Phase I/IIa study evaluating the safety, efficacy, pharmacokinetics, and pharmacodynamics of lucitanib in advanced solid tumors

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There was a spelling error in the author list in the original manuscript. The correct authors and affiliations are as above. The authors apologize for the errors.

Distal and proximal colon cancers differ in terms of molecular, pathological, and clinical features


There were some errors in the original manuscript. These have been corrected below. The authors apologize for the errors.

abstract-results

Proximal carcinomas were more often mucinous, microsatellite instable (MSI)-high, mutated in key tumorigenic pathways, expressed a B-Raf proto-oncogene, serine/threonine kinase (BRAF)-like and a serrated pathway signature, regardless of histological type. Distal carcinomas were more often chromosome instable and EGFR or human epidermal growth factor receptor 2 (HER2) amplified, and more frequently overexpressed epiregulin. While risk of relapse was not different per side, SAR was much poorer for proximal than for distal stage III carcinomas in a multivariable model including BRAF mutation status [N = 285; HR 1.95, 95% CI (1.6–2.4), p < 0.001]. Only patients with metastases from a distal carcinoma responded to anti-EGFR therapy, in line with the predictions of our pathway enrichment analysis.

materials and methods

patients

Clinicopathological data were available for a cohort of 3045 CC patients enrolled in the PETACC3 adjuvant chemotherapy trial. A subset of those patients had molecular data (N = 1404), including BRAF, KRAS, and PIK3CA mutation status, MSI status, and 18q arm loss of heterozygosity (LOS). Parallel gene expression (N = 589) and DNA copy number profiles (N = 199) were also available [16, 17]. Clinicopathological (N = 413) and molecular information (somatic mutations N = 199, RNAseq N = 325) for additional CC patients were obtained from the TCGA data portal (https://tcga-data.nci.nih.gov/tcga/) [18].

Gene expression profiles of 84 normal colon samples were derived from four datasets (TCGA CC, GSE14333, GSE8671, and GSE41258). To assess tumor side-effect on response to anti-epidermal growth factor receptor (EGFR) therapy, we studied a cohort of 435 chemorefractory metastatic CRC patients [19].

Tumors located in the splenic flexure, descending colon, and sigmoid colon were defined as distal, while cecum, ascending, and hepatic flexure were classified as proximal. Intrapertioneal rectum and distal rectum were excluded from the analysis. Transverse CCs (for the lack of clarity as to the exact location) were included exclusively when assessing feature distribution along the bowel. Further information is given in supplementary Materials and Methods, available at Annals of Oncology online.