

Supplementary Online Content

Qin S, Kudo M, Meyer T, et al. Tislelizumab vs sorafenib as first-line treatment for unresectable hepatocellular carcinoma: a phase 3 randomized clinical trial. *JAMA Oncol*. Published online October 5, 2023. doi:10.1001/jamaoncol.2023.4003

eTable 1. List of RATIONALE-301 Principal Investigators and Sites

eTable 2. Subsequent Anticancer Therapies Post Study

eFigure 1. Study Design

eFigure 2. Overall Survival by Subgroups (ITT Analysis Set)

eFigure 3. Duration of Response for Tislelizumab vs Sorafenib

This supplementary material has been provided by the authors to give readers additional information about their work.

eTable 1. List of RATIONALE-301 Principal Investigators and Sites

Principal Investigator	Site	Country
Franses, Joseph Goyal, Lipika Zhu, Andrew	1021	United States
Imagawa, David	1060	United States
Bane, Charles	1061	United States
Arora, Sukeshi	1062	United States
Costin, Dan	1074	United States
Bathini, Venu Gultawatvich, Patan Switzer, Bradley	1075	United States
Rao, Subramanya	1076	United States
Kozloff, Mark	1079	United States
Park, David	1080	United States
Pyrsoopoulos, Nikolaos	1082	United States
Levy, Anna	1100	United States
Goff, Laura	1104	United States
Finn, Richard	1117	United States
Fuloria, Jyotsna	1124	United States
Satti, Suma	1125	United States
Hassanein, Tarek	1150	United States
Loaiza-Bonilla, Arturo	1152	United States
Kayali, Zeid	1176	United States
Ducreux, Michel	33004	France
Mathurin, Philippe	33006	France
Nguyen-Khac, Eric	33008	France
Heurgue Berlot, Alexandra	33009	France
Archambeaud, Isabelle Touchefeu, Yann	33013	France
Phelip, Jean Marc	33024	France
Borg, Christophe Kim, Stefano Chong-Hun	33025	France
Ollivier-Hourmand, Isabelle	33027	France
Assenat, Eric	33028	France
Frin, Anne-Claire	33034	France
Tougeron, David	33036	France
Bouattour, Mohamed	33064	France
Decaens, Thomas	33066	France
Rosmorduc, Olivier	33072	France
Campos Marionna, Calvo	34007	Spain
Cubillo Gracian, Antonio	34021	Spain
Diaz Beveridge, Roberto	34032	Spain

Principal Investigator	Site	Country
Macarulla, Teresa	34034	Spain
Piscaglia, Fabio	39008	Italy
Pedrazzoli, Paolo	39013	Italy
Giuseppe, Aprile	39014	Italy
Villa, Erica	39015	Italy
Passalacqua, Rodolfo Tomasello, Gianluca	39016	Italy
Giannelli, Gianluigi	39017	Italy
Giovanis, Petros Pastorelli, Davide	39027	Italy
Di Maio, Massimo	39048	Italy
Soto Parra, Hector Jose	39051	Italy
Cognetti, Francesco	39052	Italy
Leo, Silvana	39053	Italy
Porta, Camillo	39062	Italy
Hubner, Richard	44012	United Kingdom
Meyer, Timothy	44024	United Kingdom
Panjak, Punia	44030	United Kingdom
Ross, Paul	44039	United Kingdom
Bar-Letkiewicz, Ilona	48019	Poland
Zaucha, Renata	48020	Poland
Wyrwicz, Lucjan	48023	Poland
Simon, Krzysztof	48024	Poland
Ettrich, Thomas	49006	Germany
Thorsten, Gotze	49007	Germany
Waldschmidt, Dirk-Thomas	49008	Germany
Christoph, Daniel Pluntke, Stefan	49009	Germany
Vogel, Arndt	49010	Germany
Wege, Henning	49011	Germany
Gonzalez-Carmona, Maria	49013	Germany
Muller, Tobias	49014	Germany
Berg, Thomas	49016	Germany
Verena, Keitel	49049	Germany
Satoh, Taroh	81001	Japan
Kondo, Yuji	81002	Japan
Wada, Yoshiyuki	81005	Japan
Sasaki, Yutaka Tanaka, Motohiko Tateyama, Masakuni	81006	Japan
Ohkawa, Kazuyoshi	81007	Japan
Kudo, Masatoshi	81008	Japan
Isomoto, Hajime	81010	Japan

