

What is the Best Way to Assess Response to Therapy?

Is complete Pathologic Response the best surrogate?

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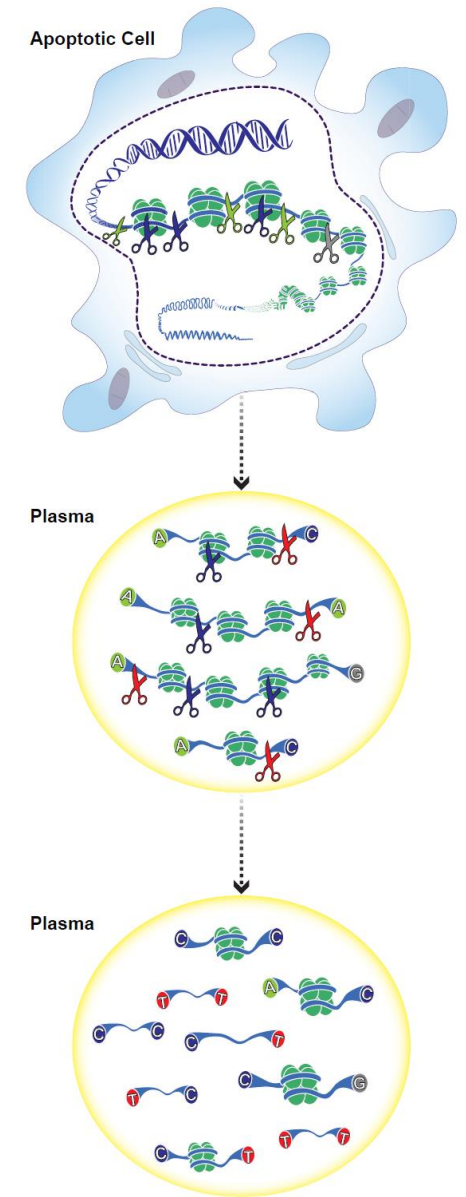
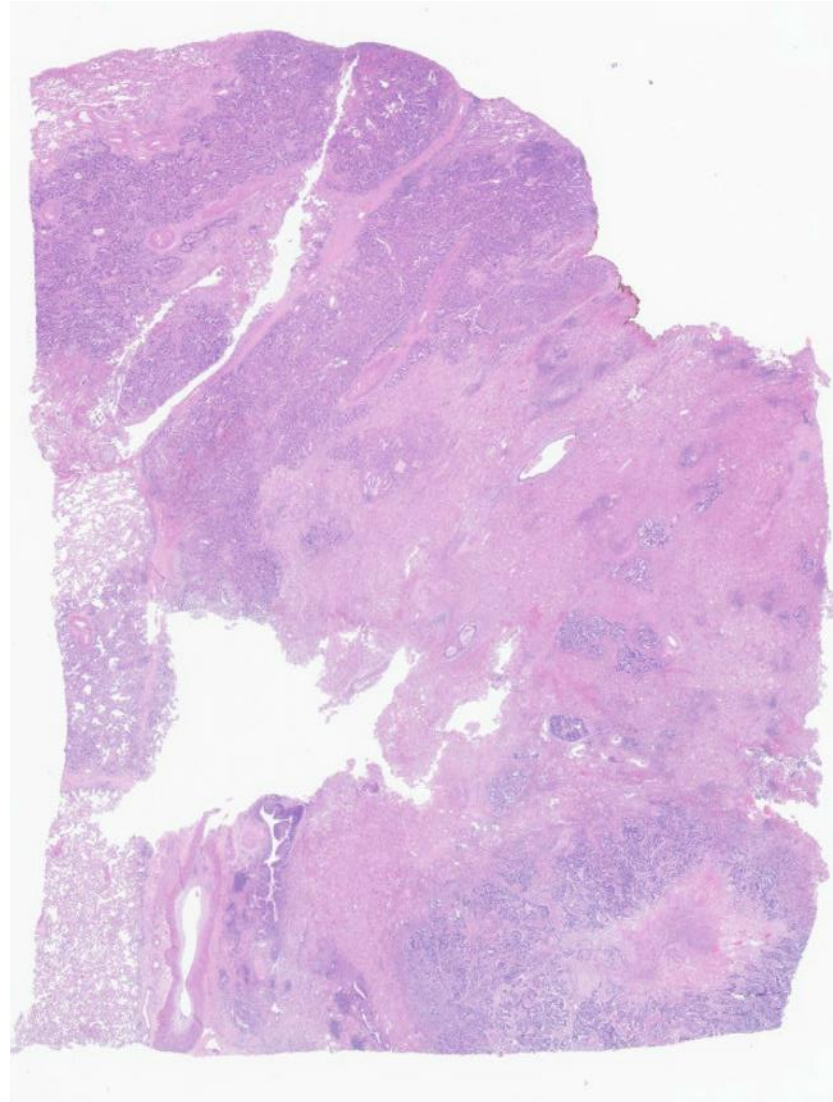
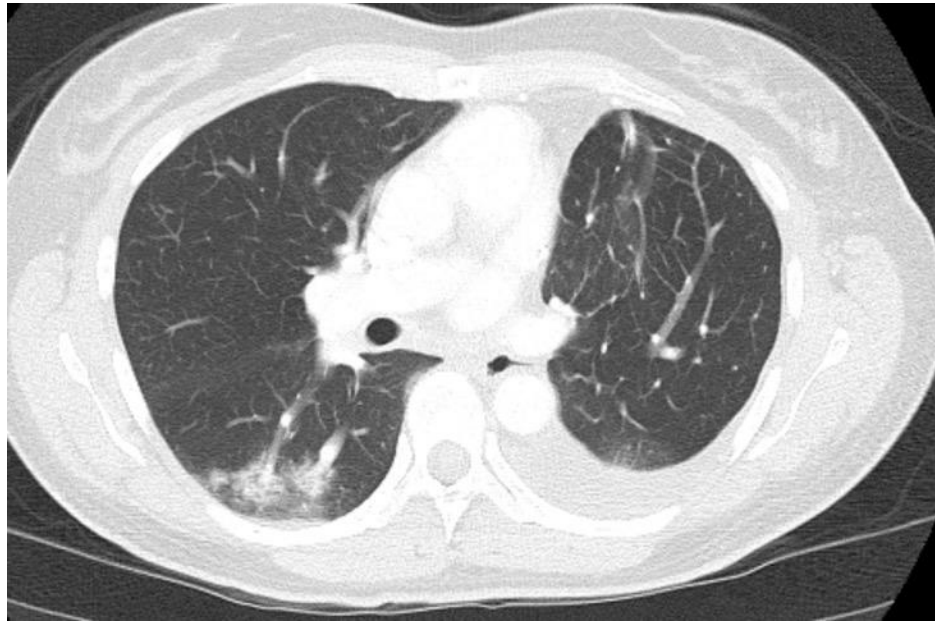
Director (Interim), Center for Advanced Molecular Diagnostics

