BeOne

ECP 2025 Industry Satellite Symposium
Vienna, Austria, September 8th, 2025

TAP (tumor area positivity):
A new PD-L1 star is born

Chair: Matteo Fassan, Padua University, Italy

SEPT · 08 · 2025

TAP (tumor area positivity):
A new PD-L1 star is born

Welcome and objectives

Welcome and housekeeping

- Please ensure your mobile devices are in silent mode

- We welcome your questions:
  - There will be an opportunity for questions at the end of the symposium

- Please complete the evaluation form to enable us to make our next event even better

Meet the experts

Matteo Fassan
Padua University and ULSS2 Marca Trevigiana
Treviso, Italy

Manuel Rodriguez-Justo
UCL and UCLH
London, UK

Mar Iglesias
Hospital del Mar
Barcelona, Spain

UCL, University College London; UCLH, University College London Hospitals; ULSS2, Unità Locale Socio Sanitaria n. 2.

Agenda

Welcome and objectives	Matteo Fassan *Italy*
PD-L1 testing in gastroesophageal cancer: Preanalytical and analytical challenges	Manuel Rodriguez-Justo *UK*
PD-L1 scoring algorithms in gastroesophageal cancer: Similarities and differences	Mar Iglesias *Spain*
TAP in the clinic: The report in clinical practice	Matteo Fassan *Italy*
Q&A and conclusions	All faculty

PD-L1, programmed cell death ligand 1; TAP, tumor area positivity.

The central dogma in the current precision oncology scenario

PD-L1 represents **the most important predictive clinical biomarker for immunotherapy** in gastroesophageal cancers

PD-L1, programmed cell death ligand 1.

It’s getting more difficult…

GOOD SCIENCE
BETTER MEDICINE
BEST PRACTICE
European Society for Medical Oncology
Guidelines

Adenocarcinoma[1,2]

- HER2
- PD-L1
- MMR/MSI
- CLDN 18.2

Squamous cell carcinoma[3]

- PD-L1

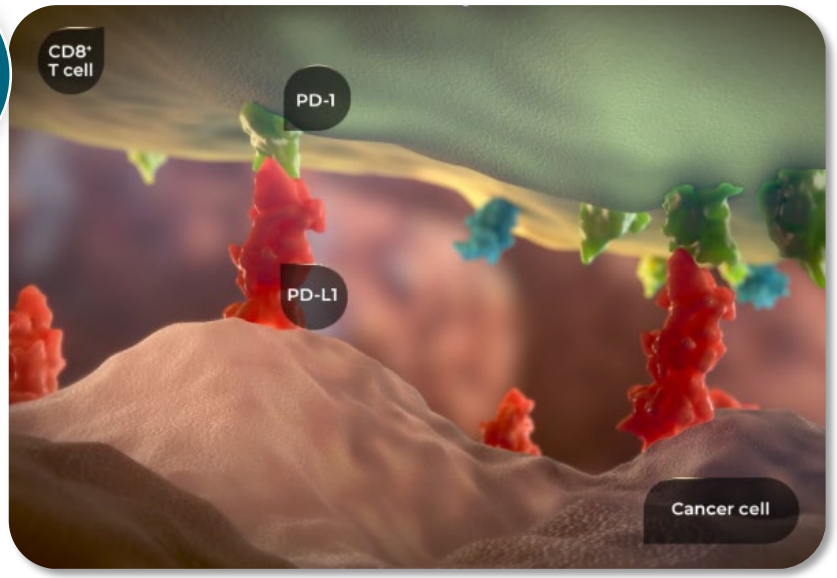
WHEN?	In case of locally advanced unresectable or metastatic disease
WHERE?	Usually in samples of the primary lesion
WHAT?	PD-L1: CPS and TAP for adenocarcinoma; CPS, TAP, and TPS for SCC
HOW?	In case of prioritization: HER2 > PD-L1 > MMR/MSI > CLDN 18.2

CLDN 18.2, Claudin 18.2; CPS, combined positive score; HER2, human epidermal growth factor receptor 2; MMR, deoxyribonucleic acid mismatch repair; MSI, microsatellite instability; PD-L1, programmed cell death ligand 1; SCC, squamous cell carcinoma; TAP, tumor area positivity; TPS, tumor proportion score.

1. Lordick F, et al. Ann Oncol. 2022;33:1005–1022; 2. ESMO. Gastric Cancer Living Guideline. Available at: https://www.esmo.org/guidelines/living-guidelines/esmo-living-guideline-gastric-cancer/diagnosis-pathology-and-molecular-biology/Accessed July 2025; 3. Obermannova R, et al. Ann Oncol. 2022;33:992–1004.

Novel PD-L1 scoring algorithm

- Tumor cells express **PD-L1**, a protein that enables them to evade the immune response and grow[1]
- Determining PD-L1 expression levels in tumor tissue is crucial for identifying gastric cancer patients eligible for **immunotherapy**[1]



Today, we will introduce a novel PD-L1 scoring algorithm based on visual estimation, the tumor area positivity (TAP) score[1,2]

TAP was established by Liu et al. and clinically tested in various upper GI cancer clinical trials, including RATIONALE-306, R-302 and R-305 (tislelizumab)[3–5] and MATTERHORN (durvalumab)[6]

TAP has the potential to standardize existing scoring methods that evaluate both TC and IC[1]

GI, gastrointestinal; IC, immune cell; PD-L1, programmed cell death ligand 1; R, RATIONALE; TC, tumor cell.

1. Liu C, et al. Diagn Pathol. 2023;18:48; 2. Klempner SJ, et al. JCO Precis Oncol. 2024:e2400230; 3. Qiu M-Z, et al. BMJ. 2024: 385:e078876; 4. Xu J, et al. Lancet Oncol. 2023; 24(5):483–95; 5. Shen L, et al. J Clin Oncol. 2022;40(26):3065–76; 6. Janjigian YY, et al. N Engl J Med. 2025. doi: 10.1056/NEJMoa2503701.

PD-L1 testing in gastroesophageal cancer: Preanalytical and analytical challenges

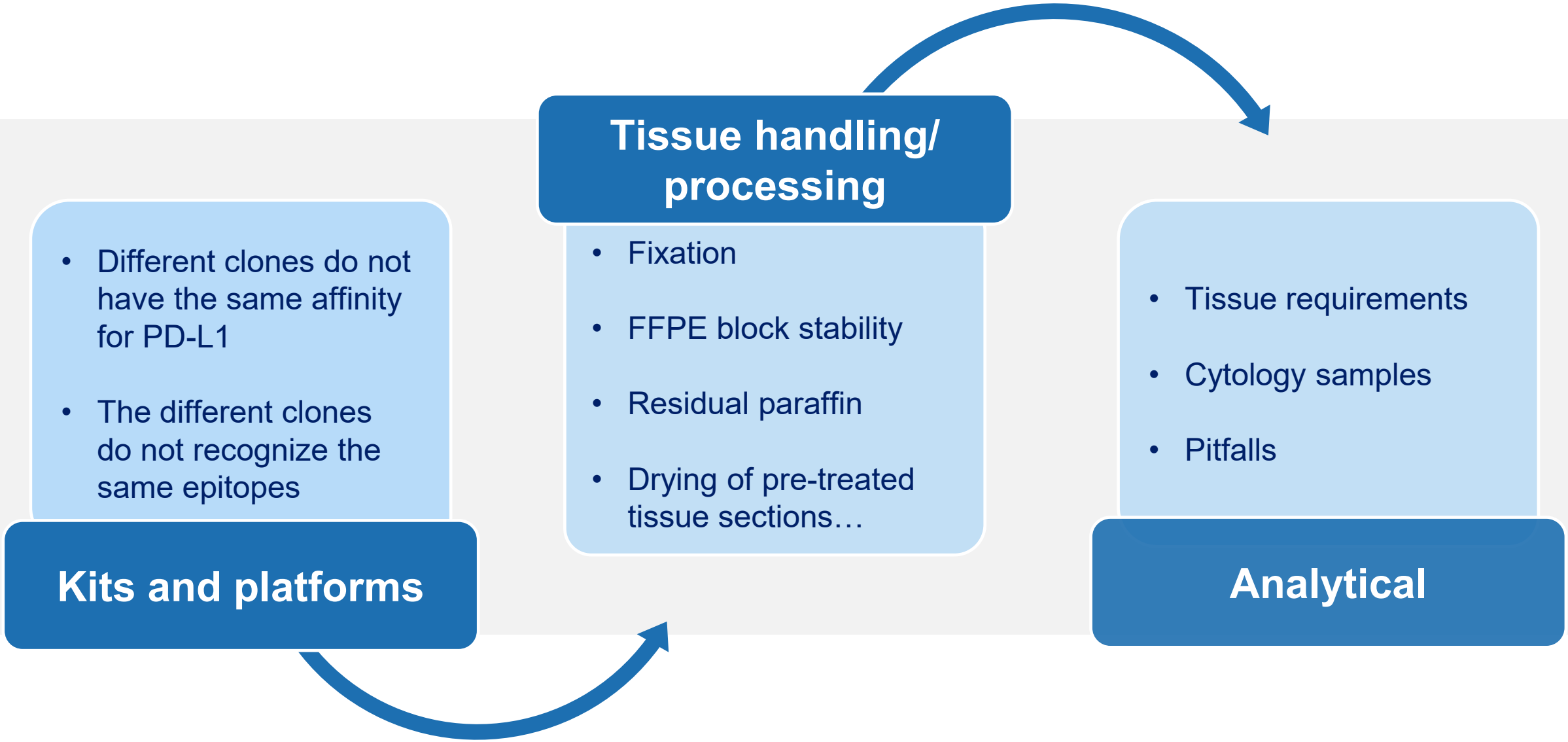
Manuel Rodriguez-Justo, FRCPath, MD

Cancer Institute - University College London and University College London Hospitals, UK

Disclosures

- **Consultancy fees:** Agilent, AstraZeneca, BeOne Medicines, Gilead, Ibex Medical, Jazz Pharmaceuticals, Roche Diagnostic Solutions, Servier
- **Research/educational grants:** Pfizer, Roche Diagnostics Limited, Hamamatsu
- **Remuneration for:** Advisory board attendance, chair of educational meetings, consultancy, travel, accommodation, and registration at national/international meetings

Considerations for PD-L1 testing in gastroesophageal cancer



FFPE, formalin-fixed paraffin-embedded; PD-L1, programmed cell death ligand 1.

Considerations for PD-L1 testing in gastroesophageal cancer

Kits and platforms

- Different clones do not have the same affinity for PD-L1
- The different clones do not recognize the same epitopes

Tissue handling/ Processing

- Fixation
- FFPE block stability
- Residual paraffin
- Drying of pre-treated tissue sections…

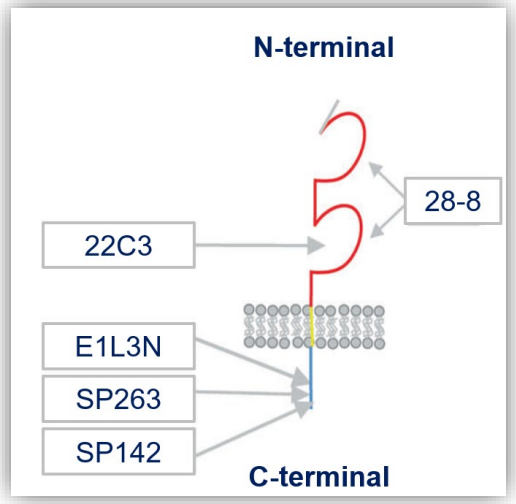
Analytical

- Tissue requirements
- Cytology samples
- Pitfalls

FFPE, formalin-fixed paraffin-embedded; PD-L1, programmed cell death ligand 1.

Commercially available antibodies

Antibody supplier	Company/Drug	Clone	Species	Antibody epitope
Dako (Agilent)[1,2]	Bristol Myers Squibb/Nivolumab	28-8	Rabbit mAb	Extracellular domain
Dako (Agilent)[3–6]	MSD/Pembrolizumab; Regeneron and Sanofi/Cemiplimab	22C3	Mouse mAb	Extracellular domain
Ventana (Roche)[6–8]	Roche/Atezolizumab	SP142	Rabbit mAb	Intracellular domain
Ventana (Roche)[6,9–12]	BeOne/Tislelizumab; AstraZeneca/Durvalumab	SP263	Rabbit mAb	Intracellular domain
Dako (Agilent)[6,13]	Merck and Pfizer/Avelumab	73-10	Rabbit mAb	Intracellular domain
Cell Signaling[6,14]	–	E1L3N	Rabbit mAb	Intracellular domain

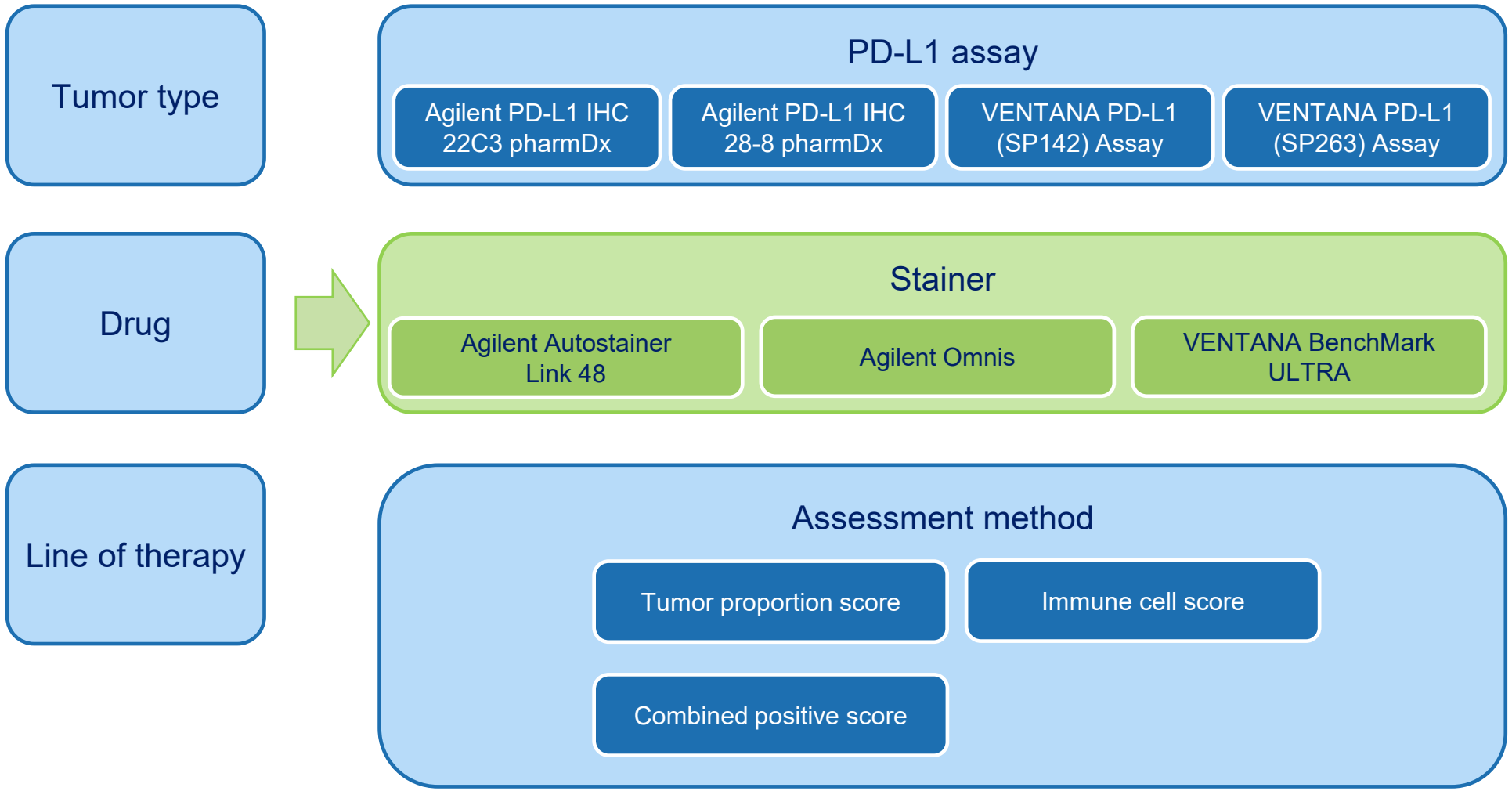


mAb, monoclonal antibody.

1. Phillips T, et al. Appl Immunohistochem Mol Morphol. 2015;23(8):541–9; 2. Agilent. PD-L1 IHC 28-8 pharmDx Interpretation Manual Non-Squamous Non-Small Cell Lung Cancer. Available at: https://www.agilent.com/; 3. Tumeh PC, et al. Nature. 2014;515(7528):568–71; 4. Agilent. PD-L1 IHC 22C3 pharmDx. Available at: https://www.agilent.com/cs/library/packageinsert/public/P03951E_26.pdf; 5. Migden MR, et al. Lancet Oncol. 2020;21(2):294–305; 6. Tsao MS, et al. In: IASLC Atlas of PD-L1 Immunohistochemistry Testing in Lung Cancer. 1st ed. North Fort Myers, FL; 2017; 7. Roche. VENTANA® PD-L1 (SP142) Assay. Available at: https://diagnostics.roche.com/; 8. Jotatsu T, et al. J Thorac Dis. 2018;10(Suppl. 18):S2127–29; 9. VENTANA® PD-L1 (SP263) Rabbit Monoclonal Primary Antibody. Available at: https://diagnostics.roche.com/; 10. Sholl LM, et al. Arch Pathol Lab Med. 2016;140(4):341–4; 11. EMA. Tevimbra, INN-tislelizumab – European Medicines Agency. Available at: https://www.ema.europa.eu/; 12. BeOne Medicines. Our Medicines. Available at: https://beonemedicines.com/science/medicines; 13. Noda Y, et al. Head Neck Pathol. 2025;19(1):65; 14. Cell Signaling Technology. PD-L1 (E1L3N®) XP® Rabbit mAb #13684. Available at: https://www.cellsignal.com/ (all links accessed June 2025).

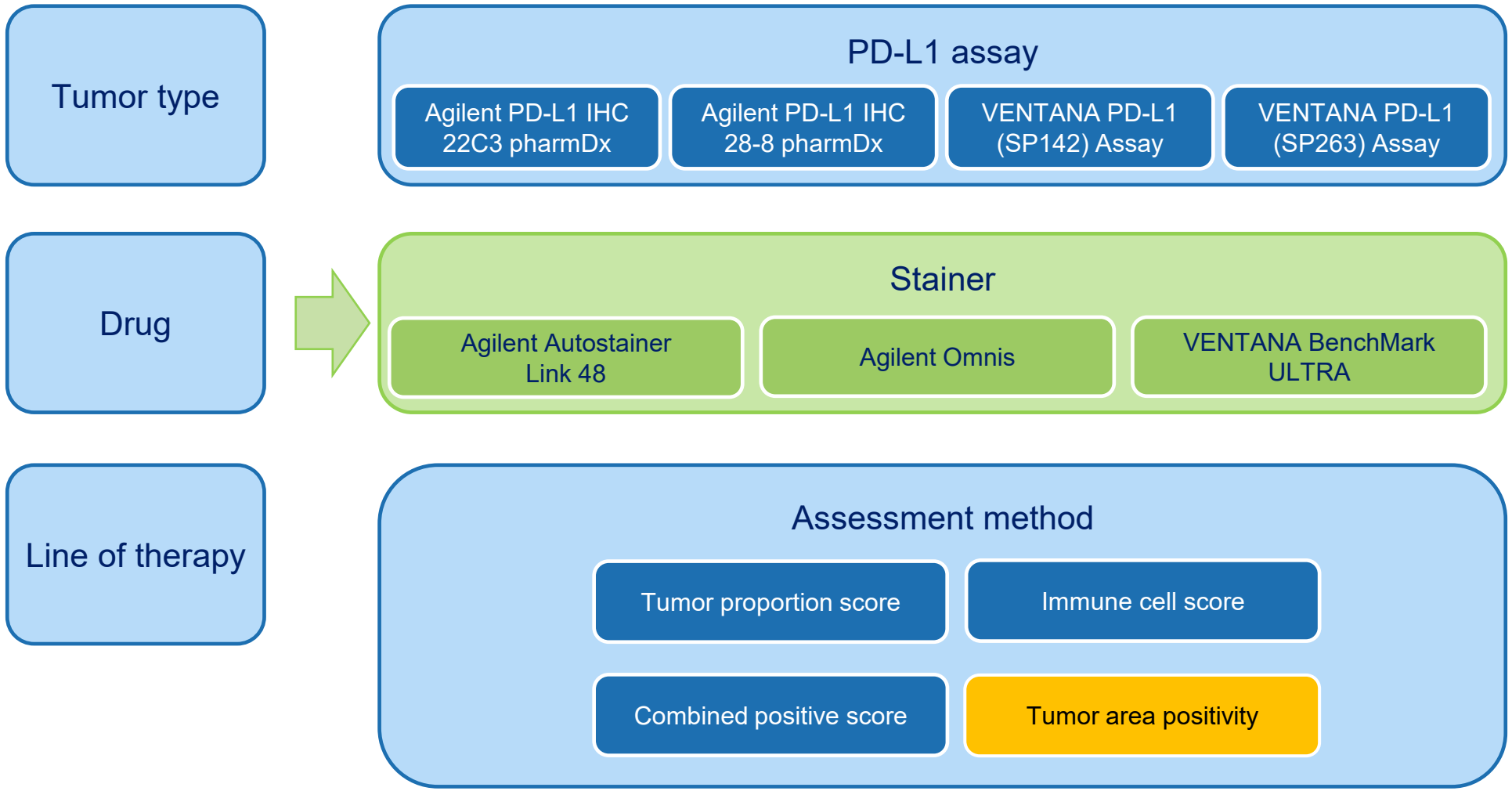
Figure adapted from: Lawson NL, et al. Mod Pathol. 2020;33(4):518–30.

PD-L1 testing platforms



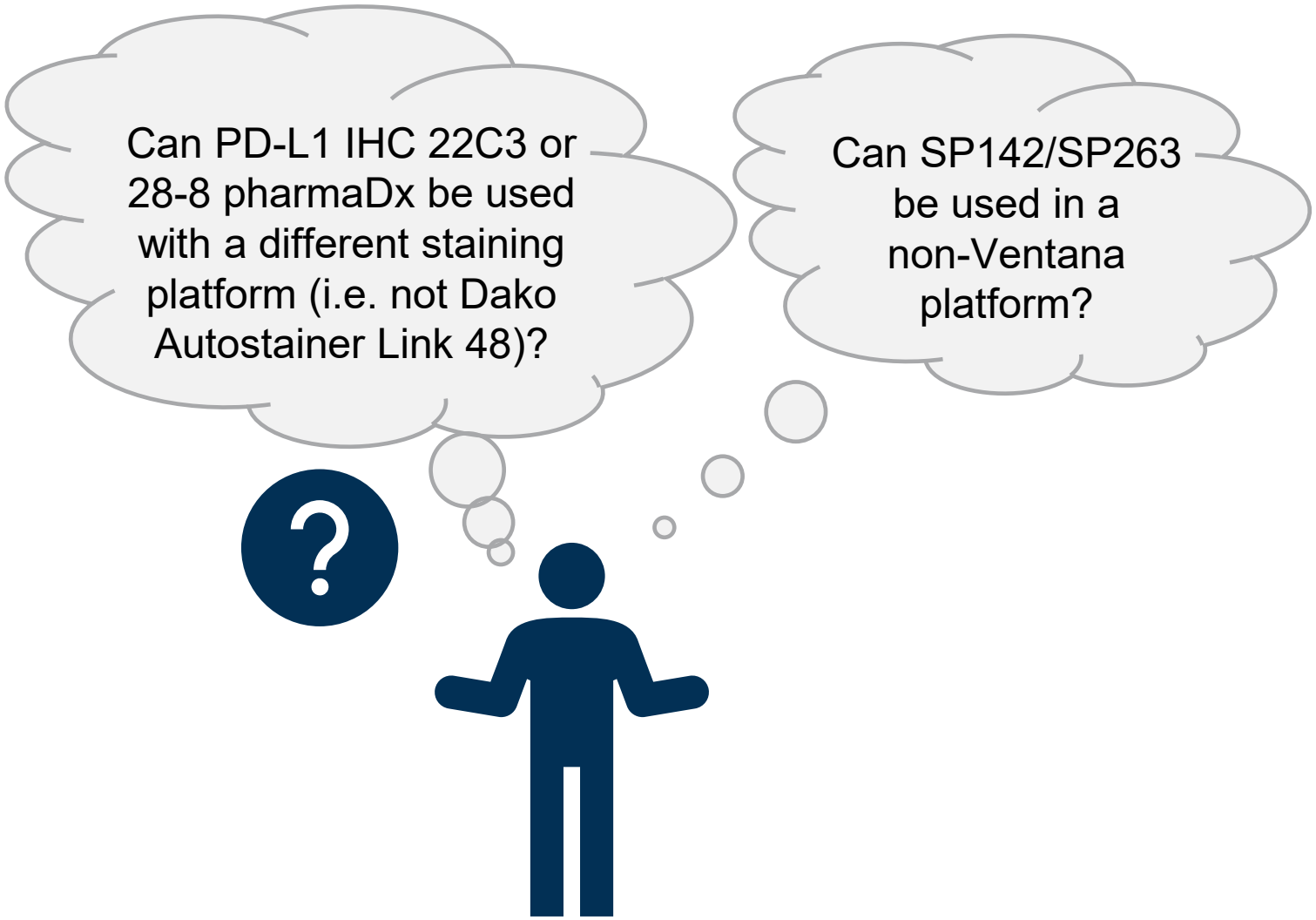
IHC, immunohistochemistry; PD-L1, programmed cell death ligand 1.

PD-L1 testing platforms



IHC, immunohistochemistry; PD-L1, programmed cell death ligand 1.

Matching assays



IHC, immunohistochemistry; PD-L1, programmed cell death ligand 1.

Matching assays

Can PD-L1 IHC 22C3 or 28-8 pharmaDx be used with a different staining platform (i.e. not Dako Autostainer Link 48)?

Can SP142/SP263 be used in a non-Ventana platform?

