High Immunoscore® is associated with good response to neo-adjuvant chemotherapy and prolonged survival in Head and Neck cancer patients

Haitham Mirghani1, Clémence Mure1, Bernhard Mlecnik2, Fabienne hermitte, Elise Martel2, Odile Casiraghi2, Mariana Iacob1, Caroline Even1, Jérôme Galon4.

1. Department of head and neck oncology - Gustave Roussy Cancer Center – 94805 Villejuif, France; 2. Department of pathology - Gustave Roussy Cancer Center – 94805 Villejuif, France; 3. Inserm, F-75006 Paris France, Inovarion, F-75013 Paris France; 4. Inserm, F-75006 Paris France

Contact: haitham.mirghani@aphp.fr

Introduction
In Head and Neck (H&N) cancer, the presence of high levels of tumour immune infiltrate has been recognized to be associated with better prognosis4. Immunoscore® (IS) is a CT-VD assay which provides an individualized risk of relapse in early-stage Colon Cancer (EC) patients by measuring the host immune response at the tumour site. The assay allows the stratification of patients into 2 (Low, High) or 3 (Low, Intermediate, High) Immunoscore categories. The primary objective of this study was to evaluate if the level of immune infiltrate measured by the Immunoscore® assay is predictive of induction chemotherapy response.

Methods

**Immunoscore methodology**
- Densities of CD3+ and cytotoxic CD8+ T cells in the core tumor (CT) and invasive margin (IM) of each patient were quantified by digital pathology.
- The complete cohort of patients was used for the definition of cut-offs for the conversion to IS.
- IS was classified in 3-groups (Low, Int, High) and as a continuous variable.

**Statistics**
The Wilcoxon-Mann-Whitney test was used for non-parametric tests. Fisher’s exact test was used to determine differences between responders and non-responders. Kaplan-Meier curves were used to visualize differences in Progression Free Survival (PFS). Significant difference of PFS among patient groups was calculated with the log-rank test. P values were corrected with the method proposed by Altman et al. Cox-proportional hazard model was used to determine hazard ratios. All tests were two-sided, and corrected with the method proposed by Altman et al.

**Predictive value of Immunoscore in Head and Neck cancer**
Among all patients with available data, 60% were good responders (N=108) as compared to 48.6% (CI 95% (39.7-57.7)) and 31.9% (CI 95% (19.4-48.7)) in Low and High patients respectively. High vs Low HR = 0.27 CI 95% (0.10-0.74); P corrected= 0.0128.

**Prognostic value of Immunoscore in Head and Neck cancer**
Kaplan-Meier estimates of PFS IS 3 groups: Low (CT<0.6-1.25), Int (0.6-1.25), High (≥1.25).
- In CT, CD3+ T cell median densities were 717 cells/mm² (95% CI 268-1030) and 304.9 cells/mm² (95% CI 156-630) in Hypopharynx and Laryngeal cancer patients respectively, p=0.0318 (Left).
- In CT, CD8+ T cell median densities were 121 cells/mm² (95% CI 51-276) and 68 cells/mm² (95% CI 30-137) in Hypopharyngeal and Laryngeal cancer patients respectively, p=0.188 (Right).
- In CT, CD8+ T cell median densities were 225 cells/mm² (95% CI 127-372) and 115 cells/mm² (95% CI 46-312) in Hypopharyngeal and Laryngeal cancer patients respectively, p=0.0368 (Right).
- Note: Densities in CT were available for only 40% of patients due to sample type biopsies.

**Immunoscore® distribution in the Head and Neck cancer cohort**

**Results**

**Patients Characteristics and IS Determination**
Out of a total of 130 patients involved in the study 82 Hypopharynx, 68 larynx. 110 patients had a valid Immunoscore® result (33 Hypopharynx, 57 larynx).
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- 108 patients had valid Immunoscore® results and complete clinical data (47 Hypopharynx, 56 larynx).
- 108 patients had valid Immunoscore® and response assessment data.

**Densities of CT cell infiltration were significantly higher in Hypopharynx as compared to Laryngeal cancer patients.**

**Statistics**

**Immunoscore® distribution in the Head and Neck cancer cohort**

**Fig. 1:** (A) Total T cell infiltration (CD3+), (B) Cytotoxic T cell infiltration (CD8+)

**Fig. 2:** IS distribution in Head and neck cancer patients (N=110)

**Fig. 3:** All patients (n=130). 5-years PFS rates of 71.4%, (CI 53.9-84.6) as compared to 54.6%, CI 95% (40.4-77.5) and 31.9%, CI 95% (13.3-74.7) in High, intermediate and low patients respectively. High vs Low HR = 0.27 CI 95% (0.10-0.74); P corrected= 0.0128.

**Fig. 4:** Hypopharynx patients (n=43). 5-years PFS rates of 57.9% (CI 25.8-100) as compared to 44.8%, CI 95% (25.9-71.7) and 31.9% (CI 95% (19.4-48.7) in High, Intermediate and low patients respectively. High vs Low HR = 0.21 CI 95% (0.05-1.26), p=0.199.

**Fig. 5:** Larynx cancer (n=85). 5-years PFS rates of 73.3%, (CI 33.3-100) as compared to 63.4 % (CI 45.8-88.1) and 36 CI 95% (15.48-61.1) in High, Intermediate and low patients respectively. High vs Low HR = 0.26 CI 95% (0.07-0.92), p=0.0255 (Right boxplots).

**Fig. 6:** Analysis of the entire cohort with valid IS expressed as a continuous variable

**Fig. 7:** IS distribution in Head and neck cancer patients

**References**