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JOHNS HOPKINS MEDICINE
RADIATION ONCOLOGY & MOLECULAR RADIATION SCIENCES

Primary Outcomes of a Phase II Randomized Trial of Observation versus Stereotactic Ablative Radiation for Oligometastatic Prostate Cancer (ORIOLE)

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Disclosures for Dr. Phillips

- Resident physician at Johns Hopkins University School of Medicine
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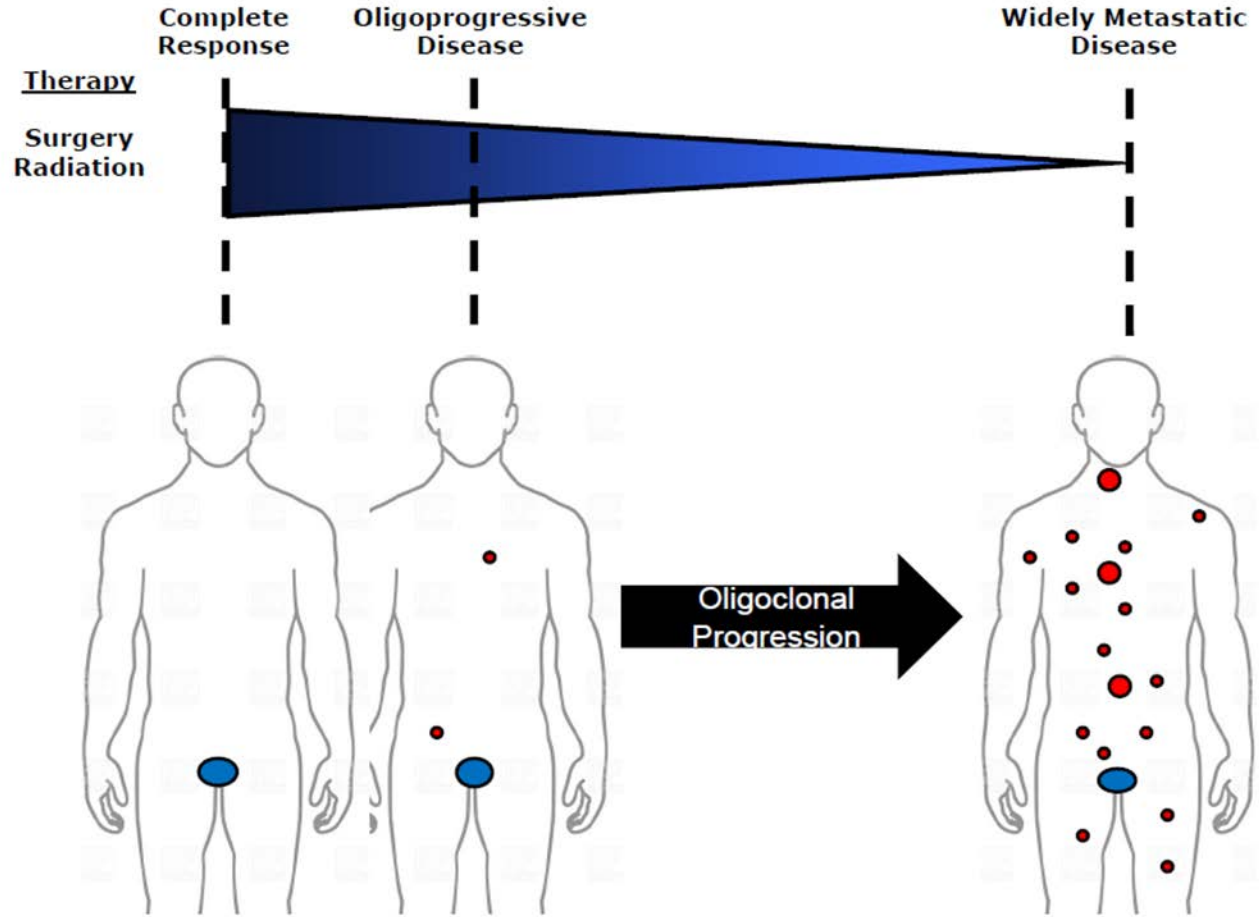
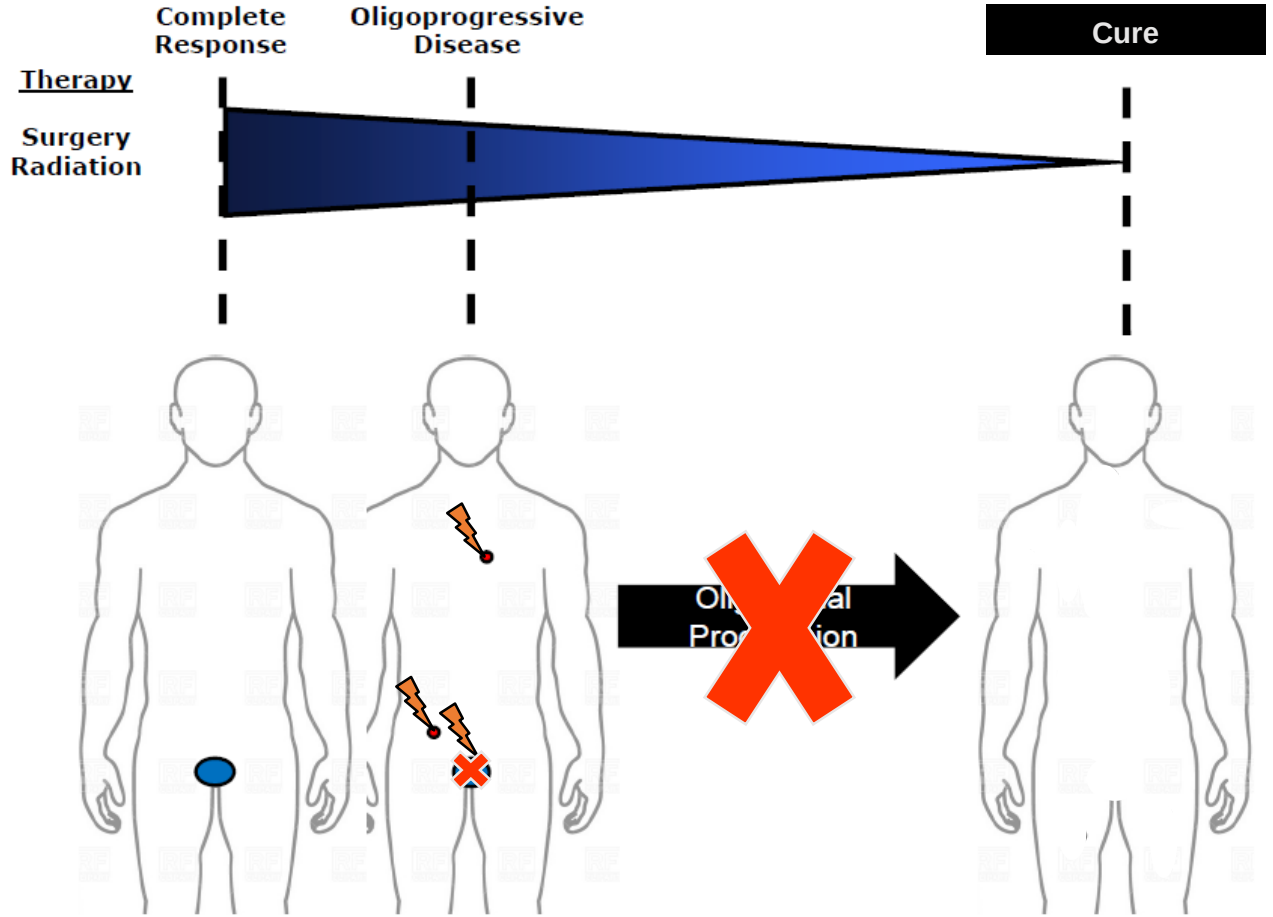
Background

