Poster 25: Evaluation of the safety and efficacy of bi-specific antibodies using organoids and colorectal cancer spheroids

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Objectives

Developing ex vivo models that replicate immune–tumor interactions with high fidelity is essential for advancing immunotherapy research, as traditional two-dimensional in vitro systems often lack the complexity required to fully represent these interactions.

Methods

In this study, we establish a comprehensive 3D redirect lysis (3D-RDL) assay using colorectal cancer spheroids and adult stem cell-derived, healthy human organoids to evaluate the efficacy and safety profile of Cibisatamab, a bispecific antibody targeting carcinoembryonic antigens (CEAs) on cancer cells and CD3 on T cells. This model allows us to assess cytotoxic activity and immune responses, capturing variations in therapeutic response not observable in simpler systems. Our model integrates live imaging and cytotoxicity analyses to enable precise, real-time tracking of antibody effects on CEA-expressing tumor cells compared to healthy cells. Additionally, by standardizing effector-to-target cell ratios in each co-culture, we establish a reproducible workflow that enhances data accuracy and comparability across assays. Flow cytometry and Granzyme B release profiling further allow us to characterize immune cell activation, revealing distinct T cell activation markers and Granzyme B release patterns tied to Cibisatamab treatment.

Results

Our results show that Cibisatamab effectively induces cell death in cancer spheroids with high CEA expression while being dose-dependent on target, off-tumor binding and killing on non-cancerous cells of healthy organoids with intermediate CEA levels. This highlights our model's potential to predict clinical immunotherapy outcomes, capturing complex responses like immune activation, therapeutic selectivity, and potential resistance mechanisms.

Conclusions

These findings underscore the utility of our model as a reliable, physiologically relevant tool for screening new immunotherapies and advancing our understanding of tumor-immune dynamics.