METRIC: A Randomized International Study of the Antibody-Drug Conjugate Glembatumumab Vedotin (GV or CDX-011) in Patients (pts) with Metastatic gpNMB-Overexpressing Triple-Negative Breast Cancer (TNBC)

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Background

Glycoprotein NMB (gpNMB)
- An internalizable transmembrane glycoprotein overexpressed in 20% of breast cancers, 40% of TNBC, and other tumors
- Shorter metastasis-free 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 potent cellular toxin monomethylauristatin E (MMAE) to gpNMB-expressing tumor cells
- Same linker-MMAE technology as that used successfully in Ad cetris® (brentuximab vedotin; Seattle Genetics)
- Three completed clinical studies in melanoma and breast cancer
  - Clinical benefit appears greatest in pts with TNBC and/or gpNMB+ tumors

Completed Phase II Study in Pts with Advanced Breast Cancer: “EMERGE”

Study designed to examine whether anti-cancer activity of glembatumumab vedotin is dependent upon distribution/intensity of gpNMB expression

Treatment
- 2:1 randomization
  - Glembatumumab vedotin (1.88 mg/kg q3w)
  - “Investigator’s Choice” (IC) single-agent chemotherapy

Population
- gpNMB+ breast cancer
- Refractory/resistant to approved therapies
- Progression within 6 months of last regimen
- 98% with metastatic disease
- Median of 6 prior lines of anticancer therapy

Results
- 99% of screened pts met eligibility for gpNMB expression (≥25% of epithelial or stromal cells positive)
- Epithelial gpNMB expression more frequent in TNBC
- Glembatumumab vedotin was well-tolerated
  - Treatment-related toxicity: Rash, neutropenia, fatigue, nausea, vomiting, alopecia, decreased appetite, and peripheral neuropathy
  - Less hematologic toxicity than IC
- Activity of glembatumumab vedotin may be enhanced in patients with gpNMB-overexpressing tumors and/or TNBC

Methodology

The “METRIC” Study Design

Objectives
- Primary:
  - Progression-free survival (PFS) per independent, blinded central review committee (RECIST 1.1)
- Secondary:
  - Objective response rate (ORR)
  - Duration of response (DOR)
  - Overall survival (OS)
  - Safety
  - Pharmacokinetics
- Exploratory:
  - Quality of life and/or cancer-related pain

Eligibility Criteria
- Tumor obtained in the advanced disease setting must show:
  - gpNMB overexpression (≥25% of tumor epithelial cells positive by central IHC)
  - 40% of TNBC expected to meet criteria (EMERGE experience)
- TNBC status:
  - ER/PR: ≤10% of cells positive by IHC
  - HER2: IHC staining of 0 or 1+, FISH < 4.0 copies or ratio < 2.0
- 0 to 2 prior chemotherapy-containing regimens for advanced breast cancer
- Prior taxane chemotherapy in any setting
- Prior anthracyline chemotherapy in any setting, unless contraindicated
- No untreated brain metastases. Pts must be asymptomatic and stable for ≥2 months.
- Measurable disease (RECIST 1.1)
- ECOG 0 or 1
- Peripheral neuropathy Grade ≤ 1
- No investigational therapy within 4 weeks of study treatment
- Resolution of all chemotherapy or radiation-related toxicities to Grade ≤ 1 severity, except for alopecia

Study Status
- Study being conducted at approximately 100 sites in US, Canada, and Australia
- For an updated listing of open sites or further details, please visit:
  - www.clinicaltrials.gov, NCT#01997333
  - www.triplenegativebc.com
  - www.facebook.com/metricstudy

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1. Rosso, et al. CCR 2010
2. L. Li, et al. APMES 2011

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