- Prostate cancer may spread to a few initial sites before widespread metastasis.



Background

- Eliminating sites of initial spread may help control or cure metastatic prostate cancer.



Trial design

- Eligibility:
  - Recurrent hormone-sensitive prostate cancer
  - 1-3 metastatic lesions ≤ 5 cm by CT, MRI, or bone scan
  - PSA doubling time < 15 months
  - ECOG performance status ≤ 2

- 54 men were randomized 2:1 to stereotactic ablative radiation (SABR) or observation for 6 months

- Follow-up every 3 months including H&P and PSA, with CT and bone scan performed at 6 months

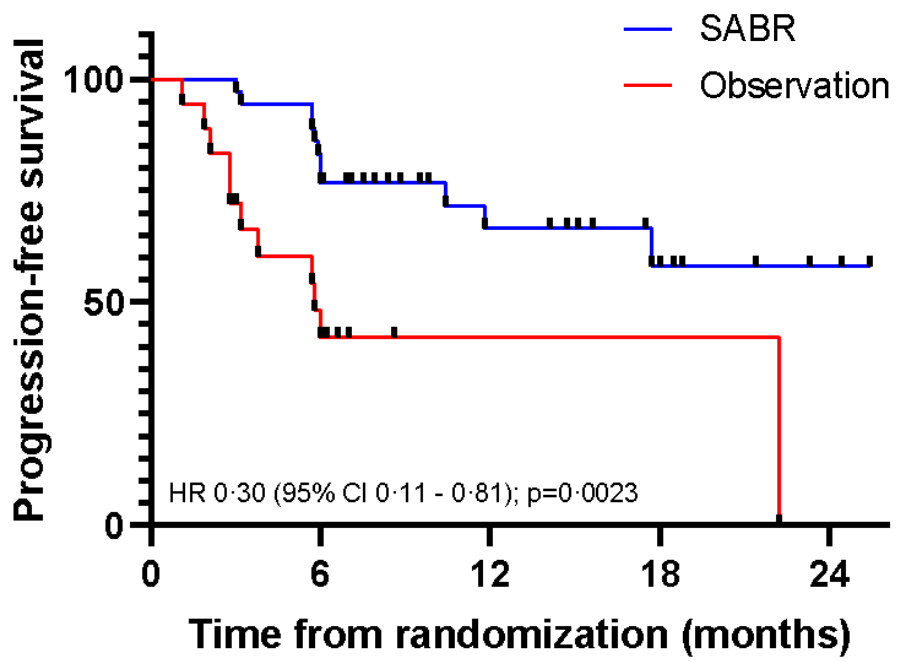
- Correlative studies included prostate-specific membrane antigen (PSMA)-PET scans as well as analysis of T-cell repertoires and circulating tumor DNA.

SABR improved progression at 6 months and progression-free survival

	Progression at 6 months	P-value
SABR (n = 36)	19%	0.005
Observation (n = 18)	61%	

Progression defined as:

- PSA increase ≥ 2 ng/mL AND ≥ 25% above nadir
- Evidence of new metastases by CT, MRI, or bone scan
- Symptomatic progression
- Initiation of ADT for any reason



Number at risk					
SABR	36	26	13	7	2
Observation	18	8	1	1	0

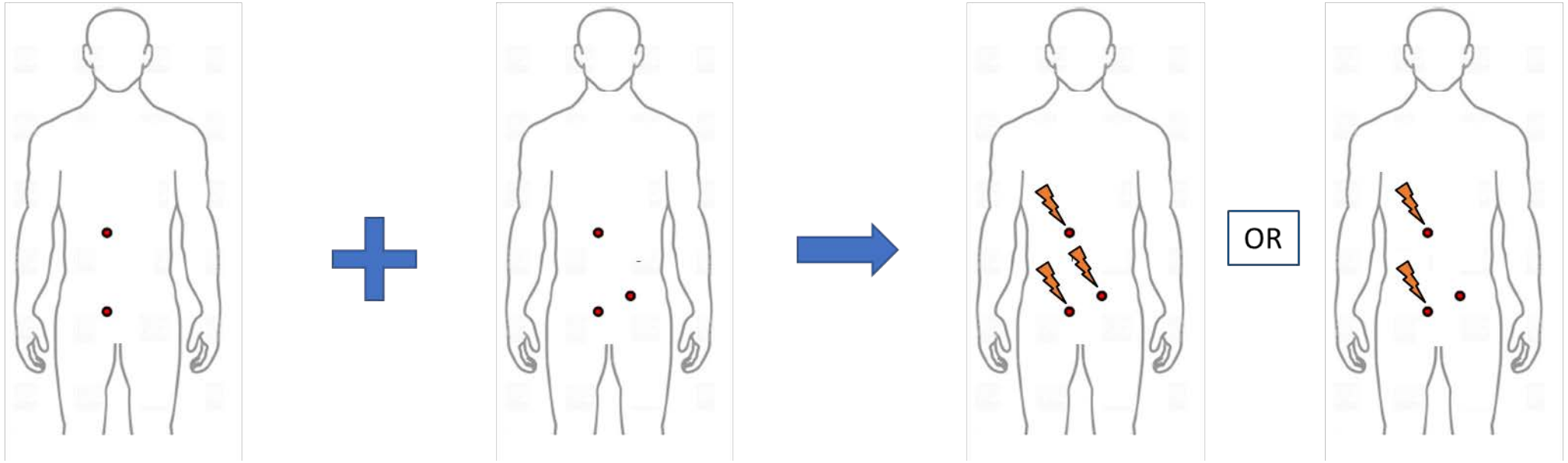
About half of men who received SABR had additional lesions detectable by PSMA-PET