Chief of Oncologic Pathology, Dana Farber Cancer Institute

Mass General Brigham Endowed Chair in Pathology

Associate Professor, Harvard Medical School





Radiology: confounded by treatment response patterns

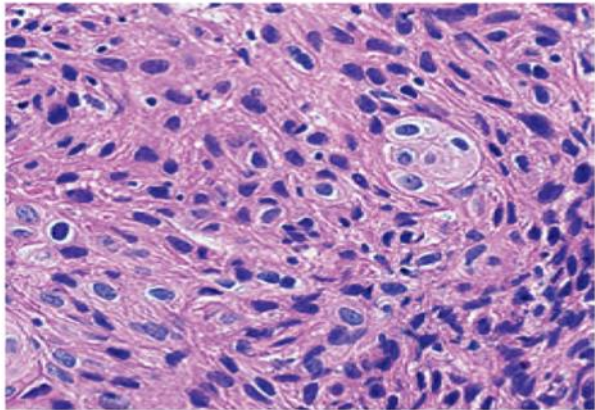
A Patient 1



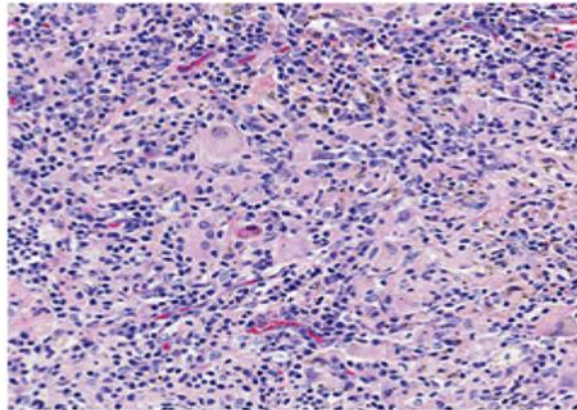
Pretreatment Imaging



Week 4 (before surgery)

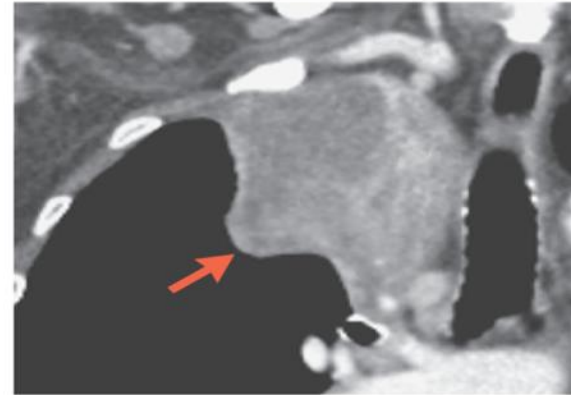


Pretreatment Tumor Biopsy

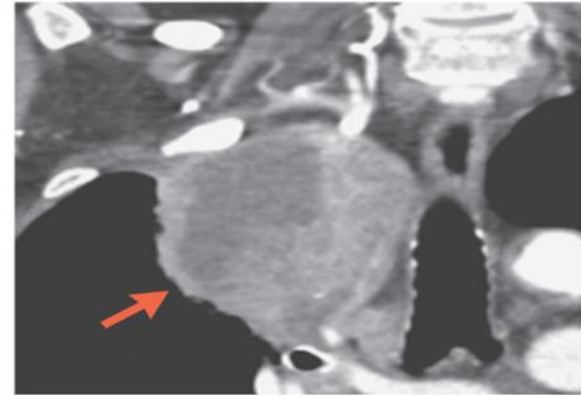


Resection Specimen

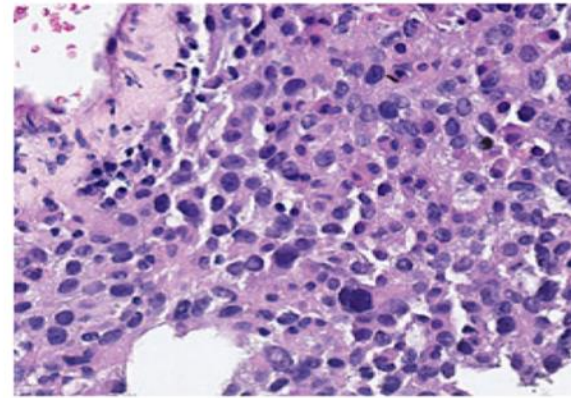
B Patient 5



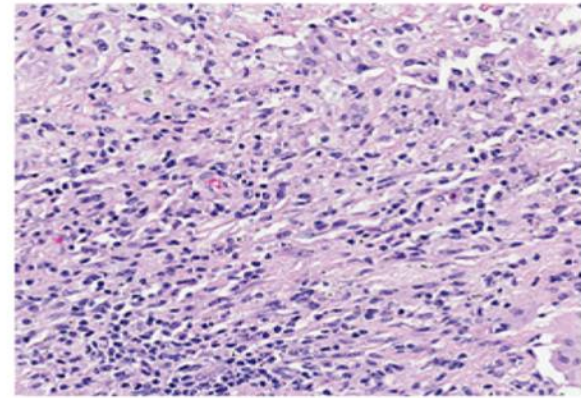
Pretreatment Imaging



Week 4 (before surgery)

