Location of colon cancer (right-sided [RC] vs. left-sided [LC]) as a predictor of benefit from Cetuximab (CET): NCIC CTG CO.17

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BACKGROUND

RC and LC differ with respect to biology, pathology, and epidemiology. Further, recent SEER data suggests a mortality difference between RC and LC that varies by stage: stage II and III RC having lower and higher mortality, respectively. We examined if the primary tumour site can also predict for outcome in pre-treated, chemotherapy refractory, metastatic colon cancer (MCC). We compared RC vs. LC as a predictor for efficacy of EGFR inhibition with CET.

METHODS

Using CO.17 (CET vs. BSC), we coded the primary tumour site for 399 pts as RC (cecum to transverse colon) or LC (splenic flexure to rectosigmoid). Fisher's exact test assessed the association between site of cancer and baseline characteristics. Univariate and multivariate analyses of overall survival (OS) and progression free survival (PFS) by site of cancer were performed using Cox regression models.

RESULTS

Pts with RC (150/399) had more poorly differentiated tumours, mutant KRAS status, and peritoneal rather than liver and lung metastases, and they more often entered the study less than two years after initial diagnosis. Among pts receiving BSC, tumour location (RC vs. LC) was not prognostic for PFS (HR 1.07 [0.79, 1.44], p=0.67) or OS (HR 0.96 [0.70, 1.31], p=0.78). Among pts with KRAS wild type tumour status, site of cancer was a predictor of benefit from CET, with much greater PFS observed for LC (interaction p=0.002).

KRAS WT subset	Median survival (months) CET vs BSC	Benefit CET vs. BSC HR (95% C.I.), p value	Predictive effect Interaction p value
PFS			
LC	5.4 vs 1.8	0.28(0.18, 0.45), p<0.0001	0.002
RC	1.9 vs 1.9	0.73 (0.42, 1.27), p=0.26	
OS			
LC	10.1 vs 4.8	0.49 (0.31, 0.77), p=0.002	0.25
RC	6.2 vs 3.5	0.66 (0.36, 1.21), p=0.18	

CONCLUSION

In refractory MCC, tumour location within the colon (RC vs. LC) is not a prognostic factor, but is a strong predictor of PFS benefit from CET therapy. Additional research is needed to understand the molecular differences between RC and LC and their interaction with EGFR inhibition.