2025 ASCO® ANNUAL MEETING

Detecting ctDNA using personalized structural variants to forecast recurrence in localized soft tissue sarcoma

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KEY TAKEAWAY POINTS

1

Detection of ctDNA using tumor-informed assays using structural variants (SV) was feasible and highly sensitive in resectable STS.

2

Positive ctDNA within the MRD window (8 weeks post-op) was associated with subsequent and earlier radiologic relapse.

3

MRD positivity should be evaluated as a predictive biomarker to better select patients for adjuvant systemic therapy.

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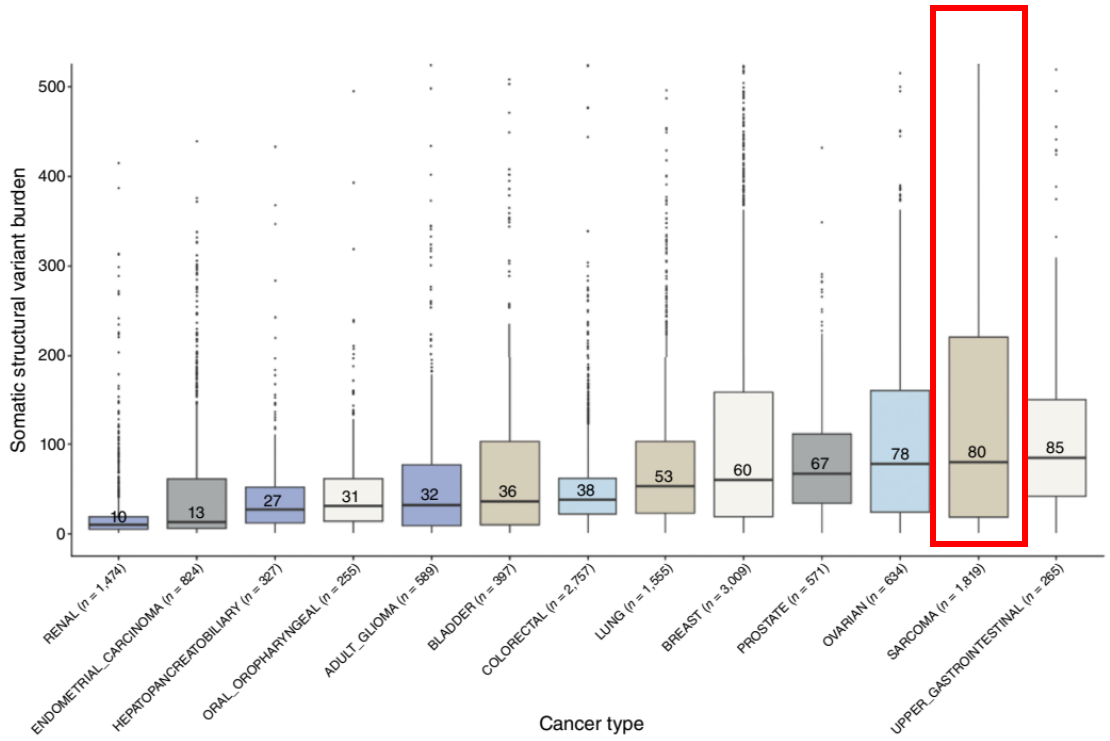
BACKGROUND

- Standard treatment for localized STS is surgery and (neo)adjuvant radiotherapy
- Up to 50% of patients with treated localized STS develop disease recurrence
- Benefit of adjuvant systemic therapy in the unselected population remains controversial
- ctDNA is a promising biomarker for MRD but the optimal modality of ctDNA detection in STS is unknown
- Among solid tumors, STS have high prevalence of genomic structural variants (SVs)



Elliott et al. Clin Cancer Res. 2025

Research Question: Can we detect ctDNA using tumor-informed structural variants to identify MRD in localized STS?

