O-10 ANCHOR CRC: Results from a single-arm, phase 2 study of encorafenib, binimetinib plus cetuximab in previously untreated BRAF V600E–mutant metastatic colorectal cancer

E. Van Cutsem[1], J. Taieb[2], R. Yaeger[3], T. Yoshino[4], E. Maiello[5], E. Elez[6], J. Dekervel[7], P. Ross[8], A. Ruiz Casado[9], J. Graham[10], T. Kato[11], J. Ruffinelli[12], T. André[13], E. Carriere Roussel[14], I. Klauck[14], M. Groc[14], A. Grothey[15], J. Vedovato[14], J. Tabernero[16]

[1]Department of Digestive Oncology, University Hospitals Leuven and KU Leuven, Leuven, Belgium; [2]Hôpital Europeen Georges Pompidou, APHP, Université de Paris, CARPEM Cancer Institute, Paris, France; [3]Memorial Sloan-Kettering Cancer Center, New York, United States; [4]National Cancer Center Hospital East, Kashiwa, Japan; [5]Oncology Unit, Foundation IRCCS Casa Sollievo della Sofferenza, San Giovanni Rotondo, Italy; [6]Department of Medical Oncology, Vall d'Hebron University Hospital, Vall d'Hebron Institute of Oncology, Barcelona, Spain; [7]University Hospital Gasthuisberg, Leuven and KU Leuven, Leuven, Belgium; [8]Guy's and St Thomas' NHS Foundation Trust, London, United Kingdom; [9]Puerta de Hierro University Hospital, Majadahonda, Spain; [10]Beatson West of Scotland Cancer Centre, Glasgow, United Kingdom; [11]Department of Surgery, National Hospital Organization, Osaka National Hospital, Osaka, Japan; [12]Catalan Institute of Oncology, Hospital Duran i Reynals, Barcelona, Spain; [13]Hôpital Saint Antoine, Assistance Publique Hôpitaux de Paris and Sorbonne Université, Paris, France; [14]Pierre Fabre Laboratories, Boulogne Billancourt, France; [15]West Cancer Center, OneOncology, Germantown, United States; [16]Vall d'Hebron University Hospital and Vall d'Hebron Institute of Oncology (VHIO), Barcelona, Spain

Background: BRAFV600E mutations are identified in 8-15% of metastatic colorectal cancer (mCRC) patients and confer a poor prognosis. The ANCHOR CRC study was designed to investigate the triplet combination of encorafenib (ENCO) + binimetinib (BINI) + cetuximab (CETUX) in the first-line setting of this population. Preliminary results reported a high confirmed objective response rate (50%) in the first 41 patients (stage 1) with a median PFS of 5 months. Having reached the minimal number of confirmed responses, the interim analysis for futility allowed continued enrolment of patients in stage 2. Results of stage 1 and stage 2 combined are presented here.

Methods: ANCHOR CRC is an open-label, single-arm, two-stage design, phase 2 study in patients with BRAFV600E-mutant mCRC who did not receive any prior systemic therapy for metastatic disease. Patients received ENCO 300 mg orally QD + BINI 45 mg orally BID and CETUX IV weekly (250mg/m 2 after a first dose of 400mg/m 2) for the first 28 weeks and then once every two weeks (500mg/m 2). In stage 2, 50 additional subjects were planned to be enrolled, for a total of 90 subjects with a centrally confirmed BRAFV600E mutation. The primary endpoint was confirmed Objective Response Rate (cORR) based on local review; other endpoints included disease control rate (DCR), progression-free survival (PFS), overall survival (OS) and safety. Results from analysis at the end of stage 2 are presented here.

Results: Ninety-five BRAFV600E-mutant mCRC patients with a median age of 65 years old (13% $\geq$ 75 years old) were enrolled and received the triplet combination as first line metastatic treatment. At study entry, 55% of patients presented with ECOG PS 1, 76% had metastases to at least 2 organs, 48% had peritoneal metastasis, 55% had synchronous metastases and 19% had received prior adjuvant systemic treatment. Ninety-two patients were evaluable for efficacy. Investigator assessed cORR was 47.8% (95% confidence interval [CI],37.3-58.5) and DCR was 88%. Median PFS was 5.8 months (95% CI, 4.6-6.4). Median OS was 17.2 months (95% CI, 14.1-NE) with only 28.4% patients having a death event. Grade 3 or higher adverse events were seen in 69.5% of patients, most commonly in $\geq$ 5% of patients: anemia (10.5%), diarrhea (9.5%), nausea (8.4%), large intestinal obstruction (6.3%), and acute kidney injury (5.3%). No new safety signals were seen.

Conclusions: The ANCHOR CRC study is the first prospective study using a BRAF inhibitor-based therapy in first-line BRAFV600E-mutant mCRC. Despite the high-risk features of the population enrolled in this study, almost half of the patients responded and most had disease control, with a median PFS of 5.8 months and a median OS of 17.2 months. The safety profile was acceptable and toxicities remained manageable.

Clinical trial identification: NCT03693170.

Legal entity responsible for the study: Pierre Fabre Medicament.

Funding: The study was funded by Pierre Fabre Medicament.

Disclosure: E. Van Cutsem: Advisory / Consultancy: Array, Astellas, AstraZeneca, Bayer, Beigene, Biocartis, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Daiichi, Halozyme, GSK, Incyte, Ipsen, Lilly, Merck Sharp & Dohme, Merck KGaA, Novartis, Pierre Fabre, Roche, Servier, Sirtex, Taiho; Research grant / Funding (institution): Amgen, Bayer, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Ipsen, Lilly, Merck Sharp & Dohme, Merck KGaA, Novartis, Roche, Servier. J. Tabernero: Honoraria (self): educational collaboration with Imedex, Medscape Education, MJH Life Sciences, PeerView Institute for Medical Education and Physicians Education Resource (PER); Advisory / Consultancy: Array Biopharma, AstraZeneca, Avvinity, Bayer, Boehringer Ingelheim, Chugai, Daiichi Sankyo, F. Hoffmann-La Roche Ltd, Genentech Inc, HalioDX SAS, Hutchison MediPharma International, Ikena Oncology, IQVIA, Lilly, Menarini, Merck Serono, Merus, MSD, Mirati, Neophore, Novartis, Orion Biotechnology, Peptomyc, Pfizer, Pierre Fabre, Samsung Bioepis, Sanofi, Seattle Genetics, Servier, Taiho, Tessa Therapeutics and TheraMyc. R. Yaeger: Advisory / Consultancy: Natera; Research grant / Funding (institution): Pfizer, Mirati Therapeutics, Boehringer Ingelheim. T. Yoshino: Honoraria (self): Bayer, Chugai, Taiho, Eli Lilly, Merck Biopharma; Research grant / Funding (institution): Daiichi Sankyo, MSD, Ono, Parexel International, Taiho, Amgen. T. Kato: Honoraria (self): Chugai Pharmaceutical Co., Ltd., ONO Pharmaceutical Co, Eli Lilly and Company; Honoraria (Institution): Chugai Pharmaceutical Co., Ltd.; Research grant / Funding (self): ONO Pharmaceutical Co; Research grant / Funding (institution): ONO Pharmaceutical Co. T. André: Honoraria (self): BMS, MSD Oncology, GSK; Advisory / Consultancy: BMS, MSD Oncology, GSK; Research grant / Funding (institution): BMS, MSD Oncology, GSK; Travel / Accommodation / Expenses: BMS, MSD Oncology. All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2021.05.014