CXCL12 Inhibition with NOX-A12 (Olaptesed) Increases T and NK Cell Infiltration and Synergizes with Checkpoint Blockade and ADCC in Tumour-Strroma Spheroids

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BACKGROUND & RATIONALE

T and NK cell-based cancer immunotherapy requires physical contact between immune effector cells and malignant cells, which is generally restricted by the tumour microenvironment (TME). CXCL12 has recently been described as a T cell exclusion factor in the TME-driven immune suppression. The clinical stage I-aptamer (Spiegelmer®) NOX-A12 (olaptesed pegol) was found to detach CXCL12 from the surface of stromal cells and to block CXCL12 binding to CXCR4 and CXCR7. In this study we aimed to investigate whether NOX-A12 is able to enhance T and NK cell infiltration into tumour-stroma spheroids, thereby facilitating effective cancer immunotherapy.

Further known modes of action of the CXCL12 inhibitor NOX-A12:

- NOX-A12 mobilizes healthy immune cells.
- NOX-A12 enhances T cell anti-cancer therapy by depriving their contact with the TME.
- NOX-A12 inhibits the formation and growth of metastases.

METHODS & RESULTS

CONCLUSIONS & OUTLOOK

- We established tumour-stroma spheroids that mimic the complexity of the tumour microenvironment, in which the CXCL12 inhibitor enhances T and NK cell infiltration.
- By facilitating physical contact of both T and NK cells with tumour cells, NOX-A12 synergizes with T cell-based checkpoint inhibition and NK cell-mediated ADCC.
- This data suggests to combine NOX-A12 with T and NK cell-based cancer immunotherapy.

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