IMMUNOSCORE® COLON*

Clinical data update - September 2017

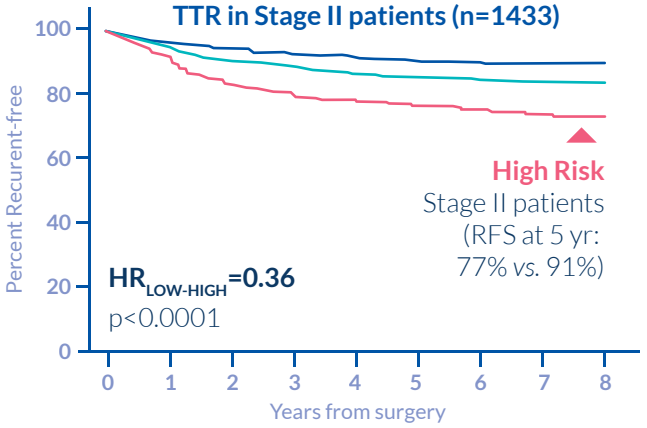
IMMUNOSCORE® CLINICAL UTILITY FOR STAGE II COLON CANCER (CC) PATIENTS

Results from the international Immunoscore® SITC study presented by Jérôme Galon, at the 2016 ASCO Meeting (manuscript submitted for publication)

There is today no consensus on risk factors to manage the approximately 20% of stage II patients who relapse; the *international Immunoscore® SITC* study validated Immunoscore® as a standardized tool to assess the risk of recurrence in this population to better manage chemotherapy prescription.

In the *Immunoscore® SITC* study (more than 3,000 patients), Immunoscore® was strongly prognostic, surpassing the TNM classification to predict outcome.

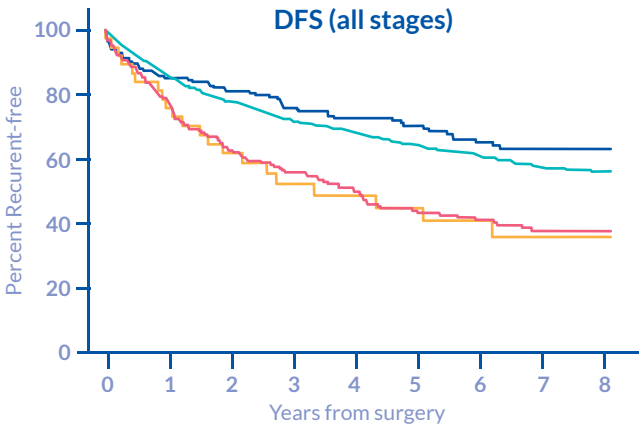
Focusing on stage II (n = 1,433 patients), Immunoscore® could identify a subgroup of high-risk stage II patients (25%) who may benefit from chemotherapy.



Classification	Events/Total	5 Year KM Est (95% CI)	Hazard Ratio (95% CI)
Immunoscore High	28/364	91.2 (87.9-94.5%)	0.36 (0.23-0.56)
Immunoscore Intermediate	88/694	85.9 (83.1-88.8%)	0.59 (0.43-0.81)
Immunoscore Low	83/375	76.8 (72.3-81.5%)	Reference

In addition, Galon et al. demonstrated that Immunoscore® was stronger than the MSI (Microsatellite Instability) status to predict relapse.

The *Immunoscore® SITC* study results demonstrate both the robustness of Immunoscore® and its clinical performance in stage II patients.



Classification	Events/Total	Time-Point	KM Est (95% CI)
Immunoscore High & MSI	71/205	3 years	77.3 (71.5-83.5%)
Immunoscore High & MSS	267/687	3 years	73.2 (69.8-76.7%)
Immunoscore Low & MSI	23/40	3 years	54.8 (40.9-73.5%)
Immunoscore Low & MSS	120/206	3 years	58.3 (51.7-65.6%)

With permission from J. Galon

HalioDx intends to further document Immunoscore® clinical utility in stage II CC as a key risk factor to guide chemotherapy prescription.

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IMMUNOSCORE® CLINICAL UTILITY FOR STAGE III CC PATIENTS

Results from the Immunoscore® validation N0147 study presented by Frank Sinicrope, at ASCO 2017 and ESMO-GI 2017 (manuscript in preparation)

Since 2004, 6 months of oxaliplatin -based treatment has been the standard of care as adjuvant therapy after surgery for stage III CC but 25% still relapse in this population. As this regimen is highly toxic, there is a need of a marker which could safely guide de-escalation therapy in patients with low-risk of relapse. In collaboration with the Mayo clinic, we investigated how Immunoscore® could be useful to identify those patients, in comparison with all other known risks factors.

