining a level of soluble BCMA (sBCMA) in a tissue sample from the patient, wherein the patient has previously been administered the first BCMA-based treatment modality comprising immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA CAR T cells), and wherein if the level of sBCMA in the tissue sample is greater than 30% of a level of sBCMA found in a tissue sample obtained from the patient prior to said administration, then the patient is a candidate for the second BCMA-based treatment modality. In a specific [embodimentexample](#), the method further comprises administering the second BCMA-based treatment modality to the candidate for the second BCMA-based treatment modality. In specific [embodimentexamples](#), the first BCMA-based treatment modality comprising immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA CAR T cells) are idecabtagene vicleucel cells. In particular [embodimentexamples](#), the disease is multiple myeloma, e.g., relapsed and refractory multiple myeloma.

[0048a] In one aspect, the present disclosure refers to a non-CAR cell therapy for use in treating a disease caused by B cell maturation antigen (BCMA) expressing cells, wherein the patient has been treated with a first BCMA-based treatment modality comprising immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA, wherein the first BCMA-based treatment modality and the second BCMA-based treatment modality are different BCMA-based treatment modalities, wherein a level of soluble BCMA (sBCMA) in a tissue sample from the patient is to be determined, wherein the patient has previously been administered the first BCMA-based treatment modality comprising immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA; and wherein if the level of sBCMA in the tissue sample is greater than 30% of a level of sBCMA found in a tissue sample obtained from the patient prior to said administration, then the patient is a candidate for the second BCMA-based treatment modality, and the second BCMA-based treatment modality is to be administered to the candidate for the second BCMA-based treatment modality.

[0048b] In one aspect, the present disclosure refers to use of a non-CAR cell therapy in the manufacture of a medicament for treating a disease caused by B cell maturation antigen (BCMA) expressing cells, wherein the patient has been treated with a first BCMA-based treatment modality comprising immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA, wherein the first BCMA-based treatment modality and the second BCMA-based treatment modality are different BCMA-based treatment modalities, wherein a level of soluble BCMA (sBCMA) in a tissue sample from the patient is to be determined, wherein the patient has previously been administered the first BCMA-based treatment modality comprising immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA; and wherein if the level of sBCMA in the tissue sample is greater than 30% of a level of sBCMA found in a tissue sample obtained from the patient prior to said administration, then the patient is a candidate for the second BCMA-based treatment modality, and the second BCMA-based treatment modality is to be administered to the candidate for the second BCMA-based treatment modality.

[0049] In particular **embodiment examples**, wherein if the level of sBCMA in the tissue sample is greater than about 20%, 25%, 30%, 35%, 40%, 45% or 50% of a level of sBCMA found in a tissue sample obtained from the patient prior to said administration, then the patient is a candidate for the second BCMA based treatment modality. Optionally, the method may further comprises administering the second BCMA based treatment modality to the candidate for the second BCMA based treatment modality.

[0050] In another **embodiment example** provided herein is a method of treating a disease caused by B Cell Maturation Agent (BCMA) expressing cells in a subject in need thereof, comprising:

(a) administering to the subject a first BCMA-based treatment modality comprising immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA CAR T cells), and (b) determining a level of soluble BCMA (sBCMA) in a tissue sample from the subject, wherein, if said level of sBCMA is greater than 4000 ng/L, the subject is subsequently provided a second BCMA-based treatment modality to treat said disease, and wherein the first BCMA-based treatment modality and the second BCMA-based treatment modality are different BCMA-based treatment modalities. In a specific **embodiment example**, said level of sBCMA is determined at 50-70 days after said administering. In another specific **embodiment example**, said level of

sBCMA is determined at 55-65 days after said administering. In another specific embodimentexample, said level of sBCMA is determined at 58-62 days after said administering. In a specific embodimentexample of the preceding embodimentexamples, the subject is provided said second BCMA-based treatment modality within three months, two months, or one month after said determining a level of sBCMA. In specific embodimentexamples, the first BCMA-based treatment modality comprising immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA CAR T cells) are idecabtagene vicleucel cells. In particular embodimentexamples, the disease is multiple myeloma, e.g., relapsed and refractory multiple myeloma.

[0050a] In one aspect, the present disclosure refers to immune cells expressing a chimeric antigen receptor (CAR) directed to B cell maturation antigen (BCMA) for use in treating a disease caused by BCMA expressing cells in a subject in need thereof, wherein: a. a first BCMA-based treatment modality comprising immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA is to be administered to the subject, and b. a level of soluble BCMA (sBCMA) in a tissue sample from the subject is to be determined wherein, if said level of sBCMA is greater than 4000 ng/L, the subject is to be subsequently provided a second BCMA-based treatment modality to treat said disease, and wherein the first BCMA-based treatment modality and the second BCMA-based treatment modality are different BCMA-based treatment modalities.

[0050b] In one aspect, the present disclosure refers to use of immune cells expressing a chimeric antigen receptor (CAR) directed to B cell maturation antigen (BCMA) in the manufacture of a medicament for treating a disease caused by BCMA expressing cells in a subject in need thereof, wherein: a. a first BCMA-based treatment modality comprising immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA is to be administered to the subject, and b. a level of soluble BCMA (sBCMA) in a tissue sample from the subject is to be determined wherein, if said level of sBCMA is greater than 4000 ng/L, the subject is to be subsequently provided a second BCMA-based treatment modality to treat said disease, and wherein the first BCMA-based treatment modality and the second BCMA-based treatment modality are different BCMA-based treatment modalities.

[0051] In another embodimentexample, provided herein is a method of treating a disease caused by B Cell Maturation Agent (BCMA) expressing cells in a subject in need thereof, comprising: (a) determining a first level of interleukin-6 (IL-6), tumor necrosis factor alpha (TNF α) or both in a tissue sample from the subject; (b) administering to the subject a first BCMA-based treatment modality comprising immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA CAR T cells), and (c) subsequently determining a second level of IL-6, TNF α or both in a tissue sample from the subject; wherein, if said second level of IL-6, TNF α or both is

not greater than said first level of IL-6, TNF α or both, then the subject is subsequently provided a second BCMA-based treatment modality to treat said disease, and wherein the first BCMA-based treatment modality and the second BCMA-based treatment modality are different BCMA-based treatment modalities. In a specific [embodimentexample](#), said first level is determined on the day of said administering to the subject the first BCMA-based treatment modality comprising immune cells expressing a CAR directed to BCMA, and said second level is determined 1-4 days after said administering. In another specific [embodimentexample](#), said second level is determined two days after said administering. In specific [embodimentexamples](#), the first BCMA-based treatment modality comprising immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA CAR T cells) are idecabtagene vicleucel cells. In particular [embodimentexamples](#), the disease is multiple myeloma, e.g., relapsed and refractory multiple myeloma.

[\[0051a\]](#) In one aspect, the present disclosure refers to immune cells expressing a chimeric antigen receptor (CAR) directed to B cell maturation antigen (BCMA) for use in treating a disease caused by BCMA expressing cells in a subject in need thereof, wherein: a. a first level of interleukin-6 (IL-6), tumor necrosis factor alpha (TNF α) or both in a tissue sample from the subject is to be determined; b. a first BCMA-based treatment modality comprising immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA is to be administered to the subject, and c. a second level of IL-6, TNF α or both in a tissue sample from the subject is to be subsequently determined; wherein, if said second level of IL-6 is not greater than said first level of IL-6, said second level of TNF α is not greater than said first level of TNF α or both are not greater than said first levels, then the subject is to be subsequently provided a second BCMA-based treatment modality to treat said disease, and wherein the first BCMA-based treatment modality and the second BCMA-based treatment modality are different BCMA-based treatment modalities.

[\[0051b\]](#) In one aspect, the present disclosure refers to use of immune cells expressing a chimeric antigen receptor (CAR) directed to B cell maturation antigen (BCMA) in the manufacture of a medicament for treating a disease caused by BCMA expressing cells in a subject in need thereof, wherein: a. a first level of interleukin-6 (IL-6), tumor necrosis factor alpha (TNF α) or both in a tissue sample from the subject is to be determined; b. a first BCMA-based treatment modality comprising immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA is to

be administered to the subject, and c. a second level of IL-6, TNF α or both in a tissue sample from the subject is to be subsequently determined; wherein, if said second level of IL-6 is not greater than said first level of IL-6, said second level of TNF α is not greater than said first level of TNF α or both are not greater than said first levels, then the subject is to be subsequently provided a second BCMA-based treatment modality to treat said disease, and wherein the first BCMA-based treatment modality and the second BCMA-based treatment modality are different BCMA-based treatment modalities.

[0052] In specific embodimentexamples of any of the above aspectexamples-or-embodiments, said disease caused by BCMA-expressing cells is multiple myeloma, chronic lymphocytic leukemia, or a non-Hodgkins lymphoma (e.g., Burkitt's lymphoma, chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL), diffuse large B cell lymphoma, follicular lymphoma, immunoblastic large cell lymphoma, precursor B-lymphoblastic lymphoma, and mantle cell lymphoma). In specific embodimentexamples, the disease is multiple myeloma, e.g., high-risk multiple myeloma or relapsed and refractory multiple myeloma. In other specific embodimentexample, the high risk multiple myeloma is R-ISS stage III disease and/or a disease characterized by early relapse (e.g., progressive disease within 12 months since the date of last treatment regimen, such as last treatment regimen with a proteasome inhibitor, an immunomodulatory agent and/or dexamethasone). In specific embodimentexamples, said disease caused by BCMA-expressing cells is a non-Hodgkins lymphoma, and wherein the non-Hodgkins lymphoma is selected from the group consisting of: Burkitt's lymphoma, chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL), diffuse large B cell lymphoma, follicular lymphoma, immunoblastic large cell lymphoma, precursor B-lymphoblastic lymphoma, and mantle cell lymphoma. In one embodimentexample, before the administration of the first BCMA-based treatment modality comprising immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA CAR T cells), the subject having a tumor has been assessed for expression of BCMA by the tumor.

[0053] In specific embodimentexamples of any of the above aspectexamples-or-embodiments, the immune cells are T cells, e.g., CD4⁺ T cells, CD8⁺ T cells or cytotoxic T lymphocytes (CTLs), T killer cells,

or natural killer (NK) cells. In another specific embodimentexample specific embodimentexample, the immune cells are administered in a dosage of from 150×10^6 cells to 450×10^6 cells.