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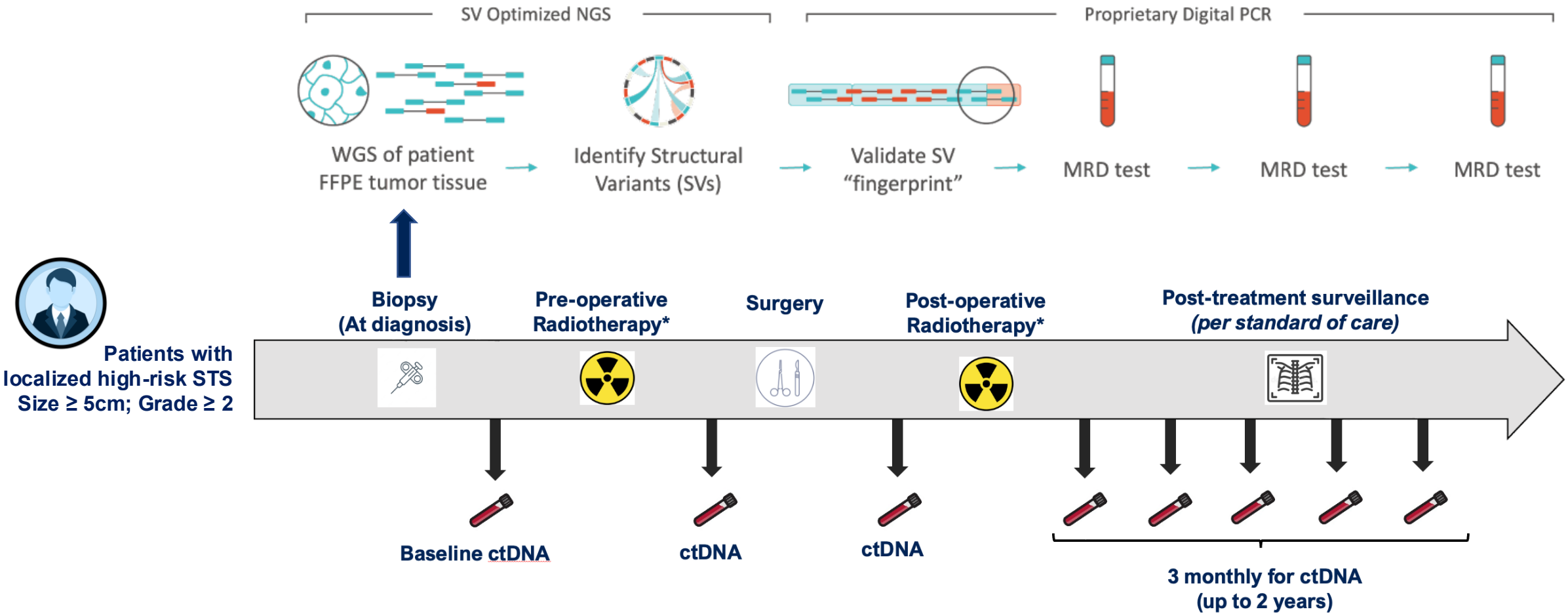
STUDY SCHEMA



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RESULTS

Patient characteristics

- 32/33 patients (97%) passed QC
  (1 patient had <4 validated SVs)
- Median of 14 SV used per fingerprint
  (range: 4-16)
- 228 plasma samples analyzed

Demographics (n=32)	
Age	
Median, years (Range)	64 (21-84)
Gender	
Male	15
Female	8
Histology	
Myxofibrosarcoma	12
Undifferentiated Pleomorphic Sarcoma	10
Dedifferentiated Liposarcoma	6
Pleomorphic Liposarcoma	2
Myxoid Liposarcoma	1
Leiomyosarcoma	1
Size of tumour at resection	
Median, cm (Range)	11.9 (4.1-38.9)
Location	
Trunk	7
Limb	24
Retroperitoneal	1
Grade	
2	15
3	17
Duration of follow-up	
Median, months (Range)	20.1 (7.6-28.7)