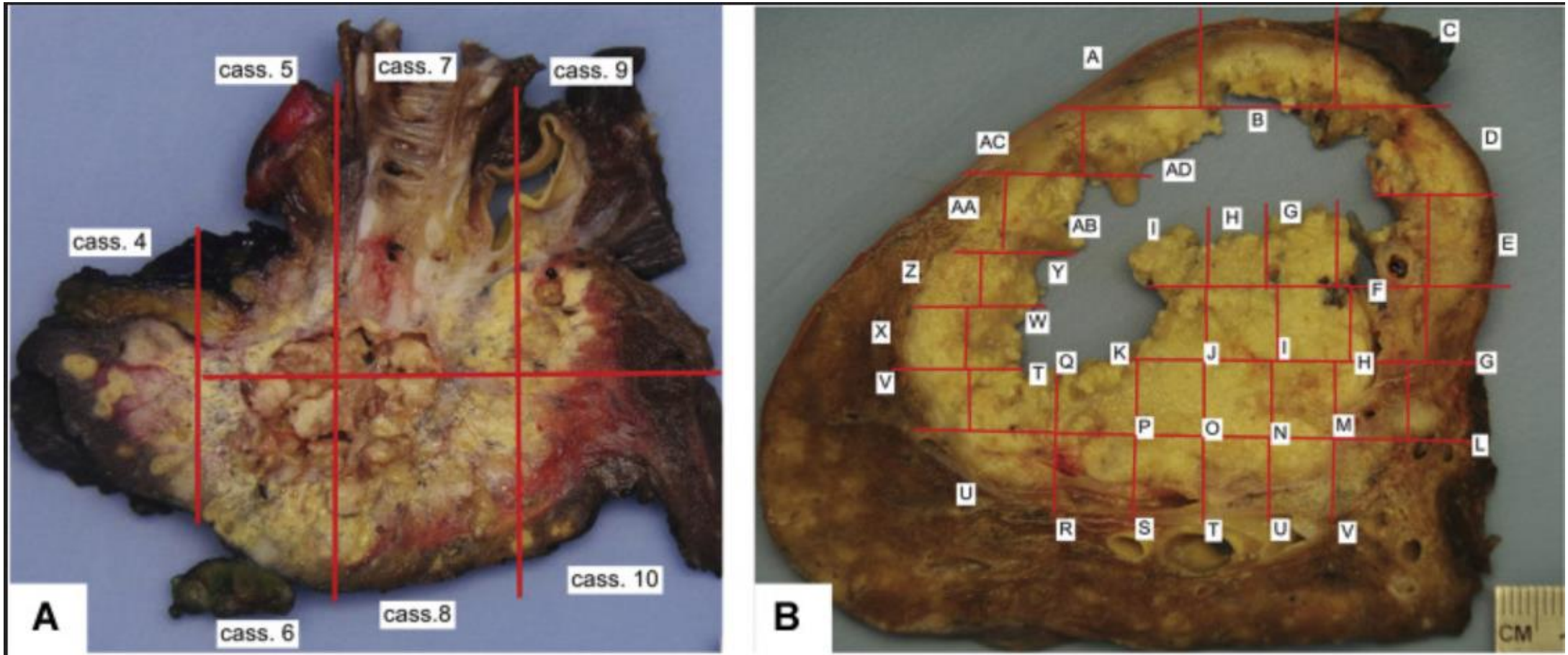


Pretreatment Tumor Biopsy



Resection Specimen

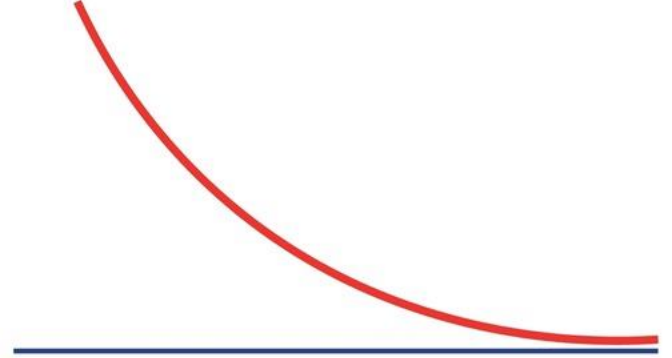
Pathologic response assessment: an exercise in standardization.



