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Old tests – New challenges

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NordiQC

Agenda

- p53: When knowledge shifts, so must we
- Melan-A: New clones, new standards
- ALK: New purpose, new expectations
- HER2: Therapy drives IHC
- CEA: From tool to target- rebirth of an old marker

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P53

When knowledge shifts, so must we

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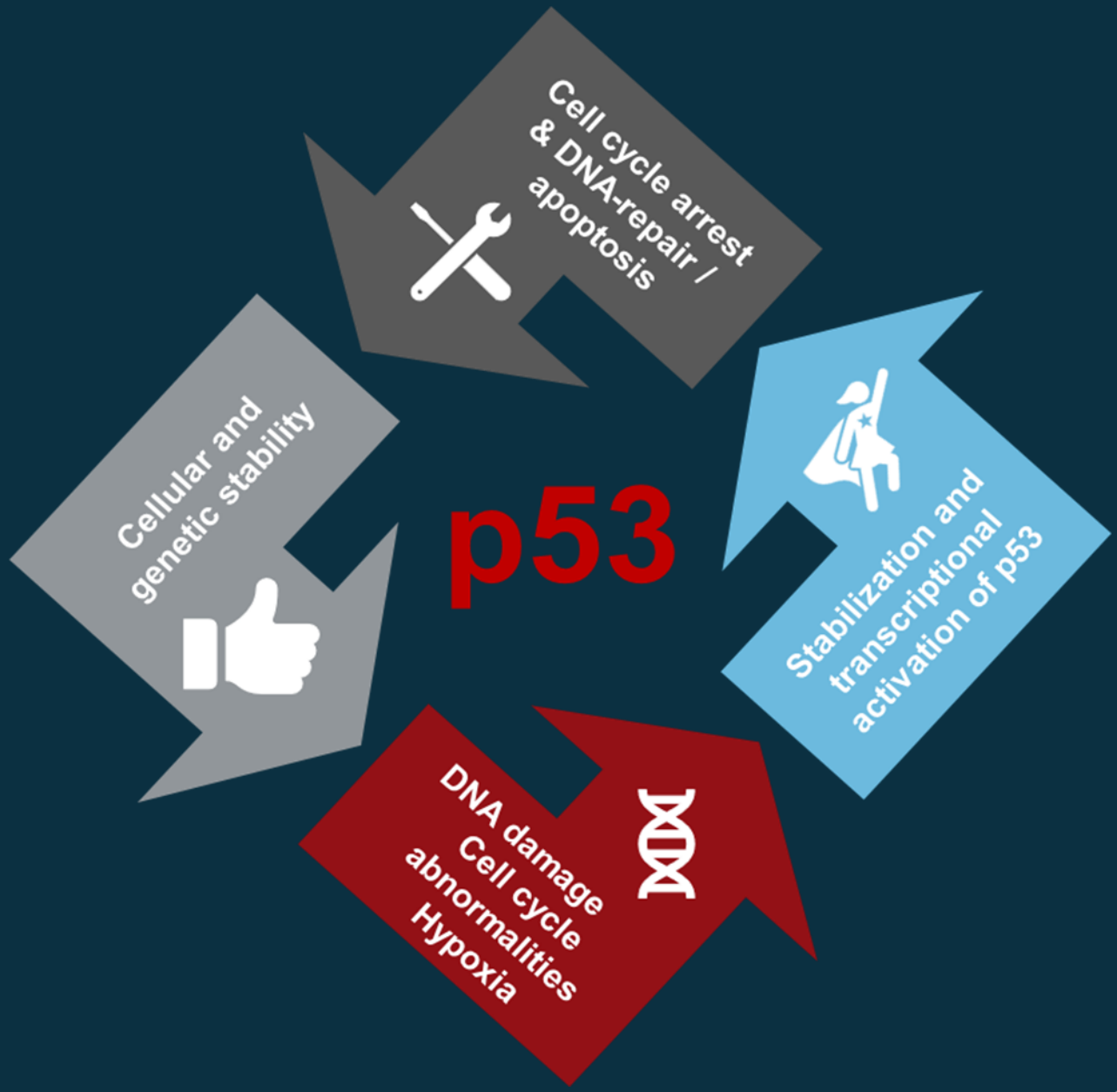
Cell cycle arrest
& DNA-repair /
apoptosis
Stabilization and
transcriptional
activation of p53
DNA damage
Cell cycle
abnormalities
Hypoxia
Cellular and
genetic stability
p53

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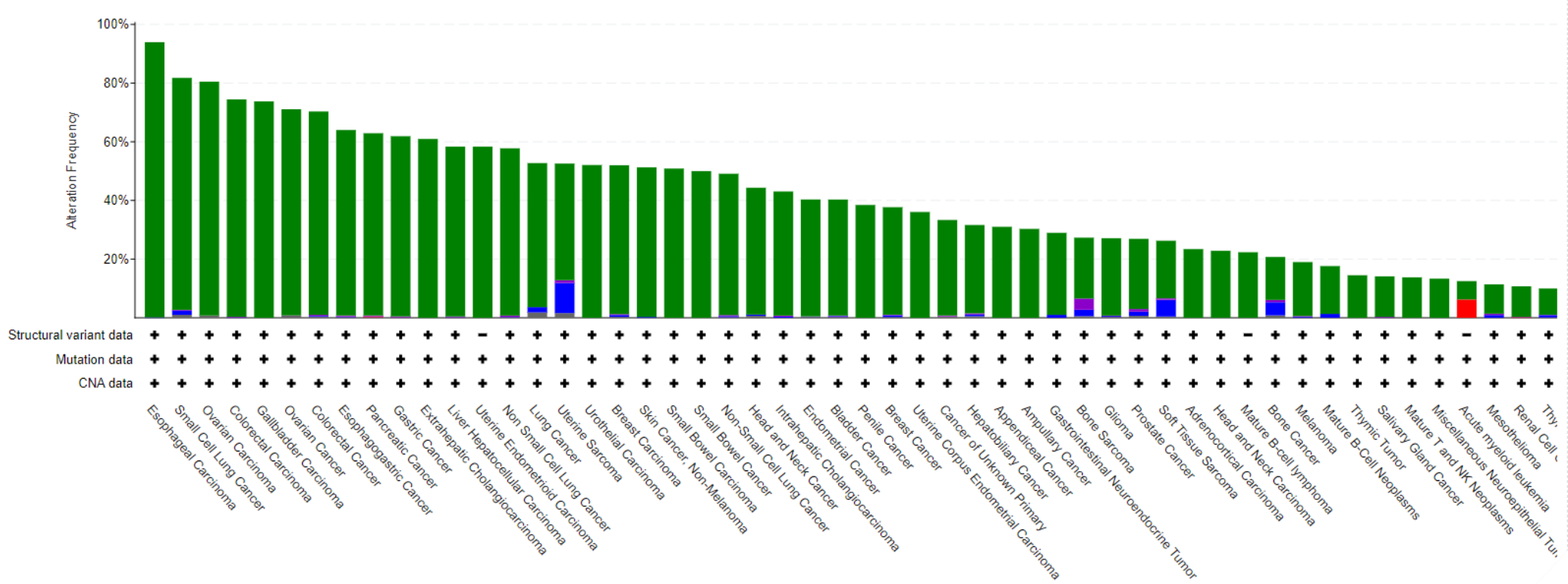
TP53 is mutated in 50% of all cancer



cBioPortal FOR CANCER GENOMICS

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Modify Query

Combined Study (101679 samples)

Querying 101679 samples / 100611 patients in 11 studies TP53

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MEDICAL SCIENCE · Volume 335, Issue 8691, P675-679, March 24, 1990 Download Full Issue

Increased expression of mutant forms of p53 oncogene in primary lung cancer

R. Iggo, MRCP [a] · J. Bartek, MD [a] · D. Lane, PhD [a] · K. Gatter, MRCPath [b] · A.L. Harris, FRCP [c] · J. Bartek [d]

Affiliations & Notes Article Info

Cite Share Set Alert

Show Outline

Abstract

Primary lung cancer samples of the

> Oncogene. 1990 Jun;5(6):893-9.

Genetic and immunochemical analysis of mutant p53 in human breast cancer cell lines

J Bartek [1], R Iggo, J Gannon, D P Lane

> Proc Natl Acad Sci U S A. 1990 Oct;87(19):7555-9. doi: 10.1073/pnas.87.19.7555.

p53 mutations in colorectal cancer

N R Rodrigues [1], A Rowan, M E Smith, I B Kerr, W F Bodmer, J V Gannon, D P Lane

Affiliations + expand

PMID: 1699228 PMCID: PMC54786 DOI: 10.1073/pnas.87.19.7555

Abstract

Immunohistological staining of primary colorectal carcinomas with antibodies specific to p53 demonstrated gross overexpression of the protein in approximately 50% of the malignant tumors examined. Benign adenomas were all negative for p53 overexpression. To determine the molecular

ne mutations were G
53 gene is the most
al methods can

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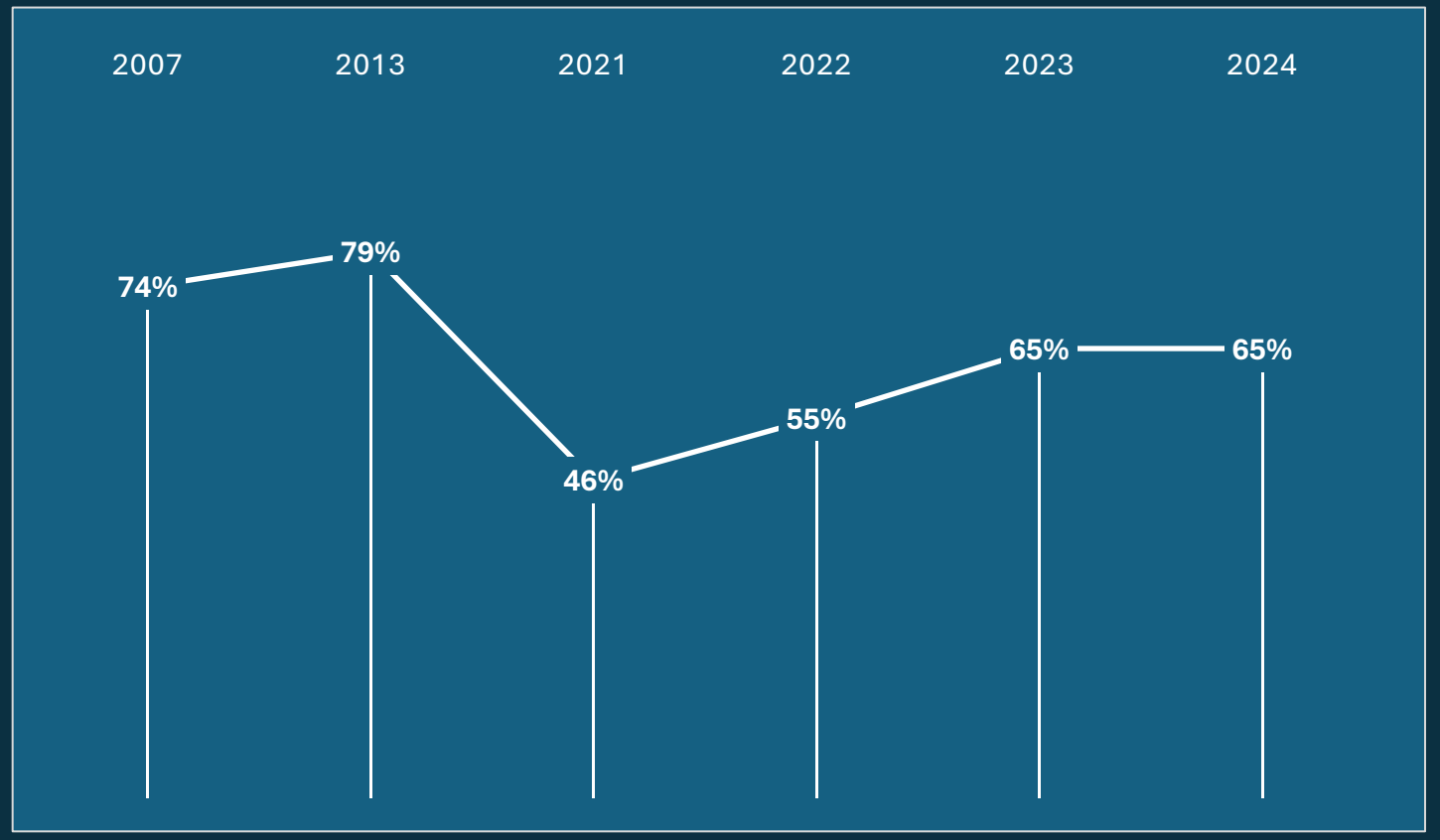
p53 Assessments in NordiQC



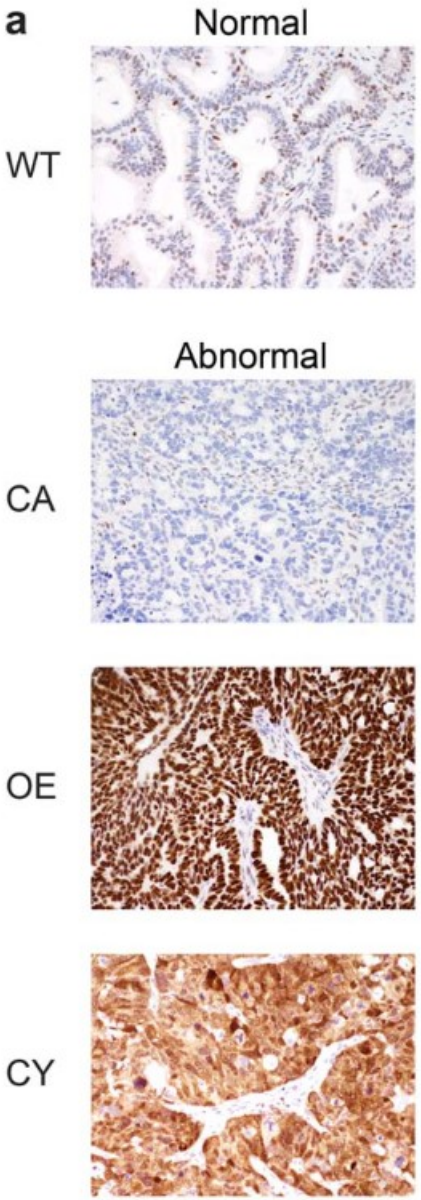
The Journal of Pathology
J Path: Clin Res October 2016
Published online 9 June 2016
(wileyonlinelibrary.com). DOI:

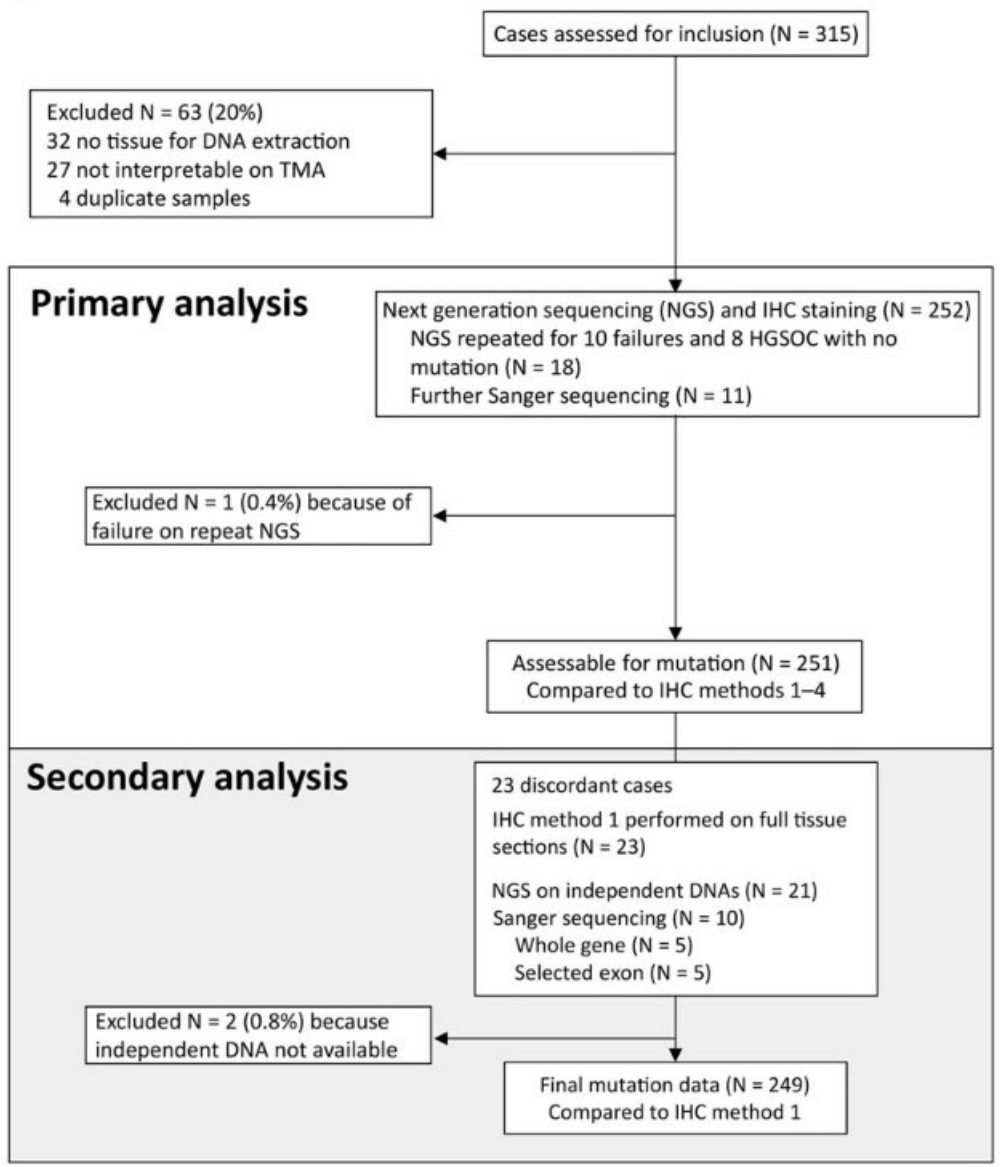
Optimized p53 i
of *TP53* mutatio

Martin Köbel,[1†] Anna M Pis
Nitzan Rosenfeld,[2] Anne-M

[1] *Department of Pathology and La*
[2] *Cancer Research UK Cambridge*
[3] *Centre de recherche du Centre h*
[4] *Institut du cancer de Montréal, M*

**Correspondence to: Dr. James D B*
Genomics of Ovarian Cancer Labo
CB2 0RE, UK. e-mail: james.brento





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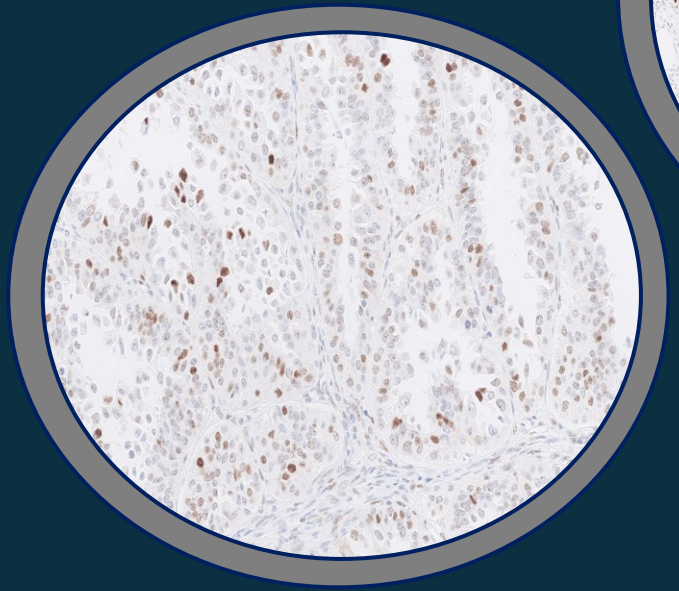
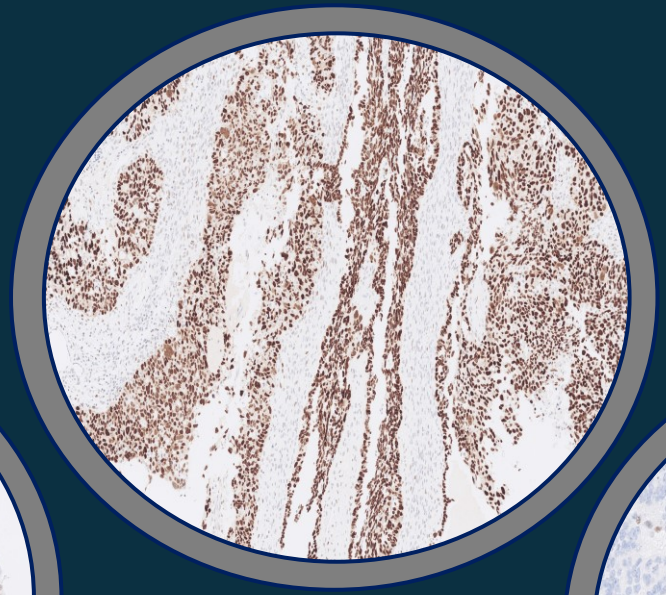
Wild type



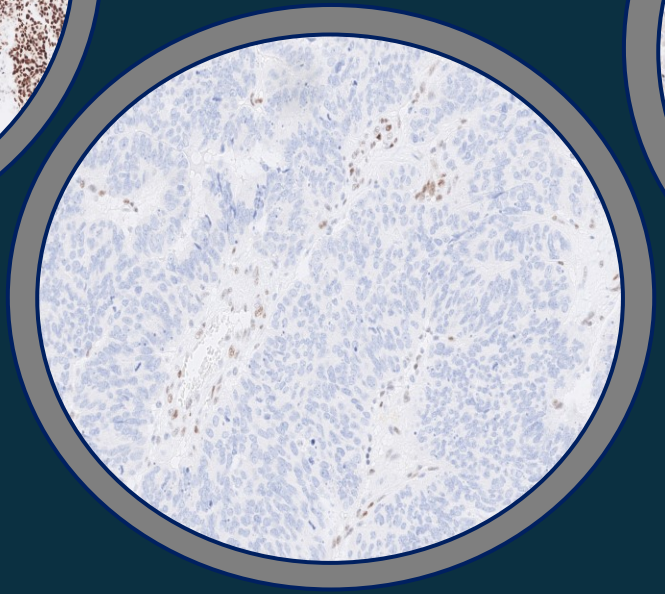
No TP53 mutation

Overexpression



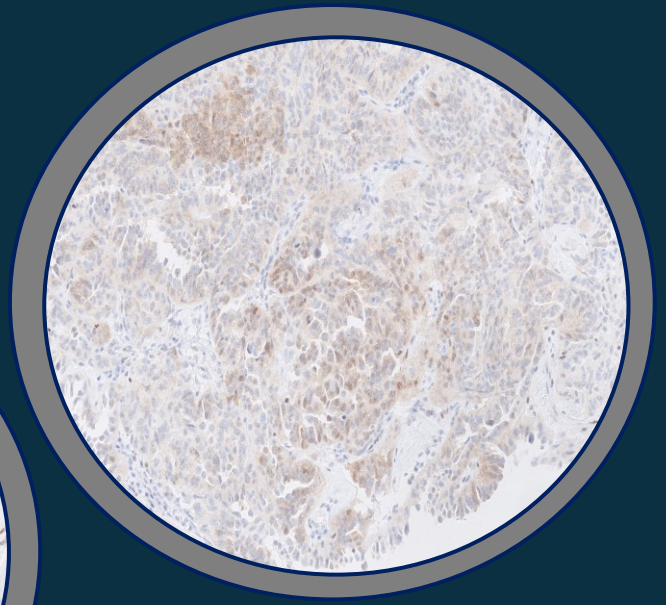
TP53 missense mutation

0-pheno-type

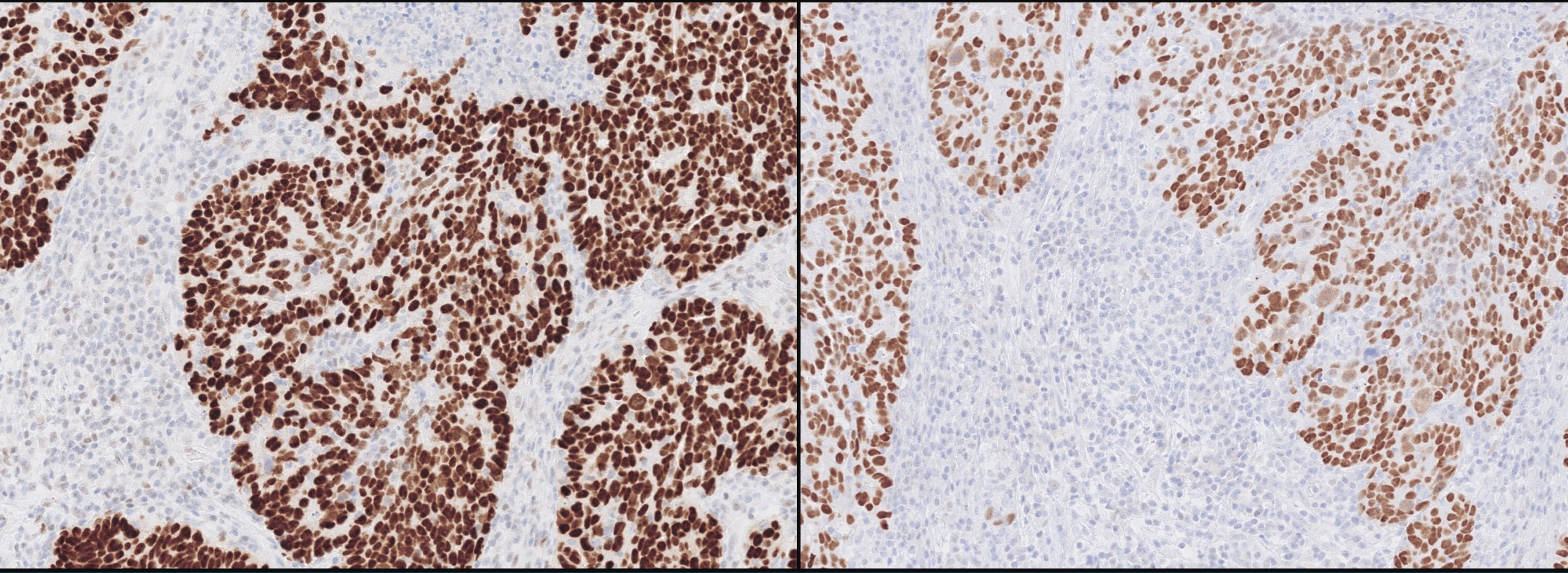


TP53 mutations resulting in absent p53 protein

Cytoplasmatic p53



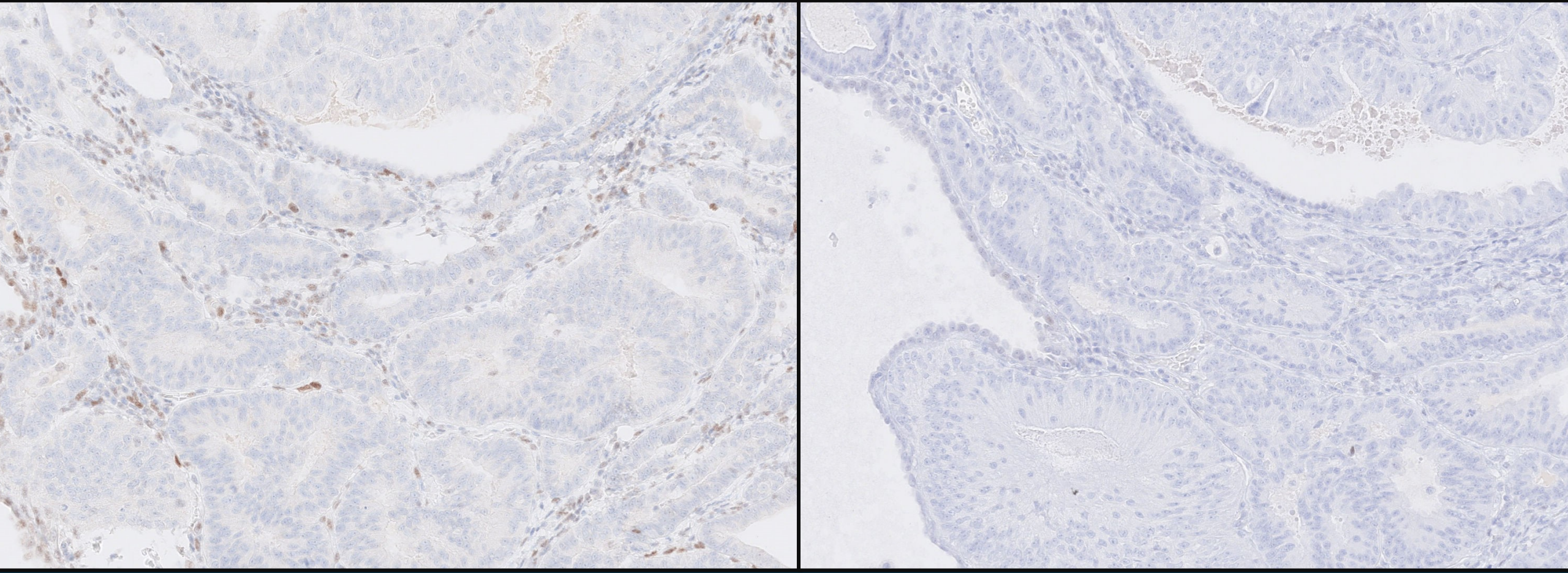
TP53 mutations affecting the nuclear localization domain or the nuclear export signal



The endometrial serous carcinoma with p53 overexpression

Protocol A:
mAb clone DO-7, RTU for Benchmark Ultra, Ventana/Roche, modified protocol settings with HIER for 64 min. in CC1, 32 min. Ab incubation and OptiView as detection system.