Conventional imaging for eligibility and treatment planning (n = 36)

Blinded PSMA-PET obtained at baseline and Day 180 (n = 35)

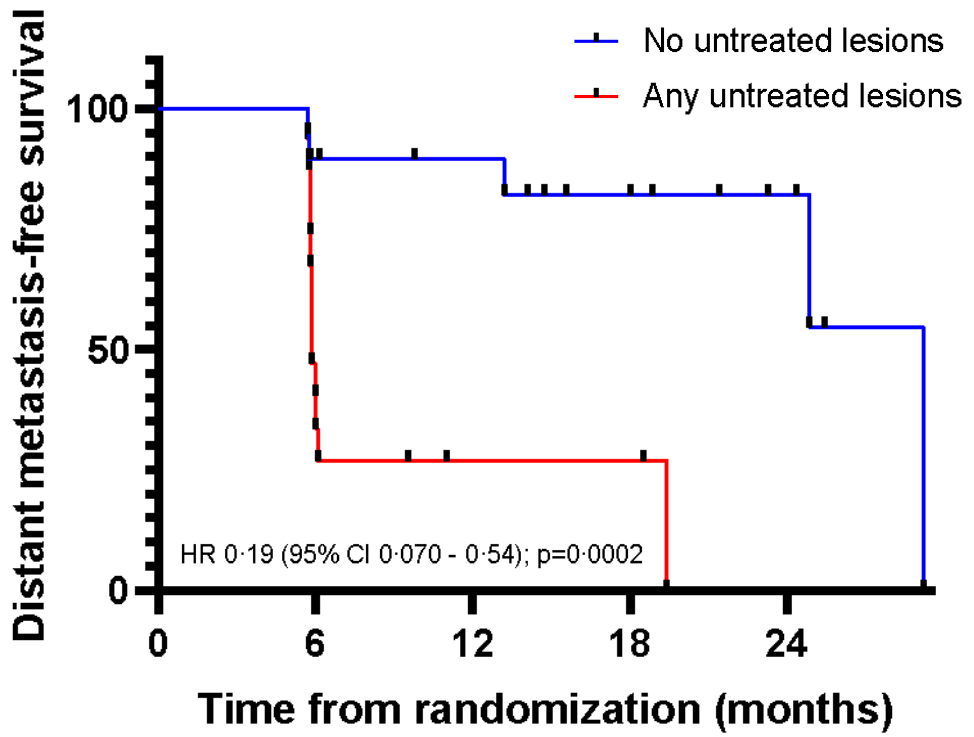
Total consolidation (n = 19)

Subtotal consolidation (n = 16)



Total consolidation of PSMA-PET detected lesions decreased risk of new metastasis formation

