

[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. SUMMARY

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

[0005] In one 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 example of either of the above examples, 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 example, said second level of sBCMA is determined at 25-35 days after said administering. In another specific example, said second level of sBCMA is determined at 28-31 days after said administering. In more specific examples, 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 examples, the immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA CAR T cells) are idecabtagene vicleucel cells. In particular examples, 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 example, 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 examples, the immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA CAR T cells) are idecabtagene vicleucel cells. In particular examples, the disease is multiple myeloma, e.g., relapsed and refractory multiple myeloma.

[0007] In another 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) 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 example, the method further

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

[0009] In particular 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 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 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: 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 example, said level of sBCMA is determined at 50-70 days after said administering. In another specific example, said level of sBCMA is determined at 55-65 days after said

administering. In another specific example, said of sBCMA is determined at 58-62 days after said administering. In a specific example of the preceding examples, 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 examples, the immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA CAR T cells) are idecabtagene vicleucel cells. In particular examples, 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 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 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 example, 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 example, said second level is determined two days after said administering. In specific examples, the immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA CAR T cells) are idecabtagene vicleucel cells. In particular examples, 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 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: 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 examples, said determining is performed within 0-4 days prior to said administering. In a specific example, said determining is performed on the same day as said administering. In another specific example, said therapy to treat CRS is first provided to said subject 0-5 days

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

[0014] In another 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) 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 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 examples, the immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA CAR T cells) are idecabtagene vicleucel cells. In particular 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 examples, 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 examples, the immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA CAR T cells) are idecabtagene vicleucel cells. In particular examples, the disease is multiple myeloma, e.g., relapsed and refractory multiple myeloma.

[0016] In another 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) 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 examples, the immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA CAR T cells) are idecabtagene vicleucel cells. In particular examples, the disease is multiple myeloma, e.g., relapsed and refractory multiple myeloma.

[0017] In another 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) 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 examples, the immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA CAR T cells) are idecabtagene vicleucel cells. In particular examples, the disease is multiple myeloma, e.g., relapsed and refractory multiple myeloma.

[0018] In certain examples 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 examples, the immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA CAR T cells) are idecabtagene vicleucel cells. In particular examples, the disease is multiple myeloma, e.g., relapsed and refractory multiple myeloma.

[0019] In certain examples 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 examples, the immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA CAR T cells) are idecabtagene vicleucel cells. In particular examples, the disease is multiple myeloma, e.g., relapsed and refractory multiple myeloma.

[0020] In another example, 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 examples, the immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA CAR T cells) are idecabtagene vicleucel cells. In particular examples, the disease is multiple myeloma, e.g., relapsed and refractory multiple myeloma.

[0021] In certain examples 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 examples, the immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA CAR T cells) are idecabtagene vicleucel cells. In particular examples, the disease is multiple myeloma, e.g., relapsed and refractory multiple myeloma.

[0022] In another 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 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 example, the method further comprises administering the non-CAR T cell therapy to the candidate for the non-CAR T cell therapy. In specific examples, the immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA CAR T cells) are idecabtagene vicleucel cells. In particular examples, 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 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 example, the method further comprises administering the non-CAR T cell therapy to the candidate for the non-CAR T cell therapy. In specific examples, the immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA CAR T cells) are idecabtagene vicleucel cells. In particular examples, the disease is multiple myeloma, e.g., relapsed and refractory multiple myeloma.

[0024] In certain examples 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 example, the method further comprises administering the non-CAR T cell therapy to the candidate for the non-CAR T cell therapy. In specific examples, the immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA CAR T cells) are idecabtagene vicleucel cells. In particular examples, the disease is multiple myeloma, e.g., relapsed and refractory multiple myeloma.

[0025] In a specific examples of any of the above examples or examples, said tissue sample is blood, plasma or serum. In another specific examples of any of the above examples or examples, 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 examples, the disease is multiple myeloma, *e.g.*, high-risk multiple myeloma or relapsed and refractory multiple myeloma. In other specific examples, 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 examples, 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 example, 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 examples of any of the above examples, 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 example, the immune cells are administered in a dosage of from 150×10^6 cells to 450×10^6 cells.

[0027] In a specific example of any of the above examples, 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 examples, 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 example, the patient has not received said non-CAR T cell therapy prior to administration of CAR T cells.