[0054] In another specific embodimentexample of any of the above aspectexamples-or-embodiments, before said administering said subject has received three or more lines of prior therapy, or one or more lines of prior therapy. In more specific embodimentexamples, said lines of prior therapy comprise a proteasome inhibitor, lenalidomide, pomalidomide, thalidomide, bortezomib, dexamethasone, cyclophosphamide, doxorubicin, carfilzomib, ixazomib, cisplatin, doxorubicin, etoposide, an anti-CD38 antibody panobinostat, or elotuzumab. In more specific embodimentexamples, before said administering said subject has received one or more lines of prior therapy comprising: daratumumab, pomalidomide, and dexamethasone (DPd); daratumumab, bortezomib, and dexamethasone (DVs); ixazomib, lenalidomide, and dexamethasone (IRd); daratumumab, lenalidomide and dexamethasone; bortezomib, lenalidomide and dexamethasone (RVd); bortezomib, cyclophosphamide and dexamethasone (BCd); bortezomib, doxorubicin and dexamethasone; carfilzomib, lenalidomide and dexamethasone (CRd); bortezomib and dexamethasone; bortezomib, thalidomide and dexamethasone; lenalidomide and dexamethasone; dexamethasone, thalidomide, cisplatin, doxorubicin, cyclophosphamide, etoposide and bortezomib (VTD-PACE); lenalidomide and low-dose dexamethasone; bortezomib, cyclophosphamide and dexamethasone; carfilzomib and dexamethasone; lenalidomide alone; bortezomib alone; daratumumab alone; elotuzumab, lenalidomide, and dexamethasone; elotuzumab, lenalidomide and dexamethasone; bendamustine, bortezomib and dexamethasone; bendamustine, lenalidomide, and dexamethasone; pomalidomide and dexamethasone; pomalidomide, bortezomib and dexamethasone; pomalidomide, carfilzomib and dexamethasone; bortezomib and liposomal doxorubicin; cyclophosphamide, lenalidomide, and dexamethasone; elotuzumab, bortezomib and dexamethasone; ixazomib and dexamethasone; panobinostat, bortezomib and dexamethasone; panobinostat and carfilzomib; or pomalidomide, cyclophosphamide and dexamethasone. In various more specific embodimentexamples, said subject has received two, three, four, five, six, seven or more of said lines of prior therapy; no more than three of said lines of prior therapy; no more than two of said lines of prior therapy; or no more than one of said lines of prior therapy.

[0055] In specific embodimentexamples of any of the above aspectexamples-or-embodiments, the immune cells are administered at a dose ranging from 150×10^6 cells to 450×10^6 cells, 300×10^6 cells to 600×10^6 cells.

x 10⁶ cells, 350 x 10⁶ cells to 600 x 10⁶ cells, 350 x 10⁶ cells to 550 x 10⁶ cells, 400 x 10⁶ cells to 600 x 10⁶ cells, 150 x 10⁶ cells to 300 x 10⁶ cells, or 400 x 10⁶ cells to 500 x 10⁶ cells. In some [embodimentexamples](#), the immune cells are administered at a dose of about 150 x 10⁶ cells, about 200 x 10⁶ cells, about 250 x 10⁶ cells, about 300 x 10⁶ cells, about 350 x 10⁶ cells, about 400 x 10⁶ cells, about 450 x 10⁶ cells, about 500 x 10⁶ cells, or about 550 x 10⁶ cells. In one [embodimentexample](#), the immune cells are administered at a dose of about 450 x 10⁶ cells. In some [embodimentexamples](#), the subject is administered one infusion of the immune cells expressing a chimeric antigen receptor (CAR) directed to B Cell Maturation Antigen (BCMA). In some [embodimentexamples](#), the administration of the immune cells expressing a CAR directed to BCMA is repeated (e.g., a second dose of immune cells is administered to the subject).

[0056] In specific [embodimentexamples](#) of any of the [embodimentexamples](#) described herein, the immune cells expressing a CAR directed to BCMA are administered in a dosage of from about 150 x 10⁶ cells to about 300 x 10⁶ cells. In specific [embodimentexamples](#) of any of the [embodimentexamples](#) described herein, the immune cells expressing a CAR directed to BCMA are administered in a dosage of from about 350 x 10⁶ cells to about 550 x 10⁶ cells. In specific [embodimentexamples](#) of any of the [embodimentexamples](#) described herein, the immune cells expressing a CAR directed to BCMA are administered in a dosage of from about 400 x 10⁶ cells to about 500 x 10⁶ cells. In specific [embodimentexamples](#) of any of the [embodimentexamples](#) described herein, the immune cells expressing a CAR directed to BCMA are administered in a dosage of from about 150 x 10⁶ cells to about 250 x 10⁶ cells. In specific [embodimentexamples](#) of any of the [embodimentexamples](#) described herein, the immune cells expressing a CAR directed to BCMA are administered in a dosage of from about 300 x 10⁶ cells to about 500 x 10⁶ cells. In specific [embodimentexamples](#) of any of the [embodimentexamples](#) described herein, the immune cells expressing a CAR directed to BCMA are administered in a dosage of from about 350 x 10⁶ cells to about 450 x 10⁶ cells. In specific [embodimentexamples](#) of any of the [embodimentexamples](#) described herein, the immune cells expressing a CAR directed to BCMA are administered in a dosage of from about 300 x 10⁶ cells to about 450 x 10⁶ cells. In specific [embodimentexamples](#) of any of the [embodimentexamples](#) described herein, the immune cells expressing a CAR directed to BCMA are administered in a dosage of from about 250 x 10⁶ cells to about 450 x 10⁶ cells. In specific [embodimentexamples](#) of any of the [embodimentexamples](#) described herein, the immune cells expressing a CAR directed to BCMA are administered in a dosage of from about 300 x 10⁶ cells to about 600 x 10⁶ cells. In specific [embodimentexamples](#) of any of the [embodimentexamples](#) described herein,

the immune cells expressing a CAR directed to BCMA are administered in a dosage of from about 250×10^6 cells to about 500×10^6 cells. In specific [embodimentexamples](#) of any of the [embodimentexamples](#) described herein, the immune cells expressing a CAR directed to BCMA are administered in a dosage of from about 350×10^6 cells to about 500×10^6 cells. In specific [embodimentexamples](#) of any of the [embodimentexamples](#) described herein, the immune cells expressing a CAR directed to BCMA are administered in a dosage of from about 400×10^6 cells to about 600×10^6 cells. In specific [embodimentexamples](#) of any of the [embodimentexamples](#) described herein, the immune cells expressing a CAR directed to BCMA are administered in a dosage of from about 400×10^6 cells to about 450×10^6 cells. In specific [embodimentexamples](#) of any of the [embodimentexamples](#) described herein, the immune cells expressing a CAR directed to BCMA are administered in a dosage of from about 200×10^6 cells to about 400×10^6 cells. In specific [embodimentexamples](#) of any of the [embodimentexamples](#) described herein, the immune cells expressing a CAR directed to BCMA are administered in a dosage of from about 200×10^6 cells to about 350×10^6 cells. In specific [embodimentexamples](#) of any of the [embodimentexamples](#) described herein, the immune cells expressing a CAR directed to BCMA are administered in a dosage of from about 200×10^6 cells to about 300×10^6 cells. In specific [embodimentexamples](#) of any of the [embodimentexamples](#) described herein, the immune cells expressing a CAR directed to BCMA are administered in a dosage of from about 450×10^6 cells to about 500×10^6 cells. In specific [embodimentexamples](#) of any of the [embodimentexamples](#) described herein, the immune cells expressing a CAR directed to BCMA are administered in a dosage of from about 250×10^6 cells to about 400×10^6 cells. In specific [embodimentexamples](#) of any of the [embodimentexamples](#) described herein, the immune cells expressing a CAR directed to BCMA are administered in a dosage of from about 250×10^6 cells to about 350×10^6 cells. In specific [embodimentexamples](#) of any of the [embodimentexamples](#) described herein, the immune cells expressing a CAR directed to BCMA are administered in a dosage of about 450×10^6 cells. In specific [embodimentexamples](#) of any of the [embodimentexamples](#) described herein, the immune cells are T cells (e.g., autologous T cells). In specific [embodimentexamples](#) of any of the [embodimentexamples](#) described herein, the subjects being treated undergo a leukapheresis procedure to collect autologous immune cells for the manufacture of the immune cells expressing a CAR directed to BCMA prior to their administration to the subject. In specific [embodimentexamples](#) of any of the [embodimentexamples](#) described herein, the immune cells (e.g., T cells) are administered by an intravenous infusion.

[0057] In a specific embodimentexample of any of any of the above aspectexamples-or-embodiments, said CAR comprises an antibody or antibody fragment that targets BCMA. In a more specific embodimentexample, said CAR comprises a single chain Fv antibody fragment (scFv). In a more specific embodimentexample, said CAR comprises a BCMA02 scFv. In a specific embodimentexample of any of the above aspectexamples-or-embodiments, said immune cells are idecabtagene vicleucel cells. In one embodimentexample, the chimeric antigen receptor comprises a murine single chain Fv antibody fragment that targets BCMA, e.g., human BCMA. In one embodimentexample, the chimeric antigen receptor comprises a murine anti-BCMA scFv that binds a BCMA polypeptide, e.g., a human BCMA polypeptide, a hinge domain comprising a CD8 α polypeptide, a CD8 α transmembrane domain, a CD137 (4-1BB) intracellular co-stimulatory signaling domain, and a CD3 ζ primary signaling domain. In one embodimentexample, the chimeric antigen receptor comprises a murine scFv that targets BCMA, e.g., human BCMA, wherein the scFv is that of anti-BCMA02 CAR of SEQ ID NO: 9. In one embodimentexample, the chimeric antigen receptor is or comprises SEQ ID NO: 9. In a more specific embodimentexample of any embodimentexample herein, said immune cells are idecabtagene vicleucel cells. In one embodimentexample, the immune cells comprise a chimeric antigen receptor which comprises a murine single chain Fv antibody fragment that targets BCMA, e.g., human BCMA. In one embodimentexample, the immune cells comprise a chimeric antigen receptor which comprises a murine anti-BCMA scFv that binds a BCMA polypeptide, e.g., human BCMA, a hinge domain comprising a CD8 α polypeptide, a CD8 α transmembrane domain, a CD137 (4-1BB) intracellular co-stimulatory signaling domain, and a CD3 ζ primary signaling domain. In one embodimentexample, the immune cells comprise a chimeric antigen receptor which is or comprises SEQ ID NO: 9.

[0058] In another aspectexample, provided herein is a method of treating a disease caused by B Cell Maturation Agent (BCMA) expressing cells in a subject in need thereof, comprising: (a) determining a first level of soluble BCMA (sBCMA) and/or a first level of interleukin-6 (IL-6), tumor necrosis factor alpha (TNF α), or both in a tissue sample from the subject; (b) administering to the subject a first BCMA-based treatment modality comprising immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA CAR T cells), and (c) determining a second level of sBCMA and/or a second level of interleukin-6 (IL-6), tumor necrosis factor alpha (TNF α), or both in a tissue sample from the subject; wherein, if said second level of sBCMA is greater than 30% of said first level of sBCMA and/or if said second level of

IL-6, TNF α or both is not greater than said first level of IL-6, TNF α or both, the subject is subsequently provided a second BCMA-based treatment modality to treat said disease, and wherein the first BCMA-based treatment modality and the second BCMA-based treatment modality are different BCMA-based treatment modalities. In specific embodiment examples, the first BCMA-based treatment modality comprising immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA CAR T cells) are idecabtagene vicleucel cells. In particular embodiment examples, the disease is multiple myeloma, e.g., relapsed and refractory multiple myeloma.

[0058a] In one aspect, the present disclosure refers to immune cells expressing a chimeric antigen receptor (CAR) directed to B cell maturation antigen (BCMA) for use in treating a disease caused by BCMA expressing cells in a subject in need thereof, wherein: a. a first level of soluble BCMA (sBCMA) and/or a first level of interleukin-6 (IL-6), tumor necrosis factor alpha (TNF α), or both in a tissue sample from the subject is to be determined; b. a first BCMA-based treatment modality comprising immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA is to be administered to the subject, and c. a second level of sBCMA and/or a second level of interleukin-6 (IL-6), tumor necrosis factor alpha (TNF α), or both in a tissue sample from the subject is to be determined; wherein, if said second level of sBCMA is greater than 30% of said first level of sBCMA and/or if said second level of IL-6 is not greater than said first level of IL-6, said second level of TNF α is not greater than said first level of TNF α or both are not greater than said first levels, the subject is to be subsequently provided a second BCMA-based treatment modality to treat said disease, and wherein the first BCMA-based treatment modality and the second BCMA-based treatment modality are different BCMA-based treatment modalities.

