

# 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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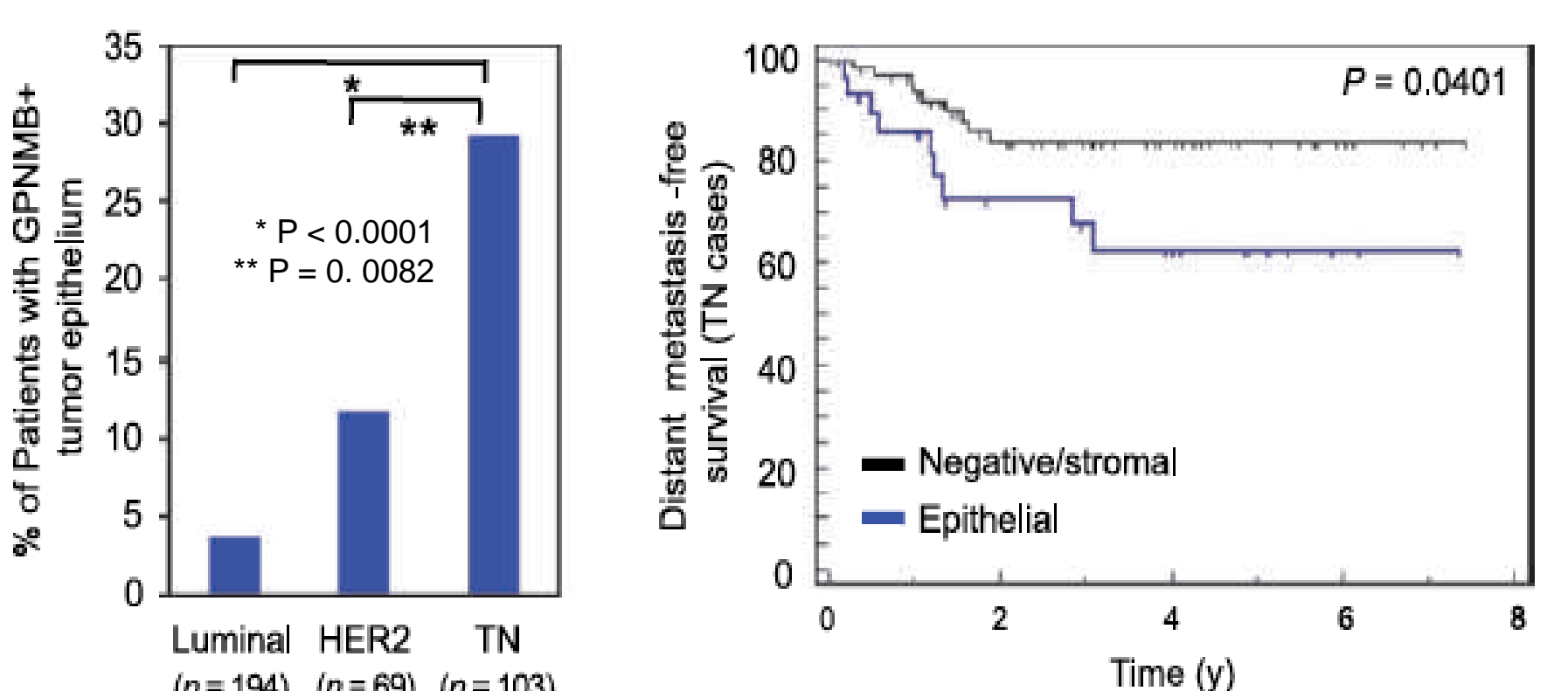
Abstract #TPS1110

