



SITC 2017

November 8-12
NATIONAL HARBOR
MARYLAND

Gaylord National Hotel
& Convention Center



Society for Immunotherapy of Cancer

SITC
2017

Standardized immune-based diagnostic tests to predict the risk of recurrence and response to therapy of cancer patients

Fabienne HERMITTE



Society for Immunotherapy of Cancer

#SITC2017

Presenter Disclosure Information

Fabienne HERMITTE

The following relationships exist related to this presentation:

HalioDx (Marseille, FRANCE) Cofounder and Full-Time Employee

Discussion of Off-Label/Investigational Uses of Commercial Products:

Immunoscore® Colon: CE-IVD in Europe - CLIA service for US

Halioseek® PD-L1/CD8 available as a CE-IVD assay and as an RUO solution in the Rest of The World

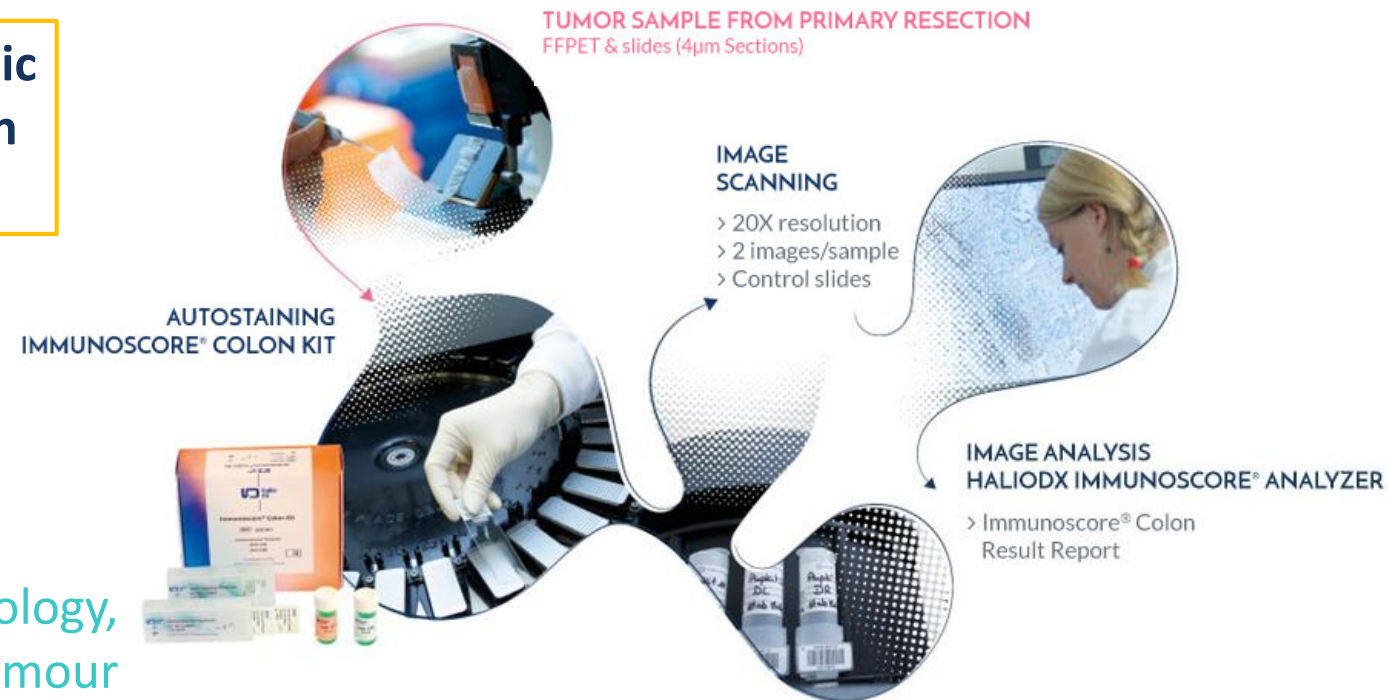
Background

- Each cancer patient needs a routine assessment of its immune response to tumor
- Immunotherapy needs better biomarkers to be more precise
- Our goal is to develop precise solutions in order to:
 - Upgrade cancer classification & solve diagnostic uncertainties with a more accurate risk assessment
 - Predict response / resistance to treatment(s)
 - Accelerate R&D of immunotherapies and discover potential CDx biomarkers

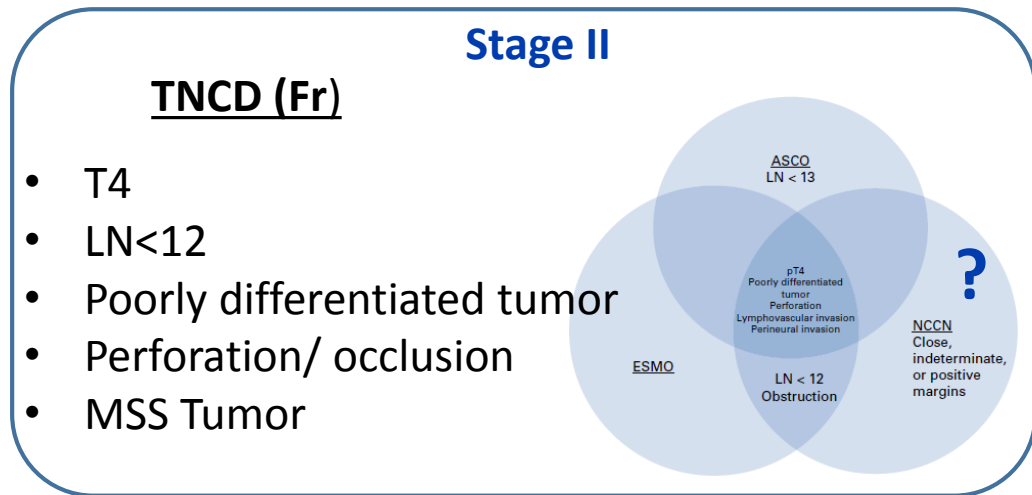
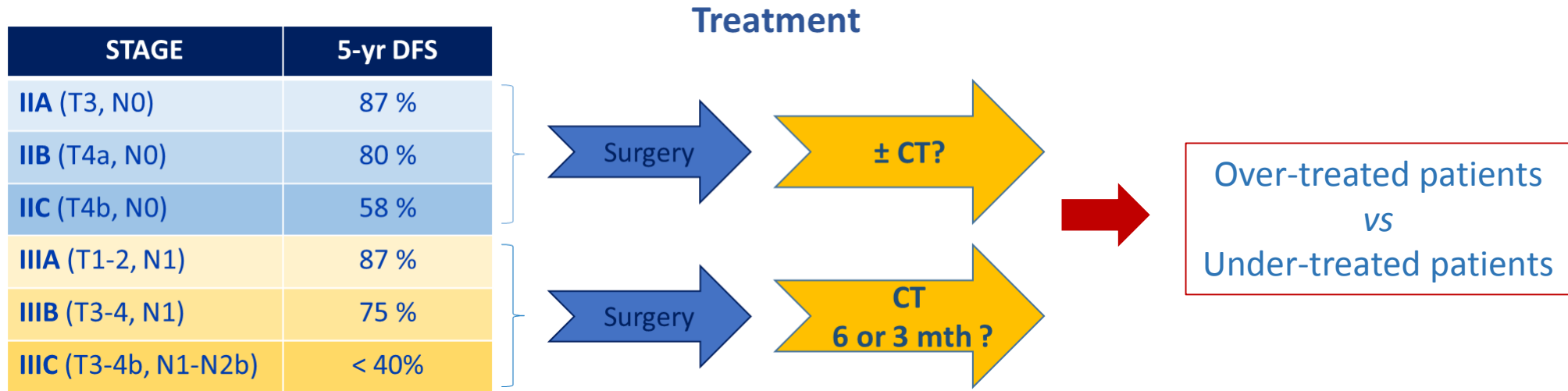
Immunoscore® Colon