[0058b] In one aspect, the present disclosure refers to use of immune cells expressing a chimeric antigen receptor (CAR) directed to B cell maturation antigen (BCMA) in the manufacture of a medicament for treating a disease caused by BCMA expressing cells in a subject in need thereof, wherein: a. a first level of soluble BCMA (sBCMA) and/or a first level of interleukin-6 (IL-6), tumor necrosis factor alpha (TNF α), or both in a tissue sample from the subject is to be determined; b. a first BCMA-based treatment modality comprising immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA is to be administered to the subject, and c. a second level of sBCMA and/or a second level of interleukin-6 (IL-6), tumor necrosis factor alpha (TNF α), or both in a tissue sample from the subject is to be determined; wherein, if said second level of sBCMA is greater than 30% of said first level of

sBCMA and/or if said second level of IL-6 is not greater than said first level of IL-6, said second level of TNF α is not greater than said first level of TNF α or both are not greater than said first levels, the subject is to be subsequently provided a second BCMA-based treatment modality to treat said disease, and wherein the first BCMA-based treatment modality and the second BCMA-based treatment modality are different BCMA-based treatment modalities.

[0059] In another aspectexample, provided herein is a method of treating a disease caused by B Cell Maturation Agent (BCMA) expressing cells in a subject in need thereof, comprising: (a) determining a first level of soluble BCMA (sBCMA) and/or a first level of interleukin-6 (IL-6), tumor necrosis factor alpha (TNF α), or both in a tissue sample from the subject; (b) administering to the subject a first BCMA-based treatment modality comprising immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA CAR T cells), (c) determining that a second level of sBCMA in a tissue sample from the subject is greater than 30% of said first level of sBCMA and/or a second level of IL-6, TNF α or both is not greater than said first level of IL-6, TNF α or both, and (d) on the basis of the determination in step c, subsequently providing a second BCMA-based treatment modality to the subject, wherein the first BCMA-based treatment modality and the second BCMA-based treatment modality are different BCMA-based treatment modalities. In specific embodimentexamples, the first BCMA-based treatment modality comprising immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA CAR T cells) are idecabtagene vicleucel cells. In particular embodimentexamples, the disease is multiple myeloma, e.g., relapsed and refractory multiple myeloma.

[0060] In another aspectexample, provided herein is a method of treating a disease caused by B Cell Maturation Agent (BCMA) expressing cells, comprising administering to a patient diagnosed with said disease a second BCMA-based treatment modality, wherein the patient has previously been administered a first BCMA-based treatment modality comprising immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA CAR T cells), wherein the first BCMA-based treatment modality and the second BCMA-based treatment modality are different BCMA-based treatment modalities, and wherein a tissue sample from the patient subsequent to said administration contained (i) a level of soluble BCMA (sBCMA) greater than 30% of a level

of sBCMA found in a tissue sample obtained from the patient prior to said administration and/or (ii) a level of IL-6, TNF α or both not greater than a level of IL-6, TNF α or both found in a tissue sample obtained from the patient prior to said administration. In specific embodiment examples, the first BCMA-based treatment modality comprising immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA CAR T cells) are idecabtagene vicleucel cells. In particular embodiment examples, the disease is multiple myeloma, e.g., relapsed and refractory multiple myeloma.

[0060a] In one aspect, the present disclosure refers to a non-CAR therapy for use in treating a disease caused by B cell maturation antigen (BCMA) expressing cells, wherein a second BCMA-based treatment modality is to be administered to a patient diagnosed with said disease, wherein the patient has previously been administered a first BCMA-based treatment modality comprising immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA, wherein the first BCMA-based treatment modality and the second BCMA-based treatment modality are different BCMA-based treatment modalities; and wherein a tissue sample from the patient subsequent to said administration contained (i) a level of soluble BCMA (sBCMA) greater than 30% of a level of sBCMA found in a tissue sample obtained from the patient prior to said administration and/or (ii) a level of IL-6, TNF α or both not greater than a level of IL-6, TNF α or both found in a tissue sample obtained from the patient prior to said administration.

[0060b] In one aspect, the present disclosure refers to use of a non-CAR therapy in the manufacture of a medicament for treating a disease caused by B cell maturation antigen (BCMA) expressing cells, wherein a second BCMA-based treatment modality is to be administered to a patient diagnosed with said disease, wherein the patient has previously been administered a first BCMA-based treatment modality comprising immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA, wherein the first BCMA-based treatment modality and the second BCMA-based treatment modality are different BCMA-based treatment modalities; and wherein a tissue sample from the patient subsequent to said administration contained (i) a level of soluble BCMA (sBCMA) greater than 30% of a level of sBCMA found in a tissue sample obtained from the patient prior to said administration and/or (ii) a level of IL-6, TNF α or both not greater than a level of IL-6, TNF α or both found in a tissue sample obtained from the patient prior to said administration.

[0061] In another aspect example, provided herein is a method of determining whether a patient diagnosed with a disease caused by B Cell Maturation Agent (BCMA) expressing cells should be administered a second BCMA-based treatment modality after treatment with a first BCMA-based treatment modality comprising immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA CAR T cells), comprising determining a level of soluble BCMA (sBCMA) and/or a level of IL-6, TNF α or both in a tissue sample from the patient, wherein the patient has previously been administered the first BCMA-based treatment modality comprising immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA CAR T cells), wherein if (i) the level of sBCMA in the tissue sample is greater than 30% of a level of sBCMA found in a tissue sample obtained from the patient prior to said administration and/or (ii) the level of IL-6, TNF α or both is not greater than a level of IL-6, TNF α or both found in a tissue sample obtained from the patient prior to said administration, then the patient is a candidate for the second BCMA-based treatment modality, and wherein the first BCMA-based treatment modality and the second BCMA-based treatment modality are different BCMA-based treatment modalities. In a specific embodiment example, the method further comprises administering the second BCMA-based treatment modality to the candidate for

the second BCMA-based treatment modality. In specific embodiment examples, the first BCMA-based treatment modality comprising immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA CAR T cells) are idecabtagene vicleucel cells. In particular embodiment examples, the disease is multiple myeloma, e.g., relapsed and refractory multiple myeloma.

[0061a] In one aspect, the present disclosure refers to a non-CAR cell therapy for use in treating a disease caused by B cell maturation antigen (BCMA) expressing cells, wherein the patient has been treated with a first BCMA-based treatment modality comprising immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA, wherein a level of soluble BCMA (sBCMA) and/or a level of IL-6, TNF α or both in a tissue sample from the patient is to be determined, wherein the patient has previously been administered the first BCMA-based treatment modality comprising immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA, wherein if (i) the level of sBCMA in the tissue sample is greater than 30% of a level of sBCMA found in a tissue sample obtained from the patient prior to said administration and/or (ii) the level of IL-6, TNF α or both is not greater than a level of IL-6, TNF α or both found in a tissue sample obtained from the patient prior to said administration, then the patient is a candidate for the second BCMA-based treatment modality, and wherein the first BCMA-based treatment modality and the second BCMA-based treatment modality are different BCMA-based treatment modalities, and the second BCMA-based treatment modality is to be administered to the candidate for the second BCMA-based treatment modality.

[0061b] In one aspect, the present disclosure refers to use of a non-CAR cell therapy in the manufacture of a medicament for treating a disease caused by B cell maturation antigen (BCMA) expressing cells, wherein the patient has been treated with a first BCMA-based treatment modality comprising immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA, wherein the first BCMA-based treatment modality and the second BCMA-based treatment modality are different BCMA-based treatment modalities, wherein a level of soluble BCMA (sBCMA) and/or a level of IL-6, TNF α or both in a tissue sample from the patient is to be determined, wherein the patient has previously been administered the first BCMA-based treatment modality comprising immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA, wherein if (i) the level of sBCMA in the tissue sample is greater than 30% of a level of sBCMA found in a tissue sample obtained from the patient prior to said administration and/or (ii) the level of IL-6, TNF α or both is not greater than a level of IL-6, TNF α or both found in a tissue sample obtained from the patient prior to said administration, then the patient is a candidate for the second BCMA-based treatment modality, and wherein the first BCMA-based treatment modality and the second BCMA-based treatment modality are different BCMA-based treatment modalities, and the second BCMA-based treatment modality is to be administered to the candidate for the second BCMA-based treatment modality.

[0062] In specific embodiment examples of any of the embodiment examples described herein, the second BCMA-based treatment modality comprises a BCMA-Antibody-Drug Conjugate (ADC), a bispecific T-cell engager (BiTE) that targets B-cell maturation antigen (BCMA), a natural killer (NK) cell engager (NKCEs) that targets B-cell maturation antigen (BCMA), or immune cells expressing a

chimeric antigen receptor (CAR) directed to BCMA (BCMA CAR T cells). In a specific [embodimentexample](#), the second BCMA-based treatment modality comprises a BCMA-Antibody-Drug Conjugate (ADC). In a specific [embodimentexample](#), the BCMA-Antibody-Drug Conjugate (ADC) comprises CC99712 or GSK2857916 (belantamab mafodotin). In a specific [embodimentexample](#), the second BCMA-based treatment modality comprises a bispecific T-cell engager (BiTE) that targets B-cell maturation antigen (BCMA). In a specific [embodimentexample](#), the bispecific T-cell engager (BiTE) that targets B-cell maturation antigen (BCMA) comprises CC-93269, AMG 420, JNJ-64007957, AMG 701, PF-06863135, REGN5458, REGN5459, or TNB-383B. In a specific [embodimentexample](#), the second BCMA-based treatment modality comprises a natural killer (NK) cell engager (NKCEs) that targets B-cell maturation antigen (BCMA). In a specific [embodimentexample](#), the natural killer (NK) cell engager (NKCEs) that targets B-cell maturation antigen (BCMA) comprises DF3001, AFM26, CTX-4419, or CTX-8573. In a specific [embodimentexample](#), the second BCMA-based treatment modality comprises immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA CAR T cells). In a specific [embodimentexample](#), the immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA CAR T cells) comprise JCARH125, KITE-585, P-BCMA-101, LCAR-B38M, CT053, anti-CD19/BCMA CAR-T cells, and CTX120.

[0063] In specific [embodimentexamples](#) of any of the [embodimentexamples](#) described herein, the immune cells in the first BCMA-based treatment modality comprising immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA CAR T cells) are idecabtagene vicleucel cells.

[0064] In specific [embodimentexamples](#) of any of the [embodimentexamples](#) described herein, the second BCMA-based treatment modality does not comprise idecabtagene vicleucel cells.

3. BRIEF DESCRIPTION OF THE DRAWINGS

[0065] Figure 1 shows a schematic of a B cell maturation antigen (BCMA) CAR construct (anti-BCMA02 CAR).

[0066] Figures 2A and 2B show post-BCMA02 CAR T cell infusion profiles of IL-6 (Fig. 2A) and TNF- α (Fig. 2B). “TNF” = TNF α , “INTLK6” = interleukin-6. Non-responders are indicated by heavy lines, and responders (patients who achieved a PR or better) are indicated by lighter lines. The fold-changes at Days 1 – 9, particularly at Day 2, significantly differentiate these two groups ($p < .02$). “Scr” = date of screening.

