In this updated analysis of the RATIONALE-307 trial, addition of tislelizumab to platinum-based chemotherapy as first-line treatment for advanced squamous NSCLC continued to demonstrate a clinically meaningful PFS benefit, higher ORR, and longer DoR versus platinum-based chemotherapy alone, and had a manageable safety profile, with no new safety signals identified.

Here, we report updated results from the final analysis (FA) of RATIONALE-307, including longer follow-up. In addition, the effect of subsequent treatment after disease progression on overall survival (OS) results is explored.

• Among patients from Arm C who crossed over to tislelizumab, median time from last dose of chemotherapy to subsequent tislelizumab was 10.3 weeks (minimum time to crossover: 0.1 weeks)

• A supportive analysis was conducted to adjust for the potential impact of in-study crossover using a two-stage model

Table 2: The reductions in HRs seen with the supportive analysis suggest the OS benefit for tislelizumab in combination with chemotherapy versus chemotherapy alone may have been partially obscured by in-study crossover.

Safety

• Tislelizumab plus chemotherapy (Arms A and B) was tolerable; no new safety signals were identified at the FA compared with the interim analysis

Table 1. IRC-Assessed Efficiency Outcomes by PD-L1 Expression Subgroup

Conclusions

Tislelizumab, a monoclonal antibody with high affinity and binding specificity for programmed cell death protein 1, was specifically engineered to minimize Fc receptor binding on macrophages.1,2

Methods

• Adults with treatment-naive, stage IIIb (not amenable to curative surgery/radiotherapy) or stage IV NSCLC were enrolled

• Patients were randomized (1:1:1) to open-label – Arm A: Tislelizumab 200 mg intravenously (IV) every 3 weeks (Q3W) plus 4-6 cycles of paclitaxel and carboplatin; – Arm B: Tislelizumab 200 mg IV Q3W plus 4-6 cycles of nab-paclitaxel and carboplatin; or – Arm C: 4-6 cycles of carboplatin and carboplatin

• Primary endpoint: Independent review committee (IRC)-assessed PFS in the intent-to-treat (ITT) analysis set

• Secondaries endpoints included: OS; IRC-assessed objective response rate (ORR) and duration of response (DoR); and safety

• Scan QR code for full methodology from the previously published interim analysis

Results

Patient Disposition and Baseline Characteristics

Between July 30, 2018, and September 30, 2020, 360 patients were randomized to Arm A (120), Arm B (n=119), or Arm C (n=121)

• Demographics and baseline characteristics were well balanced between arms

• Overall, median age was 62 years, most patients were male (91.7%), and most had stage IV disease at baseline (68.1%)

• Tumor cell programmed death ligand 1 (PD-L1) membrane expression was unavailable in 1.7% of patients, <1% in 33.8%, 1-49% in 25.3%, and 25%-99% in 34.7%

• At the FA cutoff (September 30, 2020), Median study follow-up was 10.7 months (95% confidence interval [CI]: 18.0, 20.0); 10.1 additional months compared with the interim analysis

• Overall, 25.8% of patients in Arm A and 26.8% in Arm C remained on their assigned treatment; patients in Arm C had finished study treatment after 4-6 cycles

In patients with advanced squamous (se) non-small cell lung cancer (NSCLC), interim results from the phase 3 programmed cell death ligand 1 (PD-L1)≥50% subgroup analysis of the RATIONALE-307 trial (NCT03594747) demonstrated significantly prolonged progression-free survival (PFS) and improved tumor response rates with first-line tislelizumab plus platinum-based chemotherapy versus platinum-based chemotherapy alone.

Efficacy

PFS

• The study met its primary objective of prolonging PFS with IRC in Arms A and B versus Arm C at the interim analysis.

• The improvement in median PFS in Arms A and B versus Arm C remained consistent at the final FA (Figure 1)

• PFS benefits in Arms A and B versus Arm C, respectively, were largely consistent and significant across PD-L1 expression subgroups (Table 1)

Policy

• Stratified HR

Table 1. IRC-Assessed Efficiency Outcomes by PD-L1 Expression Subgroup

Figure 1. IRC-Assessed PFS for Arms A and C (A) and Arms B and C (B) (ITT Analysis Set)

Table 2. IRC-Assessed Efficiency Outcomes by PD-L1 Expression Subgroup

Table 2. OS Analysis (ITT Set)

Acknowledgments

This study was sponsored by BeiGene, Ltd. Medical writing support, under the direction of the authors, was provided by Elizio MedComms, an Inizio company, and was funded by BeiGene, Ltd.

References


Disclosures

• Dr Ji Wang reports no potential conflicts of interest.

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