**2583** **Poster Session**

# A phase 1 study of the novel immunotoxin MT-5111 in patients with HER2+ tumors: Interim results.

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**Background:** MT-5111 is a 55kD engineered toxin body (ETB) targeting HER2 in solid tumors that binds to an epitope distinct from trastuzumab and pertuzumab, offering potential combination strategies with other HER2-targeting agents. MT-5111 may demonstrate efficacy in patients (pts) resistant to other HER2-targeting agents, as its mechanism of action induces direct cell kill via enzymatic and permanent ribosome destruction. **Methods:** This is a phase 1 study in adults with advanced HER2+ solid tumors. The dose-escalation portion (Part A) enrolls pts into sequential dose cohorts, followed by Part B expansion cohorts for HER2+ breast cancer (BC), gastroesophageal adenocarcinoma (GEA), and any other HER2+ cancer (CA). MT-5111 is dosed weekly IV over 30 min in each 21-day treatment (tx) cycle until disease progression, unacceptable toxicity, death or withdrawn consent. **Results:** As of Jan 2022, 27 pts had enrolled in Part A cohorts (0.5 to 10 μg/kg/dose) with completed DLT assessments: 9 (33%) pts were male and 18 (67%) female, median age 67 and a median of 4 prior systemic and 2 prior HER2-targeting tx. Common tissue types were BC (9/30%), biliary CA (6/22%), GEA (4/15%). The following safety data reflect 33 treated pts to date including ongoing 13 μg/kg/dose Part A and 10 μg/kg/dose BC expansion cohorts. No Grade (G) 4/5 tx-emergent adverse events (AEs) or DLTs occurred. Tx-related AEs occurred in 17 (52%) pts, most commonly G1/2 fatigue (8/24%). 3 pts had G1 troponin elevations without clinical signs or symptoms of cardiac distress: 1 at 6.75 μg/kg/dose, 2 at 10 μg/kg/dose. 2 pts (3 and 4.5 μg/kg/dose) had reversible G2 and G1, respectively, infusion-related reactions (IRR)s. A comparison of cytokines from baseline to on-treatment timepoints reveals no evidence of significant changes, even in pts with IRR. Best response per RECIST thus far was stable disease (SD) in 7 pts or non-CR/non-PD in 2 pts: 1 pt had SD for 12 weeks (wks) (4.5 μg/kg, pancreatic CA); 1 pt (1 μg/kg/dose, BC) had non-CR/non-PD for 30 wks; 1 pt (10 μg/kg/dose, GEA) has ongoing SD for 18 wks. $AUC_{last}$ data match PK simulations in non-human primate studies. $C_{max}$ at 10 μg/kg/dose is ≥5 times the $IC_{50}$ values of high HER2 expressing gastric CA and BC cell lines while approaching the $IC_{50}$ of a moderately HER2 expressing liver CA cell line. **Conclusions:** MT-5111 is well tolerated to-date with no clinically significant immuno/cardiotoxicity. Dose escalation is ongoing at a dose of 13μg/kg, expected to be required for efficacious exposure. Clinical trial information: NCT04029922. Research Sponsor: Molecular Templates, Inc.