

LIFEFEST 2026

Nashville



**SDH Research and Clinical Trials
Clinical and Translational Research at the NIH
for SDH-Deficient Gastrointestinal Stromal Tumors**

Dr. Andrew Blakely

Clinical and Translational Research at the NIH for SDH-Deficient Gastrointestinal Stromal Tumors

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Surgical Oncology Program

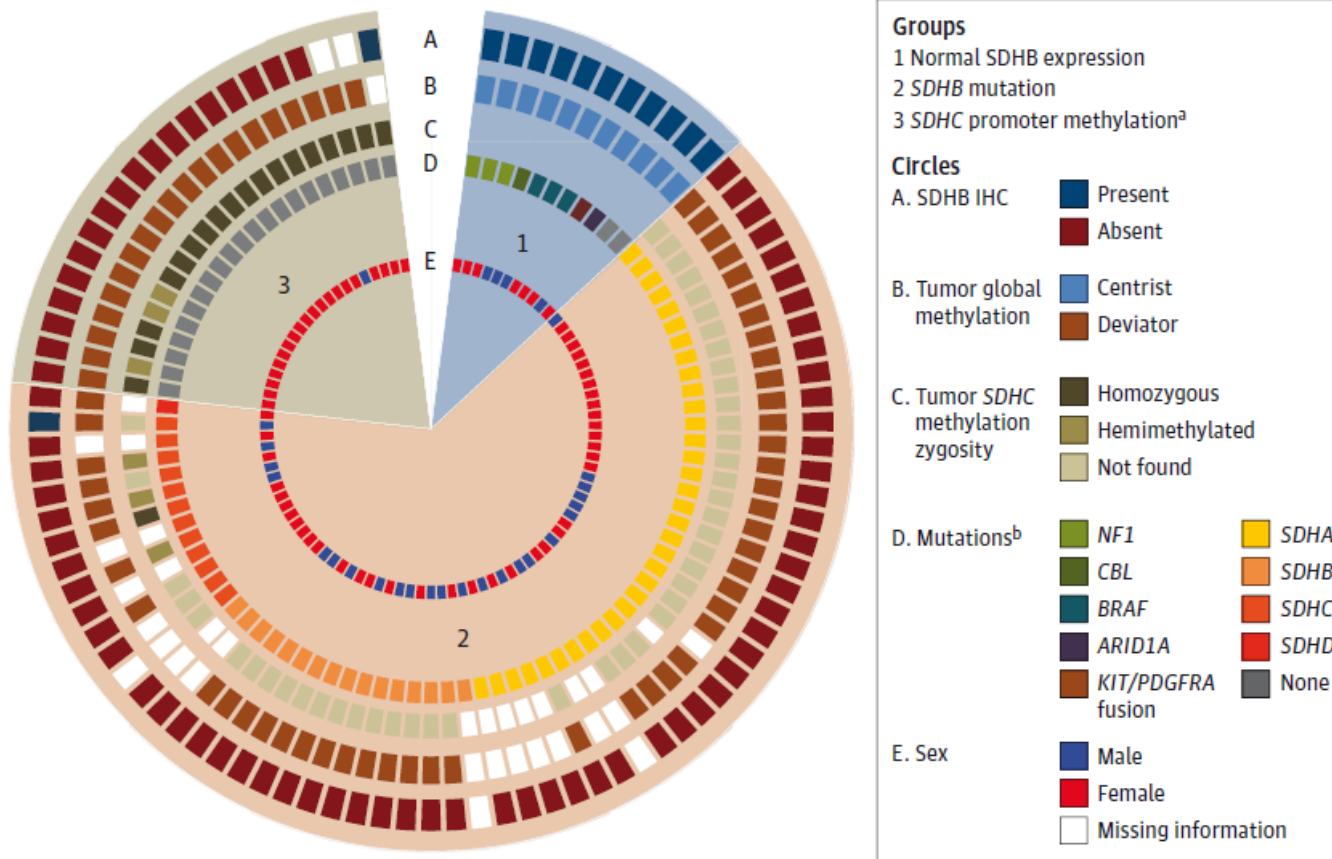
National Cancer Institute

National Institutes of Health

July 11, 2026



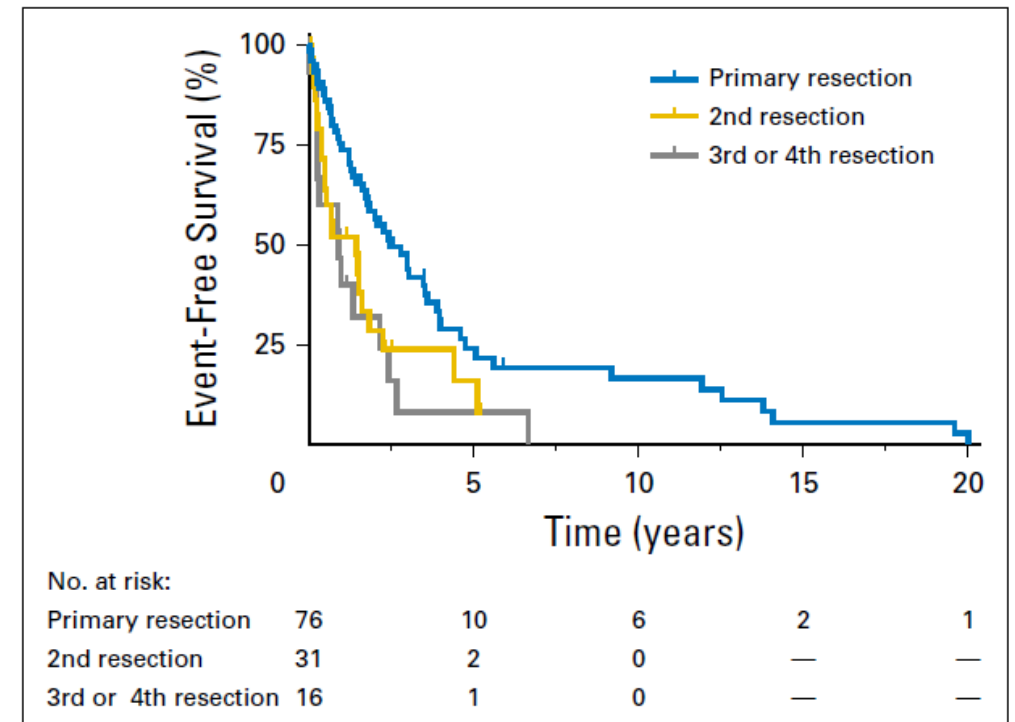
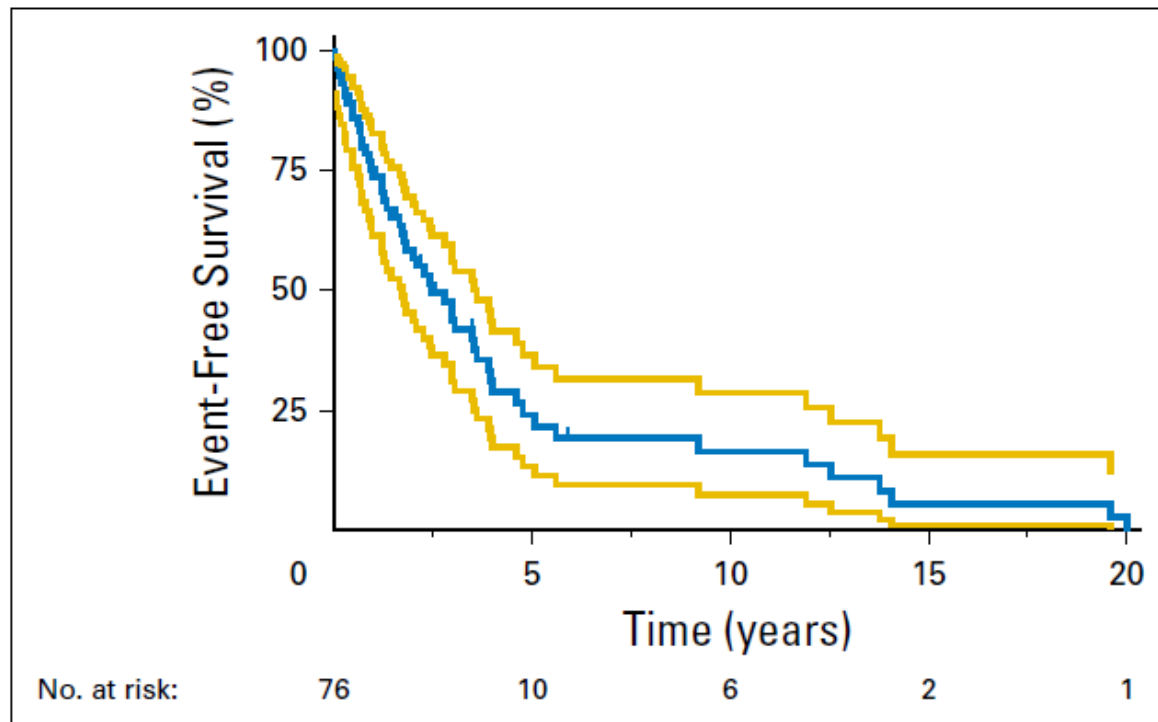
NIH History: Pediatric and WT GIST Clinic



