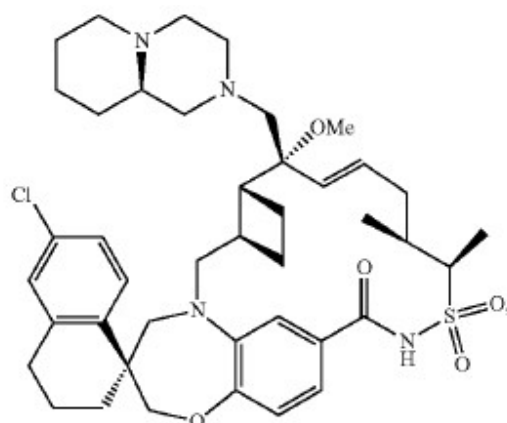


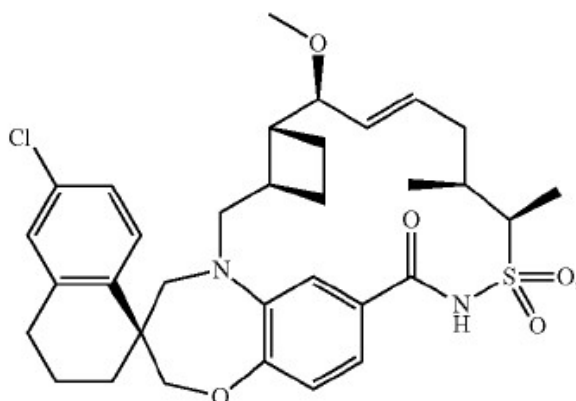


(II)

[0013] In one aspect, the disclosure provides an anti-Mcl-1 antibody or antigen-binding fragment thereof comprising the light chain complementarity determining region 1 (LCDR1) of SEQ ID NO:4, the light chain complementarity determining region 2 (LCDR2) of SEQ ID NO:5, the light chain complementarity determining region 3 of (LCDR3) SEQ ID NO:6, the heavy chain complementarity determining region 1 of SEQ ID NO:16 (HCDR1), the heavy chain complementarity determining region 2 of SEQ ID NO:17 (HCDR2), and the heavy chain complementarity determining region 3 of SEQ ID NO:18 (HCDR3), or comprising LCDR1 of SEQ ID NO:10, LCDR2 of SEQ ID NO:11, LCDR3 of SEQ ID NO:12, HCDR1 of SEQ ID NO:22, HCDR2 of SEQ ID NO:23, and HCDR3 of SEQ ID NO:24. In some examples, the antibody comprises the light chain variable region sequence of SEQ ID NO:27 or SEQ ID NO:31. In some examples, the antibody comprises the heavy chain variable region sequence of SEQ ID NO:28 or SEQ ID NO:32, including some examples in which the antibody further comprises the light chain variable region sequence of SEQ ID NO:27 if the heavy chain variable region sequence is set forth in SEQ ID NO:28, or SEQ ID NO:31 if the heavy chain variable region sequence is set forth in SEQ ID NO:32. In some examples, the antibody or fragment is a single-chain antibody or fragment, including examples in which the antibody fragment is contained in a single-chain variable fragment (scFv). In some examples, the antibody fragment is (a) a scFv; (b) a Fab; or (c) a (Fab')₂. In some examples, the antibody or fragment thereof is fully human. In some examples, the antibody or fragment thereof is an immunoglobulin G (IgG) isotype antibody or fragment. In some examples, the antibody or fragment thereof is in the form of a monoclonal antibody. In some examples, the antibody or fragment thereof is in the form of a bispecific antibody, a trispecific antibody, a single chain variable fragment (scFv), a disulfide-bond-stabilized single chain variable fragment (ds-scFv), a single domain antibody (sdAb), a single chain Fab fragment (scFab), a diabody, a triabody, a tetrabody, a minibody, a Fab, a F(ab')₂, a VHH/VH fragment, a peptibody, a chimeric antigen receptor (CAR), or a bispecific T-cell engager (BiTE).

