

CLAIMS

1. Use of an engineered NK cell in combination with an anti-CD38 antibody in the manufacture of a medicament for treating multiple myeloma or leukemia, wherein the engineered NK cell has been modified to comprise a knockout of the CD38 gene.
2. The use of claim 1, wherein the cancer comprises multiple myeloma, acute myeloid leukemia (AML), T-cell acute lymphoblastic leukemia (T-ALL), or Blastic plasmacytoid dendritic cell neoplasm (BPDCN).
3. The use of claim 1, wherein the anti-CD38 antibody comprises Daratumumab, isatuximab, TAK-079, or MOR202.
4. The use of claim 1, wherein the medicament further comprises an angiogenesis inhibitor and a steroid.
5. The use of claim 4, wherein the angiogenesis inhibitor comprises Pomalidomide, Lenalidomide, or Apremilast.
6. The use of claim 4, wherein the steroid comprises a glucocorticoid.
7. The use of claim 6, wherein the glucocorticoid comprises dexamethasone, betamethasone, prednisolone, methylprednisolone, triamcinolone, or fludrocortisone acetate.
8. Use of an engineered NK cell in the manufacture of a medicament for treating multiple myeloma or leukemia, in combination with an anti-CD38 antibody, wherein the engineered NK cell is obtained by a method comprising
 - a) obtaining a target NK cell to be modified;
 - b) obtaining gRNA specific for the target DNA sequence; and
 - c) introducing via electroporation into the target NK cell, a RNP complex comprising a class 2 CRISPR/Cas endonuclease (Cas9) complexed with a corresponding CRISPR/Cas guide RNA that hybridizes to a target sequence within the genomic DNA of the target NK cell creating an engineered NK cell.
9. The use of claim 8, wherein the NK cell is a primary NK cell that has been modified ex vivo and after modification transferred to the subject.
10. The use of claim 8, wherein the NK cell is an autologous NK cell.
11. The use of claim 8, wherein the NK cell is from an allogeneic donor source.

12. The use of claim 8, wherein the NK cell is expanded *ex vivo* with irradiated mbIL-21 expressing feeder cells.

13. The use of claim 8, wherein the medicament comprising the engineered NK cell is prepared to be administered separately from administration of IL-21 or irradiated mbIL-21

5 expressing feeder cells.

14. The use of claim 8, wherein the RNP complex targets the CD38 gene.

15. The use of claim 8, wherein the anti-CD38 antibody comprises Daratumumab, isatuximab, TAK-079, or MOR202.

16. A NK cell that has been modified to comprises a knockout of the CD38 gene in

10 combination with an anti-CD38 antibody for use in reducing NK cell fratricide in a subject receiving anti-CD38 immunotherapy.