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WHY PIPAC?

Assessing Tumor Response

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Disclosures

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This presentation has been peer-reviewed and no conflicts were noted.

Tumor regression

- Neoadjuvant chemo- and/or radiotherapy followed by surgery
- Standard of care in advanced gastrointestinal (gynecological) cancers
- Mainly in primary tumors
    - Estimation of residual tumor
    - In relation to regressive changes
    - In relation to initial tumor size

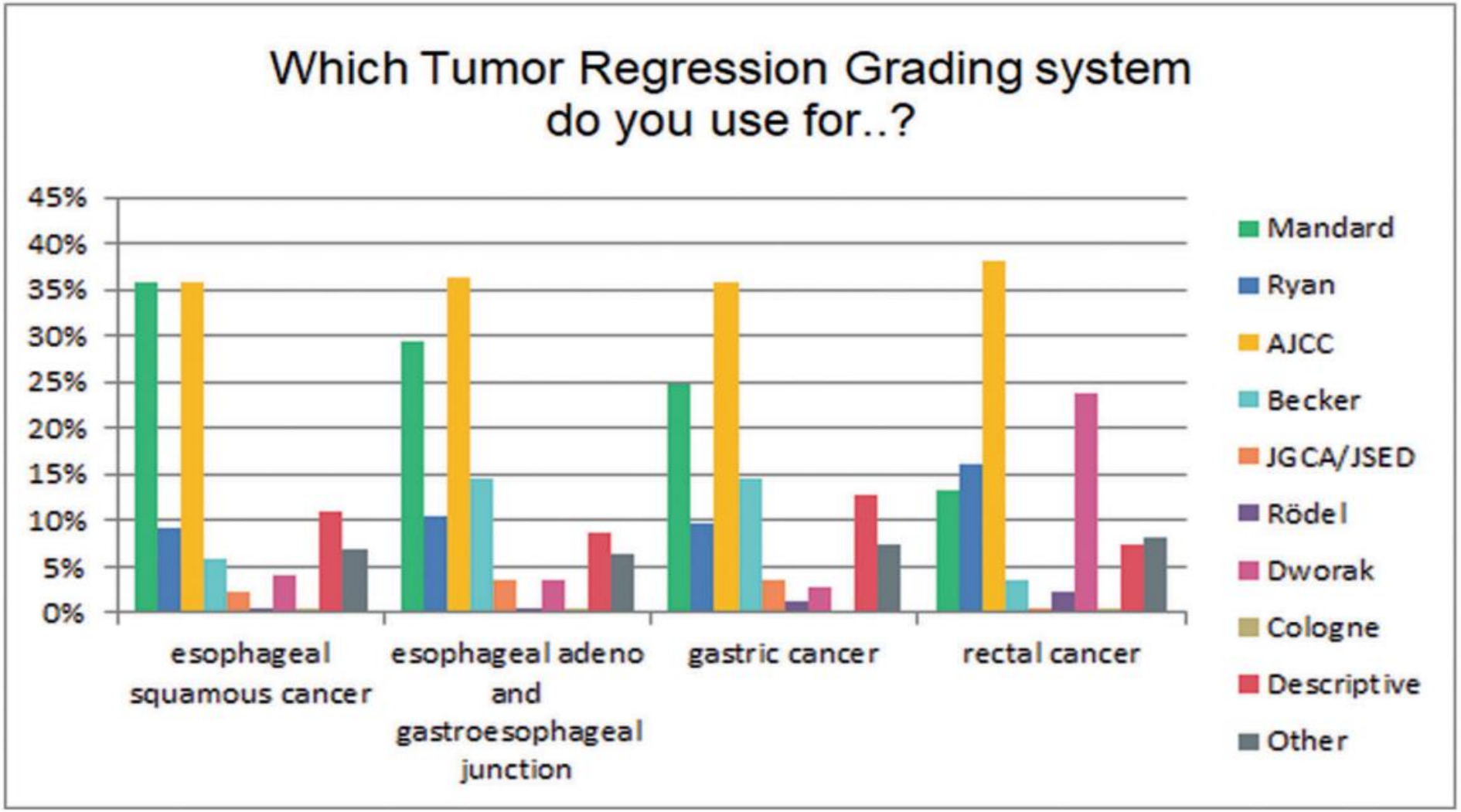
Importance of Tumor Regression Grading (TRG)

