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Nivolumab plus chemotherapy versus chemotherapy alone in patients with previously untreated advanced or recurrent gastric/gastroesophageal junction (G/GEJ) cancer: ATTRACTION-4 (ONO-4538-37) study

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Background

Nivolumab has a survival benefit for heavily pretreated patients with advanced or recurrent G/GEJ cancer. ATTRACTION-4 is a randomized, multicenter, phase 2/3 study to evaluate the efficacy and safety of nivolumab plus chemotherapy vs. chemotherapy as first-line treatment in patients with HER2-negative, advanced or recurrent G/GEJ cancer. Here we report the results of the double-blind phase III part.

Methods

Patients were randomized 1:1 to receive nivolumab plus chemotherapy (N+C, S-1 plus oxaliplatin or capecitabine plus oxaliplatin) or placebo plus chemotherapy (C). Nivolumab or placebo was intravenously administered every 3 weeks until disease progression or unacceptable toxicity. Tumor assessment was performed every 6 weeks through week 54, then repeated every 12 weeks. The co-primary endpoints were centrally-assessed PFS and OS, and it was prespecified that the primary objective is deemed to be achieved if at least one of the null hypotheses of the primary endpoints is rejected.

Results

A total of 724 Asian patients were randomized to N+C (n=362) or C (n=362) between Mar 7, 2017, and May 10, 2018. At the interim analysis primary for PFS with the median follow-up period of 11.6 mo, PFS was significantly improved in N+C vs. C (HR 0.68; 98.51% CI 0.51-0.90; p=0.0007; median PFS, 10.5 vs. 8.3 mo), meeting the primary endpoint. At the final analysis primary for OS with the median follow-up period of 26.6 mo, there was no statistically significant difference (HR 0.90; 95% CI 0.75-1.08; p=0.257; median OS, 17.5 vs. 17.2 mo), while PFS was continuously longer in N+C than in C. ORR was higher in N+C than in C (57.5 vs. 47.8%; p=0.0088). The incidences of grade 3 to 5 treatment-related adverse events were 57.9% in N+C and 49.2% in C.

Conclusions

PFS was significantly improved in N+C vs. C, achieving the primary objective. The combination of nivolumab and chemotherapy, which demonstrated clinically meaningful efficacy in PFS and ORR with a manageable safety profile but not statistically significant improvement in OS, can be considered a new first-line treatment option in advanced or recurrent G/GEJ cancer.

Clinical trial identification

NCT02746796; Study start date: March 2016.

Legal entity responsible for the study

Ono Pharmaceutical Co., Ltd.

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Disclosure

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