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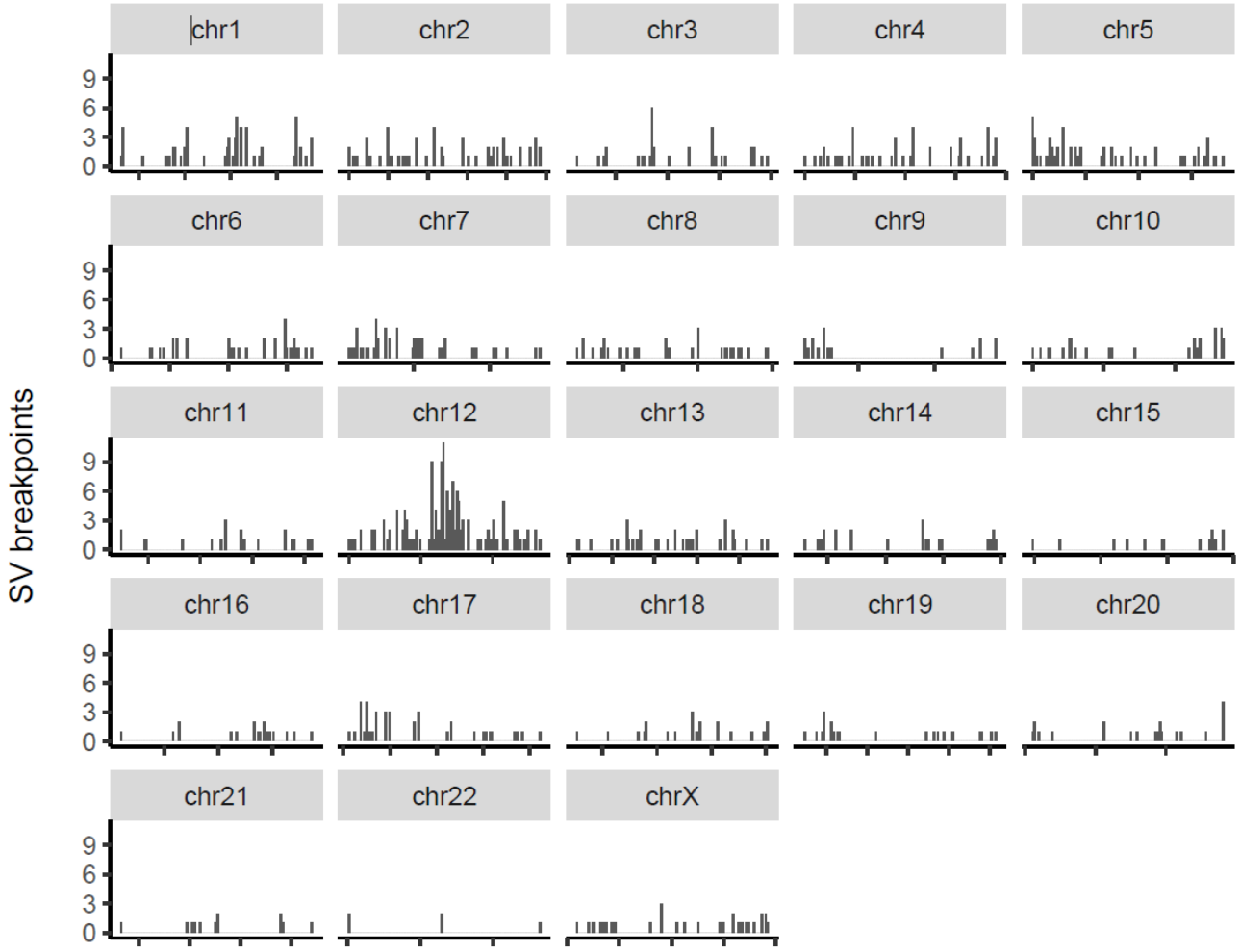
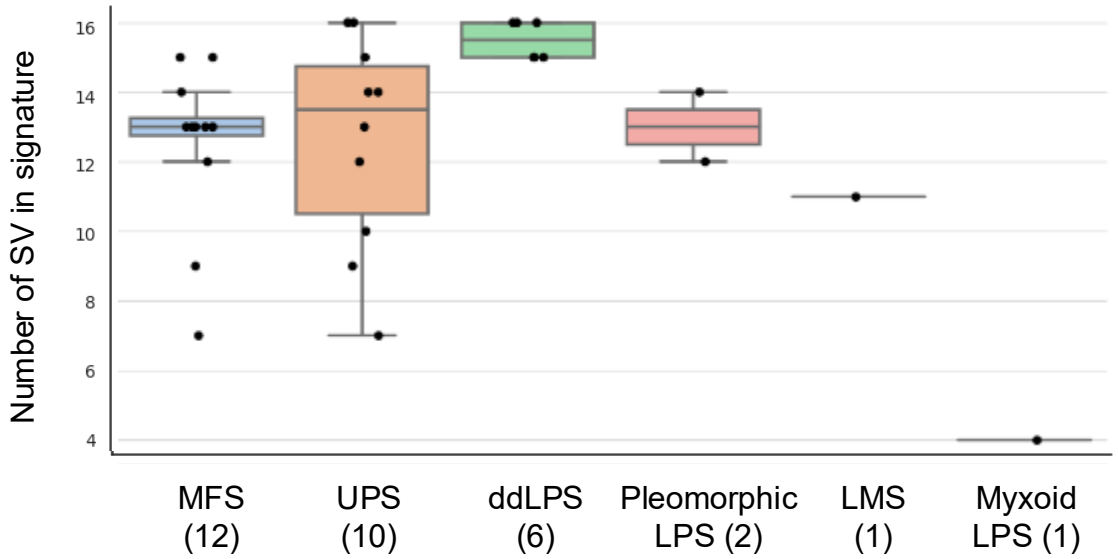
RESULTS