- Prognostic impact (complete regression or non-response)
- Surrogate parameter for therapy response
- End points in clinical trials
- However, there is no consensus which system should be used

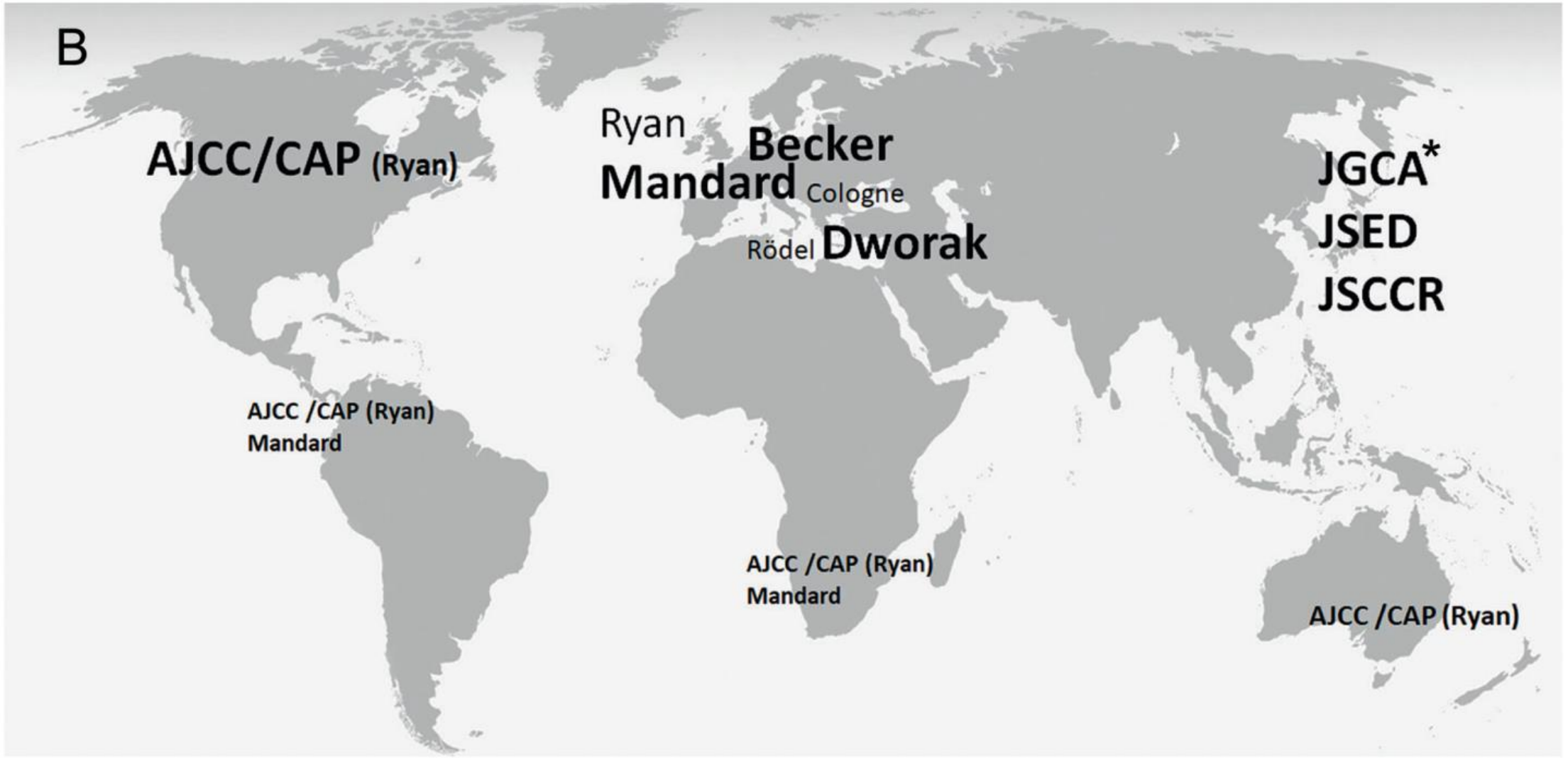
TRG in pathology practice

- Which TRG is used in daily practice is highly variable
- Histologic work-up is highly variable