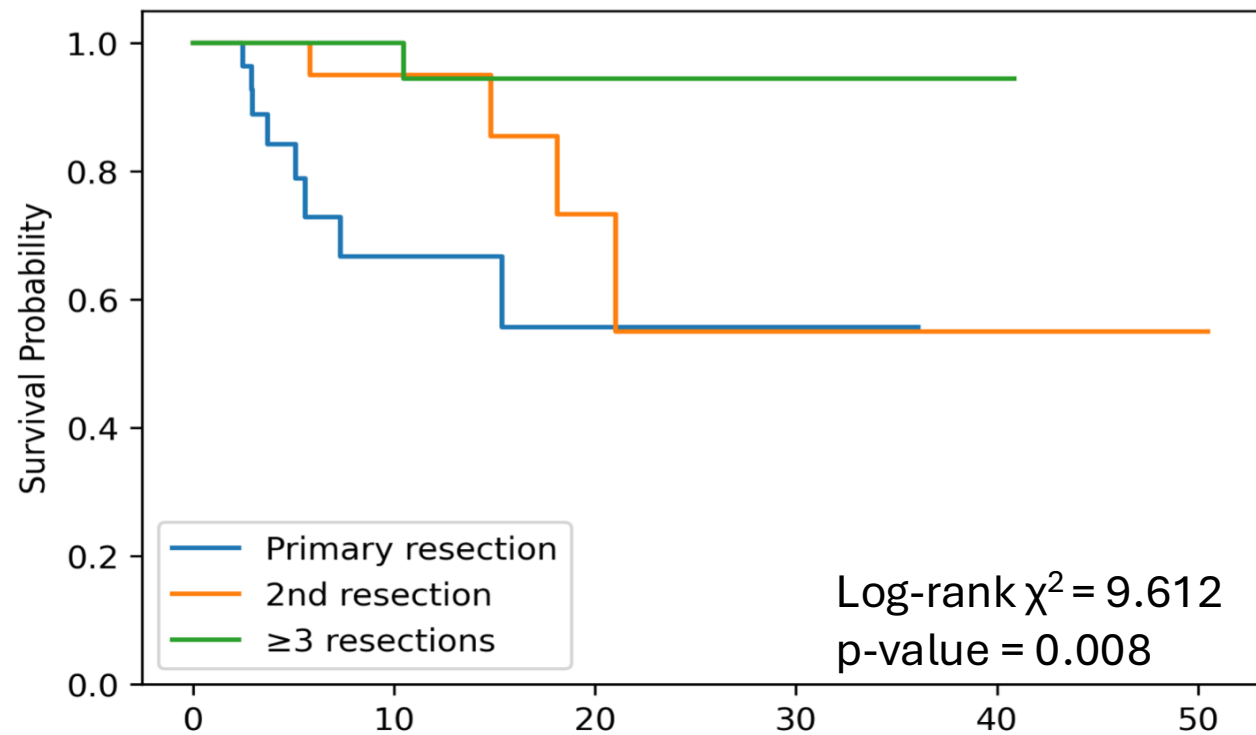
Characteristic	All Patients (n = 95)
Age, median (range), y ^a	23 (7-78)
Female sex, No. (%) ^b	66 (70)
Tumor size at resection, median (range), cm	5.6 (1.5-21)
Focality, proportion (%) ^{c,d}	
Unifocal	47/83 (57)
Multifocal	36/83 (43)
Primary location, No. (%) ^e	
Gastric	85 (89)
Small bowel	9 (9)
Abdominal	1 (1)
Histologic subtype, proportion (%) ^{d,f}	
Epithelioid	32/90 (36)
Spindle	20/90 (22)
Mixed	38/90 (42)
Metastasis at presentation, proportion (%) ^d	
Liver	19/87 (22)
Peritoneum	8/87 (9)
Lymph nodes	18/35 (51)
No liver or peritoneal metastases at presentation, proportion (%) ^d	62/87 (71)