One study (in lung) investigated whether it is possible to adapt Dako's PD-L1 22C3 pharmaDx assay to the Ventana BenchMark platform[1]

Recommendation:

CDx should be used as approved to **match specific therapies with relevant biomarkers**

- Systems for amplification and detection of the signal change the threshold of positivity of the PD-L1 signal

CDx, companion diagnostic; IHC, immunohistochemistry; PD-L1, programmed cell death ligand 1.
The content of this slide reflects the speaker's position and expert opinion.

1. Scheel AH, et al. Mod Pathol. 2016;29(10):1165–72.

PD-L1 testing accuracy: IVD vs LDT

IVD, *in vitro* diagnostic; LDT, laboratory-developed test; PD-L1, programmed cell death ligand 1.

PD-L1 testing accuracy: IVD vs LDT

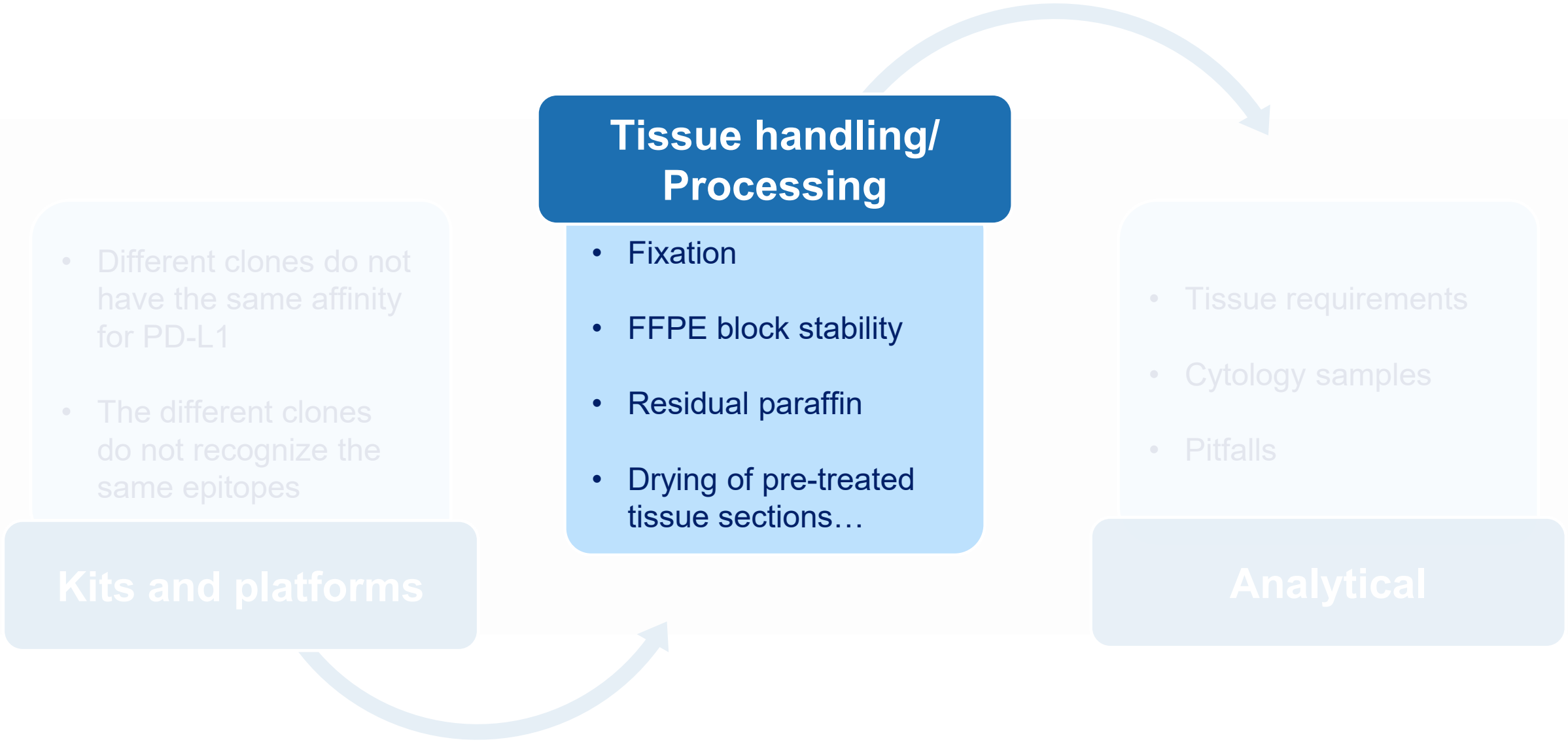
	Acceptable		False negative		False positive		Total	
	n	%	n	%	n	%	n	%
UK NEQAS								
IVD	507	92	40	7	6	1	553	69
LDT	161	66	66	27	16	7	243	31
NordiQC								
IVD	245	95	13	5	0	0	258	38
LDT	331	77	78	18	20	5	429	62
Total								
IVD	752	93	53	7	6	1	811	55
LDT	492	73	144	21	36	5	672	45

PD-L1 testing accuracy was **93% in the IVD group compared to 73% in the LDT group,** with most misclassifications being false negatives (7% of IVDs and 21% of LDTs)

IVD, *in vitro* diagnostic; LDT, laboratory-developed test; NordiQC, Nordic Immunohistochemical Quality Control; PD-L1, programmed cell death ligand 1; UK NEQAS, United Kingdom National External Quality Assessment Service.

Hurwitz JT, et al. Oncol Ther. 2022;10:391–409.

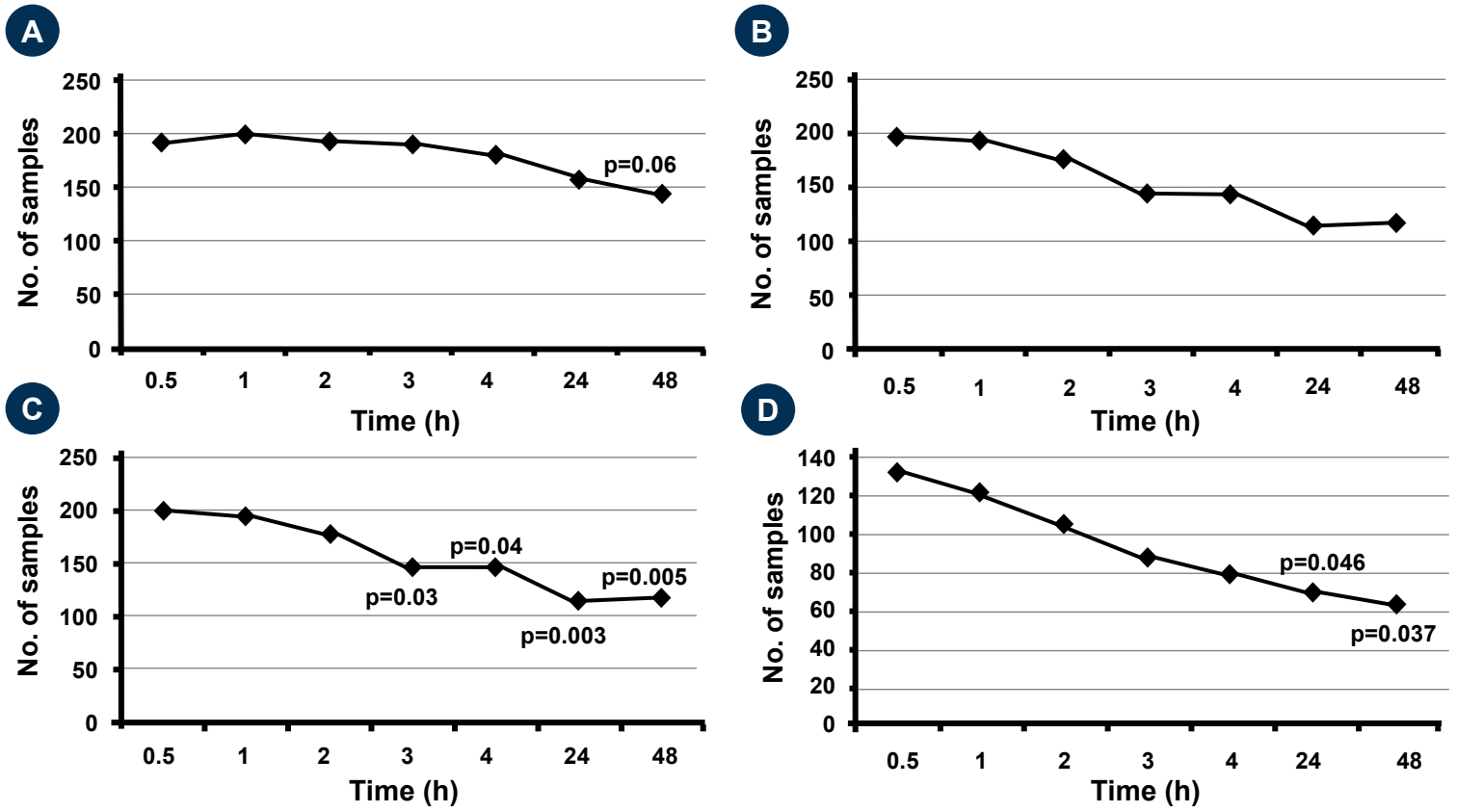
Considerations for PD-L1 testing in gastroesophageal cancer

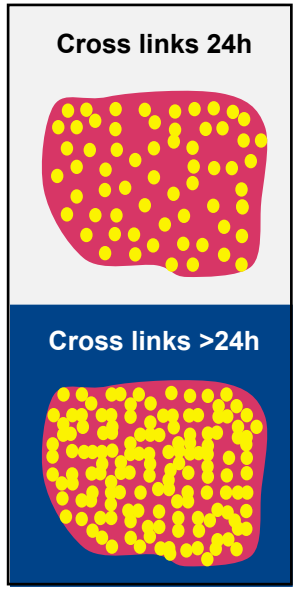


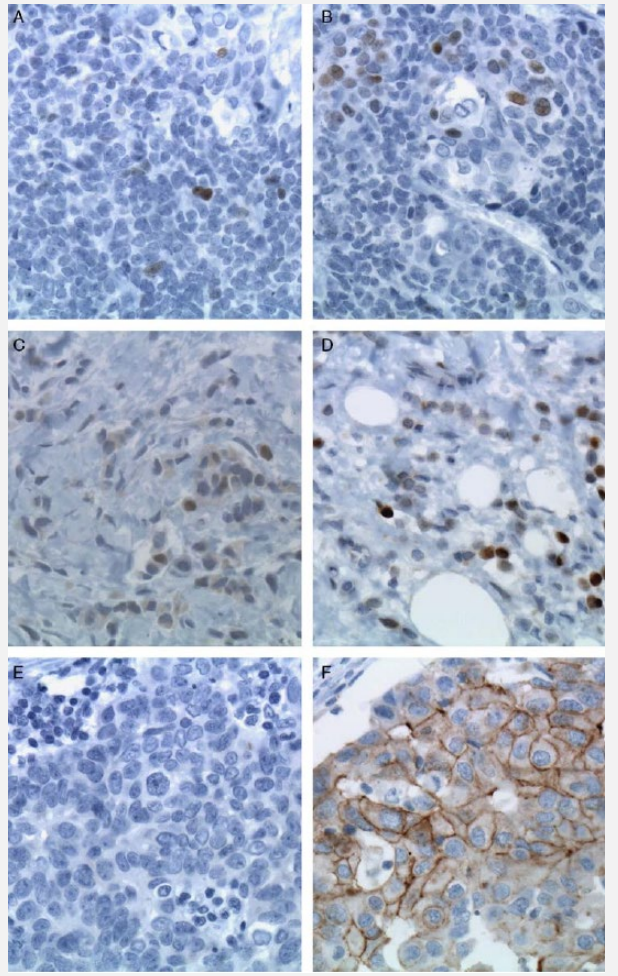
FFPE, formalin-fixed paraffin-embedded; PD-L1, programmed cell death ligand 1.

Challenges in tissue processing

Tissue fixation	• 10% neutral-buffered formalin • At least 4 hours • Ideal fixation time: 12–72 hours	• The level of expression can vary according to the level of tumor hypoxia







AQUA, automated quantitative analysis; ER, estrogen receptor; HER2, human epidermal growth factor receptor 2; PR, progesterone receptor.
The content of this slide reflects the speaker's position and expert opinion.
Figures adapted from: Khoury T. Am J Clin Pathol. 2018;149(4):275–92; Tong LC, et al. Am J Surg Pathol. 2011;35(4):545–52; Werner M, et al. Am J Surg Pathol. 2000;24(7):1016-9.

Challenges in tissue processing

Tissue fixation	• 10% neutral-buffered formalin • At least 4 hours • Ideal fixation time: 12–72 hours	• The level of expression can vary according to the level of tumor hypoxia
Block stability	• FFPE block <5 years	• Blocks >5 years: decreased and/or weaker intensity

FFPE, formalin-fixed paraffin-embedded.
The content of this slide reflects the speaker's position and expert opinion.

Challenges in tissue processing

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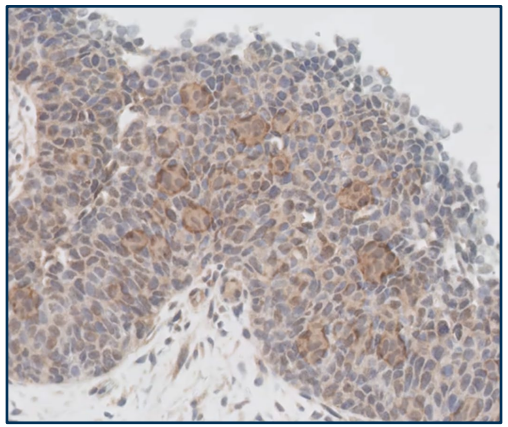
Thickness	• Sections 4–5 µm	• >5 µm → stronger intensity • <4 µm → weaker intensity

FFPE, formalin-fixed paraffin-embedded; µm, micron.
The content of this slide reflects the speaker's position and expert opinion.

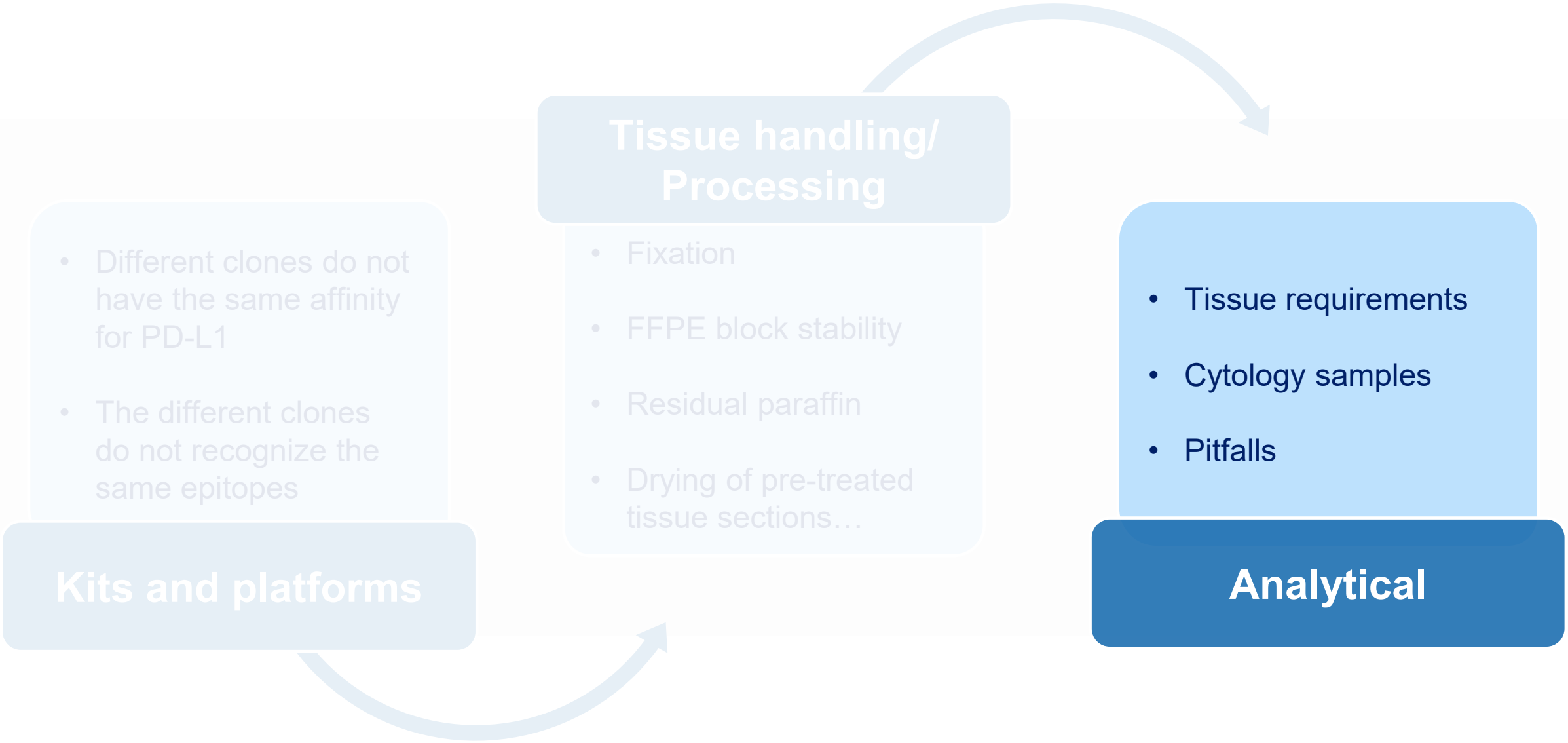
Challenges in tissue processing

Tissue fixation	• 10% neutral-buffered formalin • At least 4 hours • Ideal fixation time: 12–72 hours	• The level of expression can vary according to the level of tumor hypoxia
Block stability	• FFPE block <5 years	• Blocks >5 years: decreased and/or weaker intensity
Thickness	• Sections 4–5 µm	• >5 µm → stronger intensity • <4 µm → weaker intensity
Paraffin removal	• Incomplete deparaffinization	• False negative results • Non-specific staining (DAB droplets)



DAB, diaminobenzidine; FFPE, formalin-fixed paraffin-embedded.

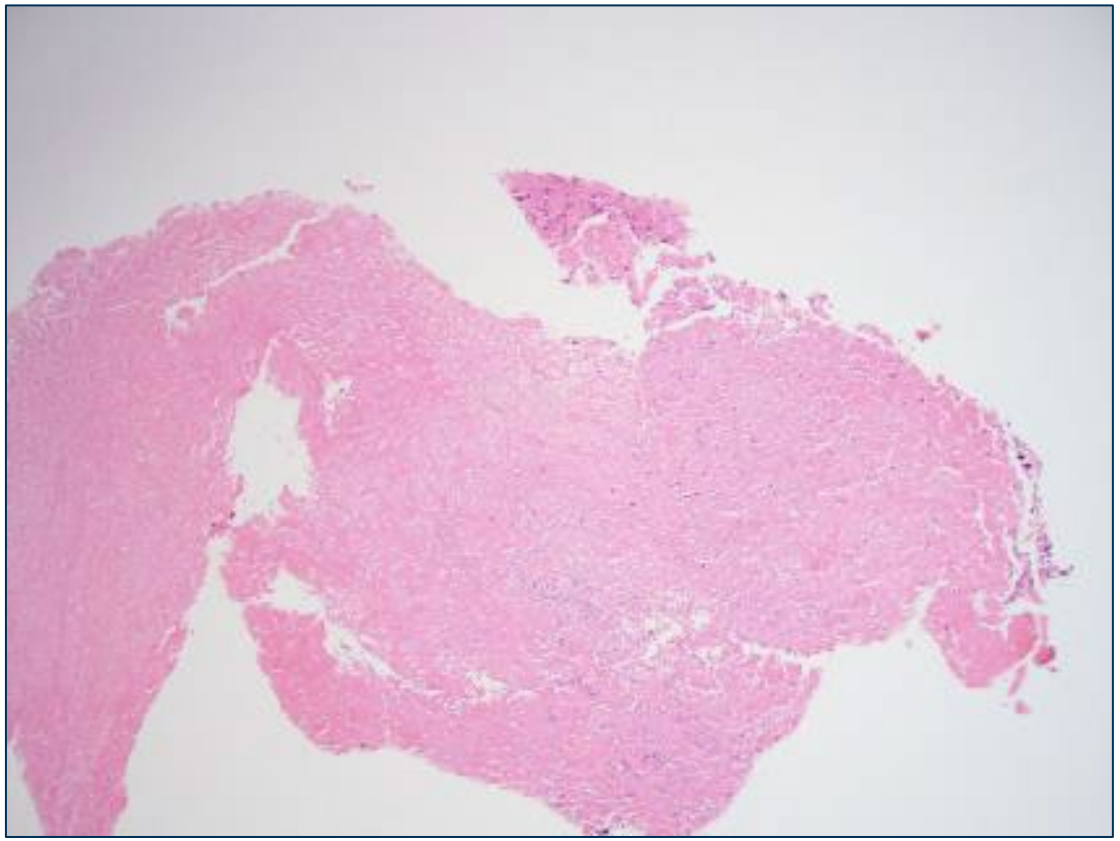
Considerations for PD-L1 testing in gastroesophageal cancer



FFPE, formalin-fixed paraffin-embedded; PD-L1, programmed cell death ligand 1.

Adequacy of biopsies

- **At least 100 viable tumor cells** are required for assessment
- **Multiple biopsies** are **preferable** than a single biopsy
- Necrotic tumor is **inadequate** for assessment
- Only **invasive components** count

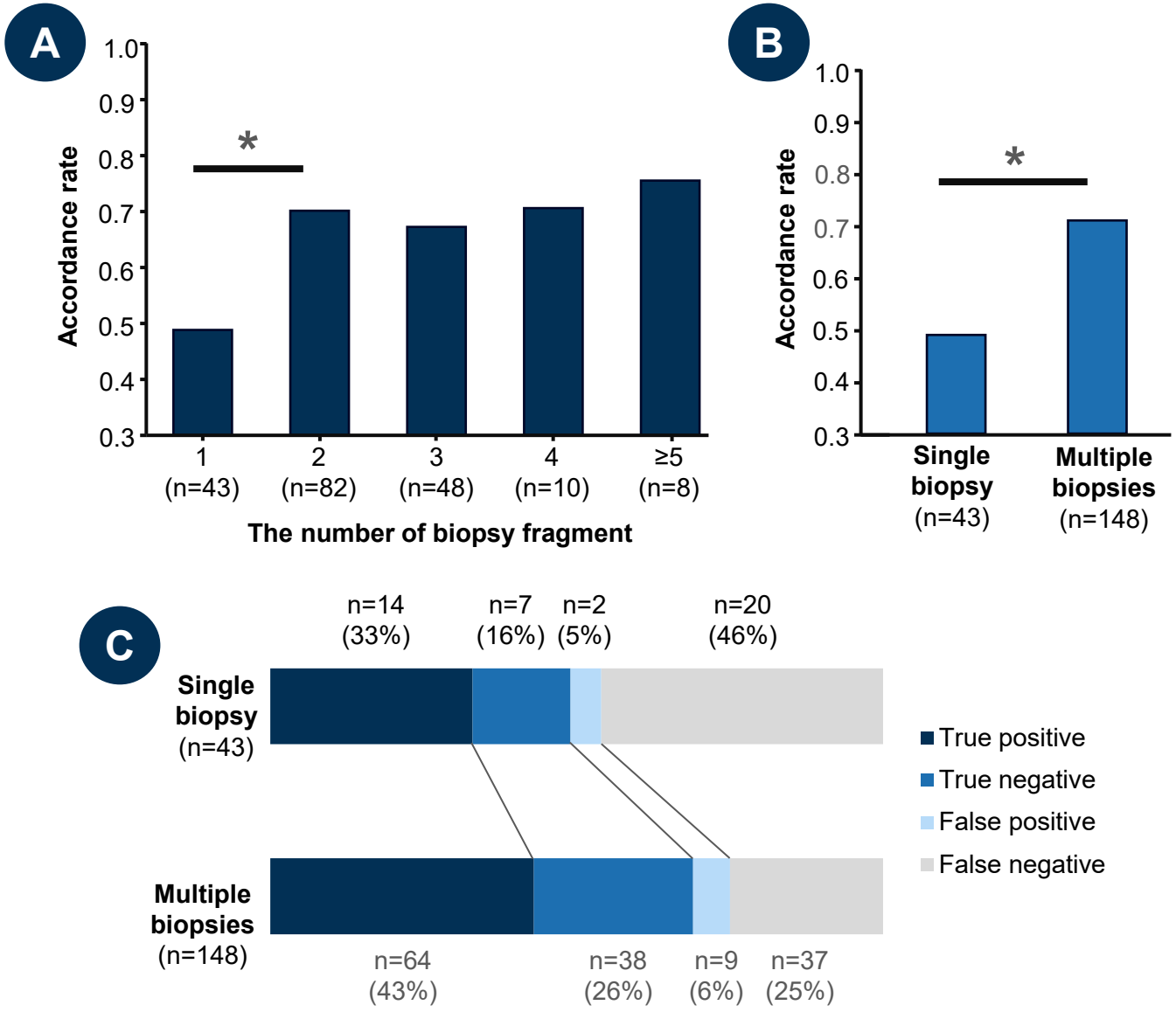


Considerations for biopsy sampling

- A **minimum of 8 biopsies** at endoscopy should be taken to harvest sufficient tumor material for biomarker testing[1]

- It is acceptable to use tissue from a metastatic lesion for biomarker testing of gastroesophageal cancers[1]

- Where multiple samples exist, only the **most recently acquired sample** should be tested for biomarker expression, provided that it meets the minimum testing requirements[1]



1. West NP, et al. Clin Oncol (R Coll Radiol). 2024;36(11):701–9.
Figures adapted from: Yamashita K, et al. Br J Cancer. 2019;121(3):278–80.