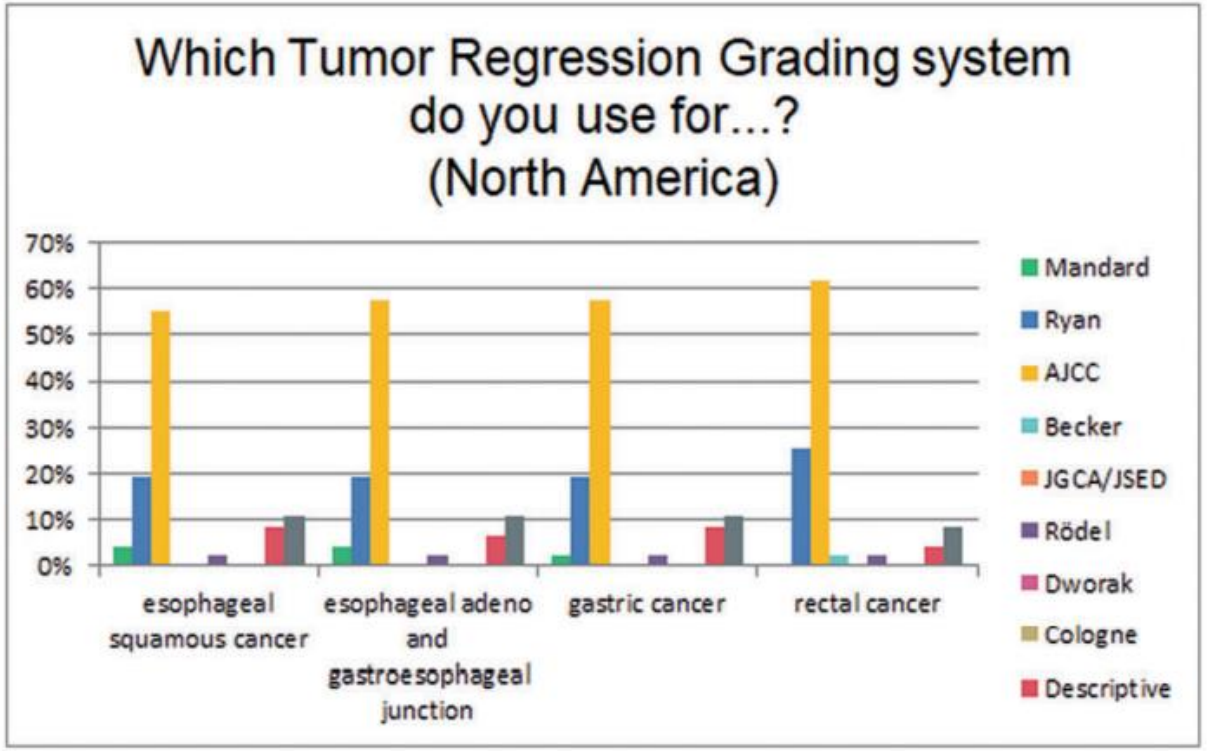
Descriptive	Mandard	AJCC	Becker	JGCA/JSED	Rödel	Dworak	Cologne	Köbel
Complete: NO tumor cells	1	0	1a	1	4	4	4	3
Subtotal	2	1	1b	2	3	3	3	2/3
Partial	3	2	2	3	2	2	2	2
Minimal regression	4	3	3	4	1	1	1	1
No regression/ abscence of regressive changes	5				0	0		1



