MLS Irvine: Radiation Oncology GU Updates

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STEVEN SEYEDIN, MD

ASST PROFESSOR OF RADIATION ONCOLOGY, UCSF

Outline

ASCO and ASTRO Annual Meeting

- Renal Cell Carcinoma
  - SBRT for oligometastatic (om) or oligoprogressive (op) disease
- Prostate Cancer
  - Intensification of systemic therapy during salvage radiation
  - AI for SBRT omCSPC
  - Protons
- Bladder Cancer
  - Adjuvant radiation

Phase 2: TKI and SBRT for omopRCC

om/op RCC

Goal: Demonstrate efficacy of combining first line systemic therapy with SBRT for oligometastatic/oligoprogressive mRCC

Single Arm Phase 2

- ≤ 5 metastatic lesions, first-line systemic therapy ≥ 3 months, ≤ 3 oligoprogressive sites
- No liver/brain metastasis
- SBRT (dose unknown) & TKI

Zhang et al ASCO Annual Meeting 2024

Phase 2: TKI and SBRT for om/opRCC

om/op RCC

30 patients enrolled, 27 evaluated

- Median age 55, 81.5% IMDC intermediate risk, 74.1% clear cell histology, 85% TKI alone

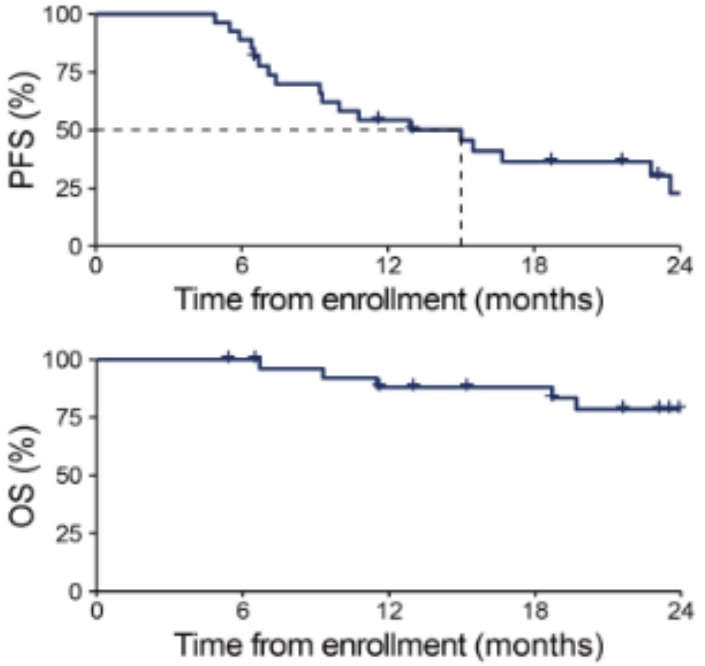
Sites of SBRT

- Bone (32.4%)
- Lymph node (23.5%)
- Lung (23.5%)

No SBRT-related grade 3-4 toxicity was observed

Median PFS 15 months

Fig 1. Progression-free survival and overall survival



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SBRT for omRCC

Single arm phase 2 studies

MDACC experience in lieu of systemic thearpy

- 30 patients with 5 or fewer mets
- 1 or fewer lines of systemic thearpy
- mPFS 22.7 months

UTSW experience

- 20 patients with oligoprogression
- 4^{th}-5^{th} line tx
- mPFS 11.1 months (24.4 months with systemic therapy)

Why PFS shorter with TKI alone?

