



Technology Offer

Ref.-No. M15/18

G_{D2} target upregulation by EZH2 inhibition in cancer therapy

Introduction

Chimeric antigen receptors (CARs) are recombinant proteins that redirect immune effector cells (T cells, NK cells) to tumor-associated antigens. CAR-modified T cells have powerful therapeutic activity against B cell malignancies. The development also for solid tumors is limited by the paucity of target antigens reliably expressed on the cell surface of cancer cells but not normal cells. One candidate antigen is the carbohydrate antigen G_{D2}, since it is aberrantly overexpressed in various cancers including neuroblastoma, osteosarcoma, Ewing sarcoma, melanoma and breast cancer.

The obstacle for effective G_{D2}-directed immune therapeutics in cancer is heterogeneous expression of G_{D2} on tumor cells, often below the detection threshold for G_{D2}-specific CARs or antibodies, resulting in immune escape. Moreover, not all cancers of the above entities are G_{D2}-positive. There is an urgent need for improved therapies in G_{D2}low or G_{D2}neg cancers or subpopulations thereof. The technical problem is to comply with this need.

Invention

The present invention relates an Enhancer of Zeste Homolog 2 (EZH2) inhibitor for use in a method of treating a solid tumor in a subject, wherein the method further comprises the administration of a G_{D2}-specific CAR-T cell or CAR-NK cell or a G_{D2}-specific antibody to the subject. Further, the present invention relates to a G_{D2}-specific CAR-T cell or CAR-NK cell or a G_{D2}-specific antibody for use in a method of treating a solid tumor in a subject, wherein (i) the method further comprises the administration of an EZH2 inhibitor to the subject; and/or (ii) the subject has been and/or is treated with an EZH2 inhibitor. Additionally, the present invention

relates to methods for increasing the surface expression of G_{D2} in solid tumor cells and kits and kits-of-part comprising an EZH2 inhibitor and a G_{D2}-specific CAR-T cell or CAR-NK cell or a G_{D2}-specific antibody.

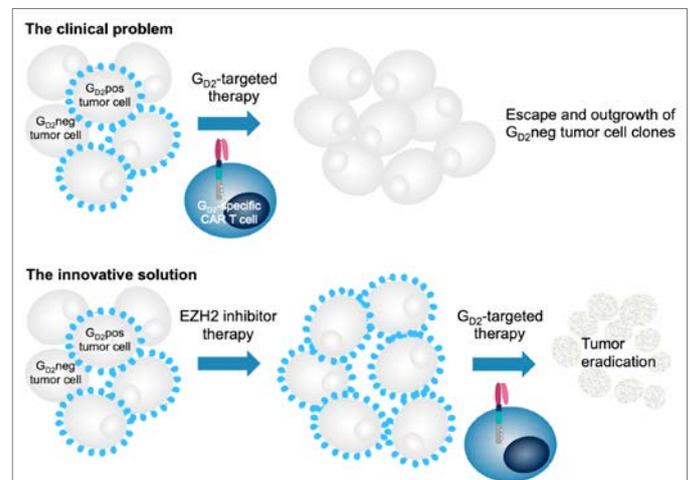


Illustration of the clinical problem of the present G_{D2}-targeted therapy and the combination of this therapy with EZH2 inhibitor therapy in order to improve tumor eradication.

Advantages of the invention

- G_{D2}neg cancers become targetable by G_{D2}-directed immune therapeutics.
- Preventing immune escape of G_{D2}low tumor cells develops G_{D2}-directed immune therapeutics to their full potential.
- A novel combined epigenetic and immunological strategy for improved cancer therapy is created.

Patent situation

Patent applications filed in Luxemburg.

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