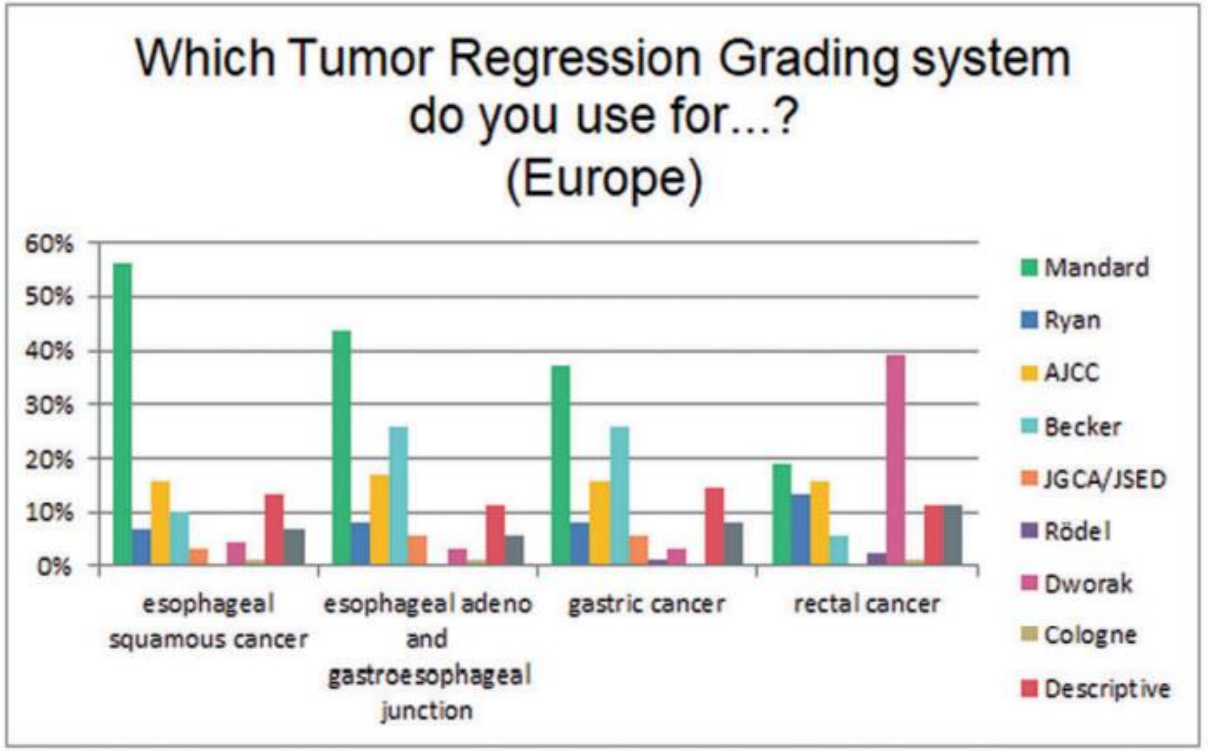
Westerhoff M et al. « Varying practices in tumor regression grading of gastrointestinal carcinomas, international survey». Mod Pathol. 2020 Apr;33(4):676-689. doi: 10.1038/s41379-019-0393-7.


B
AJCC/CAP (Ryan)
Ryan
Becker
Mandard
Cologne
Rödel
Dworak
JGCA*
JSED
JSCCR
AJCC /CAP (Ryan)
Mandard
AJCC /CAP (Ryan)
Mandard
AJCC /CAP (Ryan)

C


Which Tumor Regression Grading system do you use for...? (North America)
70%
60%
50%
40%
30%
20%
10%
0%
esophageal squamous cancer
esophageal adeno and gastroesophageal junction
gastric cancer
rectal cancer
Mandard
Ryan
AJCC
Becker
JGCA/JSED
Rödel
Dworak
Cologne
Descriptive

