A Phase 1 Study of MORAb-003, a Fully Humanized Monoclonal Antibody against Folate Receptor Alpha, in Advanced Epithelial Ovarian Cancer

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ABSTRACT

BACKGROUND: Folate receptor alpha (FRA) is over-expressed in the majority of epithelial ovarian cancers (EOC) but is largely absent from normal tissue. MORAb-003 is a fully humanized monoclonal antibody against FRA. Binding of MORAb-003 to FRA can prevent phosphorylation of substrates specific for Lyn kinase, suppress proliferation of cells over-expressing FRA, and inhibit tumor growth in rodent xenograft models. Toxicology studies in non-human primates found MORAb-003 to be well tolerated, with no dose limiting toxicity at doses up to 300 mg/m2.

METHODS: Sequential cohorts of patients received four weekly infusions at escalating dose levels of MORAb-003 from 12.5 mg/m2 to 400 mg/m2. Eligible patients had EOC, that relapsed in 6 months after platinum-based therapy, measurable organ tumors, Karnofsky Performance Status ≥70%, and no evidence of brain metastases. Patients were followed until study discontinuation or progression.

RESULTS: To date, 18 subjects have been dosed with up to 200 mg/m2. MORAb-003 was well tolerated: there were very few related adverse events (AEs) (see Table 1). No grade 3 or 4 related AEs were seen. Mild infusion reactions were seen in 2 of 22 subjects. No DLTs were observed.

CONCLUSIONS: The FRA-epitopic MORAb-003 appears to be well tolerated in patients with EOC and may have activity in platinum-resistant patients. These results support further evaluation of the efficacy of MORAb-003 in a phase 2 study.

BACKGROUND

OVARIAN CANCER:

- 1/67 women will get the disease
- 1/200 women will die from it
- Most common gynecologic malignancy
- Typically presents at Stage 3 or 4
- ~90% will achieve remission
- Bleeding AEs are rare for the therapy of choice (ovarian cancer)

MORAb-003:

- Fully humanized monoclonal antibody against Folate Receptor Alpha (FRA)
- FRA is over-expressed in >90% of human ovarian cancers
- Binding of MORAb-003 to FRA:
  - Inhibits antibody-dependent cellular toxicity
  - Inhibits complement-mediated cytotoxicity
  - Causes a reduction in cellular growth rate
  - Reduces tumor growth of human ovarian spheroids

Table 1. MORAb-003 in normal human primary ovarian tissue cultures.

Table 2. Dose-limiting toxicity.

RESULTS

DISEASE RESPONSE AND STABLE DISEASE

Table 3. Changes in CA125.

CONCLUSIONS

- Reported AEs were predominantly grade 1; no related severe or serious AEs or DLTs were observed
- 17/20 patients showed stabilization or improvement of disease
- 12/20 patients showed at least a clinical benefit
- 17/20 patients showed stabilization or improvement by RECIST criteria
- Preliminary pharmacokinetic data indicate recovery and half-life are in the expected range for humanized monoclonal antibodies
- Preliminary pharmacodynamic data indicate recovery and half-life are in the expected range for humanized monoclonal antibodies
- Realized likelihood of EOC-003 accruements at the center of interest (Figure 2).

Figure 1. RECIST and CA125 Response to MORAb-003

Figure 2. SPECT/CT images demonstrate uptake of radioactive MORAb-003 in two subjects at 48 hours after injection of 111In-DOTA MORAb-003. Representative of 3 subjects. Images show tumor tissue accumulation of radiolabeled MORAb-003.

Table 1. Change in CA125.

Table 2. Changes in tumor parameters.

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