Principal Investigator	Site	Country
Mita, Eiji	81011	Japan
Hagihara, Atsushi	81012	Japan
Hiraoka, Atsushi	81013	Japan
Numata, Kazushi	81014	Japan
Morimoto, Manabu	81016	Japan
Kojima, Yasushi	81018	Japan
Ogawa, Koji	81019	Japan
Nakata, Rto Yoshida, Hideo	81020	Japan
Itoh, Yoshito	81021	Japan
Aoki, Masaru Yamashita, Tatsuya	81024	Japan
Toyoda, Hidenori	81025	Japan
Kioka, Kiyohide	81027	Japan
Kawabe, Naoto	81028	Japan
Kuroda, Hidekatsu Takayama, Tadatoshi	81040	Japan
Kato, Naoya	81041	Japan
Kitano, Masayuki	81042	Japan
Abiru, Seigo	81043	Japan
Kuroda, Hidekatsu Takikawa, Yasuhiro	81046	Japan
Hatano, Etsuro	81047	Japan
Xing, Baocai	86001	China
Lin, Xiaoyan	86004	China
Chen, Xiaoming	86005	China
Wang, Jufeng	86006	China
Guo, Yabing	86008	China
Zhao, Haitao	86009	China
Fang, Weijia	86014	China
Zhu, Xiaoli	86015	China
Bai, Yuxian	86022	China
Liu, Xiufeng	86025	China
Li, Wei	86026	China
Ying, Jieer	86027	China
Gu, Kangsheng	86028	China
Pan, Yueyin	86029	China
Wang, Zishu	86030	China
Chen, Zhendong	86031	China
Ren, Zhenggang	86032	China
Meng, Zhiqiang	86033	China
Zhou, Fuxiang	86035	China
Lin, Hailan	86036	China

Principal Investigator	Site	Country
Wu, Jianbing	86037	China
Pan, Hongming	86038	China
Li, EnXiao	86039	China
Zhang, Tao	86040	China
Lu, Yinying	86041	China
Dai, Guanghai	86042	China
Cheng, Ying	86043	China
Zhou, Aiping	86044	China
Yu, Guohua	86045	China
Zhang, Tao	86046	China
Qiu, Wensheng	86047	China
Song, Tianqiang	86048	China
Hu, Sheng	86055	China
Yang, Jianyong	86056	China
Feng, Jifeng	86096	China
Chen, Yajin	86099	China
Xu, Bin	86145	China
Melichar, Bohuslav	420004	Czech Republic
Kral, Zdenek	420009	Czech Republic
Prausova, Jana	420010	Czech Republic
Chen, Shinn-Cherng	886001	Taiwan
Kuo, Hsing-Tao	886009	Taiwan
Lee, Teng-Yu	886011	Taiwan
Chang, Ting-Tsung	886042	Taiwan
Wang, Jing-Houng	886044	Taiwan
Chao, Yee	886045	Taiwan
Hou, Ming-Mo	886046	Taiwan
Ho, Ching-Liang	886047	Taiwan
Jeng, Long-Bin	886048	Taiwan

