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Tumour mutation profiles and circulating tumour cells in metastatic colorectal cancer patients treated with FOLFIRI + cetuximab: A prospective ancillary study of the UNICANCER PRODIGE-28 trial

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Background

We investigated the prognostic and predictive values of tumour mutation profiles determined by next-generation sequencing (NGS) and circulating tumour cell (CTC) detection.

Methods

RAS wild-type (wt) unresectable metastatic colorectal cancer (mCRC) patients (pts) with controlled disease after FOLFIRI + cetuximab (8 cycles) were randomized to receive maintenance with bi-weekly cetuximab alone or observation until disease progression. Tumour samples were centrally analysed by NGS using the AmpliSeq™ Colon and Lung Panel v2 and CTC (Cellsearch®) were assessed at baseline and during therapy. Mutation profiles and CTC counts were analysed according to objective response rate (ORR) before randomisation and progression-free survival (PFS) from randomization (in the ITT1 and the ITT2 population, respectively).

Results

A total of 214 pts (ITT1) were included in the PRODIGE28 trial according to *RAS* status locally assessed in each centre, and 139 randomized (ITT2). CTC count at baseline and mutation profiles were available in 154 and 189 pts, respectively. The median number of CTC/7.5mL at baseline was 1 [range: 0-79], and ≥ 3 in 52 (34%) pts. CTC count decreased after FOLFIRI + Cetuximab in 44 out of 78 (56%) pts. Neither baseline CTC counts nor a decrease during therapy were prognostic for ORR and PFS. Among mutations analysed by NGS, none were significantly associated with ORR. Pts with a tumour activating mutation on the MAPK pathway (defined as a mutation in at least one MAPK pathway gene) (29%) had significantly lower PFS (2.3 vs 3.7 months; HR = 1.77 [1.14-2.77], p = 0.01). This effect was maintained by adjusting on primary tumour side and performance status (HR = 1.65 [1.02-2.65], p = 0.04). Test for interaction was not statistically significant (p = 0.69), indicating that MAPK pathway activation was not a predictive factor for PFS (no treatment-dependent effect on PFS).

Conclusions

This exploratory analysis suggests that patients with any tumour mutation in MAPK pathway genes are not good candidates for maintenance treatment with cetuximab or treatment interruption after first-line FOLFIRI-cetuximab.

Clinical trial identification

NCT02404935.

Legal entity responsible for the study

UNICANCER.

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Disclosure

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