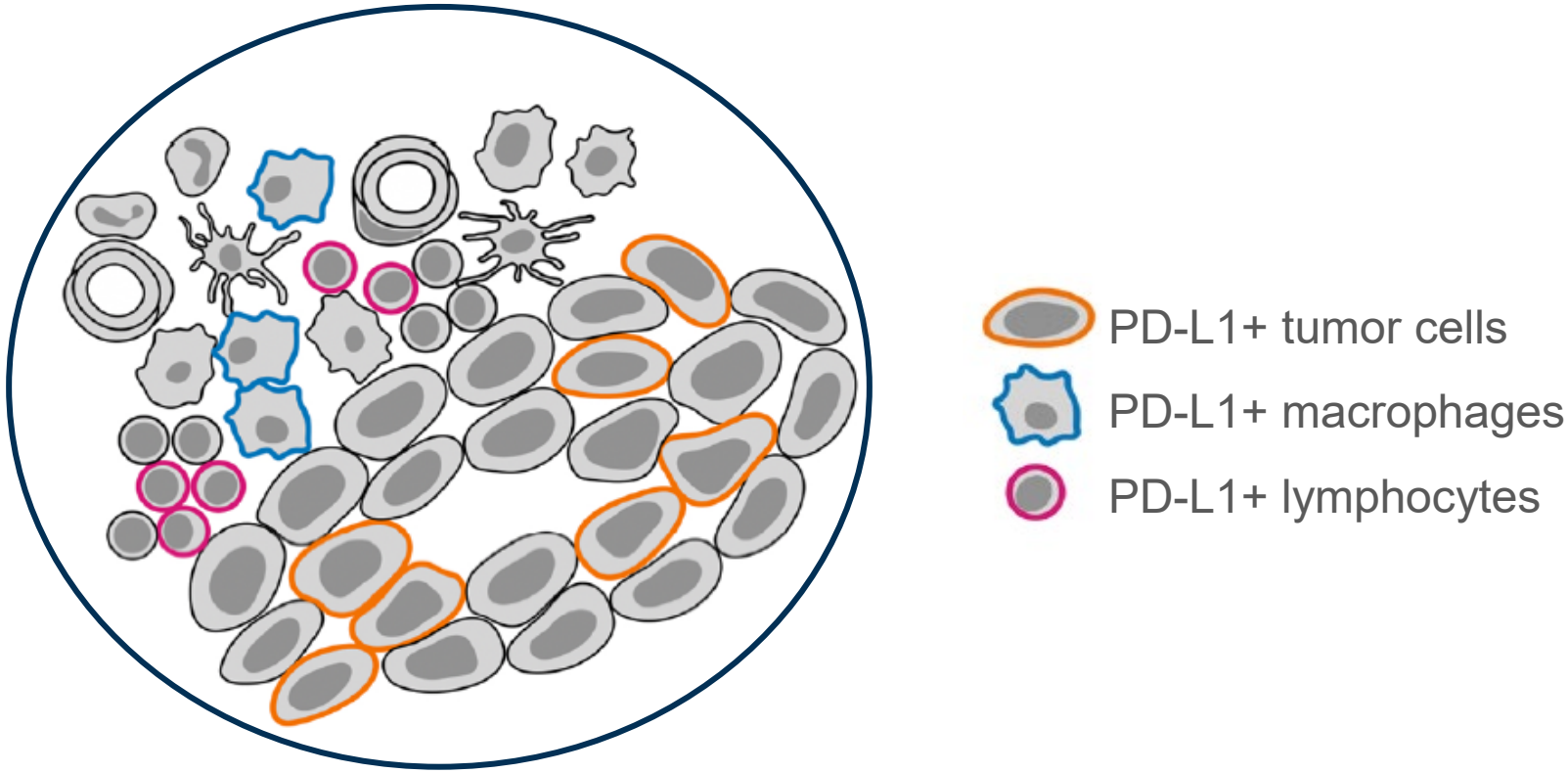
Cytology samples

Type of cytological samples	Fixative*	Results
Cellblock	Formalin	Comparable results to surgical samples
Papanicolaou-stained smears	Alcohol 96°	Comparable results to surgical samples
Unstained smears	Alcohol 96°	Slightly lower but OK
DQ and air-dried smears	No fixative	High rate of false negatives, low intensity of immunostaining
Liquid based	Methanol-based fixatives	High rate of false negatives, low intensity of immunostaining

Lack of ‘tissue architecture’ / how to assess the relationship between tumor cells and inflammatory microenvironment (CPS, TAP)?

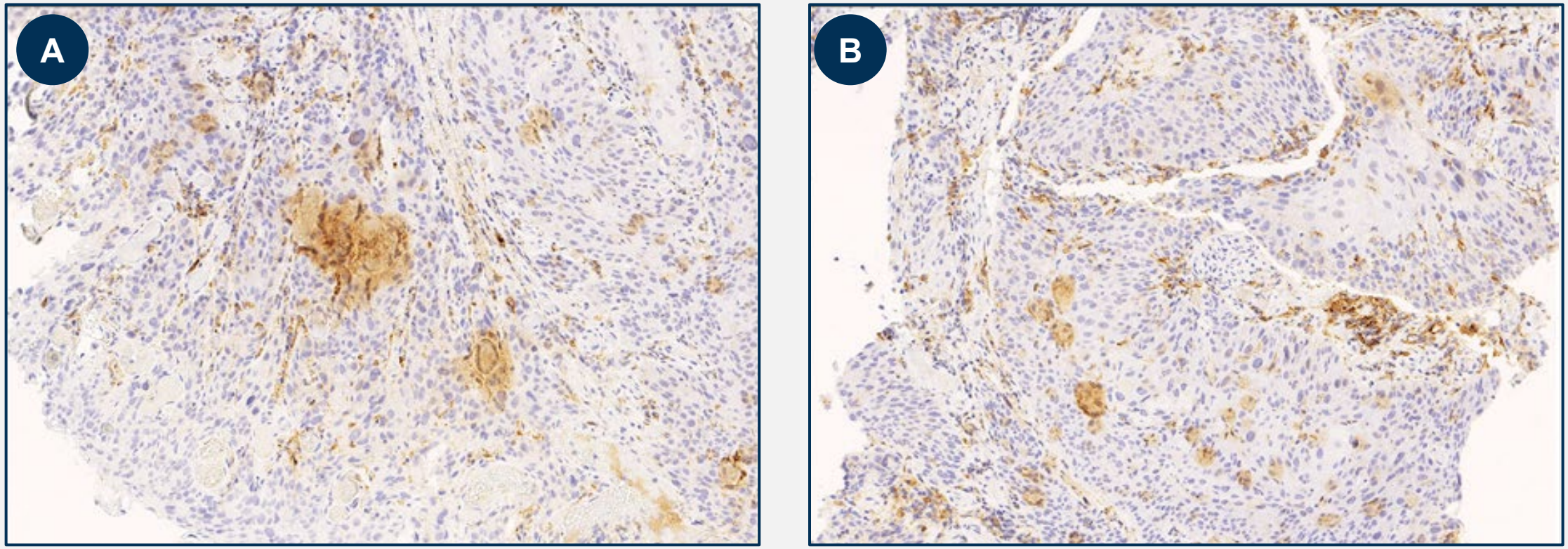
*Rigorous validation and protocol optimization should be performed in each laboratory that performs immunohistochemistry on cytology specimens (e.g. alcohol-fixed cell blocks, air-dried smears, formalin post-fixed specimens).
CPS, combined positive score; DQ, Diff-Quik; TAP, tumor area positivity.
Tejerina E, et al. Front Med (Lausanne). 2021;8:668612.

PD-L1 interpretation pitfalls



PD-L1, programmed cell death ligand 1.
Figure adapted from: Bill R, et al. Head Neck Pathol. 2023;17(4):969–75.

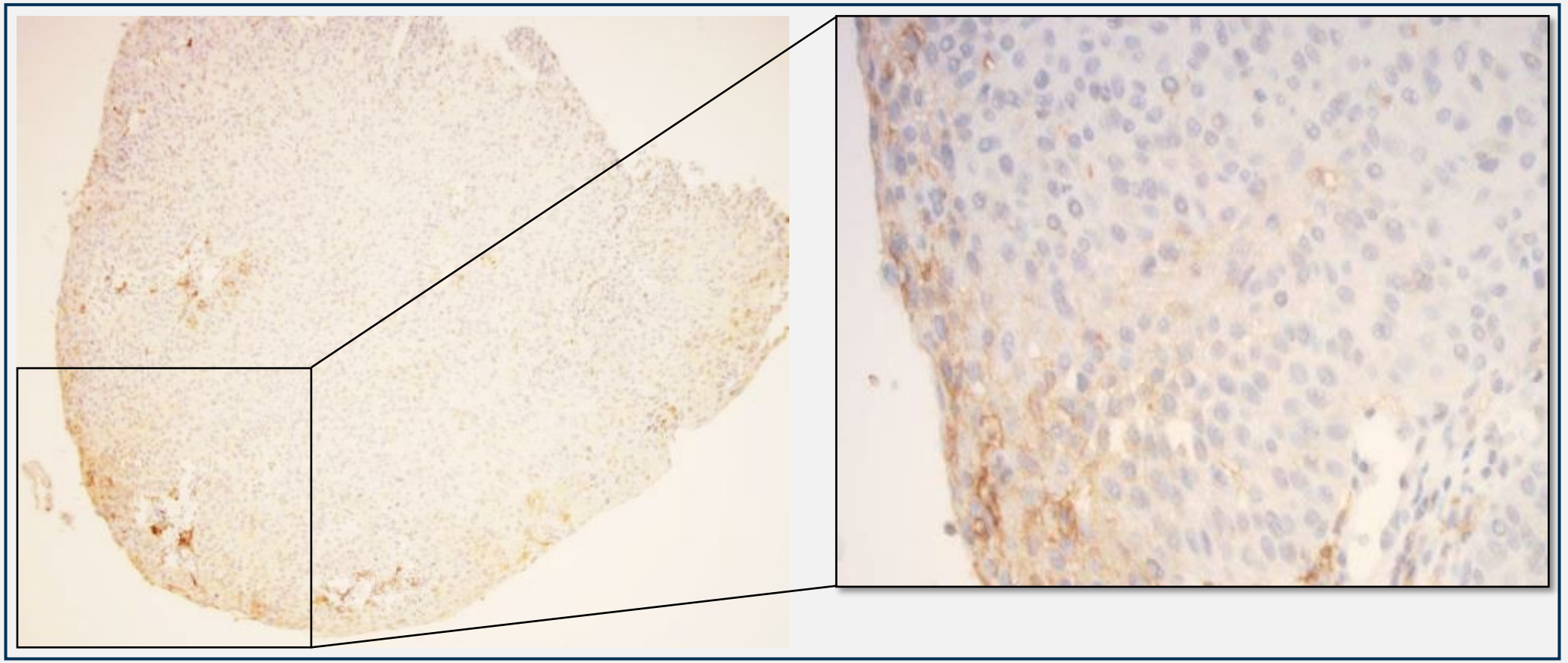
Non-specific DAB staining



ESCC biopsy specimen stained with PD-L1 antibody (Dako 22C3) exhibiting non-specific DAB staining

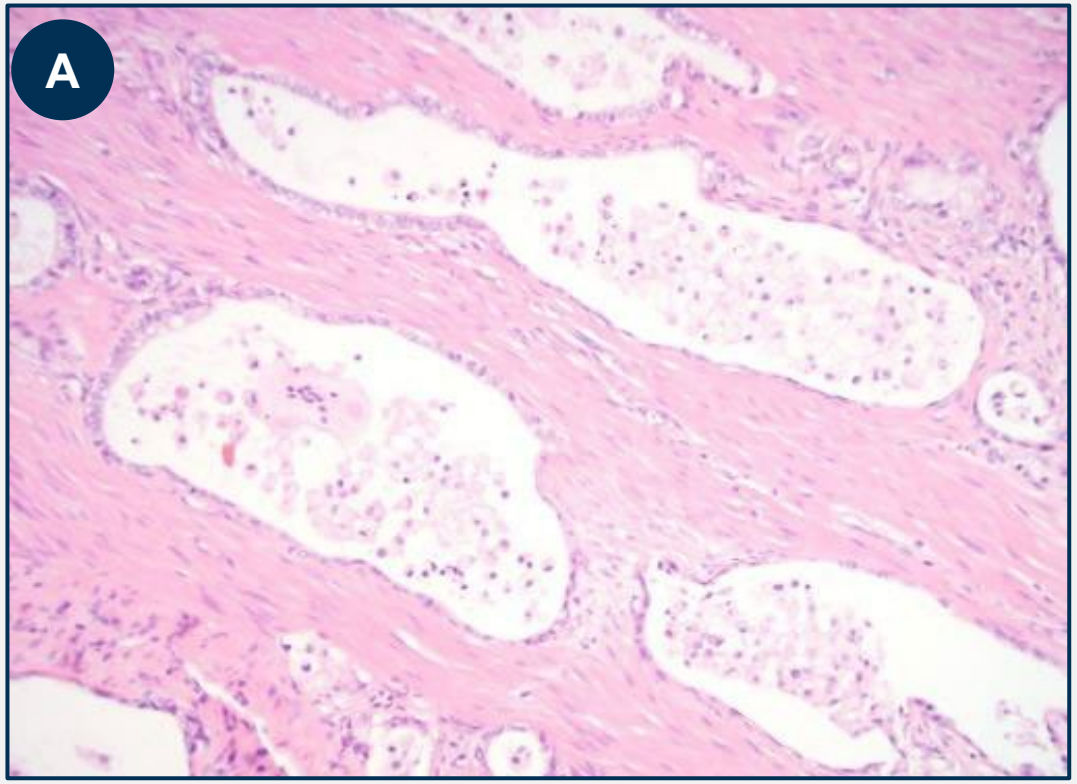
DAB, diaminobenzidine; ESCC, esophageal squamous cell carcinoma; PD-L1, programmed cell death ligand 1.
Figures taken from: Angerilli V, et al. Pathologica. 2023;115(2):57–70.

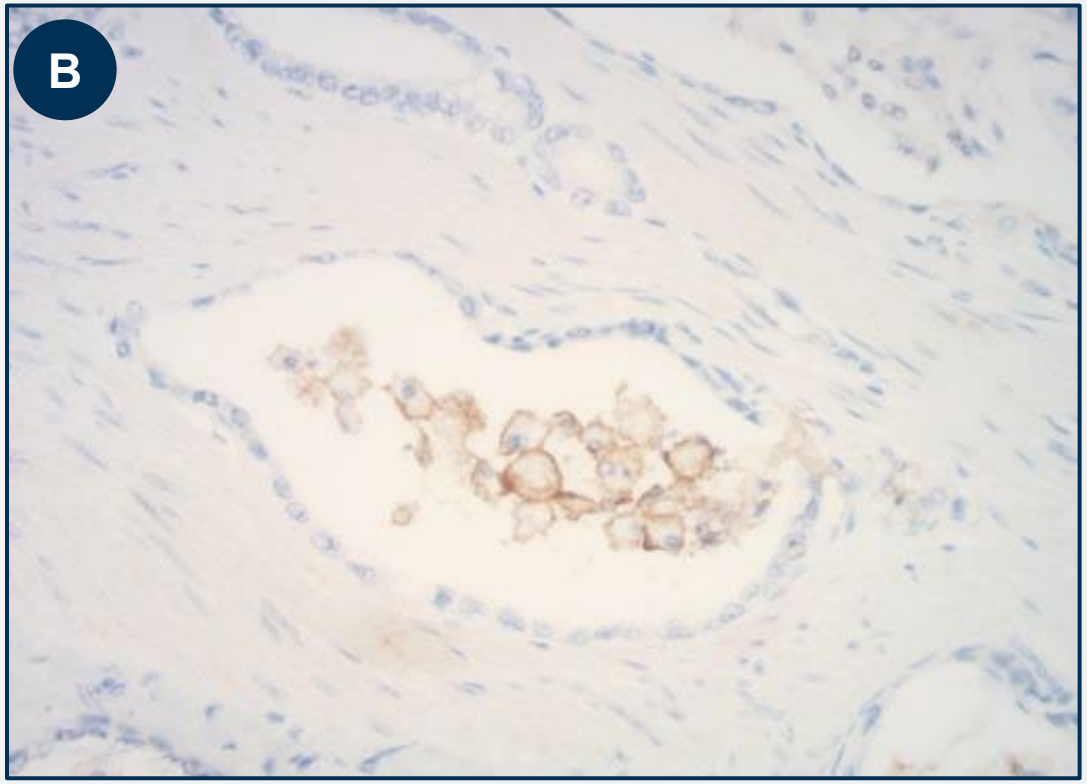
Edge effect with absent or faint staining in the central part of the tumor



The speaker confirms appropriate permissions have been obtained for the images shown.

Guidance on how to interpret macrophages in PD-L1 testing

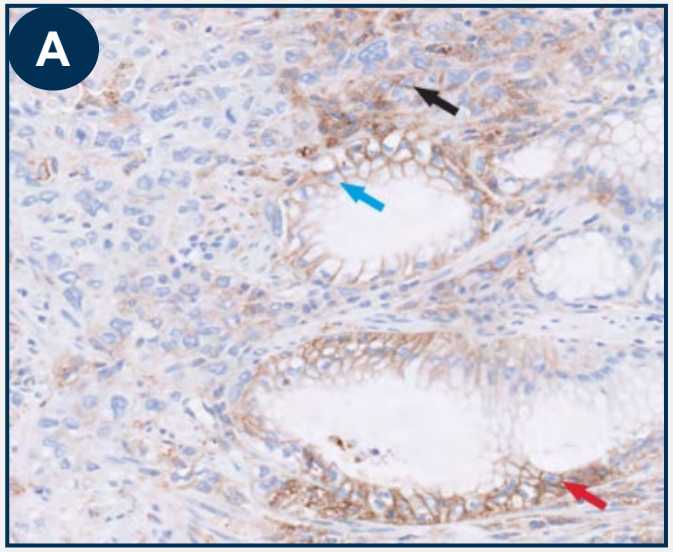


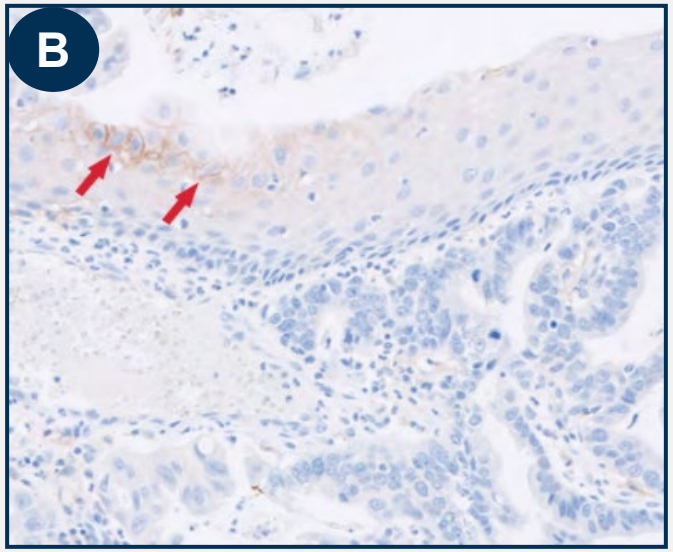


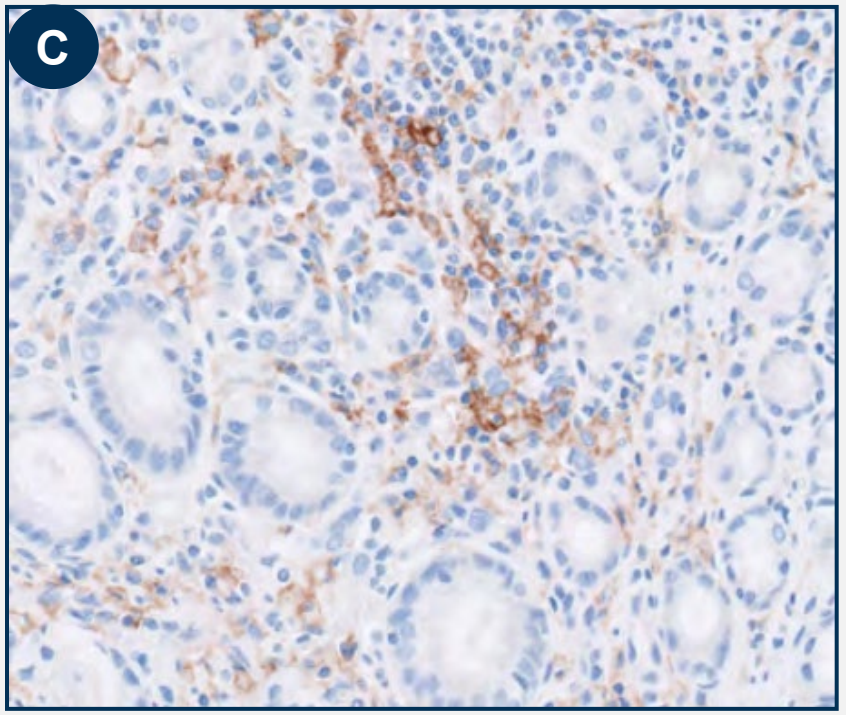
- **Macrophages** showing membrane/cytoplasmic staining (any intensity) should be included
- Conflicting data regarding macrophages within lumen glands (TAP)

The speaker confirms appropriate permissions have been obtained for the images shown.
PD-L1, programmed cell death ligand 1; TAP, tumor area positivity.

Guidance on how to interpret MICs in PD-L1 testing



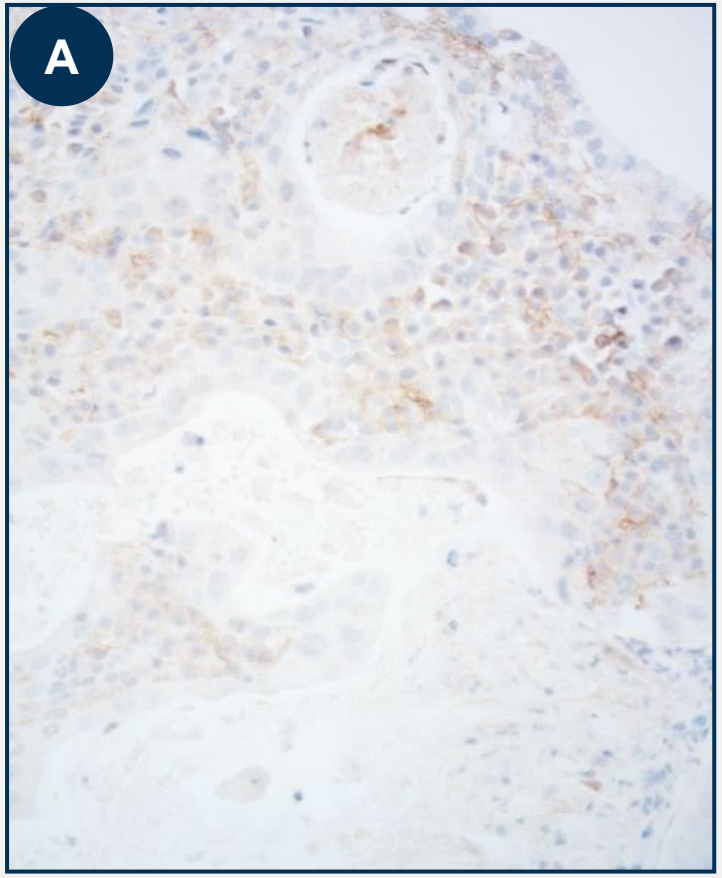


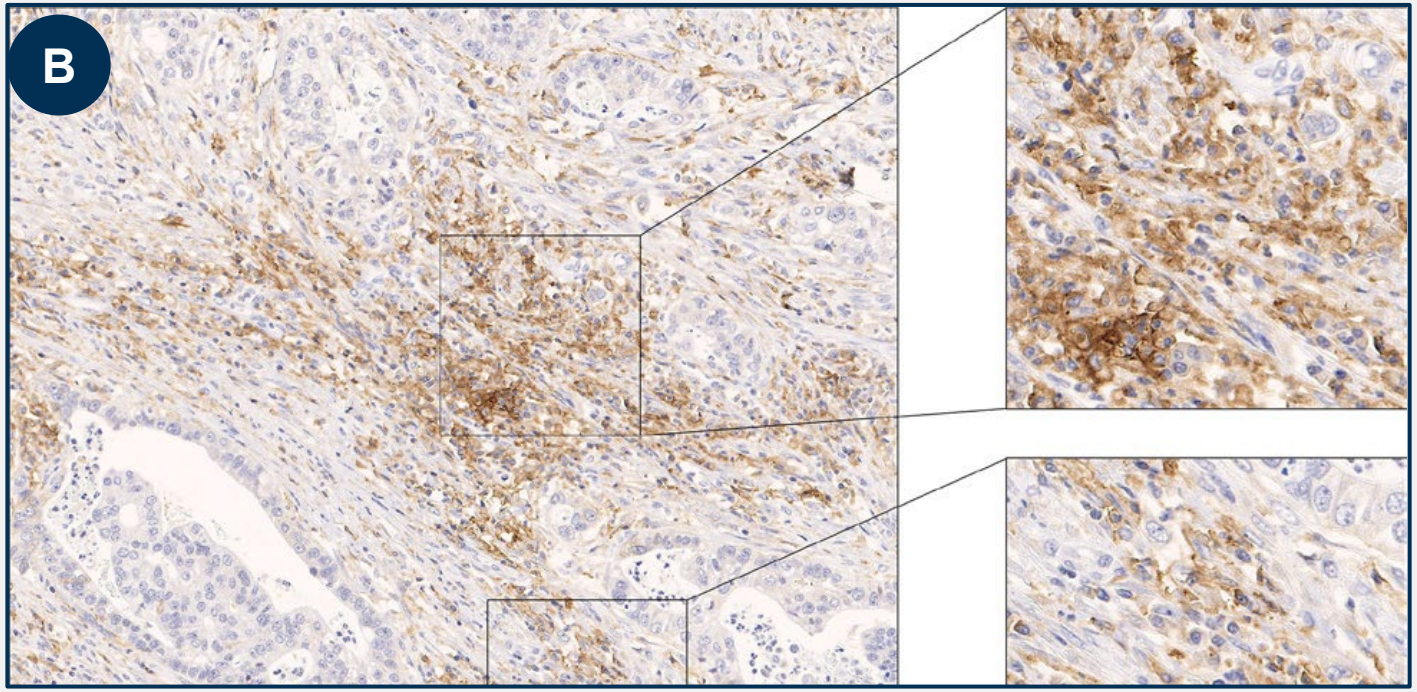


Staining of benign gastric glands/squamous epithelium and MICs associated with normal gastric glands

The speaker confirms appropriate permissions have been obtained for the images shown.
MIC, mononuclear inflammatory cell; PD-L1, programmed cell death ligand 1.

