Claims

1. A cytokine inhibitor for use in a method of treating or preventing a cytokine-related adverse event or disease in a subject, wherein the cytokine inhibitor is pomalidomide, iberdomide, lenalidomide, avadomide or Compound 1, and wherein Compound 1 is 4-(4-(4-(((2-(2,6-dioxopiperidin-3-yl)-1-oxoisoindolin-4-yl)oxy)methyl)benzyl)piperazin-1-yl)-3-fluorobenzonitrile, or an enantiomer, a mixture of enantiomers, a tautomer, an isotopolog, or a pharmaceutically acceptable salt thereof.

2. The cytokine inhibitor for use according to claim 1, wherein the cytokine-related adverse event or disease is cytokine release syndrome (CRS).

3. The cytokine inhibitor for use according to claim 1 or 2, wherein the subject has received or will receive a therapeutic agent that has caused or is likely to cause CRS.

4. The cytokine inhibitor for use according to claim 3, wherein the therapeutic agent is directed to BCMA ("BCMA therapeutic agent").

5. The cytokine inhibitor for use according to claim 1, wherein the cytokine-related adverse event or disease is Coronavirus disease 2019 (COVID-19) or cytokine-mediated neurotoxicity.

6. A BCMA therapeutic agent for use in a method of treating a disorder associated with BCMA expression in a subject, wherein the method comprises:

a) administering to the subject the BCMA therapeutic agent, wherein the administering is likely to cause or has caused CRS in the subject; and

b) administering to the subject a cytokine inhibitor at a dose to prevent or reduce the development of CRS in the subject, wherein the cytokine inhibitor is pomalidomide, iberdomide, lenalidomide, avadomide or Compound 1, and wherein Compound 1 is 4-(4-(4-(((2-(2,6-dioxopiperidin-3-yl)-1-oxoisoindolin-4-yl)oxy)methyl)benzyl)piperazin-1-yl)-3-fluorobenzonitrile, or an enantiomer, a mixture of enantiomers, a tautomer, an isotopolog or a pharmaceutically acceptable salt thereof.

7. A BCMA therapeutic agent for use in a method of treating a disorder associated with BCMA expression in a subject, wherein the method comprises:

a) administering to the subject a cytokine inhibitor (e.g. IL-6 inhibitor), wherein the cytokine inhibitor (e.g. IL-6 inhibitor) is pomalidomide, iberdomide, lenalidomide, avadomide or Compound 1, and wherein Compound 1 is 4-(4-(4-(((2-(2,6-dioxopiperidin-3-yl)-1-oxoisoindolin-4-yl)oxy)methyl)benzyl)piperazin-1-yl)-3-fluorobenzonitrile, or an enantiomer, a mixture of enantiomers, a tautomer, an isotopolog or a pharmaceutically acceptable salt thereof; and

b) following administration of the cytokine inhibitor, administering to the subject the BCMA therapeutic agent, wherein the administering is likely to cause CRS in the subject.

8. The BCMA therapeutic agent for use according to claim 7, wherein the cytokine inhibitor (e.g. IL-6 inhibitor) is administered as a first dose about 7 days before the BCMA therapeutic agent.

9. A BCMA therapeutic agent for use in a method of treating a disorder associated with BCMA expression in a subject, wherein the method comprises:

a) administering to the subject the BCMA therapeutic agent, wherein the administering is likely to cause or has caused CRS in the subject; and

b) following administration of the BCMA therapeutic agent, administering to the subject a cytokine inhibitor (e.g. IL-6 inhibitor), wherein the cytokine inhibitor (e.g. IL-6 inhibitor) is pomalidomide, iberdomide, lenalidomide, avadomide or Compound 1, and wherein Compound 1 is 4-(4-(4-(((2-(2,6-dioxopiperidin-3-yl)-1-oxoisoindolin-4-yl)oxy)methyl)benzyl)piperazin-1-yl)-3-fluorobenzonitrile, or an enantiomer, a mixture of enantiomers, a tautomer, an isotopolog or a pharmaceutically acceptable salt thereof.

10. The BCMA therapeutic agent for use according to claim 9, wherein the BCMA therapeutic agent is administered as a first dose about 7 days before the cytokine inhibitor.

11. The BCMA therapeutic agent for use according to any one of claims 6 to 10, wherein the disorder associated with BCMA expression in a subject is: multiple myeloma, optionally wherein the multiple myeloma is high-risk multiple myeloma or relapsed and refractory multiple myeloma; chronic lymphocytic leukemia; or a non-Hodgkins lymphoma, optionally wherein the non-Hodgkin's lymphoma is 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, or mantle cell lymphoma.

12. The cytokine inhibitor for use according to claim 3 or 4, or the BCMA therapeutic agent for use according to any one of claims 6 to 11, wherein the therapeutic agent that has caused or is likely to cause CRS or the BCMA therapeutic agent is a T cell engager.

13. The cytokine inhibitor for use according to claim 12, or the BCMA therapeutic agent for use according to claim 12, wherein the T cell engager is a multispecific antibody which specifically binds to a cancer antigen (e.g. BCMA) and to an antigen that promotes activation of one or more T cells, optionally wherein the antigen that promotes activation of one or more T cells is selected from the group consisting of CD3, TCRα, TCRβ, TCRγ, TCRζ, ICOS, CD28, CD27, HVEM, LIGHT, CD40, 4-1BB, OX40, DR3, GITR, CD30, TIM1, SLAM, CD2, or CD226, preferably wherein the antigen that promotes activation of one or more T cells is CD3.

