12P MSI status plus immunoscore to select metastatic colorectal cancer patients for immunotherapies

J. Galon[1], B. Mlecnik[1], F. Hermitte[2], F. Marliot[3], C. Bifulco[4], A. Lugli[5], I.D. Nagtegaal[6], A. Hartmann[7], M. van den Eynde[8], M. Roehrl[9], P. Ohashi[10], E. Zavadova[11], T. Torigoe[12], P. Patel[13], Y. Wang[14], Y. Kawakami[15], F.M. Marincola[16], P.A. Ascierto[17], B. Fox[18], F. Pagès[3]

[1]INSERM Team 15, Laboratory of Integrative Cancer Immunology, Paris, France, [2]R&D, HalioDx, Marseille, France, [3]Laboratory of Immunology, AP-HP, Georges Pompidou European Hospital, Paris, France, [4]Department of Pathology, Providence Portland Medical Center, Portland, OR, USA, [5]Department of Medical Oncology, University Hospital of Bern, Bern, Switzerland, [6]Pathology, Radboud University Medical Centre Nijmegen, Nijmegen, Netherlands, [7]Department of Surgery, University Erlangen-Nürnberg, Erlangen, Germany, [8]Department of Medical Oncology, Cliniques Universitaires St. Luc, Brussels, Belgium, [9]Department of Pathology, Memorial Sloan Kettering Cancer Center, New York, NY, USA, [10]Ontario Cancer Institute/Princess Margaret, University Health Network, Toronto, ON, Canada, [11]Pathology, General Faculty Hospital, VFN Charles University, Prague, Czech Republic, [12]Department of Pathology, Sapporo Medical University School of Medicine, Sapporo, Japan, [13]Cancer Biology, The Gujarat Cancer & Research Institute, Ahmedabad, India, [14]Institute of Cancer Research, Center of Translational Medicine, Health Science Center of Xi'an Jiaotong University, Xian, China, [15]Division of Cellular Signaling, Institute for Advanced Medical Research, Keio University School of Medicine, Tokyo, Japan, [16]Immune Oncology Discovery, AbbVie Inc., Redwood City, CA, USA, [17]Melanoma, Cancer Immunotherapy and Innovative Therapy Unit, Istituto Nazionale Tumori – I.R.C.C.S - Fondazione Pascale, Naples, Italy, [18]Laboratory of Molecular and Tumor Immunology, Earle A. Chiles Research Institute at the Robert W. Franz Cancer Center, Portland, OR, USA

Background: 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 PDL1, 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 Immunity 2016). MSI + colon 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 could clarify and extend the range of patients eligible to ICI.

Methods: Immunoscore is a robust and validated IVD test measuring the host immune reaction (CD3+ and CD8+ cells) at the tumor site. Immunoscore classifies patients' tumors into High, Intermediate or Low. We investigated the Immunoscore (IS) distribution of primary tumors of UICC-TNM stage I-III patients who experienced metachronous metastase(s) from the Immunoscore international validation cohort (Pagès The Lancet 2018). MSI status was assessed with the molecular new Bethesda panel and by IHC.

Results: We recorded 1579 UICC-TNM stage I/II/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 (89%; 282 patients) were MSS. 43 patients (13%) were IS High, 136 patients (43%) were IS Intermediate and 139 patients (44%) were IS Low. Importantly, 33 patients (12%) were classified IS High in MSS tumors. Combining MSI+ status with IS high to select patients for ICI extends from 11% to 22% the patients eligible to such immunotherapy.

Conclusions: The proportion of metastatic colon cancer patients eligible for ICI could be refined and extended by the characterization of their primary tumor immune infiltrate based on the Immunoscore status, as suggested by Le et al (Cancer Immunol Res 2017). Interventional trials are now needed to validate the predictive value of Immunoscore.

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