Intermittent or continuous panitumumab (PAN) plus FOLFIRI for first-line treatment of patients (pts) with RAS/BRAF wild-type (WT) metastatic colorectal cancer (mCRC): A randomized phase II trial (IMPROVE)


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Background: Anti-EGFR treatment demonstrated a clinical benefit limited to RAS-wt mCRC pts. In the FIRE-3 trial the depth of response was significantly associated with survival and the median time to tumor nadir was of 3.6 months in the FOLFIRI plus anti-EGFR arm. These data suggest that further exposure to combined treatment may not result in an outcome improvement, but only in an increase of side effects. Therefore, a drug holiday strategy could increase adherence to therapy and quality of life. The feasibility of intermittent use of FOLFIRI in first line was showed by the GISCAD study, but no data are available on the optimal duration of anti-EGFR monoclonal antibodies (moAbs). This issue is of particular interest given the dermatologic toxicities of anti-EGFR moAbs and the emergence of drug resistant clones. In mCRC pts recent data suggest a molecular adaptation of tumor to an intermittent drug schedule with anti-EGFR moAbs. On this basis, we designed a multicenter phase II randomized two arms study with intermittent PAN plus FOLFIRI compared to the same regimen given continuously until disease progression (PD) in the first line treatment of pts with WT RAS and BRAF unresectable mCRC, with a prospective genetic analysis of both tumor tissue and cfDNA.

Trial design: PFS on treatment (PFSOT) at 12 months is the primary endpoint. Assuming a p0=30% (corresponding to a median PFS of 7 months), and a p1=43% (corresponding to a median PFS of 10 months), setting the significance level at 10% with a power of 80% a total of 68 pts will be enrolled in each arm. At the time of enrollment, pts will be immediately randomized to one of the two arms: standard continuous or exploratory intermittent treatment.


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