## BACKGROUND

### Glycoprotein NMB (gpNMB)

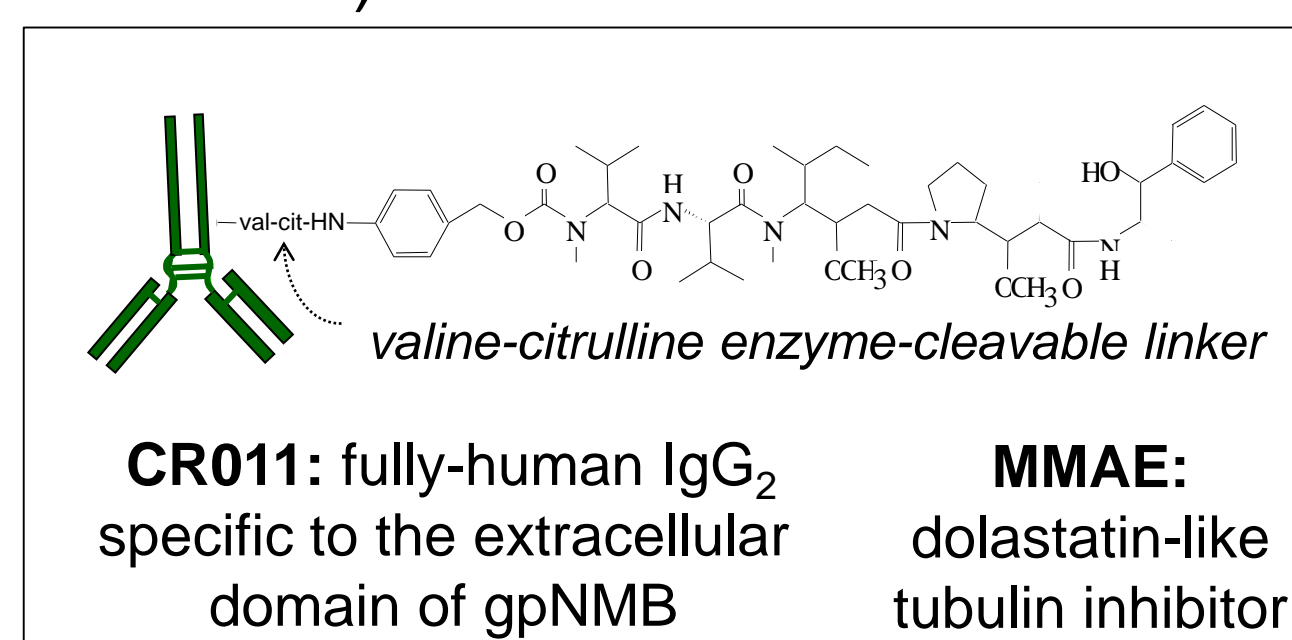
- An internalizable transmembrane glycoprotein over-expressed in 20% of breast cancers, 40% of TNBC, and other tumors
- Shorter metastasis-free and overall survival in patients with high gpNMB-expressing tumors (including breast,<sup>1</sup> small cell lung cancer<sup>2</sup>, and glioblastoma<sup>3</sup>)

Tumor Epithelial gpNMB Expression is Common in Triple Negative Breast Cancer (ER-/PR-/HER2-)\* and is Associated with Recurrence<sup>1</sup>



### 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 Adcetris<sup>TM</sup> (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"<sup>4</sup>