WHAT IS CLAIMED IS:

1. Immune cells expressing a chimeric antigen receptor (CAR) directed to B cell maturation antigen (BCMA) for use in treating a disease caused by BCMA ~~A method of treating a disease caused by B Cell Maturation Agent (BCMA)~~-expressing cells in a subject in need thereof, ~~comprising~~wherein:

- a. ~~determining~~ a first level of soluble BCMA (sBCMA) in a tissue sample from the subject is to be determined;
- b. ~~administering to the subject~~ immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA ~~(BCMA CAR T cells)~~ are to be administered to the subject, and
- c. ~~determining~~ a second level of sBCMA in a tissue sample from the subject is to be determined

and wherein, if said second level of sBCMA is greater than 30% of said first level of sBCMA, the subject is to be subsequently provided a non-CAR ~~T-cell~~ therapy to treat said disease.

2. Use of immune cells expressing a chimeric antigen receptor (CAR) directed to B cell maturation antigen (BCMA) in the manufacture of a medicament for treating a disease caused by BCMA expressing cells in a subject in need thereof, wherein:

- a. a first level of soluble BCMA (sBCMA) in a tissue sample from the subject is to be determined;
- b. immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA are to be administered to the subject, and
- c. a second level of sBCMA in a tissue sample from the subject is to be determined

and wherein, if said second level of sBCMA is greater than 30% of said first level of sBCMA, the subject is to be subsequently provided a non-CAR therapy to treat said disease.

32. ~~A method of treating a disease caused by B Cell Maturation Agent (BCMA) expressing cells in a subject in need thereof, comprising:~~ The immune cells for use of claim 1 or the use of claim 2, wherein

- a. ~~determining a first level of soluble BCMA (sBCMA) in a tissue sample from the subject;~~

- b. ~~administering to the subject immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA CAR T cells);~~
- e. ~~determining that a second level of sBCMA in a tissue sample from the subject is greater than 30% of said first level of sBCMA, and~~
- d. ~~on the basis of the determination in step c, subsequently providing thea non-CAR T cell therapy to the subject.~~

3. ~~The method of claim 1, wherein if said second level of sBCMA is greater than 40% of said first level of sBCMA, the subject is provided a non CAR T cell therapy to treat said disease.~~

4. ~~The method of any one of claims 1, 2 or 3 immune cells for use of or the use of any one of claims 1-3, wherein said second level of sBCMA is to be determined at 25-35 days after said ~~administering~~administration.~~

5. ~~The method of any one of claims 1, 2, or 3, wherein said second level of sBCMA is determined at 28-31 days after said administering.~~

6. ~~The method of any of claims 1-5, wherein the subject is provided a non CAR T cell therapy within three months, two months, or one month after said determining the second level of sBCMA.~~

57. ~~A non-CAR therapy for use in treating~~A method of treating a disease caused by B cell maturation antigen~~B-Cell Maturation Agent~~ (BCMA) expressing cells, ~~comprising wherein administering to a patient diagnosed with said disease a non-chimeric antigen receptor (CAR) T cell therapy is to be administered to a patient diagnosed with said disease~~, wherein the patient has previously been administered immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (~~BCMA CAR T cells~~) and wherein a tissue sample from the patient subsequent to said administration contained a level of soluble BCMA (sBCMA) greater than 30% of a level of sBCMA found in a tissue sample obtained from the patient prior to said administration.

6. Use of a non-CAR therapy in the manufacture of a medicament for treating a disease caused by B cell maturation antigen (BCMA) expressing cells, wherein the non-chimeric antigen receptor (CAR) therapy is to be administered to a patient diagnosed with said disease , wherein the patient has previously been administered immune cells expressing a CAR directed to BCMA and wherein a tissue sample from the patient subsequent to said administration contained

a level of sBCMA greater than 30% of a level of soluble BCMA (sBCMA) found in a tissue sample obtained from the patient prior to said administration.

78. A non-CAR cell therapy for use in treating~~A method of determining whether a patient diagnosed with~~ a disease caused by B cell maturation antigen~~B-Cell Maturation Agent~~ (BCMA) expressing cells, wherein the patient has been treated~~should be administered a non-CAR T-cell therapy after treatment~~ with immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA ~~(BCMA-CAR T-cells)~~, comprising wherein

~~determining~~ a level of soluble BCMA (sBCMA) in a tissue sample from the patient is to be determined, wherein the patient has previously been administered the immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA ~~(BCMA-CAR T-cells)~~, and wherein if the level of sBCMA in the tissue sample is greater than 30% of a level of sBCMA found in a tissue sample obtained from the patient prior to said administration, then the patient is a candidate for the non-CAR ~~T-cell~~ therapy, and

the non-CAR therapy is to be administered to the candidate for the non-CAR therapy.

8. Use of a non-CAR therapy in the manufacture of a medicament for treating a disease caused by B cell maturation antigen (BCMA) expressing cells, wherein the patient has been treated with immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA, wherein

a level of soluble BCMA (sBCMA) in a tissue sample from the patient is to be determined, wherein the patient has previously been administered the immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA, and wherein if the level of sBCMA in the tissue sample is greater than 30% of a level of sBCMA found in a tissue sample obtained from the patient prior to said administration, then the patient is a candidate for the non-CAR therapy, and

the non-CAR therapy is to be administered to the candidate for the non-CAR therapy.

9. ~~The method of claim 8, further comprising administering the non-CAR T cell therapy to the candidate for the non-CAR T cell therapy.~~

940. Immune cells expressing a chimeric antigen receptor (CAR) directed to B cell maturation antigen (BCMA) for use in treating a disease caused by BCMA~~A method of treating a disease caused by B-Cell Maturation Agent (BCMA)~~ expressing cells in a subject in need thereof, comprising wherein:

- a. ~~administering to the subject~~ immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA ~~(BCMA CAR T cells)~~ are to be administered to the subject, and
- b. ~~determining~~ a level of soluble BCMA (sBCMA) in a tissue sample from the subject is to be determined

wherein, if said level of sBCMA is greater than 4000 ng/L, the subject is to be subsequently provided a non-CAR ~~T-cell~~ therapy to treat said disease.

10. Use of immune cells expressing a chimeric antigen receptor (CAR) directed to B cell maturation antigen (BCMA) in the manufacture of a medicament for treating a disease caused by BCMA expressing cells in a subject in need thereof, wherein:

- a. immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA is to be administered to the subject, and
- b. a level of soluble BCMA (sBCMA) in a tissue sample from the subject is to be determined

wherein, if said level of sBCMA is greater than 4000 ng/L, the subject is to be subsequently provided a non-CAR therapy to treat said disease.

11. The immune cells for use of claim 9 or the use method of claim 10, wherein said level of sBCMA is to be determined at 50-70 days after said ~~administering~~ administration.

~~12. The method of claim 10 or claim 11, wherein said level of sBCMA is determined at 55-65 days after said administering.~~

~~13. The method of any of claims 10-12, wherein said level of sBCMA is determined at 58-62 days after said administering.~~

~~124.~~ The ~~method~~ immune cells for use of or use of any of claims ~~1-4 or 9-11~~ 1-13, wherein the subject is to be provided said non-CAR ~~T-cell~~ therapy within three months, two months, or one month after ~~said determining~~ determination of a level of sBCMA.

~~1345.~~ Immune cells expressing a chimeric antigen receptor (CAR) directed to B cell maturation antigen (BCMA) for use in treating a disease caused by BCMA ~~A method of treating a disease caused by B Cell Maturation Agent (BCMA)~~ expressing cells in a subject in need thereof, ~~comprising~~ wherein:

- a. ~~determining~~ a first level of interleukin-6 (IL-6), tumor necrosis factor alpha (TNF α) or both in a tissue sample from the subject is to be determined;

- b. ~~administering to the subject~~ immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA ~~(BCMA CAR T cells)~~ are to be administered to the subject, and
- c. ~~subsequently determining~~ a second level of IL-6, TNF α or both in a tissue sample from the subject is to be subsequently determined;

wherein, if said second level of IL-6 is not greater than first level of IL-6, said second level of TNF α is not greater than said first level of TNF α or both ~~is are~~ not greater than said first levels ~~of IL-6, TNF α or both~~, then the subject is to be subsequently provided a non-CAR ~~T-cell~~ therapy to treat said disease.

14. Use of immune cells expressing a chimeric antigen receptor (CAR) directed to B cell maturation antigen (BCMA) in the manufacture of a medicament for treating a disease caused by BCMA expressing cells in a subject in need thereof, wherein:

- a. a first level of interleukin-6 (IL-6), tumor necrosis factor alpha (TNF α) or both in a tissue sample from the subject is to be determined;
- b. immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA is to be administered to the subject, and
- c. a second level of IL-6, TNF α or both in a tissue sample from the subject is to be subsequently determined;

wherein, if said second level of IL-6 is not greater than first level of IL-6, said second level of TNF α is not greater than said first level of TNF α , or both are not greater than said first levels, then the subject is to be subsequently provided a non-CAR therapy to treat said disease.

1516. The ~~method~~ immune cells for use of claim 13 or the use of claim 145, wherein said first level is to be determined on the day of said ~~administering~~ administration to the subject immune cells expressing a CAR directed to BCMA, and said second level is to be determined 1-4 days or 2 days after said ~~administering~~ administration.

17. — The method of claim 16, wherein said second level is determined two days after said administering.

1618. Immune cells expressing a chimeric antigen receptor (CAR) directed to B cell maturation antigen (BCMA) for use in treating a disease caused by BCMA A method of treating a disease caused by B-Cell Maturation Agent (BCMA) expressing cells in a subject in need thereof, ~~comprising~~ wherein:

- a. ~~administering to the subject~~ immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA. ~~(BCMA CAR T cells)~~ are to be administered to the subject, and
- b. ~~determining~~ a level of ferritin in a tissue sample from the subject is to be determined;

wherein, if said level of ferritin is greater than 1500 picomoles per liter, the subject is subsequently provided a therapy to treat cytokine release syndrome (CRS).

17. Use of immune cells expressing a chimeric antigen receptor (CAR) directed to B cell maturation antigen (BCMA) in the manufacture of a medicament for treating a disease caused by BCMA expressing cells in a subject in need thereof, wherein:

- a. immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA are to be administered to the subject, and
- b. a level of ferritin in a tissue sample from the subject is to be determined;

wherein, if said level of ferritin is greater than 1500 picomoles per liter, the subject is subsequently provided a therapy to treat cytokine release syndrome (CRS).

1819. The ~~method~~ immune cells for use of claim 16 or the use of claim 178, wherein said ~~determining-determination~~ is performed within 0-4 days prior to said ~~administeringadministration~~.

20. The method of claim 18, wherein said ~~determining~~ is performed on the same day as said ~~administering~~.

1921. The ~~immune cells for use of claim 16 or the use method~~ of claim 178, wherein said therapy to treat CRS is to be first provided to said subject 0-5 days after said ~~administeringadministration~~.