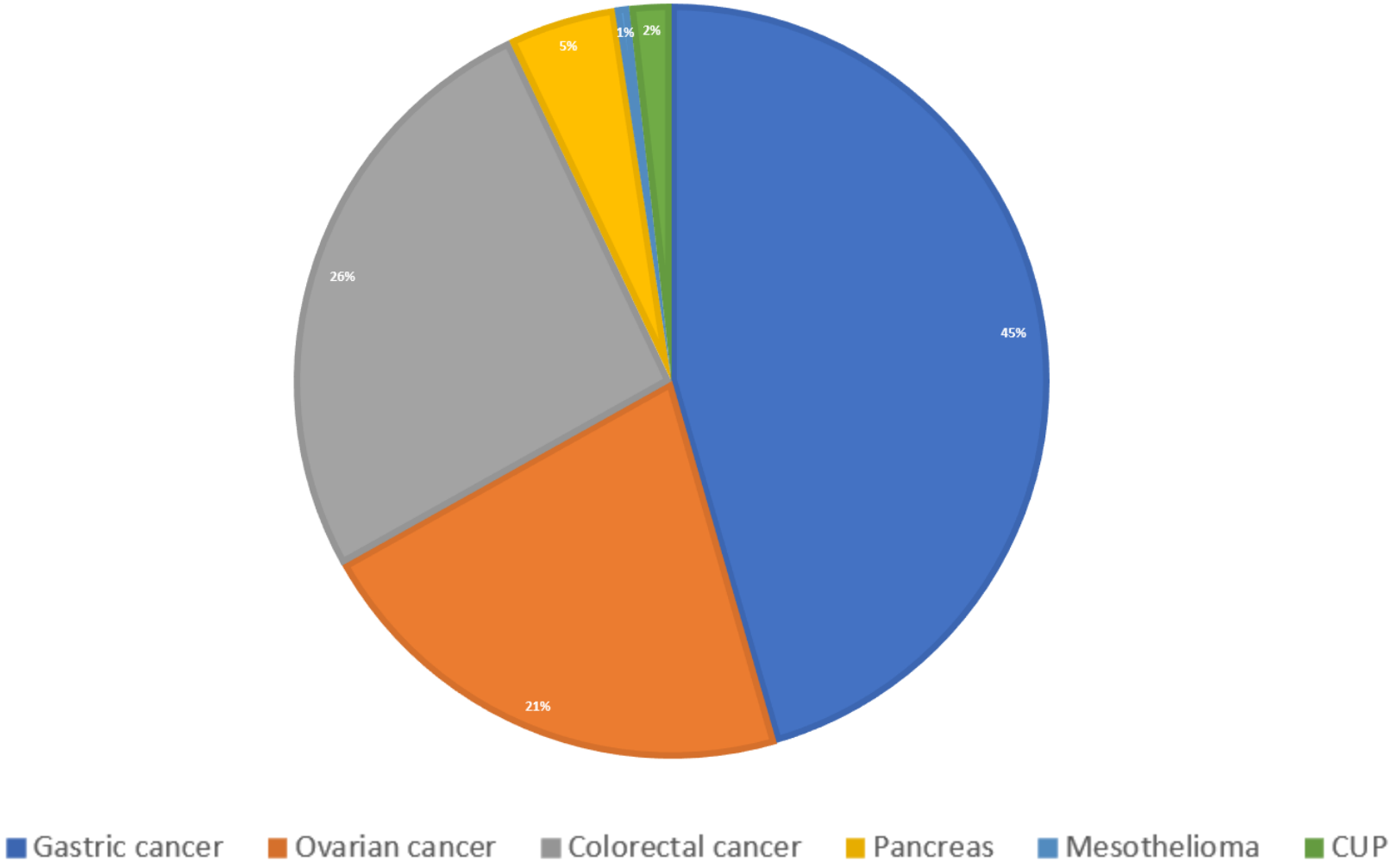
D


Which Tumor Regression Grading system do you use for...? (Europe)
60%
50%
40%
30%
20%
10%
0%
esophageal squamous cancer
esophageal adeno and gastroesophageal junction
gastric cancer
rectal cancer
Mandard
Ryan
AJCC
Becker
JGCA/JSED
Rödel
Dworak
Cologne
Descriptive

"Ideal" TRG

- Practicable in daily routine
- 4 tied score
- Document regressive features
- Amount of vital tumor

Origin of Peritoneal Metastasis



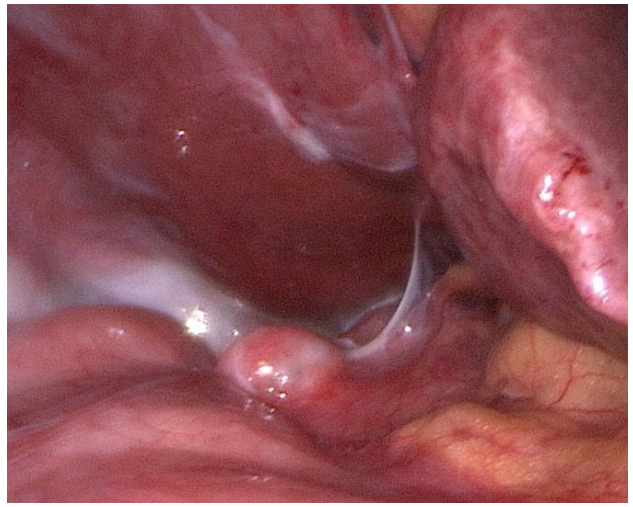
Peritoneal Regression Grading Score – PRGS

