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Cabozantinib versus placebo in patients with radioiodine-refractory differentiated thyroid cancer who have progressed after prior VEGFR-targeted therapy: Updated results from the phase III COSMIC-311 trial and prespecified subgroup analyses by prior therapy

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Background

At a preplanned interim analysis (median follow-up 6.2 mo) of the double-blind, phase 3 COSMIC-311 trial (NCT03690388), C significantly improved progression-free survival (PFS) versus P (HR 0.22, 96% CI 0.13–0.36; p<0.0001) in 187 pts with previously treated RAIR-DTC (Brose, Lancet Oncol; 2021). Pts must have received lenvatinib (L) or sorafenib (S) and progressed during or after 1–2 prior VEGFR inhibitors. We present final analysis with a longer follow-up of all randomized pts (ITT population) and for prespecified subgroups who received prior L, S, or both.

Methods

Pts were randomized 2:1 to C (60 mg QD) or P. P pts could cross over to open-label C upon disease progression per blinded independent radiology committee (BIRC). PFS (ITT) and objective response rate (ORR, first 100 randomized pts) per RECIST v1.1 by BIRC were the primary endpoints.

Results

At final analysis 258 pts (170 C, 88 P) were randomized (data cut-off 8 Feb 2021); 96 had received prior S/no L, 102 prior L/no S, and 60 prior S and L. Median follow-up was 10.1 mo. Forty pts crossed over from P to receive C. Median PFS (ITT population) was 11 mo for C vs 1.9 mo for P (HR 0.22, 96% CI 0.15–0.32; p<0.0001). For subgroups, median PFS was 16.6 vs 3.2 mo for prior S/no L (HR 0.13, 95% CI 0.06–0.26); 5.8 vs 1.9 mo for prior L/no S (HR 0.28, 95% CI 0.16-0.48), and 7.6 vs 1.9 mo for prior S and L (HR 0.27, 95% CI 0.13–0.54). ORR (ITT population) was 11% for C vs 0% for P; overall survival HR 0.76 (95% CI 0.45–1.31). Grade 3/4 treatment-emergent adverse events (TEAEs) were 62% in the C arm vs 28% in the P arm with no treatment-related grade 5 events; 67% vs 5% required dose reductions due to TEAEs; 8.8% vs 0% discontinued treatment due to TEAEs not related to disease.

Conclusions

At the final analysis of COSMIC-311 with longer follow-up, C maintained its superior efficacy vs P with a manageable safety profile in pts with previously treated RAIR-DTC. The PFS benefit was consistent with the interim analysis and irrespective of prior VEGFR-targeted therapy.

Clinical trial identification

XL184–311; NCT03690388.

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Legal entity responsible for the study

Exelixis.

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