22. The method of any of claims 1-21, wherein said ~~disease caused by BCMA-expressing cells is multiple myeloma, chronic lymphocytic leukemia, or a non-Hodgkins lymphoma.~~

23. The method of claim 22, wherein the ~~disease caused by BCMA-expressing cells is multiple myeloma.~~

24. The method of claim 23, wherein said ~~multiple myeloma is high-risk multiple myeloma or relapsed and refractory multiple myeloma.~~

~~25.—The method of claim 22, wherein said disease caused by BCMA-expressing cells is a non-Hodgkins lymphoma, and wherein the non-Hodgkins lymphoma is selected from the group consisting of: Burkitt's lymphoma, chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL), diffuse large B-cell lymphoma, follicular lymphoma, immunoblastic large cell lymphoma, precursor B-lymphoblastic lymphoma, and mantle cell lymphoma.~~

~~26.—The method of any of claims 1-25, wherein the immune cells are T cells.~~

~~27.—The method of any of claims 1-26, wherein the immune cells are administered in a dosage of from 150×10^6 cells to 450×10^6 cells.~~

~~28.—The method of any of claims 1-27, wherein before said administering said subject has received three or more lines of prior therapy.~~

~~29.—The method of any of claims 1-27, wherein before said administering said subject has received one or more lines of prior therapy.~~

~~30.—The method of claim 28 or 29, wherein said lines of prior therapy comprise a proteasome inhibitor, lenalidomide, pomalidomide, thalidomide, bortezomib, dexamethasone, cyclophosphamide, doxorubicin, carfilzomib, ixazomib, cisplatin, doxorubicin, etoposide, an anti-CD38 antibody panobinostat, or elotuzumab.~~

~~31.—The method of claim 28 or claim 29, wherein before said administering said subject has received one or more lines of prior therapy comprising:~~

- ~~a.—daratumumab, pomalidomide, and dexamethasone (DPd);~~
- ~~b.—daratumumab, bortezomib, and dexamethasone (Dvd);~~
- ~~c.—ixazomib, lenalidomide, and dexamethasone (IRd);~~
- ~~d.—daratumumab, lenalidomide and dexamethasone;~~
- ~~e.—bortezomib, lenalidomide and dexamethasone (RVd);~~
- ~~f.—bortezomib, cyclophosphamide and dexamethasone (BCd);~~
- ~~g.—bortezomib, doxorubicin and dexamethasone;~~
- ~~h.—carfilzomib, lenalidomide and dexamethasone (CRd);~~
- ~~i.—bortezomib and dexamethasone;~~
- ~~j.—bortezomib, thalidomide and dexamethasone;~~
- ~~k.—lenalidomide and dexamethasone;~~
- ~~l.—dexamethasone, thalidomide, cisplatin, doxorubicin, cyclophosphamide, etoposide and bortezomib (VTD-PACE);~~

- m. ~~lenalidomide and low dose dexamethasone;~~
- n. ~~bortezomib, cyclophosphamide and dexamethasone;~~
- o. ~~carfilzomib and dexamethasone;~~
- p. ~~lenalidomide alone;~~
- q. ~~bortezomib alone;~~
- r. ~~daratumumab alone;~~
- s. ~~elotuzumab, lenalidomide, and dexamethasone;~~
- t. ~~elotuzumab, lenalidomide and dexamethasone;~~
- u. ~~bendamustine, bortezomib and dexamethasone;~~
- v. ~~bendamustine, lenalidomide, and dexamethasone;~~
- w. ~~pomalidomide and dexamethasone;~~
- x. ~~pomalidomide, bortezomib and dexamethasone;~~
- y. ~~pomalidomide, carfilzomib and dexamethasone;~~
- z. ~~bortezomib and liposomal doxorubicin;~~
- aa. ~~cyclophosphamide, lenalidomide, and dexamethasone;~~
- bb. ~~elotuzumab, bortezomib and dexamethasone;~~
- cc. ~~ixazomib and dexamethasone;~~
- dd. ~~panobinostat, bortezomib and dexamethasone;~~
- ee. ~~panobinostat and carfilzomib; or~~
- ff. ~~pomalidomide, cyclophosphamide and dexamethasone.~~

32. ~~The method of claim 31, wherein said subject has received two, three, four, five, six, seven or more of said lines of prior therapy.~~

33. ~~The method of claim 31, wherein said subject has received no more than three of said lines of prior therapy.~~

34. ~~The method of claim 31, wherein said subject has received no more than two of said lines of prior therapy.~~

35. ~~The method of claim 31, wherein said subject has received no more than one of said lines of prior therapy.~~

36. ~~The method of any of claims 1-35, wherein said CAR comprises an antibody or antibody fragment that targets BCMA.~~

~~37. The method of any of claims 1-36, wherein said CAR comprises a single chain Fv antibody fragment (scFv).~~

~~38. The method of any of claims 1-36, wherein said CAR comprises a BCMA02 scFv.~~

~~39. The method of any of claims 1-36, wherein said immune cells are idecabtagene vicleucel cells.~~

2040. Immune cells expressing a chimeric antigen receptor (CAR) directed to B cell maturation antigen (BCMA) for use in treating a disease caused by BCMA ~~A method of treating a disease caused by B-Cell Maturation Agent (BCMA)~~ expressing cells in a subject in need thereof, ~~comprising~~wherein:

- a. ~~determining~~ a first level of soluble BCMA (sBCMA) and/or a first level of interleukin-6 (IL-6), tumor necrosis factor alpha (TNF α), or both in a tissue sample from the subject is to be determined;
- b. ~~administering to the subject~~ immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA ~~(BCMA CAR T cells)~~ are to be administered to the subject, and
- c. ~~determining~~ a second level of sBCMA and/or a second level of interleukin-6 (IL-6), tumor necrosis factor alpha (TNF α), or both in a tissue sample from the subject is to be determined

wherein, if said second level of sBCMA is greater than 30% of said first level of sBCMA and/or if said second level of IL-6 is not greater than said first level of IL-6, said second level of TNF α is not greater than said first level of; TNF α or both ~~is-are~~ not greater than said first levels ~~of IL-6, TNF α or both,~~ the subject is to be subsequently provided a non-CAR ~~T-cell~~ therapy to treat said disease.

21. Use of immune cells expressing a chimeric antigen receptor (CAR) directed to B cell maturation antigen (BCMA) in the manufacture of a medicament for treating a disease caused by BCMA expressing cells in a subject in need thereof, wherein:

- a. a first level of soluble BCMA (sBCMA) and/or a first level of interleukin-6 (IL-6), tumor necrosis factor alpha (TNF α), or both in a tissue sample from the subject is to be determined;

- b. immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA are to be administered to the subject, and
- c. a second level of sBCMA and/or a second level of interleukin-6 (IL-6), tumor necrosis factor alpha (TNF α), or both in a tissue sample from the subject is to be determined

wherein, if said second level of sBCMA is greater than 30% of said first level of sBCMA and/or if said second level of IL-6 is not greater than said first level of IL-6, said second level of TNF α is not greater than said first level of TNF α or both are not greater than said first levels, the subject is to be subsequently provided a non-CAR therapy to treat said disease.

~~2241. A method of treating a disease caused by B-Cell Maturation Agent (BCMA) expressing cells in a subject in need thereof, comprising:~~The immune cells for use of claim 20 or the use of claim 21, wherein

- a. ~~determining a first level of soluble BCMA (sBCMA) and/or a first level of interleukin-6 (IL-6), tumor necrosis factor alpha (TNF α), or both in a tissue sample from the subject;~~
- b. ~~administering to the subject immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA CAR T cells);~~
- c. ~~determining that a second level of sBCMA in a tissue sample from the subject is greater than 30% of said first level of sBCMA and/or a second level of IL-6, TNF α or both is not greater than said first level of IL-6, TNF α or both, and~~
- d. ~~on the basis of the determination in step c, subsequently providing thea non-CAR T-cell therapy to the subject.~~

~~2342. A non-CAR therapy for use in treating~~A method of treating a disease caused by B cell maturation antigen~~B-Cell Maturation Agent~~ (BCMA) expressing cells, ~~comprising wherein administering to a patient diagnosed with said disease a non-chimeric antigen receptor (CAR) T cell therapy is to be administered to a patient diagnosed with said disease,~~ wherein the patient has previously been administered immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA ~~(BCMA CAR T cells)~~ and wherein a tissue sample from the patient subsequent to said administration contained (i) a level of soluble BCMA (sBCMA) greater than 30% of a level of sBCMA found in a tissue sample obtained from the patient prior to said

administration and/or (ii) a level of IL-6, TNF α or both not greater than a level of IL-6, TNF α or both found in a tissue sample obtained from the patient prior to said administration.

24. Use of a non-CAR therapy in the manufacture of a medicament for treating a disease caused by B cell maturation antigen (BCMA) expressing cells, wherein the non-CAR therapy is to be administered to a patient diagnosed with said disease, wherein the patient has previously been administered immune cells expressing a CAR directed to BCMA and wherein a tissue sample from the patient subsequent to said administration contained (i) a level of soluble BCMA (sBCMA) greater than 30% of a level of sBCMA found in a tissue sample obtained from the patient prior to said administration and/or (ii) a level of IL-6, TNF α or both not greater than a level of IL-6, TNF α or both found in a tissue sample obtained from the patient prior to said administration.

2543. A non-CAR therapy for use in a method of treating~~A method of determining whether a patient diagnosed with~~ a disease caused by B cell maturation antigen~~B-Cell Maturation Agent~~ (BCMA) expressing cells, wherein the patient has been treated~~should be administered a non-CAR T-cell therapy after treatment~~ with immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA ~~(BCMA-CAR T-cells)~~, comprising wherein

~~determining~~ a level of soluble BCMA (sBCMA) and/or a level of IL-6, TNF α or both in a tissue sample from the patient is to be determined, wherein the patient has previously been administered the immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA ~~(BCMA-CAR T-cells)~~, and wherein if (i) the level of sBCMA in the tissue sample is greater than 30% of a level of sBCMA found in a tissue sample obtained from the patient prior to said administration and/or (ii) the level of IL-6, TNF α or both is not greater than a level of IL-6, TNF α or both found in a tissue sample obtained from the patient prior to said administration, then the patient is a candidate for the non-CAR ~~T-cell~~ therapy, and

the non-CAR therapy is to be administered to the candidate for the non-CAR therapy.

26. Use of a non-CAR therapy for use in the manufacture of a medicament for treating a disease caused by B cell maturation antigen (BCMA) expressing cells, wherein the patient has been treated with immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA, wherein

a level of soluble BCMA (sBCMA) and/or a level of IL-6, TNF α or both in a tissue sample from the patient is to be determined, wherein the patient has previously been administered the immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA, and wherein if (i) the level of sBCMA in the tissue sample is greater than 30% of a level of sBCMA found in a tissue sample obtained from the patient prior to said administration and/or (ii) the level of IL-6, TNF α or both is not greater than a level of IL-6, TNF α or both found in a tissue sample obtained from the patient prior to said administration, then the patient is a candidate for the non-CAR therapy, and

the non-CAR therapy is to be administered to the candidate for the non-CAR therapy.

2744. The ~~method-immune cells for use of or use of any of~~ claims 7-8 or claims 25-2643, ~~further comprising administering wherein~~ the non-CAR ~~T-cell~~ therapy is to be further administered to the candidate for the non-CAR ~~T-cell~~ therapy.

