ARTICLE NAVIGATION

ORAL PRESENTATIONS - PROFFERED ABSTRACTS | APRIL 25 2025

Abstract CT204: Phase 1a/b study of runimotamab, a HER2 x CD3 T cell-engaging bispecific antibody, administered as a single agent and in combination with trastuzumab in patients with HER2-expressing breast cancer (BC) FREE

Shanu Modi; Timothy A. Yap; Tira J. Tan; Armando Santoro; Valentina Gambardella; Philippe Cassier; Haeseong Park; Erika Hamilton; Chia-Chi Lin; Capucine Baldini; Philippe L. Bedard; Seock-Ah Im; Jean-Luc Canon; Iben Spanggaard; Valentina Boni; Maria de Miguel; Patricia LoRusso; Antoine Italiano; Carlos Gomez-Roca; Simon Lord; Chang-Fang Chiu; Sherene Loi; Victor Moreno; Kohei Shitara; Cristina Saura; Marloes van Dongen; Salvatore Siena; Giuseppe Curigliano; Sharareh Monemi; Sharmeen Hassan; Michelle Wilhite; Emiko Gale; Zao Li; Zhaojun Yin; Chunze Li; Luciana Molinero; Kelly DuPree; Teemu Junttila; Aditi Qamra; Lina Alon; Iris T. Chan; Kyung Hae Jung

+ Author & Article Information

Cancer Res (2025) 85 (8_Supplement_2): CT204.

https://doi.org/10.1158/1538-7445.AM2025-CT204

Abstract

Background:

Runimotamab is a HER2 x CD3 T cell-engaging bispecific antibody developed for patients with human epidermal growth factor receptor 2 (HER2)-expressing cancers that promotes cytotoxic T cell lysis of HER2-expressing cells. We hypothesized that co-treatment with trastuzumab may reduce on-target/off-tumor toxicities of runimotamab and increase its therapeutic index due to decreased runimotamab binding to low-expressing HER2 normal tissues. This first-in-human, dose-escalation study assessed the preliminary safety and anti-tumor activity of runimotamab alone and with trastuzumab in patients with HER2-expressing BC.

Methods:

Patients with locally advanced or metastatic BC received escalating doses of runimotamab IV either alone (Ph 1a) or in combination with trastuzumab (Ph 1b) to determine maximum tolerated doses. In Cycle (C) 1, runimotamab was administered using step dose fractionation, with a step-up dose given on Day (D) 1, followed by the initial target dose on D8. Subsequent runimotamab target doses were given on D1 of each 3-week cycle (Q3W). In Ph 1b, trastuzumab was administered prior to runimotamab, first on C1D-1, and then Q3W on D1 of each cycle. Study objectives included evaluation of safety and tolerability, pharmacokinetics (PK), pharmacodynamics, and anti-tumor activity. Data cut-off date was 01Aug2024.

Skip to Main Content

Results:

Overall, 73 BC patients were enrolled: 20 in Ph 1a and 53 in Ph 1b (NCT03448042). Median number of all prior therapies was 7 in Ph 1a and 8 in Ph 1b patients. The highest runimotamab doses administered in Ph 1b (100/300 mg on C1D1/D8) surpassed those in Ph 1a (1.7/5 mg). At or above pharmacologically active doses of runimotamab (≥ 0.72/2.2 mg), cytokine release syndrome (CRS) rate was lower in Ph 1b (31%, n=15/48, Grade 1-2) compared to Ph 1a (78%, n=7/9, Grade 1-2) patients. The most common treatment-related adverse events (TRAEs; ≥20% patients) among all safety-evaluable patients were CRS, hypophosphatemia, pyrexia, ALT/AST increased, headache, nausea, rash, pruritus, and fatigue. Grade ≥3 TRAEs occurred in 4 (20%) Ph 1a and 20 (37.7%) Ph 1b patients. Runimotamab PK was dose-proportional in Ph 1a/b patients. Co-administration with trastuzumab dampened runimotamab-induced T cell activation and cytokine induction. Anti-tumor activity was observed in Ph 1b only, at runimotamab doses ≥2.2/6.6 mg. Runimotamab 20/60 mg combined with trastuzumab was chosen for dose expansion. Seven of 23 (30.4%) runimotamab 20/60 mg patients had confirmed responses, including 1 CR and 6 PRs.

Conclusions:

Improved tolerability and higher runimotamab dose levels were achieved in combination with trastuzumab, compared to runimotamab alone. Runimotamab + trastuzumab demonstrated a manageable safety profile and encouraging clinical activity in heavily pretreated HER2-positive BC patients.

Citation Format:

Shanu Modi, Timothy A. Yap, Tira J. Tan, Armando Santoro, Valentina Gambardella, Philippe Cassier, Haeseong Park, Erika Hamilton, Chia-Chi Lin, Capucine Baldini, Philippe L. Bedard, Seock-Ah Im, Jean-Luc Canon, Iben Spanggaard, Valentina Boni, Maria de Miguel, Patricia LoRusso, Antoine Italiano, Carlos Gomez-Roca, Simon Lord, Chang-Fang Chiu, Sherene Loi, Victor Moreno, Kohei Shitara, Cristina Saura, Marloes van Dongen, Salvatore Siena, Giuseppe Curigliano, Sharareh Monemi, Sharmeen Hassan, Michelle Wilhite, Emiko Gale, Zao Li, Zhaojun Yin, Chunze Li, Luciana Molinero, Kelly DuPree, Teemu Junttila, Aditi Qamra, Lina Alon, Iris T. Chan, Kyung Hae Jung. Phase 1a/b study of runimotamab, a HER2 x CD3 T cell-engaging bispecific antibody, administered as a single agent and in combination with trastuzumab in patients with HER2-expressing breast cancer (BC) [abstract]. In: Proceedings of the American Association for Cancer Research Annual Meeting 2025; Part 2 (Late-Breaking, Clinical Trial, and Invited Abstracts); 2025 Apr 25-30; Chicago, IL. Philadelphia (PA): AACR; Cancer Res 2025;85(8_Suppl_2):Abstract nr CT204.

Skip to Main Content

View Metrics

PI3K Inhibitor Delays Chemotherapy Start

Drug Combo Boosts Lung Cancer Survival

Genentech, Orionis to Stick Together with Deal on Glues

View more recent articles ›

Research Watch

Ferroptosis Is Induced by Lysosomal Iron Activation in Cancer Cells

Common Blood Tests Predict CAR T-cell Therapy Response in Non-Hodgkin Lymphoma

Frequent Blood Donation Influences DNMT3A-Driven Clonal Hematopoiesis

View more recent articles ›

Online ISSN 1538-7445 **Print ISSN** 0008-5472

Molecular Cancer Therapeutics