INTRODUCTION

- In the IDEAS study, 3-month CAPOX was as effective as 6-month CAPOX in stage III colon cancer (CC) patients. The same was true for mFOLFOX6.
- Immunoscore (IS) is an IVD assay, which provides an individualized risk of relapse in early-stage CC patients by measuring the host adaptive immune response in the tumor tissue (TC) and its invasive margin (IM).
- The robustness and performance of the algorithm was assessed via an international ITC (Society for Immunotherapy of Cancer) led validation study of 3030 stage I-III CC patients from 13 countries.
- The prognostic and predictive value of IS was assessed in the mFOLFOX6 subgroup of the IDEAS France cohort study.

METHODS

IDEA France Cohort

- Phase III randomized study of stage III CC patients (IDEA France [v.2010] of the IDEAS collaboration [v.2012]).
- 3-6 months of mFOLFOX6 or CAPOX.
- Randomization stratified by center, T stage, N stage, ECOG performance status, and age.
- The choice between mFOLFOX6 and CAPOX was left to the patient and investigator decision: 90% of patients received mFOLFOX6 and 10% CAPOX.

IS Methodology

- Details of CD3+ and cytotoxic CD8+ T-cells in the CT and invasive margin (IM) of each patient were quantified by digital pathology and converted to IS using predefined published cut-offs.
- IS was classified into two (Low, Intermediate (Int)-high) and three (Low, Int, High) groups.

Statistics

- The performance of IS to predict disease-free survival (DFS) was assessed in the modified intention-to-treat population and was adjusted with clinically relevant microsatellite stability (MSS) and Mismatch Repair (MMR) status.
- The study design is registered on ClinicalTrials.gov (NCT02324301).

RESULTS

Prognostic value of IS in stage III patients treated with mFOLFOX6

- 1230 patients had available tumor samples.
- 973 (69.5%) patients with eligible samples reached the IS quality control.
- 420 (23-month arm) and 411 (6-month arm) patients were treated with mFOLFOX6 and had available IS.
- The 3-year DFS rate was 63.2% for IS Low and 77.7% for IS Int+High (p=0.0001).

Table 3: Multivariate analysis for DFS combining IS and Histopathological classifications

<table>
<thead>
<tr>
<th>IS</th>
<th>Hazard Ratio (95% CI)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>1.00 (ref)</td>
<td>1.00</td>
</tr>
<tr>
<td>Int+High</td>
<td>1.10 (0.97-1.23)</td>
<td>0.001</td>
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</tbody>
</table>

- Multivariable Analysis

- T stage, N stage, gender, M1 status and IS were independent parameters (all p < 0.05).

Table 2: Multivariate analysis for DFS combining IS and Histopathological classifications

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- T stage, N stage, gender, MSI status and IS were independent parameters (all p < 0.05).

CONCLUSIONS

- The IS in low (Low, Int-high), and three (Low, Int, High) categories was confirmed as a prognostic factor for DFS in mFOLFOX6 treated stage III CC patients in the prospective IDEA France cohort study.
- Only patients with IS Int or High benefited from 6 months of mFOLFOX6 treatment, both in low (T1-T3, N1) and high (T4-N2) IS subgroups, compared to 3-month therapy.
- The IS predictive value needs to be analyzed in CAPOX-treated population from the IDEA collaboration study to explore the use of IS for guiding the choice and duration of adjuvant treatment in stage III CC.

References

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- Flagonet et al., The Lancet 2019.
- Aridjis T et al., J Clin Oncol 2018.

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Prognostic and predictive value of the Immunoscore in stage III colon cancer patients treated with mFOLFOX6 (3 vs 6 months) in the prospective IDEA France cohort study