- **Immunoscore® Colon is an in vitro diagnostic assay for risk of relapse assessment in colon cancer patients**

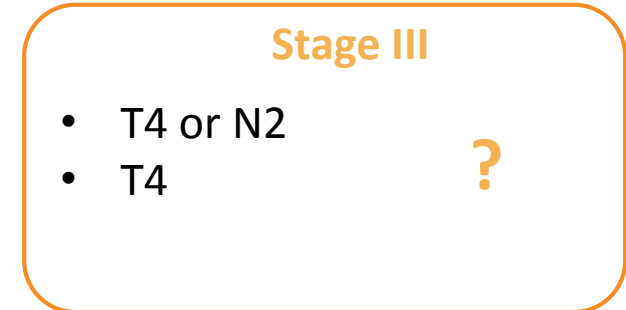
CD3+ and CD8+ lymphocytes detection by IHC
Quantification based on Digital Pathology,
combining information from the core of the tumour
(CT) and the invasive margin (IM)



TNM classification: Prediction of the risk of recurrence at 5 years is inaccurate



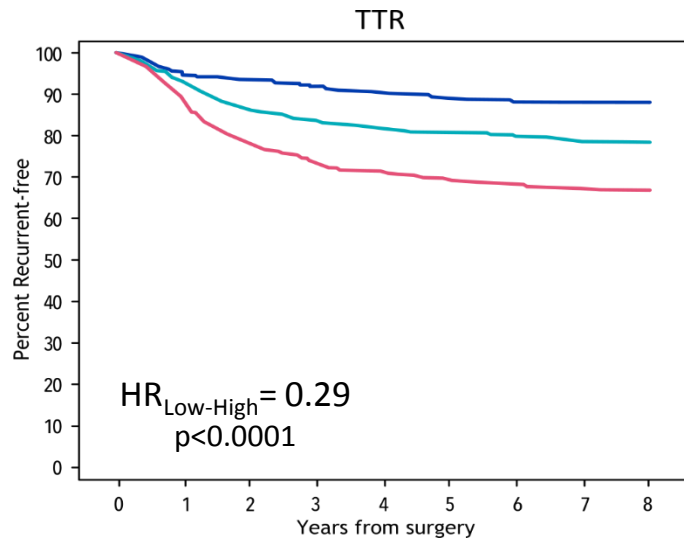
Identification of high-risk patients?



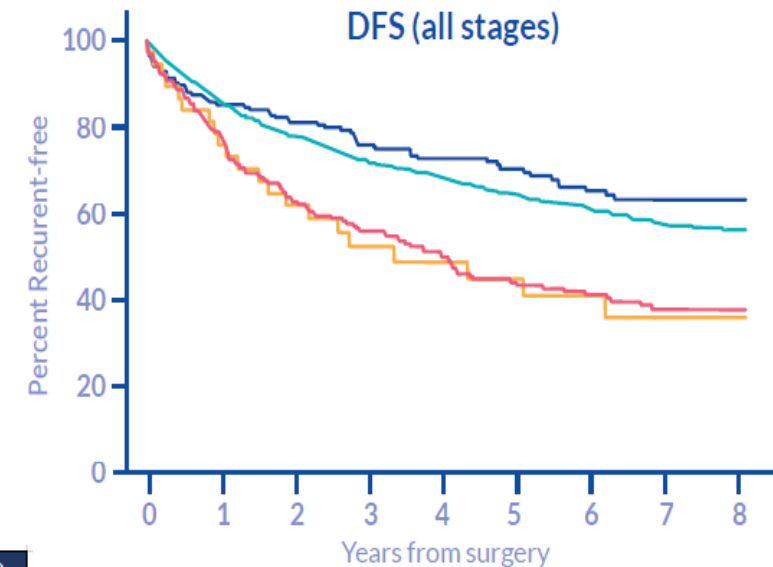
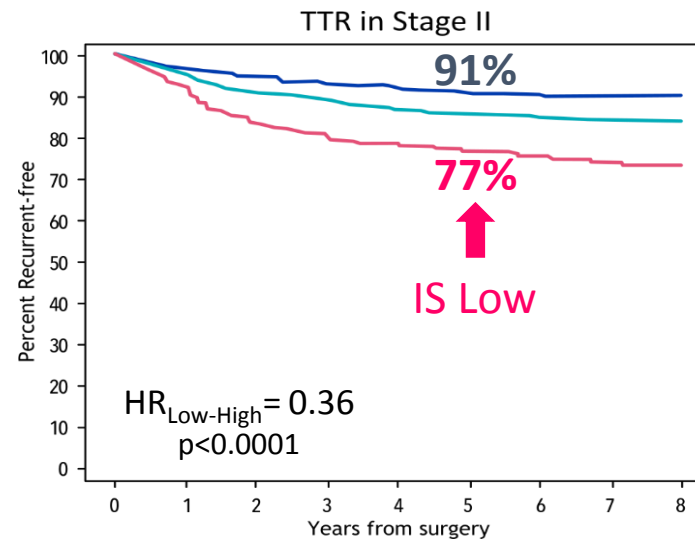
International Immunoscore® SITC study results

