A Phase 2, Randomized Study of Magrolimab Combination Therapy in Adult Patients With Unresectable Locally Advanced or Metastatic Triple-Negative Breast Cancer (ELEVATE TNBC)

TPS1130

ELEVATE TRIPLE NEGATIVE BREAST CANCER

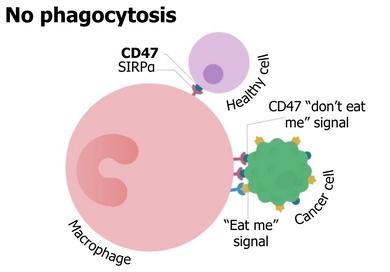
Natalie Rainey, MD,[1] Rohit Joshi, MD,[2] Joanne Chiu, MD,[3] Ann Chen, PharmD,[4] Hao Wang, PhD,[4] Jared Odegard, PhD,[4] Estibaliz Lopez Rodrigo, MD,[4] Sylvia Adams, MD[5]

[1]Cairns and Hinterland Hospital and Health Service, Cairns, QLD, Australia; [2]Cancer Research SA, Adelaide, SA, Australia; [3]Division of Hematology and Medical Oncology, Department of Medicine, Queen Mary Hospital, The University of Hong Kong, Pok Fu Lam, Hong Kong, China; [4]Gilead Sciences, Inc., Foster City, CA, USA; [5]Laura and Isaac Perlmutter Cancer Center, NYU Langone Medical Center, New York, NY, USA

Introduction

- Improving outcomes in patients with triple-negative breast cancer (TNBC) remains a high unmet need
- Immune checkpoint inhibitors (ICIs) + taxane-based chemotherapy are approved for newly-diagnosed patients with programmed death-ligand 1 (PD-L1)–positive TNBC. Sacituzumab govitecan, a trophoblast cell-surface antigen 2–targeted antibody-drug conjugate, is approved for patients who received ≥2 prior systemic therapies (≥1 for metastatic disease)[1,2]
  - However, additional options are urgently needed, particularly for patients with tumors that do not express PD-L1 and for patients with disease progression with chemotherapy ± ICIs
- Magrolimab is an antibody that blocks cluster of differentiation 47 (CD47), a "don't eat me" signal overexpressed in some cancers, including TNBC (**Figure 1**). Magrolimab has shown promising clinical activity as part of combination therapies in hematologic malignancies[3-8]
  - Magrolimab blocks CD47 and facilitates macrophage-induced phagocytosis of cancer cells, and certain chemotherapies, including taxanes, enhance prophagocytic signals on tumor cells, which may lead to synergistic antitumor activity with magrolimab[3-5,9]
- This Phase 2 study, ELEVATE-TNBC, is evaluating the safety and efficacy of magrolimab + nab-paclitaxel or paclitaxel in patients with TNBC previously untreated and magrolimab + sacituzumab govitecan in those who received at least 1 and no more than 2 prior lines of treatment in the advanced setting

Figure 1. Magrolimab Mechanism of Action[7]

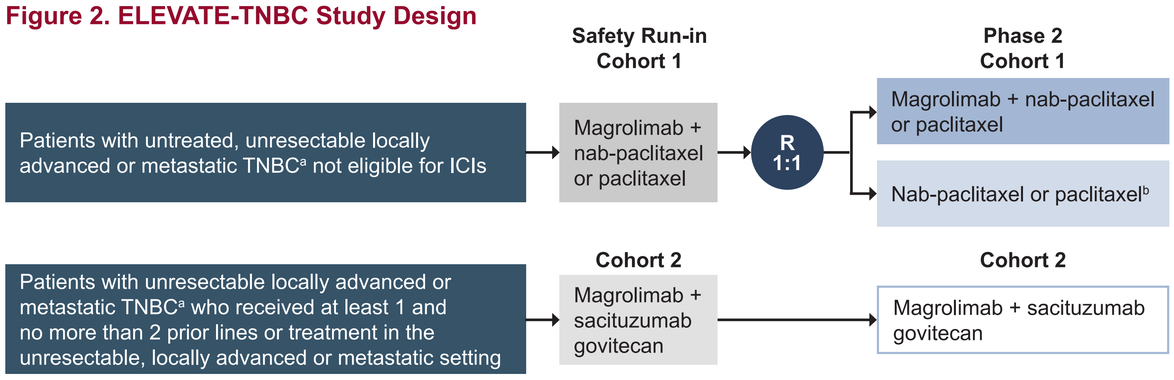


CD47, cluster of differentiation 47; SIRPα, signal-regulatory protein alpha.