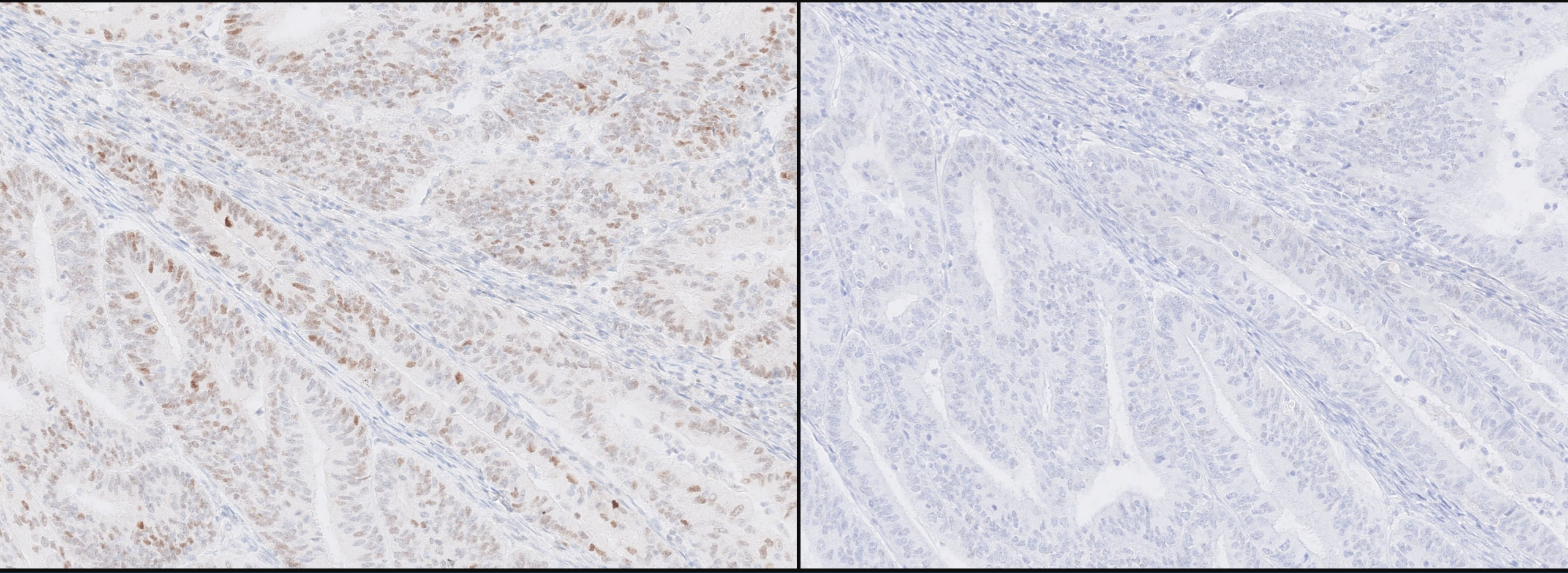
Protocol B:
mAb clone DO-7, RTU for Benchmark Ultra, Ventana/Roche, the recommended protocol settings with HIER for 32 min. in CC1, 16 min. Ab incubation and OptiView as detection system.



The endometrial serous carcinoma with absence of p53

Protocol A:
mAb clone DO-7, RTU for Benchmark Ultra, Ventana/Roche, modified protocol settings with HIER for 64 min. in CC1, 32 min. Ab incubation and OptiView as detection system.

Protocol B:
mAb clone DO-7, RTU for Benchmark Ultra, Ventana/Roche, the recommended protocol settings with HIER for 32 min. in CC1, 16 min. Ab incubation and OptiView as detection system.



The low grade endometrial carcinoma with p53 wild-type pattern

Protocol A:
mAb clone DO-7, RTU for Benchmark Ultra, Ventana/Roche, modified protocol settings with HIER for 64 min. in CC1, 32 min. Ab incubation and OptiView as detection system.

Protocol B:
mAb clone DO-7, RTU for Benchmark Ultra, Ventana/Roche, the recommended protocol settings with HIER for 32 min. in CC1, 16 min. Ab incubation and OptiView as detection system.

Results of p53 assessments in NordiQC

YEAR	Concentrated antibodies (Pass Rate)	RTU system in recommended protocol Assessment-settings (Pass Rate)	RTU system in laboratory modified protocol settings (Pass Rate)
2024	71%	30%	70%
2023	76%	41%	68%
2022	62%	33%	59%
2021	55%	18%	60%
2013	75%	100%	76%
2007	75%	60%	NA

The quality of IHC precision testing NordiQC assessment reports

Mod. prot.

3-step polymer detection

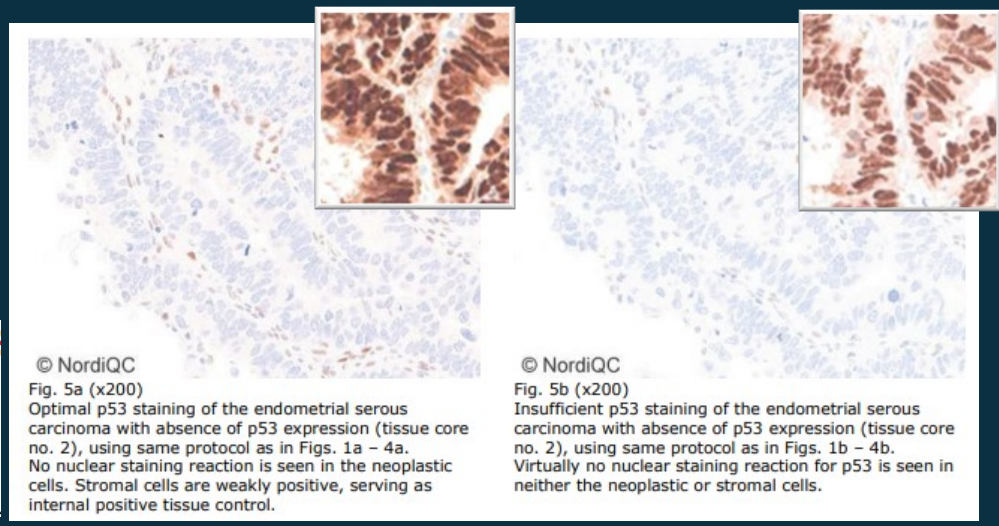
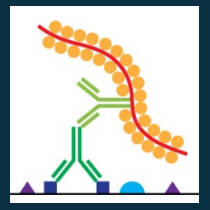


Fig. 5a (x200)
Optimal p53 staining of the endometrial serous carcinoma with absence of p53 expression (tissue core no. 2), using same protocol as in Figs. 1a – 4a.
No nuclear staining reaction is seen in the neoplastic cells. Stromal cells are weakly positive, serving as internal positive tissue control.

Fig. 5b (x200)
Insufficient p53 staining of the endometrial serous carcinoma with absence of p53 expression (tissue core no. 2), using same protocol as in Figs. 1b – 4b.
Virtually no nuclear staining reaction for p53 is seen in neither the neoplastic or stromal cells.

Rec. prot.

2-step polymer detection



p53

Assessment year	Concentrated antibodies	RTU system in laboratory modified protocol settings*	RTU system in recommended protocol settings**	Total
		PASS RATE		
2024	71%	70%	30%	65%
2023	76%	68%	41%	65%
2022	62%	59%	33%	55%
2021	55%	60%	18%	46%
2013	75%	76%	100%	79%
2007	75%	-	60%	74%

* Significant modifications: retrieval method, retrieval duration and Ab incubation time altered, detection kit – only protocols performed on the specified vendor IHC stainer integrated.
** Protocol settings recommended by vendor – Retrieval method and duration, Ab incubation times, detection kit, IHC stainer/equipment.

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Results of p53 assessments in NordiQC

Assessment year	Concentrated antibodies	RTU system
2024	24%	**76%**
2023	26%	**74%**
2022	27%	**73%**
2021	36%	**64%**
2013	63%	**37%**
2007	94%	**6%**

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ALK

new purpose, new expectations

NordiQC

Unlock ALK anaplastic lymphoma kinase

Science. 1994 Mar 4;263(5151):1281-4. doi: 10.1126/science.8122112.

Fusion of a kinase gene, ALK, to a nucleolar protein gene, NPM, in non-Hodgkin's lymphoma

S W Morris [1], M N Kirstein, M B Valentine, K G Dittmer, D N Shapiro, D L Saltman, A T Look

Affiliations + expand

PMID: 8122112 DOI: 10.1126/science.8122112

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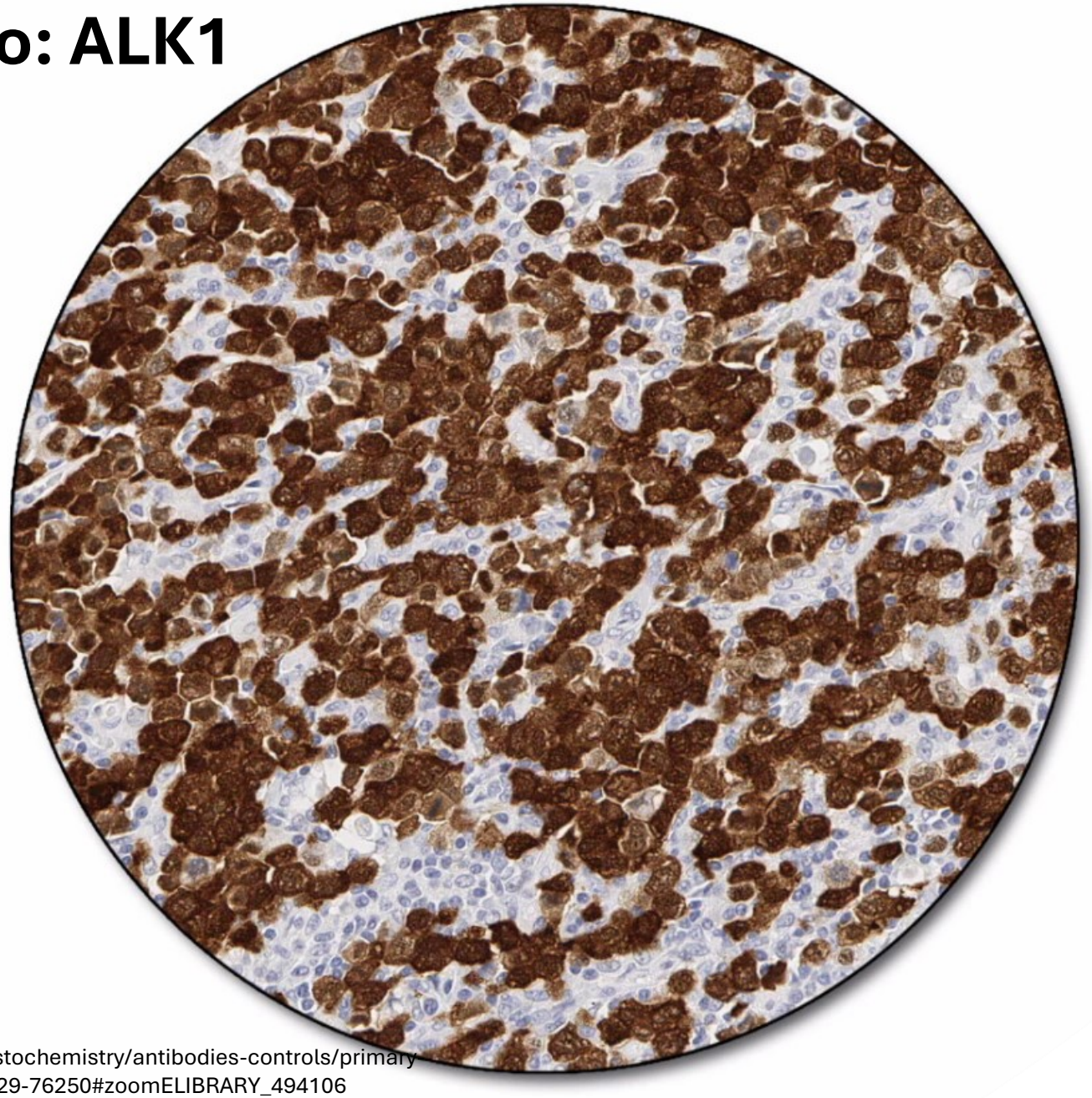
The First Hero: ALK1



https://www.agilent.com/en/product/immunohistochemistry/antibodies-controls/primary-antibodies/cd246-alk-protein-%28dako-omnis%29-76250#zoomELIBRARY_494106

A New Chapter: The ALK Story Expands

nature

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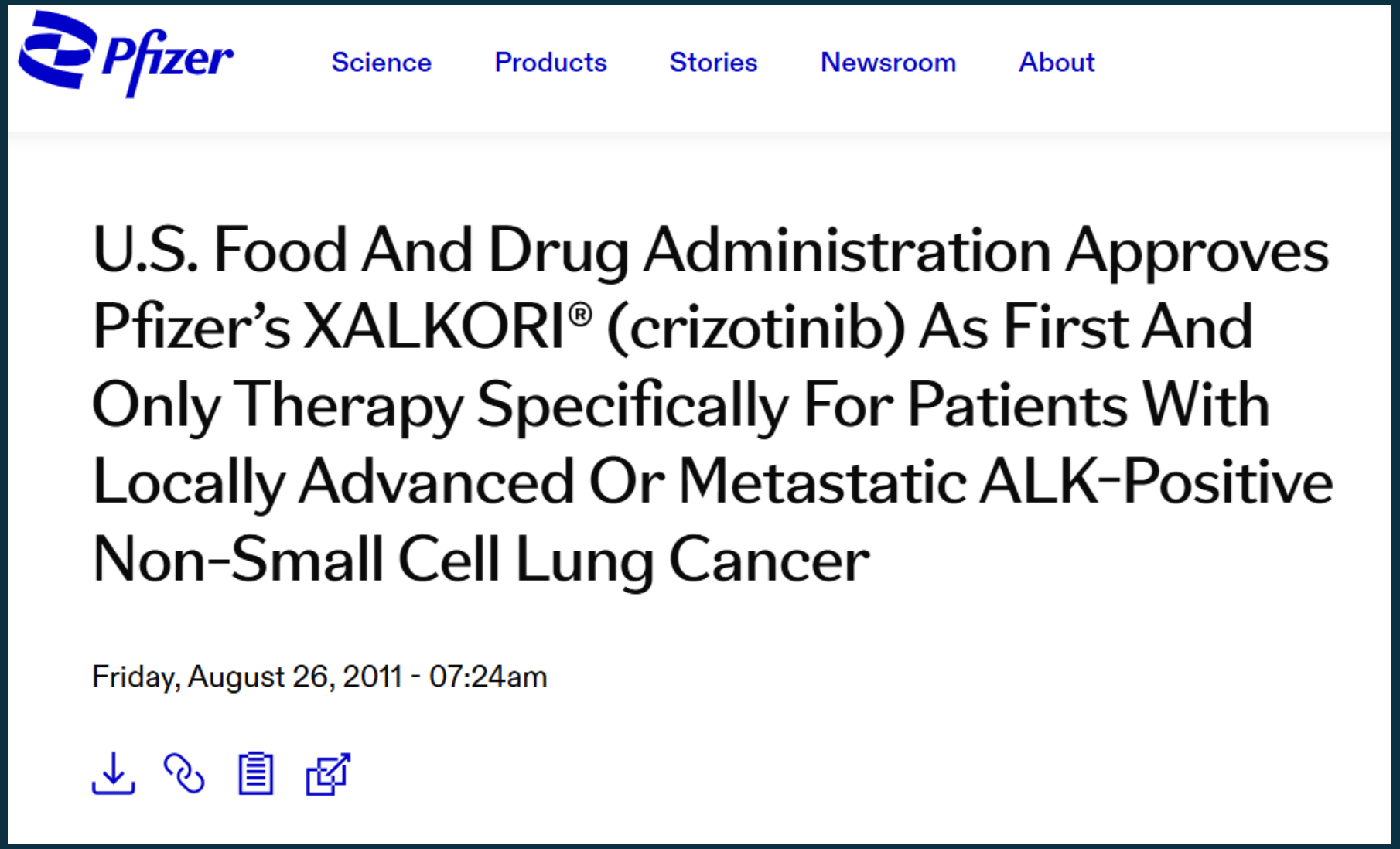
nature › articles › article

Article | Published: 11 July 2007

Identification of the transforming *EML4–ALK* fusion gene in non-small-cell lung cancer