[0028] In another specific example of any of the above examples, 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 examples, 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 examples, 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 examples, 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 examples of any of the above examples, 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 examples, 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 example, the immune cells are administered at a dose of about 450×10^6 cells. In some examples, 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 examples, 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 examples of any of the examples 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 examples of any of the examples 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 examples of any of the examples 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 examples of any of the examples 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 examples of any of the examples 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 examples of any of the examples described herein, the immune cells expressing a CAR directed to BCMA are administered in a dosage of about 450×10^6 cells. In specific examples of any of the examples described herein, the immune cells are T cells (e.g., autologous T cells). In specific examples of any of the examples 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 examples of any of the examples described herein, the immune cells (e.g., T cells) are administered by an intravenous infusion.

[0031] In specific examples of any of the examples 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 examples, LD chemotherapy comprises fludarabine and/or cyclophosphamide. In specific examples, 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 examples, LD chemotherapy comprises any of the chemotherapeutic agents described in Section 5.9. In specific examples, 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 examples, 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 examples of any of the examples 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 examples, the subject undergoes apheresis to collect and isolate said immune cells, e.g., T cells. In a specific example of any of the above examples, 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 example, 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 example of any of the above examples, 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 example, 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 example of any of any of the above examples or examples, said CAR comprises an antibody or antibody fragment that targets BCMA. In a more specific example, said CAR comprises a single chain Fv antibody fragment (scFv). In a more specific example, said CAR comprises a BCMA02 scFv. In a specific example of any of the above examples, said immune cells are idecabtagene vicleucel cells. In one example, the chimeric antigen receptor comprises a murine single chain Fv antibody fragment that targets BCMA, *e.g.*, human BCMA. In one example, 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 example, 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 example, the chimeric antigen receptor is or comprises SEQ ID NO: 9. In a more specific example of any example herein, said immune cells are idecabtagene vicleucel cells. In one example, 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 example, 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 example, the immune cells comprise a chimeric antigen receptor which is or comprises SEQ ID NO: 9.

[0034] In one 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) 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 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) 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 examples, the immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA CAR T cells) are idecabtagene vicleucel cells. In particular examples, the disease is multiple myeloma, e.g., relapsed and refractory multiple myeloma.

[0036] In another example, 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 examples, the immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA CAR T cells) are idecabtagene vicleucel cells. In particular examples, the disease is multiple myeloma, e.g., relapsed and refractory multiple myeloma.

[0037] In another 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 example, the method further comprises administering the non-CAR T cell therapy to the candidate for the non-CAR T cell therapy. In specific examples, the immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA CAR T

cells) are idecabtagene vicleucel cells. In particular examples, the disease is multiple myeloma, e.g., relapsed and refractory multiple myeloma.

[0038] In another 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) 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 example, 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 example, the lenalidomide is administered at a dosage of about 25 mg daily orally on days 1-21 of a 28-day cycle. In specific examples, the immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA CAR T cells) are idecabtagene vicleucel cells. In particular examples, 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 example of the preceding examples, the disease is Multiple Myeloma (MM). In particular examples, the disease is relapsed and refractory multiple myeloma.

[0040] In another 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) 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 example, the pomalidomide is administered at a dosage of about 1 mg, 2 mg, 3 mg, or 4 mg once daily. In another specific example, 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 examples, the immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA CAR T cells) are idecabtagene vicleucel cells. In a specific

example, the disease is Multiple Myeloma (MM). In particular examples, 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 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) 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 example, 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 example, 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 examples, the immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA CAR T cells) are idecabtagene vicleucel cells. In a

specific example, the disease is Multiple Myeloma (MM). In particular examples, 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 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) 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 example, 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 example, 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 example, 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 example, 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 examples, the immune cells expressing a chimeric antigen receptor (CAR) directed to BCMA (BCMA CAR T cells) are idecabtagene vicleucel cells. In a specific example, the disease is Multiple Myeloma (MM). In particular examples, 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 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) 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 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 examples, 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 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 examples, the disease is multiple myeloma, e.g., relapsed and refractory multiple myeloma.

[0045] In a specific example of the above examples, 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 example, said second level of sBCMA is determined at 25-35 days after said administering. In another specific example, said second level of sBCMA is determined at 28-31 days after said administering. In other specific examples, 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 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 examples, the disease is multiple myeloma, e.g., relapsed and refractory multiple myeloma.