Study Design

- This is a randomized (Phase 2 Cohort 1), open-label, multicenter, Phase 2 study consisting of safety run-in and Phase 2 cohorts that will include a total of approximately 168 patients (NCT04958785) (**Figure 2**)

Figure 2. ELEVATE-TNBC Study Design



ER, estrogen receptor; HER2, human epidermal growth factor receptor 2; ICI, Immune checkpoint inhibitors; IHC, immunohistochemistry; ISH, in situ hybridization; PR, progesterone receptor; R, randomized; TNBC, triple-negative breast cancer.
[a]TNBC defined by the American Society of Clinical Oncology/College of American Pathologists guidelines as absence of ER and PR (IHC <1% of nuclei stain for each) and HER2 (IHC 0, 1+, 2+/ISH−). [b]Patients enrolled in Cohort 1 Arm B with documented progressive disease can rescreen to enroll in Cohort 2 as long as they meet all other eligibility criteria.

Methods

Patient Eligibility

Key Inclusion Criteria	Key Exclusion Criteria
All Patients — Male or female ≥18 years of age — Adequate performance status and hematologic, renal, and liver function — Pretreatment blood crossmatch completed — Measurable disease according to RECIST version 1.1 **Cohort 1:** — Previously untreated, unresectable locally advanced or metastatic TNBC[a] — PD-L1–negative tumors **Cohort 2:** — Unresectable locally advanced or metastatic TNBC — Receipt of at least 1 and no more than 2 prior lines or treatment in the unresectable, locally advanced or metastatic setting ▪ Previous treatment with a taxane in either the neoadjuvant, adjuvant, or locally advanced setting ▪ If tumors are positive for PD-L1 expression, patients must have received an ICI for 1L treatment of locally advanced/metastatic disease	**All Patients** — Prior treatment with CD47- or signal regulatory protein α-targeting agents — History of hemolytic anemia, autoimmune thrombocytopenia, or Evans syndrome in the last 3 months — Known inherited or acquired bleeding disorder — Secondary malignancy[b] — Prior chemotherapy agents, endocrine therapy, or targeted small molecule therapy ≤2 weeks prior to magrolimab and monoclonal antibodies, antibody-drug conjugates, immunotherapy or other investigational agents ≤3 weeks prior to magrolimab — Active CNS disease[c] **Cohort 1:** — Disease progression ≤6 months following neoadjuvant/adjuvant therapy or rapid visceral progression and/or symptomatic disease for which single-agent chemotherapy would not be appropriate **Cohort 2:** — Active chronic inflammatory bowel disease and a history of bowel obstruction or GI perforation ≤6 months before enrollment — Prior receipt of topoisomerase I inhibitors or antibody-drug conjugates containing a topoisomerase I inhibitor — Receipt of high-dose systemic corticosteroids (≥20 mg of prednisone or equivalent) ≤2 weeks before Cycle 1 Day 1 — No recovery from AEs due to previously administered agent[d]

1L, first line; AE, adverse event; CNS, central nervous system; GI, gastrointestinal; RECIST, Response Evaluation Criteria in Solid Tumors.
[a]Prior systemic neoadjuvant and/or adjuvant therapy and/or curative-intent radiation therapy is permitted if completed ≥6 months prior to enrollment. [b]Excluding treated basal cell or localized squamous skin carcinomas, localized prostate cancer, or other malignancies for which patients are not receiving active anticancer therapies and who are in complete remission for >2 years. [c]Patients with asymptomatic and stable treated CNS lesions who have not received corticosteroids for ≥4 weeks are allowed. [d]Excluding any-grade neuropathy or alopecia.

