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Zanzalintinib plus atezolizumab (zanza + atezo) vs regorafenib (rego) in patients (pts) with previously treated metastatic colorectal cancer (mCRC): Primary overall survival (OS) analysis from the randomized, open-label, phase III STELLAR-303 study

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Background

Improved therapies in the salvage setting are needed for pts with mCRC. Zanzalintinib (zanza), a novel inhibitor of multiple receptor tyrosine kinases, including MET, VEGFR, and the TAM kinases (TYRO3, AXL, and MER), may improve responsiveness to immune checkpoint inhibitors. In the randomized mCRC cohort of the phase 1 STELLAR-001 study, zanza + atezo showed promising antitumor activity and manageable toxicity. STELLAR-303 (NCT05425940) was designed to evaluate efficacy and safety of zanza + atezo vs rego in pts with previously treated mCRC.

Methods

Eligible pts had relapsed/refractory mCRC, documented not to have microsatellite instability-high or mismatch repair deficient status. Pts were randomized 1:1 to oral zanza (100 mg QD) + IV atezo (1200 mg Q3W) or oral rego (160 mg QD on days 1–21 of each 28-day cycle). Dual primary endpoints were OS in the intention-to-treat (ITT) population and in the subset of pts without liver metastases (nlmITT). All data reported are for the ITT population.

Results

Overall, 901 pts were randomized. Baseline characteristics were well-balanced between groups and 82% of all pts received a prior anti-VEGF antibody. At a median follow-up of 18.0 mos, zanza + atezo significantly improved OS vs rego (HR, 0.80; 95% CI, 0.69–0.93; P=0.0045; median, 10.9 vs 9.4 mos). PFS was improved with zanza + atezo (HR, 0.68; 95% CI, 0.59–0.79; median, 3.7 vs 2.0 mos). OS and PFS benefits with zanza + atezo were consistent across prespecified subgroups including geographic region, RAS status, presence or absence of liver metastases, and prior anti-VEGF therapy. Grade 3/4 treatment-related adverse events (TRAEs) occurred in 59% (zanza + atezo) and 37% (rego) of pts; most common grade 3/4 TRAEs with zanza + atezo vs rego were hypertension (15% vs 9%), fatigue (6% vs 2%), diarrhea (6% vs 2%), and proteinuria (6% vs 2%).

Conclusions

Zanza + atezo significantly improved OS vs rego with no new safety signals, representing a potential new treatment option for pts with previously treated mCRC. The trial continues to the final OS analysis in the nlmITT population.

Clinical trial identification

NCT05425940.

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Legal entity responsible for the study

Exelixis, Inc.

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Disclosure

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