Distribution of selected structural variant breakpoints in study population





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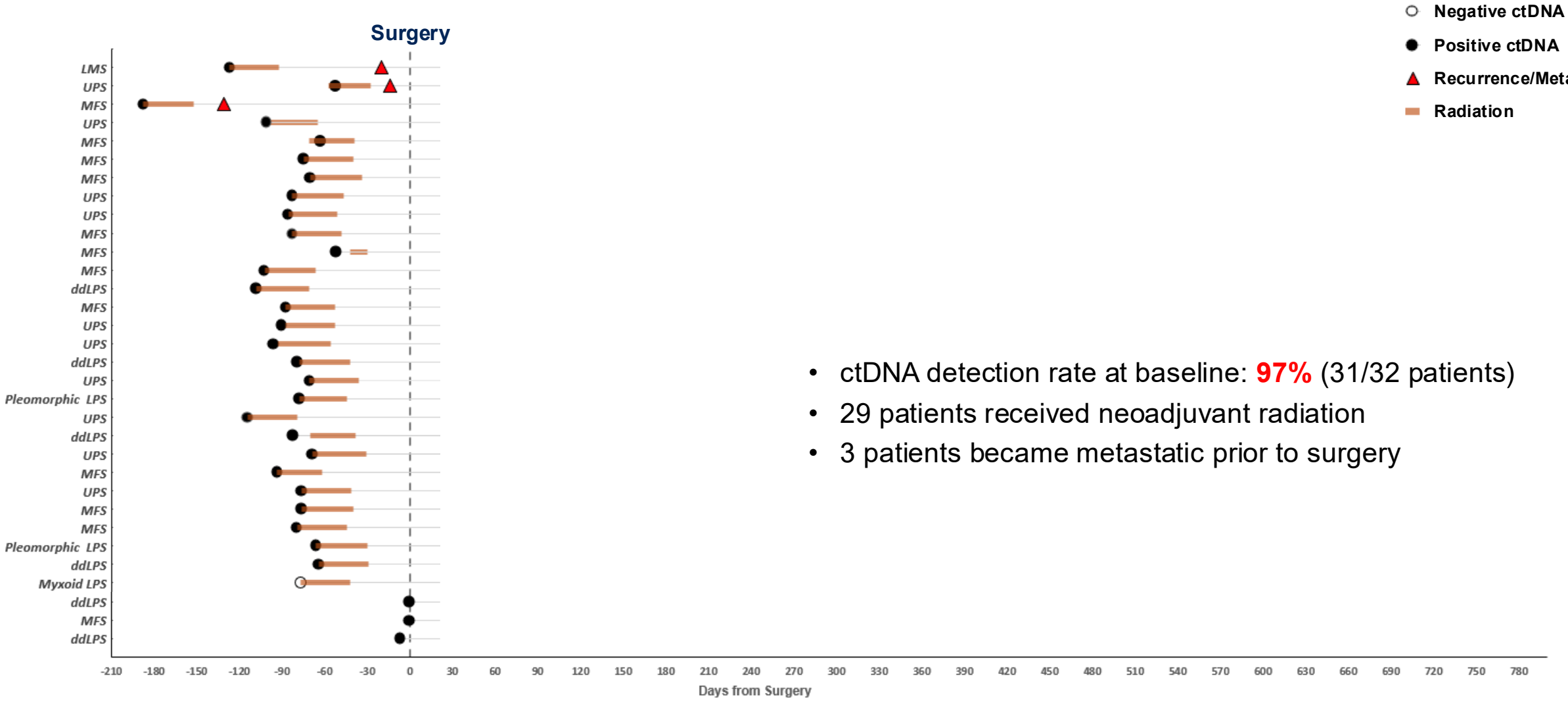
RESULTS

ctDNA was detectable at baseline with high sensitivity



- ctDNA detection rate at baseline: **97%** (31/32 patients)
- 29 patients received neoadjuvant radiation
- 3 patients became metastatic prior to surgery