2845. Immune cells expressing a chimeric antigen receptor (CAR) directed to B cell maturation antigen (BCMA) for use in treating a disease caused by BCMA ~~A method of treating a disease caused by B-Cell Maturation Agent (BCMA)~~ expressing cells in a subject in need thereof, ~~comprising~~ wherein:

- a. ~~determining~~ a first level of soluble BCMA (sBCMA) in a tissue sample from the subject is to be determined;
- b. ~~administering to the subject~~ immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA ~~(BCMA CAR T-cells)~~ is to be administered to the subject, and
- c. ~~determining~~ a second level of sBCMA in a tissue sample from the subject is to be determined

wherein, if said second level of sBCMA is greater than 30% of said first level of sBCMA, the subject is to be subsequently administered lenalidomide to treat said disease.

29. Use of immune cells expressing a chimeric antigen receptor (CAR) directed to B cell maturation antigen (BCMA) in the manufacture of a medicament for treating a disease caused by BCMA expressing cells in a subject in need thereof, wherein:

- a. a first level of soluble BCMA (sBCMA) in a tissue sample from the subject is to be determined;

- b. immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA are to be administered to the subject, and
- c. a second level of sBCMA in a tissue sample from the subject is to be determined

wherein, if said second level of sBCMA is greater than 30% of said first level of sBCMA, the subject is to be subsequently administered lenalidomide to treat said disease.

3046. The method-immune cells for use of claim 28 or the use of claim 2945, wherein the lenalidomide is to be administered at a dosage of about 2.5 mg, 5 mg, 10 mg, 15 mg, 20 mg, or 25 mg.

47.—The method of claim 45, wherein the lenalidomide is administered at a dosage of about 25 mg daily orally on days 1-21 of a 28-day cycle.

48.—The method of any one of claims 45-47, wherein the disease is Multiple Myeloma (MM).

3149. Immune cells expressing a chimeric antigen receptor (CAR) directed to B cell maturation antigen (BCMA) for use in treating a disease caused by BCMA A method of treating a disease caused by B-Cell Maturation Agent (BCMA)-expressing cells in a subject in need thereof, comprising wherein:

- a. determining a first level of soluble BCMA (sBCMA) in a tissue sample from the subject is to be determined;
- b. administering to the subject immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA CAR T cells) are to be administered to the subject, and
- c. determining a second level of sBCMA in a tissue sample from the subject is to be determined

wherein, if said second level of sBCMA is greater than 30% of said first level of sBCMA, the subject is to be subsequently administered pomalidomide to treat said disease.

32. Use of immune cells expressing a chimeric antigen receptor (CAR) directed to B cell maturation antigen (BCMA) in the manufacture of a medicament for treating a disease caused by BCMA expressing cells in a subject in need thereof, wherein:

- a. a first level of soluble BCMA (sBCMA) in a tissue sample from the subject is to be determined;

b. immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA are to be administered to the subject, and

c. a second level of sBCMA in a tissue sample from the subject is to be determined

wherein, if said second level of sBCMA is greater than 30% of said first level of sBCMA, the subject is to be subsequently administered pomalidomide to treat said disease.

3350. The method-immune cells for use of claim 31 or the use of claim 3249, wherein the pomalidomide is to be administered at a dosage of about 1 mg, 2 mg, 3 mg, or 4 mg once daily.

~~51.—The method of claim 49, wherein the pomalidomide is administered at a dosage of about 4 mg per day taken orally on days 1-21 of repeated 28-day cycles until disease progression.~~

~~52.—The method of any one of claims 49-51, wherein the wherein the disease is Multiple Myeloma (MM).~~

3453. Immune cells expressing a chimeric antigen receptor (CAR) directed to B cell maturation antigen (BCMA) for use in treating a disease caused by BCMA A—method of treating a disease caused by B Cell Maturation Agent (BCMA)—expressing cells in a subject in need thereof, comprisingwherein:

- a. ~~determining~~ a first level of soluble BCMA (sBCMA) in a tissue sample from the subject is to be determined;
- b. ~~administering to the subject~~ immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA. ~~(BCMA CAR T cells)~~ are to be administered to the subject, and
- c. ~~determining~~ a second level of sBCMA in a tissue sample from the subject is to be determined

wherein, if said second level of sBCMA is greater than 30% of said first level of sBCMA, the subject is to be subsequently administered CC-220 to treat said disease.

35. Use of immune cells expressing a chimeric antigen receptor (CAR) directed to B cell maturation antigen (BCMA) in the manufacture of a medicament for treating a disease caused by BCMA expressing cells in a subject in need thereof, wherein:

- a. a first level of soluble BCMA (sBCMA) in a tissue sample from the subject is to be determined;
- b. immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA are to be administered to the subject, and
- c. a second level of sBCMA in a tissue sample from the subject is to be determined

wherein, if said second level of sBCMA is greater than 30% of said first level of sBCMA, the subject is to be subsequently administered CC-220 to treat said disease.

3654. The method-immune cells for use of claim 34 or the use of claim 3553, wherein the CC-220 is to be administered at a dosage of about 0.15 mg, 0.3 mg, 0.45 mg, 0.6 mg, 0.75 mg, 0.9 mg, 1.0 mg, 1.1 mg, or 1.2 mg.

~~55.—The method of claim 53, wherein the CC-220 is administered orally at a dosage of about 0.15 mg, 0.3 mg, 0.45 mg, 0.6 mg, 0.75 mg, 0.9 mg, 1.0 mg, 1.1 mg, or 1.2 mg daily on days 1-21 of a 28-day cycle.~~

~~56.—The method of any one of claims 53-55, wherein the disease is Multiple Myeloma (MM).~~

3757. Immune cells expressing a chimeric antigen receptor (CAR) directed to B cell maturation antigen (BCMA) for use in treating a disease caused by BCMA-A method of treating a disease caused by B-Cell Maturation Agent (BCMA) expressing cells in a subject in need thereof, comprising wherein:

- a. ~~determining~~ a first level of soluble BCMA (sBCMA) in a tissue sample from the subject is to be determined;
- b. ~~administering to the subject~~ immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA-CAR T cells) are to be administered, and
- c. ~~determining~~ a second level of sBCMA in a tissue sample from the subject is to be determined

wherein, if said second level of sBCMA is greater than 30% of said first level of sBCMA, the subject is to be subsequently administered CC-220 and dexamethasone to treat said disease.

38. Use of immune cells expressing a chimeric antigen receptor (CAR) directed to B cell maturation antigen (BCMA) in the manufacture of a medicament for treating a disease caused by BCMA expressing cells in a subject in need thereof, wherein:

- a. a first level of soluble BCMA (sBCMA) in a tissue sample from the subject is to be determined;
- b. immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA are to be administered, and
- c. a second level of sBCMA in a tissue sample from the subject is to be determined

wherein, if said second level of sBCMA is greater than 30% of said first level of sBCMA, the subject is to be subsequently administered CC-220 and dexamethasone to treat said disease.

3958. The ~~method~~ immune cells for use of claim 37 or the use of claim 3857, wherein the CC-220 is ~~to be~~ administered at a dosage of about 0.15 mg, 0.3 mg, 0.45 mg, 0.6 mg, 0.75 mg, 0.9 mg, 1.0 mg, 1.1 mg, or 1.2 mg and the dexamethasone is to be administered at a dosage of about 20 mg, 25 mg, 30 mg, 35 mg, 40 mg, 45 mg, 50 mg, 55 mg, or 60 mg.

59. The method of claim 57 or claim 58, wherein the dexamethasone is administered at a dosage of about 20 mg, 25 mg, 30 mg, 35 mg, 40 mg, 45 mg, 50 mg, 55 mg, or 60 mg.

60. The method of claim 57, wherein the CC 220 is administered orally at a dosage of about 0.15 mg, 0.3 mg, 0.45 mg, 0.6 mg, 0.75 mg, 0.9 mg, 1.0 mg, 1.1 mg, or 1.2 mg daily on days 1-21 of a 28-day cycle.

61. The method of any one of claims 57-60, wherein the dexamethasone is administered orally at a dosage of about 20 mg, 25 mg, 30 mg, 35 mg, 40 mg, 45 mg, 50 mg, 55 mg, or 60 mg on days 1, 8, 15, and 22 of a 28-day cycle.

62. The method of any one of claims 57-61, wherein the disease is Multiple Myeloma (MM).

40. The immune cells for use of or use of any of claims 1-39, wherein the immune cells are T cells.

41. The immune cells for use of or use of any of claims 1-40, wherein the immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA are BCMA CAR T cells.

4263. Immune cells expressing a chimeric antigen receptor (CAR) directed to B cell maturation antigen (BCMA) for use in treating a disease caused by BCMA ~~A method of treating a disease caused by B Cell Maturation Agent (BCMA)~~-expressing cells in a subject in need thereof, ~~comprising~~wherein:

- a. ~~determining~~ a first level of soluble BCMA (sBCMA) in a tissue sample from the subject is to be determined;
- b. ~~administering to the subject~~ a first BCMA-based treatment modality comprising immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA ~~(BCMA-CAR T cells)~~ is to be administered to the subject, and
- c. ~~determining~~ a second level of sBCMA in a tissue sample from the subject is to be determined

wherein, if said second level of sBCMA is greater than 30% of said first level of sBCMA, the subject is subsequently provided a second BCMA-based treatment modality to treat said disease; and

wherein the first BCMA-based treatment modality and the second BCMA-based treatment modality are different BCMA-based treatment modalities.

43. Use of immune cells expressing a chimeric antigen receptor (CAR) directed to B cell maturation antigen (BCMA) in the manufacture of a medicament for treating a disease caused by BCMA expressing cells in a subject in need thereof, wherein:

- a. a first level of soluble BCMA (sBCMA) in a tissue sample from the subject is to be determined;
- b. a first BCMA-based treatment modality comprising immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA is to be administered to the subject, and
- c. a second level of sBCMA in a tissue sample from the subject is to be determined

wherein, if said second level of sBCMA is greater than 30% of said first level of sBCMA, the subject is to be subsequently provided a second BCMA-based treatment modality to treat said disease; and

wherein the first BCMA-based treatment modality and the second BCMA-based treatment modality are different BCMA-based treatment modalities.

4464. A method of treating a disease caused by B Cell Maturation Agent (BCMA) expressing cells in a subject in need thereof, comprising:The immune cells for use of claim 42 or the use of claim 43, wherein

- a. ~~—determining a first level of soluble BCMA (sBCMA) in a tissue sample from the subject;~~
- b. ~~—administering to the subject a first BCMA-based treatment modality comprising immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA CAR T cells);~~
- c. ~~—determining that a second level of sBCMA in a tissue sample from the subject is greater than 30% of said first level of sBCMA, and~~
- d. ~~—on the basis of the determination in step c, subsequently providing thea second BCMA-based treatment modality to the subject.~~

~~wherein the first BCMA-based treatment modality and the second BCMA-based treatment modality are different BCMA-based treatment modalities.~~

~~65. —The method of claim 63, wherein if said second level of sBCMA is greater than 40% of said first level of sBCMA, the subject is provided a second BCMA-based treatment modality to treat said disease.~~

4566. The ~~method~~immune cells for use of or use of any one of claims 42-4463, 64, or 65, wherein said second level of sBCMA is to be determined at 25-35 days after said ~~administering~~administration.