[0046] In another example, 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 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 examples, 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 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), 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 example, the method further comprises administering the second BCMA-based treatment modality to the candidate for the second BCMA-based treatment modality. In specific 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 examples, the disease is multiple myeloma, e.g., relapsed and refractory multiple myeloma.

[0048] In another 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), 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 example, the method further comprises administering the second BCMA-based treatment modality to the candidate for the second BCMA-based treatment modality. In specific 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 examples, 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 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 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 example, said level of sBCMA is determined at 50-70 days after said administering. In another specific example, said level of

sBCMA is determined at 55-65 days after said administering. In another specific example, said level of sBCMA is determined at 58-62 days after said administering. In a specific example of the preceding examples, 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 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 examples, 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 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) 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 example, 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 example, said second level is determined two days after said administering. In specific 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 examples, 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 examples of any of the above examples, 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 examples, the disease is multiple myeloma, e.g., high-risk multiple myeloma or relapsed and refractory multiple myeloma. In other specific examples, 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 examples, 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 example, 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 examples of any of the above examples, 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 example specific example, the immune cells are administered in a dosage of from 150×10^6 cells to 450×10^6 cells.

[0054] In another specific example of any of the above examples, 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 examples, 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 examples, 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 examples, 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 examples of any of the above examples, 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

$\times 10^6$ 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 examples, 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 example, the immune cells are administered at a dose of about 450×10^6 cells. In some examples, 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 examples, 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 examples of any of the examples 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 examples of any of the examples 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 examples of any of the examples 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 examples of any of the examples 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 examples of any of the examples described herein, the immune cells expressing a CAR directed to BCMA are administered in a dosage of from about 300×10^6 cells to about 500×10^6 cells. In specific examples of any of the examples 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 450×10^6 cells. In specific examples of any of the examples described herein, the immune cells expressing a CAR directed to BCMA are administered in a dosage of from about 300×10^6 cells to about 450×10^6 cells. In specific examples of any of the examples 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 450×10^6 cells. In specific examples of any of the examples described herein, the immune cells expressing a CAR directed to BCMA are administered in a dosage of from about 300×10^6 cells to about 600×10^6 cells. In specific examples of any of the examples 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 examples of any of the examples 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 examples of any of the examples 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 examples of any of the examples 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 examples of any of the examples 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 examples of any of the examples 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 examples of any of the examples 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 examples of any of the examples 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 examples of any of the examples 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 examples of any of the examples 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 examples of any of the examples described herein, the immune cells expressing a CAR directed to BCMA are administered in a dosage of about 450×10^6 cells. In specific examples of any of the examples described herein, the immune cells are T cells (e.g., autologous T cells). In specific examples of any of the examples 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 examples of any of the examples described herein, the immune cells (e.g., T cells) are administered by an intravenous infusion.

[0057] In a specific example of any of any of the above examples, said CAR comprises an antibody or antibody fragment that targets BCMA. In a more specific example, said CAR comprises a single chain Fv antibody fragment (scFv). In a more specific example, said CAR comprises a BCMA02 scFv. In a specific example of any of the above examples, said immune cells are idecabtagene vicleucel cells. In one example, the chimeric antigen receptor comprises a murine single chain Fv antibody fragment that targets BCMA, e.g., human BCMA. In one example, 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 example, 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 example, the chimeric antigen receptor is or comprises SEQ ID NO: 9. In a more specific example of any example herein, said immune cells are idecabtagene vicleucel cells. In one example, 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 example, 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 example, the immune cells comprise a chimeric antigen receptor which is or comprises SEQ ID NO: 9.

[0058] In another 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) 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 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 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 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) 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 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 examples, the disease is multiple myeloma, e.g., relapsed and refractory multiple myeloma.

[0060] In another example, 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 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 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 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 example, the method further comprises administering the second BCMA-based treatment modality to the candidate for

the second BCMA-based treatment modality. In specific 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 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 examples of any of the 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 example, the second BCMA-based treatment modality comprises a BCMA-Antibody-Drug Conjugate (ADC). In a specific example, the BCMA-Antibody-Drug Conjugate (ADC) comprises CC99712 or GSK2857916 (belantamab mafodotin). In a specific example, the second BCMA-based treatment modality comprises a bispecific T-cell engager (BiTE) that targets B-cell maturation antigen (BCMA). In a specific example, 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 example, the second BCMA-based treatment modality comprises a natural killer (NK) cell engager (NKCEs) that targets B-cell maturation antigen (BCMA). In a specific example, 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 example, 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 example, 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 examples of any of the examples 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 examples of any of the examples 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 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.

