**Glycoprotein NMB (gpNMB)**

- An internalization-dependent glycoprotein over-expressed in 20% of breast cancers, 47% of triple-negative breast cancer (TNBC), plus melanoma, uterine sarcoma, head and neck squamous cell cancer, and some gastrointestinal cancers.
- Shorter metastasis-free survival and overall survival in patients with high gpNMB-expressing tumors (including breast, small cell lung cancer, and glioblastoma).

**Glembatumumab Vedotin**

- Novel antibody-drug conjugate that delivers the payload metabolically activated (MMAE) to gpNMB-expressing tumor cells.
- Same single-agent MTD technology that was used successfully in AdEN.2 (breastmammary vedotin, Seattle Genetics).

**Completed Phase II Study in Patients with Advanced Breast Cancer: EMERGE**

Study designed to examine whether anti-cancer activity of glembatumumab vedotin is dependent upon gpNMB expression in tumor cells. A region of gpNMB+ stroma is delineated by the circle and a box.

**HIGH TUMOR GPMBNMB EXPRESSION CORRELATES SIGNIFICANTLY WITH RESPONSE TO GLEMBATUMUMAB VEDOTIN, BUT NOT TO IC**

High tumor gpNMB expression correlates significantly with response to glembatumumab vedotin, but not to IC.

**RESULTS**

- **Overall Response Rate (ORR)**
  - Lung: 3/4 (75%)
  - Lymph Node: 12/35 (34%)
  - Chest Wall: 3/10 (30%)
  - Breast: 6/20 (30%)
  - Liver: 5/15 (33%)
  - Metastatic Classification:
    - Mesothelioma: 2/2 (100%)
    - Colorectal: 4/22 (18%)
    - Lung: 3/7 (43%) 2/2 (100%)
    - All: 13/39 (33%)

- **Quality of life and/or cancer-related pain**
  - 2 to 3 score chemotherapy-regimens for advanced breast cancer
  - Prior taxane chemotherapy in any setting, unless contraindicated
  - Prior anthracycline chemotherapy in any setting, unless contraindicated

**METASTATIC TNBC OVEREXPRESSING GPMBNMB**

**THE STUDY DESIGN**

- **Randomization (2:1)**
  - **Treatment (2:1 randomization)**
  - Glembatumumab vedotin (GV) (1.88 mg/kg q3w IV)
  - Placebo

**EVALUATION OF TISSUE BREAST SYMPOSIUM**

- Retrospective analysis on the frequency of gpNMB overexpression (staining in ≥50% of tumor epithelial cells) from 25% of tumor epithelial cells by central IHC)

**Oncoblast Research Institute/Tennessee Cancer Institute, PLLC, Nashville, TN**

**REFERENCES**

1. Rose, et al. CCR, 2010
2. Li, et al. APMIS 2013

**MEASUREMENT OF METRICA**

- Therapeutic activity in breast cancer (EMERGE)
- Promising results obtained in the EMERGE study supported initiation of the “METRIC” study in patients with gpNMB overexpressing TNBC

**FUTURE DIRECTIONS**

- Ongoing study in metastatic TNBC gpNMB overexpression. The “METRIC” Study (Protocol CDX011-04)
- Ongoing study in advanced melanoma (Protocol CDX011-05)
- Additional studies are planned in osteosarcoma, uveal melanoma, and squamous cell lung cancer

**CONCLUSIONS**

- gpNMB overexpression in breast cancer, including in TNBC, appears consistent regardless of disease setting (early or advanced) or age
- Ongoing development of disease sites, including lung, lymph node, chest wall, liver, and breast
- gpNMB expression may be enhanced in patients with gpNMB-overexpressing tumors and/or TNBC

**STUDY Registro**

- Study ongoing in the approximate 100 sites in US, Canada, and Australia with expansion planned into Europe
- For an up-to-date listing of open sites or further details, please visit www.Celldex.com

**CONTACT**

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**Abbreviations**

- ITT: Intention To Treat
- NOS: Not Otherwise Specified