Correlation of GPNMB Expression with Outcome in Breast Cancer (BC) Patients Treated with the Antibody-Drug Conjugate (ADC), CDX-011 (CR011-vcMAE)

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BACKGROUND

GPNMB: An internalized glycoprotein expressed in more than 40% of breast cancers, as well as other tumor types, promotes the migration, invasion, and metastasis of breast cancer cells. GPNMB expression was found in the bloodstream, but to release MMAE upon internalization in the target cell-killing effect. 1,2

GPNMB DETECTION METHODS

- Immunohistochemistry (IHC) for the detection of GPNMB in paraffin-embedded tumor samples
- Western blot analysis
- Flow cytometry
- RT-PCR
- In situ hybridization
- ELISA

Anti-tumor Activity: Phase II (1.88 mg/kg)

All Patients (n=43) Triple- Negative (n=10)

Best Response (RECIST)

- Partial Response (PR): 38 (90%)
- Stable Disease (SD): 14 (33%)
- Progressive Disease (PD): 1 (2%)

Median PFS: 12 weeks

Summary: CDX-011 (CR011-vcMAE) is a promising ADC for the treatment of metastatic breast cancer with high GPNMB expression, showing promising anti-tumor activity with a manageable safety profile.

FUTURE DIRECTIONS

A Phase II trial in heavily pre-treated, advanced breast cancer patients who are refractory resistant to all approved therapies is planned. Patients will be selected for high GPNMB expression in historical tissue samples or current biopsies.

120 patients will be randomized to receive CDX-011 or an Investigator’s Choice single-agent chemotherapy.

Endpoints will include overall response rate, duration of response, PFS, overall survival, and PK/PD.

This is a positive Phase II study of CDX-011 in a population of advanced breast cancer patients who were heavily pretreated (median of seven prior regimens). The primary efficacy endpoint has been met, with 36% of patients achieving progression-free survival at 12 weeks.

Encouraging evidence of activity is seen in the subset with triple-negative disease where treatment options are limited.

These new data, using the GPNMB detection assay intended for Phase II, suggest that patients with significant expression of GPNMB on tumor cells in a biopsy may receive greatest benefit from CDX-011.

The activity of CDX-011 in patients with significant expression of GPNMB may be due to both a “bystander effect,” which in which CDX-011 is released from the GPNMB-expressing stromal cells, killing neighboring tumor populations, as well as direct depletion of supporting stromal cells.

Both patients with tumor tissue assessed by IHC who achieved objective response showed significant tumor cell and/or stromal expression of GPNMB, and continued on treatment from 27 to 54+ weeks.

These data, from a clearly small subset of patients, should be verified in a larger Phase II trial.

CDX-011 (pamidromab vedotin) is designable to be stable in the bloodstream, but to release MMAE upon internalization in the target cell-killing effect. 1,2