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.

3. The immune cells for use of claim 1 or the use of claim 2, wherein on the basis of the determination in step c, subsequently providing the non-CAR therapy to the subject.

4. The 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 administration.

5. 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.

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.

7. 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.

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. 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.

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 of claim 10, wherein said level of sBCMA is to be determined at 50-70 days after said administration.

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

13. 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.

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.

15. The immune cells for use of claim 13 or the use of claim 14, wherein said first level is to be determined on the day of said 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 administration.

16. 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).

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).

18. The immune cells for use of claim 16 or the use of claim 17, wherein said determination is performed within 0-4 days prior to said administration.

19. The immune cells for use of claim 16 or the use of claim 17, wherein said therapy to treat CRS is to be first provided to said subject 0-5 days after said administration.

20. 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.

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.

22. The immune cells for use of claim 20 or the use of claim 21, wherein on the basis of the determination in step c, subsequently providing the non-CAR therapy to the subject.

23. 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.

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.

25. 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.

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.

27. The immune cells for use of or use of any of claims 7-8 or claims 25-26, wherein the non-CAR therapy is to be further administered to the candidate for the non-CAR therapy.

28. 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.

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.

30. The immune cells for use of claim 28 or the use of claim 29, 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.

31. 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.

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.

33. The immune cells for use of claim 31 or the use of claim 32, wherein the pomalidomide is to be administered at a dosage of about 1 mg, 2 mg, 3 mg, or 4 mg once daily.

34. 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.

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.

36. The immune cells for use of claim 34 or the use of claim 35, 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.

37. 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.

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.

39. The immune cells for use of claim 37 or the use of claim 38, 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.

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.

42. 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.

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.

44. The immune cells for use of claim 42 or the use of claim 43, wherein on the basis of the determination in step c, subsequently providing the second BCMA-based treatment modality to the subject.

45. The immune cells for use of or use of any one of claims 42-44, wherein said second level of sBCMA is to be determined at 25-35 days after said administration.

46. 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.

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.

48. 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.

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.

50. 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.

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.

52. The immune cells for use of claim 50 or the use of claim 51, wherein said level of sBCMA is to be determined at 50-70 days after said administration.

53. The immune cells for use of or use of any of claims 42-45 or 50-52, wherein the subject is to be provided said second BCMA-based treatment modality within three months, two months, or one month after said determination of a level of sBCMA.

54. 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.

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.

56. The immune cells for use of claim 54 or the use of claim 55, wherein said first level is to be determined on the day of said 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 administration.

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.

59. The immune cells for use of or use of any of claims 1-58, wherein said disease caused by BCMA-expressing cells is multiple myeloma, chronic lymphocytic leukemia, or a non-Hodgkins lymphoma.

60. The immune cells for use of or use of claim 59, wherein the disease caused by BCMA-expressing cells is multiple myeloma.

61. The immune cells for use of or use of claim 60, wherein said multiple myeloma is high-risk multiple myeloma or relapsed and refractory multiple myeloma.

62. The immune cells for use of or use of claim 59, 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.

63. The immune cells for use of or use of any of claims 1-62, wherein the immune cells are to be administered in a dosage of from 150×10^6 cells to 450×10^6 cells.

64. The immune cells for use of or use of any of claims 1-63, wherein before said administration, said subject has received one or more lines of prior therapy or three or more lines or prior therapy.

65. The immune cells for use of or use of claim 63 or claim 64, 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.

66. The immune cells for use of or use of claim 63 or claim 64, wherein before said 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.

67. The immune cells for use of or use of any of claims 1-66, wherein said CAR comprises an antibody or antibody fragment that targets BCMA.

68. The immune cells for use of or use of any of claims 1-67, wherein said CAR comprises a single chain Fv antibody fragment (scFv).

69. The immune cells for use of or use of any of claims 1-67, wherein said immune cells are idecabtagene vicleucel cells.

70. 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.

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.

72. The immune cells for use of claim 70 or the use of claim 71, wherein on the basis of the determination in step c, subsequently providing the second BCMA-based treatment modality to the subject.

73. 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.

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.

75. 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.

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

77. The immune cells for use of or use of any one of claims 20-76, 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).