Guidance on how to interpret plasma cells in PD-L1 testing



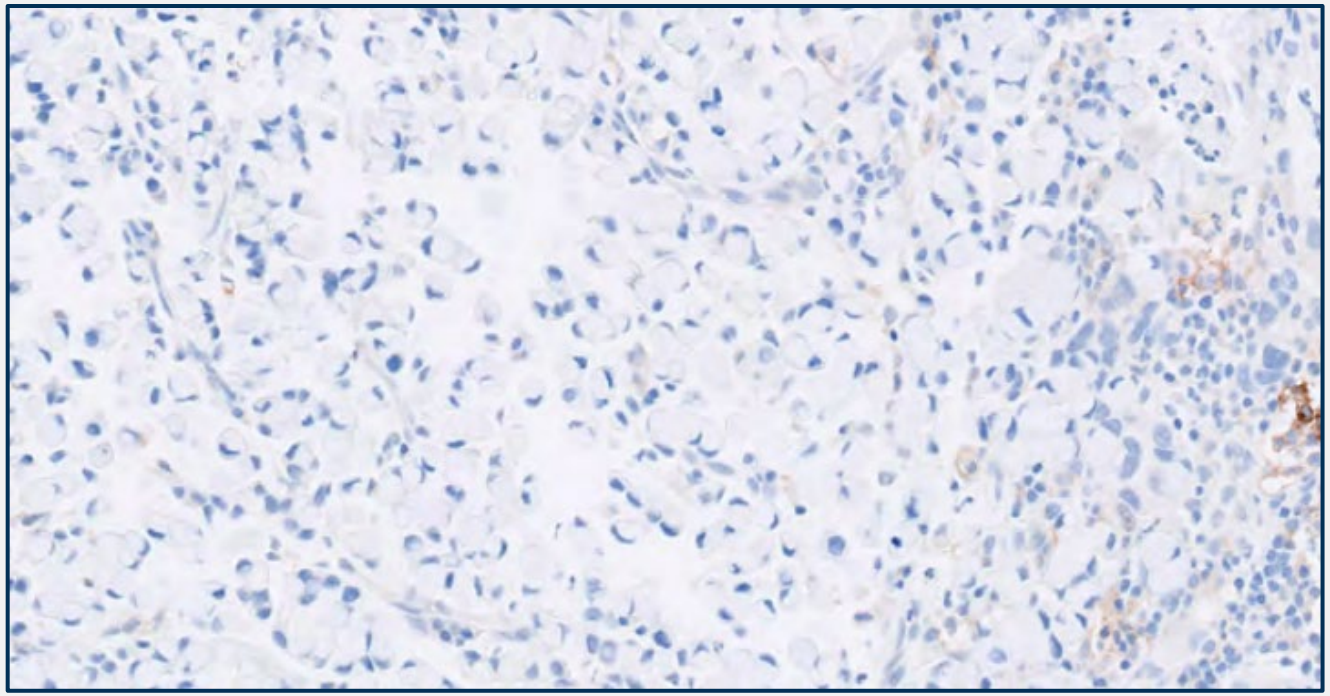


- **Plasma cells** showing membrane and/or cytoplasmic staining at any intensity should not be included in the **CPS** numerator
  - Does not apply to TAP score

The speaker confirms appropriate permissions have been obtained (Figure A).
CPS, combined positive score; TAP, tumor area positivity.
Figure B taken from: Angerilli V, et al. Pathologica. 2023;115(2):57–70.

Signet ring cell carcinoma

PD-L1 expression is lower in “diffuse” (Lauren classification) or “poorly cohesive” (WHO 2019) adenocarcinomas compared with “intestinal” type adenocarcinomas[1,2]



The speaker confirms appropriate permissions have been obtained for the images shown.

1. Taieb J, et al Eur J Cancer. 2023:195:113370; 2. Nagtegaal ID, et al. Histopathology. 2020;76:182–8.

Conclusions

Commercially available antibodies and PD-L1 testing platforms

- Different clones have different PD-L1 affinity
- Different clones do not recognize the same epitopes
- CDx should be used as approved
- Higher PD-L1 testing accuracy with IVD vs LDT

Challenges in tissue processing

- Fixation
- FFPE block stability
- Residual paraffin
- Drying of pre-treated tissue sections

Adequacy of biopsies

- 100 viable tumor cells
- A minimum of 8 biopsies

PD-L1 interpretation pitfalls

- Non-specific DAB staining
- Edge effect with absent or faint staining
- Interpretation of macrophages, MICs, and plasma cells

CDx, companion diagnostic; DAB, diaminobenzidine; FFPE, formalin-fixed paraffin-embedded; IVD, *in vitro* diagnostic; LDT, laboratory-developed test; MIC, mononuclear inflammatory cell; PD-L1, programmed cell death ligand 1.

PD-L1 scoring algorithms in gastroesophageal cancer: Similarities and differences

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Disclosures

Consultancy/honoraria: Agilent, Amgen, Astellas, BeOne Medicines, Bristol Myers Squibb, Daiichi-Sankyo, Gilead, Incyte, Merck, MSD, Roche, Servier, Taiho

How to perform PD-L1 testing

Approved drugs have companion diagnostics for PD-L1 testing, associated with specific indications

	Pembrolizumab[1]	Nivolumab[2,3]	Tislelizumab[4–6]
PD-L1 antibody/assay	22C3	28-8	SP263
Autostaining platform	Dako Autostainer Link 48	Dako Autostainer Link 48	Ventana BenchMark Series
Scoring algorithm	CPS	TPS/TC/CPS	TAP

- Products in development may use a specific assay in the clinical development program
- Each assay requires different reagents and equipment, leading to logistical issues for pathologists

CPS, combined positive score; PD-L1, programmed cell death ligand 1; TAP, tumor area positivity; TC, tumor cell; TPS, tumor proportion score.

1. Agilent. PD-L1 IHC 22C3 pharmDx. Available at: https://www.agilent.com/cs/library/packageinsert/public/P03951E_26.pdf; 2. Agilent. PD-L1 IHC 28-8 pharmDx Interpretation Manual–Gastric Adenocarcinoma, Gastroesophageal Junction (GEJ) Adenocarcinoma, and Esophageal Adenocarcinoma. Available at: https://www.agilent.com/cs/library/usermanuals/public/29456-d68866-pd-l1-28-8-gastric-interpretation-manual-en-eu.pdf; 3. Bristol-Myers Squibb. OPDIVO® (nivolumab). Prescribing Information. Revised 2025; 4. Qiu M-Z, et al. BMJ. 2024;385:e078876; 5. Roche. VENTANA PD-L1 SP263 assay package insert. 2024. Available at: https://elabdoc-prod.roche.com/eLD/api/downloads/ebfb0e7f-6178-ec11-0d91-005056a772fd?countryIsoCode=XG; 6. Moehler M, et al. Presentation at ESMO-GI. June 26–29, 2024. Munich, Germany. All links accessed June 2025.

Complex world of PD-L1 scoring systems

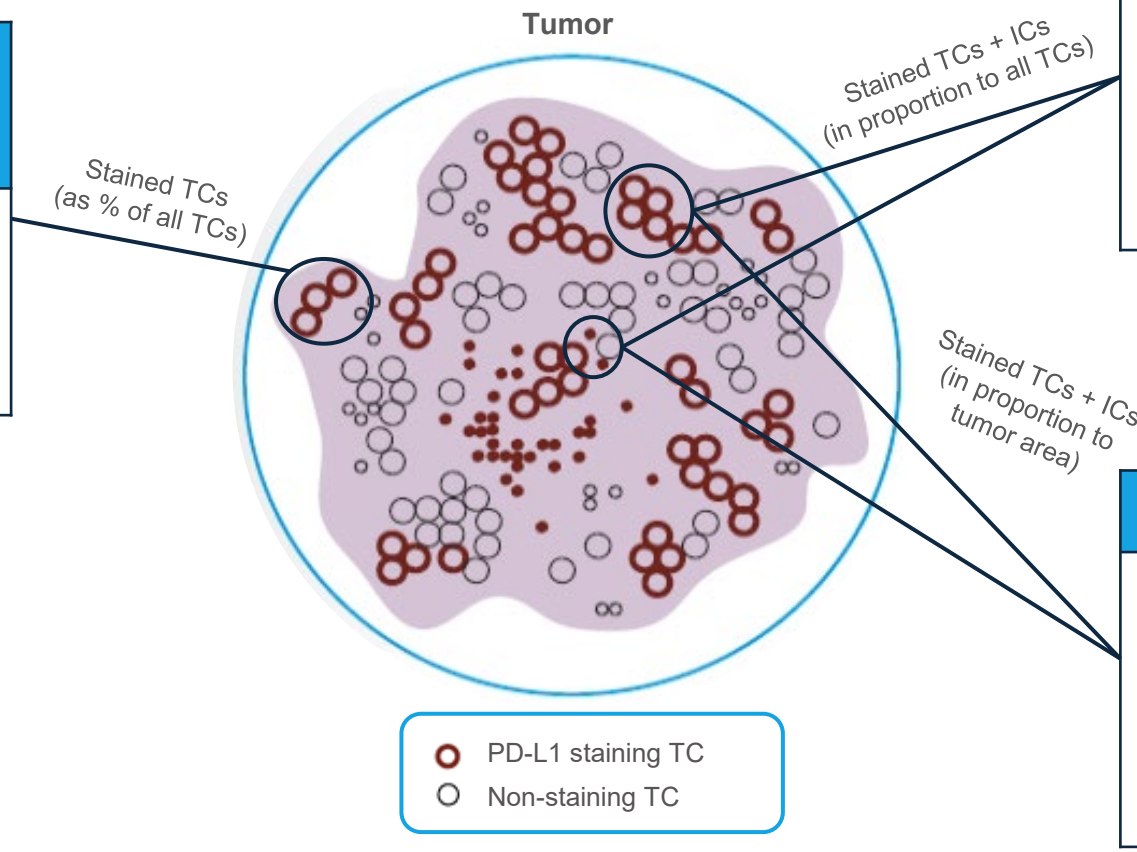
TC staining or TPS[1–5]

Dako 28-8 and 22C3, Ventana SP142 and SP263 (nivolumab, pembrolizumab, atezolizumab, durvalumab, cemiplimab-rwlc)[6–11]

$$\%\ \text{PD-L1} = \frac{\text{Number of PD-L1-staining TCs}}{\text{Total number of viable TCs}} \times 100$$

Example TC/TPS:

$\frac{50\ \text{staining TCs}}{1000\ \text{viable TCs}} \times 100 = 5\%$ tumor PD-L1 expression



CPS[1]

Dako 28-8 (nivolumab),[1] Dako 22C3 (pembrolizumab)[3]

$$\text{CPS} = \frac{\text{Number of PD-L1 staining cells (TCs, lymphocytes, macrophages)}}{\text{Total number of viable TCs}} \times 100$$

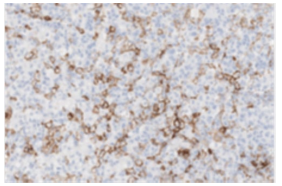
Example CPS:

$\frac{\approx 80\ \text{staining cells}}{1000\ \text{viable TCs}} \times 100 = \text{CPS}$

TAP[5,12]

Ventana SP263 (durvalumab)[5]

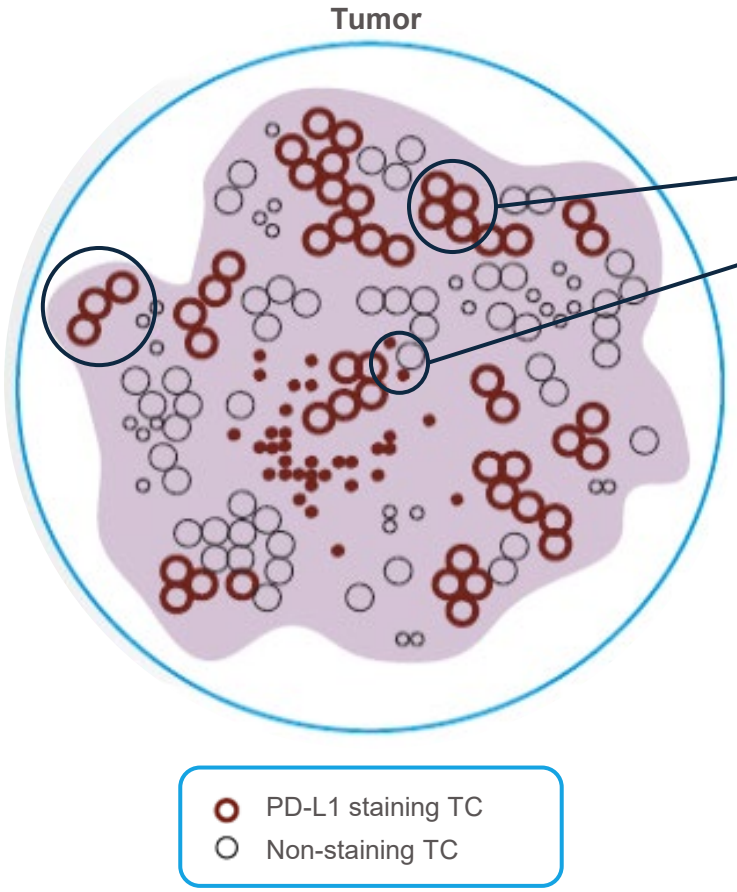
TAP = % of tumor area occupied by tumor and/or immune cells with PD-L1 staining



Example TAP:
TAP+ = ≥10%

The speaker confirms appropriate permissions have been obtained for the images shown.
CPS, combined positive score; IC+, immune cell staining; IC, immune cell; ICP, immune cell present; PD-L1, programmed cell death ligand 1; TAP, tumor area positivity; TC, tumor cell; TPS, tumor proportion score.
1. Figure adapted from: Agilent. PD-L1 IHC 28-8 pharmDx Interpretation Manual–Gastric Adenocarcinoma, Gastroesophageal Junction (GEJ) Adenocarcinoma, and Esophageal Adenocarcinoma. Available at: https://www.agilent.com/cs/library/usermanuals/public/29456-d68866-pd-l1-28-8-gastric-interpretation-manual-en-eu.pdf; 2. Agilent. PD-L1 IHC 28-8 pharmDx Interpretation Manual Non-Squamous Non-Small Cell Lung Cancer. Available at: https://www.agilent.com/cs/library/usermanuals/public/29111_pd-l1-ihc-28-8-interpretation-manual.pdf; 3. Agilent. PD-L1 IHC 22C3 pharmDx. Available at: https://www.agilent.com/cs/library/packageinsert/public/P03951E_26.pdf;
4. Roche Diagnostics. VENTANA PD-L1 (SP142) Assay. Available at: diagnostics.roche.com; 5. Roche Diagnostics. VENTANA PD-L1 (SP263) Assay Staining in Urothelial Carcinoma. Available at: diagnostics.roche.com; 6. Bristol-Myers Squibb. OPDIVO® (nivolumab). SmPC, 2025; 7. MSD. KEYTRUDA® (pembrolizumab). SmPC, 2025; 8. Roche. TECENTRIQ® (atezolizumab). SmPC, 2025; 9. AstraZeneca. IMFINZI® (durvalumab). SmPC, 2025; 10. Regeneron. LIBTAYO® (cemiplimab). SmPC, 2024; 11. Regeneron. Regeneron. LIBTAYO® (cemiplimab-rwlc). PI, 2025; 12. Liu C, et al. Diagn Pathol. 2023;18(1):48. All links accessed June 2025.

CPS captures PD-L1 expression in tumor and immune cells



Stained TCs + ICs
(in proportion to all TCs)

CPS[1,2]

Dako 28-8 (nivolumab),[1] Dako 22C3 (pembrolizumab)[2]

$$\text{CPS} = \frac{\text{Number of PD-L1 staining cells (TCs, lymphocytes, macrophages)}}{\text{Total number of viable TCs}} \times 100$$

- CPS is **highly reproducible** and concordant between observers and laboratories, after ad-hoc pathologist training[3–5]

- Calculation may equal greater than 100[1]
- But the maximum is defined as 100[1]
- CPS value is given in absolute number[1]
- The expression can be found in TC and/or IC[1]

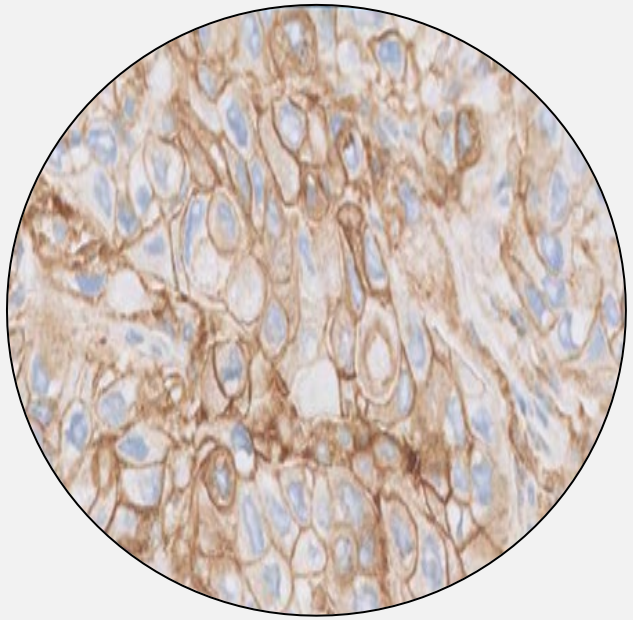
CPS, combined positive score; IC, immune cell; PD-L1, programmed cell death ligand 1; TC, tumor cell.

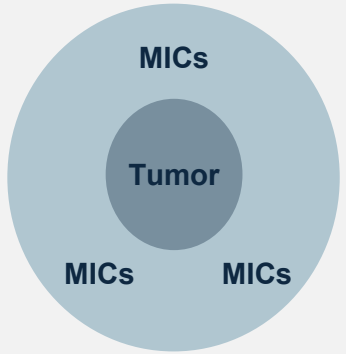
1. Figure adapted from: Agilent. PD-L1 IHC 28-8 pharmDx Interpretation Manual–Gastric Adenocarcinoma, Gastroesophageal Junction (GEJ) Adenocarcinoma, and Esophageal Adenocarcinoma. Available at: https://www.agilent.com/cs/library/usermanuals/public/29456-d68866-pd-l1-28-8-gastric-interpretation-manual-en-eu.pdf; 2. Agilent. PD-L1 IHC 22C3 pharmDx. Available at: https://www.agilent.com/cs/library/packageinsert/public/P03951E_26.pdf; 3. Brezden-Masley, et al. Curr Oncol. 2024; 31(12):7770–86; 4. Kulangara K, et al. J Clin Oncol. 2017;35(15):e14589; 5. de Ruiter EJ, et al. Mod Pathol. 2021;34(6):1125–32. All links accessed June 2025.

Considerations when using CPS

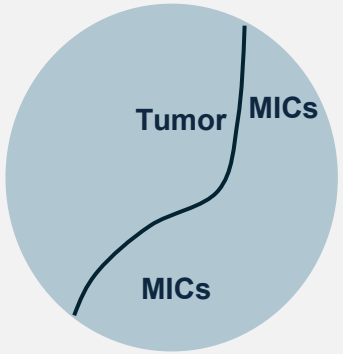
Staining on **tumor cells** at 20x:
- **Partial** or **complete**
- At **any intensity**

In **inflammatory cells**:
- **Valid membrane** or **cytoplasmic stain**
- Only assess **macrophages** and **lymphocytes** (exclude neutrophils, eosinophils, and plasma cells)
- Only count **adjacent inflammatory cells**





20x field with tumor focus in middle



20x field with edge of tumor in middle

To determine which immune cells to count, place the end of the tumor in the **center** of the **eyepiece** from a **20x field**

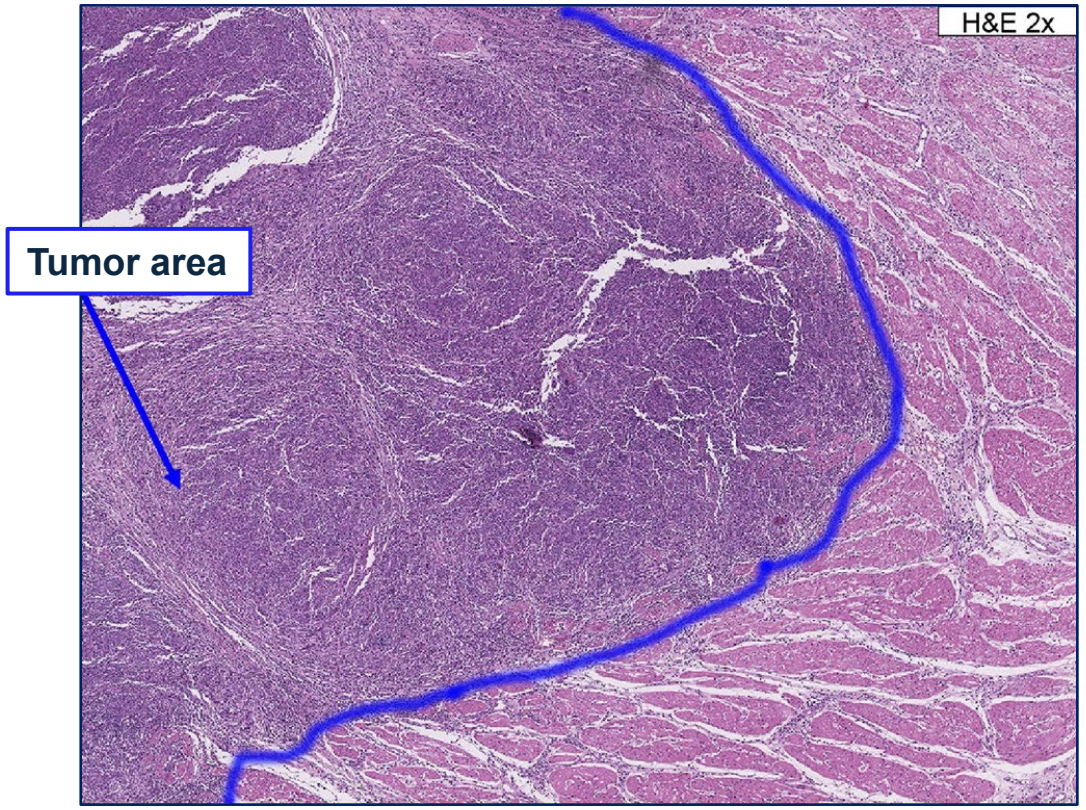
The speaker confirms appropriate permissions have been obtained for the image shown.
CPS, combined positive score; MIC, mononuclear inflammatory cell.
1. Agilent. PD-L1 IHC 28-8 pharmDx Interpretation Manual–Gastric Adenocarcinoma, Gastroesophageal Junction (GEJ) Adenocarcinoma, and Esophageal Adenocarcinoma. Available at: https://www.agilent.com/cs/library/usermanuals/public/29456-d68866-pd-l1-28-8-gastric-interpretation-manual-en-eu.pdf (accessed June 2025).

TAP is the percentage of expression in TC and IC in relation to the total tumor area

$$\text{TAP} = \frac{\%\ \text{PD-L1–positive TC and IC}}{\text{Tumor area}} \times 100$$

Cut off TAP ≥5% for ICI treatment
Antibody: SP263 (Ventana®)

Hematoxylin and eosin-stained slide to identify the tumor area



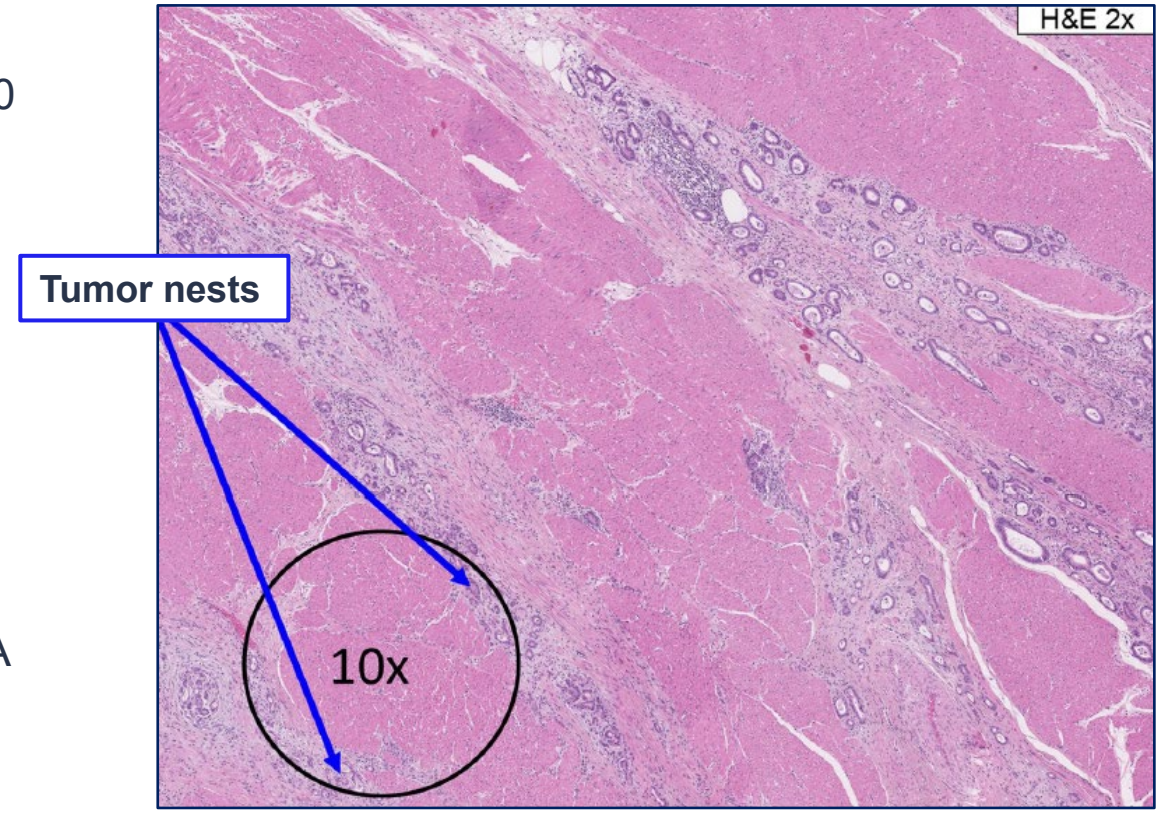
H&E, hematoxylin and eosin; IC, immune cell; ICI, immune checkpoint inhibitor; PD-L1, programmed cell death ligand 1; TAP, tumor area positivity; TC, tumor cell.
Figure adapted from: Liu C, et al. Diagn Pathol. 2023;18(1):48.