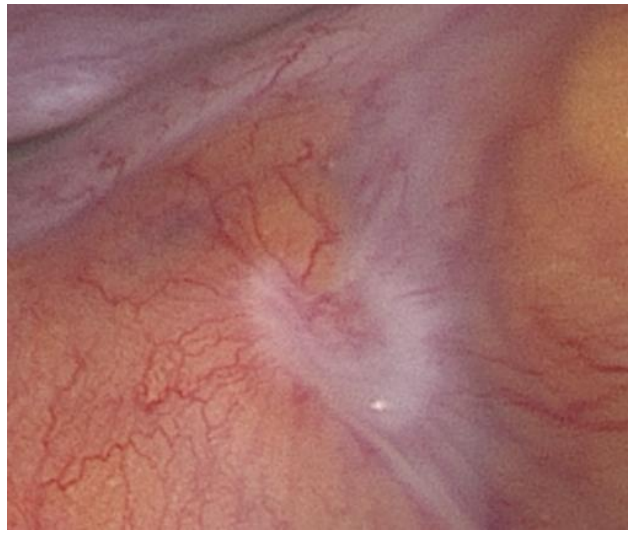
- Standardized Sampling
- Standardized Processing
- Standardized Reporting

Solass W, Sempoux C, Detlefsen S, Carr NJ, Bibeau F. Peritoneal sampling and histological assessment of therapeutic response in peritoneal metastasis: proposal of the Peritoneal Regression Grading Score (PRGS). Pleura Peritoneum. 2016 Jun 1;1(2):99-107. doi: 10.1515/pp-2016-0011.

Sampling

- The Peritoneal Carcinomatosis Index (PCI) should be documented
- At least 4 biopsies should be taken at macroscopic suspect lesions (1 / abdominal quadrant)
- Additional local peritonectomy
- Peritoneal cytology





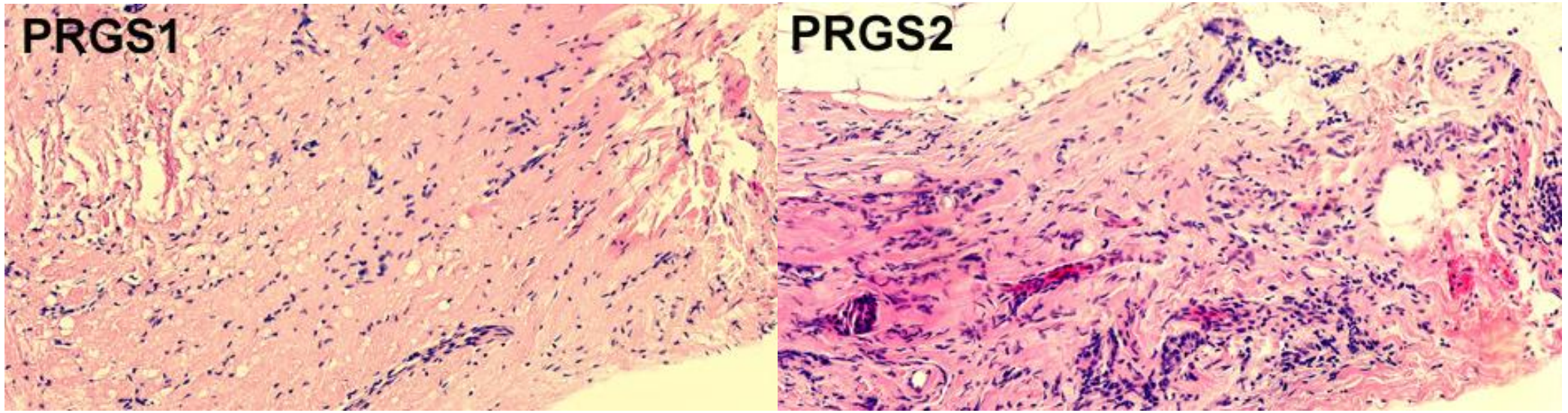
Processing

- Sample fixation (formalin for 24–48 hours)
- three-step sections are recommended
- Standard staining should be hematoxylin-eosin (HE)
- Immunohistochemical testing or molecular investigation may be needed in particular situations