J Galon et al. ASCO & SITC 2016

St. I - III (n=2667)



St. II (n= 1433)



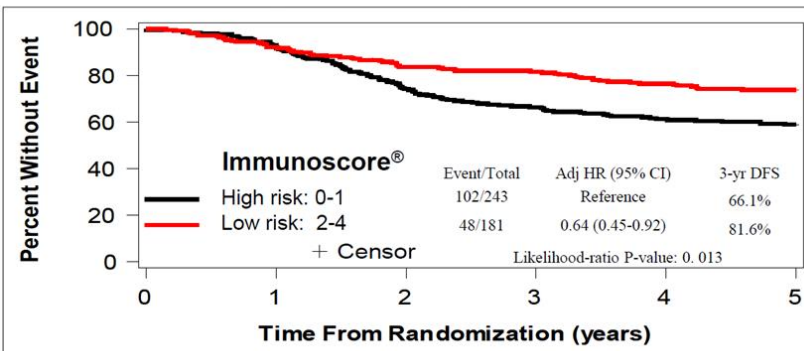
IS Result	Risk Subgroup	Events/Total	5 Year KM Est(95%CI)	Hazard Ratio (95% CI)
IS High	Low	64/687	88.9 (87.9-94.5%)	0.29 (0.21-0.38)
IS Inter	Medium	228/1306	80.6 (78.3-83.0%)	0.58 (0.48-0.71)
IS Low	High	186/674	69.9 (65.2-72.9%)	Reference

IS Result	Risk Subgroup	Events/Total	5 Year KM Est(95%CI)	Hazard Ratio (95% CI)
IS High	Low	28/364	91.2 (87.9-94.5%)	0.36 (0.23-0.56)
IS Inter	Medium	88/694	85.9 (83.1-88.8%)	0.59 (0.43-0.81)
IS Low	High	83/375	76.8 (72.3-81.5%)	Reference

Classification	Events/Total	Time-Point	KM Est (95% CI)
Immunoscore High & MSI	71/205	3 years	77.3 (71.5-83.5%)
Immunoscore High & MSS	267/687	3 years	73.2 (69.8-76.7%)
Immunoscore Low & MSI	23/40	3 years	54.8 (40.9-73.5%)
Immunoscore Low & MSS	120/206	3 years	58.3 (51.7-65.6%)

Immunoscore® Colon: Clinical evidence on randomized clinical studies

All patients



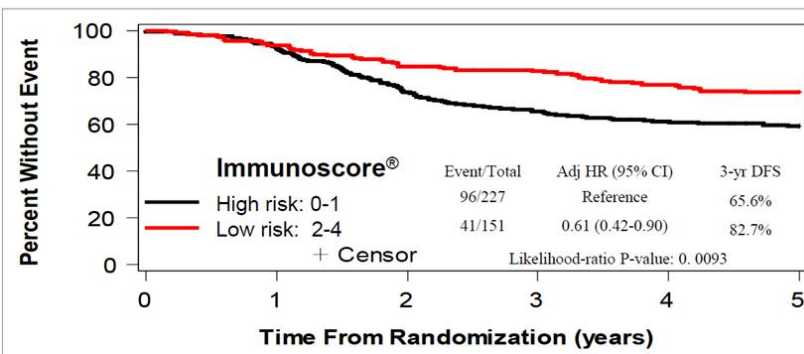
ASCO 2017 Poster

Collaboration with the Mayo Clinic - Frank A. Sinicrope

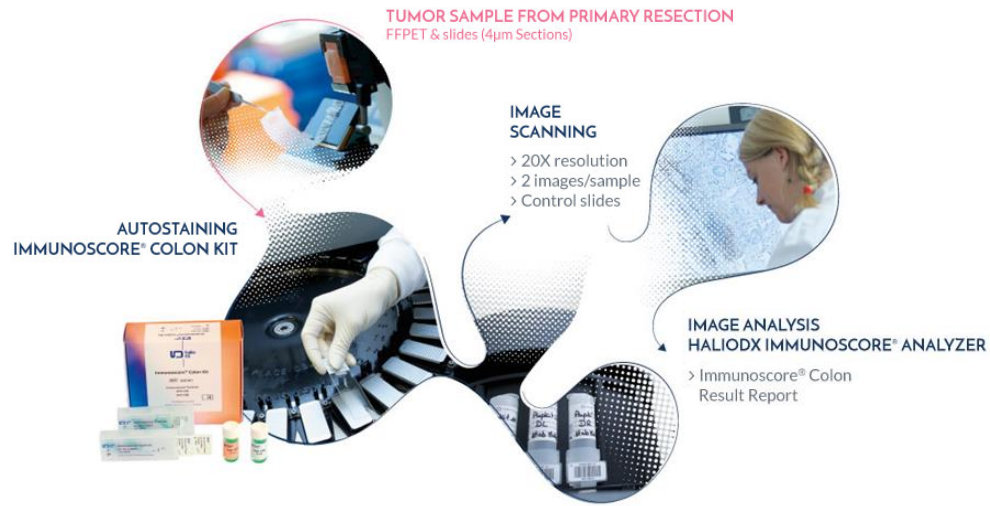
600 resected tumours of stage III CC patients from the FOLFOX arm of the prospective NCCTG N0147 clinical trial - IS analysis with predefined cut-offs

➤ *Identification of high risk patients, including in MSS population*

Excluding dMMR patients

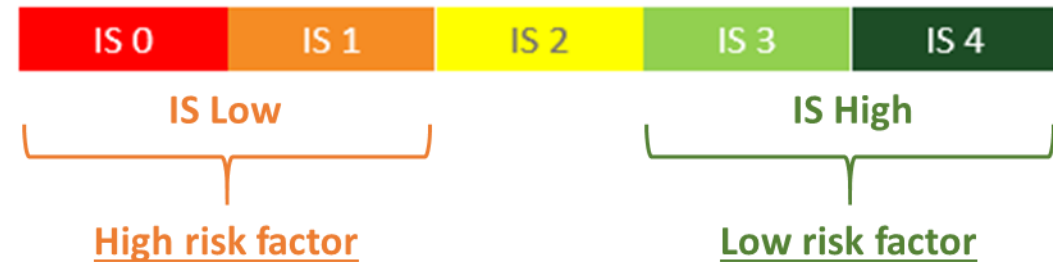


Oxaliplatin-based chemotherapy for patients with stage III colon cancer: Disease Free Survival results of the three versus six months adjuvant IDEA France Trial.



