

2095MO Pembrolizumab and trastuzumab in combination with FLOT in the perioperative treatment of HER2-positive localized esophagogastric adenocarcinoma: Interim analysis of the phase II PHERFLOT/IKF-053 trial of the AIO study group (AIO STO 0321)

E. Goekkurt¹, A. Stein¹, S-E. Al-Batran², N. Moosmann³, T.J. Ettrich⁴, T.O. Goetze⁵, C.B. Grün⁶, N. Homann⁷, S. Lorenzen⁸, R.D. Hofheinz⁹, V. Rempel¹⁰, G.M. Siegler¹¹, C. Müller¹², T.S. Broering¹³, M. Santos Cruz¹³, C. Pauligk¹⁴, M. Binder¹⁵, J. Tintelnot¹³

¹ Oncology Department, Hematology-Oncology Practice Eppendorf (HOPE), Hamburg, Germany, ² Institute of Clinical Cancer Research, Nordwest-Krankenhaus, Frankfurt am Main, Germany, ³ Oncology, Barmherzige Brüder Krankenhaus Regensburg, Regensburg, Germany, ⁴ Department of Internal Medicine I, University Hospital of Ulm - Oberer Eselsberg, Ulm, Germany, ⁵ Oncology Department, IKF - Institut für Klinische Krebsforschung GmbH, Frankfurt am Main, Germany, ⁶ Medical Oncology, German Cancer Research Center - National Center for Tumor Diseases (NCT), Heidelberg, Germany, ⁷ Medical Oncology, Klinikum Wolfsburg, Wolfsburg, Germany, ⁸ Hematology and Oncology Dept., Klinikum Rechts der Isar - Technische Universität München, Munich, Germany, ⁹ Interdisciplinary Tumor Center, UMM - Universitätsklinikum Mannheim, Mannheim, Germany, ¹⁰ Oncology, St. Anna Hospital Herne, Herne, Germany, ¹¹ Medizinische Klinik 5 Abteilung, Klinikum Nuernberg Paracelsus Medical University, Nuernberg, Germany, ¹² Klinik für Internistische Onkologie mit Integrierter Palliativmedizin, KEM | Evang. Kliniken Essen-Mitte gGmbH, Essen, Germany, ¹³ II. Department of Medicine, University Medical Center Hamburg-Eppendorf, Hamburg, Germany, ¹⁴ IKF - Institut für Klinische Krebsforschung GmbH, Frankfurt am Main, Germany ¹⁵ Medical Oncology, University Hospital Basel, Basel, Switzerland

Background

In advanced or metastatic HER2-positive esophagogastric adenocarcinoma (EGA), fluoropyrimidine-platinum chemotherapy with pembrolizumab (P) and trastuzumab (T) is standard of care. Perioperatively, FLOT (5-FU, leucovorin, oxaliplatin, docetaxel) is preferred in resectable HER2-positive disease. We evaluated adding P and T to perioperative FLOT in localized HER2-positive EGA.

Methods

PHERFLOT is an open-label, randomized, multicenter, exploratory phase II trial. Co-primary endpoints are 2-year disease-free survival rate and pathological complete response (pCR). Secondary endpoints include safety, progression-free survival, objective response rate, and translational biomarkers. This interim analysis reports baseline characteristics, pCR and safety as well as first translational analysis.

Results

From March 2023 – May 2024, 31 patients (pts) were enrolled; one declined surgery, and the remaining 30 underwent R0 resection. Median age 66 years; ECOG 0/1: 64.5/35.5%; GEJ: 77.4%; signet ring cells: 12.9%; grade 1/2/3/x: 12.9/41.9/38.7/6.5%; T1/2/3/4/x: 3.2/25.8/64.5/3.2/3.2%; N0/1/x: 32.3/58.1/9.7%; HER2 IHC 2+/3+: 19.4/80.6%; PD-L1 data (n=20): CPS ≥1 in 85% (n=17), CPS ≥10 in 50% (n=10). Of the resected pts, 70% had no postoperative complications. The pCR rate was 48.4% (n = 15/31), thereby meeting the co-primary endpoint. Pathologic subtotal response was observed in 19.4% (n = 6/31), resulting in an overall ≥ subtotal regression rate of 67.8% (n = 21/31). All pts experienced adverse events (AEs); 48.4% had at least one grade 3 treatment-related (TR) serious AE, predominantly chemotherapy-related; grade 4 neutropenia was the only ≥ grade 4 TRAE. Table: 2095MO