NIH History: Pediatric and WT GIST Clinic



NIH Update: Pediatric and WT GIST Clinic



Estimated Mean Overall Survival $\pm$ SD (years)	
Primary resection	23.32 $\pm$ 3.64 95% CI [16.19 - 30.44]
2 nd resection	35.51 $\pm$ 6.09 95% CI [23.58 - 47.44]
≥ 3 resections	39.16 $\pm$ 2.88 95% CI [35.95 - 42.38]

No. at risk:

Primary resection	32	9	3	3	0	0
2 nd resection	26	15	4	3	1	1
≥ 3 resections	22	18	8	1	1	0



Clinical Trial NCT04557969:

Surgery in Gastrointestinal Stromal Tumors (GISTs) for
Treatment, Tumor Modeling, and Genomic Analysis

PI: Andrew M. Blakely, M.D.

Open, Recruiting



Clinical Trial Specifics

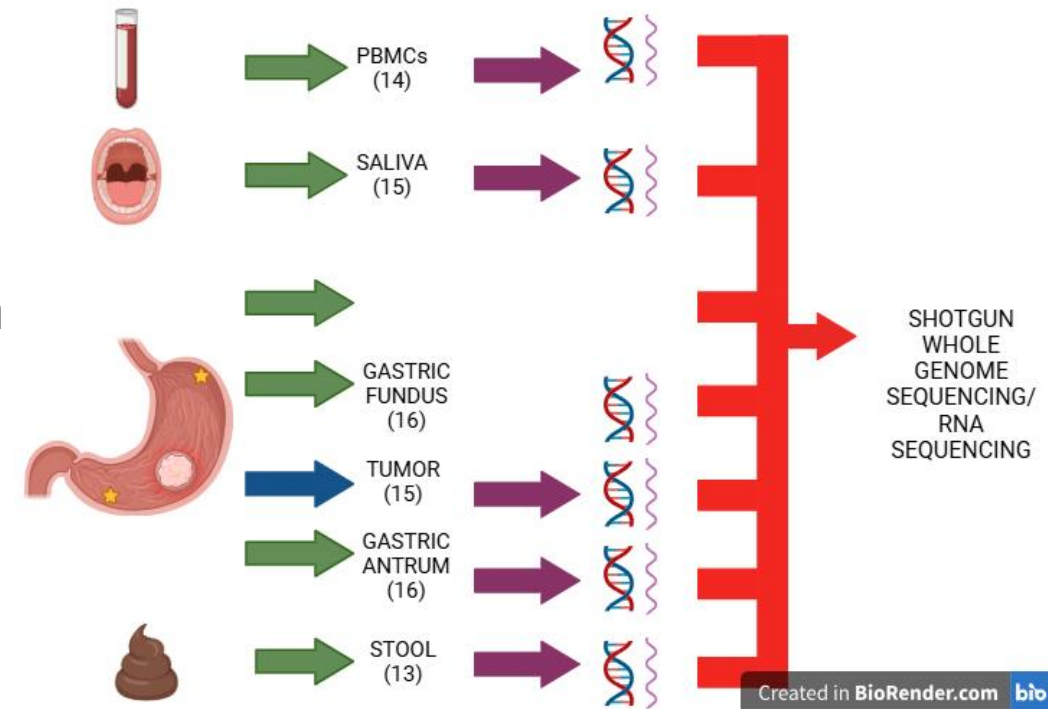


- Natural history study
- Eligibility: Suspicion of or confirmed GIST diagnosis
- Ineligibility: Medical condition that precludes surgery
- Accrual goal: 400 patients over 10 years
- Various biospecimens collected
- Tissue processing begins in the OR
 - Targeted tissue harvesting
 - Minimal warm ischemic time
 - Portion of normal adjacent tissue also taken