Objectives

Primary

- Determine safety, tolerability, and recommended phase 2 dose of magrolimab in combination with nab-paclitaxel, paclitaxel, or sacituzumab govitecan
- Compare efficacy of magrolimab in combination with nab-paclitaxel or paclitaxel vs nab-paclitaxel or paclitaxel alone via progression-free survival (PFS) (investigator-assessed)
- Evaluate efficacy of magrolimab in combination with sacituzumab govitecan via objective response rate (ORR) (investigator assessed)

Secondary

- PFS (Cohort 2, Safety Run-in, and Phase 2)
- ORR by investigator assessment (Cohort 1, Phase 2)
- Duration of response (DOR), overall survival (OS)
- Compare safety and tolerability between treatment arms
- Pharmacokinetics and immunogenicity

Exploratory

- Pharmacodynamics, mechanism of action, and therapeutic response biomarkers
- Biomarkers that may predict response to therapy
- Patient-reported outcomes/quality of life measures for patients treated with magrolimab and either nab-paclitaxel or paclitaxel

Treatment

Drug/dose/route Magrolimab + chemotherapy	Dose schedule (days per 28-day cycle)		
	Cycle 1	Cycle 2	Cycle 3+
Nab-paclitaxel 100 mg/m² IV	Days 1, 8, 15	Days 1, 8, 15	Days 1, 8, 15
Paclitaxel 90 mg/m² IV	Days 1, 8, 15	Days 1, 8, 15	Days 1, 8, 15
Safety run-in cohort 1 magrolimab administration			
Magrolimab 1 mg/kg IV	Day 1		
Magrolimab 30 mg/kg IV	Days 8, 15, 22	Days 1, 8, 15, 22	Days 1, 15
Phase 2 cohort 1 magrolimab administration			
Magrolimab 1 mg/kg IV	Day 1		
Magrolimab RP2D[a] IV	Days 8, 15, 22	Days 1, 8, 15, 22	Days 1, 15
Drug/dose/route Magrolimab + sacituzumab govitecan	**Dose schedule (days per 21-day cycle)**		
	Cycle 1	**Cycle 2**	**Cycle 3+**
Sacituzumab govitecan 10 mg/kg IV	Days 1, 8	Days 1, 8	Days 1, 8
Safety run-in cohort 2 magrolimab administration			
Magrolimab 1 mg/kg IV	Day 1		
Magrolimab 30 mg/kg IV	Days 8, 15	Days 1, 8, 15	
Magrolimab 60 mg/kg IV			Day 1
Phase 2 cohort 2 magrolimab administration			
Magrolimab 1 mg/kg IV	Day 1		
Magrolimab RP2D[a] IV	Days 8, 15	Days 1, 8, 15	Day 1

IV, intravenous; RP2D, recommended phase 2 dose.
[a]RP2D as determined in the safety run-in cohort.
Magrolimab may administered on Cycle 1 Day 1 and paclitaxel/nab-paclitaxel or sacituzumab govitecan may be administered on Cycle 1 Day 2.

Key Endpoints

Primary Endpoints

Safety Run-in Cohorts
- Dose limiting toxicity, adverse events (AE), laboratory abnormalities

Phase 2 Cohort 1
- PFS by investigator assessment

Cohort 2 (pooled safety run-in and phase 2)
- Confirmed ORR by investigator assessment