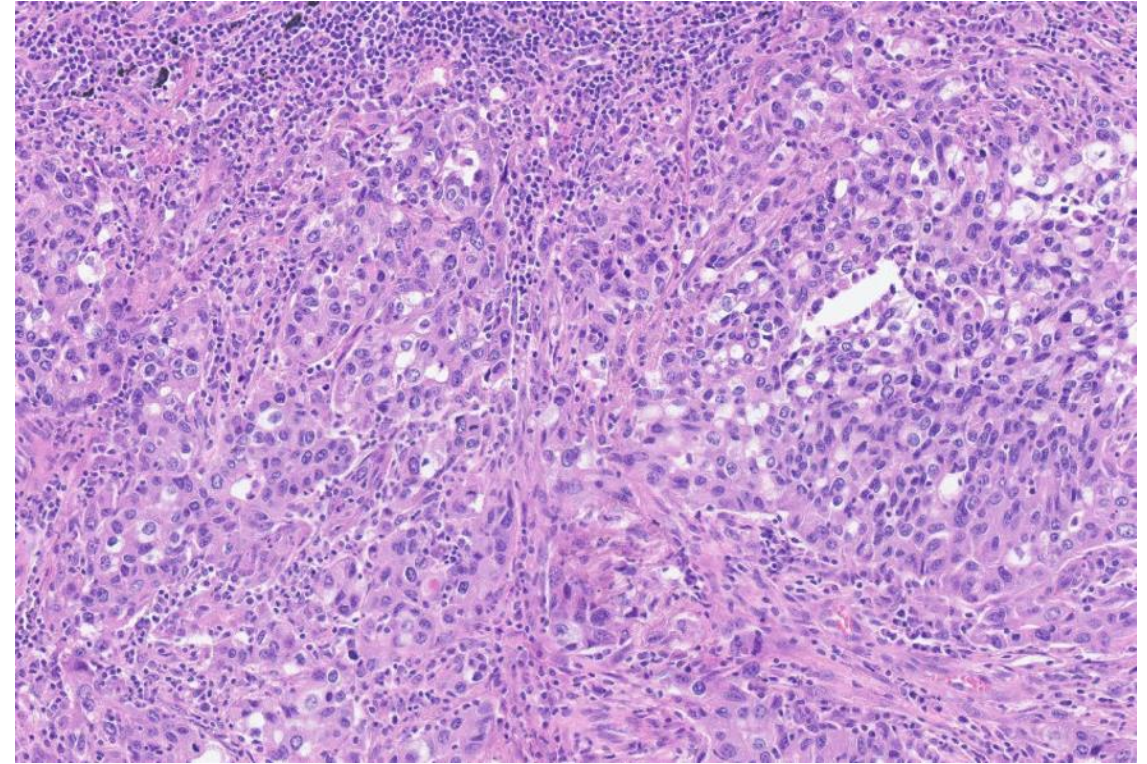
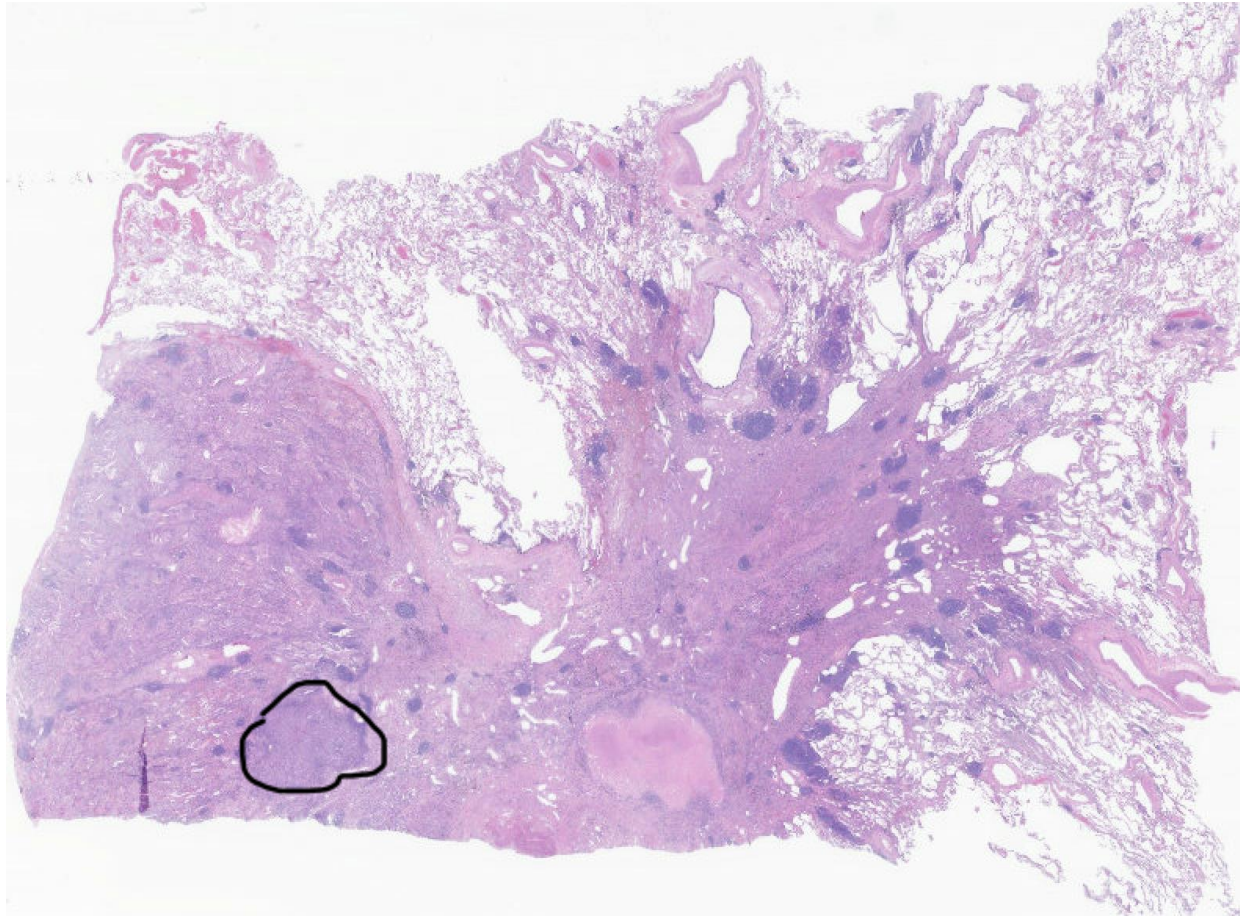
Histopathology: Limited in sensitivity and precision



