TPS2688 **Poster Session**

A phase 1 first-in-human study of the novel anti-LLT1 antibody (ZM008) alone and in combination with anti-PD1 antibody in patients with advanced solid tumors.

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Background: ZM008 is a first-in-class, fully human, IgG1 monoclonal antibody targeting the LLT1 antigen. It disrupts the interaction of LLT1-CD161, an NK-mediated innate immunity checkpoint. LLT1 expression on tumor cells has been associated with poor overall survival in multiple solid tumors. *Ex vivo* experiments with lung and bladder cancer biopsies showed significant tumor reduction and immune cell infiltration were observed with ZM008 monotherapy. Synergistic anti tumor effects were observed with ZM008 in combination with pembrolizumab. An open-label, phase 1, first-in-human study evaluating the safety, tolerability, pharmacokinetics (PKs), preliminary anti-tumor activity and the Recommended Phase 2 Dose (RP2D) of ZM008 alone and in combination with pembrolizumab in advanced solid tumors is now ongoing at 3 US sites (NCT06451497). **Methods:** The study includes a dose-escalation Part 1 and a dose-expansion Part 2. In dose escalation (part 1), ZM008 monotherapy follows 3+3 standard design starting with 0.15 mg/Kg and up to 18 mg/Kg IV Q3W. A staggered parallel arm will explore ZM008 in combination with pembrolizumab (200mg Q3W) from dose level 6. Histologically confirmed advanced or metastatic non-small cell lung, head & neck, pancreatic, biliary, prostate, colorectal, triple negative breast, urothelial, ovarian and diffuse large B cell malignancies with no standard alternative are included. Measurable disease by RECIST v1.1, adequate haematological, hepatic and renal functions are required. In Part 2, two or more doses of ZM008 will be used to select RP2D and indications of interest. Major exclusion criteria include, patients with history of uncontrolled brain metastasis, autoimmune disease, pneumonitis, active infections, and significant cardiovascular diseases. The primary objective is to determine the maximum tolerated dose (MTD) and RP2D of ZM008. Secondary objectives include PKs, incidence and severity of treatment-emergent AEs as per common terminology criteria for adverse events (CTCAE) v.5.0, immunogenicity, pharmacodynamic changes, and preliminary anti-tumor activity. Exploratory biomarkers will evaluate pharmacodynamics changes, receptor occupancy, immune and cytokine profiling, ctDNA, and transcriptomics. Paired pre- and on-treatment biopsies will be analysed using immunohistochemistry and the spatial distribution of immune and tumor cells in the tumor microenvironment. At the time of submission, enrollment of 9 subjects were completed in three dose cohorts with no reported DLTs. The study is ongoing and open for enrolment at NEXT Oncology (San Antonio and Austin sites) and Dana-Farber Cancer Institute, Boston. Clinical trial information: NCT06451497. Research Sponsor: Zumutor Biologics Inc.