LIS22: An Effective Multimodal Polyclonal Antibody Targeting T-Cell Malignancies

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Abstract

Context: T-cell lymphomas are aggressive cancers with limited treatment options. Diseases diversity limits the identification of effective therapeutic drugs. LIS22, a glyco-humanized polyclonal antibody, was developed to address these challenges by targeting simultaneously a broad spectrum of antigens associated with T-cell tumors. In this study, we extensively characterized the efficacy of LIS22 in preclinical models of T cell blood cancers.

Material and methods: LIS22 ability to induce Antibody-Dependent Cell Cytotoxicity (ADCC), Antibody-Dependent Cellular Phagocytosis (ADCP), Complement Dependent Cytotoxicity (CDC), and apoptosis was tested in a panel of hematologic malignancy cell lines, primary cells from patients and in peripheral blood mononuclear cell (PBMC). To assess the recognition of LIS22 by PTCL tumors, we evaluated the immunolabelling of LIS22 on patients' biopsies (n=119). LIS22 efficacy *in vivo* were evaluated in NMRI nude mice and SRG rats using T1301 and Jurkat cancer cell lines.

Results: LIS22 acts via several mechanisms, at 30µg/ml, it induced cytotoxicity via CDC (in 70%), ADCP (in 49%), ADCC (in 41%) and apoptosis (in 30%) of HPB-ALL human T blood cancer cell line but not in PBMC. LIS22 showed a potent *in vitro* antitumor activity in a panel of hematologic malignancy cell lines and primary patient tumors (CDC EC50=41.4±28.9ug/mL). In both CDC and apoptosis cytotoxicity assays, LIS22 displayed a significantly higher potency on T cell blood cancers and no toxicity on healthy blood cells compared to Alemtuzumab (Anti-CD52) and Belinostat (HDAC inhibitor). LIS22 demonstrated high PTCL patient biopsy recognition (staining up to 93%). *In vitro* anti-tumor activities were translated into a significant in vivo efficacy in different mice and rat xenograft models. LIS22 induced a significant reduction of tumor growth up to 86% across several tested tumors. In addition, it showed high superiority in terms of efficacy and tolerance compared to the first line standard of care in T cell lymphoma (CHOP) in SRG T1301 xenograft model.

Conclusion: LIS22 has emerged as a novel and promising antibody for the treatment of T-cell hematologic malignancies. It is currently under clinical investigation (Phase I/II) for the treatment of peripheral T-cell lymphoma (PTCL).