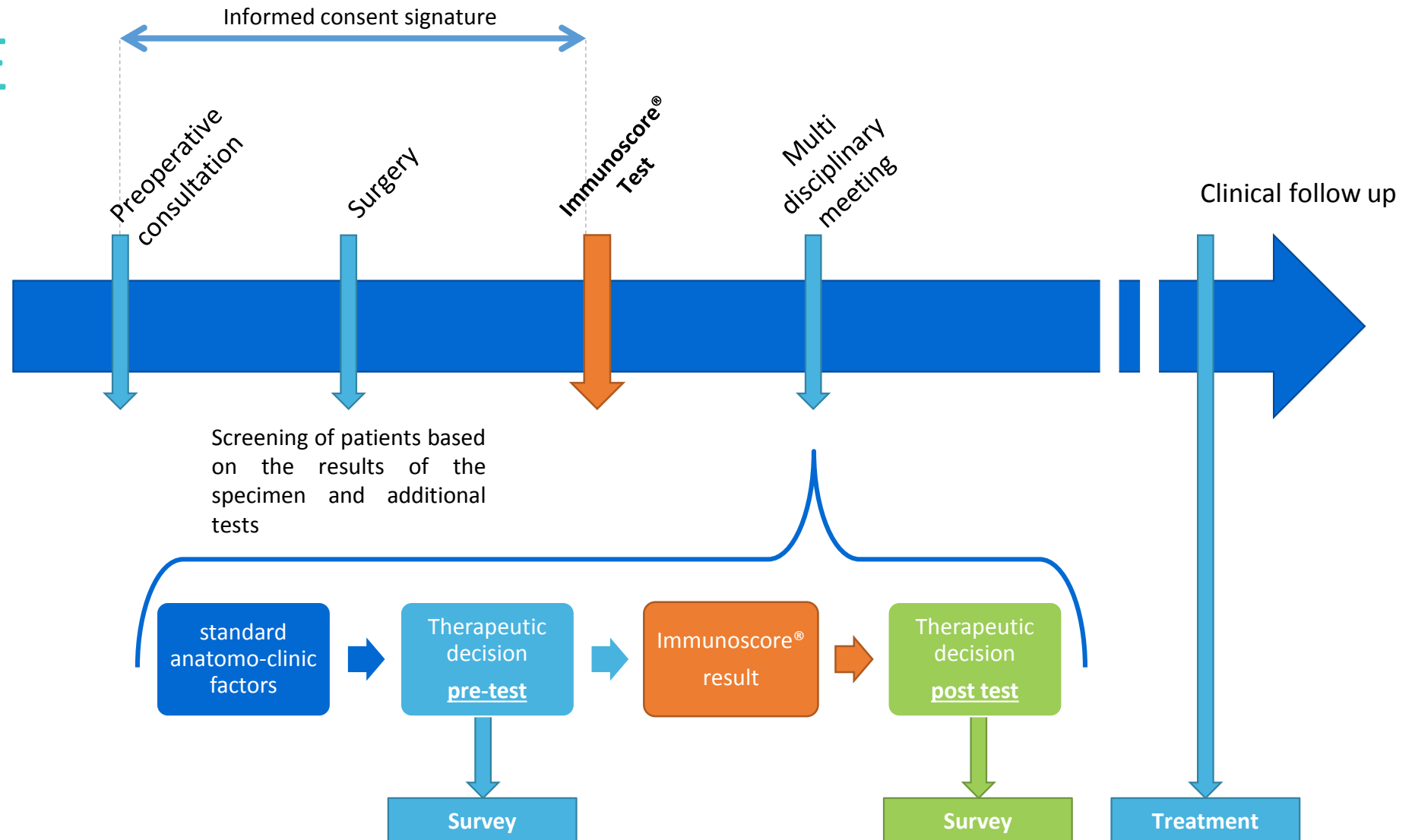
➤ **Immunoscore® Colon is a key risk factor to guide treatment strategies for stages II and III colon cancer patients.**

Immunoscore® Colon improves risk prediction and guides therapeutic choice



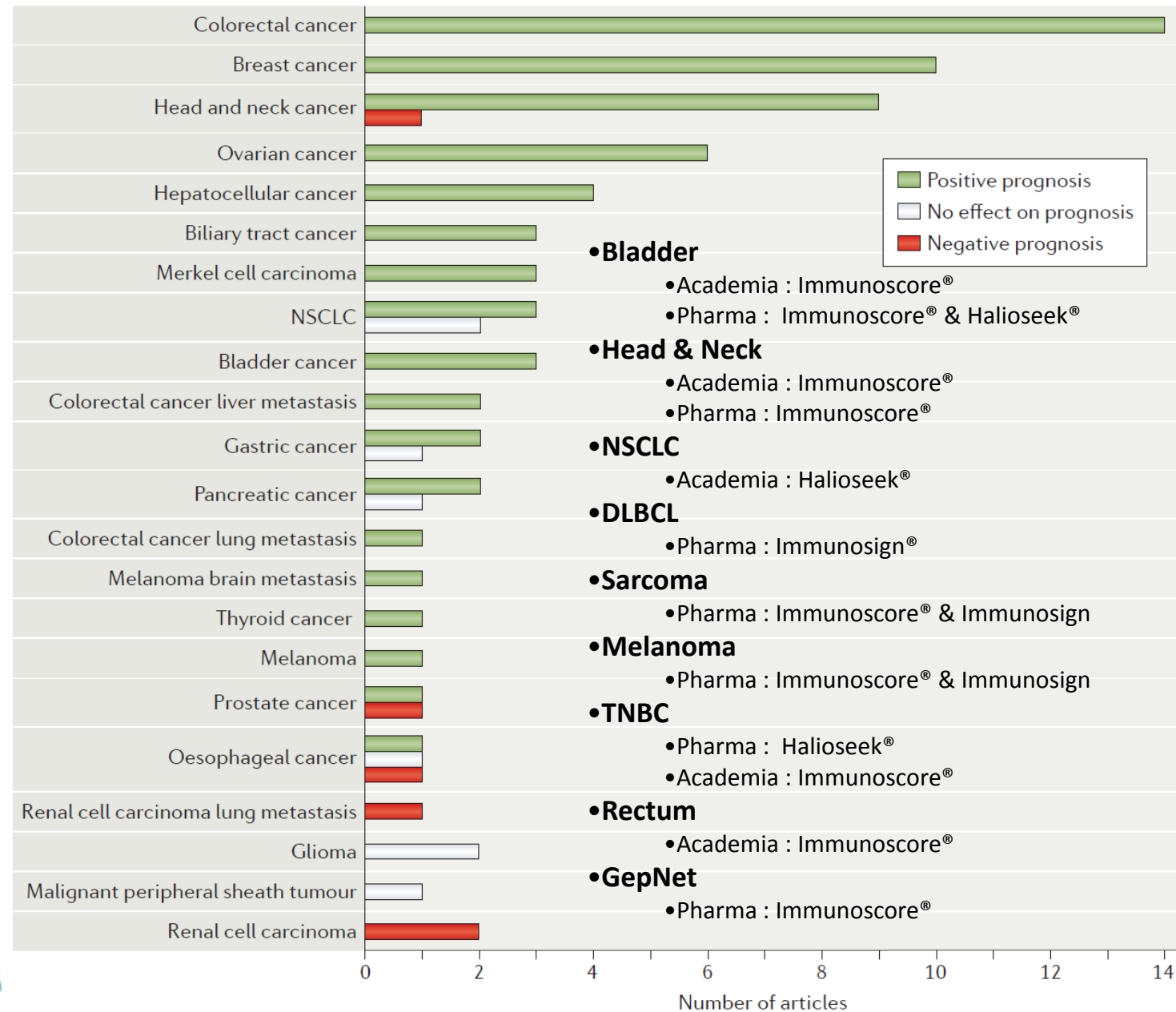
Stage II	→ In favor of the administration of Adj. CT or treatment intensification	→ In favor of surgery only
Stage III	→ In favor of 6 month Adj. CT	→ In favor of a reduction to 3 months of Adj. CT