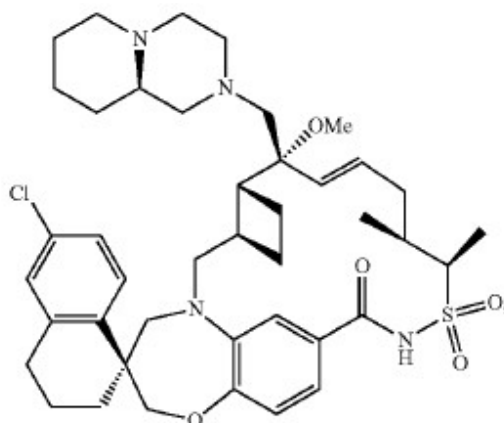
[0014] Another aspect of the disclosure is a pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of the antibody or an antigen-binding or an immunologically functional immunoglobulin fragment thereof that is disclosed herein. Thus, in one aspect, there is provided a pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of the antibody or an antigen-binding fragment thereof or an immunologically functional immunoglobulin fragment thereof that is disclosed herein.

[0015] Yet another example of the disclosure is a method of monitoring treatment of a cancer cell in a subject comprising: (a) contacting the cell of the subject with the antibody or fragment thereof of claim 1; (b) detecting binding of the antibody or fragment thereof to the cell or its contents; (c) determining the level of Mcl-1 in the cell; and (d) comparing the level of Mcl-1 in the cell to a control, wherein the control is a known level of Mcl-1 characteristic of a non-cancer cell, a level of Mcl-1 in a non-cancerous cell of the subject, or a level of Mcl-1 in a cancer cell of the subject at a different point in time. Hence, in one aspect, there is provided a method of monitoring treatment of a cancer cell in a subject comprising: (a) *in vitro* contacting the cell of the subject with the antibody or antigen-binding fragment thereof as disclosed herein; (b) detecting binding of the antibody or antigen-binding fragment thereof to the cell or its contents; (c) determining the level of Mcl-1 in the cell; and (d) comparing the level of Mcl-1 in the cell to a control, wherein the control is a known level of Mcl-1 characteristic of a non-cancer cell, a level of Mcl-1 in a non-cancerous cell of the subject, or a level of Mcl-1 in a cancer cell of the subject at a different point in time. In some examples, the monitoring comprises an assay that is an ELISA, a competitive ELISA, surface plasmon resonance analysis, *in vitro* neutralization assay, *in vivo* neutralization assay, an immunohistochemical assay with FACS sorting, or an immunohistochemical assay without FACS sorting. In some examples, the cancer cell is a leukemia cell, a lymphoma cell, or a myeloma cell. In some examples, the cancer treatment comprises administration of AMG 176 of formula I:



I.

[0016] In some examples, the cancer treatment comprises administration of AMG 397 of formula II:



II.

[0017] In some examples, the cancer cell is a myeloid leukemia cell. In some examples, the cancer cell is an organ cancer cell. In some examples, the antibody or fragment thereof is a monoclonal antibody or fragment thereof comprising the light chain complementarity determining region 1 (LCDR1) of SEQ ID NO:4, the light chain complementarity determining region 2 (LCDR2) of SEQ ID NO:5, the light chain complementarity determining region 3 (LCDR3) of SEQ ID NO:6, the heavy chain complementarity determining region 1 (HCDR1) of SEQ ID NO:16, the heavy chain complementarity determining region 2 (HCDR2) of SEQ ID NO:17, and the heavy chain complementarity determining region 3 (HCDR3) of SEQ ID NO:18, or the antibody or fragment thereof is a monoclonal antibody or fragment thereof comprising the LCDR1 of SEQ ID NO:10, the LCDR2 of SEQ ID NO:11, the LCDR3 of SEQ ID NO:12, the HCDR1 of SEQ ID NO:22, the HCDR2 of SEQ ID NO:23, and the HCDR3 of SEQ ID NO:24. In some examples, the antibody or fragment thereof comprises the light chain variable region sequence of SEQ ID NO:27, the heavy chain variable region sequence of SEQ ID NO:28, or the light chain variable region of SEQ ID NO:31 and the heavy chain variable region of SEQ ID NO:32. In some examples, the antibody or fragment thereof is in the form of a single-chain antibody, a single-chain variable fragment (scFv), a scFv, a Fab, a F(ab')₂, a bispecific antibody, a trispecific antibody, a single chain variable fragment (scFv), a disulfide-bond-

stabilized single chain variable fragment (ds-scFv), a single domain antibody (sdAb), a single chain Fab fragment (scFab), a diabody, a triabody, a tetrabody, a minibody, a Fab, a F(ab')₂, a VHH/VH fragment, a peptibody, a chimeric antigen receptor (CAR), or a bispecific T-cell engager (BiTE).

