Clinical outcomes associated with tislelizumab in patients (pts) with advanced hepatocellular carcinoma (HCC) who have been previously treated with sorafenib (SOR) or lenvatinib (LEN) in RATIONALE-208

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

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

Abstract:

Background: Tislelizumab, an anti-PD-1 monoclonal antibody, demonstrated clinical activity and was well tolerated in pts with previously treated advanced HCC in the Phase 2 RATIONALE-208 study (NCT03419897). At the time of this study, SOR and LEN were recommended first-line treatments for pts with advanced HCC and continue to have an important role in the first-line treatment of HCC despite the recent approval of new immuno-oncology-based combinations (atezolizumab and bevacizumab) in some regions. We report the clinical outcomes of pts with advanced HCC who were previously treated with SOR/LEN.

Methods: Pts who had received ≥ 1 prior line of systemic therapy for advanced HCC received tislelizumab 200 mg intravenously once every three weeks. Objective response rate (ORR) by independent review committee (IRC) (ORR_{IRC}), duration of response by IRC (DOR_{IRC}), progression-free survival by IRC (PFS_{IRC}), overall survival (OS), and safety were evaluated in pts who had been previously treated with SOR/LEN.

Results: As of February 2020, 249 pts were enrolled and 235 pts had received prior treatment with SOR/LEN, of whom 126 and 109 pts had received 1 or ≥ 2 prior lines of systemic therapy, respectively. At study entry, 211 (89.8%) pts had BCLC stage C and 187 (79.6%) pts had extrahepatic spread. Median follow-up duration for pts previously treated with SOR/LEN was 12.5 months and ORR_{IRC} was 13.6% (95% CI: 9.5, 18.7), including 2 complete responses and 30 partial responses. Median DOR_{IRC} was not reached. Median PFS_{IRC} and OS of pts previously treated with SOR/LEN was 2.7 months (95% CI: 1.6, 2.8) and 13.5 months (95% CI: 10.9, 15.8), respectively. Tislelizumab was generally well tolerated in pts previously treated with SOR/LEN (**Table**), and the most common treatment-emergent adverse events were increased aspartate aminotransferase (n=70; 28.1%) and alanine aminotransferase (n=52; 20.9%).

Conclusions: Tislelizumab was investigated beyond the first-line setting, as effective second- and third-line treatment options are limited for pts with advanced HCC and there is an unmet medical need. This analysis indicates that tislelizumab is clinically active and well tolerated in pts with advanced HCC who have received prior systemic treatment with SOR/LEN.

Table. Summary of AEs in pts previously treated with SOR/LEN

	TEAE	**TRAE**
	N=235	
≥ 1, n (%)	**223 (94.9)**	**147 (62.6)**
≥ Grade 3	116 (49.4)	32 (13.6)
Serious	87 (37.0)	15 (6.4)
Leading to discontinuation	26 (11.1)	12 (5.1)
Leading to dose delay	72 (30.6)	40 (17.0)
Leading to death	24 (10.2)	0 (0)

AE, adverse event; TEAE, treatment-emergent AE; TRAE, treatment-related treatment-emergent AE