PARIS 2022 ESMO congress

LBA22

Phase III study with FOLFIRI/cetuximab versus FOLFIRI/cetuximab followed by cetuximab (Cet) alone in first-line therapy of RAS and BRAF wild-type (wt) metastatic colorectal cancer (mCRC) patients: The ERMES study

C. Pinto[1], A. Orlandi[2], N. Normanno[3], E. Maiello[4], M.A. Calegari[5], L. Antonuzzo[6], R. Bordonaro[7], M.G. Zampino[8], S. Pini[9], F. Bergamo[10], G. Tonini[11], A. Avallone[12], T.P. Latiano[13], G. Rosati[14], A. Pazzola[15], A. Ballestrero[16], A. Zaniboni[17], M. Roselli[18], S. Tamberi[19], C.A. Barone[2]

[1] Medical Oncology, Clinical Cancer Centre Azienda USL – IRCCS di Reggio Emilia, Reggio Emilia, Italy, [2] UOC di Oncologia Medica, Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Rome, Italy, [3] Translational Research Dept., Istituto Nazionale Tumori IRCCS - Fondazione G. Pascale, Naples, Italy, [4] Oncology, IRCCS Fondazione Casa Sollievo della Sofferenza, San Giovanni Rotondo, Italy, [5] Medical Oncology, Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Rome, Italy, [6] Clinical Oncology Unit, Careggi University Hospital, and Department of Experimental and Clinical Medicine, University of Florence, Florence, Italy, [7] Oncology Department, Azienda Ospedaliera ARNAS Garibaldi, Catania, Italy, [8] Medical Oncology Department, IEO - Istituto Europeo di Oncologia, Milan, Italy, [9] Oncologia, Opsedale degli Infermi - AUSL Romagna, Faenza, Italy, [10] Dipartimento Oncologia 1, IOV - Istituto Oncologico Veneto IRCCS, Padua, Italy, [11] Medical Oncology, Policlinico Universitario Campus Bio-Medico, Rome, Italy, [12] Medical Onology, Istituto Nazionale Tumori-IRCCS Fondazione G. Pascale, Naples, Italy, [13] Oncology Dept, Fondazione IRCCS Casa Sollievo della Sofferenza, San Giovanni Rotondo, Italy, [14] Medical Oncology, Ospedale San Carlo, Potenza, Italy, [15] Medical Oncology, Oncologia Universitaria Sassari, Sassari, Italy, [16] Medical Oncology, Università degli Studi di Genova e Ospedale Policlinico San Martino IRCCS - DiMI, Genoa, Italy, [17] Medical Oncology Unit, Fondazione Poliambulanza, Brescia, Italy, [18] Medical Oncology, Policlinico Tor Vergata, Rome, Italy[19] Medical Oncology, Opsedale degli Infermi - AUSL Romagna, Faenza, Italy

Background

The optimal intensity of anti-EGFR-based first line therapy for *RAS/BRAF* wt mCRC once achieved disease control is controversial. A maintenance strategy with anti-EGFR monotherapy could be a valuable option to preserve efficacy while sparing toxicity.

Methods

Patients with untreated *RAS/BRAF* wt mCRC were randomly assigned (1:1) to receive either FOLFIRI/Cet until PD/toxicity (arm A) or FOLFIRI/Cet for 8 cycles followed by Cet alone (arm B). Co-primary endpoints were non-inferior PFS in the modified per-protocol (mPP) population (pts treated beyond cycle 8) and lower incidence of grade (G) ≥3 AEs for arm B compared to arm A. To test non-inferiority 386 events were needed, and the upper HR boundary was set at 1.33. Secondary endpoints were PFS in the intent to treatment (ITT) population (pts who received at least one dose), OS in mPP and ITT, ORR and QoL. Translational analyses on tissue sample and liquid biopsies were planned.

Results

From May 2015 to March 2020, 606 pts were randomized: 300 assigned to arm A and 306 to arm B. Median FU was 22.3 (15-33.8) months (m). Drop-out rate was around 40%. In the mPP population (arm B 183/arm A 154) 291 events occurred with mPFS of 10 *vs* 12.2 m for arm B and A, respectively (HR 1.3, 95%CI 1.03-1.64; p 0.43). In the ITT population (arm B 297/arm A 296) 503 events occurred with mPFS of 9 *vs* 10.7 m (HR 1.1, 95%CI 0.92-1.31; p 0.39). mOS was 36.6 *vs* 30.7 m (HR 0.81, 95%CI 0.6-1.09; p 0.22) and 31 *vs* 25.3 m (HR 0.9, 95%CI 0.72-1.12; p 0.32) in the mPP and ITT population, respectively. G ≥3 AEs were lower in arm B compared to arm A (39.9 *vs* 44.2%): neutropenia (9.8/14.9%), febrile neutropenia (2.7/5.2%), diarrhea (8.2/11%), oral mucositis (1.6/5.2%), fatigue (0.6/4.6%) and skin disorders (18/20.1%).

Conclusions

The ERMES study does not demonstrate non-inferiority of maintenance with Cet alone. The higher-than-expected drop-out rate and subsequent reduced statistical power might have impaired the results. The ITT analysis and OS results are suggestive for a strategy of de-escalation treatment with only cetuximab. Ongoing translational analyses might allow to select pts benefitting from de-escalation strategy.

Clinical trial identification

NCT02484833.

Legal entity responsible for the study

Fondazione Policlinico Universitario Agostino Gemelli, IRCCS, Rome.

Funding

Merck Serono S.p.A., Rome, Italy, an affiliate of Merck KGaA (CrossRef Funder ID: 10.13039/100009945).

Disclosure

C. Pinto: Non-Financial Interests, Personal, Funding: Lilly; Financial Interests, Personal, Funding: Bayer, BMS, Ipsen, AstraZeneca, Merck. A. Orlandi: Financial Interests, Personal and Institutional, Funding: MERCK; Financial Interests, Personal, Invited Speaker: Novartis, Lilly, Amgen; Financial Interests, Personal, Speaker's Bureau: Pfizer; Financial Interests, Personal, Advisory Board: Daiichi Sankio. L. Antonuzzo: Financial Interests, Personal, Advisory Board: Merck. All other authors have declared no conflicts of interest.