Original Investigation

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Effect of a Proposed Trastuzumab Biosimilar Compared With Trastuzumab on Overall Response Rate in Patients With ERBB2 (HER2)–Positive Metastatic Breast Cancer

A Randomized Clinical Trial

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Full Text

Key Points

Question Are the effects of a proposed trastuzumab biosimilar equivalent to those of trastuzumab in the treatment of ERBB2 (formerly HER2 or HER2/neu)–positive metastatic breast cancer?

Findings In this randomized clinical trial that included 458 women, the overall response rate to the proposed biosimilar plus a taxane at 24 weeks was 69.6% (95% CI, 63.62%-75.51%) compared with 64.0% (95% CI, 57.81%-70.26%) for trastuzumab plus a taxane, which was within predefined equivalence boundaries.

Meaning Although further assessment is needed to establish long-term clinical outcomes and safety, the availability of a clinically effective biosimilar treatment option for trastuzumab may lead to broader access to this therapy for patients with breast cancer.

Abstract

Importance Treatment with the anti-ERBB2 humanized monoclonal antibody trastuzumab and chemotherapy significantly improves outcome in patients with ERBB2 (HER2)–positive metastatic breast cancer; a clinically effective biosimilar may help increase access to this therapy.

Objective To compare the overall response rate and assess the safety of a proposed trastuzumab biosimilar plus a taxane or trastuzumab plus a taxane in patients without prior treatment for ERBB2-positive metastatic breast cancer.

Design, Setting, and Participants Multicenter, double-blind, randomized, parallel-group, phase 3 equivalence study in patients with metastatic breast cancer. From December 2012 to August 2015, 500 patients were randomized 1:1 to receive a proposed biosimilar or trastuzumab plus a taxane. Chemotherapy was administered for at least 24 weeks followed by antibody alone until unacceptable toxic effects or disease progression occurred.

Interventions Proposed biosimilar (n = 230) or trastuzumab (n = 228) with a taxane.
Main Outcomes and Measures The primary outcome was week 24 overall response rate (ORR) defined as complete or partial response. Equivalence boundaries were 0.81 to 1.24 with a 90% CI for ORR ratio (proposed biosimilar/trastuzumab) and −15% to 15% with a 95% CI for ORR difference. Secondary outcome measures included time to tumor progression, progression-free and overall survival at week 48, and adverse events.
Results Among 500 women randomized, the intention-to-treat population included 458 women (mean [SD] age, 53.6 [11.11] years) and the safety population included 493 women. The ORR was 69.6% (95% CI, 63.62%-75.51%) for the proposed biosimilar vs 64.0% (95% CI, 57.81%-70.26%) for trastuzumab. The ORR ratio (1.09; 90% CI, 0.974-1.211) and ORR difference (5.53; 95% CI, −3.08 to 14.04) were within the equivalence boundaries. At week 48, there was no statistically significant difference with the proposed biosimilar vs trastuzumab for time to tumor progression (41.3% vs 43.0%; −1.7%; 95% CI, −11.1% to 6.9%), progression-free survival (44.3% vs 44.7%; −0.4%; 95% CI, −9.4% to 8.7%), or overall survival (89.1% vs 85.1%; 4.0%; 95% CI, −2.1% to 10.3%). In the proposed biosimilar and trastuzumab groups, 239 (98.6%) and 233 (94.7%) had at least 1 adverse event, the most common including neutropenia (57.5% vs 53.3%), peripheral neuropathy (23.1% vs 24.8%), and diarrhea (20.6% vs 20.7%).
Conclusions and Relevance Among women with ERBB2-positive metastatic breast cancer receiving taxanes, the use of a proposed trastuzumab biosimilar compared with trastuzumab resulted in an equivalent overall response rate at 24 weeks. Further study is needed to assess safety and long-term clinical outcome.
Trial Registration clinicaltrials.gov Identifier: NCT02472964; EudraCT Identifier: 2011-001965-42

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