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HER2 gene copy number status may influence clinical efficacy to anti-EGFR monoclonal antibodies in metastatic colorectal cancer patients.

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Source

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Abstract

BACKGROUND:

In metastatic colorectal cancer (mCRC), KRAS is the only validated biomarker used to select patients for administration of epidermal growth factor receptor (EGFR)-targeted therapies. To identify additional predictive markers, we investigated the importance of HER2, the primary EGFR dimerisation partner, in this particular disease.

METHODS:

We evaluated the HER2 gene status by fluorescence in situ hybridisation (FISH) in 170 KRAS wild-type mCRC patients treated with cetuximab or panitumumab.

RESULTS:

Depending on HER2 gene copy number status, patients showed three distinct cytogenetic profiles: 4% of patients had HER2 gene amplification (R:HER2/CEP17 $\geq$ 2) in all neoplastic cells (HER2-all-A), 61% of patients had HER2 gain due to polysomy or to gene amplification in minor clones (HER2-FISH+*), and 35% of patients had no or slight HER2 gain (HER2-FISH-). These subgroups were significantly correlated with different clinical behaviours, in terms of response rate (RR; P=0.0006), progression-free survival (PFS; P<0.0001) and overall survival (OS; P<0.0001). Patients with HER2-all-A profile experienced the worst outcome, patients with HER2-FISH- profile showed an intermediate behaviour and patients with HER2-FISH+* profile were related to the highest survival probability (median PFS in months: 2.5 vs 3.9 vs 7.6, respectively; median OS in months: 4.2 vs 9.7 vs 13, respectively).

CONCLUSION:

HER2 gene copy number status may influence the clinical response to anti-EGFR-targeted therapy in mCRC patients.