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

ESMO 2019 Abstract #2016

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Introduction

In Head and Neck (H&N) cancer, the presence of high levels of tumor immune infiltrate has been recognized to be associated with better prognosis[1-3]. Immunoscore® (IS) is a CE-IVD assay which provides an individualized risk of relapse in early-stage Colon Cancer (CC) patients by measuring the host immune response at the tumor site[4]. 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 hazards model was used to determine hazard ratios. All tests were two-sided, and P < 0.05 was considered statistically significant. All analyses were performed with R statistical software (survival package).

Results

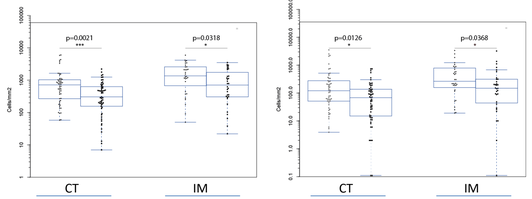
Patients Characteristics and IS Determination

Out of a total of 130 patients involved in the study (62 hypopharynx, 68 larynx):

- 110 patients had a valid Immunoscore® results (53 hypopharynx, 57 larynx).
- 103 patients had valid Immunoscore® results and complete clinical data (47 Hypopharynx, 56 larynx).
- 108 patients had valid Immunoscore® and response assessment data

Densities of T cell infiltration were significantly higher in Hypopharyngeal as compared to Laryngeal cancer patients.

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



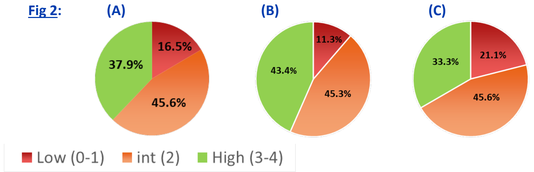
(A): In CT, CD3+ T cell median densities were 717 cells/ mm² (95% CI 268-1030) and 304,9 cells/mm² (95% CI 156-630) in Hypopharyngeal and Laryngeal cancer patients respectively, p=0.0021 (Left). In IM, CD3+ T cell median densities were 1361 cells/mm² (95% CI 674-2578) and 705 cells/ mm² (95% CI 307-1540) in Hypopharyngeal and Laryngeal cancer patients respectively, p=0.0318 (Right).

(B): In CT, CD8+ T cell median densities were 121 cells/mm² (95% CI 51-276) and 68 cells/ mm² (95% CI 15-137) in Hypopharyngeal and Laryngeal cancer patients respectively, p=0.0126 (Left). In IM, CD8+ T cell median densities were 263 cells/mm² (95% CI 172-751) and 149 cells/ mm² (95% CI 46-311) in Hypopharyngeal and Laryngeal cancer patients respectively, p=0.0368 (Right).

Note: Densities in IM were available for only 40% of patients due to sample type (biopsies).

Immunoscore® distribution in the Head and Neck cancer cohort

Fig 2: **(A)** **(B)** **(C)**



(A): IS distribution in Head and neck cancer patients (N=110)

(B): IS distribution in Hypopharyngeal cancer patients (N=53)

(C): IS distribution in Laryngeal cancer patients (N=57)

Prognostic value of Immunoscore in Head and Neck cancer

Kaplan-Meier estimates of PFS

IS 3 groups: Low (0-1), Int (2), High (3-4)

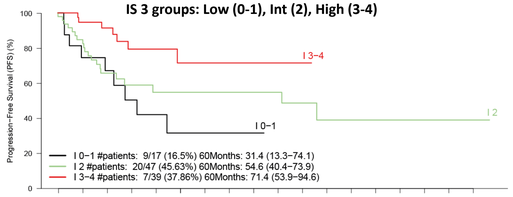


Fig 3: All patients (n=103). 5-years PFS rates of 71.4%, (CI 53.9–94.6) as compared to 54.6%, CI 95% (40.4–73.9) and 31.4%, CI 95% (13.3–74.1) in high, intermediate and low IS patients respectively.

High vs Low HR = 0.27 CI 95% (0.10–0.74), P corrected= 0.0214.

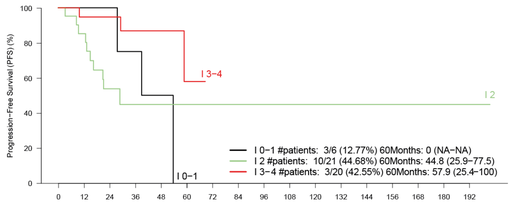


Fig 4: Hypopharynx patients (n=47). 5-years PFS rates of 57.9% (CI 25.4–100) as compared to 44.8 CI 95% (25.9–77.5) and 0% CI 95% (NA) in high, intermediate and low IS patients respectively.

High vs Low HR = 0.21 CI 95% (0.035–1.26), ns.

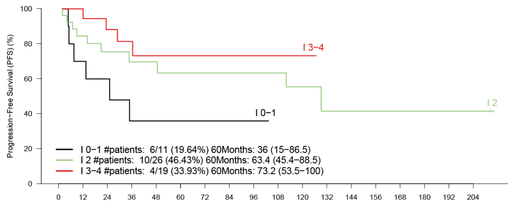


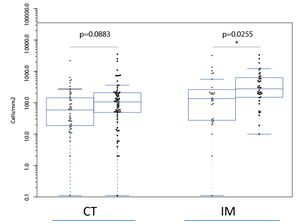
Fig 5: Larynx cancer (n=56). 5-years PFS rates of 73.2% (CI 53.5–100) as compared to 63.4 CI 95% (45.4–88.5) and 36 CI 95% (15–86.5) in high, intermediate and low IS patients respectively.

High vs Low HR = 0.26 CI 95% (0.07–0.92), ns.

Predictive value of Immunoscore in Head and Neck cancer

Among all patients with available data, 60% were good responders (N=108)

(A) Cytotoxic T cell infiltration (CD8+)



(B) IS distribution

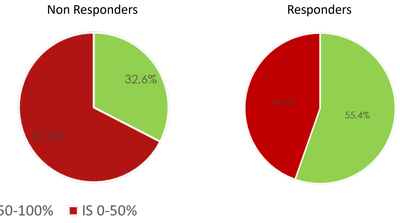


Fig 6: Analysis of the entire cohort with valid IS expressed as a continuous variable

(A): In CT, CD8+ T cell median densities were 59 cells/mm² (95% CI 18.8-144) and 107 cells/ mm² (95% CI 49-209) in Non-Responders and Responders patients respectively, ns (Left boxplots). In IM, CD8+ T cell median densities were 136 cells/mm² (95% CI 27.5-263.5) and 278 cells/ mm² (95% CI 149-634) in Non-Responders and Responders patients respectively, *p*=0.0255 (Right boxplots).

(B): Responders had a higher proportion of High Immunoscore® (55.4%) than Non-Responders (32.6%). *PV*=0.0297 with OR=2.5485 [1.0742-6.259].

Conclusion

- ✓ Analysis of the entire cohort showed that Immunoscore® in 3 categories (Low, Int, High) had prognostic value in Head and Neck cancer. Analysis in Laryngeal and Hypopharyngeal cancer patient cohorts separately showed similar trend.
- ✓ Potential predictive value of Immunoscore® for the response to induction chemotherapy.

Future directions

- ✓ Prognostic and predictive values of Immunoscore® in Head and Neck cancer should be confirmed in an enlarged cohort.

References

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