TPS3161: A Multi-center, Open-Label Phase 1/1b Dose Finding, Safety, and Pharmacokinetic Study of MBRC-101, an Anti-EphA5 Monomethyl Auristatin (MMAE) Antibody Drug Conjugate, in Advanced Refractory Solid Tumors

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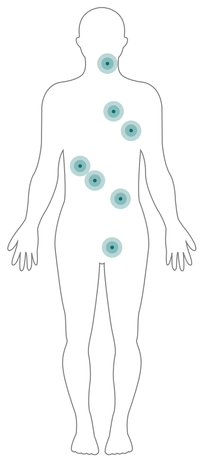
Background

1. **Ephrin A5 (EphA5) is a receptor tyrosine kinase**
2. **Highly & selectively expressed in:**



- Non-small cell lung carcinoma (NSCLC)
- Breast cancer (including HR+/HER2- & triple negative)
- Head and neck squamous cell carcinoma
- Colorectal adenocarcinoma
- Pancreatic ductal carcinoma
- Gastric adenocarcinoma
- Hepatocellular carcinoma

3. **MBRC-101 is a novel antibody-drug conjugate (ADC) composed of:**
   - Humanized anti-EphA5 IgG1 antibody
   - MMAE payload (DAR 4)
   - A valine citrulline cleavable linker

A Phase 1/1b trial of MBRC-101 is open and currently enrolling patients (NCT06014658)

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Current Status

1 MAY 2024 — **3 escalating Dose Levels completed without DLT (n = 13 patients):**

- **0.5 mg/kg** (n=4 patients)
- **1.0 mg/kg** (n=4 patients)
- **1.5 mg/kg** (n=5 patients)

APRIL 2024 — **Enrollment to Dose Level 4 (2.0 mg/kg) began**

Methods

First-in-human, Phase 1/1b, multicenter, open-label study of MBRC-101 in patients with advanced metastatic solid tumors refractory to standard treatment.

MBRC-101-001 Phase 1/1b: Study Schema

Phase 1 Escalation (n ≈ 30)

Will **identify potential optimal biologically relevant doses** (OBRD)

Maximum tolerated dose (MTD) at one or more dosing regimens

Modified toxicity probability interval (mTPI-2) method method will **guide dose escalation**

Phase 1b Expansion (n ≈ 60)

- **Cohort A** (n ≈ 20): Non-small cell lung cancer (NSCLC)
- **Cohort B** (n ≈ 20): Breast Cancer (Triple negative or HR+/HER2-)
- **Cohort C** (n ≈ 20): Pancreatic, gastric, hepatic, ovarian adenocarcinomas, squamous cell carcinomas, and primary head and neck malignancies

Primary Endpoints

MTD | Dose Limiting Toxicities (DLTs) | Clinical Laboratory Tests | Treatment Emergent Adverse Events (TEAEs)

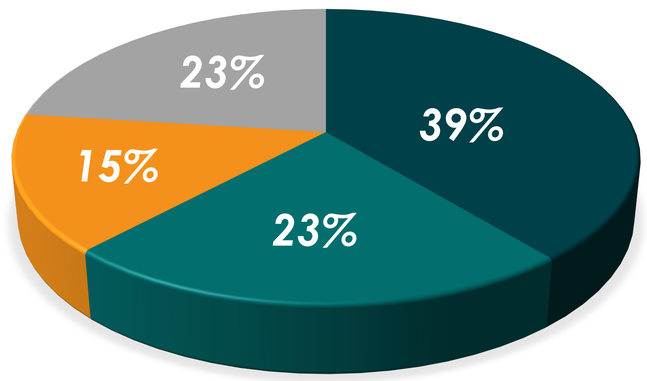
Primary Endpoints

TEAEs | **Investigator-Assessed Objective Response Rate (ORR)** by RECIST v1.1and clinical evaluation

Secondary Endpoints for Ph1 and 1b: PK Analytes | EphA5 expression as determined by IHC

Tumor Types

n=13 patients



- NSCLC & Breast
- Colorectal
- Pancreas
- Ovarian & Other