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Session E. Gastrointestinal (colorectal) cancer

E06 Circulating microRNAs in metastatic colorectal cancer (mCRC) patients (pts) treated with regorafenib

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Background: Regorafenib is indicated for the treatment of mCRC patients who have failed all other therapies. Nevertheless a substantial percentage of patients experiences rapid disease progression (PD) and serious adverse events may occur. For these reasons, clinical and/or molecular markers able to improve the cost/benefit ratio are urgently needed. Circulating microRNAs (c-miRNAs) have been recognized as possible prognostic and diagnostic markers in mCRC. The aim of this study was to describe the early changes in plasma levels of 10 selected c-miRNAs during the treatment with regorafenib and to investigate their correlation with clinical outcome.

Patients and methods: Plasma samples of patients treated with regorafenib at our Institution were collected at baseline (D1) and after 15 days of treatment (D15). Plasma levels of c-miR-17, c-miR-21, c-miR-29, c-miR-34, c-miR-92, c-miR-126, c-miR-141, c-miR-221, c-miR-601, c-miR-760 were analysed by means of real-time PCR. Paired levels at D1 and D15 were compared by means of Wilcoxon test for each c-miRNA. C-miRNAs showing significant changes were further analysed in order to identify possible correlations with outcome.

Results: Thirty-four patients were included in the present study. Main characteristics were the following: M/F = 50%/50%; median age = 65 (range 48-78 years); ECOG-PS 0/1-2 = 71%/29%; time from diagnosis of metastases </ = 18 months 15%/85%. Median PFS and OS were 2.4 and 6.5 months, respectively. One (3%) patient achieved a response and 16 (47%) had disease stabilization (disease control rate: 50%). As compared to D1, the following c-miRNAs increased at D15: c-miR-601 (p = 0.01), c-miR-141 (p = 0.04) and c-miR-21 (p = 0.06). Despite a median increase in the overall population, 12 (35%) out of 34 patients showed reduced level of c-miR-21 at D15. Nine out of 12 (75%) patients with reduced levels of c-miR-21 achieved disease control, as compared to 8 out of 23 (35%) patients with increased levels (Fisher 's Exact Test, p = 0.035). Median PFS of patients with increased and decreased level of levels of c-miR-21 were 2.1 and 3.9 months, respectively (HR = 1.89 95%CI 0.92-4.14 p = 0.08). Data on OS are not yet mature. Early modifications of c-miR-21 levels showed a sensitivity of 82% in predicting benefit from regorafenib.

Conclusions: The early modulation of c-miR-21 levels may predict benefit from regorafenib in terms of disease control. These results need validation in independent series.