VIRTUAL ESMO congress 2020

LBA68

Results of the randomized, placebo (PL)-controlled phase II study evaluating the efficacy and safety of regorafenib (REG) in patients (pts) with metastatic relapsed Ewing sarcoma (ES), on behalf of the French Sarcoma Group (FSG) and UNICANCER

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Background

REGOBONE is non-comparative phase II, double-blind, PL-controlled trial designed to evaluate the activity and safety of REG, in 5 independent cohorts of sarcoma originating in bone. We report here the ES cohort results.

Methods

Key-eligibility criteria were histologically confirmed diagnosis of bone ES, age ≥10 years, confirmed measurable PD not amenable to curative-intent, 1-2 previous chemotherapy (CT) regimens for metastatic disease, ECOG 0-1. Eligible ES pts were randomized (2:1) to receive either REG (160 mg/d, 21/28 d) or matched PL with optional cross-over at the time of centrally confirmed progressive disease (PD). 24 pts were planned in the REG arm based on a A'Hern's single-stage design for phase II trials (1-sided α=0.05, and 80% power) to detect a 27% improvement in the progression-free rate (PFR) at 8 weeks (P_0=40%) as evaluated by central review per RECIST1.1. Secondary endpoints included PFS, OS and safety.

Results

From September 2014 to November 2019, 41 ES pts were included. Five pts were not eligible for efficacy analysis. Of 36 efficacy-evaluable pts (13 in PL arm and 23 in REG arm); 28 were men, median age was 32 (16-59) years. 13/23 pts in REG arm (56.5%; one-sided CI95% = [37.5-[) were non-progressive at 8 weeks vs. 1/13 pts in PL arm (7.7%; CI95% = [0.4-[). Median PFS was 11.4 (CI95% = 4.6-22.9) vs. 3.9 (CI95%= 3.3-7.3) weeks for REG and PL arms, respectively. 5 (21.7%) partial responses were observed on REG. Median OS was 34.9 (CI95%=17.6-58.7) and 30.4 (CI95%=10.0-NE) weeks for REG and PL arms, respectively. Ten out of 13 pts crossed-over to REG after centrally-confirmed PD on PL. The most common ≥ Gr3 REG-related AEs during the double blind period were diarrhea (13%), hand-foot skin reaction (13%), asthenia (9%), thrombocytopenia (9%), mucosal inflammation (9%) and febrile neutropenia (9%), with one toxic death due to thrombocytopenia.

Conclusions

Despite a PFR at 8 weeks lower than expected, this randomized non comparative study shows a promising signal of benefit of REG in relapsed ES, with a median of PFS of 11.4 weeks, and a moderate toxicity.

Clinical trial identification

EudraCT: 2013-003910-42; NCT02389244.

Legal entity responsible for the study

UNICANCER.

Funding

Bayer.

Disclosure

F. Duffaud: Advisory/Consultancy: Bayer; Travel/Accommodation/Expenses: Leo Pharma; Travel/Accommodation/Expenses: PharmaMar. J-Y. Blay: Honoraria (institution), Advisory/Consultancy: Bayer. O. Mir: Honoraria (self): Amgen; Honoraria (self), Honoraria (institution): Astra-Zeneca; Honoraria (self), Research grant/Funding (institution): Bayer; Honoraria (self): Bristol Myers-Squibb; Honoraria (self), Speaker Bureau/Expert testimony, Research grant/Funding (institution): Eli-Lilly; Honoraria (self), Honoraria (institution), Advisory/Consultancy, Shareholder/Stockholder/Stock options: Ipsen; Honoraria (self): Lundbeck; Honoraria (self): MSD; Honoraria (self), Honoraria (institution): Novartis; Honoraria (self), Honoraria (institution), Speaker Bureau/Expert testimony, Travel/Accommodation/Expenses: Pfizer; Honoraria (self), Honoraria (institution), Speaker Bureau/Expert testimony, Travel/Accommodation/Expenses: Roche; Honoraria (self), Speaker Bureau/Expert testimony: Servier; Honoraria (self): Vifor pharma; Honoraria (institution), Advisory/Consultancy, Research grant/Funding (institution): Blueprint Medicines; Honoraria (institution): PharmaMar; Research grant/Funding (institution): Agios pharmaceutical; Research grant/Funding (institution): Epizyme; Travel/Accommodation/Expenses: Amgen; Shareholder/Stockholder/Stock options: Amplitude surgical; Shareholder/Stockholder/Stock options: Transgene. C.M. Chevreau: Honoraria (self), Advisory/Consultancy, Travel/Accommodation/Expenses: BMS; Honoraria (self), Advisory/Consultancy, Travel/Accommodation/Expenses: Ipsen; Honoraria (self), Advisory/Consultancy: Novartis. P. Boudou Rouquette: Advisory/Consultancy, Travel/Accommodation/Expenses: Takeda; Advisory/Consultancy: BMS; Travel/Accommodation/Expenses: PharmaMar. N. Penel: Research grant/Funding (institution): Bayer HealthCare. C. Perrin: Advisory/Consultancy, Travel/Accommodation/Expenses: Pfizer; Advisory/Consultancy, Travel/Accommodation/Expenses: Eisai; Travel/Accommodation/Expenses: Roche; Travel/Accommodation/Expenses: Daiichi; Travel/Accommodation/Expenses: Novartis. N. Gaspar: Advisory/Consultancy: Eisai; Advisory/Consultancy: Ipsen. All other authors have declared no conflicts of interest.