PROSCORE Impact study

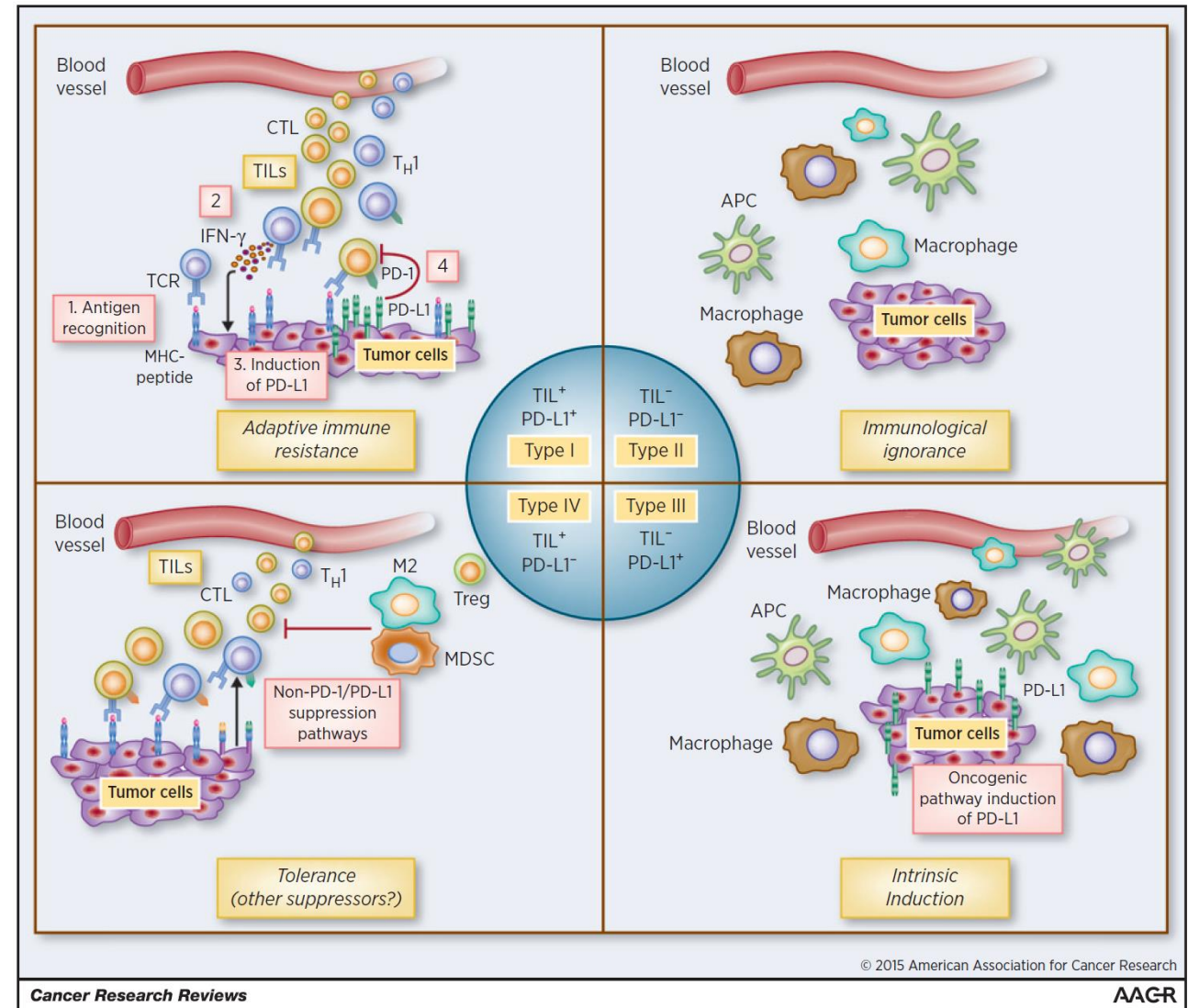


Association between CD8+ T-cell infiltration and survival

Fridman et al Nature Reviews Clinical Oncology 2017



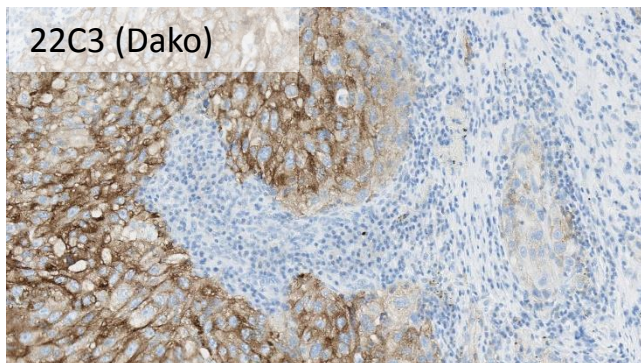
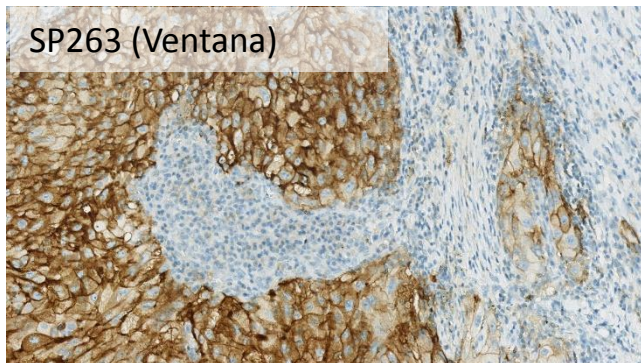
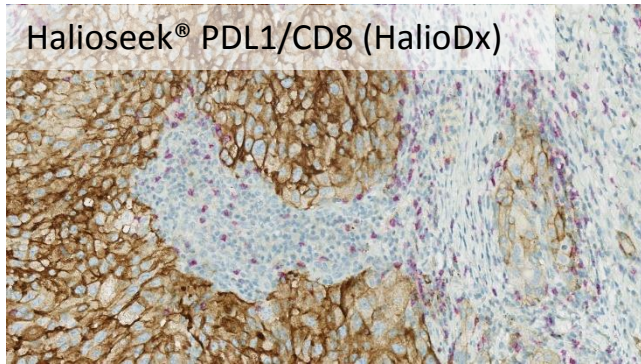
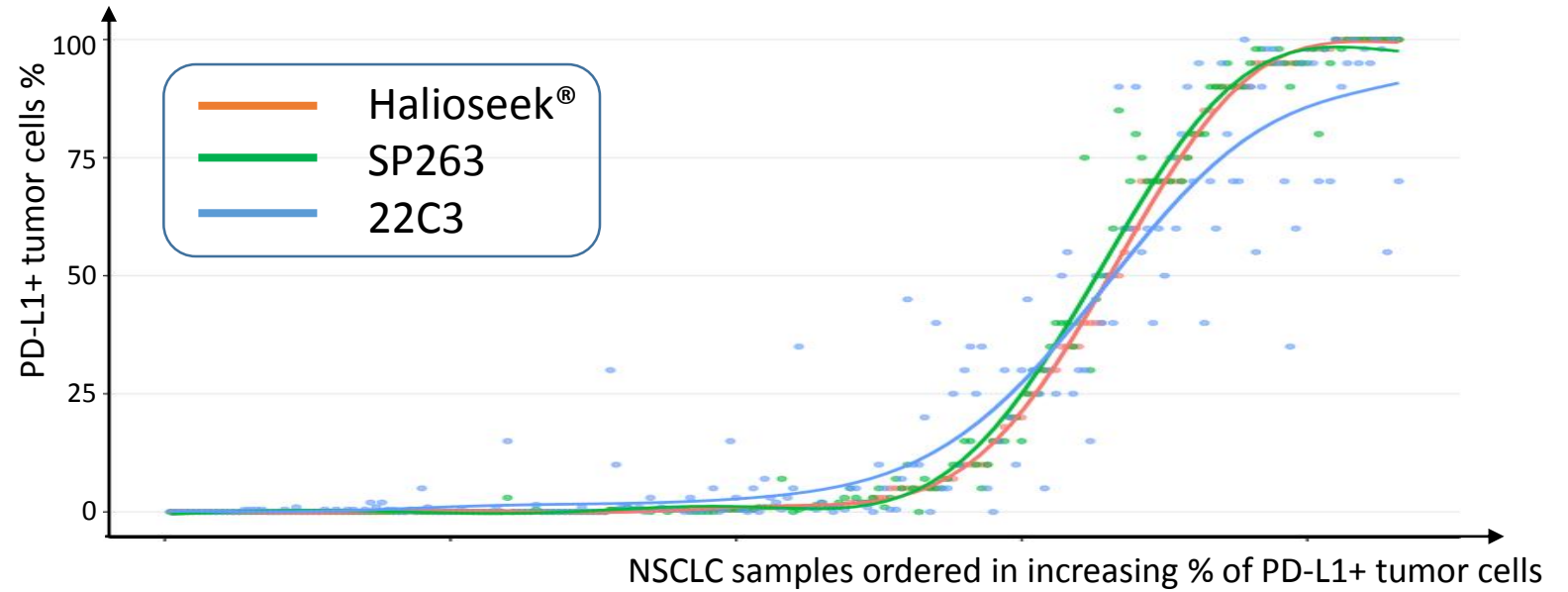
Towards a more precise framework of stratifying tumors to discuss the immunotherapeutic strategies