Considerations when using TAP: Tumor nests in tumor area

$$\text{TAP} = \frac{\%\ \text{PD-L1–positive TC and IC}}{\text{Tumor area}} \times 100$$

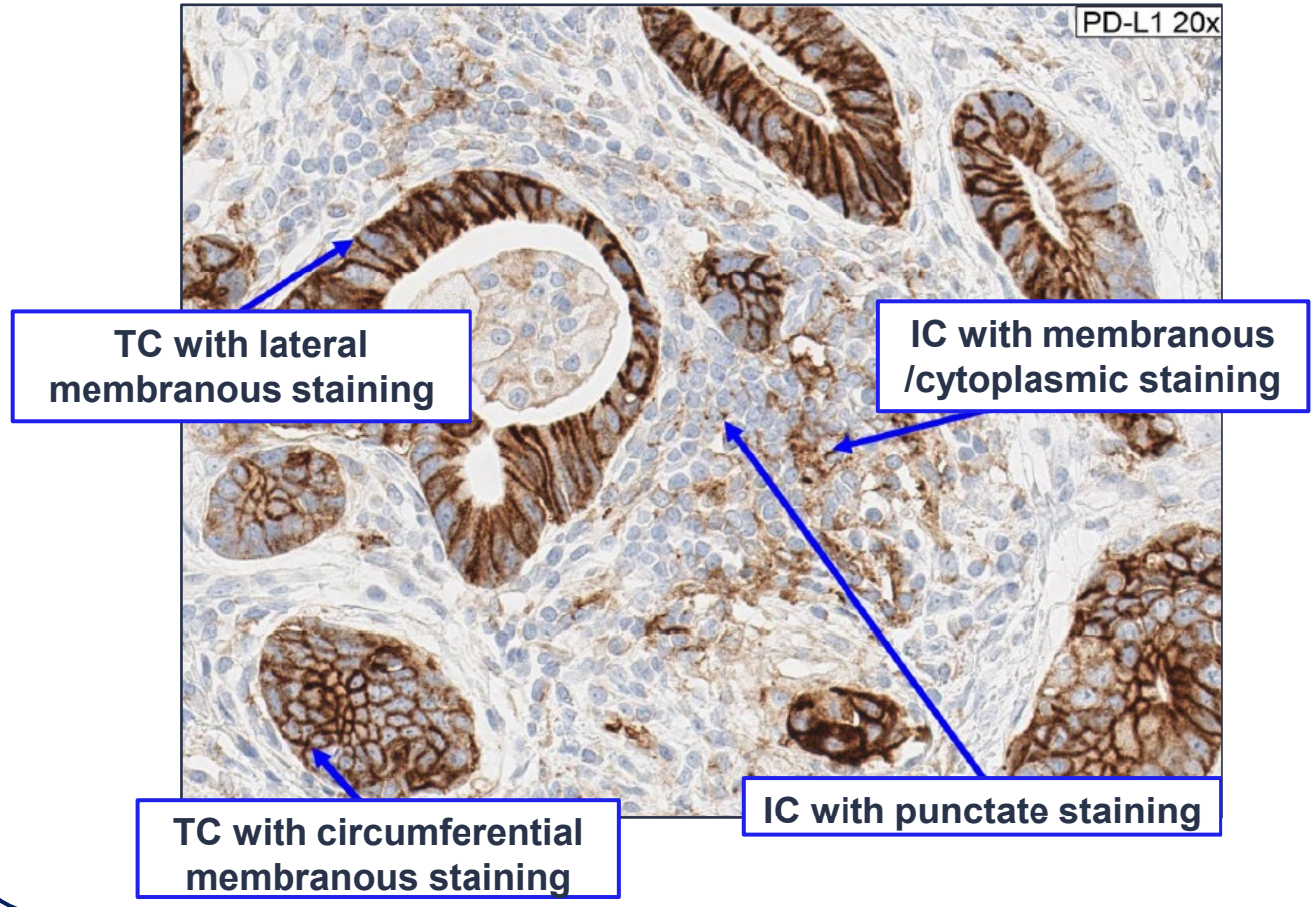
If tumor nests are separated by non-neoplastic tissue, they are included as part of the tumor area as long as the tumor nests are **bordered** on **both sides of a 10x field**

- **Pools of mucin and glandular luminal spaces** in the presence or absence of viable TC are **included** in the TA
- **Tumor nests within the lymphovascular** spaces are **included**



H&E, hematoxylin and eosin; IC, immune cell; PD-L1, programmed cell death ligand 1; TA, tumor area; TAP, tumor area positivity; TC, tumor cell.
Figure adapted from: Liu C, et al. Diagn Pathol. 2023;18(1):48.

Considerations when using TAP: Positive TC and IC

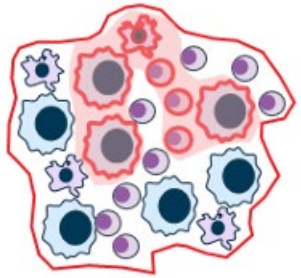


Tumor cells:
- Circumferential and partial/lateral membrane staining
- At any intensity
- Cytoplasmic staining is disregarded

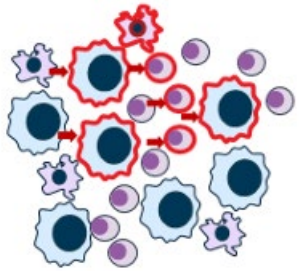
Immune cells:
- Membranous, cytoplasmic, and punctate staining
- At any intensity
- Any cell

IC, immune cell; PD-L1, programmed cell death ligand 1; TAP, tumor area positivity; TC, tumor cell.
Figure adapted from: Liu C, et al. Diagn Pathol. 2023;18(1):48.

TAP compared with CPS

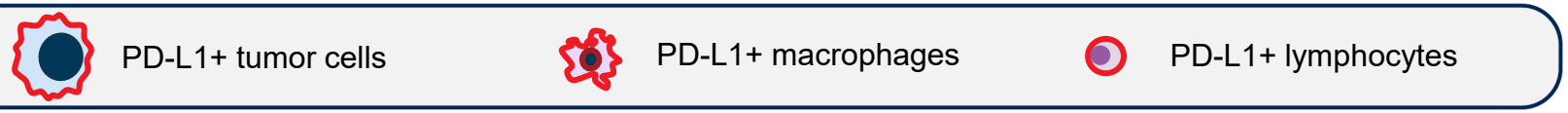


Visual estimation



Cell counting

TAP	CPS
$\frac{\text{Area occupied by PD−L1 – stained TCs and ICs}}{\text{Tumor area}}$ x 100%	$\frac{\text{Number of PD−L1 – stained TCs and ICs}}{\text{Total number of viable TCs}}$ x 100
Include PD-L1–positive tumor cells and all tumor-associated immune cells	Include PD-L1–positive tumor cells, lymphocytes, and macrophages



CPS, combined positive score; IC, immune cell; PD-L1, programmed cell death ligand 1; TAP, tumor area positivity; TC, tumor cell.
Figure adapted from: US Food and Drug Administration. September 26, 2024: Meeting of the Oncologic Drugs Advisory Committee Meeting Announcement. Available at: https://www.fda.gov/media/182209/download (accessed June 2025); Moehler M, et al. Mod Pathol. 2025;38(9):100793.

Advantages and limitations

TAP vs CPS: Advantages and limitations

	TAP	CPS
Methodology	Area covered by PD-L1 staining TC and IC relative to total tumor area	Number of PD-L1 staining TC and IC relative to all viable tumor cells
Calculation	$\frac{\text{\% PD-L1-positive TCs and ICs}}{\text{Tumor area}}$	$\frac{\text{Number of PD-L1-positive TCs and ICs}}{\text{Total number of TC}}$
Advantages	• **Reduced time needed (vs CPS and TPS)** for the visual estimation process[1] • **High concordance** with CPS[1] • **Simple IC counting approach** (all types) vs CPS[1]	• **High familiarity** among pathologists (FDA approved)[2,3] • **Proven efficacy** with use in approved therapies[2]
Limitations	• **Less familiarity** among pathologists and oncologists[3] • **Difficult to use in complex histologies** (i.e. presence of non-neoplastic cells)[3]	• **Time-consuming** due to cell counting process[1] • **Complex IC counting approach** (mononuclear only)[3,4]

Same slide for both methodologies!

CPS, combined positive score; FDA, US Food and Drug Administration; IC, immune cell; PD-L1, programmed cell death ligand 1; TAP, tumor area positivity; TC, tumor cell; TPS, tumor proportion score.

1. Moehler M, et al. Mod Pathol. 2025;38(9):100793; 2. US Food and Drug Administration; 2. FDA approves pembrolizumab for HER2 positive gastric or gastroesophageal junction adenocarcinoma expressing PD-L1 (CPS ≥1). Available at: https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-pembrolizumab-her2-positive-gastric-or-gastroesophageal-junction-adenocarcinoma (accessed June 2025); 3. Liu C, et al. Diagn Pathol. 2023;18(1):48; 4. Ulas EB, et al. JTO Clin Res Rep. 2023;4(9):100532.

Concordance

High concordance rate between TAP score and CPS

Percentage agreement between TAP (cutoff of 1% and 5%) and CPS (cutoff of 1):

- PPA, NPA, and OPA of the two comparisons were ≥85%
- In theory, samples in which the tumor stroma does not comprise large portions of tumor areas, such as mucosal biopsy specimens, have even greater potential for higher concordance of the two scoring methods (TAP and CPS)

Agreement between TAP (1% cutoff) and CPS (cutoff of 1) scoring algorithms

Statistic	Agreement
PPA%	100.0
n/N	39/39
95% CI	91.0, 100.0
NPA %	84.6
n/N	11/13
95% CI	57.8, 95.7
OPA %	96.2
n/N	50/52
95% CI	87.0, 98.9

Agreement between TAP (5% cutoff) and CPS (cutoff of 1) scoring algorithms

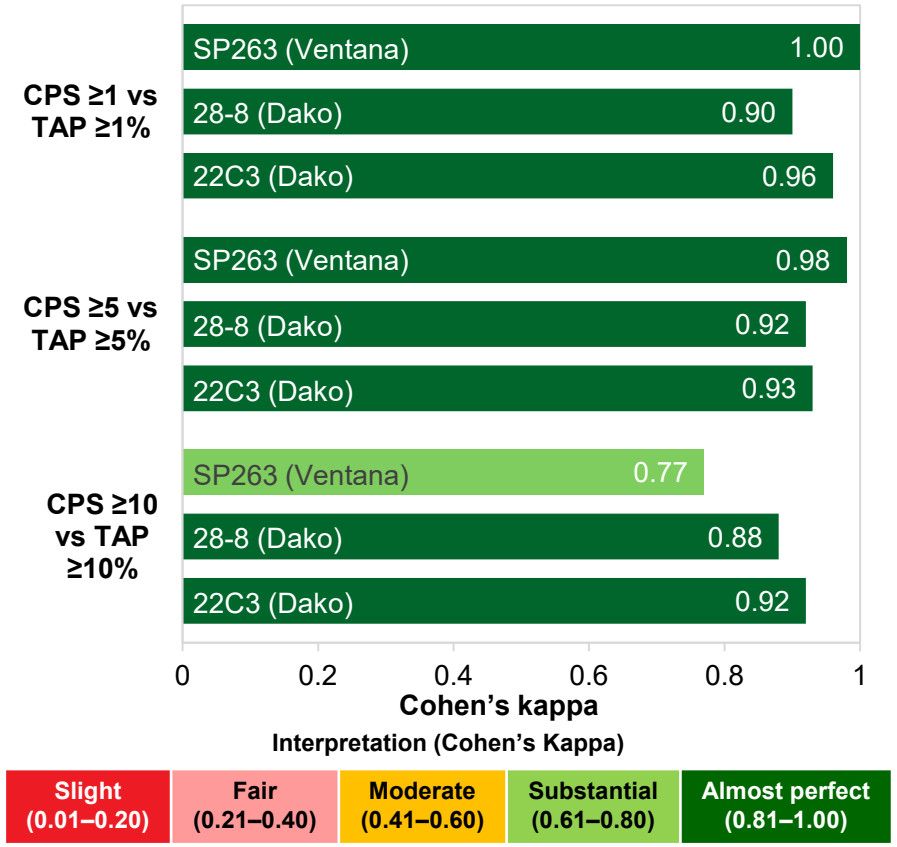
Statistic	Agreement
PPA%	89.7
n/N	35/39
95% CI	76.4, 95.9
NPA %	100.0
n/N	13/13
95% CI	77.2, 100.0
OPA %	92.3
n/N	48/52
95% CI	81.8, 97.0

CI, confidence interval; CPS, combined positive score; NPA, negative percent agreement; OPA, overall percent agreement; PPA, positive percent agreement; TAP, tumor area positivity.

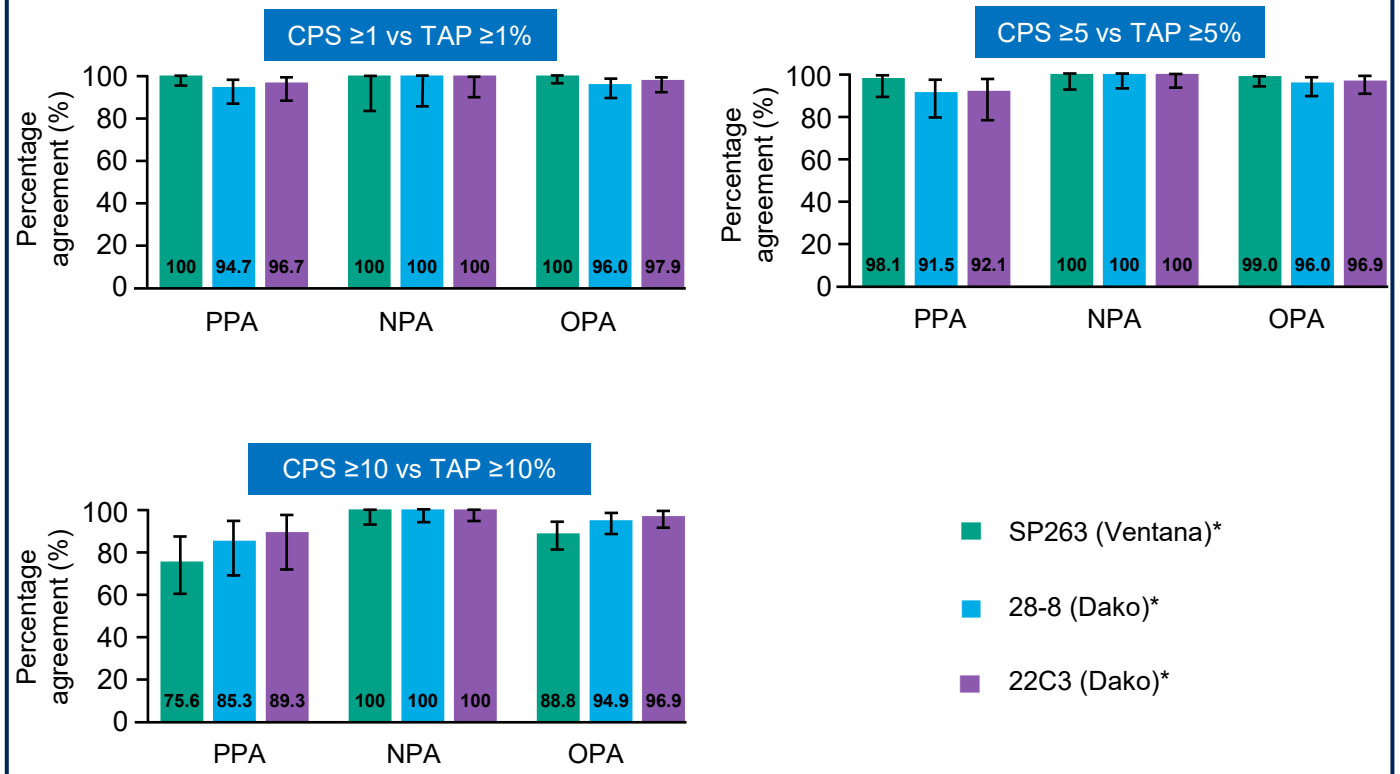
Liu C, et al. Diagn Pathol. 2023;18(1):48.

High concordance rate between TAP score and CPS

Inter- and intra-assay assessments demonstrated **substantial to almost-perfect agreement**



Interpathologist (n=3) assessment exhibited a **significant level of concordance**

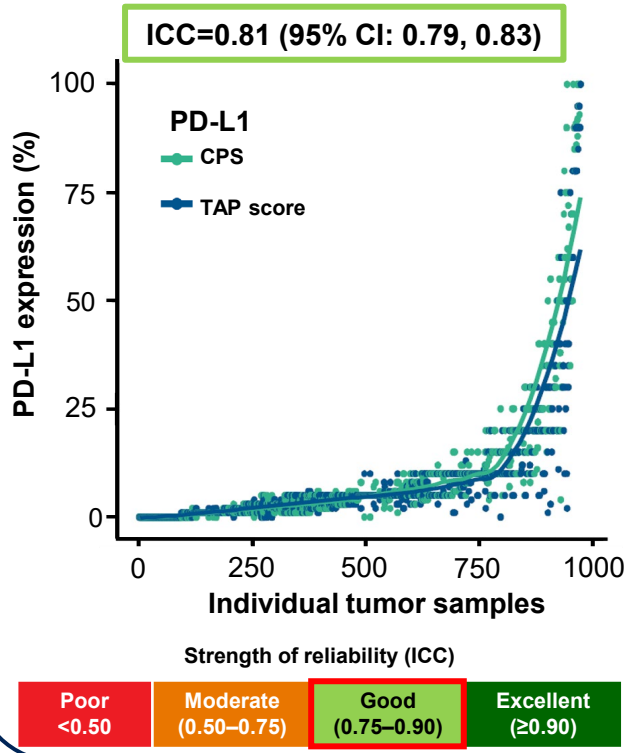


100 resection specimens; PD-L1 28-8, 22C3, and SP263; three trained pathologists blindly and independently scored CPS and TAP.
*The 22C3 and 28-8 PD-L1 assays used CPS as the denominator, and the SP263 assay used TAP.
CPS, combined positive score; NPA, negative percent agreement; OPA, overall percent agreement; PD-L1, programmed cell death ligand 1; PPA, positive percent agreement; TAP, tumor area positivity.
Figures adapted from: Klempner SJ, et al. JCO Precis Oncol. 2024:e2400230.

RATIONALE-305:
Substantial correlation and concordance between TAP score and CPS[1,2]

- Of 997 patients randomized, 997 had evaluable TAP scores and 974 had evaluable *post hoc* CPS results

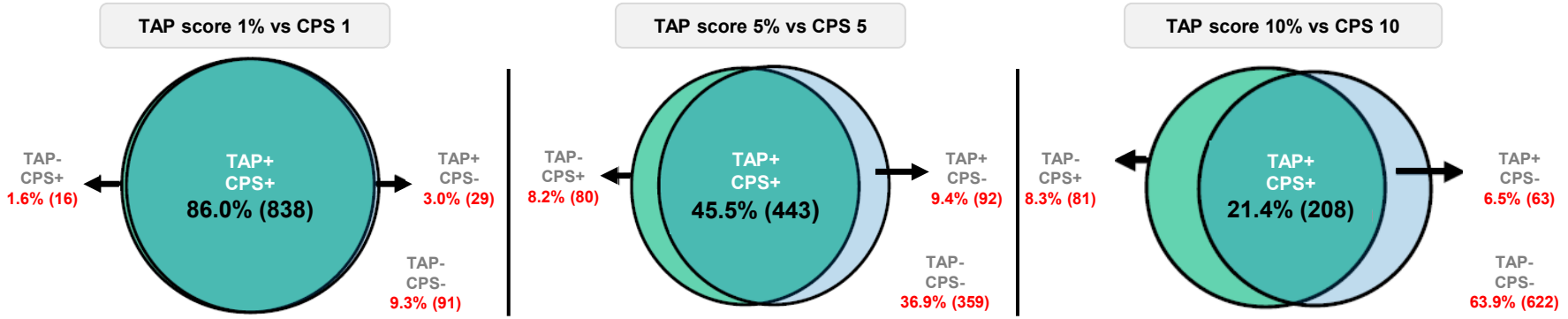
Good correlation between TAP score and CPS based on interclass correlation coefficient



Strength of reliability (ICC)

Poor	Moderate	Good	Excellent
<0.50	(0.50–0.75)	(0.75–0.90)	(≥0.90)

TAP score and CPS showed substantial concordance in terms of OPA and Cohen's kappa at matched thresholds for each score



	n/N	Agreement		n/N	Agreement		n/N	Agreement
PPA, % (95% CI)	838/854	98 (97, 99)	PPA, % (95% CI)	443/523	85 (81, 88)	PPA, % (95% CI)	208/289	72 (66, 77)
NPA	91/120	76 (68, 83)	NPA	359/451	80 (76, 83)	NPA	622/685	91 (89, 93)
OPA	929/974	**95 (94, 97)**	OPA	802/974	**82 (80, 85)**	OPA	830/974	**85 (83, 87)**
Cohen's kappa	**0.78 (0.71, 0.84)**		**Cohen's Kappa**	**0.64 (0.60, 0.69)**		**Cohen's Kappa**	**0.64 (0.59, 0.69)**	

Strength of agreement (Cohen's Kappa)

Slight	Fair	Moderate	Substantial	Almost perfect
(0.01–0.20)	(0.21–0.40)	(0.41–0.60)	(0.61–0.80)	(0.81–1.0)

CI, confidence interval; CPS, combined positive score; ICC, interclass correlation coefficient; NPA, negative percent agreement; OPA, overall percent agreement; PD-L1, programmed cell death ligand 1; PPA, positive percent agreement; TAP, tumor area positivity.

1. Figures and tables adapted from: Moehler M, et al. Mod Pathol. 2025;38(9):100793; 2. Moehler M, et al. Mini oral presentation at ESMO-GI 2024. June 26–29 2024. Munich, Germany.

RATIONALE-305:
Clinically confirmed concordance between TAP score and CPS[1–3]

PD-L1 biomarker analysis*

PD-L1 status TAP score/CPS	TAP score, n (%) n=997		CPS, n (%) n=974	
	Tislelizumab + chemotherapy n=501	Placebo + chemotherapy n=496	Tislelizumab + chemotherapy n=491	Placebo + chemotherapy n=483
≥1%/≥1	432 (86.2)	453 (91.3)	420 (85.5)	434 (89.9)
<1%/<1	69 (13.8)	43 (8.7)	71 (14.5)	49 (10.1)
≥5%/≥5	274 (54.7)	272 (54.8)	254 (51.7)	269 (55.7)
<5%/<5	227 (45.3)	224 (45.2)	237 (48.3)	214 (44.3)
≥10%/≥10	136 (27.1)	145 (29.2)	151 (30.8)	138 (28.6)
<10%/<10	365 (72.9)	351 (70.8)	340 (69.2)	345 (71.4)

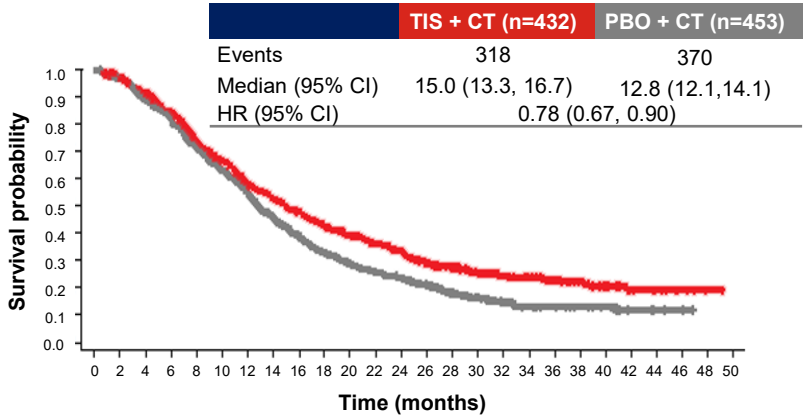
- Prevalence was comparable across arms by TAP score or CPS under different thresholds

*The RATIONALE-305 study (n=997) evaluated the efficacy and safety of tislelizumab plus chemotherapy vs placebo plus chemotherapy, as a first-line treatment for adult patients with locally advanced unresectable or metastatic gastric/gastroesophageal junction adenocarcinoma. Minimum study follow-up was 24.6 months at the final analysis (data cut-off: 28 February 2023).
CPS, combined positive score; CT, chemotherapy; PBO, placebo; PD-L1, programmed cell death ligand 1; TAP, tumor area positivity; TIS, tislelizumab.
1. Moehler M, et al. Mod Pathol. 2025;38(9):100793; 2. Moehler M, et al. Mini oral presentation at ESMO-GI 2024. June 26–29 2024. Munich, Germany; 3. Qiu M-Z, et al. BMJ. 2024:385:e078876.