Tang et al Lancet Oncol 2021

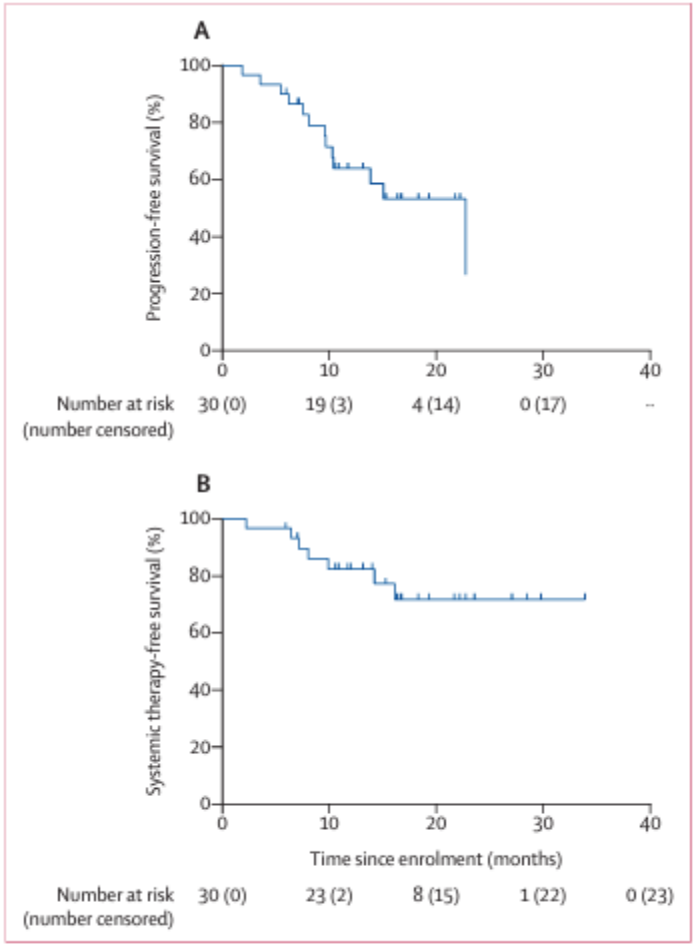


Figure 2: **Kaplan-Meier plots of progression-free survival (A) and systemic therapy-free survival (B)**

Hannan et al Euro Urol 2023

RTOG 3506: STEEL

Post-prostatectomy

Goal: Adding enzalutamide to ADT during salvage RT (SRT) for high-risk patients with biochemical failure after surgery would improve PFS

Enrolled

- Pts with biochemical failure after RP with 1 high risk factor (RF)
- RFs: GS 8-10, SVI, pN1, persistent PSA > 0.1 after RP, and PSA ≥ 0.7
- Intervention: 24 months of GnRH agonist +/- Enza 160 mg daily + SRT
- Endpoint: 35% reduction in PFS at 5-years
  - Progression = first occurrence of BF (PSA ≥ 0.05), clinical failure, or starting new tx

