Introduction

- Immunoscore® (IS) is an IVD assay, which provides an individualized risk of relapse in early-stage colon cancer (CC) patients by measuring the host adaptive immune response in the tumor core and its invasive margin. It is a clinically driven tool to provide a prognosis (High/Intermediate and more accurately than the AJCC-UICC TNM classification). 1

- It is not routinely and prognostic performance has been consolidated through an international validation study of 3,533 patients’ stage III CC-GCs from 13 countries led by the Society for Immunotherapy of Cancer (SITC). 2

- IS was assessed in the French IS cohort study1 investigating 3 vs 6 months of oxaliplatin-based adjuvant chemotherapy in stage III CC patients. The primary objective was to validate whether the immunoscore test is able to identify patients with high risk of relapse or death whichever occur first among stage III patients under oxaliplatin-based adjuvant therapy.

Methods

IDEA France Cohort

- Phase III randomized study of stage III CC patients (IDEA France part) between 2010 and 2018. 3
- 3 vs 6 months of chemotherapy with mFOLFOX6 or CAPOX. 4
- Randomization stratified by centre, stage, N stage, EGFR PS, and age. 5
- mFOLFOX or CAPOX left to the patient and investigator decision. 60% of patients were treated with mFOLFOX, 10% with CAPOX.

Immunoscore Methodology

- Dense set of CD3+ and CD8+ T cells in the tumor core (CT) and invasive margin (CIM) of each patient were quantified by digital image analysis, and were categorized into IS using predefined published cut-offs. 7
- IS was classified into 2 groups (Low, Intermediate) and as a continuous score. 8

Statistics

- The performance of IS to predict disease-free survival (DFS) was assessed in the modified intention-to-treat population, in each study arm and was adjusted with clinical feature in multivariable Cox models. Harel’s C-statistic was used to investigate the IS performance.

- The study design is registered on ClinicalTrials.gov (NCT01028001).

Results

Patients Characteristics and IS Determination

1,322 patients with available tumor sample. A linear proportion of low-risk patients (T1-T3,N1) vs T4 tumors was observed in those with sample available for the IS characterization. 3 All samples were excluded due to poor-quality non-continuous (1%), 962 patients (66.6%) reached the quality control, 973 treated with mFOLFOX6 and 98 by CAPOX. 10

- Local (L) disease: 18 + 14% (T1,T2, 70.95% and 77.14% [95%CI 73.50-79.46] and 78.05% [95%CI 74.94-81.06]) vs 80.35% [95%CI 75.00-84.59] respectively (p=0.0001).

- High risk patients (T1-T3, N1) were treated with mFOLFOX6 and 89 by CAPOX. 11

- Only patients with IS Intermediate or High dial benefit from 6 months of mFOLFOX6 treatment compared with 3 months, both in low-risk (T1-T3,N1) and in the high-risk groups (T4 and N2). In contrast, no significant benefit of the 6-month FOLFOX regimen was observed for patients with IS Low. A moderate benefit of the 6-month FOLFOX regimen was observed in the first 3 years and was multiplied thereafter.

Prognostic value of IS in stage III patients

(A) IS 2 groups (Low, Intermediate) 12

(B) IS 3 groups (Low, Intermediate, High) 13

(C) Low-risk / High-risk (IS 2-group) 14

(A) Among patients’ groups stratified by IS in 2 categories (Low vs Intermediate), the 3-year DFS rates were 66.83% (95%CI 62.23-71.50) and 71.41% (95%CI 66.48-76.88) for IS Low and Intermediate, respectively (p=0.04).

- With IS in 3 categories, the 3-year DFS rate of 81% was observed in patients with IS High, vs 67% in patients with IS Low (p<0.001) (I1). In continuous variables, the p-value was also significantly different for IS 2 groups (p<0.002) (I2).

- The deleterious effect of IS Low in terms of DFS was higher in patients with T1-3 than in patients with T4 tumors (p<0.002) (I3).

Multivariable analysis

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

Multivariable analysis for DFS combining IS and Histopathological classifications

- Patients are stratified into 4 groups based on IS and a combination of histopathological factors

The efficacy of 3 vs 6 months of mFOLFOX6 therapy according to IS status

(A) All patients

(B) High risk (T1-T3, N1)

(C) High risk (T4 and N2)

(A) The beneficial effect of the 6 months vs 3 months FOLFOX regimen was observed in patients with IS Intermediate and IS Low (p<0.001). 15

(B) This benefit was observed in the low-risk (T1-T3, N1) and in the high-risk groups (T4 and N2). In contrast, no significant benefit of the 6-month FOLFOX regimen was observed for patients with IS Low. A moderate benefit of the 6-month FOLFOX regimen was observed in the first 3 years and was multiplied thereafter.

Conclusion

The immunoscore is a 2 categories (Low, Intermediate) 3 categories (Low, Intermediate, High) stage and sex as a continuous variable is confirmable as a prognostic factor for DFS in stage III CC patients in the prospective IDEA France cohort study.

- Only patients with IS Intermediate or High dial benefit from 6 months of mFOLFOX6 treatment compared with 3 months, both low-risk (T1-T3, N1) and high-risk (T4 and N2) stage III groups.

- These results need to be confirmed on another patients’ population included in the IDEA international study, to evaluate the impact of IS stratification of 3 vs 6 months of CAPOX treatment, and to validate its use to guide the choice of oxaliplatin-based adjuvant chemotherapy duration in stage III CC.

References