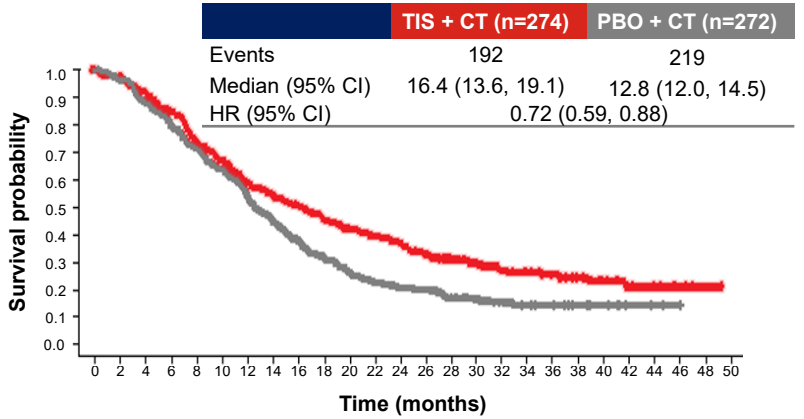
RATIONALE-305:
Clinically confirmed concordance between TAP score and CPS[1,2]

PD-L1 biomarker analysis

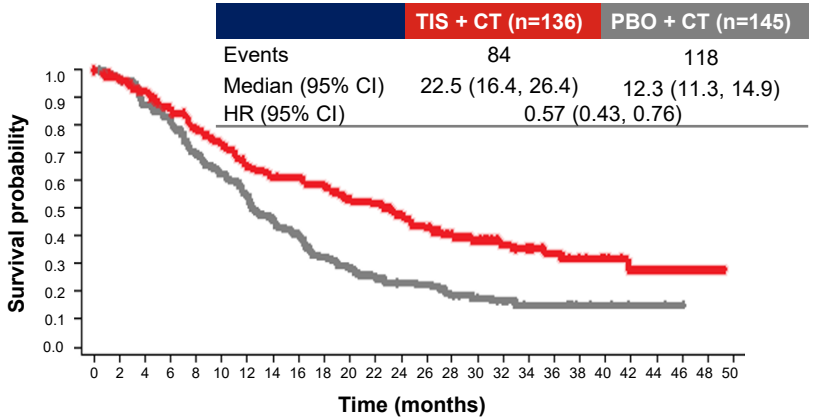
TAP ≥1%



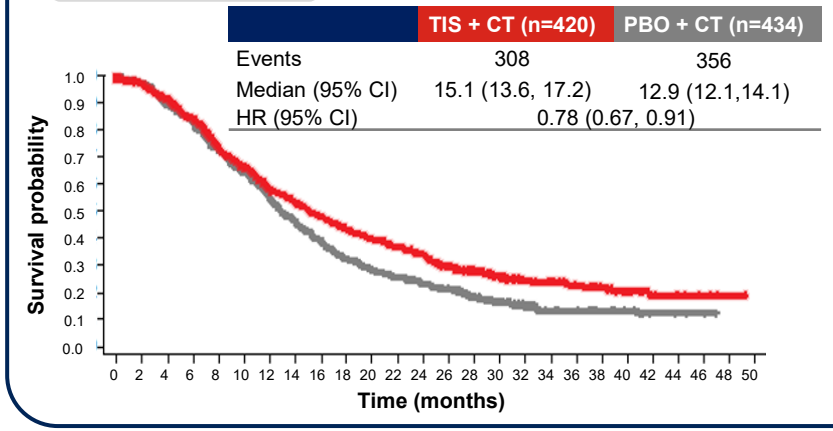
TAP ≥5%



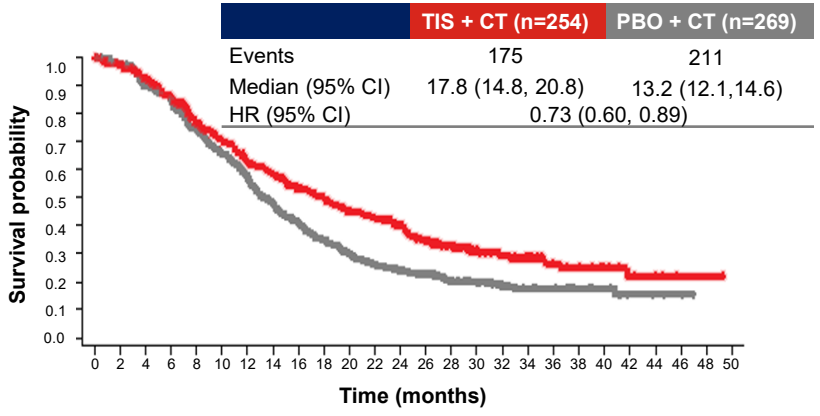
TAP ≥10%



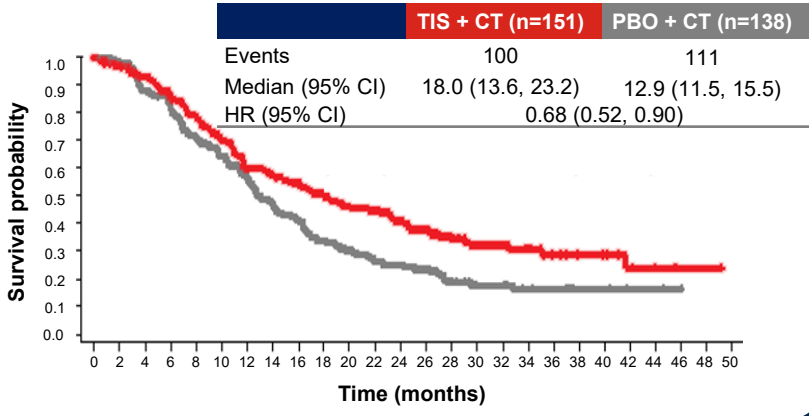
CPS ≥1



CPS ≥5



CPS ≥10



CI, confidence interval; CPS, combined positive score; CT, chemotherapy; HR, hazard ratio; PBO, placebo; PD-L1, programmed cell death ligand 1; TAP, tumor area positivity; TIS, tislelizumab.

1. Figures adapted from: Moehler M, et al. Mod Pathol. 2025;38(9):100793; 2. Moehler M, et al. Mini oral presentation at ESMO-GI 2024. June 26–29 2024. Munich, Germany.

Conclusions

Different methodologies to test PD-L1, and as pathologists, we need to be aware of these

There is a good correlation between determinations (testing and clinical response)

Mandatory to talk to the oncologist, to use the right method, depending on the therapeutic options

TAP has advantages – let's expand our knowledge and establish expertise in this methodology

PD-L1, programmed cell death ligand 1; TAP, tumor area positivity.

TAP in the clinic: The report in clinical practice

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Padua University, Padua

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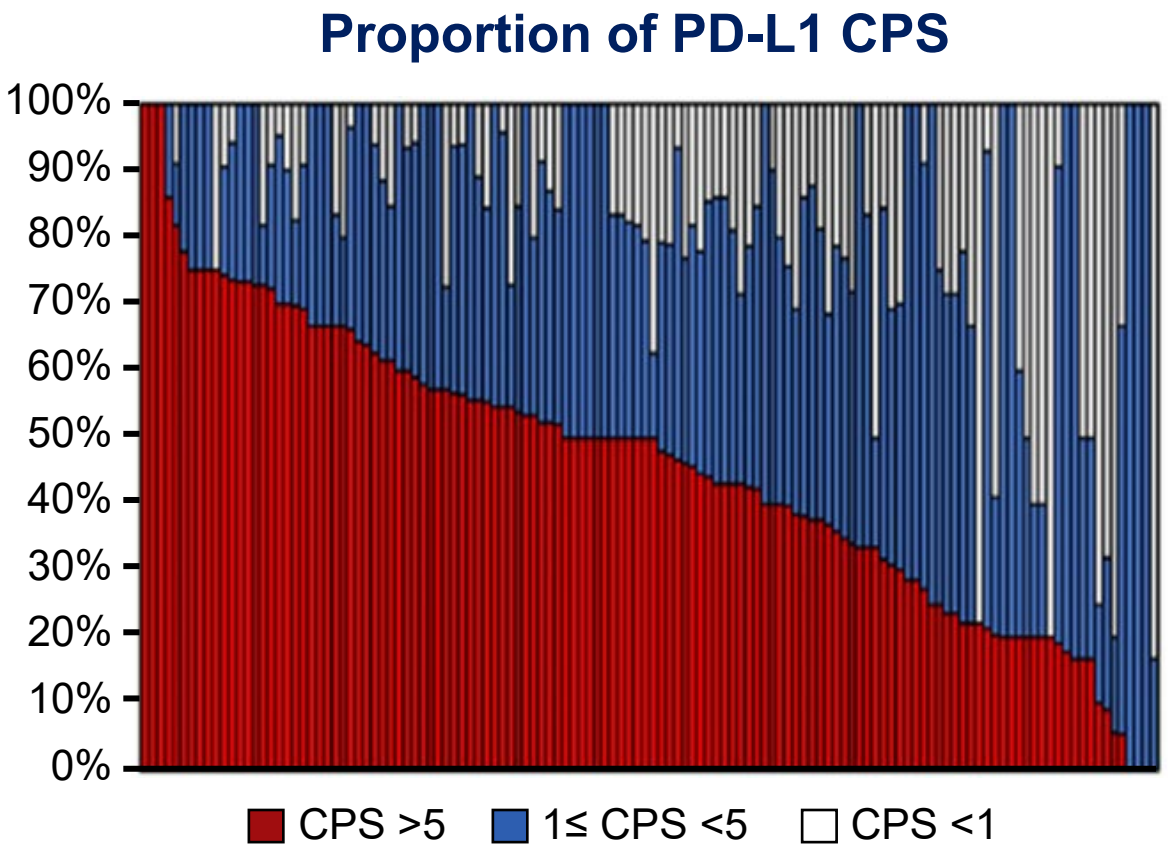
Disclosures

- **Consultancy fees:** Amgen, Astellas, BeOne Medicines, Bristol Myers Squibb, Diaceutics, Diapath, Eli Lilly, GSK, Incyte, IQVIA, MSD, Novartis, Sanofi

- **Research/educational grants:** Thermo Fisher Scientific, Roche

Are we good enough in PD-L1 assessment in clinical practice?[1–5]



2,533 cases

	Cases (n)	Observed (%)	Expected (%)
CPS <1	480	19	15–25
CPS 1–5	855	34	20
CPS ≥5	1,198	47	60

155 institutions

Proportions of each score in each institution using 100% stacked bar charts

CPS, combined positive score; PD-L1, programmed cell death ligand 1.

1. Figure and data adapted from: Abe H, et al. Gastric Cancer. 2025;28(2):294–300; 2. OncLive. TAP Score and CPS May Be Viable for PD-L1 Expression Measurement in Advanced Gastric Cancers. Available at: https://www.onclive.com/view/tap-score-and-cps-may-be-viable-for-pd-l1-expression-measurement-in-advanced-gastric-cancers/Accessed August 2025; 3. Cortes J, et al. Lancet. 2020;396(10265):1817–28; 4. Janjigian YY, et al. Lancet. 2021; 398(10294):27–40; 5. FDA. September 26, 2024: Meeting of the Oncologic Drugs Advisory Committee Meeting Announcement. Available at: https://www.fda.gov/advisory-committees/advisory-committee-calendar/september-26-2024-meeting-oncologic-drugs-advisory-committee-meeting-announcement-09262024/Accessed August 2025.

Real-world issues in PD-L1 testing implementation

The sample

The methods of analysis

Staining interpretation

PD-L1, programmed cell death ligand 1.

Example of PD-L1 IHC report

- Biopsy/surgical sample(s) representative of neoplastic tissue (fixed in formalin and embedded in paraffin) identified as n. XXX of the Surgical Pathology Unit of the XXX Hospital
- Histologically, >100 viable tumor cells are present

Tumor histotype	@ (Adenocarcinoma; Describe if other)
Site	@ (Primary neoplasm; Metastasis [if metastasis, define site])
Test material	@ (Biopsy specimen; Surgical specimen)
Sample adequacy	@ (Adequate; Inadequate)
Cause of inadequacy	@ (Lack of tumor tissue; Electrocution/fixation artifacts; Less than 6 biopsies to be tested; Other [define])
IHC clone	@ (xxx [Company])

Immunoreaction evaluation

• CPS (combined positive score)	Positive/negative – XX
• TPS (tumor proportion score)	Positive/negative – XX%
• TAP (tumor area positivity)	Positive/negative – XX%

Note: Enter if the laboratory regularly participates in national/international external quality assessment programs

Bibliographical references: xxx

IHC, immunohistochemistry; PD-L1, programmed cell death ligand 1.

Example of PD-L1 IHC report

Qualification of the specimen

- Biopsy/surgical sample(s) representative of neoplastic tissue (fixed in formalin and embedded in paraffin) identified as n. XXX of the Surgical Pathology Unit of the XXX Hospital
- Histologically, >100 viable tumor cells are present

Analytical variables

Tumor histotype	@ (Adenocarcinoma; Describe if other)
Site	@ (Primary neoplasm; Metastasis [if metastasis, define site])
Test material	@ (Biopsy specimen; Surgical specimen)
Sample adequacy	@ (Adequate; Inadequate)
Cause of inadequacy	@ (Lack of tumor tissue; Electrocution/fixation artifacts; Less than 6 biopsies to be tested; Other [define])
IHC clone	@ (xxx [Company])

Evaluation of the biomarker

Immunoreaction evaluation

• CPS (combined positive score)	Positive/negative – XX
• TPS (tumor proportion score)	Positive/negative – XX%
• TAP (tumor area positivity)	Positive/negative – XX%

Laboratory qualification

Note: Enter if the laboratory regularly participates in national/international external quality assessment programs

Bibliographical references: xxx

IHC, immunohistochemistry; PD-L1, programmed cell death ligand 1.

Example of PD-L1 IHC report

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Analytical variables

IHC clone	@ (xxx [Company])

Evaluation of the biomarker

Immunoreaction evaluation

• CPS (combined positive score)	Positive/negative – XX
• TPS (tumor proportion score)	Positive/negative – XX%
• TAP (tumor area positivity)	Positive/negative – XX%

Laboratory qualification

Note: Enter if the laboratory regularly participates in national/international external quality assessment programs

Bibliographical references: xxx

IHC, immunohistochemistry; PD-L1, programmed cell death ligand 1.

What is the best tissue sample for PD-L1 testing?

Biopsy

- **Heterogeneity** of expression
- Often PD-L1 overexpression is observed at **invasive edge**
- **Ulcer** can be a problem
- **At least 5–6** neoplastic biopsies required

Surgical specimen

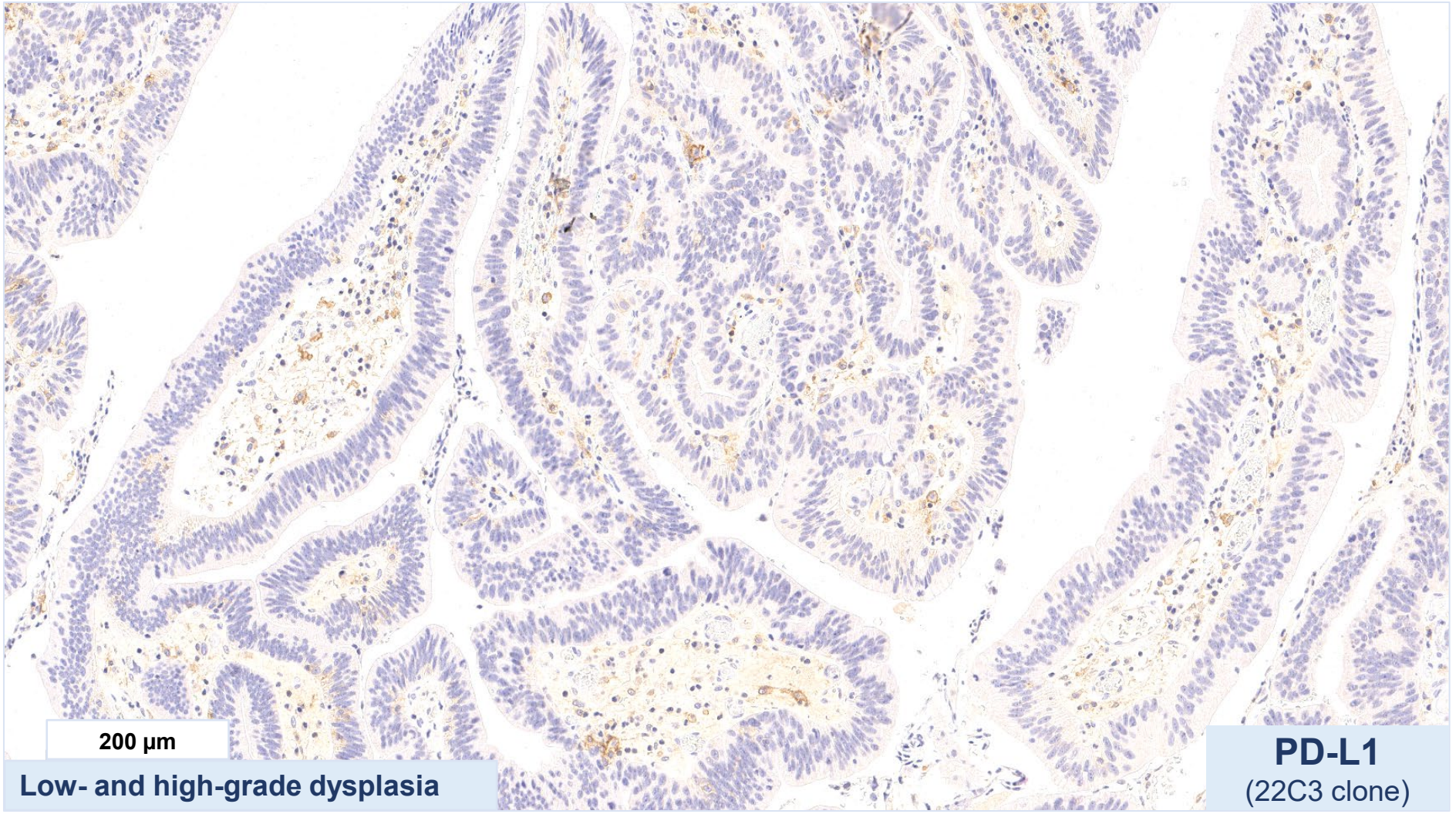
- **One FFPE block** is enough
- Potential **pre-analytical problems**
- May not be representative of the **clinical situation**
- Impact of **neoadjuvant treatment** on PD-L1 expression?

Metastasis

- Probably **reflects** the **ongoing clinical situation**
- No robust data in GEJ oncological setting
- **Heterogeneity** between the **primary tumor** and **metastases**?
- **Heterogeneity** between the different **metastatic sites**?

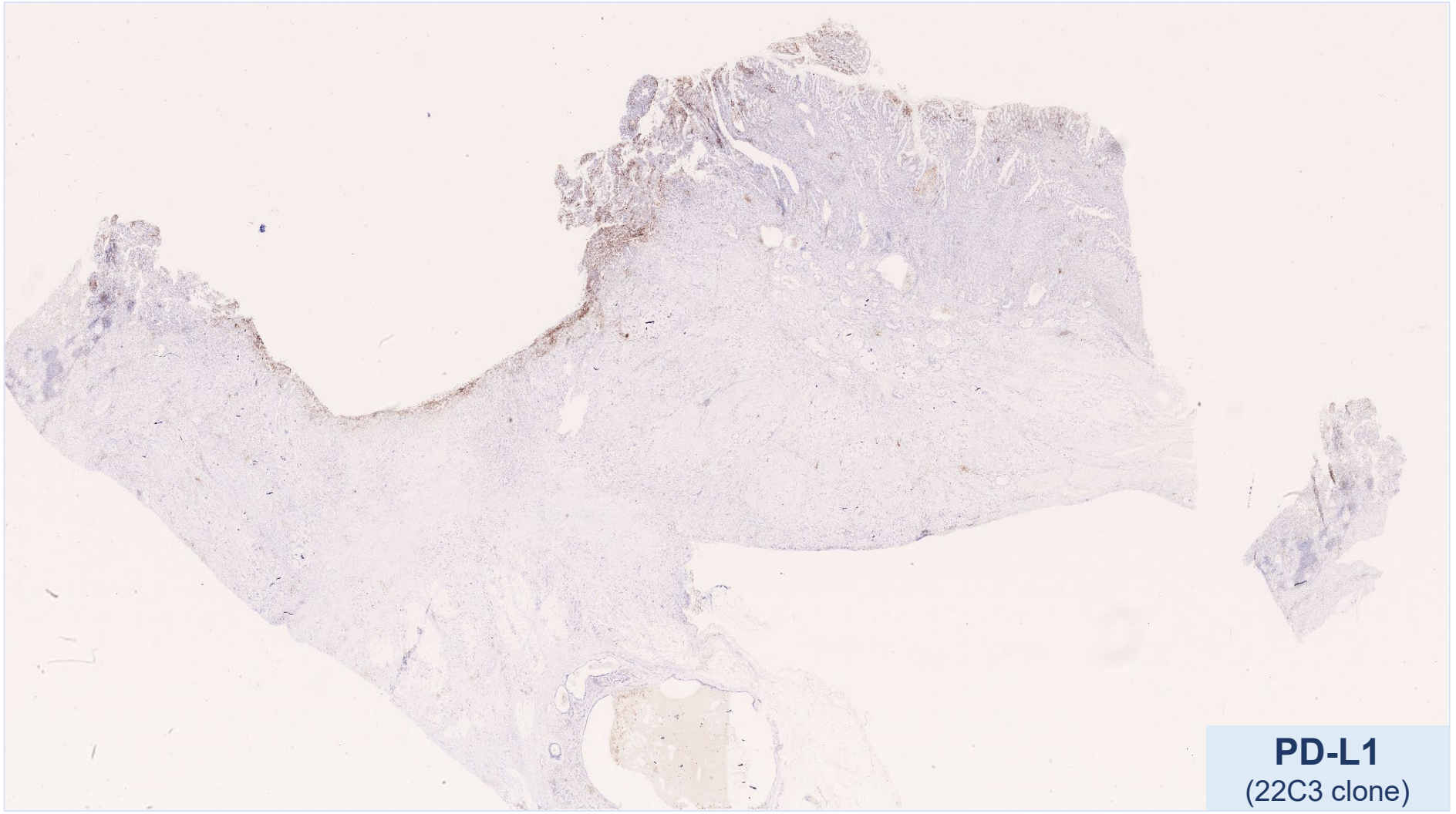
FFPE, formalin-fixed paraffin-embedded; GEJ, gastroesophageal junction; PD-L1, programmed cell death ligand 1.

The need for experienced GI pathologists in biomarker evaluation!



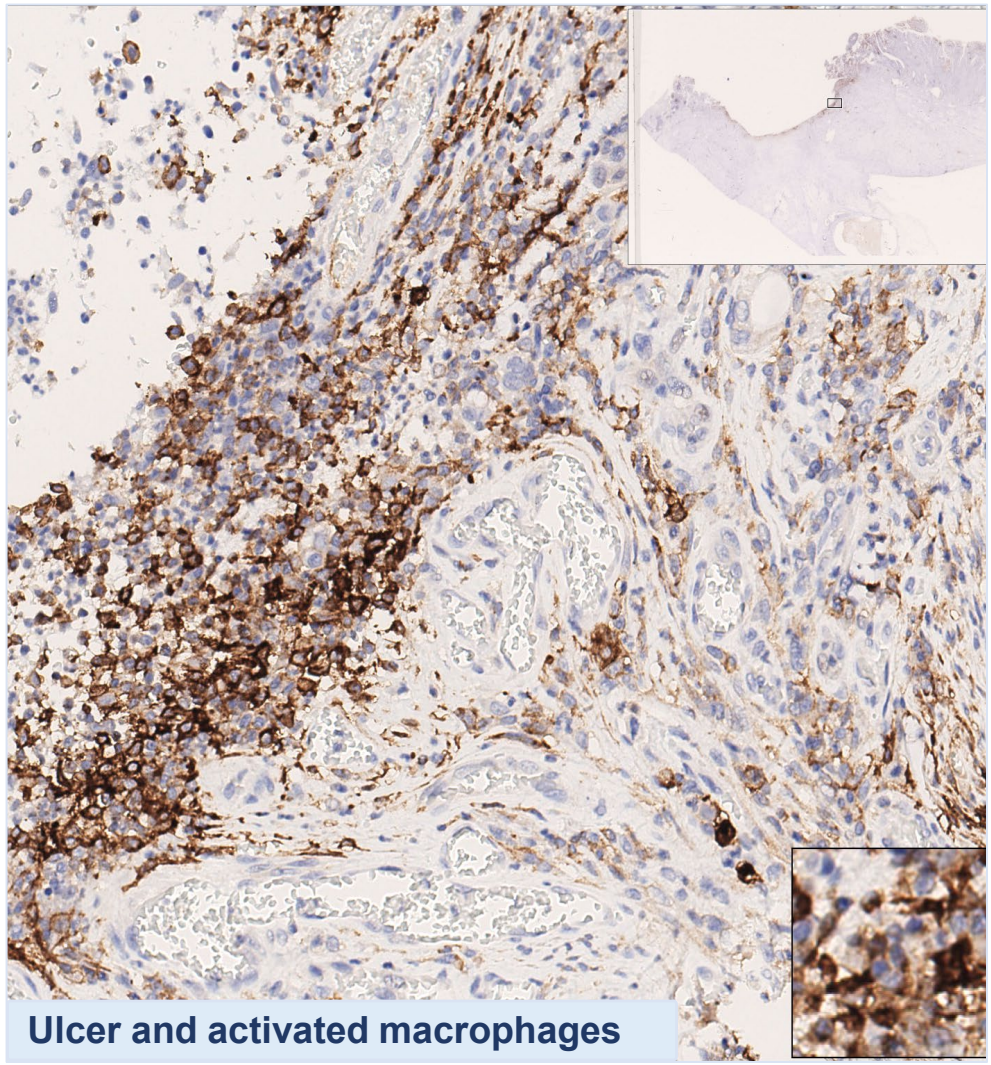
The speaker confirms appropriate permissions have been obtained for the image shown.
GI, gastrointestinal; PD-L1, programmed cell death ligand 1.