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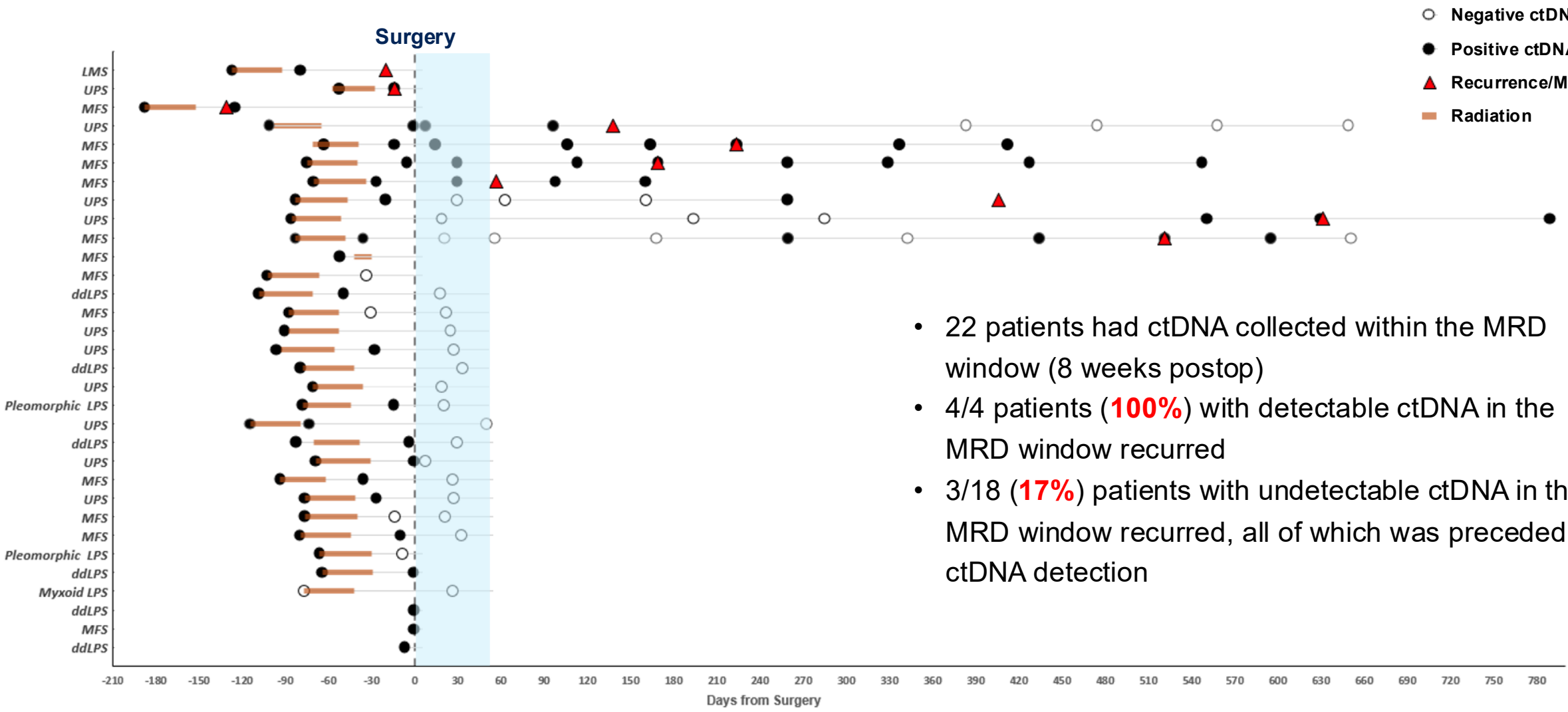
RESULTS

ctDNA positivity in the MRD window was predictive of subsequent recurrence



- 22 patients had ctDNA collected within the MRD window (8 weeks postop)
- 4/4 patients (**100%**) with detectable ctDNA in the MRD window recurred
- 3/18 (**17%**) patients with undetectable ctDNA in the MRD window recurred, all of which was preceded by ctDNA detection