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

### Treatment

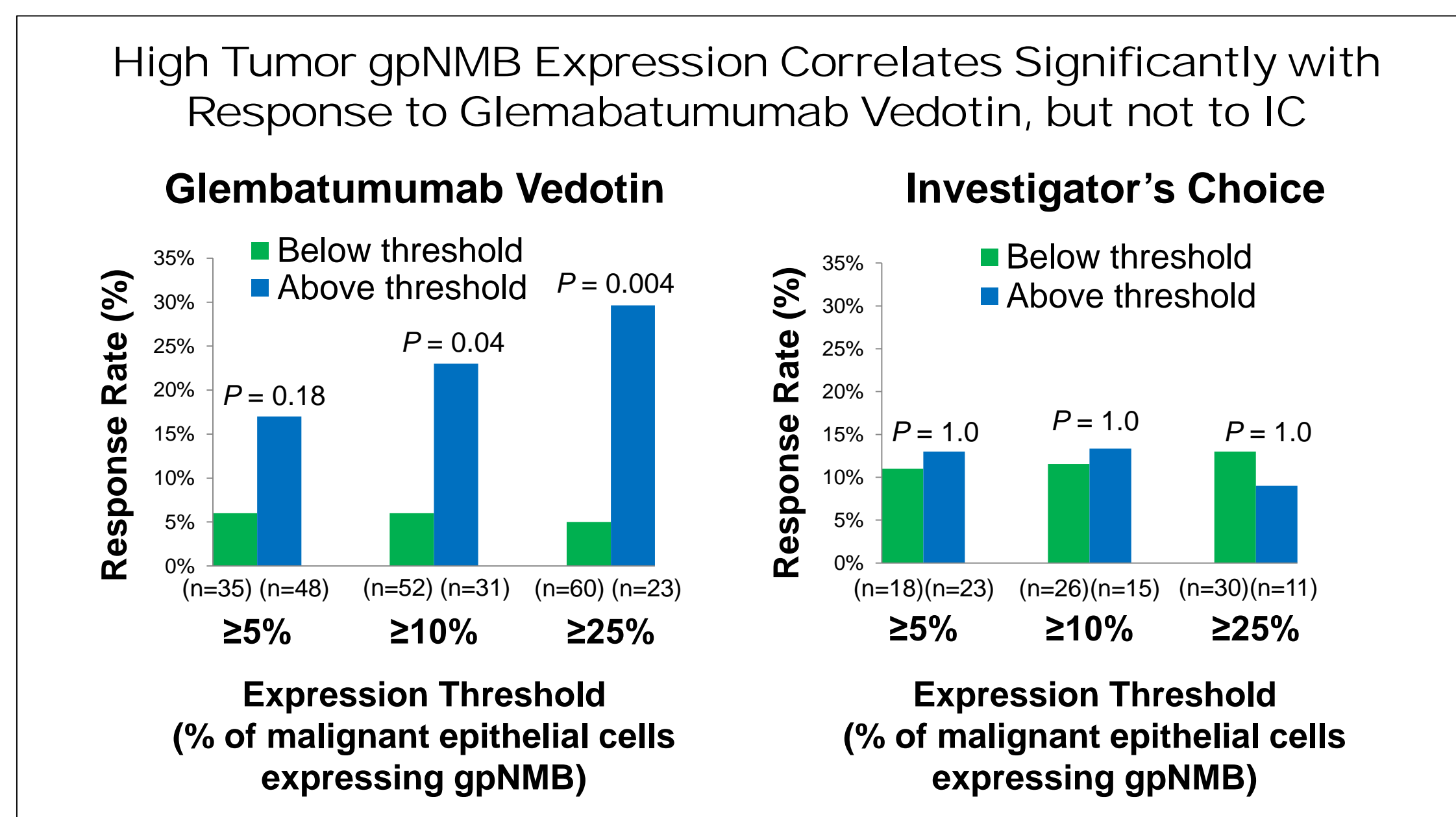
- 2:1 randomization
  - Glembatumumab vedotin (1.88 mg/kg q3w)
  - "Investigator's Choice" (IC) single-agent chemotherapy
- Cross-over from IC to glembatumumab vedotin permitted at progression