The ulcerated GC: An example of intratumor heterogeneity

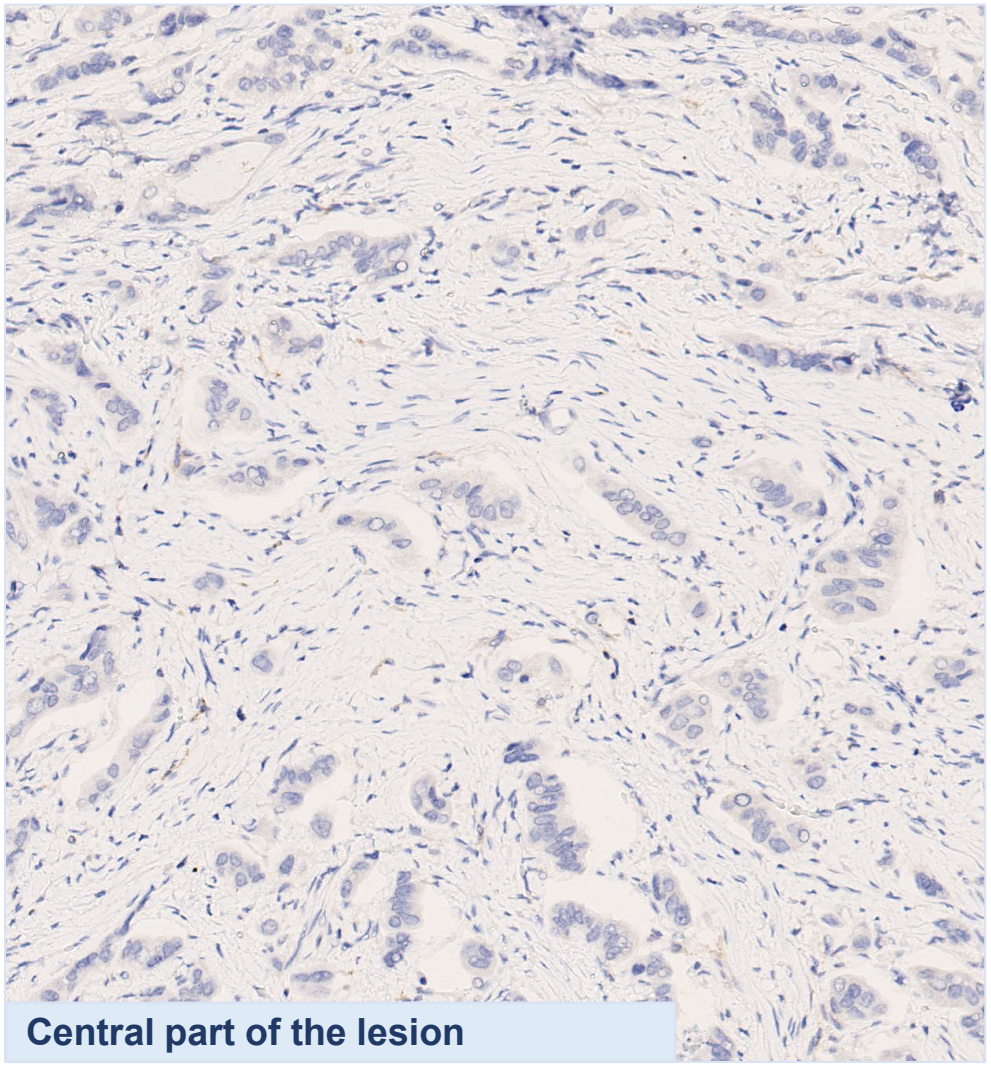


The speaker confirms appropriate permissions have been obtained for the image shown.
GC, gastric cancer; PD-L1, programmed cell death ligand 1.

Tumor-associated macrophages in GC



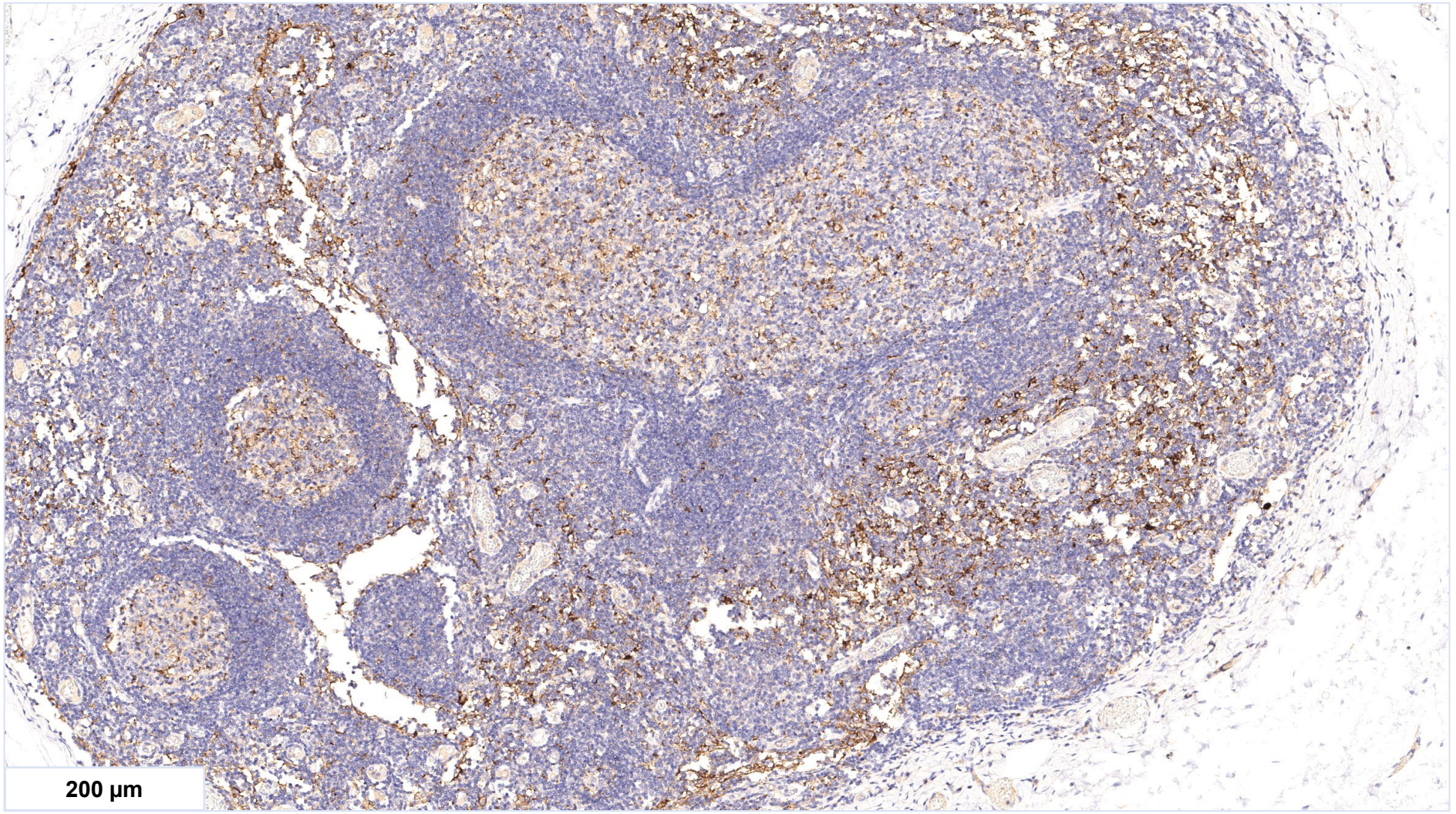
Ulcer and activated macrophages



Central part of the lesion

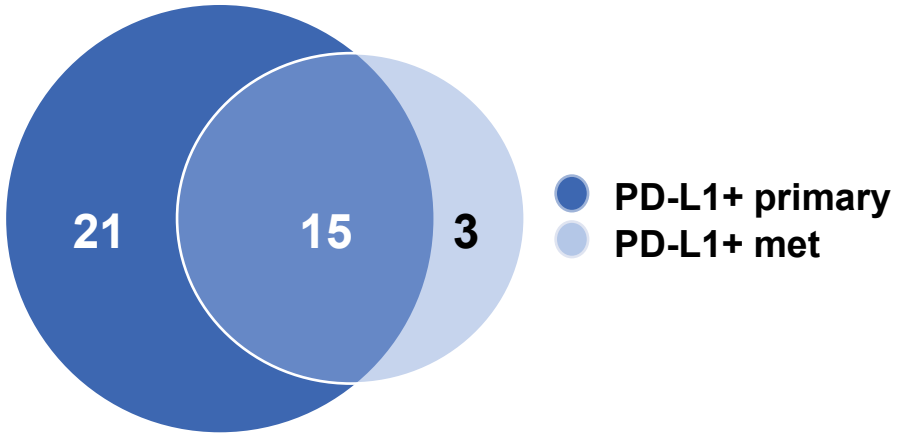
The speaker confirms appropriate permissions have been obtained for the image shown.
GC, gastric cancer.

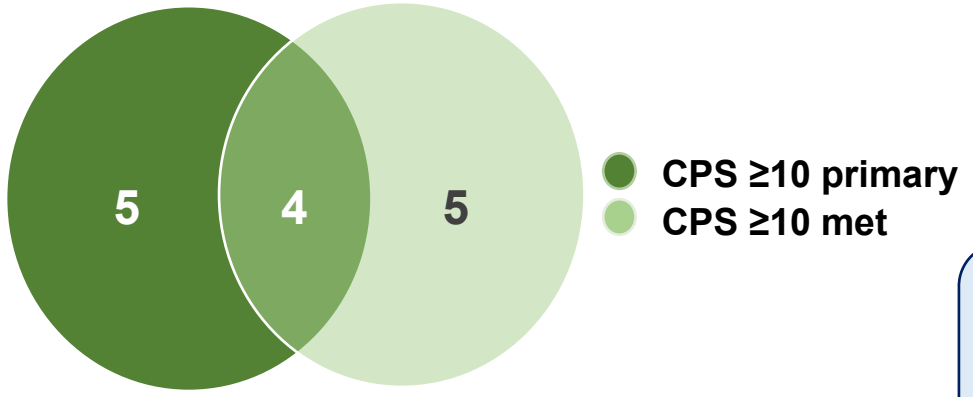
Non-metastatic LN is characterized by PD-L1+ elements

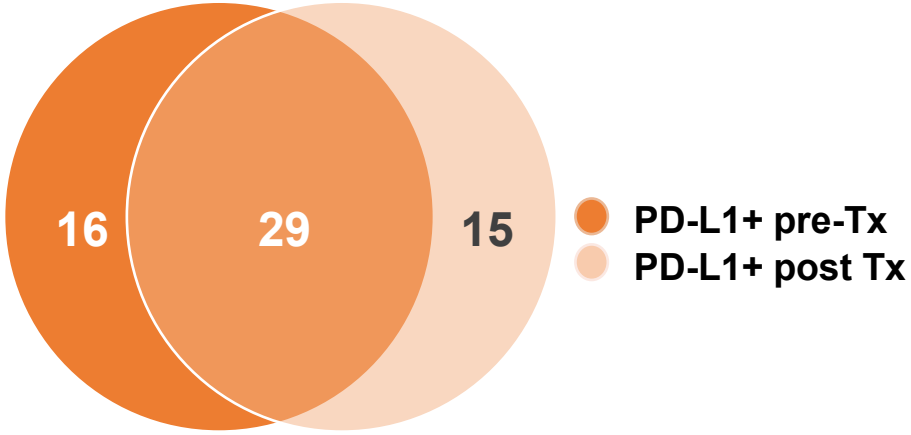


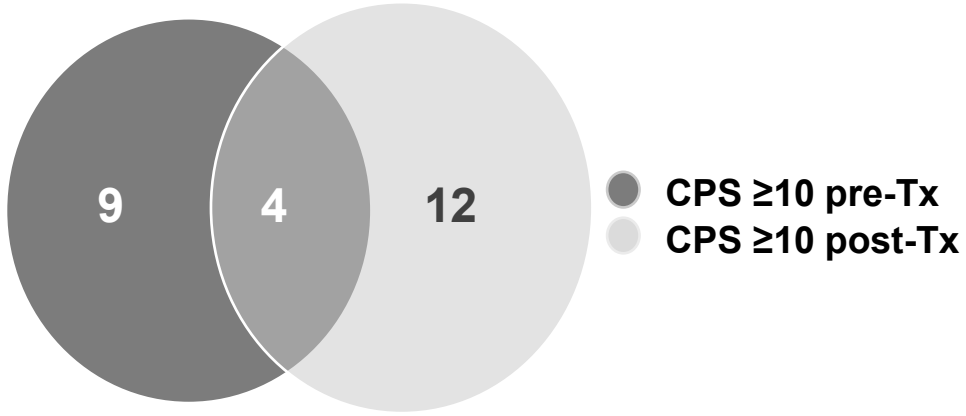
The speaker confirms appropriate permissions have been obtained for the image shown.
LN, lymph node; PD-L1, programmed cell death ligand 1.

Timing of testing: PD-L1 spatial and temporal heterogeneity









PD-L1 expression exhibits marked spatial and temporal heterogeneity in GECs

CPS, combined positive score; GEC, gastroesophageal cancer; met, metastatic tumor; PD-L1, programmed cell death ligand 1; primary, primary tumor; Tx, treatment.
Figures adapted from: Zhou KI, et al. Clin Cancer Res. 2020;26(24):6453–63.

Example of PD-L1 IHC report

Qualification of the specimen

- Biopsy/surgical sample(s) representative of neoplastic tissue (fixed in formalin and embedded in paraffin) identified as n. XXX of the Surgical Pathology Unit of the XXX Hospital
- Histologically, >100 viable tumor cells are present

Tumor histotype	@ (Adenocarcinoma; Describe if other)
Site	@ (Primary neoplasm; Metastasis [if metastasis, define site])
Test material	@ (Biopsy specimen; Surgical specimen)
Sample adequacy	@ (Adequate; Inadequate)
Cause of inadequacy	@ (Lack of tumor tissue; Electrocution/fixation artifacts; Less than 6 biopsies to be tested; Other [define])

Analytical variables

IHC clone	@ (xxx [Company])

Evaluation of the biomarker

Immunoreaction evaluation	
• CPS (combined positive score)	Positive/negative – XX
• TPS (tumor proportion score)	Positive/negative – XX%
• TAP (tumor area positivity)	Positive/negative – XX%

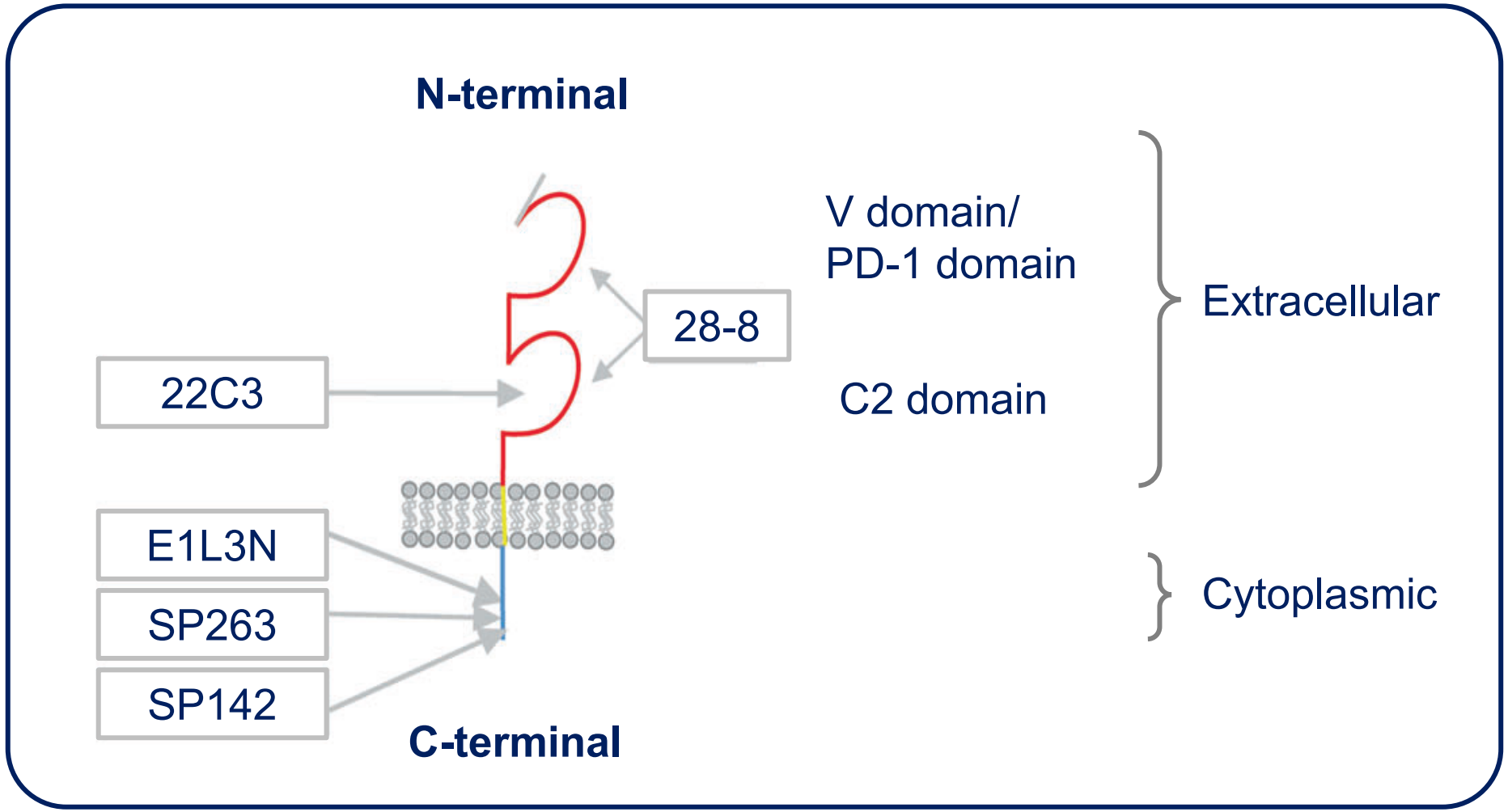
Laboratory qualification

Note: Enter if the laboratory regularly participates in national/international external quality assessment programs

Bibliographical references: xxx

IHC, immunohistochemistry; PD-L1, programmed cell death ligand 1.

The different Ab clones are targeting different epitopes of the PD-L1 protein



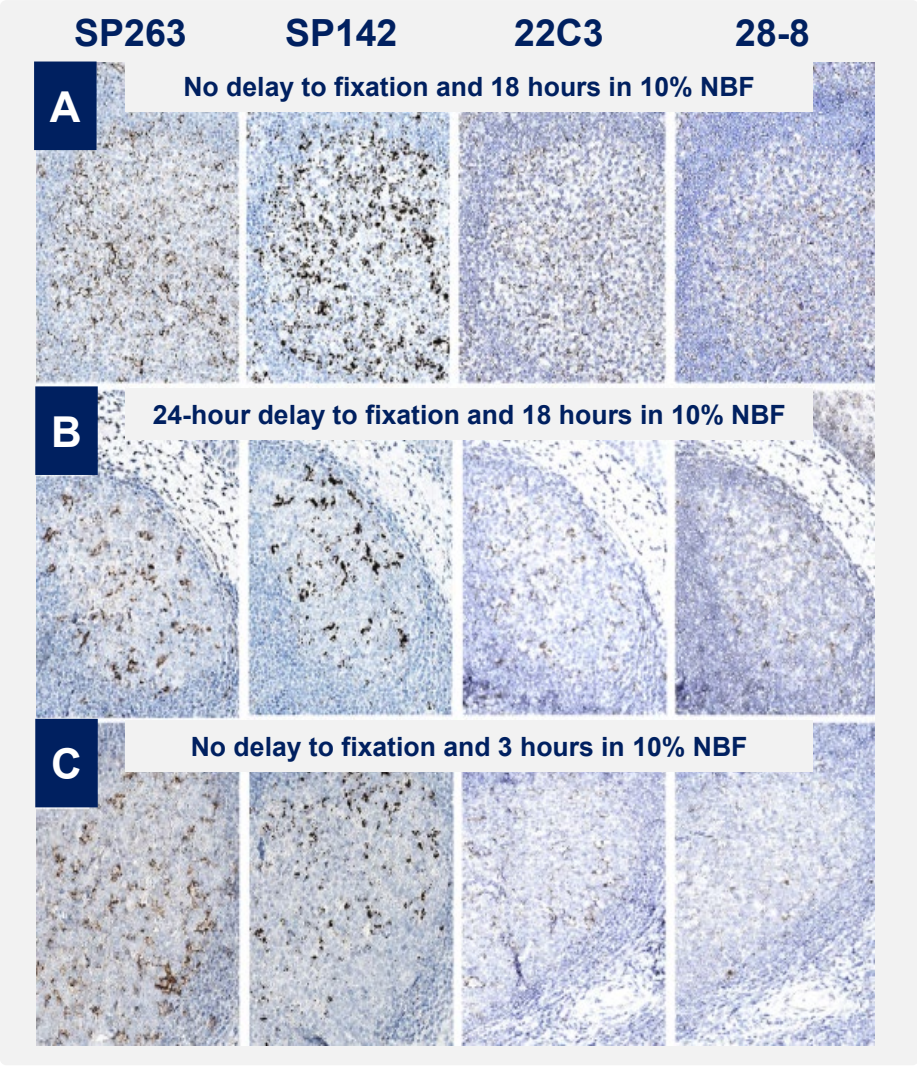
Ab, antibody; PD-1, programmed cell death 1; PD-L1, programmed cell death ligand 1.
Figure adapted from: Lawson NL, et al. Mod Pathol. 2020;33(4):518–30.

Performance of internal and external domain antibodies under suboptimal conditions

- **Under suboptimal decalcification** or **fixation** conditions, the performance of **internal** domain **antibodies** is **less detrimentally affected** than that of **external** domain antibodies

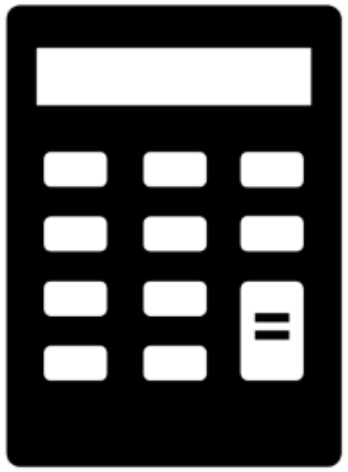
- The **binding sites** of **external** domain antibodies are susceptible to **deglycosylation** and **conformational** structural **changes**, leading to IHC staining reduction or loss

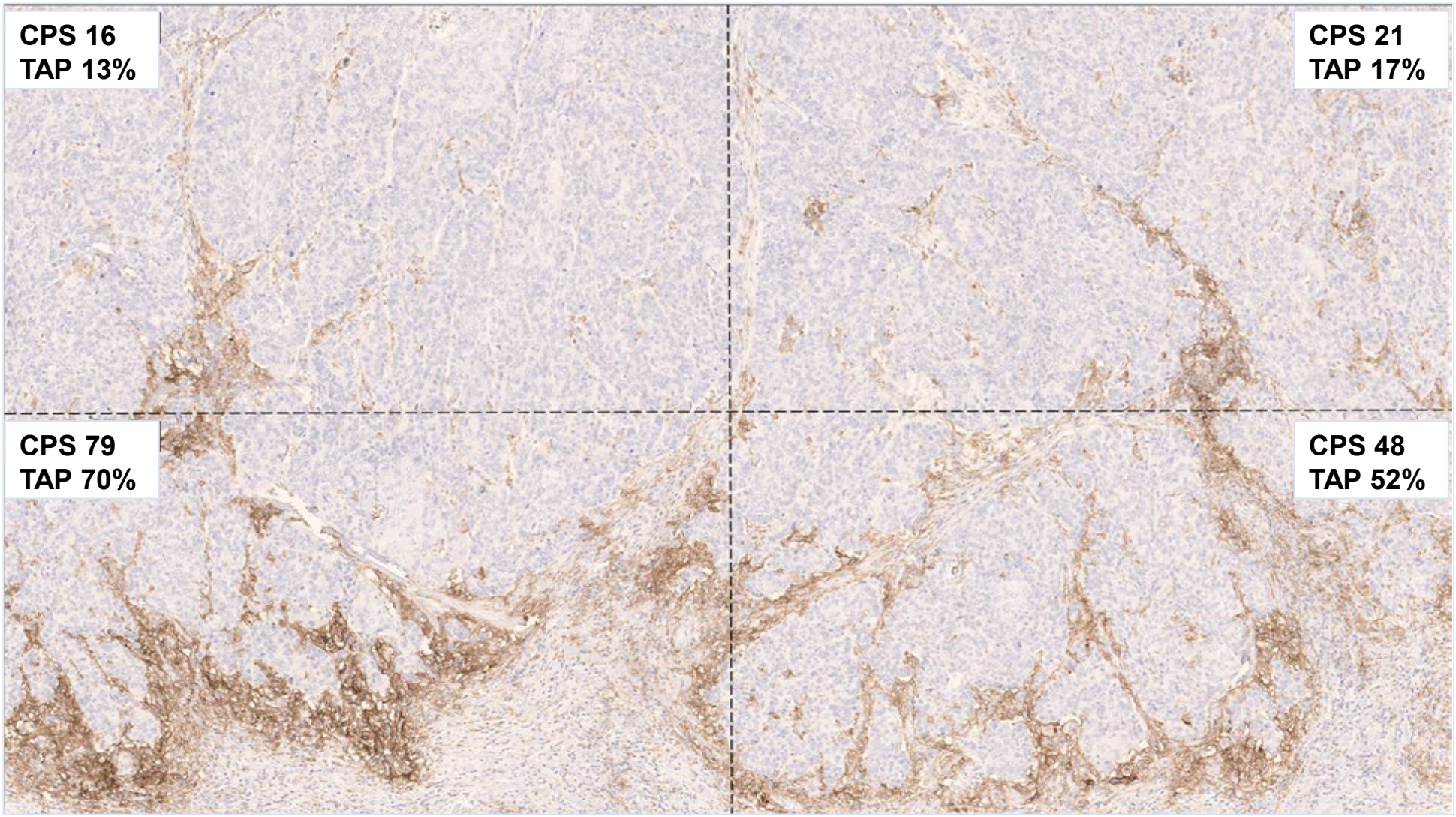
- **Do all tissue types lose antigenicity in the same way?**
- **Are tonsils the same as adenocarcinoma?**
- **Do neoplastic cells lose antigenicity in the same way as inflammatory cells?**



IHC, immunohistochemistry; NBF, neutral buffered-formalin.
Figure adapted from: Lawson NL, et al. Mod Pathol. 2023;36(9):100220.

It is not a hot-spot evaluation!*





*CPS and TAP calculations have been rescored by the speaker.
CPS, combined positive score; TAP, tumor area positivity.
Figure adapted from: Angerilli V, et al. Pathologica. 2023;115(2):57–70.

