

MEDIA UPDATE

Novartis announces tislelizumab demonstrated efficacy and tolerability in first-line advanced liver cancer in Phase III trial

- *RATIONALE 301 trial met its objective at final analysis, demonstrating non-inferior overall survival (OS) for tislelizumab (median OS: 15.9 months) versus sorafenib (median OS: 14.1 months) in patients with previously untreated unresectable hepatocellular carcinoma (HCC)¹*
- *Tislelizumab demonstrated a favorable safety profile compared to sorafenib, with fewer grade ≥ 3 adverse events (AEs) and fewer AEs leading to discontinuation*
- *Results from RATIONALE 301 study, the eighth positive clinical trial readout for tislelizumab, presented as late-breaking oral at ESMO*

Basel, September 10, 2022 — Novartis today announced new data from the Phase III RATIONALE 301 trial that show tislelizumab demonstrated non-inferior overall survival (OS) compared to sorafenib (median OS: 15.9 months vs. 14.1 months; stratified HR=0.85 [95.003% CI: 0.712, 1.019]) in patients with previously untreated, unresectable hepatocellular carcinoma (HCC). The trial met its primary objective of non-inferiority for OS; superiority was subsequently tested, which was not met. These data were presented at a late-breaking oral session at the 2022 European Society for Medical Oncology (ESMO) Congress (Abstract #LBA36) in collaboration with BeiGene.

"People living with advanced liver cancer face poor survival outcomes and frequently suffer from cirrhosis, which further complicates their treatment," said Richard S. Finn, MD, professor of medicine, Department of Medicine, Division of Hematology/Oncology, David Geffen School of Medicine and Jonsson Comprehensive Cancer Center at UCLA and the lead US investigator on the trial. "These positive results show that tislelizumab has the potential to deliver a meaningful clinical benefit for patients with HCC who need more safe and effective therapeutic options."

OS results were consistent across pre-specified subgroups, including regions. Tislelizumab was associated with higher objective response rate (ORR, 14.3% vs. 5.4%) and more durable responses (duration of response [DoR]; median DoR: 36.1 months vs. 11.0 months) compared with sorafenib. Median progression-free survival (PFS) was 2.1 months with tislelizumab compared to 3.4 months with sorafenib (HR=1.11 [CI: 0.92, 1.33]). Median treatment duration was longer with tislelizumab (4.1 months) versus sorafenib (2.7 months).

"HCC is an aggressive disease with poor survival outcomes, and there is an urgent need for additional treatment options with improved tolerability in the first line setting," said Jeff Legos,

Executive Vice President, Global Head of Oncology & Hematology Development. “We are excited to see the positive efficacy results and favorable safety profile of tislelizumab monotherapy in this setting and will begin discussing these data with regulatory authorities.”

The safety profiles of both agents were consistent with previous reports, and no new safety signals were identified. Incidence rates of grade ≥ 3 adverse events (AEs) were lower with tislelizumab (48.2%) compared with sorafenib (65.4%), as were AEs leading to discontinuation (10.9% vs 18.5%). AEs leading to death were low across both tislelizumab (4.4%) and sorafenib (5.2%). Immune-mediated AEs occurring in at least 5% of tislelizumab-treated patients were hepatitis (5.3%) and hypothyroidism (5.3%).

HCC is the most common type of liver cancer globally and constitutes 75-85% of liver cancer diagnoses.⁴ In 2022, it is estimated that there will be more than 800,000 new liver cancer diagnoses and 700,000 deaths worldwide.⁵ Over 70% of HCC patients in the United States are diagnosed with unresectable cancers, and US patients with metastasized cancers face a five-year survival rate of 12% or less.^{6,7}

RATIONALE 301 (NCT03412773) is a multi-regional, open-label, randomized Phase III study of tislelizumab versus sorafenib in previously untreated patients with unresectable HCC. In the trial, 674 participants were randomized 1:1 to receive tislelizumab or sorafenib. The primary objective is to compare OS between the two treatment groups. Secondary endpoints include ORR, PFS, DoR, safety and tolerability, and health-related quality of life measures.

About Tislelizumab

Tislelizumab is a uniquely designed anti-PD-1 monoclonal antibody currently under review by the US Food and Drug Administration (FDA) and the European Medicines Agency (EMA) for advanced or metastatic esophageal squamous cell carcinoma (ESCC) after prior chemotherapy. The EMA is also reviewing tislelizumab for advanced or metastatic non-small cell lung cancer (NSCLC) after prior chemotherapy, and in combination with chemotherapy for previously untreated advanced or metastatic NSCLC.

Tislelizumab is being evaluated within a global clinical development program consisting of 17 pivotal clinical trials across a broad array of solid tumors, with more than 9,000 patients enrolled to date in 35 countries and regions. Novartis is committed to advancing immunology (IO) therapies to increase the depth and durability of treatment response across more tumor types and to make transformational treatment improvements for more patients living with cancer.

Novartis has the rights to develop, manufacture and commercialize tislelizumab in North America, Europe and Japan through a collaboration and license agreement with BeiGene.

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