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3-years follow-up of double-blind randomized phase II comparing concurrent high-dose cisplatin chemoradiation plus xevinapant or placebo in high-risk patients with locally advanced squamous cell carcinoma of the head and neck

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Background

This was a double-blind, randomized phase 2 study of 96 patients with poor prognosis locally advanced, squamous cell carcinoma of the head and neck (LA-SCCHN). Previously reported data showed significant improvements of xevinapant (Debio 1143) versus placebo in addition to chemoradiation (CRT) for the primary endpoint of locoregional control (LRC) rate at 18 months, and demonstrated that addition of Debio 1143 was feasible, safe and did not compromise backbone therapy. Here we report up-dated data on PFS and overall survival (OS).

Methods

Patients, stratified by node involvement, tumor localization and HPV-16 status, were randomized (1:1) to receive Debio 1143 or matching placebo at 200 mg/day, oral once daily D1–14 q3w (3 cycles) when added to standard high-dose cisplatin CRT. PFS and OS were analyzed using a Cox model in the intention-to-treat population. Median and survival rates at 36 months were estimated by the Kaplan-Meier method.

Results

As of 21 Jul 2020, the median follow-up was 33 months. Debio 1143 combined with CRT showed a statistically significant improvement in OS vs placebo by reducing the risk of mortality by 51% (HR=0.49, [95%CI: 0.26-0.92], P=0.0261). The 3 years OS rate was 66% (95% CI: 49–78) in the Debio 1143 arm versus 51% (95% CI: 34–65) in the placebo arm; the median OS is not reached with Debio 1143 vs. 36.1 months with placebo (95%CI: 21.8-46.7). Statistically significant improvement in PFS was demonstrated, reducing the risk of disease progression or death by 66% (HR=0.34 [95%CI, 0.17-0.68], p=0.0023) and improving probability of PFS at 36 months to 72% in the Debio 1143 arm compared to 36% in the placebo arm. The predictable and manageable safety profile observed with Debio 1143 + CRT after 2 years remained unchanged after 3 years.

Conclusions

These results with extended follow-up confirm those previously reported, showing now in addition a statistically and clinically significant OS benefit by adding Debio 1143 to standard CRT. The confirmatory phase III Trilynx study (EudraCT Number: 2020-000377-25) is ongoing.

Clinical trial identification

EudraCT: 2013-000044-25; NCT02022098.

Legal entity responsible for the study

Debiopharm.

Funding

Debiopharm.

Disclosure

J. Bourhis: Advisory/Consultancy: BMS; Advisory/Consultancy: MSD; Advisory/Consultancy: Merck; Advisory/Consultancy: AstraZeneca; Advisory/Consultancy: Debiopharm. C. Le Tourneau: Honoraria (self), Advisory/Consultancy: BMS; Honoraria (self), Advisory/Consultancy: MSD; Honoraria (self), Advisory/Consultancy: Merck Serono; Honoraria (self), Advisory/Consultancy: AstraZeneca; Honoraria (self): Rakuten; Honoraria (self), Advisory/Consultancy: Nanobiotix; Honoraria (self), Advisory/Consultancy: GSK; Honoraria (self), Advisory/Consultancy: Roche. Y. Pointreau: Honoraria (self), Advisory/Consultancy: MSD; Honoraria (self), Advisory/Consultancy: Merck; Honoraria (self), Advisory/Consultancy: BMS. M-C. Kaminsky-Forrett: Honoraria (self), Advisory/Consultancy: Merck; Honoraria (self), Advisory/Consultancy: Novartis; Advisory/Consultancy: EMD Serono. P. Boisselier: Honoraria (institution), Advisory/Consultancy: Merck; Advisory/Consultancy: BMS; Advisory/Consultancy: Roche. J-P. Delord: Advisory/Consultancy: BMS; Advisory/Consultancy: Roche; Advisory/Consultancy: MSD; Advisory/Consultancy: Novartis; Advisory/Consultancy: Merck. F. Clatot: Advisory/Consultancy: Merck; Advisory/Consultancy: BMS; Advisory/Consultancy: Lilly. F. Rolland: Advisory/Consultancy: BMS; Advisory/Consultancy: Novartis; Advisory/Consultancy: Ipsen; Advisory/Consultancy: Pfizer; Advisory/Consultancy: Merck. K. Gollmer: Full/Part-time employment: Debiopharm. S.A. Szyldergemajn: Full/Part-time employment: Debiopharm. C. Even: Advisory/Consultancy: BMS; Advisory/Consultancy: Merck; Advisory/Consultancy: MSD; Advisory/Consultancy: Innate Pharma. All other authors have declared no conflicts of interest.

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