MSI status has been used to select metastatic colorectal cancer patients for immunotherapies. Introduction

Only a fraction of patients with metastatic disease respond to immune checkpoint inhibitors (ICI). Responders are more likely to be defective in mismatch repair genes (MSI). MSI+ patients are over-represented in the group of tumors with high densities of CD8+ T-cells. Patients with high T-cell infiltration have a higher expression of PD-1 and PD-L1, and are more likely to respond to ICI. These observations suggest that the response to ICI is strongly dependent on the presence of an established in situ adaptive immune reaction (Mlecnik et al. Immunology 2018).

Principle of the Immunoscore test

The Immunoscore® test is a standardized tool measuring the host immune reaction (CD3+ T-cells, CD10+ T-cells, CD8+ T-cells, and B-cells) within the primary tumor together with MSI status. The test is based on the International Immunoscore® SITC study, which included 282 patients with metastatic colorectal cancer, of whom 129 (44%) were high risk, 43% (81) were intermediate risk, and 28% (36) were low risk. The study showed that up to 20% of the MSS patients (n=129/652) had a High Immunoscore (IS3-4) associated with a low risk of relapse. The Immunoscore® test is a standard tool measuring the host immune reaction (CD3+ and CD8+ cells) in the primary tumor together with MSI status, which can help identify patients likely to benefit from immunotherapy.

Background & Rationale

In the Immunoscore International validation study (Pagès et al. The Lancet 2018), we recorded 1579 UICC–TNM Stage III patients with available MSI status and IS. 318 patients (20%) experienced a relapse. Among those patients, 36 patients (11%) were MSI+ whereas the vast majority of them (83%; 282 patients) were MSS. Patients who relapsed, combining MSI+ status (n=36 patients) with IS high (n=33 patients) to select patients for ICI extends from 11% to 22% the patients eligible to such immunotherapy.

Results: Immunoscore® versus MSI/MSS status in Stage I-IIII patients

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Eligibility of mCRC patients to ICI treatments

MSI color cancer Stage IV patients are eligible to ICI. However, this only concerns a minority of patients. Taking into account the evaluation of the in situ immune reaction in the primary tumor together with MSI status can clarify and extend the range of patients eligible to ICI.

Conclusions

• In our series of 318 Stage I-IIII CC patients, the relative proportion of patients who relapsed extends from 11% to 22% the patients eligible to such immunotherapy.

• The proportion of metastatic cancer patients eligible for ICI could be refined and extended by the characterization of their primary tumor immune infiltrate based on the Immunoscore, as suggested by Czeczot et al. Cancer Immunol Res. 2017.

• Interventional trials are now needed to validate the predictive value of Immunoscore.

• Immunoscore could also be helpful in identifying a subgroup of patients eligible for ICI in the early-stage setting, in order to select the MSI+ patients who could benefit from ICI.

References


• Czeczot J, Korn S, Hermitte F et al. Immunoscore to provide prognostic information in low- (T1–3N1) and high-risk (T4 or N2) subsets of Stage III colon carcinoma patients treated with adjuvant FOLFOX in a phase III trial (NCCTG N0147; Alliance). J Clin Oncol. 2018;36:4s(suppl;abstr614)


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