Gut. 2015 Jun;64(6):921-8. doi: 10.1136/gutjnl-2014-307234. Epub 2014 Jul 10.

FCGR polymorphisms and cetuximab efficacy in chemorefractory metastatic colorectal cancer: an international consortium study.

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Abstract

OBJECTIVE:

We aimed to better clarify the role of germline variants of the FCG2 receptor, FCGR2A-H131R and FCGR3A-V158F, on the therapeutic efficacy of cetuximab in metastatic colorectal cancer (mCRC). A large cohort with sufficient statistical power was assembled.

DESIGN:

To show a HR advantage of 0.6 in progression-free survival (PFS) for FCGR2A-HH versus the rest and FCGR3A-VV versus the rest, with an 80% power, 80 Kirsten Rat Sarcoma Viral Oncogene Homolog (KRAS) wild-type (KRAS-WT) and 52 KRAS-WT patients are required, respectively. This leads to a total sample size of 952 and 619 patients, respectively. Samples were collected from 1123 mCRC patients from 15 European centres treated with cetuximab alone or in combination with chemotherapy. Fc gamma receptor (FCGR) status was centrally genotyped. Two additional externally genotyped series were included.

RESULTS:

Incidences of FCGR2A-HH and FCGR3A-VV in KRAS-WT patients were 220/660 (33%) and 109/676 (16.1%) respectively. There was no difference in median PFS (mPFS) for KRAS-WT patients with FCGR2A-HH (22.0 weeks; 95% CI18.8 to 25.2) versus non-HH (22.0 weeks; 95% CI 19.4 to 24.6) or for FCGR3A-VV (16.4 weeks; 95% CI 13.0 to 19.8) versus non-VV (23 weeks; 95% CI 21.1 to 24.9) (p=0.06). Median overall survival, response rate and disease control rate assessments showed no benefit for either HH or VV.

CONCLUSIONS:

No differences in mPFS were found between the FCGR polymorphisms HH and the others and VV versus the others in KRAS-WT mCRC patients refractory to irinotecan, oxaliplatin and 5-fluorouracil treated with cetuximab. We cannot confirm the effects of other IgG1 antibodies, which may be weaker than previously suggested. Other markers may be needed to study the actual host antibody response to cetuximab.