Potential drug targets in small-bowel adenocarcinoma

Most small-bowel adenocarcinomas have genomic alterations that are potentially targetable, according to findings from a recent genomic profiling study. Currently, few treatment options exist for this rare malignancy, which has a median overall survival of 20 months, and until now it has not undergone a comprehensive genomic analysis.

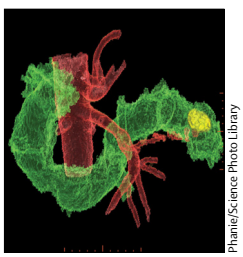
In a recent paper by Alexa Schrock (Foundation Medicine Inc, Cambridge, MA, USA) and colleagues, the investigators performed hybridisation capture-based genomic profiling of clinical samples of small-bowel adenocarcinomas (n=317), colorectal cancers (n=6353), and gastric adenocarcinomas (n=889). Genomic alterations (base substitutions, insertions/deletions, copy number changes, and cancer-associated rearrangements) were assessed in cancer-related genes. Potentially targetable genomic alterations associated with available therapeutics or drugs in clinical trials were detected in 290 (92%) of 317 small-bowel adenocarcinomas, especially *ERBB2*/*HER2* mutation/amplification, *EGFR* mutation/amplification, microsatellite instability, and PI3K pathway-activating alterations. The genomic alterations in small-bowel adenocarcinomas showed distinct differences compared with colorectal cancers and gastric adenocarcinomas.

Schrock commented, "We are encouraged at the number of alterations that were identified in small-bowel carcinomas that are potentially treatable with currently approved drugs in other tumour types or with drugs that can be accessed through clinical trials." Schrock hopes that the study will encourage the use and further development of genomically guided therapy for patients with these tumours.

"This study showed that small-bowel carcinoma is a unique cancer that we need to think of independently," said co-author Robert McWilliams (Mayo Clinic, Rochester, MN, USA). He noted that the incidence of high microsatellite instability could mean that the immunotherapeutic drug pembrolizumab is now accessible to some patients with small-bowel carcinomas .

Robert Coffey Jr (Vanderbilt-Ingram Cancer Center, Nashville, TN, USA) commented, "The investigators have analysed a much larger set of these tumours than has been done previously and compared them to gastric cancer and colorectal cancer…Whether the mutations found are driver mutations or merely passenger mutations is yet to be determined."

Judith A Gilbert



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For the **study by Schrock and colleagues** see *JAMA Oncol* 2017; published online June 15. http://dx.doi.org/10.1001/jamaoncol.2017.1051