~~67. —The method of any one of claims 63, 64, or 65, wherein said second level of sBCMA is determined at 28-31 days after said administering.~~

~~68. —The method of any of claims 63-67, wherein the subject is provided a second BCMA-based treatment modality within three months, two months, or one month after said determining the second level of sBCMA.~~

4669. A non-CAR therapy for use in treating~~A method of treating~~ a disease caused by B cell maturation antigen~~B Cell Maturation Agent (BCMA)~~ expressing cells, comprising wherein ~~administering to a patient diagnosed with said disease~~ a second BCMA-based treatment modality is to be administered to a patient diagnosed with said disease, wherein the patient has previously

been administered a first BCMA-based treatment modality comprising immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (~~BCMA-CAR T cells~~), wherein the first BCMA-based treatment modality and the second BCMA-based treatment modality are different BCMA-based treatment modalities; and wherein a tissue sample from the patient subsequent to said administration contained a level of soluble BCMA (sBCMA) greater than 30% of a level of sBCMA found in a tissue sample obtained from the patient prior to said administration.

47. Use of a non-CAR therapy in the manufacture of a medicament for treating a disease caused by B cell maturation antigen (BCMA) expressing cells, wherein a second BCMA-based treatment modality is to be administered to a patient diagnosed with said disease, wherein the patient has previously been administered a first BCMA-based treatment modality comprising immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA, wherein the first BCMA-based treatment modality and the second BCMA-based treatment modality are different BCMA-based treatment modalities; and wherein a tissue sample from the patient subsequent to said administration contained a level of soluble BCMA (sBCMA) greater than 30% of a level of sBCMA found in a tissue sample obtained from the patient prior to said administration.

4870. A non-CAR cell therapy for use in treating~~A method of determining whether a patient diagnosed with~~ a disease caused by B cell maturation antigen~~B-Cell Maturation Agent~~ (BCMA) expressing cells, wherein the patient has been treated~~should be administered a second BCMA-based treatment modality after treatment~~ with a first BCMA-based treatment modality comprising immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (~~BCMA-CAR T cells~~), wherein the first BCMA-based treatment modality and the second BCMA-based treatment modality are different BCMA-based treatment modalities, ~~comprising~~ wherein determining a level of soluble BCMA (sBCMA) in a tissue sample from the patient is to be determined, wherein the patient has previously been administered the first BCMA-based treatment modality comprising immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (~~BCMA-CAR T cells~~); and wherein if the level of sBCMA in the tissue sample is greater than 30% of a level of sBCMA found in a tissue sample obtained from the patient prior to said administration, then the patient is a candidate for the second BCMA-based treatment modality, and

the second BMCA-based treatment modality is to be administered to the candidate for the second BCMA-based treatment modality.

49. Use of a non-CAR cell therapy in the manufacture of a medicament for treating a disease caused by B cell maturation antigen (BCMA) expressing cells, wherein the patient has been treated with a first BCMA-based treatment modality comprising immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA, wherein the first BCMA-based treatment modality and the second BCMA-based treatment modality are different BCMA-based treatment modalities, wherein

a level of soluble BCMA (sBCMA) in a tissue sample from the patient is to be determined, wherein the patient has previously been administered the first BCMA-based treatment modality comprising immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA; and wherein if the level of sBCMA in the tissue sample is greater than 30% of a level of sBCMA found in a tissue sample obtained from the patient prior to said administration, then the patient is a candidate for the second BCMA-based treatment modality, and

the second BCMA-based treatment modality is to be administered to the candidate for the second BCMA-based treatment modality.

~~71.—The method of claim 70, further comprising administering the second BCMA-based treatment modality to the candidate for the second BCMA-based treatment modality.~~

5072. Immune cells expressing a chimeric antigen receptor (CAR) directed to B cell maturation antigen (BCMA) for use in treating a disease caused by BCMA~~method of treating a disease caused by B Cell Maturation Agent (BCMA)~~ expressing cells in a subject in need thereof, ~~comprising~~wherein:

- a. ~~administering to the subject~~ a first BCMA-based treatment modality comprising immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA ~~(BCMA-CAR T-cells)~~ is to be administered to the subject, and
- b. ~~determining~~ a level of soluble BCMA (sBCMA) in a tissue sample from the subject is to be determined

wherein, if said level of sBCMA is greater than 4000 ng/L, the subject is to be subsequently provided a second BCMA-based treatment modality to treat said disease, and wherein the first BCMA-based treatment modality and the second BCMA-based treatment modality are different BCMA-based treatment modalities.

51. Use of immune cells expressing a chimeric antigen receptor (CAR) directed to B cell maturation antigen (BCMA) in the manufacture of a medicament for treating a disease caused by BCMA expressing cells in a subject in need thereof, wherein:

- a. a first BCMA-based treatment modality comprising immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA is to be administered to the subject, and
- b. a level of soluble BCMA (sBCMA) in a tissue sample from the subject is to be determined

wherein, if said level of sBCMA is greater than 4000 ng/L, the subject is to be subsequently provided a second BCMA-based treatment modality to treat said disease, and wherein the first BCMA-based treatment modality and the second BCMA-based treatment modality are different BCMA-based treatment modalities.

5273. The ~~method-immune cells for use of claim 50 or the use~~ of claim 5172, wherein said level of sBCMA is to be determined at 50-70 days after said ~~administering~~administration.

74. ~~The method of claim 72 or claim 73, wherein said level of sBCMA is determined at 55-65 days after said administering.~~

75. ~~The method of any of claims 72-74, wherein said level of sBCMA is determined at 58-62 days after said administering.~~

5376. The ~~method-immune cells for use of or use~~ of any of claims 42-45 or 50-5273-75, wherein the subject is to be provided said second BCMA-based treatment modality within three months, two months, or one month after said ~~determining~~determination of a level of sBCMA.

5477. Immune cells expressing a chimeric antigen receptor (CAR) directed to B cell maturation antigen (BCMA) for use in treating a disease caused by BCMAA ~~method of treating a disease caused by B-Cell Maturation Agent (BCMA)~~ expressing cells in a subject in need thereof, ~~comprising~~wherein:

- a. ~~determining~~a first level of interleukin-6 (IL-6), tumor necrosis factor alpha (TNF α) or both in a tissue sample from the subject is to be determined;
- b. ~~administering to the subject~~a first BCMA-based treatment modality comprising immune cells expressing a chimeric antigen receptor (CAR)

directed to BCMA (~~BCMA CAR T-cells~~) is to be administered to the subject, and

- c. ~~subsequently determining~~ a second level of IL-6, TNF α or both in a tissue sample from the subject is to be subsequently determined;

wherein, if said second level of IL-6 is not greater than said first level of IL-6, said second level of TNF α is not greater than said first level of TNF α or both ~~is-are~~ not greater than said first levels ~~of IL-6, TNF α or both~~, then the subject is to be subsequently provided a second BCMA-based treatment modality to treat said disease, and wherein the first BCMA-based treatment modality and the second BCMA-based treatment modality are different BCMA-based treatment modalities.

55. Use of immune cells expressing a chimeric antigen receptor (CAR) directed to B cell maturation antigen (BCMA) in the manufacture of a medicament for treating a disease caused by BCMA expressing cells in a subject in need thereof, wherein:

- a. a first level of interleukin-6 (IL-6), tumor necrosis factor alpha (TNF α) or both in a tissue sample from the subject is to be determined;
- b. a first BCMA-based treatment modality comprising immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA is to be administered to the subject, and
- c. a second level of IL-6, TNF α or both in a tissue sample from the subject is to be subsequently determined;

wherein, if said second level of IL-6 is not greater than said first level of IL-6, said second level of TNF α is not greater than said first level of TNF α or both are not greater than said first levels, then the subject is to be subsequently provided a second BCMA-based treatment modality to treat said disease, and

wherein the first BCMA-based treatment modality and the second BCMA-based treatment modality are different BCMA-based treatment modalities.

5678. The ~~method-immune cells for use of claim 54 or the use~~ of claim 5577, wherein said first level is to be determined on the day of said ~~administering-administration~~ to the subject the first BCMA-based treatment modality comprising immune cells expressing a CAR directed to BCMA, and said second level is to be determined 1-4 days or 2 days after said ~~administering-administration~~.

~~79. The method of claim 78, wherein said second level is determined two days after said administering.~~

57. The immune cells for use of or use of any of claims 42-56, wherein the immune cells are T cells.

58. The immune cells for use of or use of any of claims 42-57, wherein the immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA are BCMA CAR T cells.

5980. The ~~method-immune cells for use of or use~~ of any of claims 1-~~5879~~, wherein said disease caused by BCMA-expressing cells is multiple myeloma, chronic lymphocytic leukemia, or a non-Hodgkins lymphoma.

6084. The ~~method-immune cells for use of or use~~ of claim ~~5980~~, wherein the disease caused by BCMA-expressing cells is multiple myeloma.

6182. The ~~method-immune cells for use of or use~~ of claim ~~6084~~, wherein said multiple myeloma is high-risk multiple myeloma or relapsed and refractory multiple myeloma.

6283. The ~~method-immune cells for use of or use~~ of claim ~~5980~~, wherein said disease caused by BCMA-expressing cells is a non-Hodgkins lymphoma, and wherein the non-Hodgkins lymphoma is selected from the group consisting of: Burkitt's lymphoma, chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL), diffuse large B cell lymphoma, follicular lymphoma, immunoblastic large cell lymphoma, precursor B-lymphoblastic lymphoma, and mantle cell lymphoma.

~~84. The method of any of claims 1-83, wherein the immune cells are T cells.~~

6385. The ~~method-immune cells for use of or use~~ of any of claims 1-~~6284~~, wherein the immune cells are to be administered in a dosage of from 150×10^6 cells to 450×10^6 cells.

~~86. The method of any of claims 1-85, wherein before said administering said subject has received three or more lines of prior therapy.~~

6487. The ~~method-immune cells for use of or use~~ of any of claims 1-~~6385~~, wherein before said ~~administering administration~~, said subject has received one or more lines of prior therapy or three or more lines or prior therapy.

6588. The ~~method-immune cells for use of or use~~ of claim ~~6386~~ or claim 6487, wherein said lines of prior therapy comprise a proteasome inhibitor, lenalidomide, pomalidomide, thalidomide, bortezomib, dexamethasone, cyclophosphamide, doxorubicin, carfilzomib, ixazomib, cisplatin, doxorubicin, etoposide, an anti-CD38 antibody panobinostat, or elotuzumab.

6689. The ~~method-immune cells for use of or use~~ of claim 6386 or claim 6487, wherein before said ~~administering-administration~~, said subject has received one or more lines of prior therapy comprising:

- a. daratumumab, pomalidomide, and dexamethasone (DPd);
- b. daratumumab, bortezomib, and dexamethasone (DVd);
- c. ixazomib, lenalidomide, and dexamethasone (IRd);
- d. daratumumab, lenalidomide and dexamethasone;
- e. bortezomib, lenalidomide and dexamethasone (RVd);
- f. bortezomib, cyclophosphamide and dexamethasone (BCd);
- g. bortezomib, doxorubicin and dexamethasone;
- h. carfilzomib, lenalidomide and dexamethasone (CRd);
- i. bortezomib and dexamethasone;
- j. bortezomib, thalidomide and dexamethasone;
- k. lenalidomide and dexamethasone;
- l. dexamethasone, thalidomide, cisplatin, doxorubicin, cyclophosphamide, etoposide and bortezomib (VTD-PACE);
- m. lenalidomide and low-dose dexamethasone;
- n. bortezomib, cyclophosphamide and dexamethasone;
- o. carfilzomib and dexamethasone;
- p. lenalidomide alone;
- q. bortezomib alone;
- r. daratumumab alone;
- s. elotuzumab, lenalidomide, and dexamethasone;
- t. elotuzumab, lenalidomide and dexamethasone;
- u. bendamustine, bortezomib and dexamethasone;
- v. bendamustine, lenalidomide, and dexamethasone;
- w. pomalidomide and dexamethasone;
- x. pomalidomide, bortezomib and dexamethasone;
- y. pomalidomide, carfilzomib and dexamethasone;
- z. bortezomib and liposomal doxorubicin;
- aa. cyclophosphamide, lenalidomide, and dexamethasone;

- bb. elotuzumab, bortezomib and dexamethasone;
- cc. ixazomib and dexamethasone;
- dd. panobinostat, bortezomib and dexamethasone;
- ee. panobinostat and carfilzomib; or
- ff. pomalidomide, cyclophosphamide and dexamethasone.

