E59. Use of a BTN3A activating antibody, in the manufacture of a medicament for treating cancer in a subject in need thereof, wherein a therapeutically efficient amount of said medicament is to be administered to said subject, in combination simultaneously, sequentially or separately, with a therapeutically efficient amount of a Bcl2 inhibitor compound, optionally further in combination with a hypomethylating agent.

FIGURES

Figure 1: Activation of Vγ9Vδ2 T Cells with ICT01 Protects Them from Venetoclax Induced Cell Death. A) Mean±SEM frequencies of Live (black), Apoptotic (light grey) or Dead (dark grey) Vγ9Vδ2 T cells in HD-PBMC 48h after treatment with Venetoclax (left) or 5-Azacytidine (right). N=4 HD. B) Mean frequency of Live Vγ9Vδ2 T cells in HD-PBMC after treatment with Venetoclax, 5-Azacytidine or the combination for 48h. N=4 HD. C) Mean±SEM frequencies of Live (black), Apoptotic (light grey) or Dead (dark grey) Vγ9Vδ2 T cells in HD-PBMC 48h after treatment with Venetoclax in the presence of ICT01 (right) or its isotype control (hIgG1S, left). N=4 HD. D) Mean±SEM frequency of Live Vγ9Vδ2 T cells in HD-PBMC 48h after treatment with Venetoclax in the presence of ICT01 (black) or its isotype control (hIgG1S, light grey), normalized to no Venetoclax conditions. N=4 HD, each dot represents one healthy donor. *** p<0,005, 2-way ANOVA. E) Mean±SEM CD69 median mean fluorescence intensity (MFI) of Vγ9Vδ2 T cells in HD-PBMC treated for 48h with ICT01 (black) or its isotype control (hIgG1S, light grey). N=5 HD, each dot represents one healthy donor.

Figure 2: Activation of Vγ9Vδ2 T Cells with ICT01 Protects Them from Bcl-2 Family Member Inhibitors (Navitoclax, ABT-737 and MIK665) Induced Cell Death. A) Heatmap showing the mean frequency of live Vγ9Vδ2 T cells in HD-PBMC assessed by flow cytometry after treatment with increasing concentration of the indicated Bcl-2 family member inhibitor for 48h. N=3 HD for ABT-737 and N=5 for Navitoclax and MIK665. B-D) Frequency of live Vγ9Vδ2 T cells (Mean±SEM) in HD-PBMC assessed by flow cytometry after 48h of treatment with indicated concentration of ABT-737 (N=3 HD) (B), Navitoclax (N=5 HD) (C), or MIK665 (N=5 HD) (D), in the presence of 1 µg/mL of ICT01 (black) or its isotype control hIgG1S (light grey). Data were normalized to no ABT-737, Navitoclax or MIK665 treatment and each dot represents one healthy donor. * p<0.05, ** p<0.01, *** p<0.001, **** p<0.0001, 2way ANOVA.

Figure 3: ICT01-Mediated Activation Prior to Treatment Decreases Venetoclax Sensitivity of Vγ9Vδ2 T Cells. A) Schematic representation of the treatment sequence. B) Mean±SEM frequency of CD25+ Vγ9Vδ2 T cells in HD-PBMC on day 3 of treatment with ICT01 (black) or its isotype control (hIgG1S, light grey) and Venetoclax. N=6 HD. C) Mean±SEM relative number of Live Vγ9Vδ2 T cells and D) Mean±SEM % of Live Vγ9Vδ2 T cells relative

to no Venetoclax condition on day 3 of treatment with ICT01 (black) or its isotype control (hIgG1S, light grey) and Venetoclax. N=5 HD. Each dot represents one healthy donor. *p<0,05, 2-way ANOVA.

Figure 4: Vγ9Vδ2 T Cell Phenotypic Activation and Proliferation in HD-PBMC Stimulated with ICT01 is Mainly Unaffected by Treatment with Venetoclax and 5-Azacytidine: A) Schematic representation of the treatment sequence (left) and Mean±SEM frequency of CD25

CLAIMS

1. Use of a BTN3A activating antibody, in the manufacture of a medicament for treating cancer in a subject in need thereof, wherein a therapeutically efficient amount of said medicament is to be administered to said subject, in combination simultaneously, sequentially or separately, with a therapeutically efficient amount of a Bcl2 inhibitor compound, optionally further in combination with a hypomethylating agent.

2. The use according to Claim 1, wherein said Bcl2 inhibitor is Venetoclax.

3. The use according to any one of Claims 1-2, wherein said BTN3A activating antibody comprises (a) a variable heavy chain (VH) polypeptide comprising an amino acid sequence that is at least about 95%, 96%, 97%, 98%, 99% or 100% identical to the amino acid sequence of SEQ ID NO: 1, and (b) a variable light chain (VL) polypeptide comprising an amino acid sequence that is at least about 95%, 96%, 97%, 98%, 99% or 100% identical to of SEQ ID NO: 2;

4. The use according to any one of Claims 1-3, wherein the anti-BTN3A antibody is an antibody comprising a heavy chain of SEQ ID NO: 4 and a light chain of SEQ ID NO: 6.

5. The use according to any one of Claims 1-4, wherein said medicament is to be administered in combination simultaneously, sequentially or separately with Venetoclax, further in combination with Azacytidine or Decitabine.

6. The use according to any one of Claims 1-5, wherein said cancer is a hematological malignancy, for example acute myeloid leukemia.

7. The use according to any one of Claims 1-6, wherein said cancer is acute myeloid leukemia, and wherein said BTN3A activating antibody is an antibody comprising a heavy chain of SEQ ID NO: 4 and a light chain of SEQ ID NO: 6, and said medicament is to be administered in combination simultaneously, sequentially or separately with Venetoclax, further in combination with Azacytidine or Decitabine.

8. The use according to any one of Claims 1-7, wherein said subject is not eligible for intensive chemotherapy.

9. The use according to any one of Claims 1-8, wherein said medicament is to be administered once every three weeks, or once every four weeks.

10. The use according to any one of Claims 1-9, wherein the medicament is to be administered intravenously.

11. The use according to any one of Claims 1-10, wherein the medicament is to be administered at a unit dose of 7 to 200 mg of the BTN3A activating antibody.

12. The use according to any one of Claims 1-11, wherein Venetoclax is to be administered orally, once a day.

13. The use according to any one of Claims 1-12, wherein Venetoclax is to be administered orally at a unit dose of 50 mg to 500 mg.

14. The use according to any one of Claims 1-13, wherein the hypomethylating agent comprises Azacitidine.

15. The use according to any one of Claims 1-14, wherein the hypomethylating agent is to be administered at a dose of 50 mg/m^2 to 100 mg/m^2.