### 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

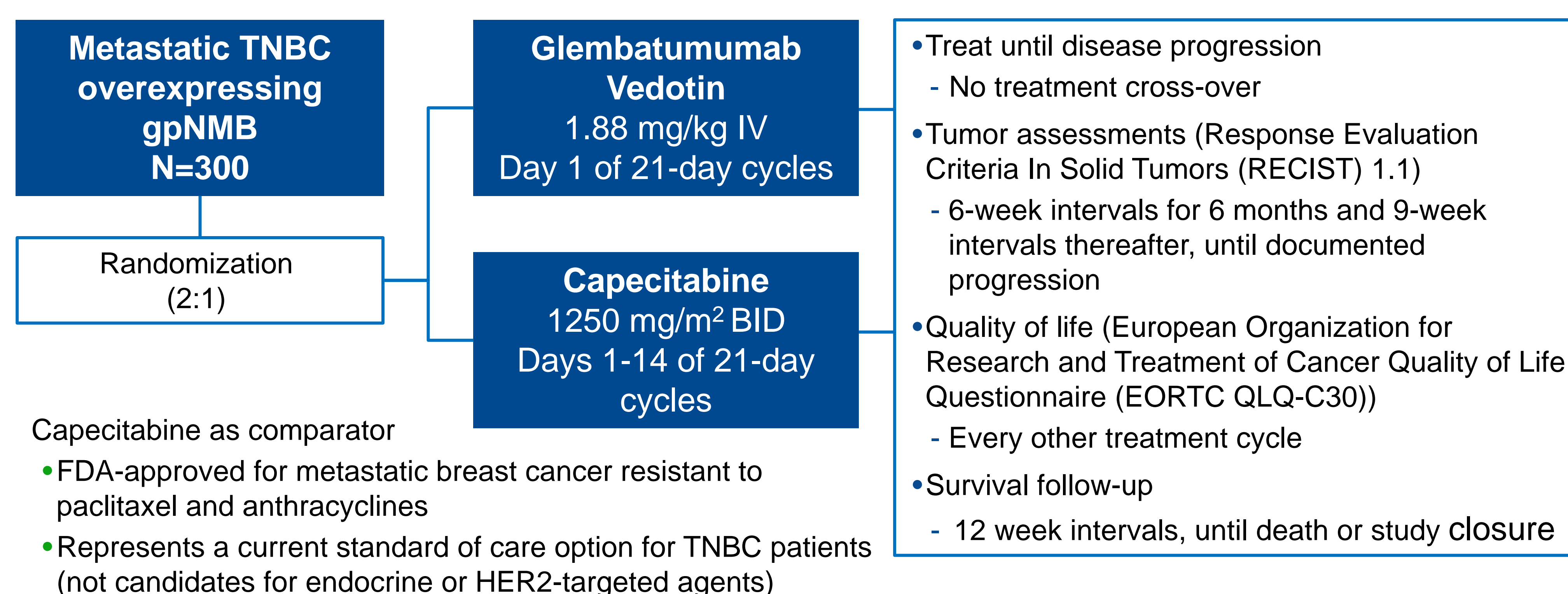
- 99% of screened pts met eligibility for gpNMB expression (≥5% of epithelial or stromal cells positive)
  - Epithelial gpNMB expression more frequent in TNBC
- Glembatumumab vedotin was well-tolerated
  - Treatment-related toxicity: Rash, neutropenia, fatigue, nausea, vomiting, alopecia, decreased appetite, and peripheral neuropathy
  - Less hematologic toxicity than IC
- Activity of glembatumumab vedotin may be enhanced in patients with gpNMB-overexpressing tumors and/or TNBC



	High gpNMB Expression <sup>§</sup>		TNBC & High gpNMB <sup>§</sup>	
	GV (n=23)	IC (n=11)	GV (n=10)	IC (n=6)
<b>Overall Response Rate (ORR)</b>	7 (30%)	1 (9%)	4 (40%)	0 (0%)
<b>Confirmed PR</b>	3 (13%)	1 (9%)	1 (10%)	0 (0%)
<b>Stable Disease or Better</b>	15 (65%)	3 (27%)	9 (90%)	1 (17%)
<b>Median PFS (months)</b>	2.8	1.5	3.5	1.5
	HR=0.63, p=0.18		HR=0.11, p=0.0017*	
<b>Median OS (months)</b>	10.0	5.7	10.0	5.5
	HR=0.67, p=0.31		HR=0.14, p=0.003*	

GV, Glembatumumab vedotin; IC, Investigator's Choice Therapy; HR, Hazard Ratio  
Intention-To-Treat (ITT) analysis of all randomized patients  
§ ≥ 25% of tumor epithelial cells expressing gpNMB by IHC  
\* Statistically significant

## 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

### Statistical Design

- Type I error rate ( $\alpha$ ): 0.05 (2-sided)
- Power: 85%
- Hypothesized PFS Hazard Ratio: 0.64
- Hypothesized median PFS for two arms:
  - Capecitabine: 4.0 months
  - Glembatumumab vedotin: 6.25 months
- Targeted PFS events = 203

### 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 anthracycline 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