

## **MEDIA & INVESTOR RELEASE**

# **New Phase III data show Novartis tislelizumab significantly extended median overall survival by more than 6 months in first-line advanced esophageal cancer in combination with chemotherapy**

- *First-line tislelizumab plus chemotherapy showed median overall survival of 17.2 months versus 10.6 months for chemotherapy and reduced risk of death by 34% in patients with advanced esophageal squamous cell carcinoma<sup>1</sup>*
- *Statistically significant survival benefit with tislelizumab plus chemotherapy was observed regardless of PD-L1 status and consistent across all patient subgroups<sup>1</sup>*
- *Novartis to discuss results of multi-regional RATIONALE 306 study, the seventh positive Phase III trial readout for tislelizumab, with regulatory health authorities*

**Basel, June 30, 2022** — Today Novartis announced results from the Phase III RATIONALE 306 trial showing tislelizumab plus chemotherapy significantly improved overall survival (OS) as a first-line treatment for adult patients with unresectable, locally advanced or metastatic esophageal squamous cell carcinoma (ESCC), regardless of PD-L1 status. Tislelizumab plus chemotherapy demonstrated a median OS of 17.2 months (CI, 15.8-20.1 months) versus 10.6 months (CI, 9.3-12.1 months) in patients receiving chemotherapy plus placebo and reduced the risk of death by 34% (hazard ratio=0.66; CI, 0.54-0.80, p<0.0001).<sup>1</sup> In collaboration with BeiGene, these data were presented today during a late-breaking oral session at the 2022 European Society for Medical Oncology (ESMO) World Congress on Gastrointestinal Cancer (Abstract #LBA-1).

“These data, which show tislelizumab plus chemotherapy extended patients’ lives by a median of more than six months, are a promising outcome in the treatment of this aggressive cancer,” said Dr. Ken Kato, Chief of Head and Neck Medical Oncology, National Cancer Center Hospital, Tokyo, Japan. “Importantly, the significant overall survival benefit was observed across all patient subgroups in the trial, indicating that tislelizumab plus chemotherapy may be a viable treatment option for patients regardless of their PD-L1 score.”

In patients with PD-L1 score ≥10% (secondary endpoint), tislelizumab plus chemotherapy showed a median OS of 16.6 months (CI, 15.3-24.4 months) versus 10.0 months (CI, 8.6-13.0 months) in patients receiving chemotherapy plus placebo and reduced risk of death by 38% (HR=0.62; CI, 0.44-0.86, p=0.0020). In those with PD-L1 score <10% (exploratory analysis), median OS with tislelizumab plus chemotherapy was 16.7 months (CI, 13.0-20.1 months) versus 10.4 months (CI, 9.1-13.0 months; HR=0.72; CI, 0.55-0.94). Survival benefit was consistent across all other subgroups, including race, geographical region and investigator choice of chemotherapy. Tislelizumab plus chemotherapy also significantly improved progression-free survival (7.3 months vs 5.6 months; HR=0.62; CI, 0.52-0.75, p<0.0001) and objective response rate (63.5% vs 42.4%; odds ratio=2.38, p<0.0001).<sup>1</sup>

“The prognosis for ESCC remains poor, with a five-year survival rate of just five percent, and patients are in need of more treatment options, especially in earlier lines of therapy,” said Jeff Legos, Executive Vice President, Global Head of Oncology & Hematology Development, Novartis. “These results add to the growing body of evidence demonstrating the potential for tislelizumab to help patients with esophageal cancer, and reinforce our commitment to studying tislelizumab alone and in synergistic combinations across additional tumor types that may benefit from an immunotherapy.”

The incidence of treatment-related adverse events (TRAEs) was similar in both arms. Most common TRAEs for tislelizumab plus chemotherapy versus chemotherapy were anemia (68% vs 61%), decreased neutrophils (78% vs 80%), decreased white blood cell count (55% vs 65%), decreased appetite (39% vs 38%), nausea (37% vs 42%) and peripheral sensory neuropathy (26% vs 21%).<sup>1</sup>

ESCC is the most common type of esophageal cancer globally, with an estimated 604,000 new cases and 544,000 deaths from esophageal cancer internationally in 2020.<sup>2</sup> In the United States, it is estimated there will be more than 20,000 new diagnoses and more than 16,000 deaths from esophageal cancers.<sup>3</sup>

RATIONALE 306 (NCT03783442) is a multi-regional Phase III, randomized, placebo-controlled, double-blind study of tislelizumab in combination with chemotherapy versus chemotherapy in patients with unresectable, locally advanced recurrent or metastatic ESCC. Approximately 649 study participants were randomized 1:1 to receive either tislelizumab plus chemotherapy or chemotherapy plus placebo. The primary endpoint is OS in the all-comer intent-to-treat population. Secondary endpoints include OS in patients with PD-L1 score  $\geq 10\%$ , progression-free survival, objective response rate, duration of response, health-related quality of life measures and safety.

#### **About Tislelizumab**

Tislelizumab is currently under review by the US Food and Drug Administration (FDA) and the European Medicines Agency (EMA) for advanced or metastatic 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 a uniquely designed anti-PD-1 monoclonal antibody, in 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 broad portfolio of advanced therapeutic approaches offer a unique opportunity to study tislelizumab in differentiated, potentially synergistic combinations.

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

#### **Disclaimer**

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### **About Novartis**

Novartis is reimagining medicine to improve and extend people's lives. As a leading global medicines company, we use innovative science and digital technologies to create transformative treatments in areas of great medical need. In our quest to find new medicines, we consistently rank among the world's top companies investing in research and development. Novartis products reach nearly 800 million people globally and we are finding innovative ways to expand access to our latest treatments. About 108,000 people of more than 140 nationalities work at Novartis around the world. Find out more at <https://www.novartis.com>.

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### **References**

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3. American Cancer Society. Key statistics for esophageal cancer. Accessed March 1, 2022. <https://www.cancer.org/cancer/esophagus-cancer/about/key-statistics.html>

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