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

Natalie Raineri, MD,1 Rohit Joshi, MD,2 Joanne Chiu, MD,3 Ann Chen, PharmD,4 Hao Wang, PhD,1 Jared Odgard, PhD,1 Estibaliz Lopez Rodrigo, MD,5 Sylvia Adams, MD,6
1Cairns and Hinterland Hospital and Health Service, Cairns, QLD, Australia; 2Cancer Research SA, Adelaide, SA, Australia; 3Division of Hematology and Medical Oncology, Department of Medicine, Queen Mary Hospital, The University of Hong Kong, Pok Fu Lam, Hong Kong, China; 4Gilead Sciences, Inc., Foster City, CA, USA; 5Laura 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 govhrect, a trophoblast cell-surface antigen 2–targeted antibody-drug conjugate, is approved for patients who received 3 prior systemic therapies (pts; p<0.001 for metastatic disease).
— However, additional options are urgently needed, particularly for pts with tumors that do not express PD-L1 and for pts with disease progression with chemotherapy.
— 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.
— Magrolimab blocks CD47 and facilitates macrophage-induced phagocytosis of cancer cells, and certain chemotherapies, including taxanes, enhance phagocytic signals on tumor cells, which may lead to synergistic antitumor activity with magrolimab.
— 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 govhrect in those who received at least 1 and no more than 2 prior lines of treatment in the advanced setting.

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 1. Magrolimab Mechanism of Action

No phagocytosis

Magrolimab blocks CD47 and facilitates macrophage-induced phagocytosis.

Figure 2. ELEVATE-TNBC Study Design

Methods

Key Inclusion 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
— PD-L1-negative tumors

Cohort 2:
— Unresectable locally advanced or metastatic TNBC
— Receipt of at least 1 and no more than 2 prior lines of treatment in the unresectable, locally advanced or metastatic setting
— Previous treatment with a taxane in the neoadjuvant, adjuvant, or locally advanced setting
— If tumors are positive for PD-L1 expression, patients must have received an IC1 for 1 or 2 line treatment

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
— Prior chemotherapy agents, endocrine therapy, or targeted small molecule therapy 52 weeks prior to magrolimab and monoclonal antibodies, antibody-drug conjugates, immunotherapy or other investigational agents 53 weeks prior to magrolimab
— Active CNS disease

Cohort 1:
— Disease progression 56 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 within 56 months before enrolment
— Prior receipt of topoisomerase I inhibitors or antibody-drug conjugates containing a topoisomerase I inhibitor
— Receipt of dose-dense systemic corticosteroids (≥20 mg of prednisone or equivalent) ≤5 weeks before Cycle 1 Day 1
— Patients who received at least 1 and no more than 2 prior lines of treatment in the advanced setting

Key Assumptions and Timing

— Blood type and screen (ABO/Rh), DAT, and extended RBC phenotyping
— LDH testing
— Tumor biopsy
— Tumor biopsy from for therapeutic response biomarkers
— Rituximab, nab-paclitaxel or paclitaxel

Cohort 1, each cycle is 28 days; in Cohort 2, each cycle is 21 days

Cohort 1
— Cycle 1: PRO assessment (Day 1; Phase 2 Cohort 1 only)
— Cycle 2: PRO assessment (Day 1; Phase 2 Cohort 1 only)

Cohort 2
— Cycle 1: PRO assessment (Day 1; Phase 2 Cohort 1 only)
— Cycle 2: PRO assessment (Day 1; Phase 2 Cohort 1 only)
— Cycle 3: PRO assessment (Day 1; Phase 2 Cohort 1 only)

References:

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

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

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