Teng et al. Cancer Res. 2015

Halioseek® PD-L1/CD8 staining compared to approved PD-L1 CDx assays

216 NSCLC samples of which 21 biopsies



HS® Vs SP263

1% cut off

OA = 97.7% with 95% IC [94.7;99.0]

50% Cut off

OA = 99.1% with 95% IC [96.7;99.7]

HS® Vs 22C3

1% cut off

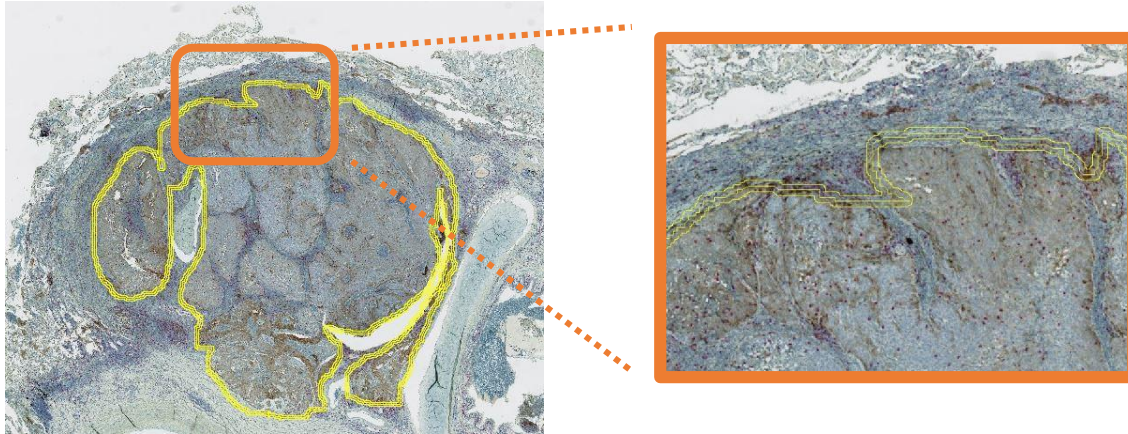
OA = 91.2% with 95% IC [86.7;94.3]