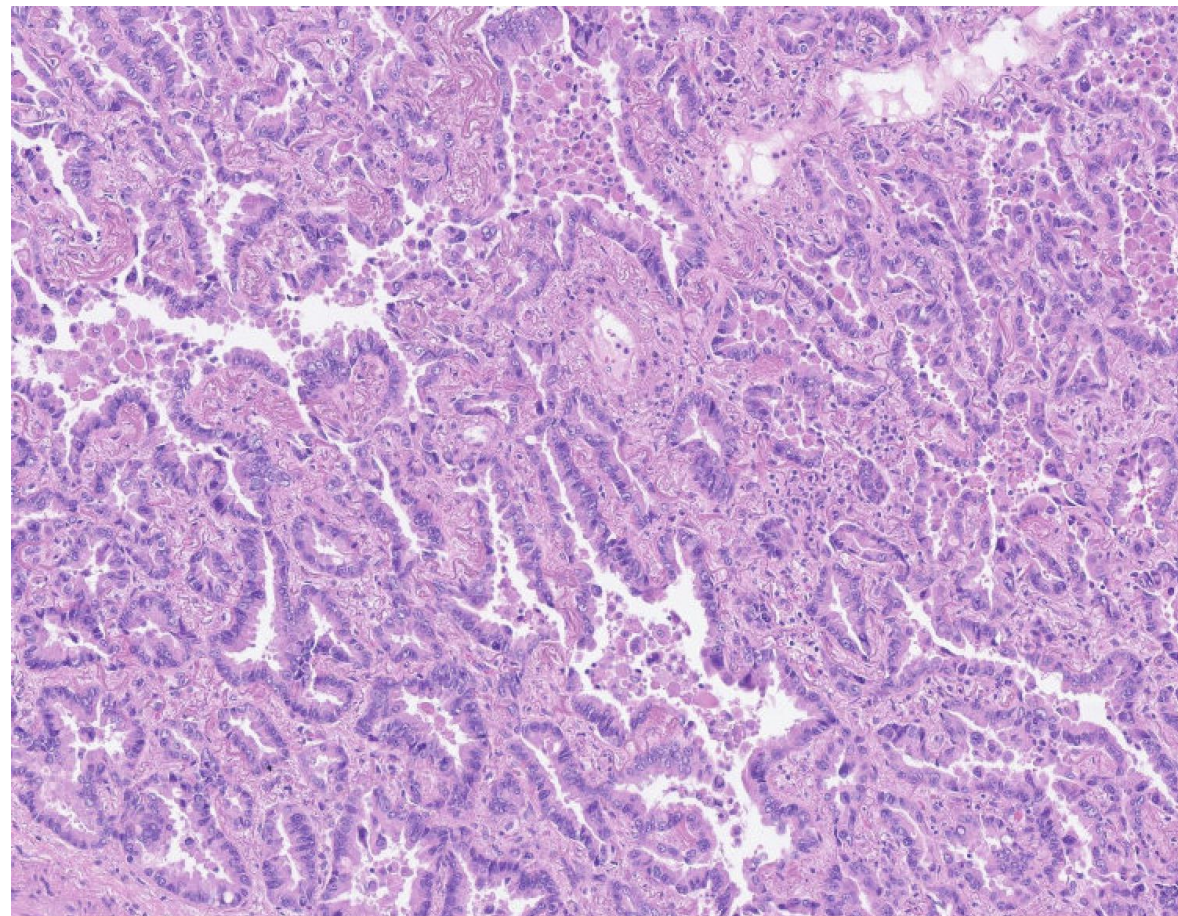
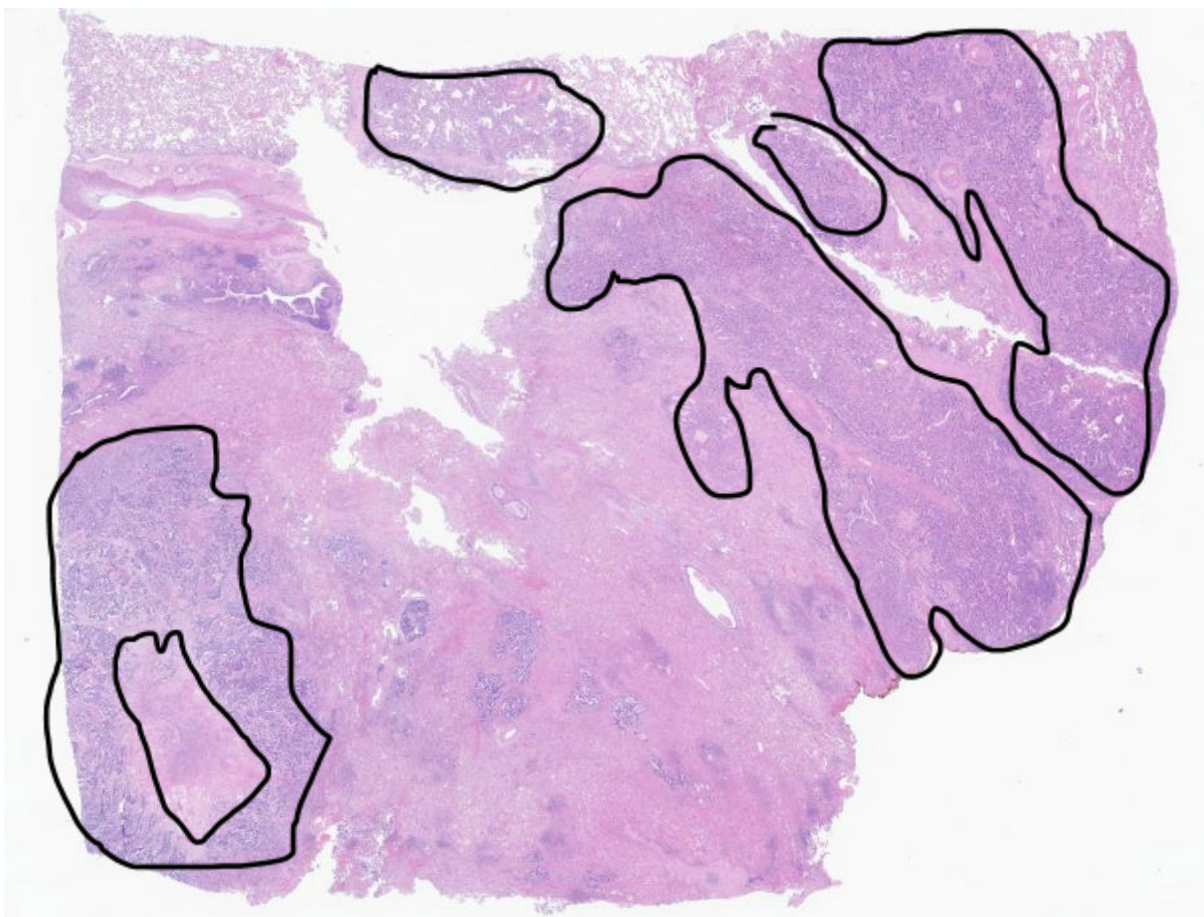
Wikimedia Commons



