A Phase 1 Study of the Anti-Erbb3 Antibody MM-121 in Combination with Weekly Paclitaxel in Patients with Advanced Gynecological and Breast Cancers

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Background

The study evaluated the combination of MM-121 with weekly paclitaxel to treat patients with advanced gynecological and metastatic breast cancers.

MM-121 is a fully human monoclonal antibody designed to target ErbB3, a signaling receptor believed to be responsible for triggering tumor growth and playing a role in the resistance to conventional chemotherapies and targeted agents in solid tumors including breast, ovarian, gastric, esophageal and bladder cancers.

Methodology

- A total of 28 patients with certain platinum resistant gynecological cancers or HER2 non-overexpressing breast cancer received a combination of MM-121 and weekly paclitaxel until disease progression or intolerable toxicity was reported. Response was assessed every eight weeks.
- In the dose-expansion cohorts, pre- and post-treatment fresh tumor biopsies were obtained to assess ErbB3 signaling status and its potential as a predictive marker for MM-121 response.
- The median patient age was 57 years and patients had received a median of four prior lines of therapy in the adjuvant or metastatic setting including chemotherapies and anti-hormonal therapies.
- Common adverse events include fatigue, peripheral neuropathy, diarrhea, rash and neutropenia. Other toxicities included anemia, stomatitis, mucosal inflammation, dyspnoe and hypokalemia.

Results

- 23 patients were evaluable
- The overall clinical benefit rate (CBR) was 70 percent.
- The progression free survival rate was 33 weeks.
    - Other clinical studies have shown patients typically experience a progression free survival rate of 12 weeks on weekly paclitaxel alone.
    - Patients in advanced and resistant ovarian cancer expect to have a PFS of 18 weeks on paclitaxel alone
- Forty-eight percent of patients achieved a partial response (PR); of those, 39 percent achieved a confirmed PR with a median duration of 2.7 months.
- Twenty-two percent achieved stable disease (SD) >4 months with a median duration of 5.3 months.
- Twenty-six percent remain on study with a median on-study time of 13.5 months.

- The observed safety profile of MM-121 in combination with weekly paclitaxel was shown to be comparable to treatment with weekly paclitaxel alone.

In partnership with Sanofi, this combination regimen is currently being evaluated in two Phase II studies in advanced ovarian cancer and neoadjuvant breast cancer.

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