50% Cut off

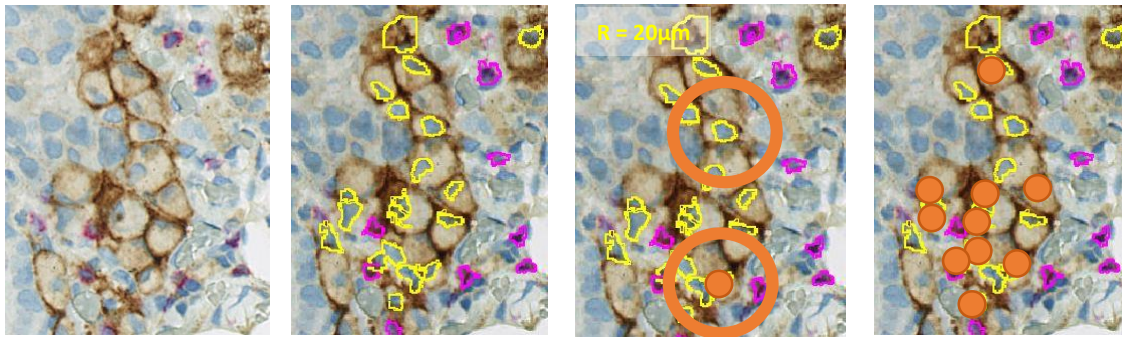
OA = 95.8% with 95% IC [92.3;97.8]





Halioseek® PD-L1/CD8 dedicated DP tool for NSCLC samples typing

ROI definition and automated margin growing




Proximity index calculation between CD8+ and PD-L1+ cells



 Detected PD-L1+ cell nucleus -
  Detected CD8+ cell -
  20µm radius circle surrounding PD-L1 cell -
  PD-L1+ cell with at least 1 CD8+ cell around 20µm

9 PD-L1+ cells
 (out of 19
 detected) have a
 CD8+ cell at less
 than 20µm.
**Proximity index =
 47%**


Report # 564013

Halioseek® PD-L1/CD8 Report

Customer order #: CC-06-082938
 Laboratory: PathChange
 Address: Borolring avenue
 NewCity
 Tel: 985 678 0054
 Email: pathchange@free.com

Samples ID:
 FFPE Block ID: IS4I43570
 Unstained slide ID: IS4I43570US546
 Stained slide ID: IS4I43570HTAS
 Image ID: IS4I43570IDA
 Date of reception: 14/09/2017

Digital pathology results

CD8			PD-L1		
	Tumor	Margin		Tumor	Margin
Total cell count	2111 cells	172 cells	Total cell count	33872 cells	1024 cells
Density	150 cells/mm ²	190 cells/mm ²	Density	1914 cells/mm ²	1423 cells/mm ²
Cluster index			Cluster index		
< 20 µm	58 %	50 %	< 20 µm	96 %	90 %
< 40 µm	85 %	88 %	< 40 µm	99 %	98 %

PD-L1 – CD8 proximity index		
Proximity radius	Tumor	Margin
< 20 µm	7 %	9 %
< 40 µm	18 %	21 %

PD-L1 centered proximity values are expressed in terms of PD-L1-positive cell percentage whose nearest CD8-positive neighbor is detected at less than 20µm or 40µm.

CD8 cluster index is expressed in terms of CD8-positive cell percentage whose nearest PD-L1-positive neighbor is detected at less than 20µm or 40µm.

PD-L1 cluster index is expressed in terms of PD-L1-positive cell percentage whose nearest PD-L1-positive neighbor is detected at less than 20µm or 40µm.

Quality controls:

Integrity & quality of sample: PASS / FAIL Sample fulfill test requirements: PASS / FAIL

Integrity & quality of control sample: PASS / FAIL Control sample fulfill test requirements: PASS / FAIL

Comments:

I, the undersigned, verify that the interpretation of the results is correct as reported.
 Name: Dr John Doe
 Date: 16th Oct 2017

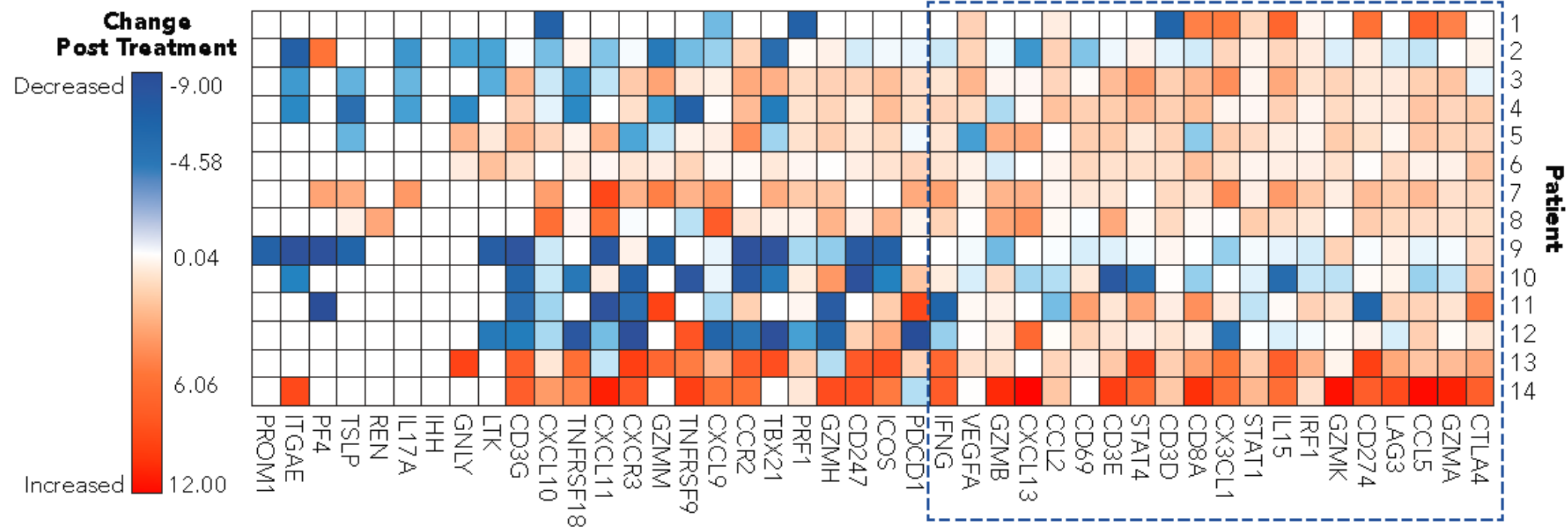
If you have any questions, please contact Customer Support at tech.support@haliodx.com or Call + 33 (0)4 91 29 30 90

