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End-of-study analysis from JACOB: A phase III study of pertuzumab (P) + trastuzumab (H) and chemotherapy (CT) in HER2-positive metastatic gastric or gastro-esophageal junction cancer (mGC/GEJC)

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Background

In JACOB (NCT01774786), a double-blind, placebo-controlled, randomised, multicentre, phase III study in patients (pts) with HER2-positive mGC/GEJC, addition of P to H + CT did not significantly improve overall survival (OS) *v* placebo (PLA) at >24.4 months (m) median follow-up; median OS: 17.5 m with P + H + CT *v* 14.2 m with PLA + H + CT, HR 0.84 (95% CI 0.71, 1.00); p=0.057 (Tabernero et al. *Lancet Oncology* 2018). Here we report the end-of-study analysis at >44.4 m median follow-up.

Methods

Pts with previously untreated disease were randomised 1:1 to P + H + CT or PLA + H + CT. P (840 mg) + H (8 mg/kg loading and 6 mg/kg maintenance doses) were given intravenously every 3 weeks until disease progression or unacceptable toxicity. CT was a standard cisplatin/fluoropyrimidine regimen. The primary endpoint was OS. Secondary endpoints included progression-free survival (PFS), objective response rate (ORR), duration of response (DoR) and safety. All results are considered descriptive.

Results

The date of this database lock snapshot was 24 Jan 2020. Overall, 388 pts were randomised to P + H + CT *v* 392 to PLA + H + CT (intention-to-treat population). Efficacy / safety results are shown in the Table.Table: 1423MO

	PLA + H + CT (n = 392)	P + H + CT (n = 388)
Efficacy		
Median OS, m	14.2	18.1
Stratified HR (95% CI)	0.85 (0.72, 0.99)	
Median duration of follow-up, m	44.4	46.1
Median PFS, m	7.2	8.5
Stratified HR (95% CI)	0.73 (0.62, 0.85)	
Median duration of follow-up, m	47.4	50.4
Baseline measurable disease	n = 352	n = 351
ORR, % (CR + PR)	48.6	57.0
Median DoR, m (95% CI)	n = 175 8.4 (6.8, 9.1)	n = 203 10.2 (8.5, 12.0)
Safety, pts (%)	n = 388	N = 385
AE	385 (99.2)	381 (99.0)
AE with fatal outcome	31 (8.0)	27 (7.0)
Serious AE	156 (40.2)	178 (46.2)
Grade ≥ 3 AE	288 (74.2)	310 (80.5)
AE leading to P/PLA + H discontinuation	46 (11.9)	48 (12.5)
AE leading to P/PLA dose interruption and / or delay	94 (24.2)	110 (28.6)

The incidence of symptomatic left ventricular systolic dysfunction / heart failure was low and similar in both arms (P + H + CT: 0.8%; PLA + H + CT: 0.3%). The incidence of all-grade diarrhoea was higher in the P + H + CT arm (62.6% *v* 35.8% in the PLA + H + CT arm); the majority of events were grade 1 or 2 in severity.

Conclusions

The end-of-study analysis from JACOB confirmed evidence of treatment activity, with a 15% reduction in risk of death when adding P to H + CT in previously untreated pts with mGC/GEJC. The overall safety profile of P + H + CT was considered acceptable.

Clinical trial identification

NCT01774786.

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Legal entity responsible for the study

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Disclosure

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