O-15 Randomized, phase 3 study of second-line tislelizumab vs chemotherapy in advanced or metastatic esophageal squamous cell carcinoma (RATIONALE 302) in the overall population and Europe/North America subgroup

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Background: The global Phase 3 study RATIONALE 302 (NCT03430843) evaluated the efficacy and safety of second-line tislelizumab, an anti-PD-1 antibody, in patients with advanced or metastatic esophageal squamous cell carcinoma (ESCC). Here, we report data from the overall and Europe/North America (EU/NA) populations.

Methods: Eligible adult patients had disease progression during or after first-line systemic therapy, ≥1 evaluable lesion per RECIST v1.1 and an Eastern Cooperative Oncology Group performance score (ECOG PS) of ≤1. Patients were randomized (1:1) to receive tislelizumab 200 mg intravenously Q3W or investigator-chosen chemotherapy (paclitaxel, docetaxel, or irinotecan) and treated until disease progression, intolerable toxicity, or withdrawal. Stratification factors included chemotherapy option, region, and ECOG PS. The primary endpoint was overall survival (OS) in all patients (ITT population). The key secondary endpoint was OS in PD-L1 positive (vCPS ≥10%) patients; other secondary endpoints included progression-free survival (PFS), overall response rate (ORR), duration of response (DoR), health-related quality of life and safety.

Results: 512 patients (overall population) were randomized to tislelizumab (n=256) or chemotherapy (n=256), of which 108 (21%) patients were enrolled into EU/NA subgroup (n=55 tislelizumab, n=53 chemotherapy). On 1 December 2020 (data cut-off), median follow-up was 6.9 and 6.8 months in the overall population and EU/NA subgroup, respectively. Tislelizumab improved OS vs chemotherapy in the overall population (median OS 8.6 vs 6.3 months; HR 0.70, 95% CI 0.57–0.85; p=0.0001); survival benefit was consistently observed in the EU/NA subgroup (median OS 11.2 vs 6.3 months; HR 0.55; 95% CI 0.35–0.87). Treatment with tislelizumab was associated with improved ORR (20.3% [95% CI 15.6%–25.8%] vs 9.8% [95% CI 6.4%–14.1%]) and median DoR (7.1 vs 4.0 months; HR 0.42, 95% CI 0.23–0.75) vs chemotherapy in the overall population. Improvement in ORR (20.0% [95% CI 10.4%–33.0%] vs 11.3% [95% CI 4.3%–23.0%]) and median DOR (5.1 vs 2.1 months; HR 0.42, 95% CI 0.13–1.39) was also observed in the EU/NA subgroup. Fewer patients had Grade ≥3 treatment-emergent adverse events (TEAE) with tislelizumab vs chemotherapy in both the overall and EU/NA populations (46% vs 68% and 56% vs 71%, respectively). Of these, fewer Grade ≥3 AEs were treatment-related with tislelizumab vs chemotherapy (overall: 19% vs 56%; EU/NA: 13% vs 51%). AEs leading to death were similar with tislelizumab vs chemotherapy (overall: 14% vs 12%; EU/NA: 6% vs 5%).

Conclusions: Second-line tislelizumab demonstrated statistically significant and clinically meaningful improvement in OS versus chemotherapy in patients with advanced or metastatic ESCC. Tislelizumab demonstrated a tolerable safety profile. Efficacy and safety results from the EU/NA subgroup were consistent with the overall population.

Clinical trial identification: NCT03430843.

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O-16 HEPANOVA: Final efficacy and safety results from a phase 2 study of Tumor Treating Fields (TTFields, 150 kHz) concomitant with sorafenib in advanced hepatocellular carcinoma

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Background: Tumor Treating Fields (TTFields) are an anti-mitotic, regional treatment modality, utilizing low intensity alternating electric fields delivered non-invasively to the tumor using a portable medical device. TTFields are approved by the FDA for the treatment of glioblastoma and malignant pleural mesothelioma. In vitro and in vivo TTFields at 150 kHz reduced the proliferative potential of hepatocelluar carcinoma (HCC) cell lines. In patients with Barcelona clinic liver cancer (BCLC) stage C or stage B following failure of loco-regional treatments, systemic therapies are the standard of care in eligible patients. Most HCC patients are not amenable to curative therapies and are treated with best supportive care following failure of loco-regional treatment options. The HEPANOVA EF-30 Phase II trial (NCT03606590) was a prospective study investigating the efficacy and safety of TTFields as a treatment option for advanced HCC concomitant with sorafenib. We present the finaly efficacy and safety data of the HEPANOVA trial.

Trial design: Patients (N=25) with unresectable HCC, amenable to systemic therapy with sorafenib following failure of loco-regional treatment options were enrolled in this study. Patients had ECOG score 0-2; Barcelona clinic liver cancer (BCLC) stage 0-C, Child-Turcotte-Pugh score between 5 and 8 points and measurable disease per RECIST. Implanted electronic devices in the torso was exclusionary. Standard sorafenib treatment was administered 400 mg (2 x 200 mg tablets). TTFields (150 kHz) were delivered for 18 hours/day until local disease progression (RECIST). Clinical follow up was performed q4w, with CT/MRI scan q12w. Primary end point was overall response rate (ORR); secondary: in-field control rate, 12-month progression-free survival rate 12 month (PFS12), 1-year OS rate and incidence and severity of adverse events (AE). A sample size of 25 patients would achieve 77% power at 0.05 one-sided alpha to detect overall radiological response rate of 20% in TTFields-treated patients. The final safety and efficacy results of the HEPANOVA trial are currently under final analyses. Our hypothesis is that treatment with TTFields as a novel modality for HCC will be efficacious and safe in treatment of advanced HCC.

Methods: Patients (N=25) with unresectable HCC, amenable to systemic therapy with sorafenib following failure of loco-regional treatment options were enrolled in this study. Patients had ECOG score 0-2; Barcelona clinic liver cancer (BCLC) stage 0-C, Child-Turcotte-Pugh score between 5 and 8 points and measurable disease per RECIST. Implanted electronic devices in the torso was exclusionary. Standard sorafenib treatment was administered 400 mg (2 x 200 mg tablets). TTFields (150 kHz) were delivered for 18 hours/day until local disease progression (RECIST). Clinical follow up was performed q4w, with CT/MRI scan q12w. Primary endpoint was overall response rate (ORR); secondary: in-field control rate, 12-month progression-free survival rate (PFS12), 1-year OS rate and incidence and severity of adverse events (AE). A sample size of 25 patients would achieve 77% power at 0.05 one-sided alpha to detect overall radiological response rate of 20% in TTFields-treated patients.

Conclusions: The final safety and efficacy results of the HEPANOVA trial are currently under final analyses. Our hypothesis is that treatment with TTFields as a novel modality for HCC will be efficacious and safe in treatment of advanced HCC.

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