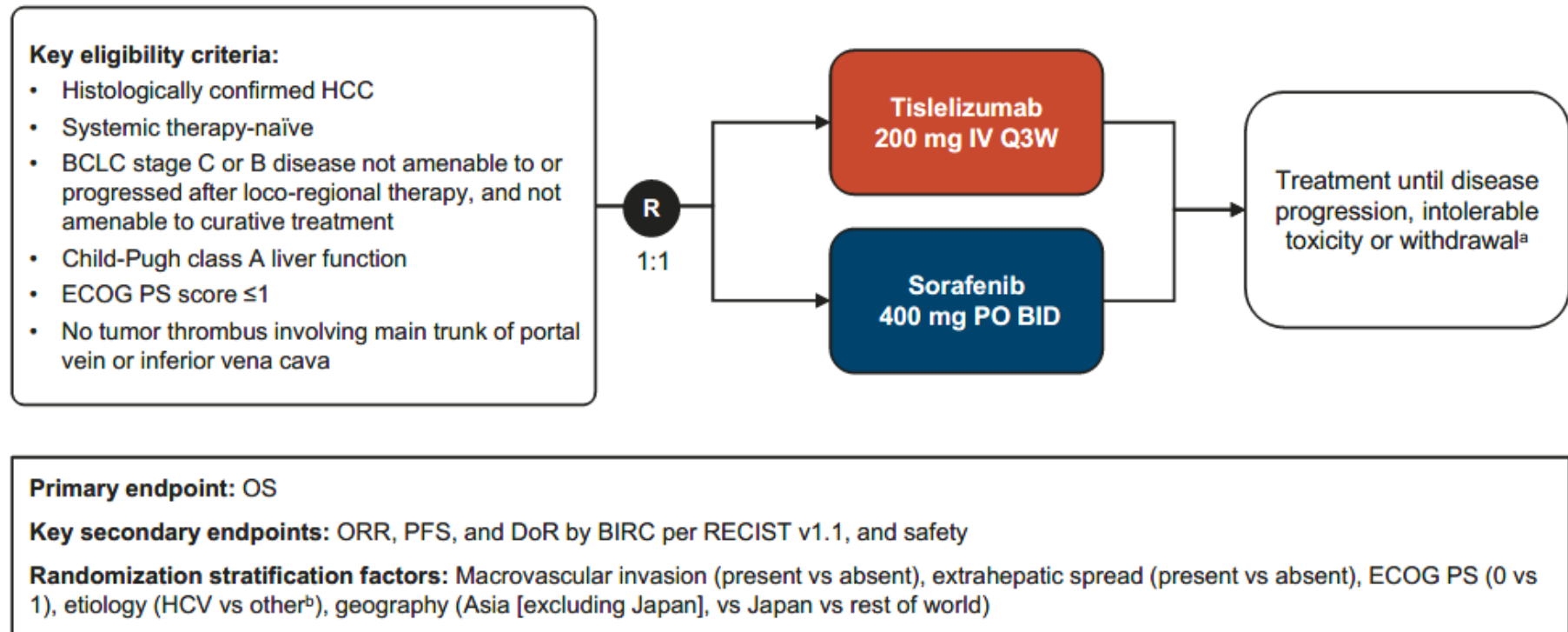
eTable 2. Subsequent Anticancer Therapies Post Study

n (%) ^a	Tislelizumab (n = 342)	Sorafenib (n = 332)
Any subsequent anti-cancer treatment	207 (60.5)	222 (66.9)
Procedure, radiotherapy, embolization or surgery	82 (24.0)	78 (23.5)
Systemic therapy	185 (54.1)	199 (59.9)
TKI ^b	175 (51.2)	137 (41.3)
Sorafenib	104 (30.4)	15 (4.5)
Lenvatinib	73 (21.3)	66 (19.9)
Regorafenib	25 (7.3)	48 (14.5)
Cabozantinib	15 (4.4)	22 (6.6)
Apatinib	12 (3.5)	12 (3.6)
Rivoceranib	7 (2.0)	7 (2.1)
Catequentinib	3 (0.9)	4 (1.2)
Immunotherapy ^b	33 (9.6)	87 (26.2)
Atezolizumab	11 (3.2)	17 (5.1)
Sintilimab	9 (2.6)	8 (2.4)
Camrelizumab	6 (1.8)	10 (3.0)
Pembrolizumab	6 (1.8)	11 (3.3)
Toripalimab	3 (0.9)	6 (1.8)
Nivolumab	2 (0.6)	11 (3.3)
Monoclonal antibodies	2 (0.6)	20 (6.0)
Anti-angiogenesis (non-TKI) ^b	18 (5.3)	19 (5.7)
Bevacizumab	13 (3.8)	16 (4.8)
Ramucirumab	5 (1.5)	6 (1.8)
Chemotherapy ^b	12 (3.5)	15 (4.5)
Investigational agent ^b	3 (0.9)	27 (8.1)
Other ^c	3 (0.9)	27 (8.1)

Abbreviations: TKI, tyrosine kinase inhibitor.

^aSubsequent anticancer therapies received by ≥1% of patients in either treatment arm are reported. ^bReceived as systemic therapy. ^cOther^c included antineoplastic agents, mtl cebpa, onatasertib, avdoralimab, bay 1895344, capmatinib, lenalidomide, pomalidomide, and *Streptococcus pyogenes*.