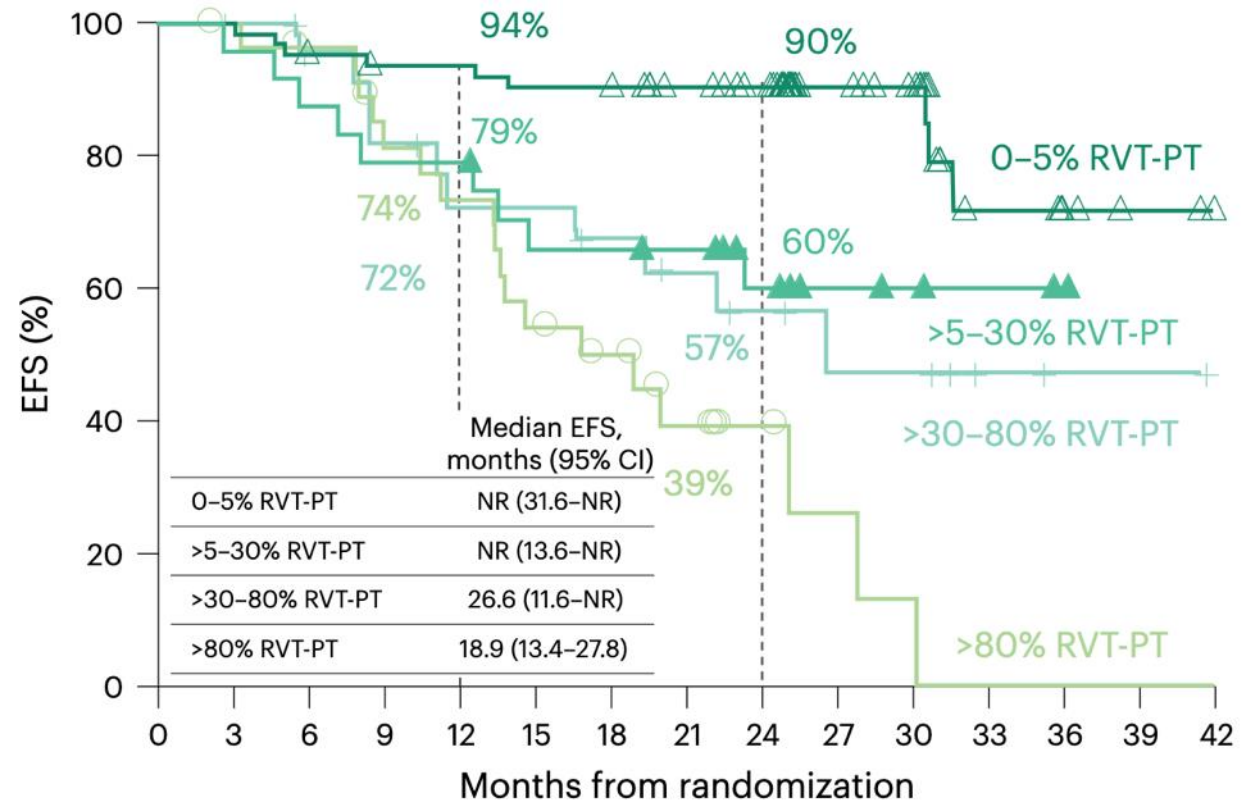
MPR



Not MPR



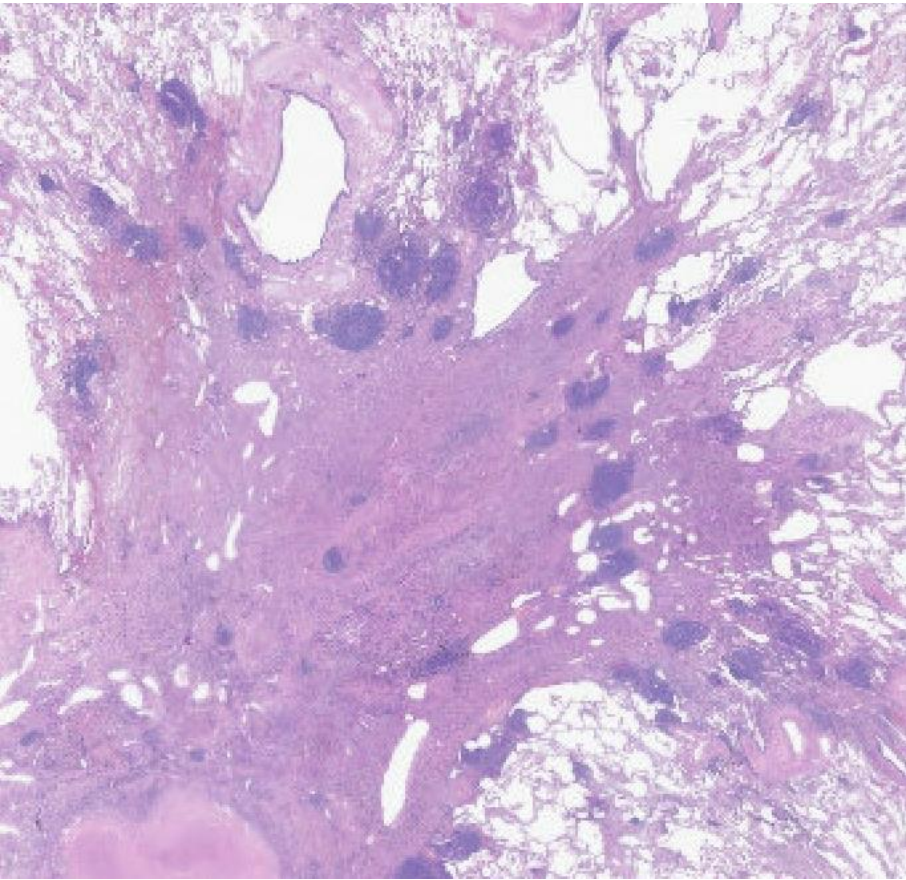
Checkmate 816: EFS at incremental RVT cutpoints