Posadas et al ASCO Annual Meeting 2024

RTOG 3506: STEEL

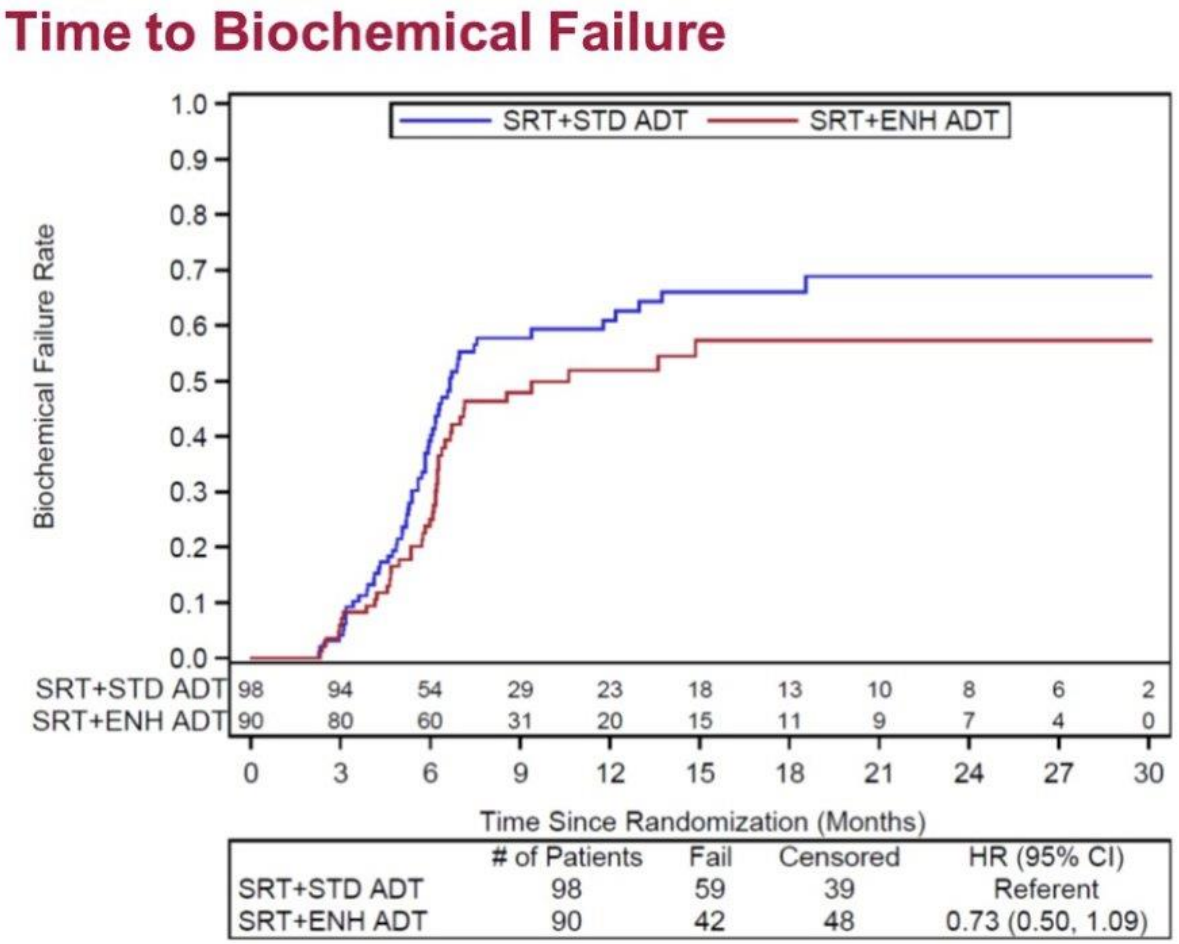
Post-prostatectomy

188 patients enrolled (> 70% with 2+ high RFs)

- pN1: 22%
- pT3a-b: 77%
- GS 9: 52%

Grade 3+ AEs: HTN, decreased lymphocytes

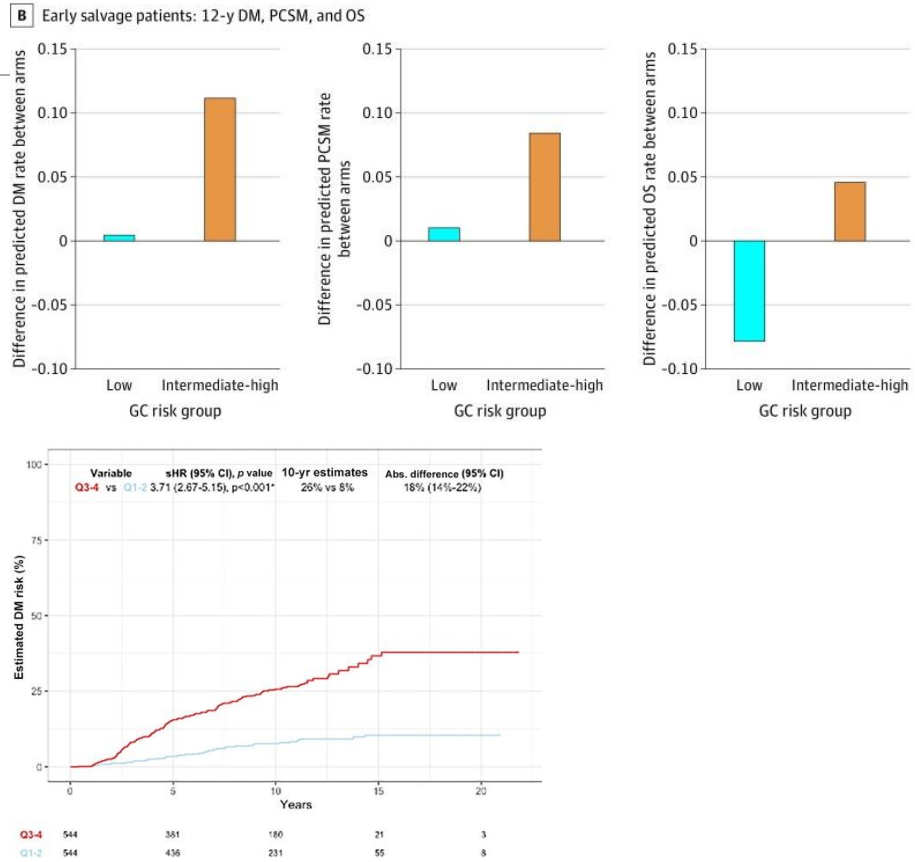
PFS: “Favored” enza arm (HR 0.72, 80% CI: 0.56 – 0.94, p = 0.14)