PD-L1 inter-pathologist agreement

Summary of inter-reader variability

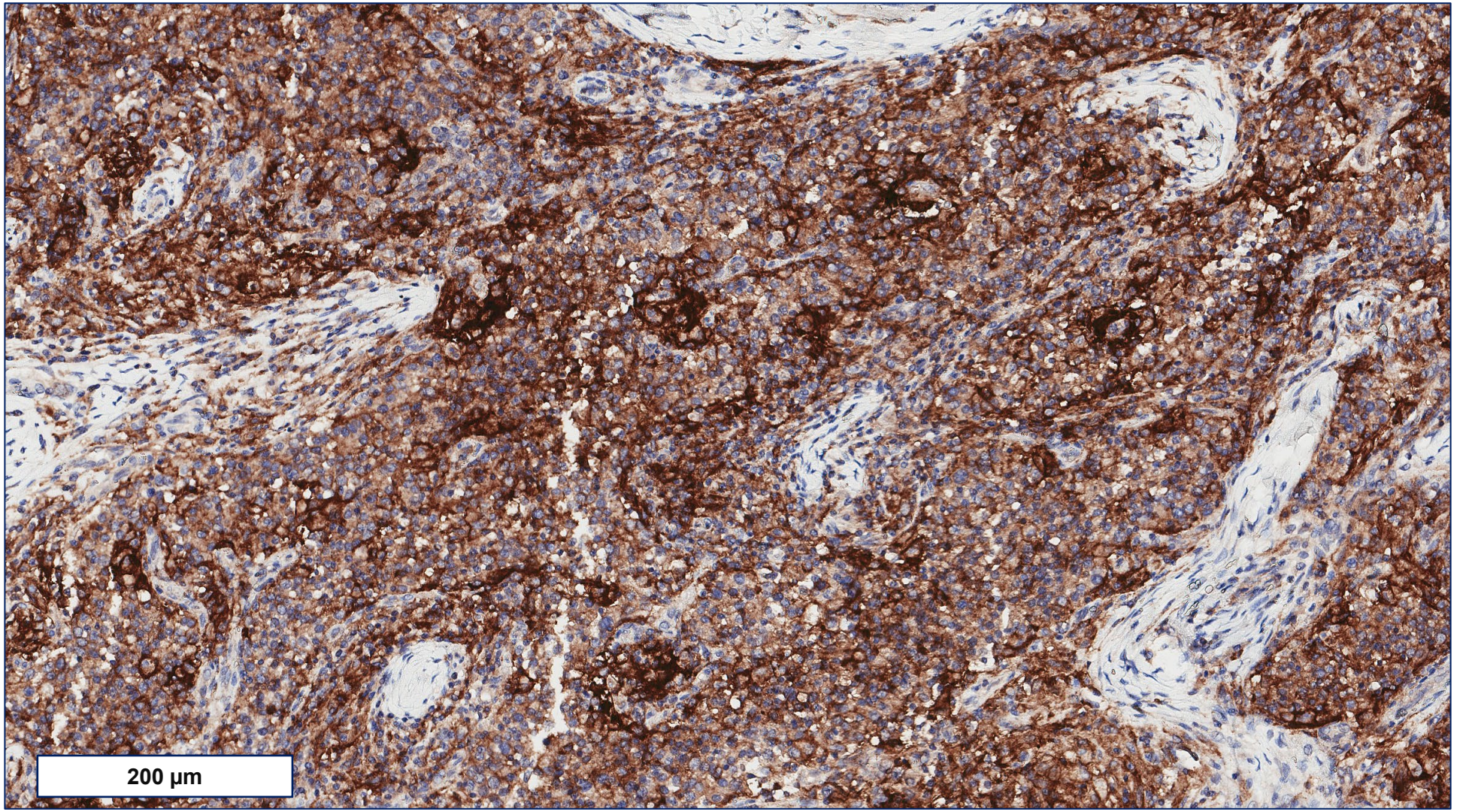
Reference	PD-L1 assay	n	Scoring algorithm	Reader	ICC (95% CI)	Mean bias to reference (95% CI)
P1	28-8	97	CPS	P2	0.92 (0.89, 0.95)	–4.80 (–6.12, –3.48)
				P3	0.95 (0.93, 0.97)	–2.95 (–4.01, –1.89)
			TAP	P2	0.95 (0.93, 0.97)	–1.77 (–2.62, –0.91)
				P3	0.94 (0.92, 0.96)	0.47 (–0.40, 1.34)
	22C3	96	CPS	P2	0.96 (0.94, 0.97)	–3.08 (–4.21, –1.95)
				P3	0.97 (0.96, 0.98)	–2.25 (–3.26, –1.24)
			TAP	P2	0.99 (0.98, 0.99)	–0.53 (–1.16, 0.11)
				P3	0.98 (0.98, 0.99)	0.52 (–0.13, 1.16)
	SP263	98	CPS	P2	0.94 (0.92, 0.96)	–4.25 (–5.96, –2.54)
				P3	0.95 (0.93, 0.97)	–3.74 (–5.32, –2.17)
			TAP	P2	0.98 (0.97, 0.98)	–1.03 (–2.01, –0.05)
				P3	0.97 (0.96, 0.98)	0.13 (–0.91, 1.17)

The inter-pathologist analysis for CPS and TAP demonstrated high correlation, with ICCs ranging from 0.92 to 0.99

CI, confidence interval; CPS, combined positive score; ICC, intraclass correlation coefficient; P, pathologist; PD-L1, programmed cell death ligand 1; TAP, tumor area positivity.

Klempner SJ, et al. JCO Precis Oncol. 2024:e2400230.

Example 1: EBV-related GC



The speaker confirms appropriate permissions have been obtained for the image shown.
EBV, Epstein–Barr virus; GC, gastric cancer.

Example 1: EBV-related GC

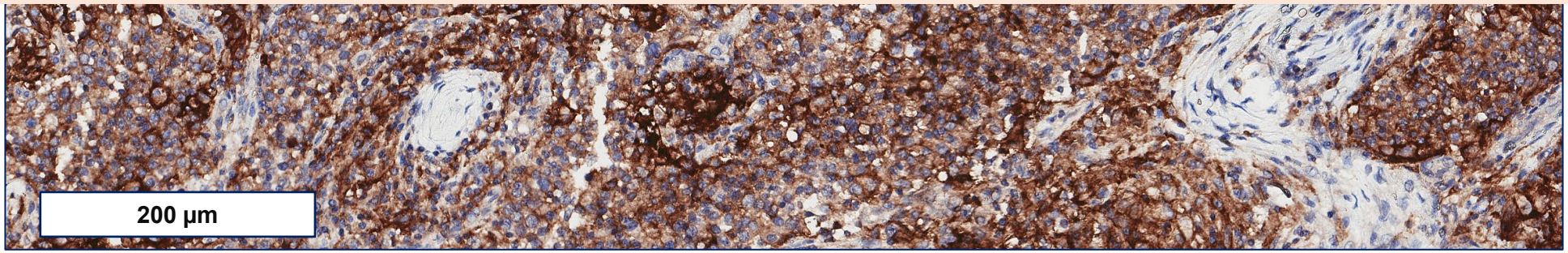
Histology report

- Surgical sample representative of neoplastic tissue (FFPE). Histologically, >100 viable tumor cells are present

Tumor histotype	Adenocarcinoma
Site	Primary neoplasm
Sample adequacy	Adequate
IHC clone	22C3 (Agilent)

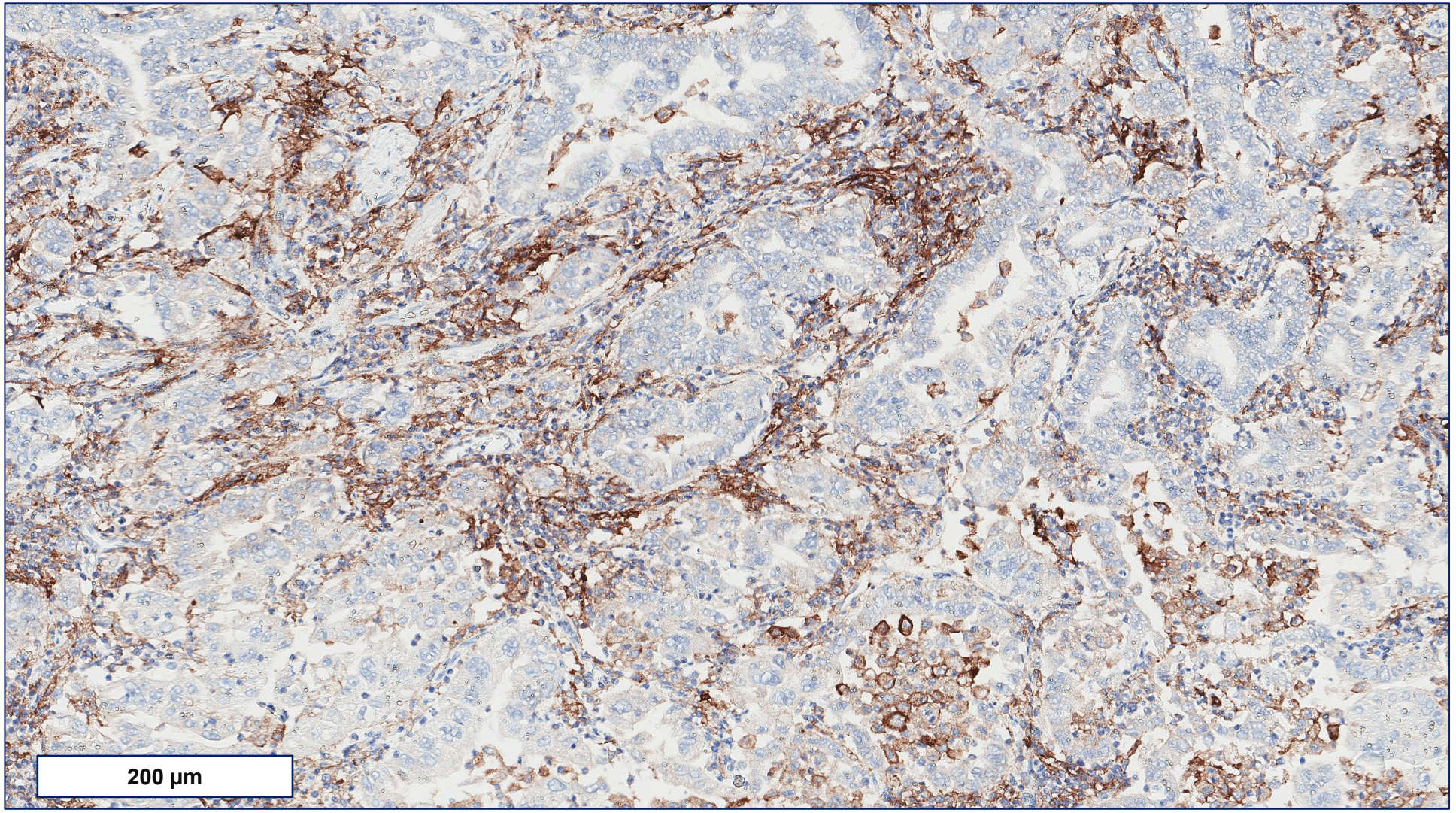
Immunoreaction evaluation

• CPS (combined positive score)	Positive* – 100
• TAP (tumor area positivity)	Positive* – 98%



The speaker confirms appropriate permissions have been obtained for the image shown.
*According to current cutoffs.
EBV, Epstein–Barr virus; FFPE, formalin-fixed paraffin-embedded; GC, gastric cancer; IHC, immunohistochemistry.

Example 2: MMRd/MSI GC



The speaker confirms appropriate permissions have been obtained for the image shown.
GC, gastric cancer; MMRd, mismatch repair deficient; MSI, microsatellite instability.

Example 2: MMRd/MSI GC

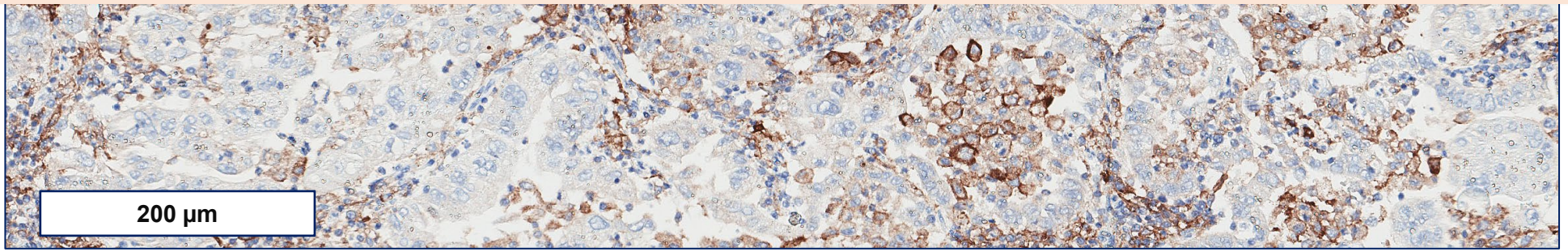
Histology report

- Surgical sample representative of neoplastic tissue (FFPE). Histologically, >100 viable tumor cells are present

Tumor histotype	Adenocarcinoma
Site	Primary neoplasm
Sample adequacy	Adequate
IHC clone	22C3 (Agilent)

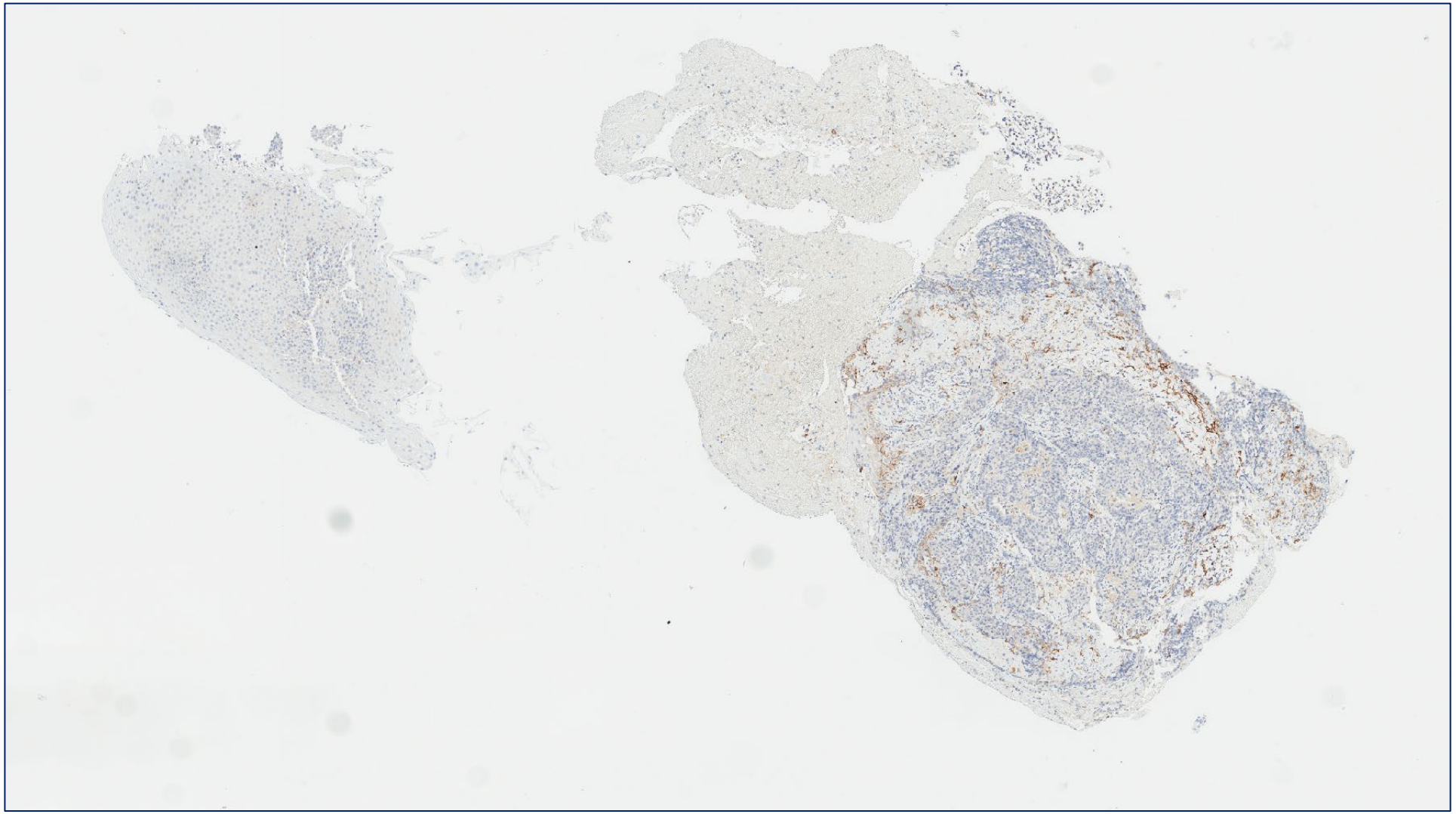
Immunoreaction evaluation

- CPS (combined positive score) — Positive* – 67
- TAP (tumor area positivity) — Positive* – 69%



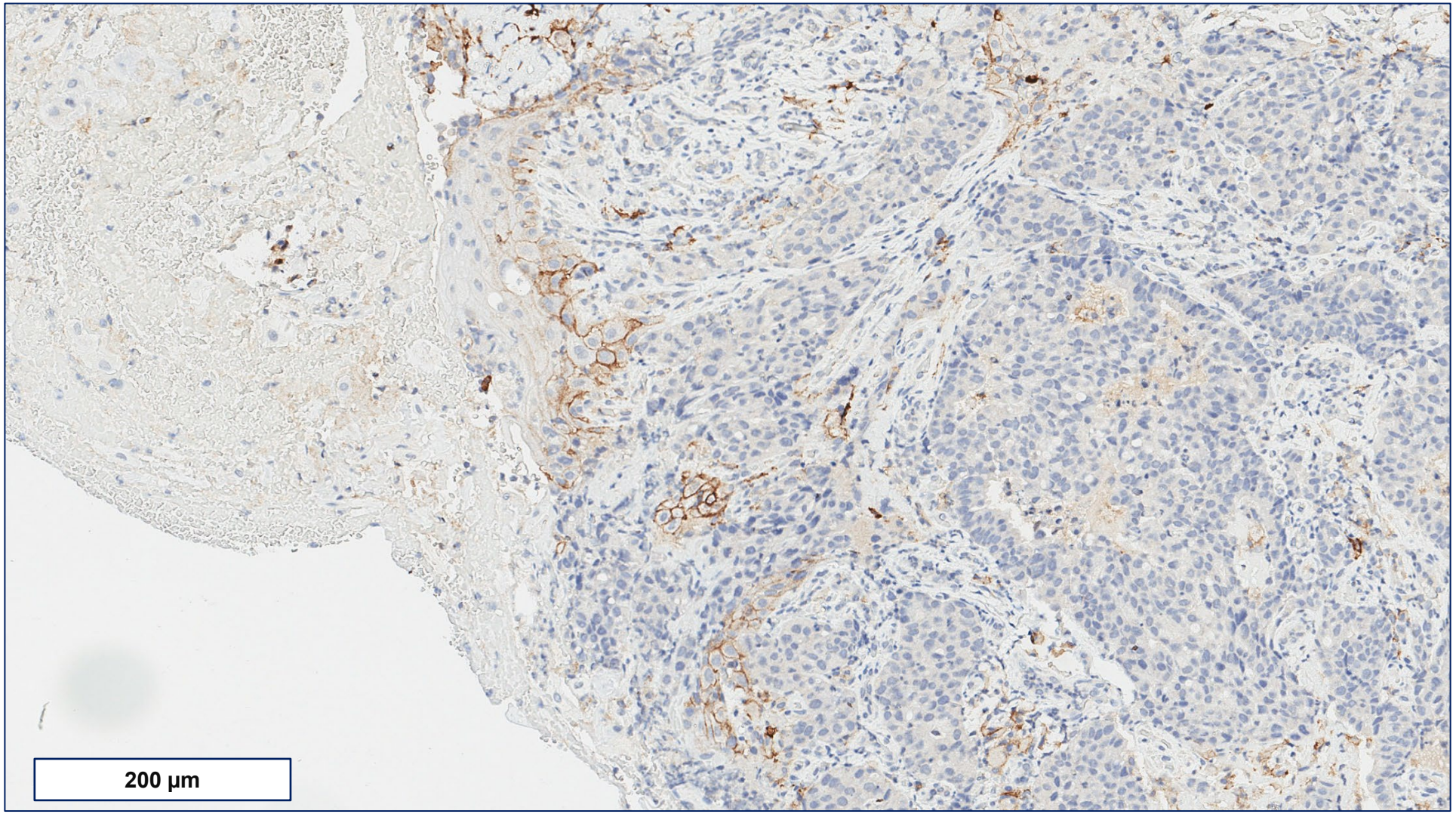
The speaker confirms appropriate permissions have been obtained for the image shown.
*According to current cutoffs.
FFPE, formalin-fixed paraffin-embedded; GC, gastric cancer; IHC, immunohistochemistry; MMRd, mismatch repair deficient; MSI, microsatellite instability.

Example 3: ESCC



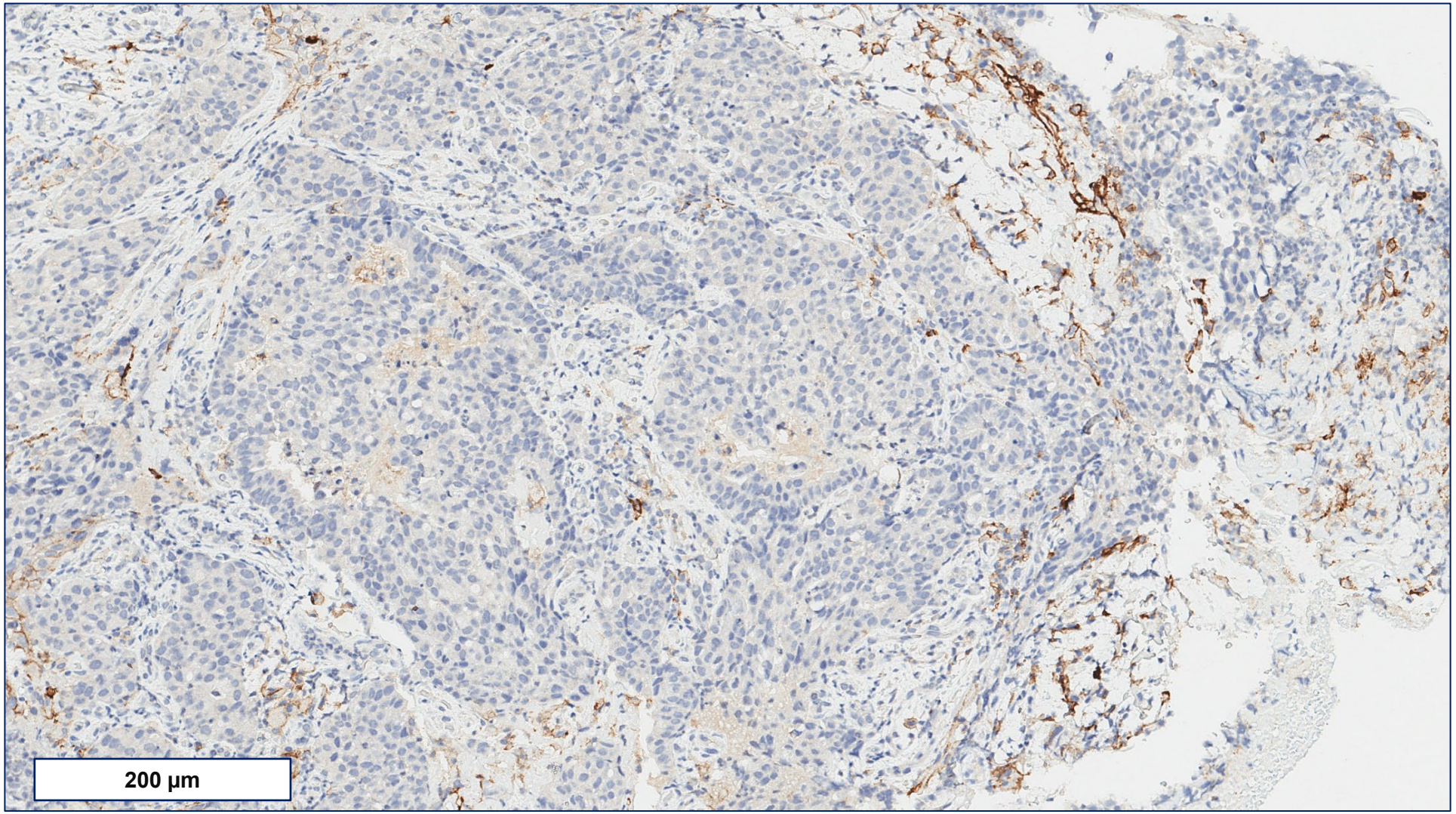
The speaker confirms appropriate permissions have been obtained for the image shown.
ESCC, esophageal squamous cell carcinoma.

Example 3: ESCC



The speaker confirms appropriate permissions have been obtained for the image shown.
ESCC, esophageal squamous cell carcinoma.

Example 3: ESCC



The speaker confirms appropriate permissions have been obtained for the image shown.
ESCC, esophageal squamous cell carcinoma.

Example 3: ESCC

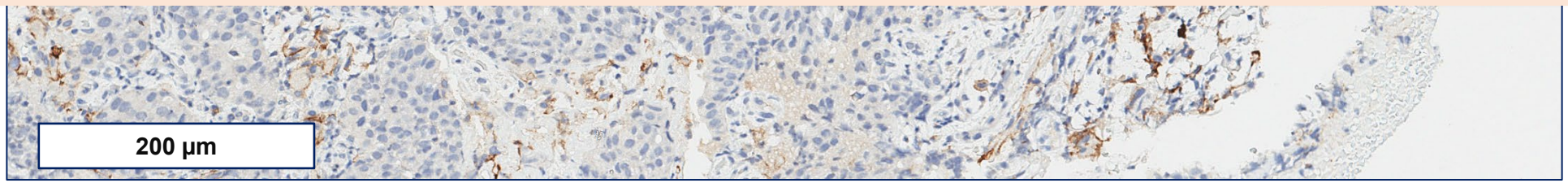
Histology report

- Surgical sample representative of neoplastic tissue (FFPE). Histologically, >100 viable tumor cells are present

Tumor histotype	ESCC
Site	Primary neoplasm
Sample adequacy	Inadequate
Cause of inadequacy	<6 biopsies tested
IHC clone	22C3 (Agilent)

Immunoreaction evaluation

• TPS (tumor proportion score)	Negative – 0%
• CPS (combined positive score)	Negative* – 4
• TAP (tumor area positivity)	Negative* – 3%



The speaker confirms appropriate permissions have been obtained for the image shown.
*According to current cutoffs.
ESCC, esophageal squamous cell carcinoma; FFPE, formalin-fixed paraffin-embedded; IHC, immunohistochemistry.

Take-home messages: TAP in the clinic

Another PD-L1 scoring system to be added in a relatively complex diagnostic world…

- **No additional costs**
- **Easier to use than other systems with visual evaluation**
- **More standardizable than other PD-L1 scoring systems**
- **Of clinical value!**

PD-L1, programmed cell death ligand 1; TAP, tumor area positivity.

BeOne

ECP 2025 Industry Satellite Symposium
Vienna, Austria, September 8th, 2025

TAP (tumor area positivity):
A new PD-L1 star is born

Chair: Matteo Fassan, Padua University, Italy

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