~~90. The method of claim 89, wherein said subject has received two, three, four, five, six, seven or more of said lines of prior therapy.~~

~~91. The method of claim 89, wherein said subject has received no more than three of said lines of prior therapy.~~

~~92. The method of claim 89, wherein said subject has received no more than two of said lines of prior therapy.~~

~~93. The method of claim 89, wherein said subject has received no more than one of said lines of prior therapy.~~

6794. The ~~method-immune cells for use of or use~~ of any of claims 1-~~6693~~, wherein said CAR comprises an antibody or antibody fragment that targets BCMA.

6895. The ~~method-immune cells for use of or use~~ of any of claims 1-~~6794~~, wherein said CAR comprises a single chain Fv antibody fragment (scFv).

~~96. The method of any of claims 1-94, wherein said CAR comprises a BCMA02 scFv.~~

6997. The ~~method-immune cells for use of or use~~ of any of claims 1-~~6794~~, wherein said immune cells are idecabtagene vicleucel cells.

7098. Immune cells expressing a chimeric antigen receptor (CAR) directed to B cell maturation antigen (BCMA) for use in treating a disease caused by BCMA~~A method of treating a disease caused by B-Cell Maturation Agent (BCMA)~~ expressing cells in a subject in need thereof, ~~comprising~~wherein:

- a. ~~determining~~ a first level of soluble BCMA (sBCMA) and/or a first level of interleukin-6 (IL-6), tumor necrosis factor alpha (TNF α), or both in a tissue sample from the subject is to be determined;
- b. ~~administering to the subject~~ a first BCMA-based treatment modality comprising immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA ~~(BCMA-CAR T-cells)~~ is to be administered to the subject, and

- c. ~~determining~~ a second level of sBCMA and/or a second level of interleukin-6 (IL-6), tumor necrosis factor alpha (TNF α), or both in a tissue sample from the subject is to be determined;

wherein, if said second level of sBCMA is greater than 30% of said first level of sBCMA and/or if said second level of IL-6 is not greater than said first level of IL-6, said second level of TNF α is not greater than said first level of TNF α or both ~~is-are~~ not greater than said first levels ~~of IL-6, TNF α or both~~, the subject is to be subsequently provided a second BCMA-based treatment modality to treat said disease, and

wherein the first BCMA-based treatment modality and the second BCMA-based treatment modality are different BCMA-based treatment modalities.

71. Use of immune cells expressing a chimeric antigen receptor (CAR) directed to B cell maturation antigen (BCMA) in the manufacture of a medicament for treating a disease caused by BCMA expressing cells in a subject in need thereof, wherein:

- a. a first level of soluble BCMA (sBCMA) and/or a first level of interleukin-6 (IL-6), tumor necrosis factor alpha (TNF α), or both in a tissue sample from the subject is to be determined;
- b. a first BCMA-based treatment modality comprising immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA is to be administered to the subject, and
- c. a second level of sBCMA and/or a second level of interleukin-6 (IL-6), tumor necrosis factor alpha (TNF α), or both in a tissue sample from the subject is to be determined;

wherein, if said second level of sBCMA is greater than 30% of said first level of sBCMA and/or if said second level of IL-6 is not greater than said first level of IL-6, said second level of TNF α is not greater than said first level of TNF α or both are not greater than said first levels, the subject is to be subsequently provided a second BCMA-based treatment modality to treat said disease, and

wherein the first BCMA-based treatment modality and the second BCMA-based treatment modality are different BCMA-based treatment modalities.

~~7299. A method of treating a disease caused by B Cell Maturation Agent (BCMA) expressing cells in a subject in need thereof, comprising: The immune cells for use of claim 70 or the use of claim 71, wherein~~

- ~~a. determining a first level of soluble BCMA (sBCMA) and/or a first level of interleukin-6 (IL-6), tumor necrosis factor alpha (TNF α), or both in a tissue sample from the subject;~~
- ~~b. administering to the subject a first BCMA-based treatment modality comprising immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA-CAR T cells);~~
- ~~c. determining that a second level of sBCMA in a tissue sample from the subject is greater than 30% of said first level of sBCMA and/or a second level of IL-6, TNF α or both is not greater than said first level of IL-6, TNF α or both, and~~
- ~~d. on the basis of the determination in step c, subsequently providing thea second BCMA-based treatment modality to the subject;~~

~~wherein the first BCMA-based treatment modality and the second BCMA-based treatment modality are different BCMA-based treatment modalities.~~

~~73400. A non-CAR therapy for use in treating~~A method of treating a disease caused by B cell maturation antigen~~B Cell Maturation Agent~~ (BCMA) expressing cells, ~~comprising wherein administering to a patient diagnosed with said disease~~ a second BCMA-based treatment modality is to be administered to a patient diagnosed with said disease, wherein the patient has previously been administered a first BCMA-based treatment modality comprising immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA ~~(BCMA-CAR T cells)~~, wherein the first BCMA-based treatment modality and the second BCMA-based treatment modality are different BCMA-based treatment modalities; and wherein a tissue sample from the patient subsequent to said administration contained (i) a level of soluble BCMA (sBCMA) greater than 30% of a level of sBCMA found in a tissue sample obtained from the patient prior to said administration and/or (ii) a level of IL-6, TNF α or both not greater than a level of IL-6, TNF α or both found in a tissue sample obtained from the patient prior to said administration.

74. Use of a non-CAR therapy in the manufacture of a medicament for treating a disease caused by B cell maturation antigen (BCMA) expressing cells, wherein a second BCMA-based treatment modality is to be administered to a patient diagnosed with said disease, wherein

the patient has previously been administered a first BCMA-based treatment modality comprising immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA, wherein the first BCMA-based treatment modality and the second BCMA-based treatment modality are different BCMA-based treatment modalities; and wherein a tissue sample from the patient subsequent to said administration contained (i) a level of soluble BCMA (sBCMA) greater than 30% of a level of sBCMA found in a tissue sample obtained from the patient prior to said administration and/or (ii) a level of IL-6, TNF α or both not greater than a level of IL-6, TNF α or both found in a tissue sample obtained from the patient prior to said administration.

~~75404. A non-CAR cell therapy for use in treating~~A method of determining whether a patient diagnosed with a disease caused by B cell maturation antigen~~B-Cell Maturation Agent (BCMA) expressing cells, wherein the patient has been treated should be administered a second BCMA-based treatment modality after treatment~~ with a first BCMA-based treatment modality comprising immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA ~~(BCMA-CAR T-cells), comprising wherein determining~~ a level of soluble BCMA (sBCMA) and/or a level of IL-6, TNF α or both in a tissue sample from the patient is to be determined, wherein the patient has previously been administered the first BCMA-based treatment modality comprising immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA ~~(BCMA-CAR T-cells)~~, wherein if (i) the level of sBCMA in the tissue sample is greater than 30% of a level of sBCMA found in a tissue sample obtained from the patient prior to said administration and/or (ii) the level of IL-6, TNF α or both is not greater than a level of IL-6, TNF α or both found in a tissue sample obtained from the patient prior to said administration, then the patient is a candidate for the second BCMA-based treatment modality, and

wherein the first BCMA-based treatment modality and the second BCMA-based treatment modality are different BCMA-based treatment modalities, and

the second BCMA-based treatment modality is to be administered to the candidate for the second BCMA-based treatment modality.

76. Use of a non-CAR cell therapy in the manufacture of a medicament for treating a disease caused by B cell maturation antigen (BCMA) expressing cells, wherein the patient has been treated with a first BCMA-based treatment modality comprising immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA, wherein the first BCMA-based treatment

modality and the second BCMA-based treatment modality are different BCMA-based treatment modalities, wherein

a level of soluble BCMA (sBCMA) and/or a level of IL-6, TNF α or both in a tissue sample from the patient is to be determined, wherein the patient has previously been administered the first BCMA-based treatment modality comprising immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA, wherein if (i) the level of sBCMA in the tissue sample is greater than 30% of a level of sBCMA found in a tissue sample obtained from the patient prior to said administration and/or (ii) the level of IL-6, TNF α or both is not greater than a level of IL-6, TNF α or both found in a tissue sample obtained from the patient prior to said administration, then the patient is a candidate for the second BCMA-based treatment modality, and

wherein the first BCMA-based treatment modality and the second BCMA-based treatment modality are different BCMA-based treatment modalities, and

the second BCMA-based treatment modality is to be administered to the candidate for the second BCMA-based treatment modality.

~~102.—The method of claim 101, further comprising administering the second BCMA-based treatment modality to the candidate for the second BCMA-based treatment modality.~~

~~77103. The method immune cells for use of or use of any one of claims ~~2063-76102~~, wherein the second BCMA-based treatment modality comprises a BCMA-Antibody-Drug Conjugate (ADC), a bispecific T-cell engager (BiTE) that targets B-cell maturation antigen (BCMA), a natural killer (NK) cell engager (NKCEs) that targets B-cell maturation antigen (BCMA), or immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA CAR T cells).~~

~~104.—The method of claim 103, wherein the second BCMA-based treatment modality comprises a BCMA-Antibody-Drug-Conjugate (ADC).~~

~~105.—The method of claim 104, wherein the BCMA-Antibody-Drug-Conjugate (ADC) comprises CC99712 or GSK2857916 (belantamab mafodotin).~~

~~106.—The method of claim 103, wherein the second BCMA-based treatment modality comprises a bispecific T-cell engager (BiTE) that targets B-cell maturation antigen (BCMA).~~

~~107.—The method of claim 106, wherein the bispecific T cell engager (BiTE) that targets B cell maturation antigen (BCMA) comprises CC-93269, AMG-420, JNJ-64007957, AMG-701, PF-06863135, REGN5458, REGN5459, or TNB-383B.~~

~~108.—The method of claim 103, wherein the second BCMA-based treatment modality comprises a natural killer (NK) cell engager (NKCEs) that targets B cell maturation antigen (BCMA).~~

~~109.—The method of claim 108, wherein the natural killer (NK) cell engager (NKCEs) that targets B cell maturation antigen (BCMA) comprises DF3001, AFM26, CTX-4419, or CTX-8573.~~

~~110.—The method of claim 103, wherein the second BCMA-based treatment modality comprises immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA-CAR T cells).~~

~~111.—The method of claim 103 or 110, wherein the immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA-CAR T cells) comprise JCARH125, KITE-585, P-BCMA-101, LCAR-B38M, CT053, anti-CD19/BCMA-CAR T cells, and CTX120.~~

~~112.—The method of any one of claims 98-111, wherein the immune cells in the first BCMA-based treatment modality comprising immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA-CAR T cells) are idecabtagene vicleucel cells.~~

~~113.—The method of any one of claims 63-112, wherein the second BCMA-based treatment modality does not comprise idecabtagene vicleucel cells.~~