14. The cytokine inhibitor for use according to claim 13, or the BCMA therapeutic agent for use according to claim 13, wherein the multispecific antibody is a bispecific antibody, optionally wherein the bispecific antibody comprises two Fab fragments of an anti-BCMA antibody, one Fab fragment of an anti-CD3 antibody, and one Fc portion and the bispecific antibody is in the format BCMA Fab - Fc - CD3 Fab - BCMA Fab.

15. The cytokine inhibitor for use according to claim 12, or the BCMA therapeutic agent for use according to claim 12, wherein the T cell engager is a chimeric antigen receptor (CAR) directed to a cancer antigen (e.g. BCMA), or a T cell expressing at least one CAR directed to a cancer antigen (e.g. BCMA).

16. The cytokine inhibitor for use according to claim 4 or any one of claims 12 to 14 when dependent on claim 4, or the BCMA therapeutic agent for use according to any one of claims 6 to 15, wherein the BCMA therapeutic agent comprises a CDR1H, CDR2H, CDR3H, CDR1L, CDR2L, and CDR3L region combination selected from:

a) CDR1H region of SEQ ID NO:21, CDR2H region of SEQ ID NO:22, CDR3H region of SEQ ID NO:17, CDR1L region of SEQ ID NO:27, CDR2L region of SEQ ID NO:28,

and CDR3L region of SEQ ID NO:20, optionally wherein the BCMA therapeutic agent comprises a VH of SEQ ID NO: 10 and a VL of SEQ ID NO: 14;

b) CDR1H region of SEQ ID NO:21, CDR2H region of SEQ ID NO:22, CDR3H region of SEQ ID NO:17, CDR1L region of SEQ ID NO:25, CDR2L region of SEQ ID NO:26, and CDR3L region of SEQ ID NO:20, optionally wherein the BCMA therapeutic agent comprises a VH of SEQ ID NO: 10 and a VL of SEQ ID NO: 13; and

c) CDR1H region of SEQ ID NO:15, CDR2H region of SEQ ID NO:16, CDR3H region of SEQ ID NO:17, CDR1L region of SEQ ID NO:18, CDR2L region of SEQ ID NO:19, and CDR3L region of SEQ ID NO:20, optionally wherein the BCMA therapeutic agent comprises a VH of SEQ ID NO: 9 and a VL of SEQ ID NO: 11.

17. The cytokine inhibitor for use according to claim 13 or 14, or the BCMA therapeutic agent for use according to claim 13 or 14, wherein the multispecific antibody comprises a heavy and light chain set of the polypeptides set forth in SEQ ID NO:48, SEQ ID NO:55, SEQ ID NO:56, and two copies of SEQ ID NO:57.

18. The cytokine inhibitor for use according to claim 4 or any one of claims 12 to 15 when dependent on claim 4, or the BCMA therapeutic agent for use according to any one of claims 6 to 15, wherein the BCMA therapeutic agent comprises a VH comprising a CDR1H of SEQ ID NO:64, a CDR2H of SEQ ID NO:65 a CDR3H of SEQ ID NO:66, and a VL comprising a CDR1L, a CDR2L and a CDR3L set of sequences selected from:

a) CDR1L of SEQ ID NO:67, CDR2L of SEQ ID NO:68, and CDR3L of SEQ ID NO:69, optionally wherein the BCMA therapeutic agent comprises a VH of SEQ ID NO:76 and a VL of SEQ ID NO:77;

b) CDR1L of SEQ ID NO:70, CDR2L of SEQ ID NO:71, and CDR3L of SEQ ID NO:72, optionally wherein the BCMA therapeutic agent comprises a VH of SEQ ID NO:76 and a VL of SEQ ID NO:78; or

c) CDR1L of SEQ ID NO:73, CDR2L of SEQ ID NO:74, and CDR3L of SEQ ID NO:75 optionally wherein the BCMA therapeutic agent comprises a VH of SEQ ID NO:76 and a VL of SEQ ID NO:79.

19. The cytokine inhibitor for use according to any one of claims 3, 4, or 12 to 18, or the BCMA therapeutic agent for use according to any one of claims 6 to 18, wherein:

(a) the cytokine inhibitor is administered before (e.g. within 12 or 24 hours before) administration of the therapeutic agent (e.g. BCMA therapeutic agent);
(b) the cytokine inhibitor is administered on the same day as administration of the therapeutic agent (e.g. BCMA therapeutic agent);
(c) the cytokine inhibitor is administered after (e.g. within 12 or 24 hours after) administration of the therapeutic agent (e.g. BCMA therapeutic agent); or
(d) the cytokine inhibitor is administered within 12 hours after diagnosis of CRS.

20. The cytokine inhibitor or the BCMA therapeutic agent for use according to any one of the preceding claims, wherein the cytokine inhibitor is a proinflammatory cytokine inhibitor.

21. The cytokine inhibitor or the BCMA therapeutic agent for use according to any one of the preceding claims, wherein the cytokine-related adverse event or disease is not breast cancer.