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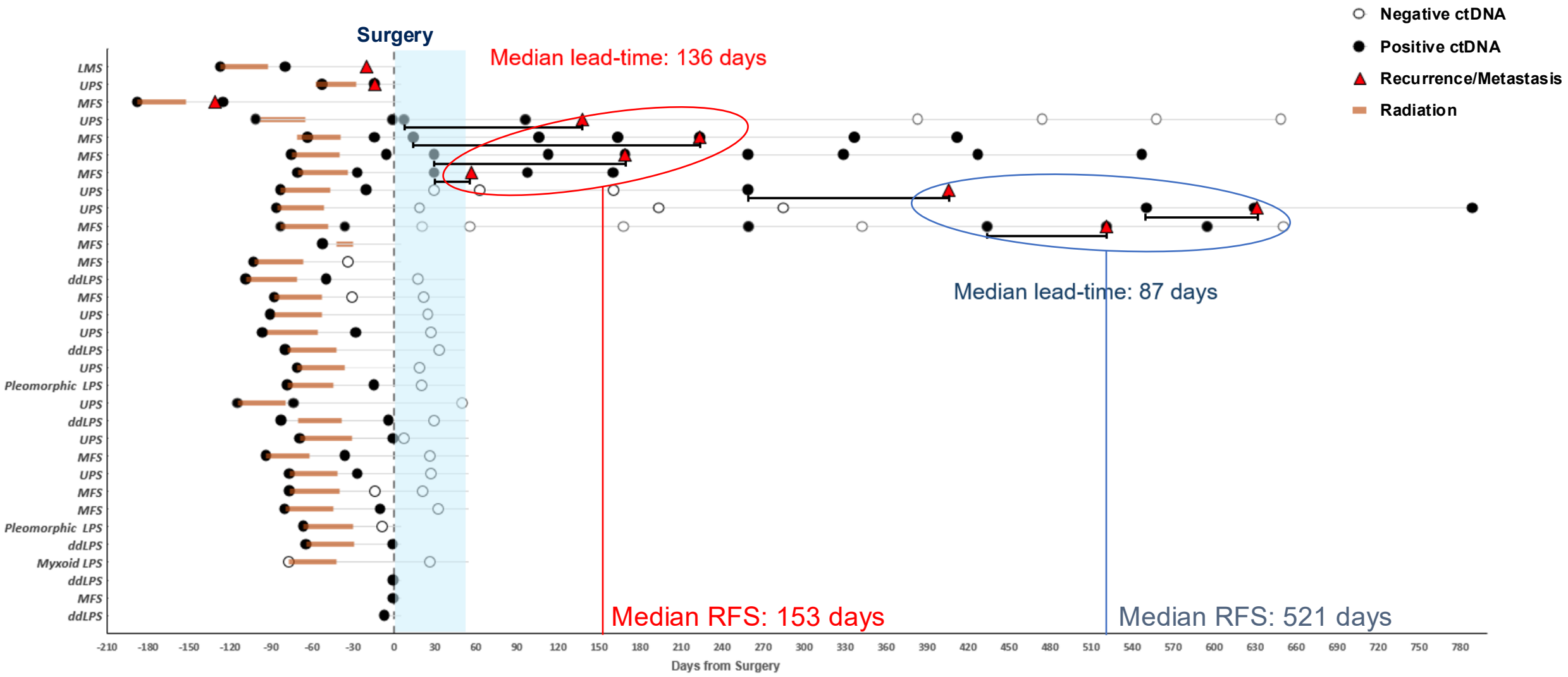
RESULTS