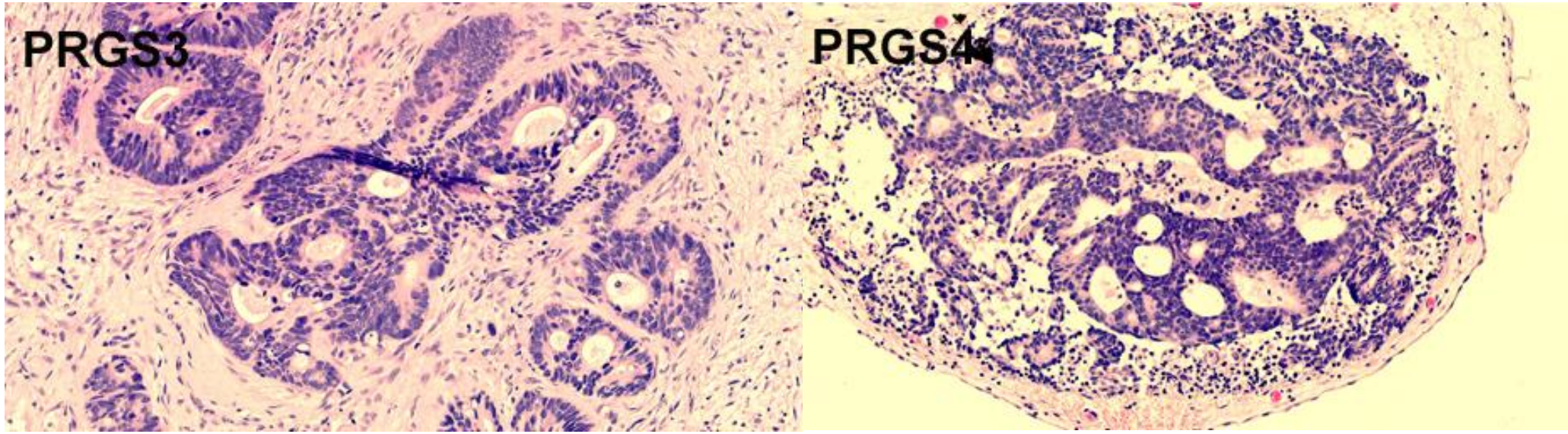
Peritoneal Regression Grading Score PRGS

Grade	Tumor cells	Regressive Features
PRGS 1 – complete Response	No tumor cells	Abundant fibrosis And/or acellular mucin pools And/or infarct like necrosis
PRGS 2- major response	Few tumor cells (isolated or small clusters)	Fibrosis And/or acellular mucin pools And/or infarct- like necrosis Predominant over tumor cells
PRGS 3 – minor response	Predominant tumor cells	Tumor cells predominat over fibrosis And/or acellular mucin pools And/or infact-like necrosis
PRGS 4 – no response	Visible tumor cells (at lowest magnification)	No regressive changes

Peritoneal Regression Grading Score PRGS



Peritoneal Regression Grading Score PRGS



PRGS

- Is a validated TRG with moderate to good/substantial interobserver agreement (1)
- And good to excellent/almost perfect in intraobserver agreement
- Additional stainings/immunohistochemistry helps in complex cases (2)
- Endpoint in multiple clinical trials worldwide
- Easy to handle

(1) Solass W et al. Reproducibility of the peritoneal regression grading score for assessment of response to therapy in peritoneal metastasis. Histopathology. 2019 Jun;74(7):1014-1024.

(2) Detlefsen S et al . Role of immunohistochemistry for interobserver agreement of Peritoneal Regression Grading Score in peritoneal metastasis. Hum Pathol. 2022 Feb;120:77-87.

Pathologist is the pilot of cancer surgery

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