Press release

A large-scale international clinical study validates the prognostic value of Immunoscore® in colon cancer

- An international consortium confirms the strong prognostic value of the Immunoscore® assay in early stage colon cancer.
- Published in *The Lancet* on May 11, 2018, these results validate the reliability of Immunoscore® Colon in identifying patients with a high risk of recurrence, independently of the TNM[1] staging system.

Marseille, France, May the 14th, 2018 – HalioDx, an immuno-oncology company pioneering immunological diagnosis of tumours, announces the publication of the positive results of a clinical study validating Immunoscore® in early stage colon cancer. This study, led by the International Society for Immunotherapy of Cancer (SITC), was conducted in 14 expert centres in North America, Asia and Europe. Published in *The Lancet*, the results confirm the crucial prognostic value of Immunoscore® and support the implementation of Immunoscore® Colon in cancer classification using a new staging system termed TNM-I (I for Immune).

Immunoscore® exceeds all other clinicopathological parameters in predicting the risk of recurrence and survival in colon cancer patients

Following the STARD reporting guidelines (*Standards for Reporting of Diagnostic Accuracy*), this large clinical study was conducted on 2681 early stage colon cancer patients (stages 1 to 3) and demonstrates that the relative contribution of Immunoscore® in predicting patient survival exceeds that of all clinicopathological criteria, including the AJCC/UICC TNM classification system.

By measuring the density of CD3 and CD8 T lymphocyte populations in the centre and the periphery of the tumour, Immunoscore® stratified patients into three distinct prognostic groups in terms of risk of recurrence (primary endpoint) and survival (secondary outcome). Five years after surgical resection of the tumours, patients with a high Immunoscore® had the lowest rate of recurrence and death: 8% of patients recurred (log rank test $p < 0.0001$) and 18% died. In contrast, among patients with a low Immunoscore®, 32% recurred (log rank test $p < 0.0001$) and 38% died in the same period post-surgery.

A Cox multivariable analysis showed that only the international classification system (AJCC/UICC TNM) and Immunoscore® are significantly associated to survival. It further demonstrated that the prognostic value of Immunoscore® is independent of all other biological and clinical variables, including age, sex, histopathological classification (AJCC/UICC TNM), molecular profile of the tumour and microsatellite instability. Finally, despite the heterogeneity in the biological samples collected (the study included centres from 13 different countries), the quantification by Immunoscore® demonstrated to be robust and highly reproducible.

Over 10 years of research and development

Jerôme Galon and his co-workers demonstrated for the first time in 2006 that the density, localisation and functionality of adaptive immune cells at the centre and the periphery of a tumour (the immune contexture) determine the risk of recurrence and the probability of survival in colon cancer patients, and do so independently of any other biological or clinical parameter[2]. The Immunoscore® test was developed as a result of these observations and was validated through a number of retrospective studies[3], which prompted HalioDx to develop and commercialize the Immunoscore® Colon assay (CE-IVD in Europe, and available in CLIA laboratories in the USA).

"It's a crucial step that demonstrates the prognostic value of the very first diagnostic test based on the antitumour immune response" **highlights Dr Jérôme GALON, Research Director at the Inserm, head of the Laboratory for Integrative Immunology and Cancer Research in the Cordeliers Research Centre, co-founder and chairman of the Scientific Advisory Board of HalioDx and co-author of this publication** *"This publication further results from a remarkable collective effort, as suggested by its 99 co-authors; we have built what is today the largest international consortium in immuno-oncology".*

"This new study undeniably proves that the prognostic value of Immunoscore® in early stage colon cancer exceeds that of all other biological and clinical parameters" **declares Dr Bernard Fox, Harder Family Chair for Cancer Research at the Earle A. Chiles Research Institute, Robert W. Franz Cancer Center in Portland, OR and co-author of this work.** *"On the basis of these results, we aim to improve the current TNM cancer staging system to include the Immunoscore® quantification and give rise a new prognostic standard, the TNM-I (Immune)".* He went on to say, "*These results provide a basis for clinical trials to evaluate vaccines and other immunotherapies that might increase Immunoscore® and improve outcomes of patients with colon cancer*".

"It is definitely a key finding for early stage colon cancer patients for whom no biomarker was available before Immunoscore® to reliably evaluate the risk of recurrence after surgery" **indicates Vincent FERT, CEO and co-founder of HalioDx.** *"This work advocates for Immunoscore® Colon to be included in routine diagnosis, and identifies the need to make it widely available throughout healthcare systems".*

[1] The TNM Classification of Malignant Tumours (TNM) describes the stage of a cancer which originates from a solid tumor with alphanumeric codes. T describes the size of the original (primary) tumour and whether it has invaded nearby tissue, N describes nearby (regional) lymph nodes that are involved, M describes distant metastasis (spread of cancer from one part of the body to another). It is a classification of the anatomical extent of disease which has gained wide international acceptance for many solid tumour cancers.

[2] Galon et al Science 2006.

[3] Pagès et al JCO 2009, Mlecnik et al JCO 2011, Mlecnik et al Immunity 2016, Mlecnik et al JNCI 2018.

About HalioDx

The Immune Response to Cancer Diagnostics

HalioDx is an immuno-oncology diagnostic company providing oncologists with first-in-class Immune-based diagnostic products and services to guide cancer care and contribute to precision medicine in the era of immuno-oncology and combination therapies.
Immunoscore® proprietary technology, pioneered by Jérôme Galon at the Cordeliers Research Center, Paris, France, integrates immunohistochemistry combined with sophisticated algorithm and advanced imaging analysis enabling extraction of spatially-organized tissue molecular information. Immunoscore® is a platform for many cancers, as immune response to tumor is a key hallmark of disease progression. HalioDx collaborates with renowned international clinical groups to support clinical utility and ensure rigorous performance validation of its assays in selected cancer indications.

Two additional assays, Halioseek® & Immunosign®, have been developed by HalioDx and provide tools to help stratifying patients for immunotherapies.

HalioDx has an experienced team of more than 130 employees, a CLIA-certified laboratory and compliant facilities to develop, manufacture, register and market in vitro diagnostic (IVD) products. HalioDx executes biomarker studies and companion diagnostic assay development in conformity with regulations and in partnership with biopharmaceutical companies. The company co-founded the European immunology cluster Marseille Immunopôle (MI).

For more information, please visit our websites www.haliodx.com and www.immunoscore-colon.com and follow the company on Twitter @HalioDx.

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