Manabu Soda, Young Lim Choi, Munehiro Enomoto, Shuji Takada, Yoshihiro Yamashita, Shunpei Ishikawa, Shin-ichiro Fujiwara, Hideki Watanabe, Kentaro Kurashina, Hisashi Hatanaka, Masashi Bando, Shoji Ohno, Yuichi Ishikawa, Hiroyuki Aburatani, Toshiro Niki, Yasunori Sohara, Yukihiko Sugiyama & Hiroyuki Mano

A New Chapter: The ALK Story Expands



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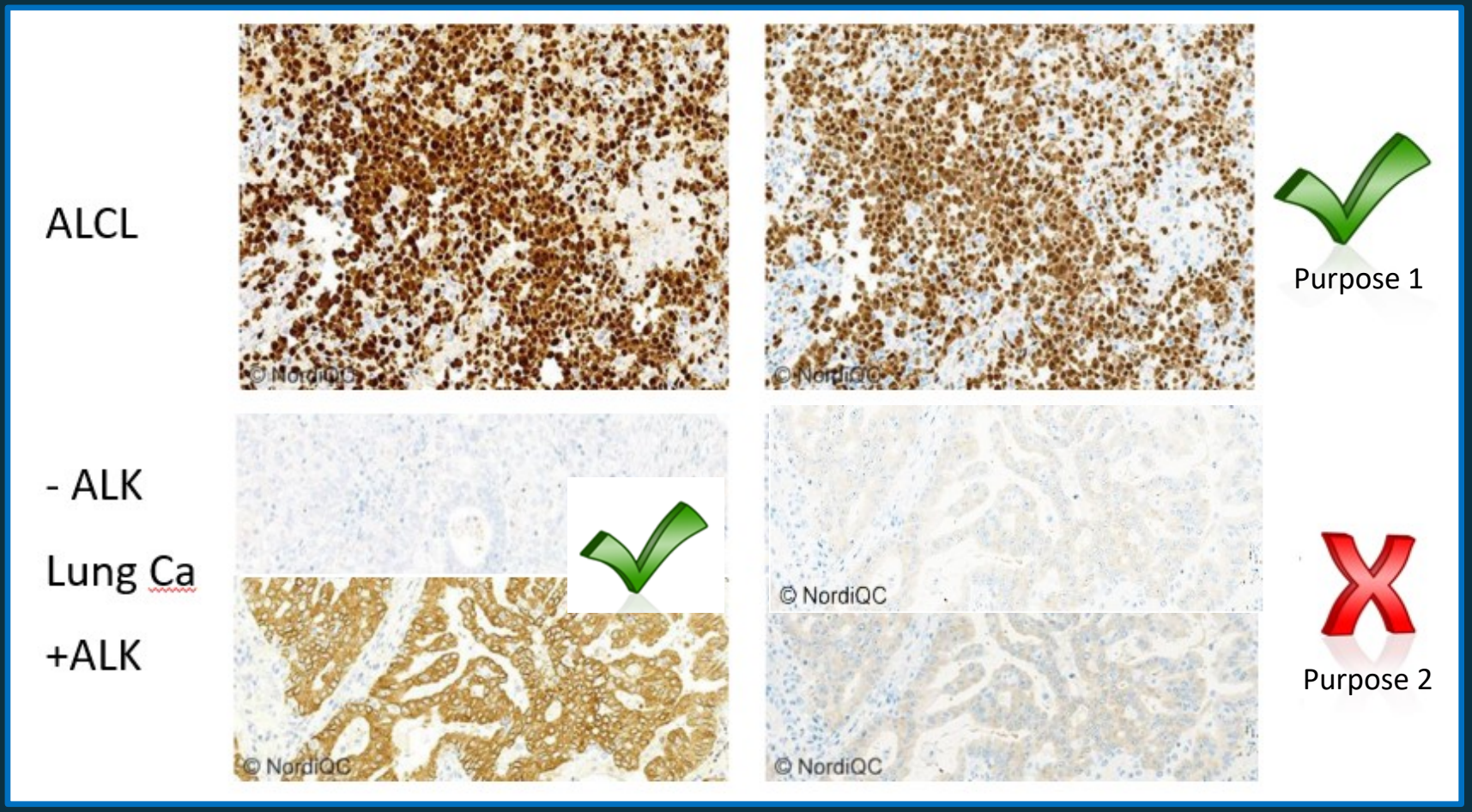
The quality of IHC precision testing
Fit-For-Purpose IHC - ALK



Typically **high** antigen expression level

Typically **low** antigen expression level

IHC protocol 1 **IHC protocol 2**

Slide from Søren Nielsen

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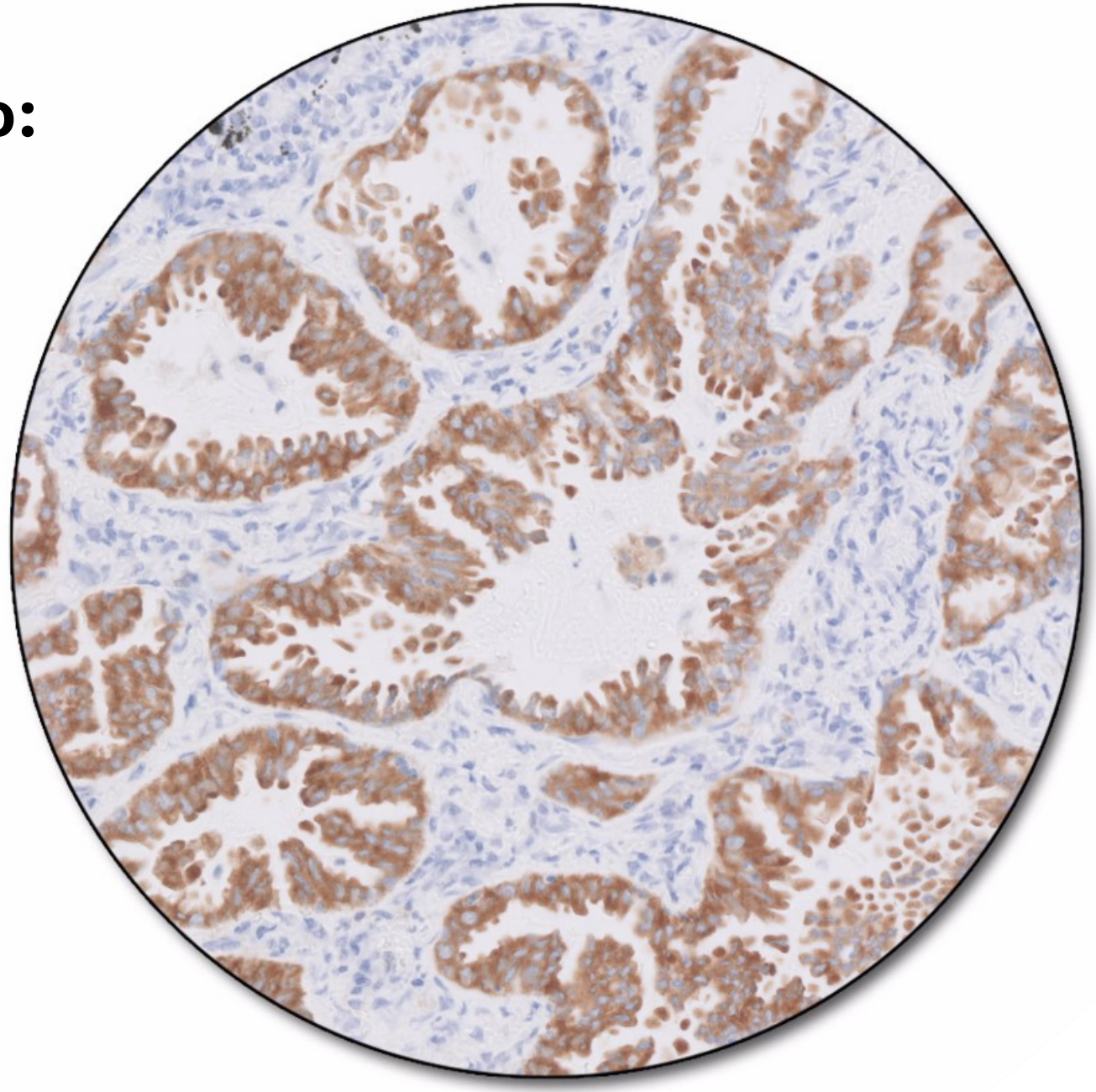
The Second Hero: super-sensitive ALK antibody clones



https://www.agilent.com/en/product/immunohistochemistry/antibodies-controls/primary-antibodies/cd246-alk-protein-dako-omnis-1931656#zoomELIBRARY_1065463

NordiQC

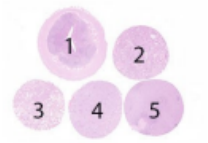
Assessment Run 73 2025

Lung Anaplastic Lymphoma Kinase (ALK (lung))

Purpose
Evaluation of the technical performance and level of analytical sensitivity and specificity of IHC tests among NordiQC participants for EML4-ALK translocations in lung adenocarcinomas. The EML4-ALK translocation occurs through a paracentric inversion between EML4 and ALK genes located in the short arm of chromosome 2 and induces an EML4-ALK fusion protein being expressed in 2–4% of lung adenocarcinomas and is a target for ALK tyrosine inhibitors as crizotinib, ceritinib, and alectinib.

Material
The slide to be stained for ALK (lung) comprised:

1. Appendix, 2. Lung adenocarcinoma without EML4-ALK translocation*, 3. Lung adenocarcinoma with EML4-ALK translocation*, 4. Merkel cell carcinoma, 5. Anaplastic large cell lymphoma (ALCL) with ALK translocation*.
*confirmed by Next Generation Sequencing (NGS)



All tissues were fixed in 10% neutral buffered formalin.

Criteria for assessing ALK (lung) staining as optimal included:

- A distinct, moderate to strong nuclear and cytoplasmic staining reaction of virtually all neoplastic cells in the anaplastic large cell lymphoma (ALCL).
- An at least weak to moderate granular cytoplasmic staining reaction of virtually all neoplastic cells in the lung adenocarcinoma with EML-ALK translocation.
- An at least weak to moderate granular cytoplasmic staining reaction with membrane accentuation of virtually all neoplastic cells in the Merkel cell carcinoma.
- An at least weak to moderate granular cytoplasmic staining reaction of ganglion cells and dispersed axons in the appendix.
- No staining of neoplastic cells in the lung adenocarcinoma without ALK rearrangement.
- No staining of epithelial cells in the appendix and tonsil.

KEY POINTS FOR ALK (lung) IMMUNOASSAYS
- The mAb clone **OTI1A4** is recommendable both as a concentrated Ab and a RTU.
- The mAb clone **ALK-1** should not be used for lung adenocarcinomas.
- Appendix is a recommendable, external positive tissue control

Participation

Number of laboratories registered for ALK (lung), run 73	330
Number of laboratories returning slides	307 (93%)

Results
At the date of assessment, 93% of the participants had returned the circulated NordiQC slides. All slides returned after the assessment were assessed and laboratories received advice if the result was insufficient, but the data were not included in this report.

307 laboratories participated in this assessment. 180 (59%) achieved a sufficient mark (optimal or good), see Table 1a (see page 3). Tables 1b and 1c summarizes the antibodies (Abs) used and assessment marks (see page 3-4).

The most frequent causes of insufficient staining reactions were:
- Unexpected and aberrant cytoplasmic staining reaction on the BenchMark platform.
- Less successful primary antibodies (mAb clone ALK1)

Consentrates:
OTI1A4
5A4

RTU-systems:
OTI1A4
5A4
D5F3

~~ALK1~~

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Melan A

New clones, new standards

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Assessment Run 74 2025

Melan A (MLA)

Updated 11.07.2025

Purpose

Evaluation of the technical performance, level of analytical sensitivity and specificity of IHC tests among the NordiQC participants for MLA, identifying malignant melanomas in the characterization of tumours of unknown origin. Relevant clinical tissues, both normal and neoplastic, were selected displaying a broad spectrum of antigen densities for MLA (see below). This was the second NordiQC assessment of MLA, excluding steroid hormone producing cells and corresponding tumours (only applicable for mAb clone A103), focusing only on intended use in relation to the diagnosis of malignant melanomas.

Material

The slide to be stained for MLA comprised:

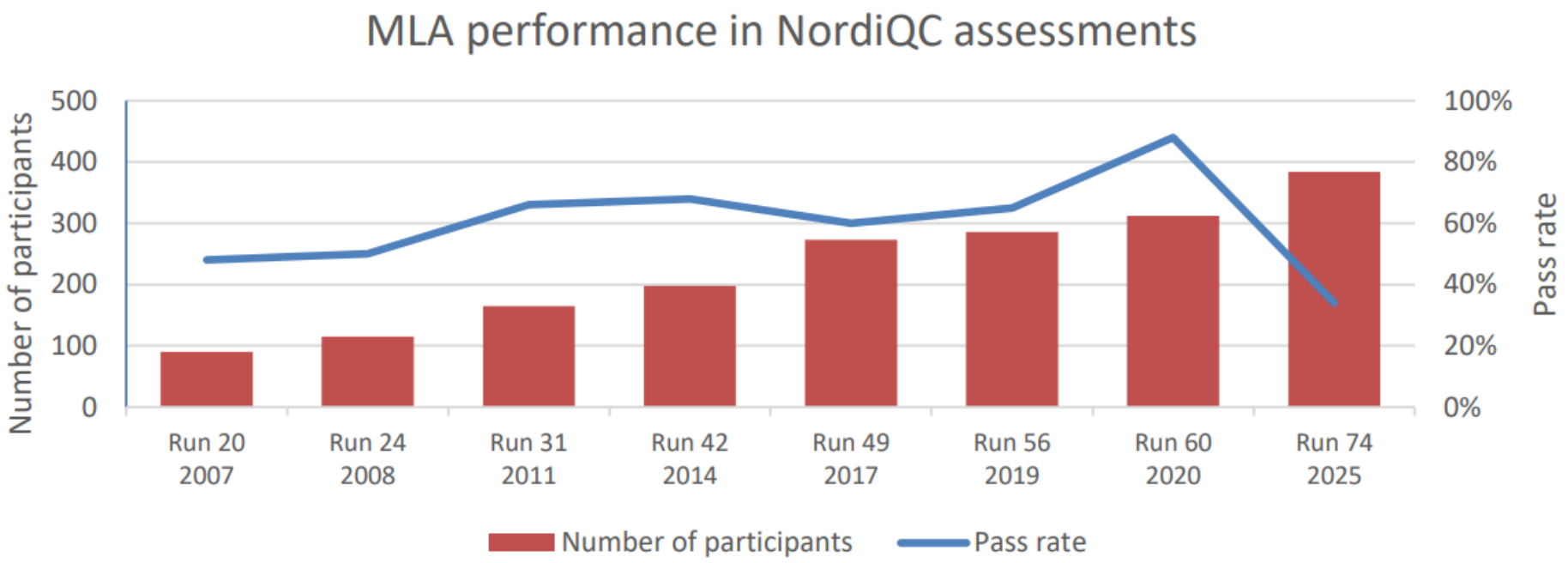
1. Skin, 2. Kidney, 3. Colon Adenocarcinoma, 4-5. Malignant melanoma

All tissues were fixed in 10% neutral buffered formalin.

Criteria for assessing a MLA staining as optimal included:

- A moderate to strong, distinct cytoplasmic staining reaction of virtually all melanocytes in the skin. The dendrites of melanocytes should display a crisp and precise staining reaction.