Pathological response	n (%)
Missing value due to withdrawal from surgery	1 (3.2%)
Complete Response (pCR) - no tumor cells visible, but signs of regression	15 (48.4%)
Subtotal Response (pSR) - morphologically intact neoplastic cells in <10% of tumor bed	6 (19.4%)
Partial Response (pPR) - morphologically intact neoplastic cells in 10 –50% of tumor bed	3 (9.7%)
Minor Response (pMR) - morphologically intact neoplastic cells in >50% of tumor bed	6 (19.4%)

Conclusions

Perioperative FLOT plus P and T is feasible, with an expected safety profile and strong antitumor activity, suggesting superiority over current standards.

Clinical trial identification

NCT05504720.

Legal entity responsible for the study

Institute of Clinical Cancer Research (IKF Frankfurt).

Funding

MSD Sharp & Dohme GmbH.

Disclosure

E. Goekkurt: Financial Interests, Institutional, Advisory Board: MSD, BMS, Daiichi, Servier; Financial Interests, Institutional, Local PI: msd, Daiichi, AstraZeneca, BMS, Novartis. A. Stein: Financial Interests, Institutional, Advisory Board: BMS, MSD, Amgen, Merck, Takeda, Daiichi Sankyo, Roche, BeiGene, Servier, Taiho; Financial Interests, Institutional, Writing Engagement: Daiichi Sankyo, BMS; Financial Interests, Institutional, Research Grant: BMS, MSD, Servier, German Cancer Aid, Pierre Fabre, Merck, BeiGene, Takeda; Financial Interests, Institutional, Steering Committee Member: Novartis; Non-Financial Interests, Member: DGHO, ASCO. S. Al-Batran: Financial Interests, Personal, Advisory Board: Bristol Myers Squibb, Lilly, MSD Sharp & Dohme; Financial Interests, Personal, Speaker, Consultant, Advisor: MCI Deutschland GmbH; Financial Interests, Personal, Ownership Interest, CEO: Institut für Klinische Krebsforschung IKF GmbH; Financial Interests, Institutional, Research Grant: AstraZeneca, Bristol Myers Squibb, Celgene, Eurozyto, Federal Ministry of Education and Research, German Cancer Aid (Krebshilfe), German Research Foundation, Immutep, Ipsen, Lilly, MSD Sharp & Dohme, Roche, Sanofi. T.O. Goetze: Financial Interests, Personal, Invited Speaker: Lilly, Servier; Financial Interests, Personal, Advisory Board: MSD Oncology, Bayer, Roche, BMS, Sanofi, Jazz Pharmaceuticals, Amgen; Financial Interests, Personal and Institutional, Funding, Reserach grant: Deutsche Forschungsgemeinschaft (DFG); Financial Interests, Personal and Institutional, Funding, Research Grant: Gemeinsamer Bundesausschuss, Deutsche Krebshilfe, Lilly, AstraZeneca; Financial Interests, Personal and Institutional, Funding: Incyte, Taiho Oncology, Servier. S. Lorenzen: Financial Interests, Personal, Invited Speaker: Servier, Lilly, MSD, BMS, AstraZeneca; Financial Interests, Personal, Advisory Board: Astellas. R.D. Hofheinz: Financial Interests, Personal, Advisory Board: Amgen, BMS, MSD, Sanofi, Roche, AstraZeneca, Lilly, Roche, Merck, Daichi, Nordic Pharma, AbbVie, BeiGene, Takeda, WALA, Servier, GSK, Pierre Fabre, Onkowissen. G.M. Siegler: Financial Interests, Personal, Other: Aurikamed, AstraZeneca, Servier, Ipsen, Janssen, MCI Deutschland, Meet the Experts Academy, Astellas Pharma, Amgen; Financial Interests, Personal, Officer: Deutsche Röntgengesellschaft; Financial Interests, Personal, Advisory Board: Novartis, Merck, Amgen, MSD Oncology, Roche, Servier. All other authors have declared no conflicts of interest.

© European Society for Medical Oncology