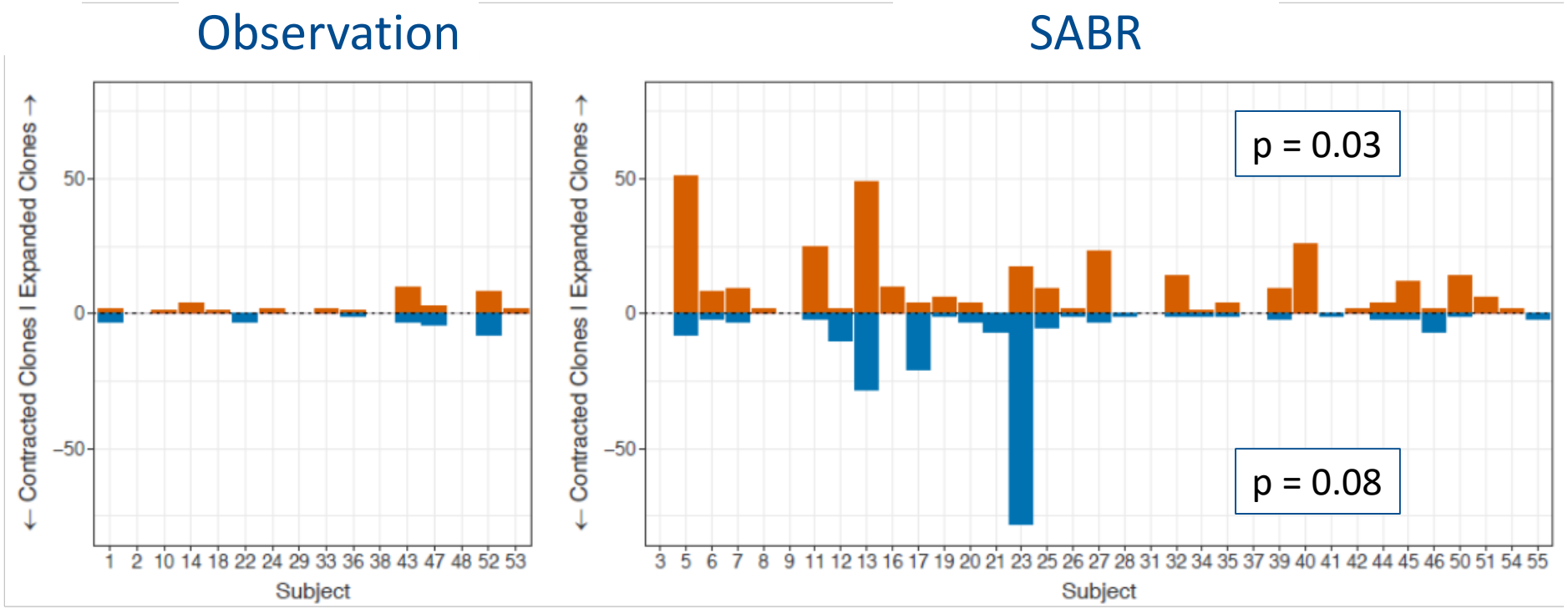
Consolidation	New metastases at 6 months	P-value
Total (n = 19)	16%	0.006
Subtotal (n = 16)	63%	