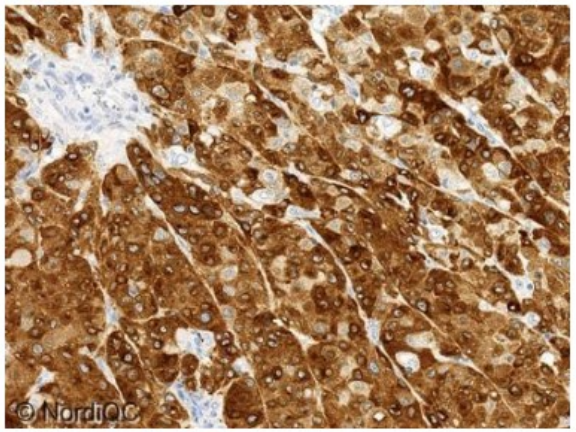
Pass rate 34%

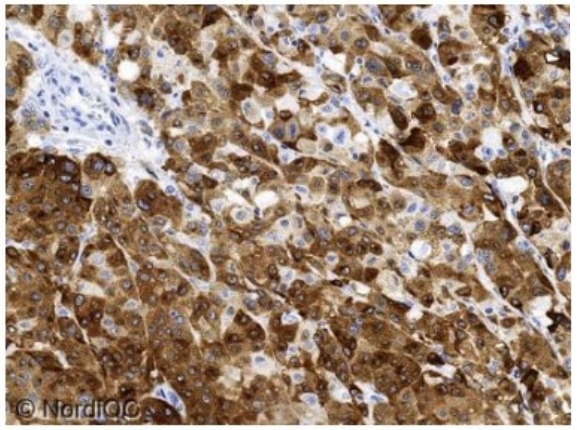


Identification of purpose of the test

E Torlakovic et al. AIMM 2017;25:4-11
Evolution of Quality Assurance for Clinical Immunohistochemistry in the Era of Precision Medicine: Part 1

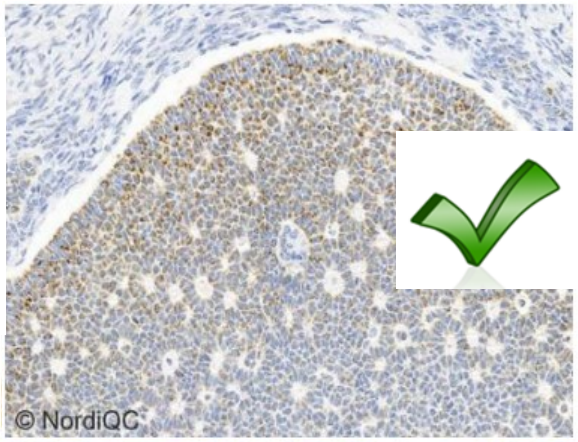
Melanoma

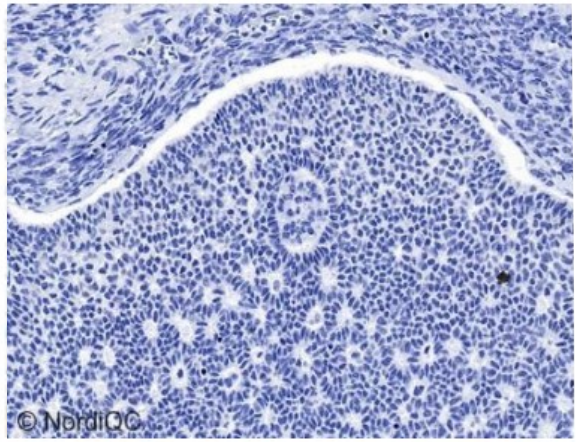




Purpose 1

Sex cord tumour





Purpose 2

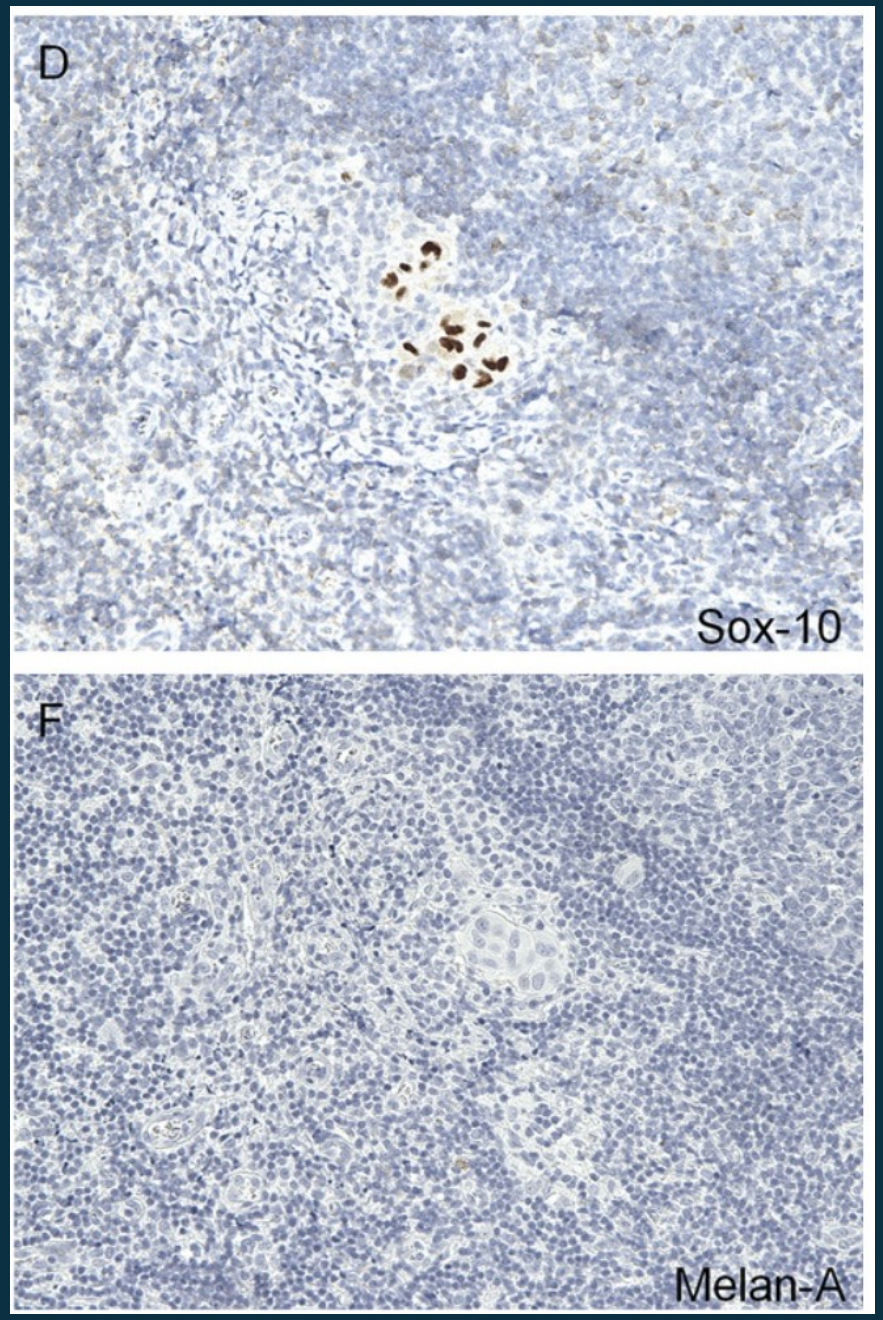
IHC method 1 **IHC method 2**

IHC for Melan A

Typically **mod.- high** antigen expression level

Typically **low – mod.** antigen expression level and only for clone A103

Slide from Søren Nielsen



ORIGINAL STUDY

Identification of Nodal Metastases in Melanoma Using Sox-10

Jennings, Charay MD, PhD*; Kim, Jinah MD, PhD*†

Author Information

The American Journal of Dermatopathology 33(5):p 474-482, July 2011. | ***DOI:*** 10.1097/DAD.0b013e3182042893

SDC

RESEARCH ARTICLES

SOX10

A Useful Marker for Identifying Metastatic Melanoma in Sentinel Lymph Nodes

Willis, Brian C. MD; Johnson, Gina MD; Wang, Jason MD; Cohen, Cynthia MD

Author Information

Applied Immunohistochemistry & Molecular Morphology 23(2):p 109-112, February 2015. | ***DOI:*** 10.1097/PAI.0000000000000097

Assessment Run 74 2025

Melan A (MLA)

Updated 11.07.2025

Purpose

Evaluation of the technical performance, level of analytical sensitivity and specificity of IHC tests among the NordiQC participants for MLA, identifying malignant melanomas in the characterization of tumours of unknown origin. Relevant clinical tissues, both normal and neoplastic, were selected displaying a broad spectrum of antigen densities for MLA (see below). This was the second NordiQC assessment of MLA, excluding steroid hormone producing cells and corresponding tumours (only applicable for mAb clone A103), focusing only on intended use in relation to the diagnosis of malignant melanomas.

Material

The slide to be stained for MLA comprised:

KEY POINTS FOR MLA IMMUNOASSAYS

- A historically low pass rate of 34% was observed during Run 74 with only 9.5% being optimal.
- The mAb clone **A103** was used by 90% of all participants either as a concentrate or RTU product.
- The mAb clone **A103** seemed to have less affinity for low-level MLA expression in malignant melanomas compared to other clones.
- The LD assays using mAb clone **BS52** and rmAb clone **EP43** had the highest pass rate and optimal result could be obtained on all main fully automated IHC platforms.

Participation

Number of laboratories registered for MLA, run 74	430
Number of laboratories returning slides	391 (91%)

Results

At the date of assessment, 91% of the participants had returned the circulated NordiQC slides. All slides returned after the assessment were assessed and laboratories received advice if the result was insufficient, but the data were not included in this report.

391 laboratories participated in this assessment, however 7 laboratories submitted inappropriate antibodies, and the data were not included in this report. 34% achieved a sufficient mark (optimal or good). Table 1a-c summarizes antibodies (Abs) used and assessment marks (see page 3 and 4).

NordiQC internal study
MelanA Diagnostic Performance:
Clone A103 vs. Newer Clones

71 melanomas + 36 non-melanomas

A103 shows lower sensitivity: The widely used **A103 clone** has a significantly lower diagnostic sensitivity for melanomas compared to newer clones.

A103: 82% sensitivity
EP43: 94% sensitivity
BS52: 93% sensitivity

A103 has weaker staining intensity: A103 also showed weaker H-scores, indicating a less intense stain and fewer positive cells, increasing the risk of **misdiagnosis**.

Median H-scores:

EP43 & BS52: 260
A103: 160

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HER 2

Therapy drives IHC

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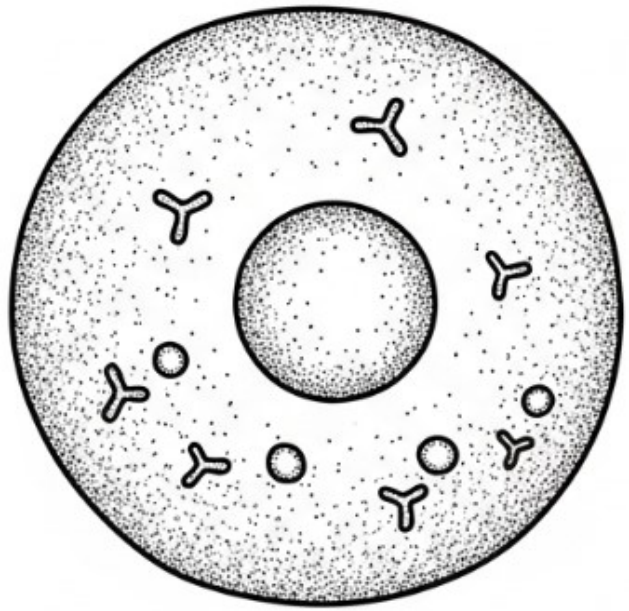
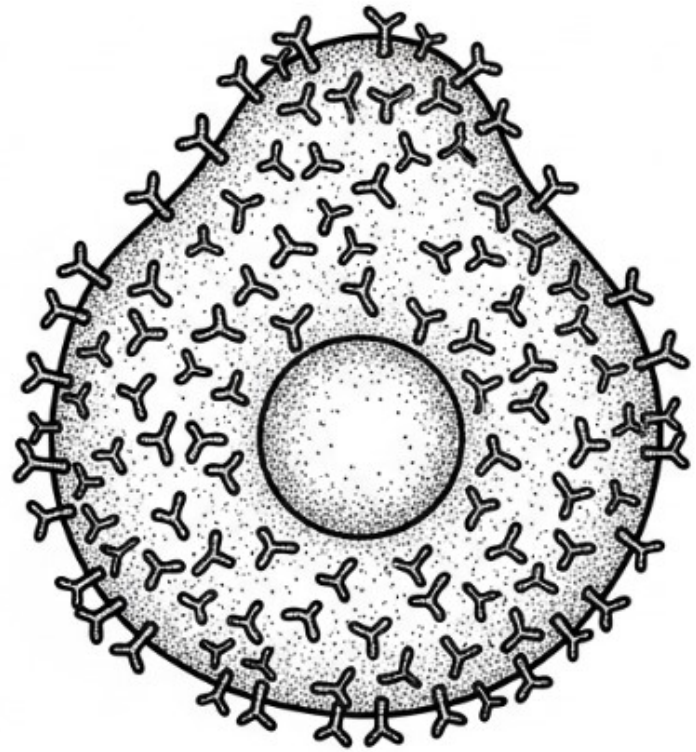


Normal breast cell



HER2-positive cancer

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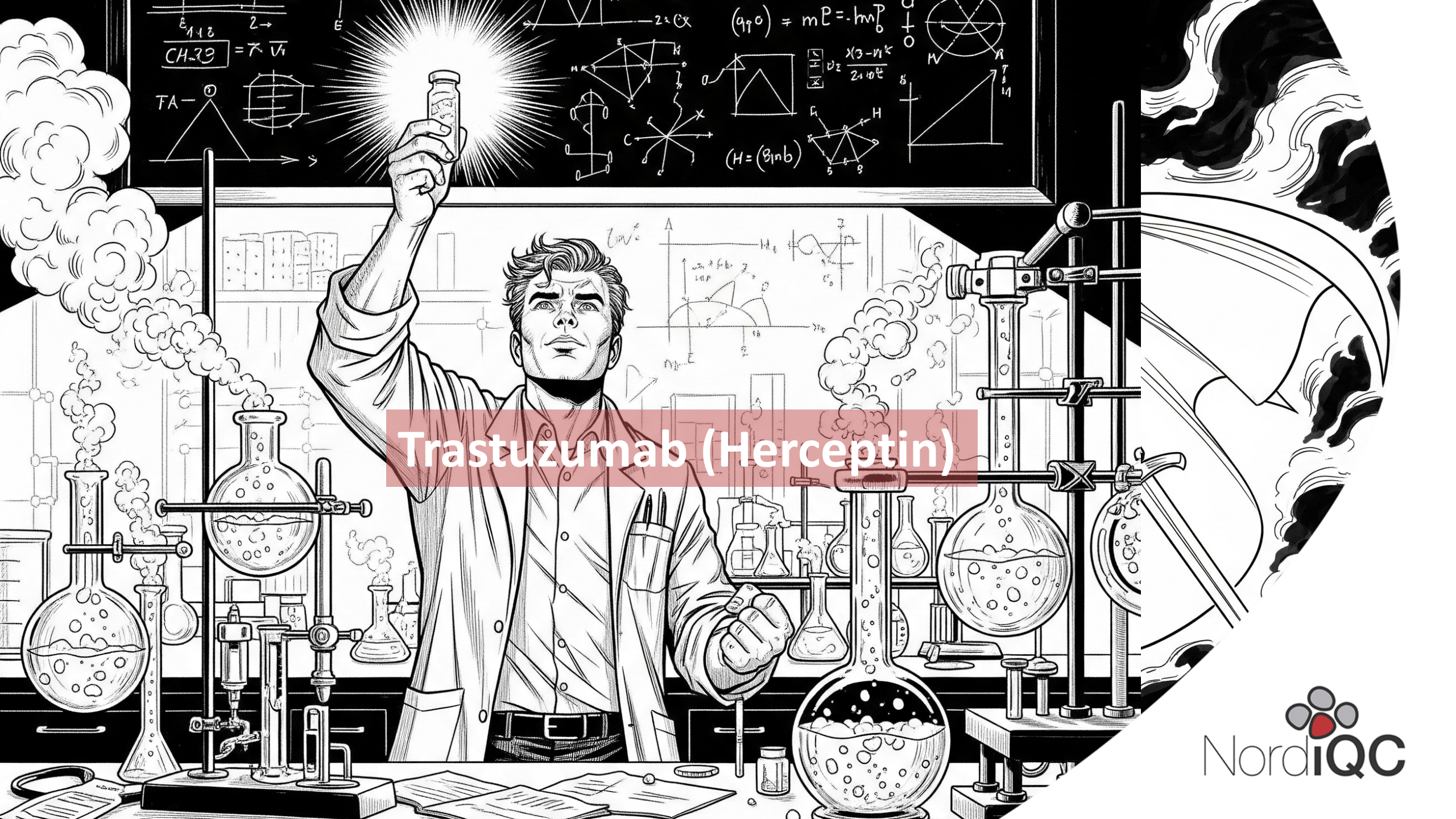

