A Phase 1 Study of MM-111; a Bispecific HER2/HER3 Antibody Fusion Protein, Combined with Multiple Treatment Regimens in Patients with Advanced HER2 Positive Solid Tumors

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Background

The Phase 1, multi-arm study examined the safety, pharmacokinetics and anti-tumor activity of MM-111 combined with the standard of care HER2-targeting regimens in patients with breast, gastric, esophageal and bladder cancers.

MM-111 is a bispecific antibody targeting the HER2/HER3 complex that inhibits HER3 (ErbB3) from binding with HER2 (ErbB2) and the ligand heregulin to signal cell growth. ErbB3 is also thought to play a role in causing resistance to HER2-targeted therapies.

Methodology

- This was a multi-arm Phase 1 study in which MM-111 was combined with commonly used HER2-targeting regimens. Each arm of the study ran as a separate Phase 1 study using standard 3+3 dose escalation. Safety, tolerability, PK and responses were evaluated.
    - Capecitabine, cisplatin and trastuzumab
    - Lapatinib +/- trastuzumab
    - Paclitaxel with trastuzumab
- A total of 46 patients with documented advanced HER2 + cancer received weekly doses of MM-111 at 10 mg/kg and escalated up to 20 mg/kg.

Results

- Across all dosing regimens, the overall clinical benefit rate, defined as complete response (CR), partial response (PR) and stable disease (SD) at least 4 months, was 52 percent in 29 evaluable patients.
- Responses were observed across various tumor types including, breast, bladder, esophageal, colorectal and ovarian cancers.
- MM-111 was tolerable and could be safely combined at full dose with lapatinib / trastuzumab and paclitaxel / trastuzumab regimens. The capecitabine containing arm required dose reduction of capecitabine. Re-escalation of MM-111 is ongoing.
- The toxicity profile of the MM-111 combinations was consistent with that generally observed in patients receiving the underlying HER2 therapy.

Phase 2 studies will further examine the role of MM-111 in the treatment of a variety of tumors, the first of which is expected to be initiated late this year.