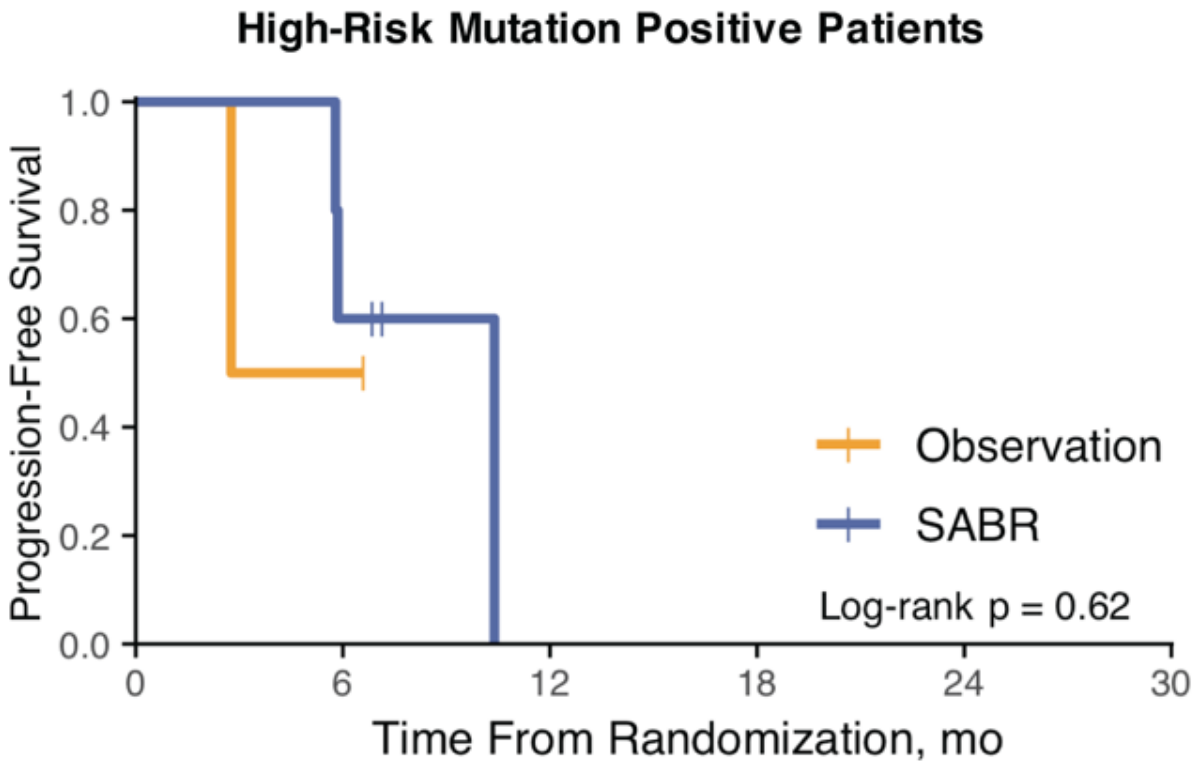
Number at risk

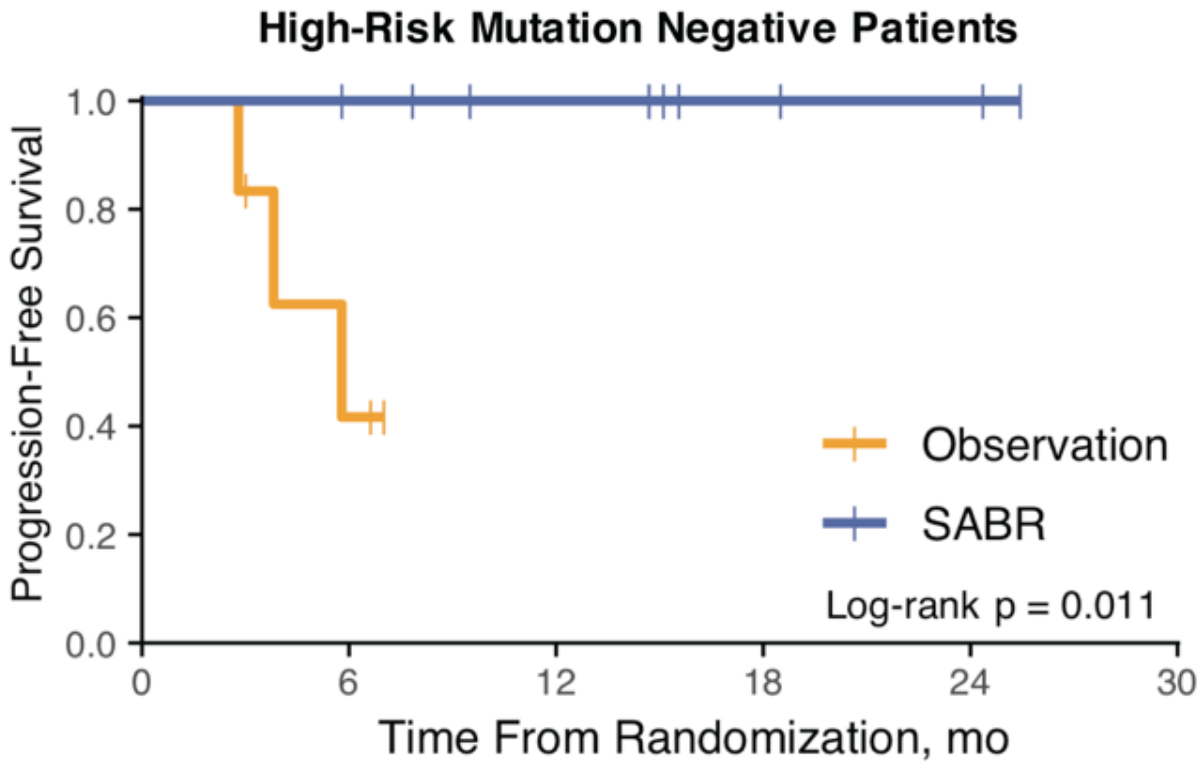
No untreated	19	14	12	8	4
Any untreated	16	6	2	2	0

SABR resulted in expansion of more T-cell clones, suggesting a systemic immune response



Presence of high-risk mutations by circulating tumor DNA was associated with progression after SABR





Conclusions

- SABR improves PFS in men with oligometastatic prostate cancer compared to observation alone.
- Total consolidation of PSMA radiotracer-avid lesions may decrease risk of new metastases and alter the natural history of this disease.
- SABR induced a systemic immune response in a prototypically "cold" tumor type.
- Continued biomarker development and validation may help us tailor individualized treatment approaches.