Immunoscore® is an in vitro diagnostic test that predicts the risk of relapse in patients with early-stage Colon Cancer (CC) by measuring the host immune response at the tumor site. It is a risk-assessment tool that provides independent and superior prognostic value than traditional risk parameters and is intended to be used as an adjunct to the TNM classification. Currently, the target population for Immunoscore is stage II & III CC patients, for whom individual risk-assessment plays a critical role to guide post-surgery decisions. In stage I, survival rates are high and adjuvant chemotherapy is not typically recommended. However, approximately 10% of stage I CC tumors will recur even after surgical resection.

• A subgroup analysis was performed on the stage I patients (n=451) from the Immunoscore international validation study (Pagès et al. The Lancet 2018). Patients were classified by Immunoscore based on predefined cutoffs, either in 5 (IS 0-4), in 3 (IS 0-1, IS 2, IS 3-4) or in 2 categories (IS 0-1, IS 2-3-4).
• Time to recurrence (TTR) was compared between Immunoscore categories.
• When stratified into 3 categories, IS 0-1 vs IS 3-4 was significantly associated with worse 5 yrs TTR rates of 91.5% (95% CI 93.4-100.0) vs 97.1% (95% CI 83.8-98.9) (unadjusted and stratified by participating center HRlow vs high=7.82; 95% CI 1.49−41.01; p=0.015), with the highest relative contribution of IS to the risk of relapse (Chi2).
• Immunoscore was stronger than all standard clinical parameters, showing the highest contribution to predict relapse.
• Significant results were found using the Immunoscore percentiles as numeric continuous parameter.

### Association of Immunoscore with clinical outcome in Stage I Colon Cancer Patients

**Relative contribution of IS to the risk of relapse (Chi2)**
- IS 3-4, 2 and 0-1 were observed in 39%, 47% and 14% of the cohort, respectively.
- IS was positively and significantly correlated with TTR.
- In multivariate analysis, when adjusting the model with IS, age, gender, T-stage sidedness and MSI, IS remained the sole significant parameter (stratified by participating center HRlow vs high =7.82; 95% CI 1.49−41.01; p=0.015), with the highest relative contribution for prediction of relapse (chi squared proportion (χ2) =62%) compared to the other parameters in the model.
- **Immunoscore is a robust prognostic indicator of the risk of recurrence in stage I CC.**
- This risk assessment tool reliably identifies a sub-group of patients with an increased risk of relapse for whom a more intensive surveillance program after curative resection may be recommended.

#### Distribution of Immunoscore among 451 Stage I CC patients

- IS 0-1: 36%
- IS 2: 19%
- IS 3-4: 45%

#### Correlation between Immunoscore classification and TTR

<table>
<thead>
<tr>
<th>Immunoscore classification</th>
<th>Events/total</th>
<th>5y event-free survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>IS4</td>
<td>1/27</td>
<td>100%</td>
</tr>
<tr>
<td>IS3</td>
<td>4/149</td>
<td>96.6%</td>
</tr>
<tr>
<td>IS2</td>
<td>13/214</td>
<td>94.9%</td>
</tr>
<tr>
<td>IS1</td>
<td>4/45</td>
<td>90.5%</td>
</tr>
<tr>
<td>IS0</td>
<td>2/16</td>
<td>92.3%</td>
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</tbody>
</table>