

788R0

Encorafenib plus cetuximab (EC) beyond progression in combination with FOLFIRI in BRAF V600E metastatic colorectal cancer (mCRC) patients (pts) progressing on EC: Results from the ECLYPse phase II trial

M.A. Calegari¹, L. Salvatore², M. Basso¹, G. Trovato¹, G. Caira¹, L. Di Francesco², A. Cosmai², M. Prisciandaro³, D. Giannarelli⁴, L. Giannone¹, M. Ventola¹, C. Barbagallo², A. Spring², F. Schietroma², R. Fazio³, M. Bensi², C. Pozzo¹, F. Morano³, G. Tortora²

¹ Department of Medical Oncology, Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Rome, Italy, ² Medical Oncology, Università Cattolica del Sacro Cuore, Comprehensive Cancer Center, Fondazione Policlinico Universitario Agostino Gemelli, IRCCS Rome, Rome, Italy, ³ Department of Medical Oncology, Fondazione IRCCS - Istituto Nazionale dei Tumori, Milan, Italy ⁴ Biostatistics, Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Rome, Italy

Background

There is an unmet need for effective treatments in pts with *BRAF* V600E mCRC progressing on targeted therapy. ECLYPse was designed to address this issue based on two key premises: first, the hypothesis that due to intratumoral heterogeneity at progression, a disease subset may remain sensitive to EC; and second, the evidence of a synergistic activity of targeted agents in combination with chemotherapy (Cht) in first-line setting.

Methods

ECLYPse (NCT06640166) is a multicenter, single-arm, phase II study evaluating EC continuation beyond progression (E 300 mg daily, C 500mg/m² i.v. every 2 weeks) in combination with FOLFIRI in pts with *BRAF* V600E mCRC progressing on second-line EC. The primary endpoint was investigator-assessed 6-month PFS rate in the ITT population. The study design (single-stage, $\alpha=0.05$, 80% power) required enrolling 25 patients and observing ≥ 7 patients alive without progression at 6 months to reject the null hypothesis (H_0 : 6-month PFS $\leq 10\%$). Secondary endpoints included OS and safety.

Results

Between June 12, 2024 and April 15, 2026, 25 patients were enrolled. Main pts' characteristics were: men 68%, median age 65 yrs (range 37–84 yrs), ECOG PS 0 68%, right-sided primary tumor 64%, synchronous metastases 72%, peritoneal metastases 64%, liver metastases 64%, pMMR tumor 92%. As of May 8, 2026, with a median follow-up of 7.6 months, 14 disease progression events were observed. The investigator-assessed 6-month PFS rate was 69.5% (95% CI, 51.7–93.6%), and the mPFS was 7.1 months (95% CI, 6.2–NE months). Median OS was not reached; 6- and 12-month OS rates were 94.1% (95% CI, 83.6–100%) and 83.7% (95% CI, 64.5–100%), respectively. No new safety signal were observed, with adverse events occurring with the expected frequency and grade.

Conclusions

ECLYPse met its primary endpoint, with about two-thirds of the pts progression-free at 6 months. Continuing EC beyond progression on second-line plus Cht appears to extend disease control in this poor-prognosis population. These findings may serve as a pathfinder to guide future research in the post-BREKWATER era and help identify the optimal therapeutic strategy.

Clinical trial identification

EU CT Number: 2023-508615-24-00; NCT06640166.

Legal entity responsible for the study

Fondazione Policlinico Universitario Agostino Gemelli, IRCCS.

Funding

Pierre Fabre Italy.

Disclosure

M.A. Calegari: Financial Interests, Personal, Invited Speaker: Merck, Amgen, Takeda, Bayer, Pierre Fabre, Servier; Financial Interests, Institutional, Funding: Pierre Fabre. L. Salvatore: Financial Interests, Personal, Advisory Board: Takeda, Pierre Fabre, GSK, Servier, Bayer,

MSD, Amgen, Merck, Leopharma; Financial Interests, Personal, Invited Speaker: Takeda, Pierre Fabre, Servier, Bayer, MSD, Incyte, AstraZeneca, Amgen, Merck, GSK; Financial Interests, Personal, Other, Advisory board: Incyte, Nordic Pharma; Financial Interests, Personal, Other, advisory board: AstraZeneca; Financial Interests, Institutional, Local PI: Amgen; Financial Interests, Institutional, Funding: Merck. C. Pozzo: Financial Interests, Personal, Invited Speaker, Internal training courses: Servier; Financial Interests, Personal, Advisory Board: Astellas, Merck Serono, Lilly, Daiichi Sankyo, Amgen, Italfarmaco; Financial Interests, Institutional, Local PI: Amgen, Astellas; Non-Financial Interests, Personal, Other, AI Training: Medicorp. G. Tortora: Financial Interests, Personal, Advisory Board: BMS, AstraZeneca, MSD, Merck, Servier. All other authors have declared no conflicts of interest.

© *European Society for Medical Oncology*