UCGI 34 - PROSCORE: A prospective study assessing whether Immunoscore® Colon test impacts the choice of adjuvant chemotherapy, in a multidisciplinary meeting, for treating non-metastatic colon cancer patients after curative-intent surgery

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Background

The prognosis and treatment of patients with resected colon cancer are based on the TNM staging classification. However, this approach fails to account for the important role of the immune system.

The immune response can now be accurately measured in clinical practice with the Immunoscore® Colon assay. This assay provides a standardized quantification of CD3+ and CD8+ T cell densities both in the tumor center and invasive margin.

Immunoscore® was shown to predict patient outcome more accurately than TNM classification plus other parameters including microsatellite instability status in a large international multicenter study, supporting its implementation as a new component of a TNM-Immune classification of colon cancer.

The objective of PROSCORE study is to assess the impact of Immunoscore® on adjuvant chemotherapy decision making in patients with resected stage II-III colon cancer.

Objectives

Primary objective :

To assess whether the Immunoscore® (IS) Colon test results will impact the choice of therapy, during a multidisciplinary meeting, in two cohorts of patients (stage II and stage III colon cancer) after curative-intent surgery of non -metastatic colon cancer for which adjuvant chemotherapy is being considered

Secondary objectives :

To assess:

- The consistency of decisions with the current recommendations
- The decision-making impact of IS Colon test results on treatment selection according to clinical sub-groups
- The feasibility of IS Colon test in clinical standard practice, samples and information flow
- The correlation of IS Colon test result with relapse-free survival (RFS), disease -free survival (DFS) and disease-specific survival (DSS)
- RFS rate at 3 and 5 years
- Overall survival at 5 years
- The budget impact of IS Colon test use

Trial Rationale

TNM classification in combination with conventional clinicopathological factors provides the most reliable reference for routine prognostication and for guiding treatment decisions for colon carcinoma. However, the information provided by those classification tools remains imperfect in predicting the outcome of patients

Immunoscore® allows us to identify sub-groups of patients (see fig.1 &2):

1) **Patients at high risk of relapse** who may benefit from adjuvant chemotherapy (for stage II patients) or treatment intensification (for stage III patients).

2) **Patients at low risk of relapse** who may benefit from reduced adjuvant chemotherapy (decreased intensity and/or shorter duration) in stage III patients or absence of adjuvant chemotherapy in stage II patients.

Immunoscore® is an additional objective criterion for making individualized therapeutic decision with an improved risk assessment. The use of Immunoscore® aims to improve the treatments for patients and potential reduce treatment costs for the national health system.

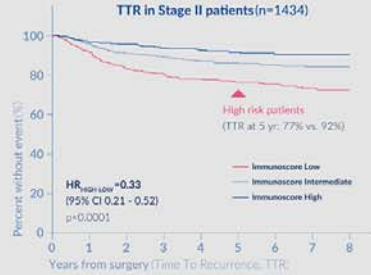


Figure 1 - TTR in stage II colon cancer

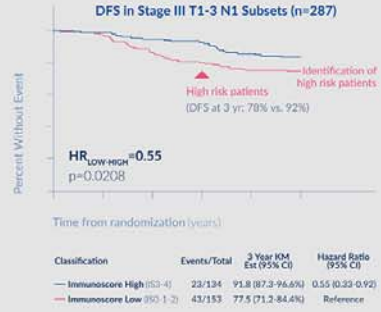
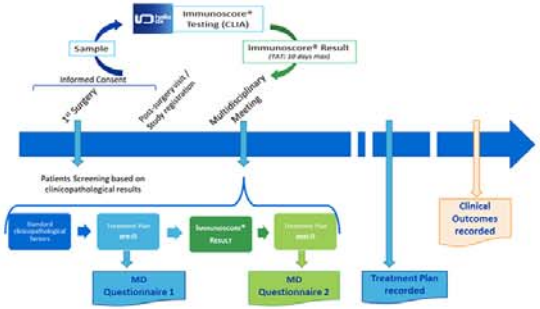


Figure 2 - DFS in stage III colon cancer

Study design

PROSCORE is a multicenter, non-randomized, prospective study.

The medical decisions (MDs) will be taken during one multidisciplinary meeting (MM). Alternatively, the MDs can be taken during two distinct MMs.



IS test result disclosing

During a multidisciplinary meeting, a **first therapeutic decision (n°1)** concerning adjuvant chemotherapy will be made and documented.

Once the initial decision is made, the IS Colon test result will be **disclosed** (eCRF and IVRS systems).

A second **therapeutic decision (n°2)** will then be made and documented.

Statistical considerations

The primary endpoint is the **rate of therapeutic modifications** due to IS Colon test result.

Sample size: **280 patients enrolled** (140 stage II and 140 stage III CRC)

With a one-stage Fleming design (α=5%, β=5%, p0=10% and p1=20%) we will include 133 evaluable per cohort. Taking into account an estimate of 5% of non -evaluable patients, we will enrol a total of 140 patients in each cohort.

The strategy will be considered effective if we observed at least 19 successes out of 133 evaluable patients. A success being defined as a therapeutic modification due to the IS Colon test result.

Study Population

Main Inclusion Criteria

- Patients ≥ 18 year of age
- Cytologically or histologically proven stage II or III colon adenocarcinoma (patients with rectal cancer are not eligible)
- Non-metastatic cancer assessed using appropriate imaging within 3 months of study registration and during per operative exploration
- Surgical resection within 2 months of study registration
- Adjuvant chemotherapy considered during multidisciplinary meeting
- Performance status ECOG ≤ 2

Main Exclusion Criteria

- Patients for which adjuvant chemotherapy is not indicated
- Other invasive cancer within 5 years of the diagnosis of colon cancer being studied, except for adequately treated squamous cell carcinoma, in situ cervical carcinoma and basal cell carcinoma
- Any previous systemic or loco regional anticancer therapy for the studied colon cancer (e.g. neoadjuvant therapy)
- Patient enrolled or planned to be enrolled in another clinical trial that may influence the therapeutic decision

References:

Pagès, F et al., The Lancet, May 2018

Sinicrope, F et al., J Clin Oncol 36, 2018

Study start: January 2019
End of recruitment: June 2020

Conflict of interests

First author disclosed relationships with Amgen, Roche, Sanofi-Aventis, Servier, Merck, Merck Serono, HalioDx, Bayer and Shire

Co-authors F. Hermitte and A. Catteau disclosed relationships with HalioDx

Information

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