No. at risk

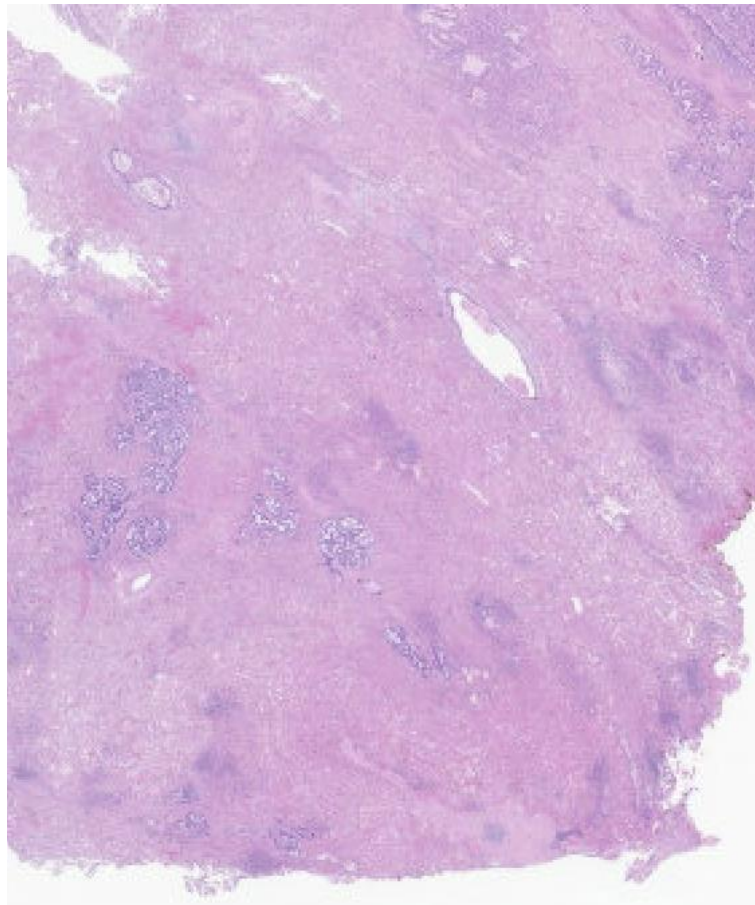
63	63	59	57	57	55	55	50	46	26	21	9	4	2	0
24	23	21	19	19	15	15	14	10	5	4	2	1	0	0
25	24	21	18	15	15	13	11	9	5	5	2	1	1	0
29	28	26	22	19	14	11	7	4	2	1	0	0	0	0

Tumor response assessment: can it be more than tumor + necrosis + stroma %?

