Subgroup analysis of the number of prior lines of systemic therapy and clinical outcomes associated with tislelizumab in patients with previously treated advanced hepatocellular carcinoma (HCC)

Authors: *†Philippe Merle,[1] Julien Edeline,[2] Weijia Fang,[3] Eric Assenat,[4] Hongming Pan,[5] Lorenza Rimassa,[6,7] Zhiwei Li,[8] Jean-Frédéric Blanc,[9] Chia-Jui Yen,[10] Paul Ross,[11] Sheng Hu,[12] Tao Zhang,[13] Albert Tran,[14] Guoliang Shao,[15] Mohamed Bouattour,[16] Yajin Chen,[17] John Wu,[18] Bai Li,[19] Sandra Chica-Duque,[20] Zhenggang Ren[21]

Affiliations:

[1]Hepatology Unit, Croix-Rousse Hospital, Lyon, France; [2]Department of Medical Oncology, Eugene Marquis Center, Rennes, France; [3]Department of Medical Oncology, The First Affiliated Hospital, Zhejiang University, Hangzhou, China; [4]Department of Oncology, St-Eloi University Hospital, Montpellier, France; [5]Department of Medical Oncology, Sir Run Run Shaw Hospital, Zhejiang University School of Medicine, Zhejiang, China; [6]Department of Biomedical Sciences, Humanitas University, Milan, Italy; [7]Medical Oncology and Hematology Unit, IRCCS Humanitas Research Hospital, Humanitas Cancer Center, Milan, Italy; [8]Division of Hepatobiliary and Pancreatic Surgery, The First Affiliated Hospital, Zhejiang University, Hangzhou, China; [9]Service Hépato-Gastroentérologie et Oncologie Digestive, Hôpital Haut-Lévêque, CHU de Bordeaux, Bordeaux, France; [10]Clinical Medicine Research Center, National Cheng Kung University Hospital, Tainan, Taiwan; [11]Department of Gastroenterology, Guy's and St. Thomas' NHS Foundation Trust and King's College London, London, United Kingdom; [12]Department of Internal Medicine-Oncology, Hubei Cancer Hospital, Wuhan, China; [13]Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, Cancer Center, Wuhan, China; [14]Département Digestif, CHU de Nice-Hôpital Archet, Nice, France; [15]Department of Radiology, Zhejiang Cancer Hospital, Hangzhou, China; [16]Department of Medical Oncology, Beaujon University Hospital, Paris, France; [17]Department of Hepatobiliary Surgery, Sun Yat-Sen Memorial Hospital, Sun Yat-Sen University, Guangzhou, China; [18]BeiGene (Ridgefield Park) Co., Ltd., Ridgefield Park, NJ, USA; [19]BeiGene (Beijing) Co., Ltd., Beijing, China; [20]BeiGene (San Mateo) Co., Ltd., San Mateo, CA, USA; [21]Liver Cancer Institute, Zhongshan Hospital, Fudan University, Shanghai, China

Abstract text:

Background: Tislelizumab, an anti-programmed cell death protein 1 (PD-1) monoclonal antibody, showed clinical activity and was well tolerated in patients with previously treated advanced HCC in the Phase 2 RATIONALE-208 study (NCT03419897). This analysis examined the number of prior lines of systemic therapy and clinical outcomes associated with tislelizumab.

Methods: Patients who received ≥ 1 prior line of systemic therapy for advanced HCC, excluding immune checkpoint inhibitors, received tislelizumab 200 mg IV every 3 weeks. The primary endpoint was objective response rate by independent review committee (IRC) (ORR_{IRC}) per RECIST version 1.1. Secondary endpoints included investigator-

assessed (INV) ORR_{INV}, duration of response by IRC (DoR_{IRC}), DoR by INV (DoR_{INV}), overall survival (OS), progression-free survival by IRC (PFS_{IRC}), and safety.

Results: As of June 2021, 249 patients were enrolled; 138 had received 1 prior line of therapy and 111 patients had received ≥ 2 prior lines of therapy. Median (m) follow-up duration was 13.3 months and 11.9 months, respectively. Response rate assessed by IRC (1 prior line, ORR_{IRC}=13.0% [95% CI: 7.9, 19.8]; ≥ 2 prior lines, ORR_{IRC}=12.6% [95% CI: 7.1, 20.3]) and by INV (1 prior line, ORR_{INV}=15.2% [95% CI: 9.7, 22.3]; ≥ 2 prior lines, ORR_{INV}=13.5% [95% CI: 7.8, 21.3]) was generally consistent between subgroups. Number of prior lines of therapy did not impact OS (1 prior line, mOS=13.8 months [95% CI: 10.5, 19.1]; ≥ 2 prior lines, mOS=12.4 months [95% CI: 9.9, 15.2]) or PFS (1 prior line, $mPFS_{IRC}$=2.6 months [95% CI: 1.4, 2.8]; ≥ 2 prior line, $mPFS_{IRC}$=2.7 months [95% CI: 1.4, 2.8]). $mDOR_{IRC}$ was not reached in either subgroup. $mDoR_{INV}$ was not reached in the 1 prior line subgroup and was 14.6 months [95% CI: 7.6, 27.3] in the ≥ 2 prior lines subgroup. Treatment-emergent adverse events (TEAEs) were consistent between the 1 prior line and ≥ 2 prior lines subgroups; 94.2% vs 95.5% experienced any TEAE, 50.0% vs 48.6% experienced ≥ Grade 3 TEAEs, 38.4% vs 36.0% experienced serious TEAEs, 13.0% vs 9.0% experienced TEAEs that led to treatment discontinuation, 32.6% vs 30.6% experienced TEAEs that led to dose delay, and 11.6% vs 9.0% experienced TEAEs that led to death in the 1 prior line and ≥ 2 prior lines subgroups, respectively. Similarly, treatment-related adverse events (TRAEs) were consistent between the 1 prior line and ≥ 2 prior lines subgroups; 65.9% vs 60.4% experienced any TRAE, 17.4% vs 12.6% experienced ≥ Grade 3 TRAEs, 9.4% vs 4.5% serious TRAEs, 7.2% vs 2.7% experienced TRAEs that led to treatment discontinuation, 19.6% vs 17.1% experienced TRAEs that led to dose delay, and 0% vs 0% experienced TRAEs that led to death in the 1 prior line and ≥ 2 prior lines subgroups, respectively.

Conclusions: Effective second- and third-line treatment options are limited for patients with advanced HCC. This analysis indicates Tislelizumab is clinically active and well tolerated in patients with advanced HCC, regardless of the number (1 or ≥ 2) of prior lines of systemic therapy. Tislelizumab is being investigated further in a Phase 3 study (NCT03412773).