

LBA58

Results of the randomized, placebo (PL)-controlled phase II study evaluating the efficacy and safety of regorafenib (REGO) in patients (pts) with relapsed advanced or metastatic chordoma, on behalf of the French Sarcoma Group (FSG) and Unicancer

F. Duffaud¹, S. Chabaud², C.M. Chevreau³, A. Italiano⁴, C. Perrin⁵, N. Isambert⁶, S. Piperno-Neumann⁷, E. Saada-Bouzid⁸, F. Bertucci⁹, D. Cupissol¹⁰, E. Kalbacher¹¹, B. Narciso¹², C. Schiffler¹³, N. de Sousa Carvalho¹⁴, L. Monard¹⁵, C. Bouvier¹⁶, V. Vidal¹⁷, J-Y. Blay¹⁸, O. Mir¹⁹

¹ APHP Marseille, APHP Marseille, Marseille, France, ² Biostatistics and Therapeutics Evaluation Unit, Centre Léon Bérard, Lyon, France, ³ Oncology Department, Institut Universitaire du Cancer -Toulouse- Oncopole, Toulouse, Haute-Garonne, France, ⁴ Early Phase Trials Unit, Institute Bergonié, Bordeaux, France, ⁵ Medical Oncology, Centre Eugene Marquis, Rennes, France, ⁶ Oncologie 3, Centre Georges-François Leclerc (Dijon), Dijon, France, ⁷ Medecine, Institut Curie, Paris, France, ⁸ Medical Oncology, Centre Antoine Lacassagne, Nice, France, ⁹ Medecine, Institut Paoli Calmettes, Marseille, France, ¹⁰ Medecine, Institut du cancer de Montpellier, Montpellier, France, ¹¹ Medecine, Hôpital Jean Minoz, Besançon, France, ¹² Medical Oncology, Centre Hospitalier Universitaire de Tours, Tours, France, ¹³ Statistics, Centre Léon Bérard, Lyon, France, ¹⁴ Research and Development, Unicancer, Le Kremlin Bicetre, France, ¹⁵ UCGI, Unicancer, Paris, France, ¹⁶ Français Anglais Anatomopathology, APHM Hopital la Timone Adultes, Marseille, France, ¹⁷ Radiology, APHM Hopital la Timone Adultes, Marseille, France, ¹⁸ Medicine Department, Centre Léon Bérard, Lyon, France ¹⁹ Cancer Medicine Department, Institut Gustave Roussy, Villejuif, France

Background

REGOBONE is a non-comparative phase 2, double-blind, PL-controlled trial designed to evaluate the activity and safety of REGO, in 5 independent cohorts of sarcomas originating in bone. We report here the chordoma cohort results.

Methods

Eligibility criteria included histologically centrally confirmed diagnosis of chordoma, age ≥ 18 years, confirmed measurable progressive disease (PD) not amenable to curative-intent, with ≤ 2 prior lines of treatment, and ECOG 0-1. Eligible pts were randomized (2:1) to receive either REGO (160 mg/d, 21/28 d) or PL with optional cross-over at the time of centrally confirmed progressive disease (PD). 18 pts were planned in the REG arm to detect a 35% improvement (1-sided $\alpha=0.05$, and 80% power) in the Progression-Free Rate (PFR) at 6 months ($P_0=40\%$), by central review per RECIST1.1. Main secondary endpoints were PFS, Response Rate, OS and safety.

Results

From March 2016 to February 2020, 27 chordoma pts were enrolled. Of 23 efficacy-evaluable pts (7 in PL arm and 16 in REG arm); 16 were men, median age was 66 (32-85) years. At 6 months, in REGO arm; one pt was not evaluable, 6/15 were non-progressive (PFR: 40.0%; one-sided CI95% = [19.1-]), and 4/15 discontinued REGO due to toxicity; and in PL arm; 2/5 were non-progressive (PFR: 40.0%; CI95% = [7.6-]), 2 pts were non evaluable. Median PFS was 8.2 (CI95% = 4.5-12.9) vs. 10.1 (CI95%= 0.8-NE) months for REGO and PL arms respectively. Median OS was 28.3 months on REGO but not reached in PL arm. Four out of 7 pts crossed-over to REGO after centrally-confirmed PD on PL. Of the 25 safety-evaluable pts, the most common \geq Gr3 REGO-related AEs during the double blind period were hand-foot skin reaction (22%), hypertension (17%) and diarrhea (17%), with no toxic death.

Conclusions

This randomized non comparative study failed to show any signal of benefit for REGO in pts with advanced/metastatic incurable chordoma, with toxicities in REGO arm leading to early treatment discontinuation in this small group of patients.

Clinical trial identification

EudraCT 2013-003910-42; NCT02389244.

Legal entity responsible for the study

Unicancer.

Funding

Bayer.

