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TARGETED THERAPIES

MATCH-AND-MIX OR MATCH-AND-MISS?

The goal of personalized medicine is to treat the right person with the right drug at the right time. In clinical oncology, the first step to achieve this chain of events is to obtain a molecular profile of the tumours and match whatever aberrations are identified with the available drugs designed to target those specific aberrations. This approach of combining treatments designed to target specific aberrations in individual tumours has proven to be very effective in certain types of cancer, such as melanoma or lung cancer. Can we extend the benefits of match-and-mix to all types of cancer, though?

The team led by Josep Tabernero at the Molecular Therapeutics Research Unit of Vall d'Hebrón Institute of Oncology has enrolled many patients with metastatic colorectal cancer (mCRC) in cohorts of phase I trials according to molecular profiling of tumours. "Our impression was that these patients did not derive significant benefit with a matched therapy, as opposed to those presenting breast, lung and gynaecological malignancies or advanced melanoma," says Tabernero.

To assess this observation further, the researchers evaluated retrospectively the benefit of matched targeted agents in 68 patients with mCRC who had been enrolled in 15 different phase I trials, in which they had received 82 targeted drugs in total. The study compared time to treatment failure (TTF) between treatment with the therapy selected according to the molecular profile of the tumour and the most-recent unmatched therapy on which the patient had experienced progression. Median TTF with matched targeted therapy was 7.9 weeks, compared with 16.3 weeks obtained with standard regimens, chemotherapy in most cases.

Although these result might be disappointing, Tabernero remains contagiously hopeful: "we are performing more comprehensive analysis of molecular aberrations and enrolling patients in clinical trials with new agents/targets based on solid preclinical data. Combination of targeted agents and chemotherapies is another way to move forward in order to increase the benefit for the patients."

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Original article Dienstmann, R. *et al.* Molecular profiling of patients with colorectal cancer and matched targeted therapy in phase 1 clinical trials. *Mol. Cancer Ther.* doi:10.1158/1535-7163.MCT-12-0290

Further reading Rodón, J. *et al.* Molecular prescreening to select patient population in early clinical trials. *Nat. Rev. Clin. Onc.* **9**, 359–366 (2012).