Abstract 2219

Dynamic changes of pro-angiogenic factors during FOLFIRI-aflibercept treatment – interim analysis of DISTINCTIVE trial

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Background

To date, no biomarkers for second-line anti-angiogenic treatment in RAS wild type (wt) metastatic colorectal cancer (mCRC) patients (pts) with progression after first-line anti-epidermal growth factor receptor (EGFR) agents have been validated. Data on dynamic change of circulating pro-angiogenic factors levels during treatment from the pre-planned interim analysis of DISTINCTIVE trial (NCT04252456) are presented.

Methods

RAS wt mCRC pts progressing on first-line oxaliplatin-based + anti-EGFR are treated with second-line FOLFIRI-aflibercept. They are prospectively allocated to a favorable (>4 ng/ml) or unfavorable (≤4 ng/ml) prognostic group, according to Elisa-assessed baseline VEGFR2 plasma levels. Circulating angiogenic factors changes between baseline (BL), first tumor assessment (TA1) and disease progression (PD) are assessed. Primary endpoint is overall survival (OS) according to VEGFR2 levels. Secondary endpoints are OS, progression free survival (PFS), response rate, safety and angiogenic factors levels. Statistical analysis is performed with MedCalc (survival distribution: Kaplan-Meier; survival comparison: log-rank test).

Results

Globally, 73 pts were enrolled from 04/2018 to 06/2020; 44 were eligible for interim analysis. Median OS was 11.9 months (m) (95%CI:10-14.2). OS was significantly improved (not reached [NR] vs 11.2 m, 95%CI:8.2-14.2) in pts with increase of interleukin-8 levels between BL and PD (HR 0.30, p=0.0226) and between TA1 and PD (HR 0.16, p=0.0092) and increase of neuropilin-1 between TA1 and PD (HR 0.18, p=0.0143). Median PFS was 8.3 m (95% CI 4.2-24.2). PFS was longer in pts with decreased levels between BL and PD of endoglin (9.8 m [95%CI, 4.7-11.6] vs 4 m [95%CI:2.2-24.2), HR 0.3, p=0.0128), C reactive protein (10.6 m [95%CI:8.3-11.9] vs 5.3 m [95%CI:3.7-24.2], HR 0.40, p=0.0158) and serum amyloid protein (10 m [95%CI:5.8-14.2] vs 4.7 m, [95%CI:2.5-24.2], HR 0.39,p=0.0175).

Conclusions

Change of pro-angiogenic factors during FOLFIRI-aflibercept might be a promising predictive factor for treatment efficacy.

Clinical trial identification

NCT04252456

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