[0018] Still another example of the disclosure is a method of treating cancer in a subject comprising administering a therapeutically effective amount of the anti-Mcl-1 antibody or fragment thereof disclosed herein to the subject. In another aspect of the disclosure is a use of the anti-Mcl-1 antibody or antigen-binding fragment thereof of the disclosure in the manufacture of a medicament for treating cancer. In some examples, the cancer cell is a leukemia cell, a lymphoma cell, or a myeloma cell. In some examples, the cancer cell is a myeloid leukemia cell. In some examples, the cancer cell is an organ cancer cell. In some examples, the antibody or fragment thereof is a monoclonal antibody or fragment thereof comprising the light chain complementarity determining region 1 (LCDR1) of SEQ ID NO:4, the light chain complementarity determining region 2 (LCDR2) of SEQ ID NO:5, the light chain complementarity determining region 3 (LCDR3) of SEQ ID NO:6, the heavy chain complementarity determining region 1 (HCDR1) of SEQ ID NO:16, the heavy chain complementarity determining region 2 (HCDR2) of SEQ ID NO:17, and the heavy chain complementarity determining region 3 (HCDR3) of SEQ ID NO:18, or the antibody or fragment thereof is a monoclonal antibody or fragment thereof comprising the LCDR1 of SEQ ID NO:10, the LCDR2 of SEQ ID NO:11, the LCDR3 of SEQ ID NO:12, the HCDR1 of SEQ ID NO:22, the HCDR2 of SEQ ID NO:23, and the HCDR3 of SEQ ID NO:24. In some examples, the antibody or fragment thereof comprises the light chain variable region sequence of SEQ ID NO:27, the heavy chain variable region sequence of SEQ ID NO:28, or the light chain variable region of SEQ ID NO:31 and the heavy chain variable region of SEQ ID NO:32. In some examples, the antibody or fragment thereof is in the form of a single-chain antibody, a single-chain variable fragment (scFv), a scFv, a Fab, a F(ab')₂, a bispecific antibody, a trispecific antibody, a single chain variable fragment (scFv), a disulfide-bond-stabilized single chain variable fragment (ds-scFv), a single domain antibody (sdAb), a single chain Fab fragment (scFab), a diabody, a triabody, a tetrabody, a minibody, a Fab, a F(ab')₂, a VHH/VH fragment, a peptibody, a chimeric antigen receptor (CAR), or a bispecific T-cell engager (BiTE).

[0019] Other features and advantages of the disclosure will become apparent from the following detailed description, including the drawing. It should be understood, however, that the detailed description and the specific examples, while indicating preferred examples, are provided for illustration only, because various changes and modifications within the spirit and scope of the disclosure will become apparent to those skilled in the art from the detailed description.

Brief Description of the Drawing

[0020] Figure 1. Rabbit antibody immune response to Mcl-1 immunogen. ELISA assays were run by serially diluting rabbit sera on 384-well plates coated with biotin-labeled Mcl-1 protein. Sample absorbance values yielded the curves shown. A) Mcl-1 immune response

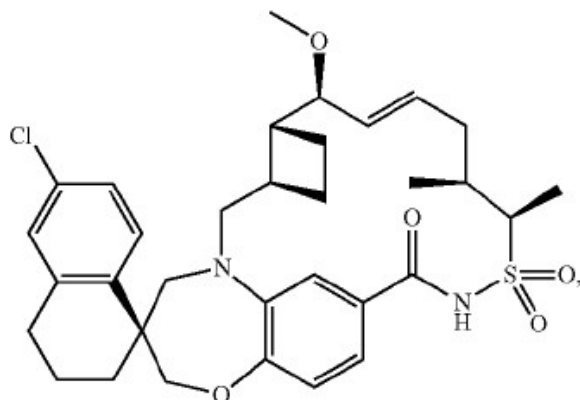
CLAIMS

WHAT IS CLAIMED IS:

1. An anti-Mcl-1 antibody or antigen-binding fragment thereof comprising the light chain complementarity determining region 1 (LCDR1) of SEQ ID NO:4, the light chain complementarity determining region 2 (LCDR2) of SEQ ID NO:5, the light chain complementarity determining region 3 of (LCDR3) SEQ ID NO:6, the heavy chain complementarity determining region 1 of SEQ ID NO:16 (HCDR1), the heavy chain complementarity determining region 2 of SEQ ID NO:17 (HCDR2), and the heavy chain complementarity determining region 3 of SEQ ID NO:18 (HCDR3), or comprising LCDR1 of SEQ ID NO:10, LCDR2 of SEQ ID NO:11, LCDR3 of SEQ ID NO:12, HCDR1 of SEQ ID NO:22, HCDR2 of SEQ ID NO:23, and HCDR3 of SEQ ID NO:24.
2. The antibody or antigen-binding fragment thereof of claim 1 comprising the light chain variable region sequence of SEQ ID NO:27 and the heavy chain variable region sequence of SEQ ID NO:28.
3. The antibody or antigen-binding fragment thereof of claim 1 comprising the light chain variable region sequence of SEQ ID NO:31 and the heavy chain variable region sequence of SEQ ID NO:32.
4. The antibody or antigen-binding fragment thereof of claim 1 wherein the antibody or antigen-binding fragment thereof is a single-chain antibody or antigen-binding fragment thereof.
5. The antibody or antigen-binding fragment thereof of claim 4 contained in a single-chain variable fragment (scFv).
6. The antibody or antigen-binding fragment thereof of claim 5, wherein the antibody or antigen-binding fragment thereof is
 - (a) a scFv;
 - (b) a Fab; or
 - (c) a (Fab')₂.
7. The antibody or antigen-binding fragment thereof of claim 1, which is fully humanized.

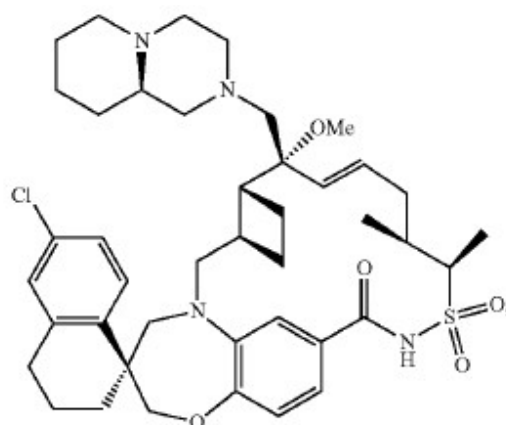
8. The antibody or antigen-binding fragment thereof of claim 1 that is an immunoglobulin G (IgG) isotype antibody or antigen-binding fragment thereof.
9. The antibody or antigen-binding fragment thereof of claim 1 in the form of a monoclonal antibody.
10. The antibody or antigen-binding fragment thereof of claim 1 in the form of a bispecific antibody, a trispecific antibody, a single chain variable fragment (scFv), a disulfide-bond-stabilized single chain variable fragment (ds-scFv), a single domain antibody (sdAb), a single chain Fab fragment (scFab), a diabody, a triabody, a tetrabody, a minibody, a Fab, a F(ab')₂, a VHH/VH fragment, a peptibody, a chimeric antigen receptor (CAR), or a bispecific T-cell engager (BiTE).
11. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of the antibody or an antigen-binding fragment thereof or an immunologically functional immunoglobulin fragment thereof of claim 1.
12. A method of monitoring treatment of a cancer cell in a subject comprising:
 - (a) *in vitro* contacting the cell of the subject with the antibody or antigen-binding fragment thereof of claim 1;
 - (b) detecting binding of the antibody or antigen-binding fragment thereof to the cell or its contents;
 - (c) determining the level of Mcl-1 in the cell; and
 - (d) comparing the level of Mcl-1 in the cell to a control, wherein the control is a known level of Mcl-1 characteristic of a non-cancer cell, a level of Mcl-1 in a non-cancerous cell of the subject, or a level of Mcl-1 in a cancer cell of the subject at a different point in time.
13. The method of claim 12 wherein the monitoring comprises an assay that is an ELISA, a competitive ELISA, surface plasmon resonance analysis, *in vitro* neutralization assay, *in vivo* neutralization assay, an immunohistochemical assay with FACS sorting, or an immunohistochemical assay without FACS sorting.
14. The method of claim 12 wherein the cancer cell is a leukemia cell, a lymphoma cell, or a myeloma cell.

15. The method of claim 12 wherein the cancer treatment comprises administration of AMG 176 of formula I:



I.

16. The method of claim 12 wherein the cancer treatment comprises administration of AMG 397 of formula II:



II.

