

Real-world dosing of regorafenib in patients with unresectable hepatocellular carcinoma (uHCC): Final analysis of the prospective, observational REFINE study.

Richard S. Finn, Philippe Merle, Masafumi Ikeda, Heinz-Josef Klumpen, Gianluca Masi, Alessandro Granito, Ho Yeong Lim, Masatoshi Kudo, Shukui Qin, René Gerolami, Yi-Hsiang Huang, Do Young Kim, Matthias Pinter, Naoya Kato, Masayuki Kurosaki, Kazushi Numata, Javeed Khan, Kirhan Ozgurdal, Yoon Jun Kim; David Geffen School of Medicine at UCLA, UCLA Medical Center, Los Angeles, CA; Groupement Hospitalier Lyon Nord, Hepatology Unit, Lyon, France; National Cancer Center Hospital East, Kashiwa, Japan; Amsterdam University Medical Centers, University of Amsterdam, Amsterdam, Netherlands; Azienda Ospedaliera-Universitaria Pisana, Pisa, Italy; University of Bologna, Bologna, Italy; Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, South Korea; Kindai University Faculty of Medicine, Osaka, Japan; Chinese People's Liberation Army Cancer Center of Nanjing Bai Hospital, Nanjing, China; CHU La Timone, Marseille, France; Division of Gastroenterology and Hepatology, Taipei Veterans General Hospital, Taipei, Taiwan; Severance Hospital, Seoul, South Korea; Medical University of Vienna, Vienna, Austria; Chiba University Hospital, Chiba, Japan; Musashino Red Cross Hospital, Tokyo, Japan; Yokohama City University Medical Center, Yokohama, Japan; Bayer plc, Reading, United Kingdom; Bayer Consumer Care AG, Basel, Switzerland; Seoul National University Hospital, Seoul, South Korea

Background: Final results from the real-world REFINE study confirmed the safety and effectiveness of regorafenib (REG) in a broad population of patients (pts) with uHCC that was consistent with the results from RESORCE, in which REG prolonged overall survival (OS) vs placebo in pts with uHCC who progressed on prior sorafenib. Here we evaluate baseline characteristics and outcomes according to the initial REG dose. **Methods:** REFINE (NCT03289273), an international, prospective, multicenter study, enrolled pts with uHCC for whom a decision to treat with REG was made by the treating physician prior to enrollment according to the local health authority approved label (160 mg/day, 3 weeks on/1 week off). The primary objective was safety (NCI-CTCAE v4.03); secondary endpoints included OS and progression-free survival (PFS). **Results:** Of 1005 pts eligible for analysis, 47%, 11%, 40%, and 3% initiated REG at 160 mg, 120 mg, 80 mg, and 40 mg, respectively. A higher proportion of pts from Asia initiated REG at 160 mg (51%) vs non-Asian countries (42%), and 67% were Child–Pugh A in Asia vs 54% in non-Asian countries at study entry. Pts initiating REG at 160 mg were more likely to be Child–Pugh A and albumin–bilirubin (ALBI) grade 1 vs pts initiating REG at <160 mg (Table). A higher proportion of pts (53%) who initiated REG at 160 mg ended prior sorafenib at 800 mg/day. Of the pts intolerant to prior sorafenib (n=91), more pts started REG at 80 mg (49%), followed by 160 mg (32%) and 120 mg (9%). Median duration of REG treatment was similar across initial dose levels (overall 3.7 months). Any-grade TEAEs were reported for 90%, 93%, and 93% of pts initiating REG at 160 mg, 120 mg, and 80 mg, respectively. TEAEs led to dose modifications in 49%, 51%, and 38% and to dose reductions in 34%, 26%, and 17% of pts. Median OS was 15.8 months in pts who initiated REG at 160 mg, 13.3 months at 120 mg, and 11.1 months at 80 mg. Median PFS was similar across doses (overall 3.9 months). **Conclusions:** In this real-world study, most pts with uHCC initiated REG at 160 mg or 80 mg/day. A higher proportion of pts from Asia initiated REG at the recommended dose, and a higher proportion of pts initiating REG at 160 mg had relatively better liver function at study entry. Safety was generally similar regardless of initial dose, and OS was observed to be longer in pts initiating REG at 160 mg vs lower doses. Clinical trial information: NCT03289273. Research Sponsor: Bayer.

REG initial daily dose, %	160 mg (n=469)	120 mg (n=106)	80 mg (n=398)
Child–Pugh class A/B/C	73/9/<1	58/18/0	50/15/1
ALBI grade 1/2/3	37/48/3	32/55/3	27/47/5
Eastern Cooperative Oncology Group performance status 0/1/≥2	45/41/4	39/50/5	38/38/9
Etiology of uHCC (multiple responses)			
Hepatitis B	41	32	38
Alcohol use	27	26	22
Hepatitis C	21	25	27
Nonalcoholic steatohepatitis/genetic or metabolic	8/3	4/1	6/2
Other/unknown	3/9	1/13	4/12