Immunosign® Clinical Research Assay Panel Evaluates Key Immune Pathways Within the Tumor Microenvironment

IMMUNOSIGN 15	T Cell Cytotoxicity	T Cell Differentiation	T Cell Attraction	T Cell Adhesion	Adaptive Immunity
	Immune Orientation	Angiogenesis Suppression	Immune Co-inhibition	Cancer Stem Cell	Immune Suppression
IMMUNOSIGN 21	T Cell Cytotoxicity	T Cell Activation	T Cell Attraction	Th1 Orientation	Adaptive Immunity

- The Immunosign Clinical Research assay utilizes the nCounter® technology (Nanostring) to measure the gene expression level of multiple immune genes in a multiplex format
- The assay has been optimized for utilizing minimal amount of RNA

Axi-cel–Related Signature in Tumor Microenvironment



Blue box indicates cytokines included in Table 2.

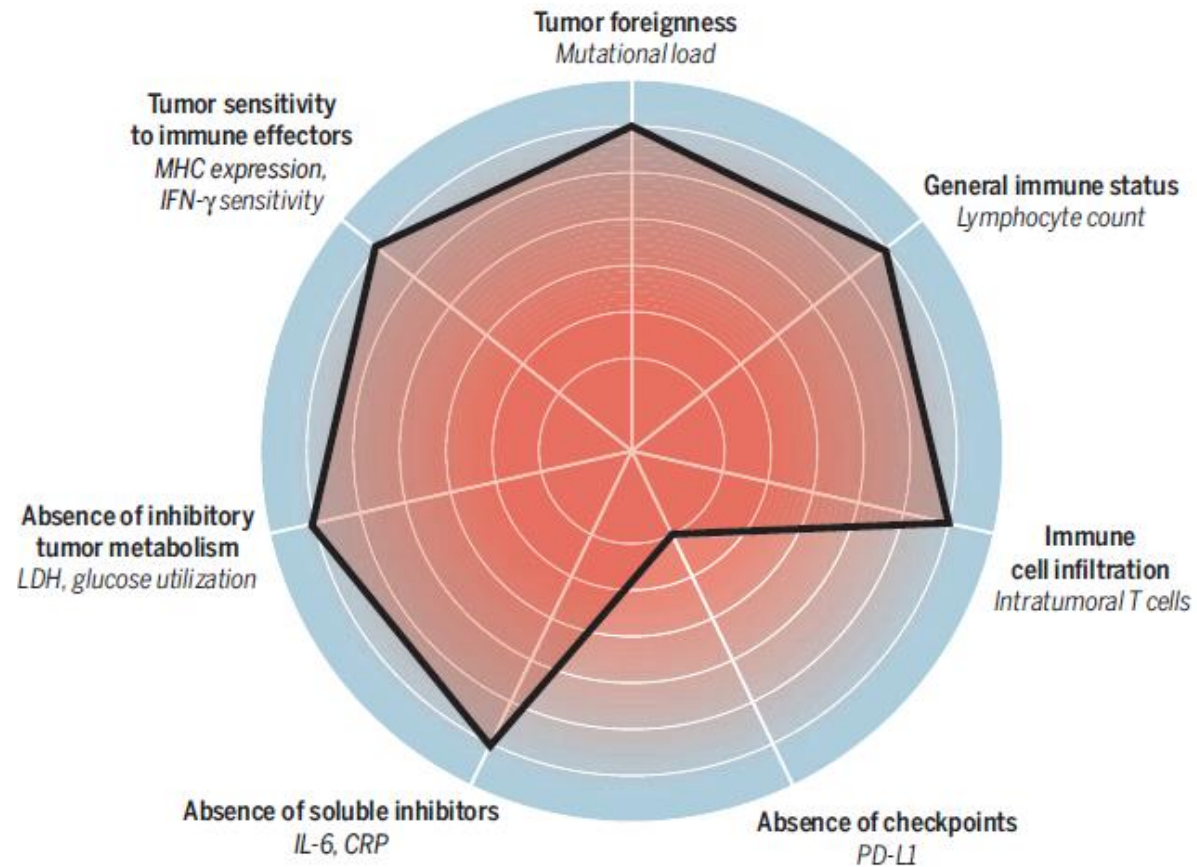
Common names are given in parenthesis for the following: CCL2 (MCP-1), CCL5 (RANTES), CX3CL1 (fractalkine), CXCL9 (MIG), CXCL10 (IP-10), CXCL11 (I-TAC), CXCL13, TBX21 (TBET), CD274 (PD-L1), PDCD1 (PD-1), CD247 (CD3z), PRF1 (perforin), TNFRSF9 (4-1BB), TNFRSF18 (GITR).

Tissue-based predictive biomarkers of a response to immune-checkpoint inhibition

Biomarker	Method	HalioDx Tests
Target molecule expression CTLA-4, PD-1, PD-L1	IHC	Halioseek® + on demand assays
Neoantigens / Tumor Foreignness	Whole-exome sequencing and bioinformatic analyses TMB	Halioseq
Immune gene signatures	Nanostring nCounter®	Immunosign®
T-Cell receptor clonality	RNAseq	Halioseq
TILs	IHC + DP	Immunoscore®

Adapted from Fridman et al Nature Reviews, Clinical Oncology 2017

Lessons & Take Home Messages



HalioDx Services for
standardized
Immunogram
assessment on clinical
samples under CLIA /
GCLP

Blank CU et al. Science. 2016