Disclosure

F. Duffaud: Other, Attending oncology meetings: Léo Pharma; Other, Invited Speaker, Attending to meetings (ESMO and ASCO meetings): PharmaMar. C.M. Chevreau: Financial Interests, Personal, Advisory Board: Ipsen; Financial Interests, Personal, Advisory Board: BMS; Financial Interests, Personal, Advisory Board: LEO; Financial Interests, Personal, Advisory Board: MSD; Financial Interests, Institutional, Principal Investigator: MSD; Financial Interests, Institutional, Principal Investigator: Ipsen; Financial Interests, Institutional, Principal Investigator: Karyopharm; Financial Interests, Institutional, Principal Investigator: Exelisis. A. Italiano: Financial Interests, Personal, Advisory Board: Bayer; Financial Interests, Personal, Advisory Board: Chugai; Financial Interests, Personal, Advisory Board: GSK; Financial Interests, Personal, Advisory Board: Philips; Financial Interests, Personal, Advisory Board: Roche; Non-Financial Interests, Institutional, Principal Investigator: AstraZeneca; Non-Financial Interests, Institutional, Principal Investigator: Bayer; Non-Financial Interests, Institutional, Principal Investigator: Ipsen; Non-Financial Interests, Institutional, Principal Investigator: Merck; Non-Financial Interests, Institutional, Principal Investigator: MSD; Non-Financial Interests, Institutional, Principal Investigator: Roche. C. Perrin: Financial Interests, Personal, Advisory Board: Daiichi Sankyo; Financial Interests, Personal, Advisory Board: Pfizer; Non-Financial Interests, Personal, Invited Speaker: Novartis; Non-Financial Interests, Personal, Invited Speaker: Pfizer; Non-Financial Interests, Personal, Invited Speaker: Roche. S. Piperno-Neumann: Financial Interests, Personal, Advisory Board: Immunocore. E. Kalbacher: Financial Interests, Institutional, Advisory Role: GSK Tesaro; Financial Interests, Institutional, Advisory Role: AstraZeneca; Financial Interests, Institutional, Advisory Role: Pharmamar; Financial Interests, Institutional, Advisory Role: Roche; Financial Interests, Institutional, Advisory Role: Leopharma; Financial Interests, Institutional, Advisory Role: Bayer; Financial Interests, Institutional, Advisory Role: Sanofi. J. Blay: Financial Interests, Personal, Leadership Role, Supervisory Board: Innate Pharma; Financial Interests, Personal, Other, Honoraria: Bayer; Financial Interests, Personal, Other, Honoraria: Roche; Financial Interests, Personal, Other, Honoraria: Novartis; Financial Interests, Personal, Other, Honoraria: Deciphera; Financial Interests, Personal, Other, Honoraria: Pfizer; Financial Interests, Institutional, Other, Honoraria: Novartis; Financial Interests, Institutional, Other, Honoraria: Bayer; Financial Interests, Institutional, Other, Honoraria: Pfizer; Financial Interests, Institutional, Other, Honoraria: Deciphar; Financial Interests, Institutional, Other, Honoraria: Roche; Financial Interests, Personal, Advisory Role: Novartis; Financial Interests, Personal, Advisory Role: GSK; Financial Interests, Personal, Advisory Role: Bayer; Financial Interests, Personal, Advisory Role: Pfizer; Financial Interests, Personal, Advisory Role: Deciphera; Financial Interests, Personal, Advisory Role: Roche; Financial Interests, Personal, Advisory Role: BMS; Financial Interests, Personal, Advisory Role: MSD; Financial Interests, Personal, Advisory Role: AstraZeneca; Financial Interests, Institutional, Research Grant: Novartis; Financial Interests, Institutional, Research Grant: Bayer; Financial Interests, Institutional, Research Grant: GSK; Financial Interests, Institutional, Research Grant: Pfizer; Financial Interests, Institutional, Research Grant: Deciphera; Financial Interests, Institutional, Research Grant: Roche; Financial Interests, Institutional, Research Grant: BMS; Financial Interests, Institutional, Research Grant: MSD; Financial Interests, Institutional, Research Grant: AstraZeneca; Non-Financial Interests, Personal, Research Grant, Medical writing: F Hoffmann-La Roche Ltd. O. Mir: Financial Interests, Personal, Advisory Board: Bayer; Financial Interests, Personal, Advisory Board: Blueprint Medicines; Financial Interests, Personal, Invited Speaker: BMS; Financial Interests, Personal, Invited Speaker: Eli-Lilly; Financial Interests, Personal, Advisory Board: MSD; Financial Interests, Personal, Advisory Board: Pfizer; Financial Interests, Personal, Invited Speaker: Roche; Financial Interests, Personal, Invited Speaker: Servier; Financial Interests, Institutional, Other, Local PI: Bayer; Financial Interests, Institutional, Other, Local PI: Blueprint Medicines; Financial Interests, Institutional, Other, Local PI: Eli Lilly; Financial Interests, Institutional, Other, Local PI: Epizyme. All other authors have declared no conflicts of interest.

© European Society for Medical Oncology