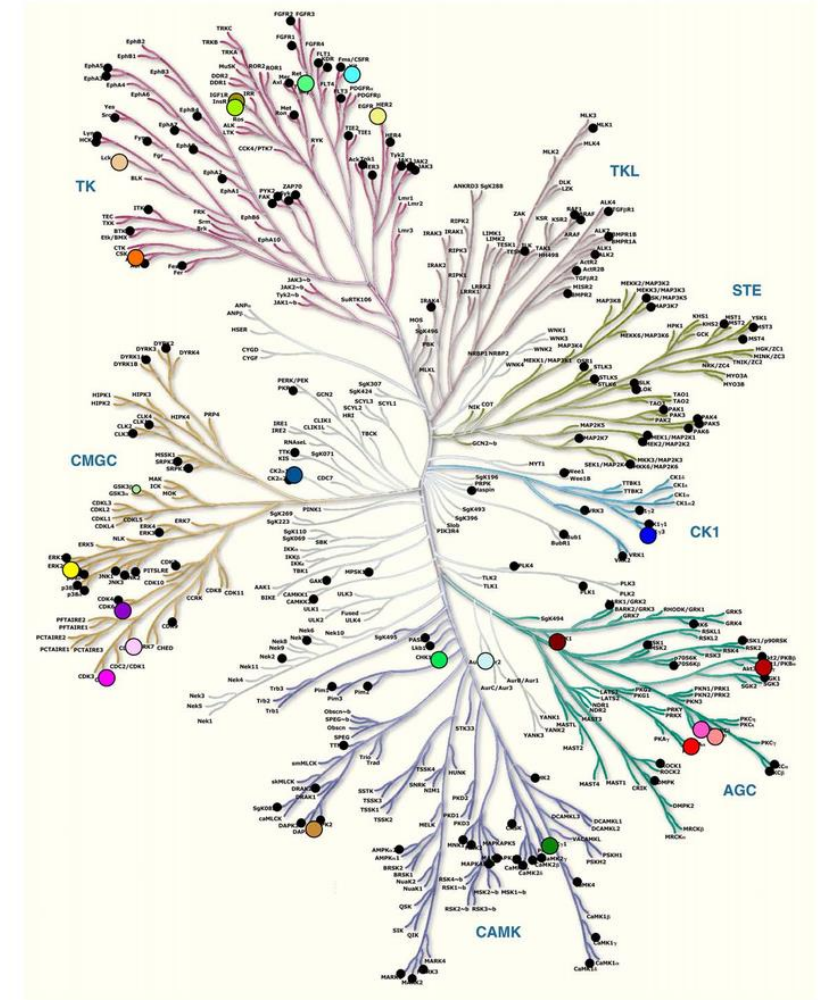
Microbiome Assessment

- Added into the protocol as of September 2023
 - Close to 100 patients so far
- Pre-operative: blood, saliva, stool
- Intra-operative EGD: lavage, fundus, antrum
 - All patients, after induction, prior to antibiotics
- Post-operative at 1 year: blood, saliva, stool
- Dietary questionnaires at both time points



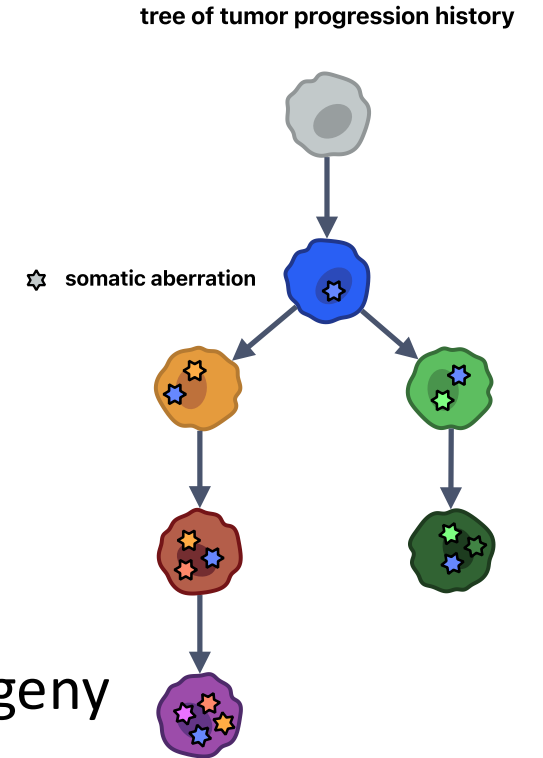
Translational Research Initiatives

- (Phospho)proteomics assessment spanning mutational subtypes
 - Short warm ischemic time (~7 minutes) minimizes degradation of phosphorylation prior to snap freezing and later analysis
 - Research initiatives to identify similarities and differences in serine/threonine and tyrosine kinases across GIST subtypes