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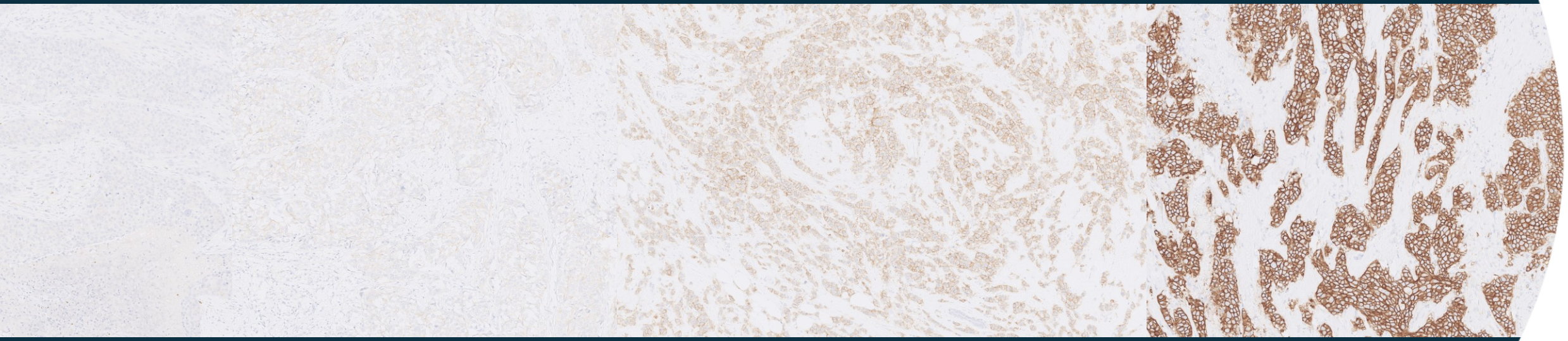
Traditional Breast HER2-scoring

0 1+ 2+ 3+



HER2 No-overepression:
0, 1+ or 2+ISH non-amplified

HER2 2+:
Send ISH

HER2 Overepression:
3+ or 2+ISH amplified

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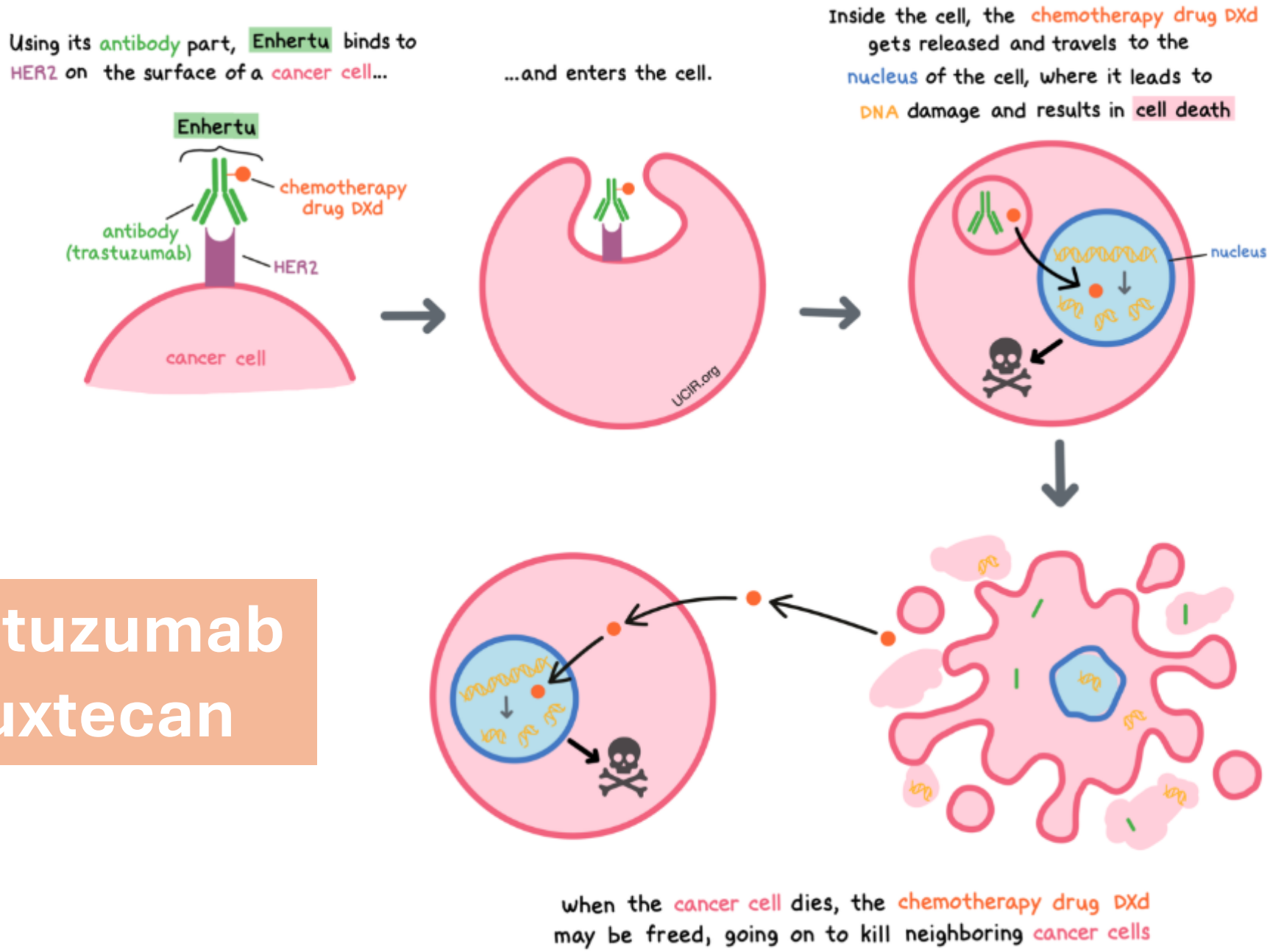
Illustration adapted from M. Troxell, *Repurposing HER2 IHC: Pan-HER2 and Low-HER2*, USCAP 2025.

Trastuzumab deruxtecan



https://www.ucir.org/immunotherapy-drugs/fam-trastuzumab-deruxtecan-nxki-enhertu

Breast HER2-scoring in 2020's

0 1+ 2+ 3+

HER2 low expression:
1+ or 2+ISH non-amplified

HER2 No-overepression:
0, 1+ or 2+ISH non-amplified

HER2 2+:
Send ISH

HER2 Overepression:
3+ or 2+ISH amplified

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Destiny Breast 04
Illustration adapted from M. Troxell, *Repurposing HER2 IHC: Pan-HER2 and Low-HER2*, USCAP 2025.

Breast HER2-scoring in 2025

0 1+ 2+ 3+

HER2- low:
1+ or 2+ISH non-amplified

HER2 ultra-low:
0+

HER2 No-overepression:
0, 1+ or 2+ISH non-amplified

HER2 2+:
Send ISH

HER2 Overepression:
3+ or 2+ISH amplified

Destiny Breast 06
Illustration adapted from M. Troxell, *Repurposing HER2 IHC: Pan-HER2 and Low-HER2*, USCAP 2025.

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Are HER2 assays comparable?

Impact of different CE-IVD IHC assays on HER2 status in breast cancer with focus on HER2-low & HER2-ultralow

Kristi Bøgh Anderson, Søren Nielsen, Birgit Truumees, Rasmus Røge
NordiQC, Aalborg University Hospital, Denmark

Background and objective

The European Medicines Agency (EMA) recently approved trastuzumab deruxtecan for treating patients with unresectable or metastatic HR-positive breast cancer (BC) that is HER2-low or HER2-ultralow. HER2 status is at present determined by immunohistochemistry (IHC) most frequently using a CE-IVD-approved assay. While staining differences among IHC-assays are well known, a direct comparison of the three main CE-IVD-approved HER2 IHC assays is lacking. Additionally, previously published comparisons provide limited information on analytical performance and inter-assay concordance due to post-analytical variability in the studies.
This study evaluates the analytical performance of three most frequently used CE-IVD-approved HER2 IHC assays and their clinical implications for categorizing HER2-low and HER2-ultralow BC.

Methods

Two tissue microarrays (TMAs) were constructed for other quality control studies, including triple-negative and ductal BCs. Serial sections, minimizing tumor heterogeneity, were stained with three CE-IVD approved HER2 IHC assays: PATHWAY rmAb 4B5, 790-2991 (Ventana/Roche), HercepTest pAb, SK001 (Dako/Agilent) and HercepTest rmAb DG44, GE001 (Dako/Agilent). All BCs were scored by three observes and classified as HER2 0, ultralow, 1+, 2+ or 3+. The amplification status was available for HER2 2+ cases based on fluorescence in situ hybridization of the original tissue.

Results

In total 109 BCs were analyzed. A 97% concordance was observed across all three assays, classifying samples into the classical two groups: HER2 negative (0, ultralow, 1+, 2+ unamplified) and HER2 positive (3+, 2+ amplified) (Table 1). For HER2-low and HER2-ultralow a low inter-assay agreement was seen as the HER2 0 classification differed between assays: PATHWAY rmAb 4B5 classified 34% (37 samples) as HER2 0, compared to 31% (34 samples) with HercepTest pAb SK001 and 25% (27 samples) with HercepTest rmAb DG44 (Graph 1, Figure 1).

Table 1. Frequency of Different HER2 Scores Across CE-IVD-approved Assays.

HER2 Group	PATHWAY 4B5	HercepTest SK001	HercepTest DG44
HER2-negative	88	90	87
HER2-positive	21	19	22
Total	109	109	109

Graph 1. HER2 Status Across CE-IVD-approved IHC-assays.

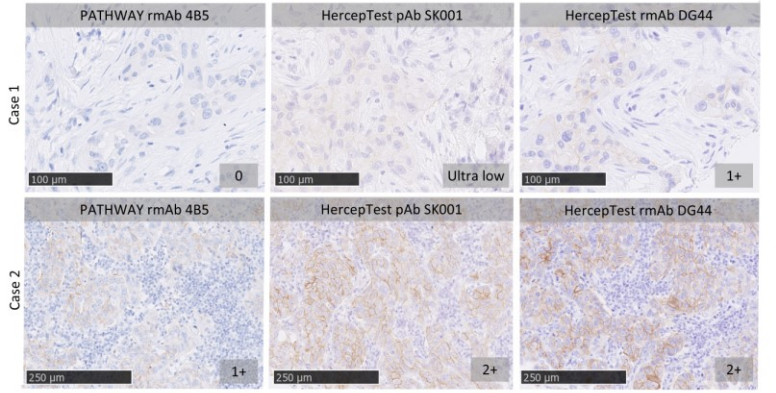


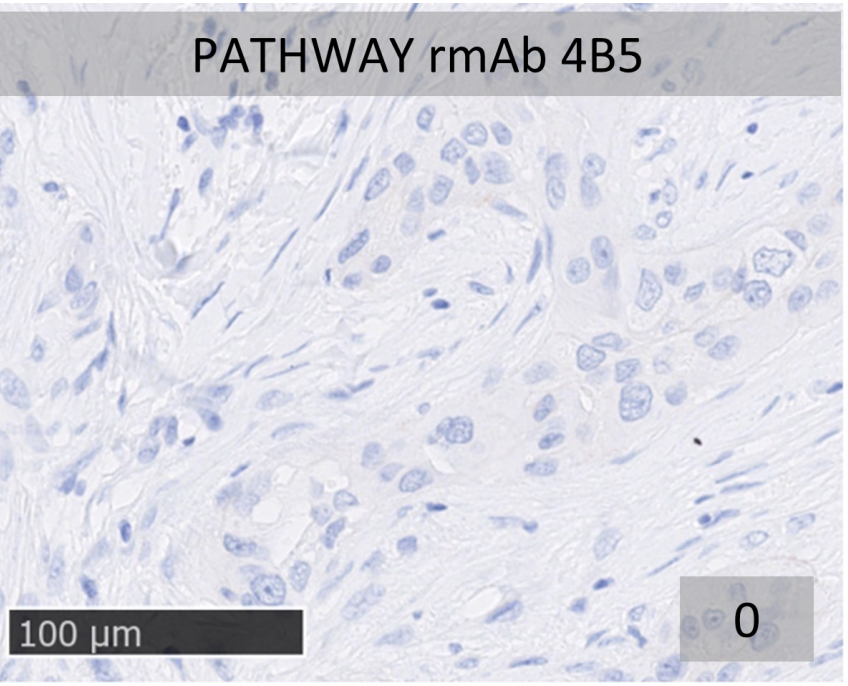
Figure 1. HER2 IHC on three serial sections of two different breast carcinoma cases using three different IHC assays: PATHWAY rmAb 4B5, HercepTest pAb SK001 and HercepTest rmAb DG44. All assays were performed using vendor-recommended protocol settings (VRPS).
Top row: Case 1, showing HER2 expression score "0" using PATHWAY rmAb 4B5, "ultralow" with HercepTest pAb SK001 and "1+" with HercepTest rmAb DG44.
Bottom row: Case 2, showing HER2 expression score "1+" using PATHWAY rmAb 4B5, "2+" with HercepTest pAb SK001 and "2+" with HercepTest rmAb DG44.
Scale bars: 100 µm (top row), 250 µm (bottom row).

