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FOLFIRI plus ramucirumab versus paclitaxel plus ramucirumab as second-line therapy for taxane-pretreated patients with advanced or metastatic gastroesophageal adenocarcinoma—Final results of the phase III IKFs602/AIO RAMIRIS Study

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Background

Ramucirumab (Ram) as monotherapy or plus paclitaxel is approved as 2nd-line treatment for advanced gastroesophageal adenocarcinoma (GEA). Many patients (pts) are pretreated with a taxane in previous lines, these may benefit from a non-cross resistant chemotherapy backbone regimen which was indicated by results from the phase II part of this trial.

Methods

This is an international, randomized, investigator initiated, phase II/III trial. Taxane-pretreated pts with GEA who have progressed after a fluoropyrimidine/platinum-containing regimen were randomized 1:1 to either FOLFIRI plus Ram q2w (Arm A) or paclitaxel (d 1, 8, 15 q28d) plus Ram q2w (Arm B). Co-primary endpoints were overall survival (OS) and objective overall response rate (ORR), further endpoints included DCR, PFS, quality of life and safety. Efficacy was assessed in the intention-to-treat (ITT) population.

Results

319 pts were enrolled between 2019 and 2024 and 317 analyzed within ITT (Arm A, 158; Arm B, 159; median age 60 years, 76% male). There was no significant difference in median OS (A, 8.7 vs. B, 7.5 mo, HR 0.95, p=.33, median FU A, 52, B, 31 mo) and ORR (A, 25.3% vs. B, 22.6%, p=.29). Median PFS was longer in Arm A with 5.5 vs. B, 3.7 mo (HR 0.7, p=.003) and DCR was A, 64% and B, 61%. Combination of Ram and FOLFIRI was not associated with more grade 3-5 adverse events in Arm A vs. B (70% vs. 68% of safety population N=304). Most common grade 3/4 adverse events included neutropenia (A, 17%, B, 12%), hypertension (A, 10%, B, 8%), anemia (A, B, 6%), and lung infection (A, 3%, B, 6%). 47% of the pts in Arm A and 55% in Arm B had at least one serious adverse event.

Conclusions

The RAMIRIS trial demonstrated feasibility of the combination of FOLFIRI and Ram. The co-primary endpoints were not met, however, PFS was clearly improved and trends towards a benefit of Ram/FOLFIRI regarding all other efficacy endpoints were seen. These findings support the personalization of treatment decisions in pts with taxane-pretreated advanced GEA after failure of standard therapy. More data will be presented at the meeting.

Clinical trial identification

EU CT No. 2024-512934-14-00.

Legal entity responsible for the study

Frankfurter Institut für Klinische Krebsforschung IKF GmbH.

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Disclosure

S. Lorenzen: Financial Interests, Personal, Invited Speaker: Servier, Lilly, MSD, BMS, AstraZeneca, Jazz Pharmaceuticals; Financial Interests, Personal, Advisory Board: Astellas, Takeda. E. Goekkurt: Financial Interests, Institutional, Advisory Board: MSD, BMS, Daiichi, Servier; Financial Interests, Institutional, Local PI: MSD, Daiichi, AstraZeneca, BMS, Novartis. G. Stocker: Financial Interests, Personal, Advisory Board, Discussion latest results on upper GI Cancer: BMS; Financial Interests, Personal, Other, virtual Access to ASCO GI 2025: AstraZeneca; Financial Interests, Personal, Other, travel compensation ESMO GI 2024: Gilead; Non-Financial Interests, Member, regular Member: Deutsche Gesellschaft für Hamatologie und Onkologie, Arbeitsgemeinschaft für Internistische Onkologie (AIO), Deutsche Gesellschaft für Innere Medizin. M. Venerito: Financial Interests, Personal, Advisory Role: MSD, BMS, AstraZeneca, Amgen, Roche, Servier, Daiichi Sankyo, Sirtex. M.K. Scheck: Financial Interests, Personal, Advisory Role: AstraZeneca, Daiichi Sankyo; Financial Interests, Personal, Other: Lilly, BeiGene, Astellas; Financial Interests, Personal, Stocks/Shares: Merck. F. De Vita: Financial Interests, Personal, Advisory Role: Amgen, Merck KGaA, MSD, Roche, Servier, Lilly, Daiichi Sankyo, BMS. B. Grünberger: Financial Interests, Personal, Advisory Role: BMS, MSD, Eli Lilly, Roche, Bayer, Servier, AstraZeneca, Amgen, Daiichi Sankyo, Pierre Fabre, Incyte, Merck, Novartis, BeiOne, Takeda, Jazz Pharma. S. Al-Batran: Financial Interests, Personal, Advisory Board: Lilly, Bristol-Myers Squibb, MSD Sharp & Dohme; Financial Interests, Personal, Invited Speaker: MCI Deutschland GmbH; Financial Interests, Personal, Ownership Interest, CEO: Frankfurter Institut für Klinische Krebsforschung IKF GmbH; Financial Interests, Institutional, Research Grant: Sanofi, Roche, Celgene, Lilly, Eurozyto, Immutep, Ipsen, Bristol-Myers Squibb, MSD Sharp & Dohme, AstraZeneca, German Cancer Aid (Krebshilfe), German Research Foundation, Federal Ministry of Education and Research. All other authors have declared no conflicts of interest.

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