17. The method of claim 12 wherein the cancer cell is a myeloid leukemia cell.
18. The method of claim 12 wherein the cancer cell is an organ cancer cell.
19. The method of claim 12 wherein the antibody or fragment thereof is a monoclonal antibody or antigen-binding fragment thereof comprising the light chain complementarity determining region 1 (LCDR1) of SEQ ID NO:4, the light chain complementarity determining region 2 (LCDR2) of SEQ ID NO:5, the light chain complementarity determining region 3 (LCDR3) of SEQ ID NO:6, the heavy chain complementarity determining region 1 (HCDR1) of SEQ ID NO:16, the heavy chain complementarity determining region 2 (HCDR2) of SEQ ID NO:17, and the heavy chain complementarity determining region 3 (HCDR3) of SEQ ID NO:18,

- or the antibody or antigen-binding fragment thereof is a monoclonal antibody or antigen-binding fragment thereof comprising the LCDR1 of SEQ ID NO:10, the LCDR2 of SEQ ID NO:11, the LCDR3 of SEQ ID NO:12, the HCDR1 of SEQ ID NO:22, the HCDR2 of SEQ ID NO:23, and the HCDR3 of SEQ ID NO:24.
20. The method of claim 12 wherein the antibody or antigen-binding fragment thereof comprises the light chain variable region sequence of SEQ ID NO:27, the heavy chain variable region sequence of SEQ ID NO:28, or the light chain variable region of SEQ ID NO:31 and the heavy chain variable region of SEQ ID NO:32.
 21. The method of claim 12 wherein the antibody or antigen-binding fragment thereof is in the form of a single-chain antibody, a single-chain variable fragment (scFv), a scFv, a Fab, a F(ab')₂, a bispecific antibody, a trispecific antibody, a single chain variable fragment (scFv), a disulfide-bond-stabilized single chain variable fragment (ds-scFv), a single domain antibody (sdAb), a single chain Fab fragment (scFab), a diabody, a triabody, a tetrabody, a minibody, a Fab, a F(ab')₂, a VHH/VH fragment, a peptibody, a chimeric antigen receptor (CAR), or a bispecific T-cell engager (BiTE).
 22. Use of the anti-Mcl-1 antibody or antigen-binding fragment thereof of claim 1 in the manufacture of a medicament for treating cancer.
 23. The use of claim 22 wherein the cancer cell is a leukemia cell, a lymphoma cell, or a myeloma cell.
 24. The use of claim 22 wherein the cancer cell is a myeloid leukemia cell.
 25. The use of claim 22 wherein the cancer cell is an organ cancer cell.
 26. The use of claim 22 wherein the antibody or antigen-binding fragment thereof is a monoclonal antibody or antigen-binding fragment thereof comprising the light chain complementarity determining region 1 (LCDR1) of SEQ ID NO:4, the light chain complementarity determining region 2 (LCDR2) of SEQ ID NO:5, the light chain complementarity determining region 3 (LCDR3) of SEQ ID NO:6, the heavy chain complementarity determining region 1 (HCDR1) of SEQ ID NO:16, the heavy chain complementarity determining region 2 (HCDR2) of SEQ ID NO:17, and the heavy chain complementarity determining region 3 (HCDR3) of SEQ ID NO:18, or the antibody or antigen-binding fragment thereof is a monoclonal antibody or antigen-binding fragment thereof comprising the LCDR1 of SEQ ID NO:10, the LCDR2 of SEQ ID NO:11, the LCDR3 of SEQ ID NO:12, the HCDR1

of SEQ ID NO:22, the HCDR2 of SEQ ID NO:23, and the HCDR3 of SEQ ID NO:24.

27. The use of claim 22 wherein the antibody or antigen-binding fragment thereof comprises the light chain variable region sequence of SEQ ID NO:27, the heavy chain variable region sequence of SEQ ID NO:28, or the light chain variable region of SEQ ID NO:31 and the heavy chain variable region of SEQ ID NO:32.
28. The use of claim 22 wherein the antibody or antigen-binding fragment thereof is in the form of a single-chain antibody, a single-chain variable fragment (scFv), a scFv, a Fab, a F(ab')₂, a bispecific antibody, a trispecific antibody, a single chain variable fragment (scFv), a disulfide-bond-stabilized single chain variable fragment (ds-scFv), a single domain antibody (sdAb), a single chain Fab fragment (scFab), a diabody, a triabody, a tetrabody, a minibody, a Fab, a F(ab')₂, a VHH/VH fragment, a peptibody, a chimeric antigen receptor (CAR), or a bispecific T-cell engager (BiTE).