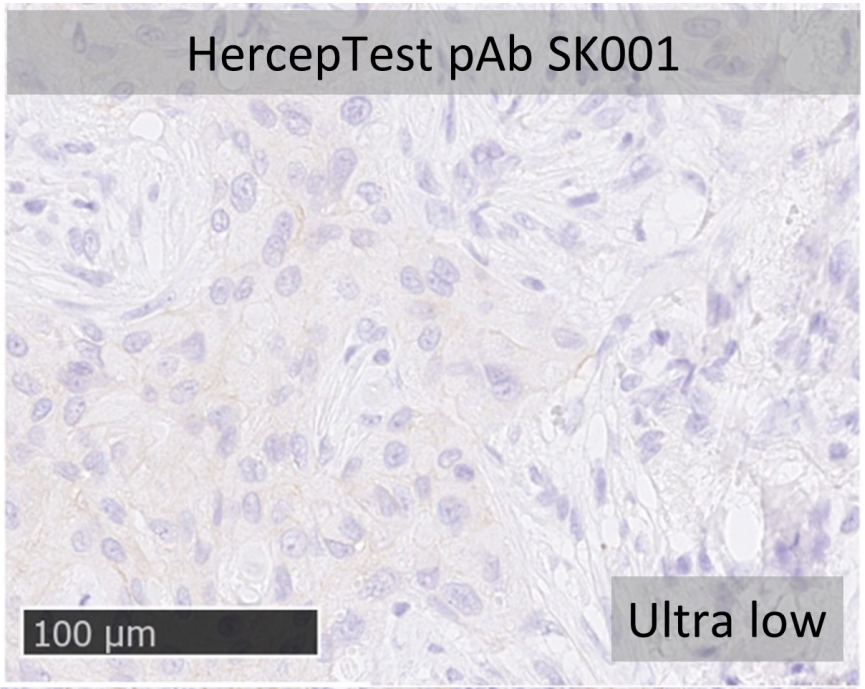
Conclusion

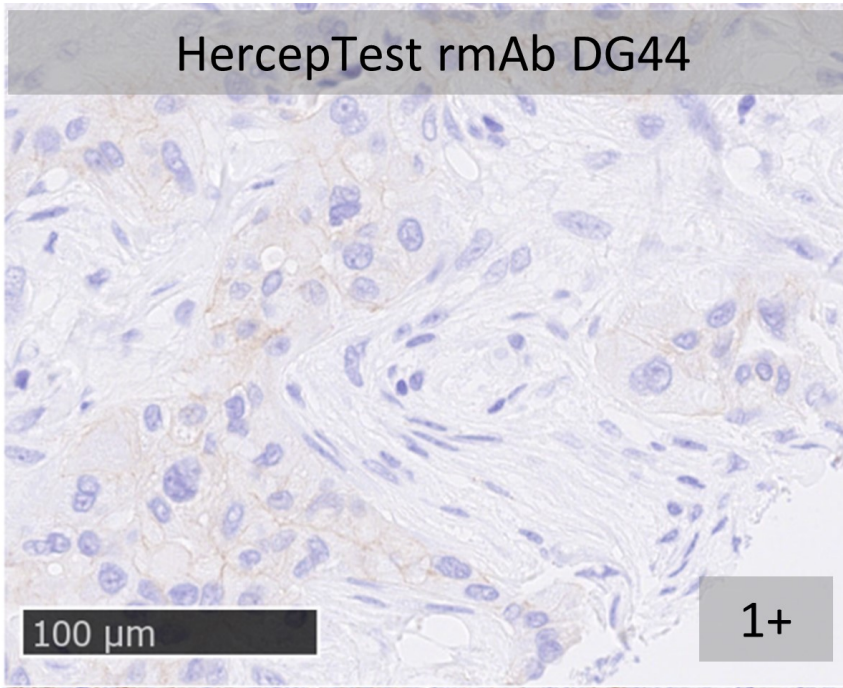
This study shows strong agreement among the three IHC assays when using the classical interpretation that classifies BC as either HER2-positive or HER2-negative. However, under the new treatment approach, where only HER2 0 patients do not receive therapy, the choice of assay becomes important. The PATHWAY rmAb assay identifies more patients as HER2 0 compared to the two HercepTest assays, potentially influencing treatment decisions.

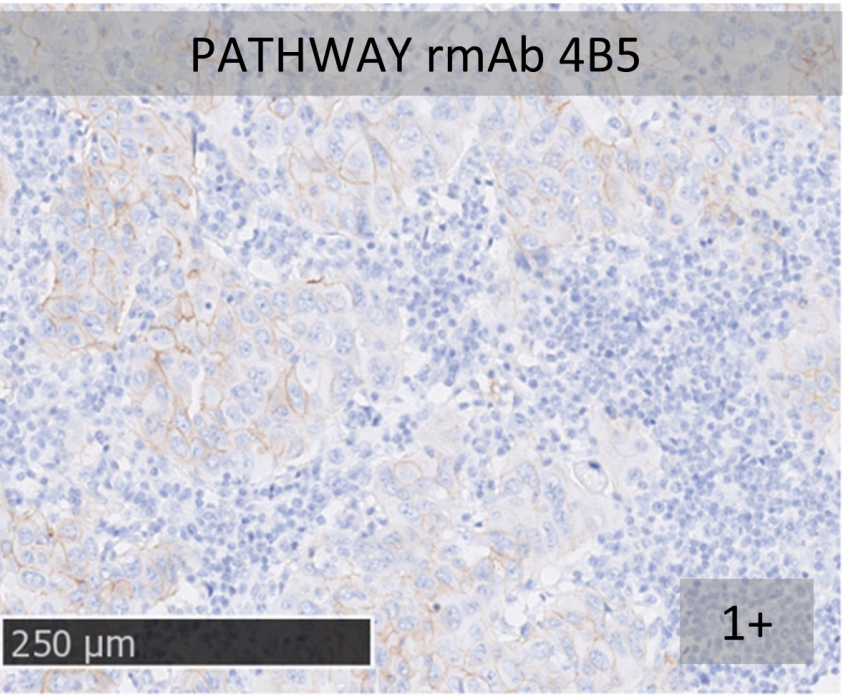
← Download the poster here!

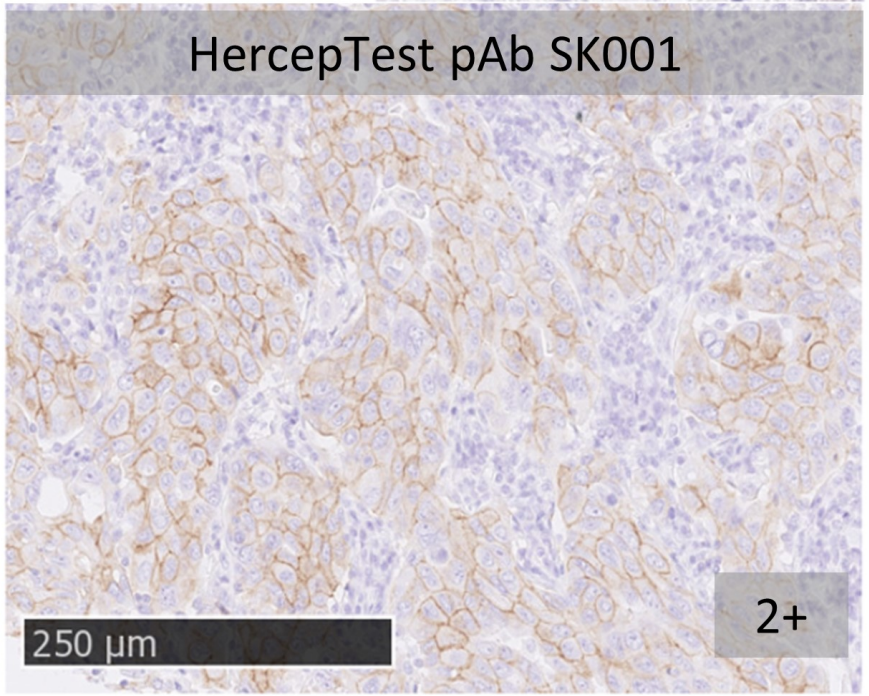
The authors have no conflict of interest related to the content of this work.

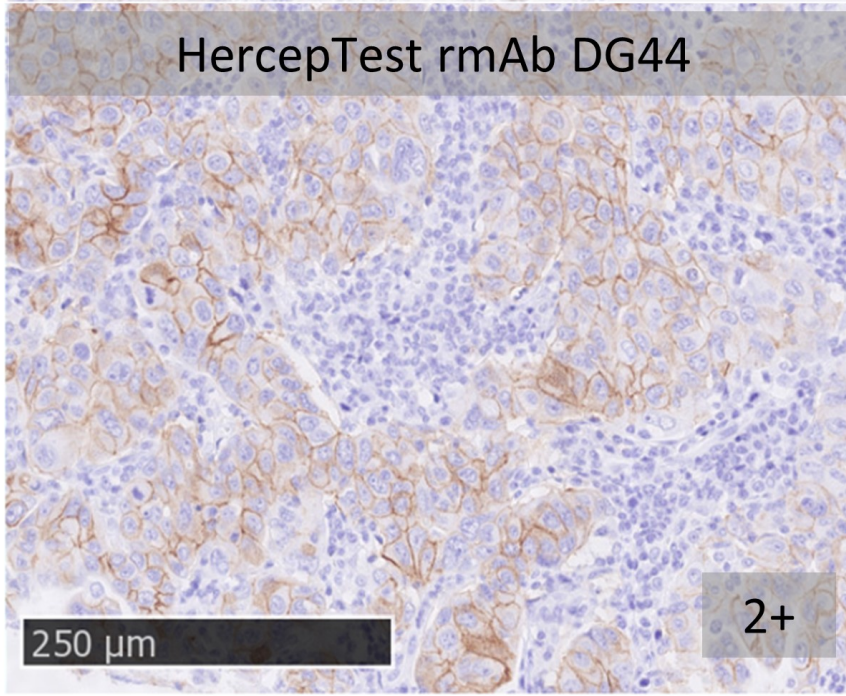

PATHWAY rmAb 4B5
100 µm
0


HercepTest pAb SK001
100 µm
Ultra low

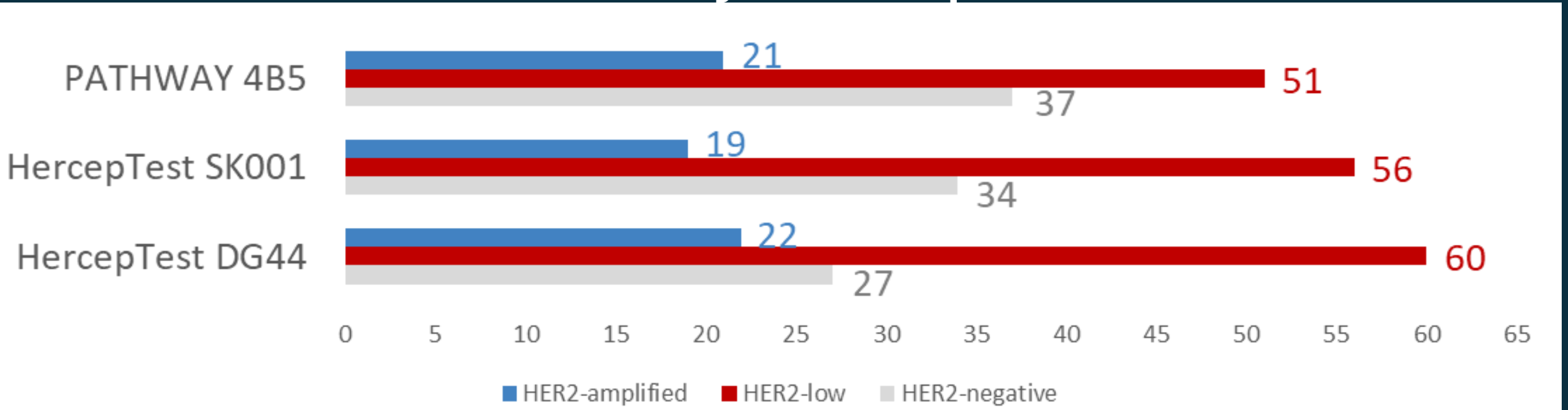

HercepTest rmAb DG44
100 µm
1+


PATHWAY rmAb 4B5
250 µm
1+


HercepTest pAb SK001
250 µm
2+


HercepTest rmAb DG44
250 µm
2+

Are HER2 assays comparable?



HER2 Group	PATHWAY 4B5	HercepTest SK001	HercepTest DG44
HER2-negative	88	90	87
HER2-positive	21	19	22
Total	109	109	109

Two TMAs: triple-negative and ductal BC

Three CE-IVD approved IHC-assays:
PATHWAY rmAb 4B5, 790-2991 (Ventana/Roche) HercepTest pAb, SK001 (Dako/Agilent)
HercepTest rmAb DG44, GE001 (Dako/Agilent)

Scored as HER2 0, ultralow, 1+, 2+ or 3+

Amplification FISH status for HER2 2+

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CEA = Carcinoembryonic Antigen

CEA
From tool to target- rebirth of an old marker

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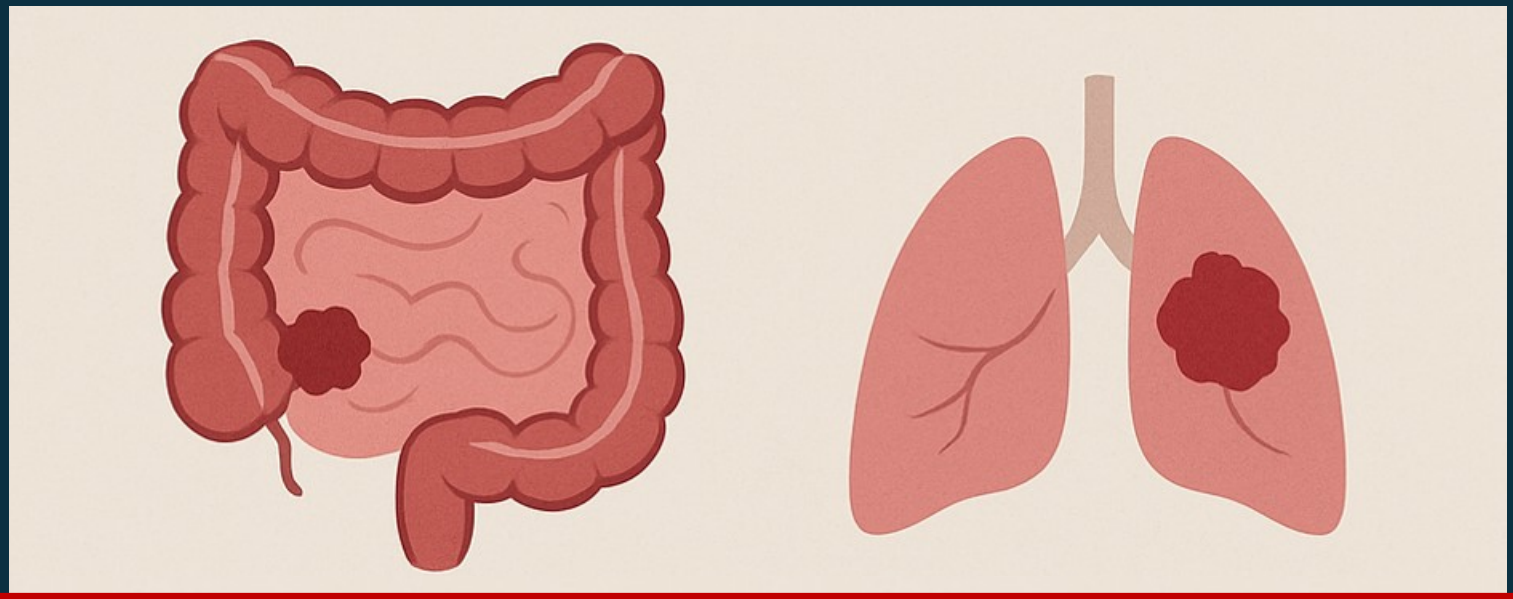
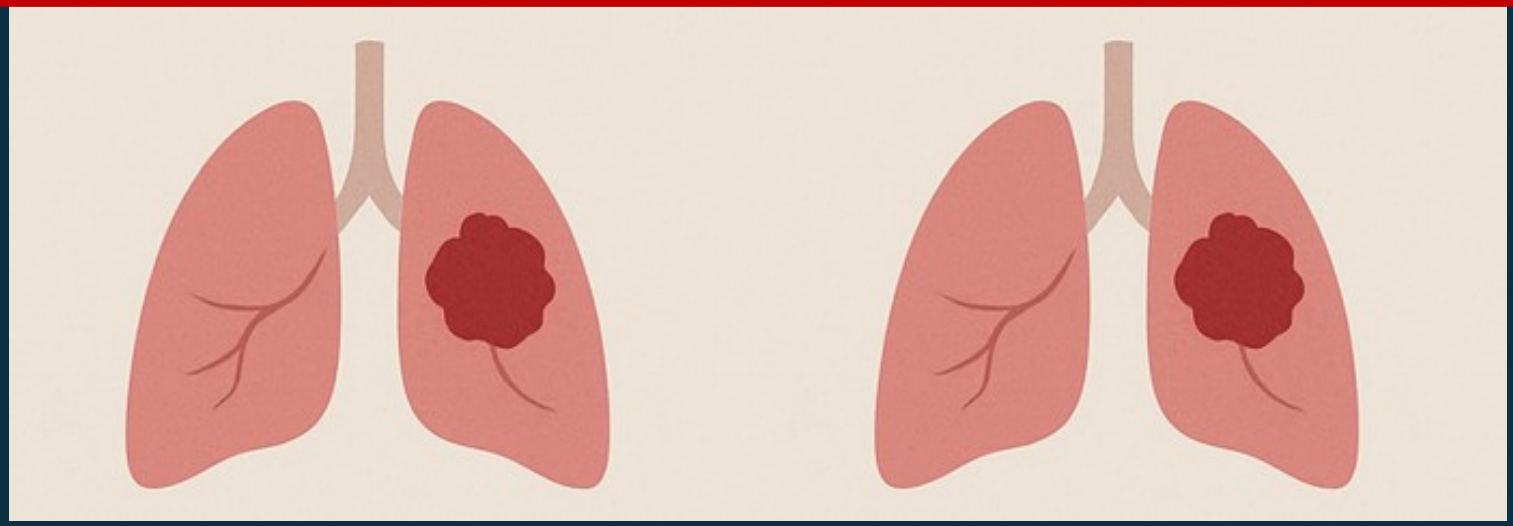
If CEA-negative, tumor unlikely to be colonic AC