ctDNA positivity in the MRD window was predictive of early recurrence



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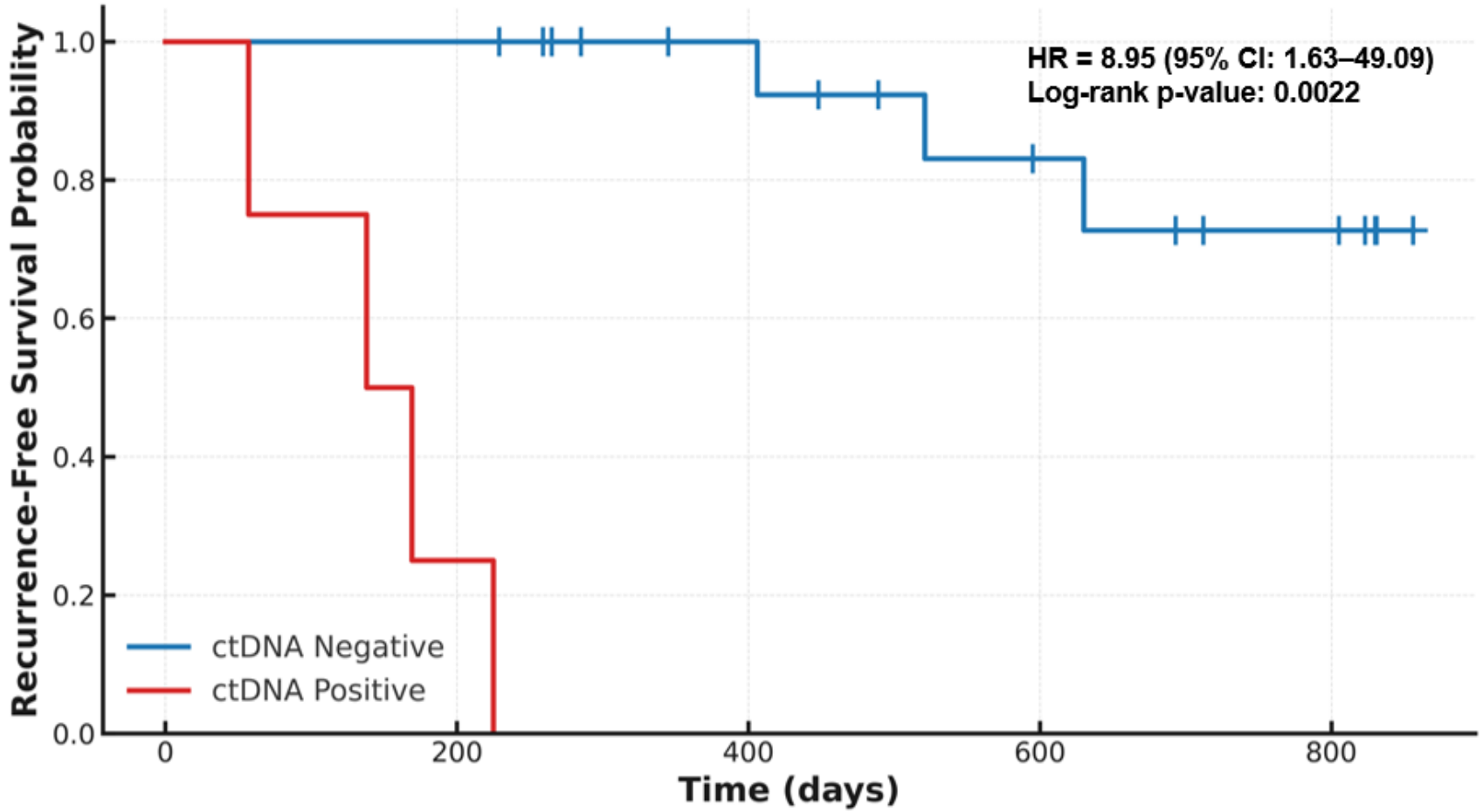
RESULTS