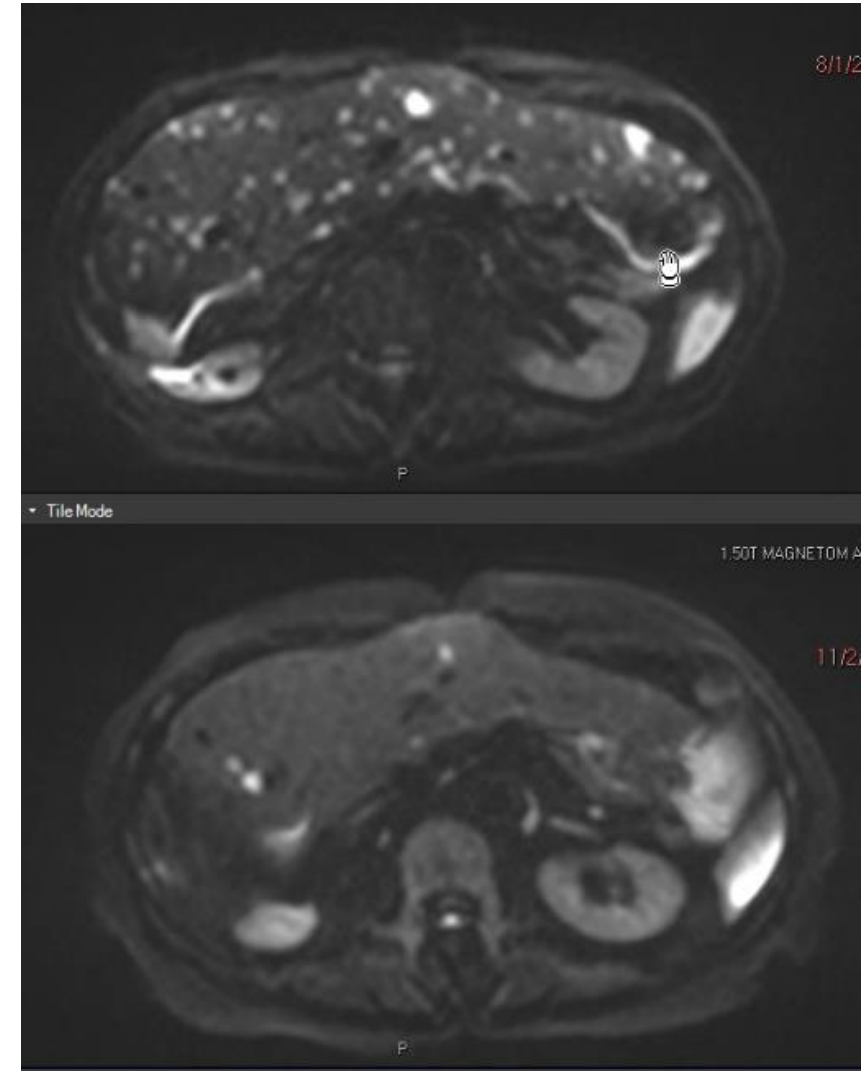
Translational Research Initiatives

- Range of primaries and variety of metastases
- Move beyond genomic heterogeneity to:
 - Tumor clonality: whole-exome seq and methylation for phylogeny
 - Multi-omics assessment: spatial transcriptomics, proteomics, ? metabolomics to identify changes associated with stability versus progression



Clinical Research Initiatives

- Updated assessment of the NIH Pediatric and Wild-Type GIST Clinic
- International collaborations to develop driver-specific recurrence risk nomograms
- Outcomes of liver debulking for SDH-def GIST
- GIST subtype-specific outcomes of peritoneal and hepatic cytoreduction



A Word about Surgery

- The treatment frontier for SDH-deficient GIST is expanding
 - Surgery remains a mainstay of treatment
 - Candidacy for surgery expands with effective systemic treatment
- Everyone deserves at least a couple surgical opinions
 - Dynamic assessment that changes in the context of time and treatment
 - Tailoring treatment to the individual is critical to optimize outcomes

Thank You

Surgical Oncology (NCI)

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