If CEA-positive, likely lung AC, not mesothelioma



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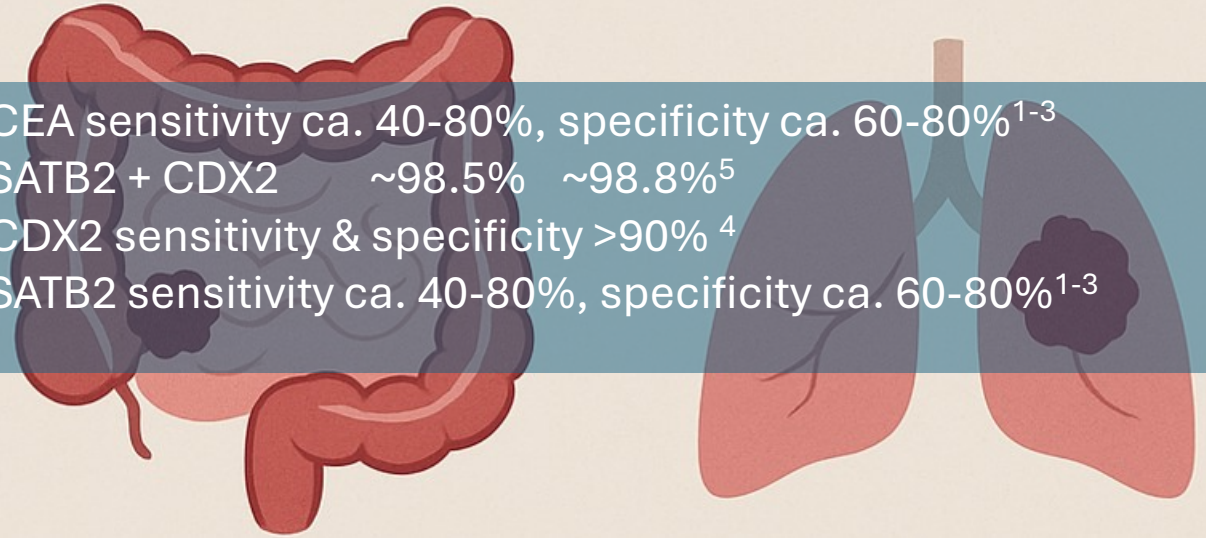
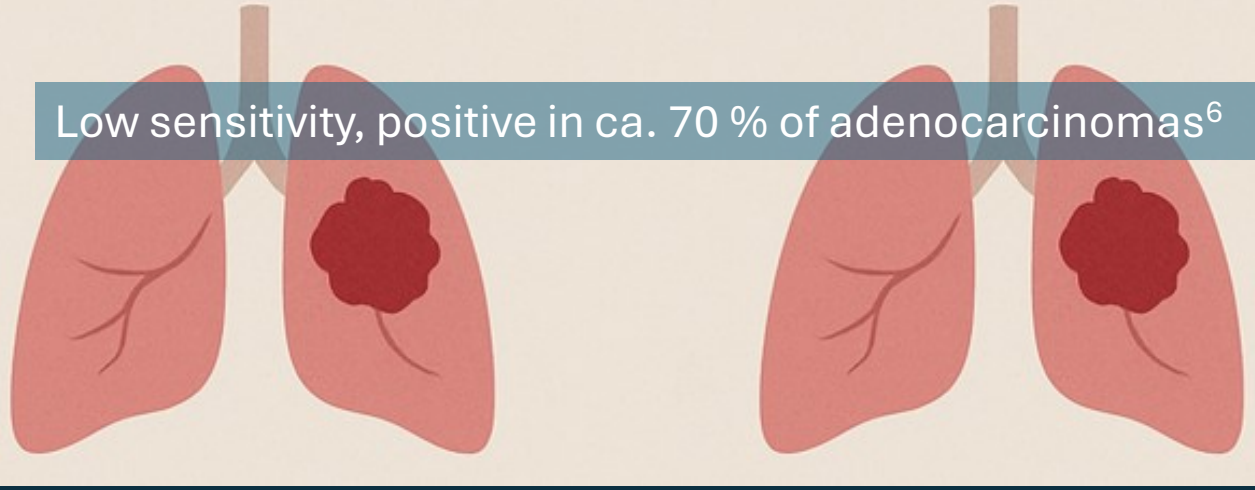
1. Kankanala VL, Zubair M, Mukkamalla SKR. Carcinoembryonic Antigen. 2024 Dec 11. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan–. PMID: 35201700.
2. Sørensen CG, Karlsson WK, Pommergaard HC, Burcharth J, Rosenberg J. The diagnostic accuracy of carcinoembryonic antigen to detect colorectal cancer recurrence - A systematic review. Int J Surg. 2016 Jan;25:134-44. doi: 10.1016/j.ijsu.2015.11.065. Epub 2015 Dec 15. PMID: 26700203.
3. Fakih MG, Padmanabhan A. CEA monitoring in colorectal cancer. What you should know. Oncology (Williston Park). 2006 May;20(6):579-87; discussion 588, 594, 596 passim. PMID: 16773844.
4. Oh HH, Joo YE. Novel biomarkers for the diagnosis and prognosis of colorectal cancer. Intest Res. 2020 Apr;18(2):168-183. doi: 10.5217/ir.2019.00080. Epub 2019 Nov 30. PMID: 31766836; PMCID: PMC7206347.
5. Elnady MS, Eltatawy FA, Nosseir AG, Zamzam YA, El-Guindya DM. Diagnostic accuracy of SATB2 in identifying primary and metastatic colorectal carcinoma: a comparative immunohistochemical study. Ecancermedicalscience. 2022 Dec 19;16:1491. doi: 10.3332/ecancer.2022.1491. PMID: 36819801; PMCID: PMC9935057.
6Wang J, Ma Y, Zhu ZH, Situ DR, Hu Y, Rong TH. Expression and prognostic relevance of tumor carcinoembryonic antigen in stage IB non-small cell lung cancer. J Thorac Dis. 2012 Oct;4(5):490-6. doi: 10.3978/j.issn.2072-1439.2012.09.01. PMID: 23050113; PMCID: PMC3461079.

If CEA-negative, tumor unlikely to be colonic AC



CEA sensitivity ca. 40-80%, specificity ca. 60-80%[1-3]
SATB2 + CDX2 ~98.5% ~98.8%[5]
CDX2 sensitivity & specificity >90% [4]
SATB2 sensitivity ca. 40-80%, specificity ca. 60-80%[1-3]

If CEA-positive, likely lung AC, not mesothelioma



Low sensitivity, positive in ca. 70 % of adenocarcinomas[6]

CARMEN-LC03: Tusamitamab Ravtansine vs Docetaxel in Previously Treated Advanced Nonsquamous NSCLC

By Julia Cipriano, MS

Posted: 10/22/2024 11:30:00 AM
Last Updated: 10/22/2024 10:34:07 AM

Benjamin Besse, MD, PhD

The multicenter phase III CARMEN-LC03 trial did not meet its dual primary endpoints of progression-free and overall survival with the CEACAM5-directed antibody-drug conjugate tusamitamab ravtansine vs standard chemotherapy with docetaxel in previously treated patients with advanced nonsquamous non–small cell lung cancer (NSCLC), according to the final progression-free survival and first interim overall survival analyses.[1] At the International Association for the Study of Lung Cancer (IASLC) 2024 World Conference on Lung Cancer, **Benjamin Besse, MD, PhD**, of Gustave Roussy, Villejuif, France, and colleagues presented these findings, which led to the termination of the study in December 2023.

Dr. Besse reported trends toward improved overall survival in the overall population and improved progression-free and overall survival in the subgroup of patients with CEACAM5 expression levels of at least 80%, along with a favorable safety profile.

"CEACAM5 is a transmembrane glycoprotein, which is overexpressed in up to 25% of patients with nonsquamous NSCLC," Dr. Besse explained. He noted that an exploratory analysis aiming to understand the high performance of the control arm, which was also presented during the conference, revealed a potential prognostic role for CEACAM5 expression.[2]

The ASCO Post

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CARMEN-LC03: Tusamitamab Ravtansine vs Docetaxel in Previously Treated Advanced Nonsquamous NSCLC

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Press Release: Sanofi announces end of program evaluating tusamitamab ravtansine after a 2L NSCLC Phase 3 trial did not meet a primary endpoint

December 21, 2023

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Meeting Abstract: 2025 ASCO Annual Meeting I

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Precemtabart tocentecan (M9140), an anti-CEACAM5 ADC with exatecan payload, in patients with metastatic colorectal cancer (mCRC): Results from the dose optimization of the phase 1 PROCEADE CRC-01 study.

Authors: Scott Kopetz, Rocio Garcia-Carbonero, Sae-Won Han, Ildefonso Ismael Rodriguez Rivera, Jose Carlos Ruffinelli, Valentina Boni, Maria Vieito Villar, ... SHOW ALL ... , and Ken Kato | AUTHORS INFO & AFFILIATIONS

Publication: Journal of Clinical Oncology • Volume 43, Number 16_suppl • https://doi.org/10.1200/JCO.2025.43.16_suppl.3038

224 Am score 5

Recruiting

Anti-CEACAM5 ADC M9140 in Advanced Solid Tumors (PROCEADE-CRC-01)

ClinicalTrials.gov ID NCT05464030

Sponsor EMD Serono Research & Development Institute, Inc.

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Last Update Posted 2025-07-25

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Antibody-Drug Conjugate (ADC)

CEACAM5

Carcinoembryonic antigen-related cell adhesion molecule 5 (CEACAM5) is a cell surface glycoprotein that is overexpressed on tumor cells and is associated with tumor differentiation, invasion, and metastasis.[1,2] While expression of CEACAM5 is high in several tumor types, such as gastric, colorectal, and pancreatic cancers, expression in normal epithelial tissues is low.[3,4] Thus, CEACAM5 presents a potential target for anticancer therapy.

M9140 – CEACAM5 ADC

M9140 is an investigational CEACAM5 ADC that is designed to deliver a cytotoxic topoisomerase 1 (TOP1) inhibitor payload to CEACAM5-expressing tumor cells.[5-7] The TOP1 inhibitor payload enters the nucleus and disrupts DNA replication and repair, thereby killing CEACAM5-expressing tumor cells.[5-7] The payload can also enter and kill neighboring tumor cells via a bystander effect.[5]

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CEACAM5 is high in several tumor types, such as
gastric,
colorectal
and pancreatic cancers,
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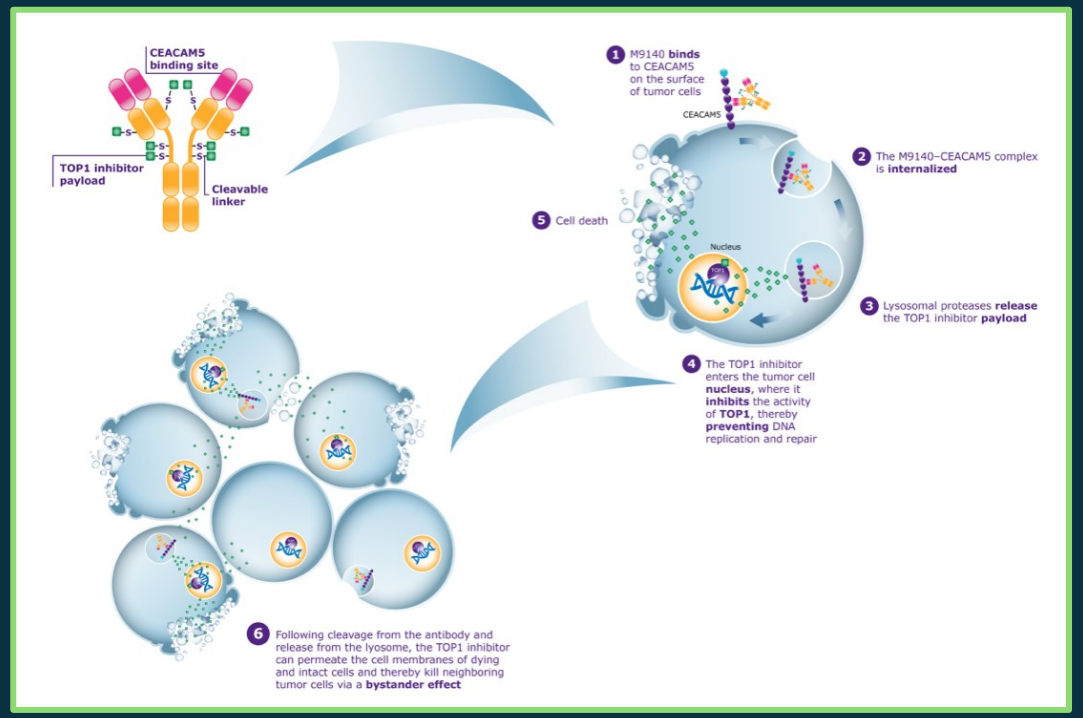

1. Decary S, Berne P-F, Nicolazzi C, et al. Preclinical activity of SAR408701: a novel anti-CEACAM5-maytansinoid antibody-drug conjugate for the treatment of CEACAM5-positive epithelial tumors. *Clin Cancer Res*. 2020;26(24):6589-6599.
2. Boogerd LSF, Vuijk FA, Hoogstins CES, et al. Correlation between preoperative serum carcinoembryonic antigen levels and expression on pancreatic rectal cancer tissue. *Biomark Cancer*. 2017;9:1179299X17710016.

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Thank you!

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