SOPHIA: A Phase 3, Randomized Study of Margetuximab (M) Plus Chemotherapy (CTX) vs Trastuzumab (T) Plus CTX in the Treatment of Patients with HER2+ Metastatic Breast Cancer (MBC)

Hope S. Rugó1, Mark D. Pegram2, William J. Gradishar1, Javier Cortes1, Giuseppe Curigliano3, Jan Baughman1, Sutton Edlich1, Naimish Pandya1, Jon M. Wigginton1, Fatima Cardoso2

University of California San Francisco, San Francisco, CA; 1Stanford School of Medicine, Stanford, CA; 2Lurie Comprehensive Cancer Center of Northwestern University, Chicago, IL; 3Vall d’Hebron Institute of Oncology (VHIO), Barcelona, Spain; 4Istituto Europeo di Oncologia, Milano, Italy; 5MacroGenics, Inc., Rockville, MD; 6Chapmanwald Cancer Centre, Lisbon, Portugal.

Background

Margetuximab acts against HER2+ tumors by a combination of potential mechanisms:

- Margetuximab induces ADCC through interaction with CD16A.
- Margetuximab binds with high affinity to HER2, resulting in growth retardation.
- Margetuximab indirectly induces apoptosis through the death receptor signaling pathway.

Margetuximab demonstrates single-agent activity in heavily pretreated HER2+ MBC patients.

Margetuximab produces superior engagement of effector cells and ADCC compared to trastuzumab.

Phase 1 Study Results

Outcomes in Heavily Pre-treated Patients

<table>
<thead>
<tr>
<th>Margetuximab</th>
<th>Trastuzumab</th>
<th>p-value</th>
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</thead>
<tbody>
<tr>
<td>PFS (median)</td>
<td>1.9 months</td>
<td>0.035</td>
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<tr>
<td>OS (median)</td>
<td>15.0 (p=0.008)</td>
<td>1.0 (p=0.008)</td>
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</tbody>
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Trastuzumab activity may differ by Fc-

disease-free survival (DFS) for patients with high affinity isoform.

Margetuximab was well tolerated with mild to moderate infusion-related reactions, cytokine release syndrome, and growth retardation or induction of apoptosis.

Related adverse events: All that occurred in ≥10% of patients:

- Fatigue
- Nausea
- Infusion-related reactions
- Diarrhea
- Influenza-like illness
- Cytokine release syndrome
- Hypertension

Entry Criteria

- Histologically-proven metastatic or locally-advanced relapsed/metastatic HER2+ solid cancers
- Prior chemotherapy for HER2+ solid cancers
- History of prior allogeneic bone marrow, stem-cell, or solid organ transplantation
- History of clinically significant cardiovascular disease
- History of prior adjuvant/neoadjuvant trastuzumab

Ongoing Phase 3 Study

Key Study Objectives:

- To evaluate efficacy, as measured by PFS assessed by independent central review, and overall survival (OS) of margetuximab plus chemotherapy compared to trastuzumab plus chemotherapy in patients with advanced HER2+ breast cancer.
- To evaluate PFS, as assessed by study investigators, of margetuximab plus chemotherapy vs. trastuzumab plus chemotherapy.
- To evaluate by independent review the objective response rate (ORR) of margetuximab plus chemotherapy vs. trastuzumab.
- To evaluate health-related quality of life (HRQoL), as assessed using the Functional Assessment of Cancer Therapy-Breast Cancer Symptom Index (FACT-B13) and EQ-5D-5L.
- To characterize safety profile of margetuximab plus chemotherapy vs. trastuzumab plus chemotherapy.

Study Status

- Ongoing: 12 Countries, ~200 Sites
- Ongoing: 16 Countries, ~280 Sites
- Ongoing; 16 Countries, ~200 Sites
- Ongoing; 16 Countries, ~200 Sites
- Denmark, Republic of Korea
- Ireland, Spain
- France, United Kingdom
- Germany, United States
- France, United Kingdom
- Germany, United States
- France, United Kingdom
- Germany, United States

References


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