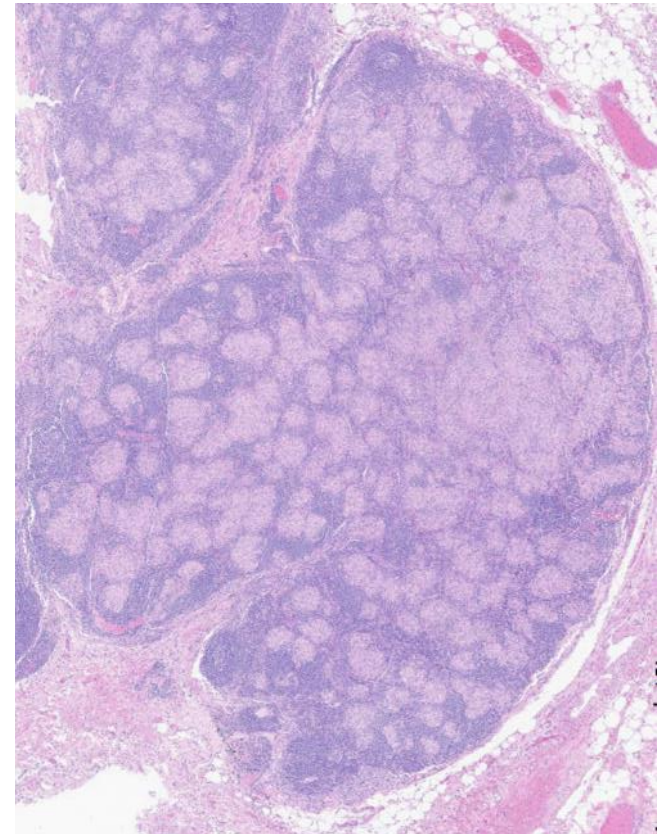


TLS's

vs

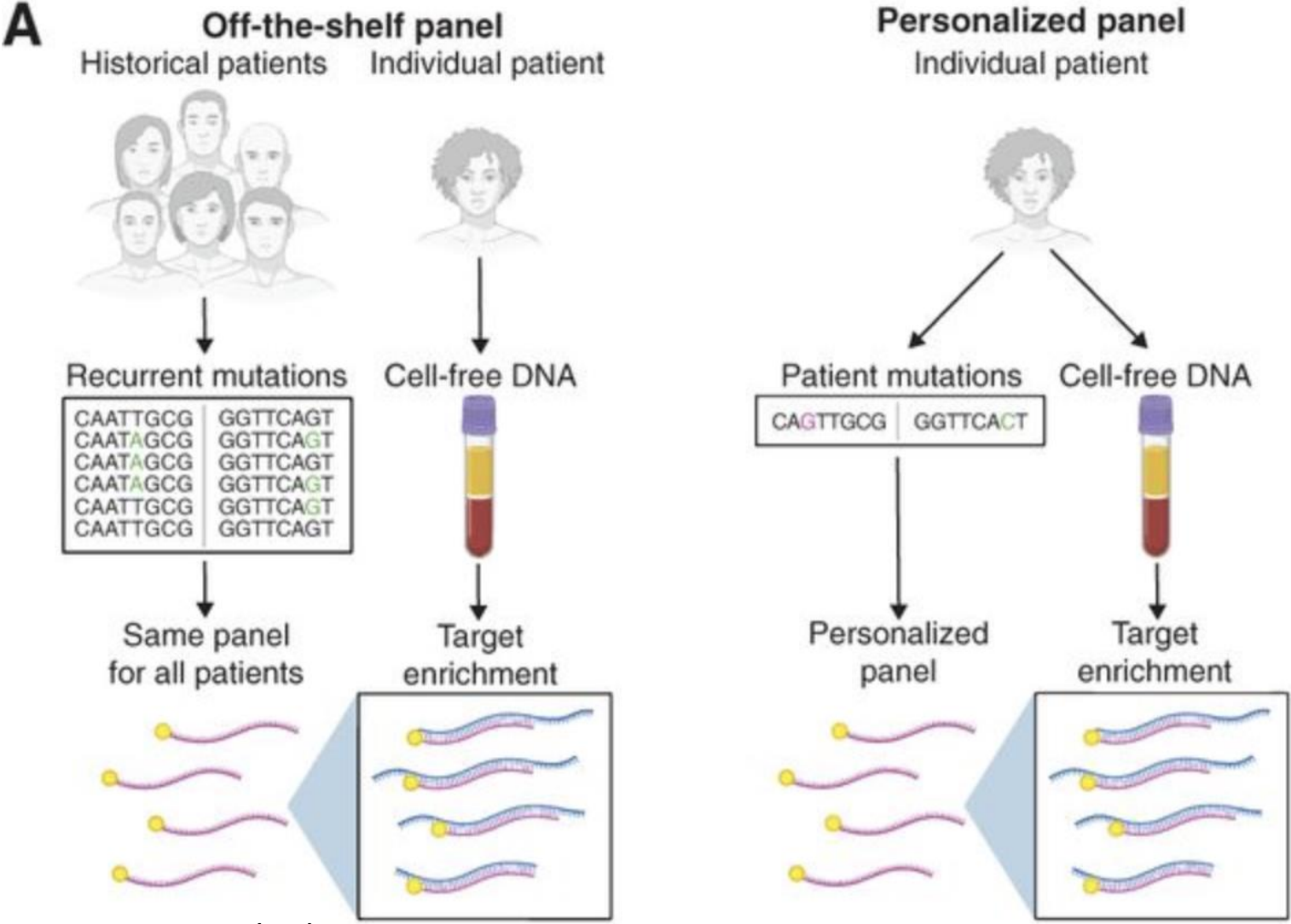


No TLS's

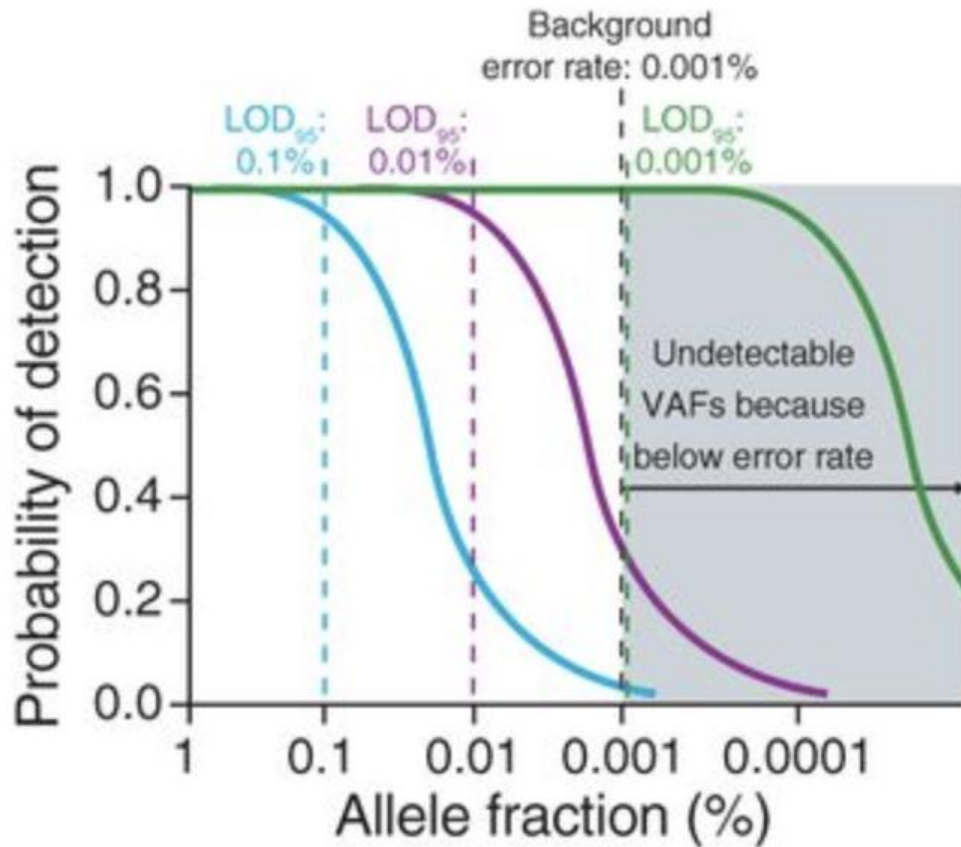


"sarcoidal response" in lymph nodes

Tumor agnostic vs Bespoke cfDNA for MRD



Sensitivity challenges remain... technical specs for available commercial tests unclear.



	Mutations	cfDNA Input	Depth
—	+	+	+
—	++	++	++
—	+++	+++	+++

Unanswered questions

- What is the right cutpoint for defining MPR?
- And is our standard sampling strategy the right one?
- Can we explain recurrences in patients with pCR?
- Can assessment of the TME further inform response outcomes?
- When and how should plasma cfDNA testing be used post-op?