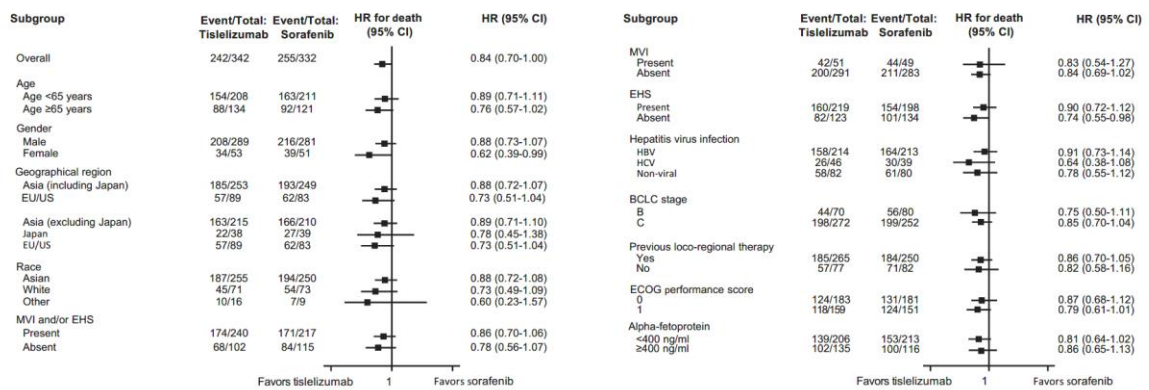
eFigure 1. Study Design



Abbreviations: BCLC, Barcelona Clinic Liver Cancer; BID, twice daily; BIRC, blinded independent review committee; DoR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; HBV, hepatitis B virus; HCC, hepatocellular carcinoma; HCV, hepatitis C virus; IV, intravenous; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; PO, oral; Q3W, once every 3 weeks; RECIST, Response Evaluation Criteria in Solid Tumors.

^aPatients in both arms could continue treatment after disease progression providing there was no symptomatic deterioration, ECOG PS remained ≤1, and there was no rapid progression of disease or progression at a critical anatomical site. ^bIncludes HBV.

eFigure 2. Overall Survival by Subgroups (ITT Analysis Set)

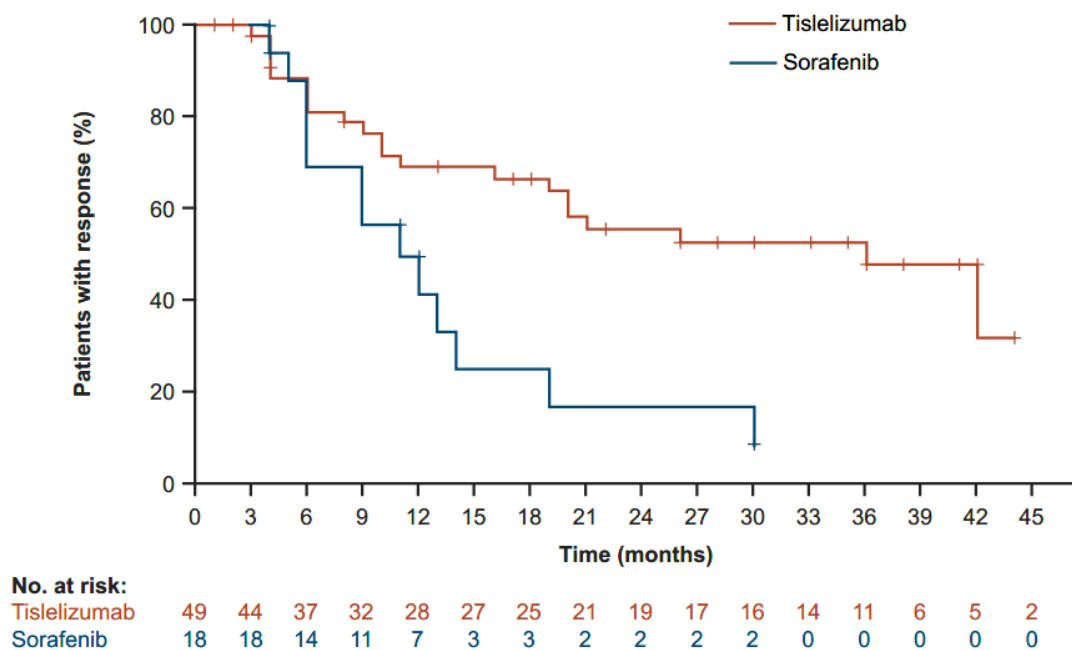


Abbreviations: BCLC, Barcelona Clinic Liver Cancer; CI, confidence interval; ECOG, Eastern Cooperative Oncology Group; EHS, extrahepatic spread; EU, Europe; HBV, hepatitis B virus; HCV, hepatitis C virus; HR, hazard ratio; ITT, intent-to-treat; MVI, macrovascular invasion; US, United States.

Data cutoff: July 11, 2022.

All subgroups were predefined.

eFigure 3. Duration of Response for Tislelizumab vs Sorafenib



Data cutoff: July 11, 2022. Data for patients who started to receive new anticancer therapy or were lost to follow-up were censored at the last valid tumor assessment date.