The prognostic value of Immunoscore® was confirmed in stage III CC patients treated with FOLFOX alone (n=600) from the randomized Phase III adjuvant trial NCCTG N0147.
Immunoscore High was associated with significantly better prognosis than Immunoscore Low (81.6% *vs.* 66.1% 3-yr DFS; p<0.003). Results were similar regardless of the MSI status.

These results obtained in the context of a retro-prospective design with pre-specified cut-offs and endpoints, validate the clinical performance of Immunoscore® in the stage III setting.

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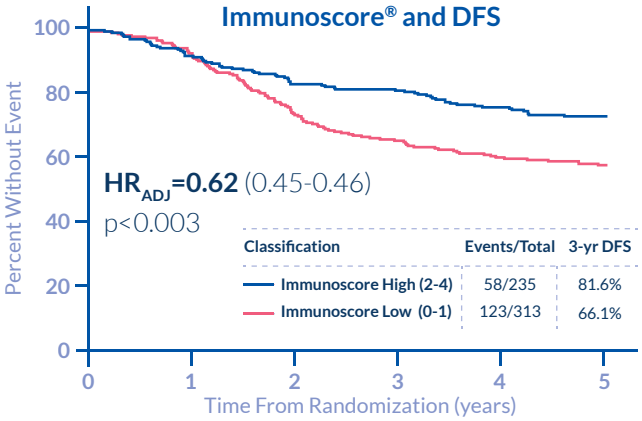


With permission from F Sinicrope

Importantly, the IDEA international collaboration results presented at the ASCO 2017 meeting showed that in patients with stage III colon cancer, a 3-month course of chemotherapy was almost as effective as a standard 6-month course while reducing the risk of neurotoxicity. A subgroup analysis further showed that the 3-month course was most appropriate for low-risk patients. Thus, a risk-based approach is now recommended by the IDEA collaboration to guide adjuvant chemotherapy prescription.

Considering IDEA clinical results, HalioDx is conducting additional studies to further demonstrate that Immunoscore® is a key risk factor to optimally adapt chemotherapy prescription in stage III CC patients.

A COMPREHENSIVE BODY OF CLINICAL EVIDENCE - AS OF SEPTEMBER 2017

Immunoscore® surpasses TNM for prediction of tumor recurrence and survival in CRC patients

- Galon J et al. - Science 2006
- Pages F et al. - JCO 2009
- Mlecnik B et al. - JCO 2011
- Galon J et al. - ASCO 2016

Immunoscore® is a stronger predictor of survival than MSI in CC

- Mlecnik B et al. - Immunity 2016, Stage II CC patients with Immunoscore Low have a higher risk of recurrence
- Galon J et al. - SITC 2016 - Oral presentation of the SITC Immunoscore® study *(manuscript submitted)*

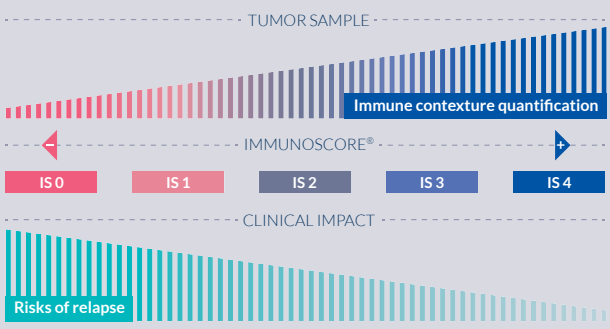
Stage III CC patients with Immunoscore High have a lower risk of recurrence regardless of the MSI status

- Sinicrope FA et al. - ASCO 2017 - Poster *(manuscript in preparation)*

HalioDx is conducting multiple studies to reach a higher level of clinical evidence. This will further support the Immunoscore®-based risk assessment for CC patients management.

PRINCIPLE AND CLINICAL UTILITY

Immunoscore® is a standardized IHC assay enhanced by digital pathology enabling the robust quantification of immune cells in the tumor (immune contexture).
A high density of immune cells indicates a robust immune response against tumor cells and a low-risk of relapse. A low infiltration indicates a weak anti-tumor immune response and a high-risk of relapse.
In localized CC, Immunoscore® strongly predicts the risk of relapse, independently of usual risks factors.



HalioDx intends to expand Immunoscore® clinical utility beyond CC, in a variety of cancer types and treatment regimens including immunotherapies.

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