Relapse-free survival by ctDNA status in the MRD window



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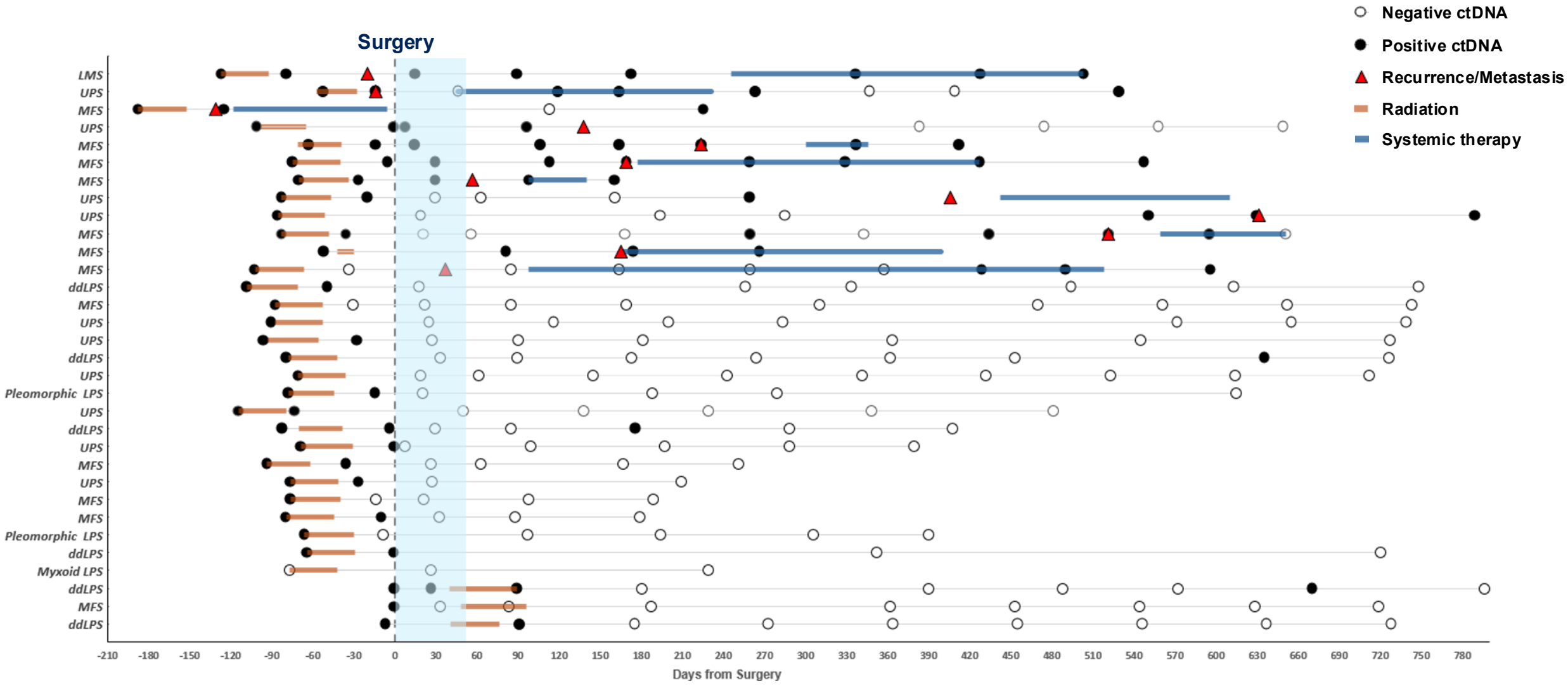
RESULTS

ctDNA kinetics in the study population



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CONCLUSIONS AND FUTURE DIRECTIONS

- Detection of ctDNA using tumor-informed assays for somatic SV tracking was feasible and highly sensitive in resectable STS.
- Positive ctDNA within the MRD window was associated with subsequent and earlier radiologic relapse.
- Positive ctDNA may serve as a biomarker to better select patients for adjuvant systemic therapy.
- Analyses of circulating ecDNA detection are ongoing
- An interception trial of adjuvant systemic therapy for MRD-positive STS patients is planned

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Acknowledgements

- All patients and their relatives
- Dr. Albiruni Abdul Razak and my co-authors
- All members of the Toronto Sarcoma Program
- Collaborator: SAGA Diagnostics

This study was supported by:

Sarcoma Cancer Foundation of Canada

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Lay Summary Slide

- Patients with localized soft tissue sarcoma treated with surgery and radiation have a high chance of recurrence
- It is unclear which patients will benefit from the addition of chemotherapy
- Our study successfully detected circulating tumour DNA (ctDNA) using personalized genomic structural changes, which are common in sarcomas
- Presence of ctDNA within a window of 8 weeks following radiation and surgery was predictive of future recurrence
- This test may serve as a biomarker to better select candidates for adjuvant chemotherapy, and we are currently designing a trial to answer this question

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