Secondary Endpoints

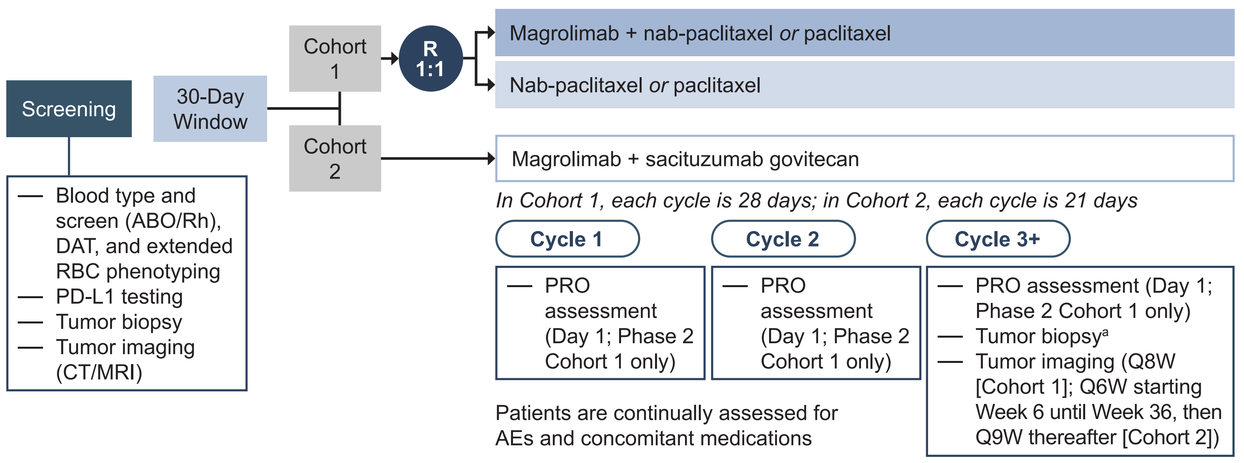
Safety Run-in Cohorts
- Magrolimab concentration vs time and antidrug antibodies (ADA) to magrolimab

Phase 2 Cohort 1
- Confirmed ORR by investigator assessment
- PFS
- DOR by investigator assessment
- OS
- AEs and laboratory abnormalities
- Magrolimab concentration vs time and ADAs to magrolimab

Cohort 2 (pooled safety run-in and phase 2)
- Confirmed ORR
- PFS by investigator assessment
- DOR by investigator assessment
- OS
- AEs and laboratory abnormalities
- Magrolimab concentration vs time and ADAs to magrolimab

- Key assessments and timing are shown in **Figure 3**

Key Assessments and Timing



AE, adverse events; CT, computed tomography; DAT, direct antiglobulin test; MRI, magnetic resonance imaging; PD-L1, programmed death-ligand 1; PRO, patient-reported outcome; Q6W, every 6 weeks; Q8W, every 8 weeks; Q9W, every 9 weeks; R, randomization; RBC, red blood cell; Rh, rhesus.
[a]On-treatment tumor biopsy can be collected any time between Cycle 3 Day 1 and Cycle 4 Day 1.

Enrollment: The study is currently enrolling in the US, Australia, and Hong Kong. ClinicalTrials.gov identifier: NCT04958785.

References: **1.** Keytruda (pembrolizumab). Prescribing information. Merck Sharp & Dohme Corp; 2022. Accessed May 5, 2023. **2.** Trodelvy (sacituzumab govitecan). Prescribing information. Gilead Sciences; 2022. Accessed May 5, 2023. **3.** Daver NG, et al. *J Clin Oncol*. 2022;40(16 suppl):7020-7020. **4.** Sallman DA, et al. *J Clin Oncol*. 2022;40(16 suppl):7017-7017. **5.** Liu J, et al. *PLoS One*. 2015;10(9):e0137345. **6.** Advani R, et al. *N Engl J Med*. 2018;379(18):1711-1721. **7.** Chao MP, et al. *Front Oncol*. 2020;9:1380. **8.** Yuan J, et al. *Oncol Lett*. 2019;18(3):3249-3255. **9.** Kiss B, et al. *J Clin Oncol*. 2020;38(15 suppl):e17035.

Acknowledgments: We extend our thanks to the patients and their families, friends, and caregivers, as well as to the study staff. This study was funded by Gilead Sciences, Inc. Medical writing support was provided by Michelle Sulzinski, of SciMentum, Inc, a Nucleus Group Holdings, Inc, company, Hamilton, NJ, and was funded by Gilead Sciences, Inc.

Correspondence:
Natalie Rainey,
Natalie.Rainey@health.qld.gov.au

Presented at American Society for Clinical Oncology (ASCO), June 2-6, 2023, Chicago, IL & Online