Posadas et al ASCO Annual Meeting 2024

Is STEEL practice changing?
Post-prostatectomy

Feng et al JAMA Onc 2021



Spratt et al Eur Urol 2024

- Not yet
  - Is there a particular RF driving the need?
  - Definition of BF
- FORMULA 509: 6 months ADT +/- Apa + AAP (Nguyen et al ASCO GU 2023)
  - PFS: HR 0.71 (90% CI 0.49-1.03)
  - Benefit primary for those with PSA > 0.5
- Duration of ADT (RADICALS HD)
- Biomarkers

AI for Prognostication

omCSPC

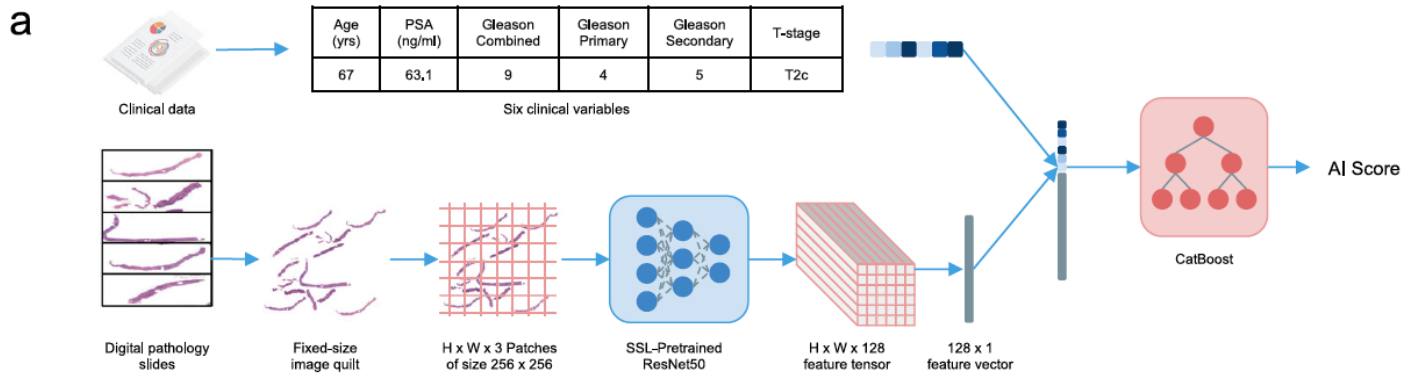
Goal: Previously shown multimodal artificial intelligence (MMAI) for high risk prostate cancer can be used to prognosticate those with oligometastatic CSPC and predict which patients benefit from SBRT

Multi-instituitional retrospective study of those with omCSPC and ≤ 5 metastases

Endpoint: OS

Second analysis of those from STOMP and ORIOLE looking at role of MDT

Endpoint: MFS



Esteva et al Npj Digital Medicine 2022

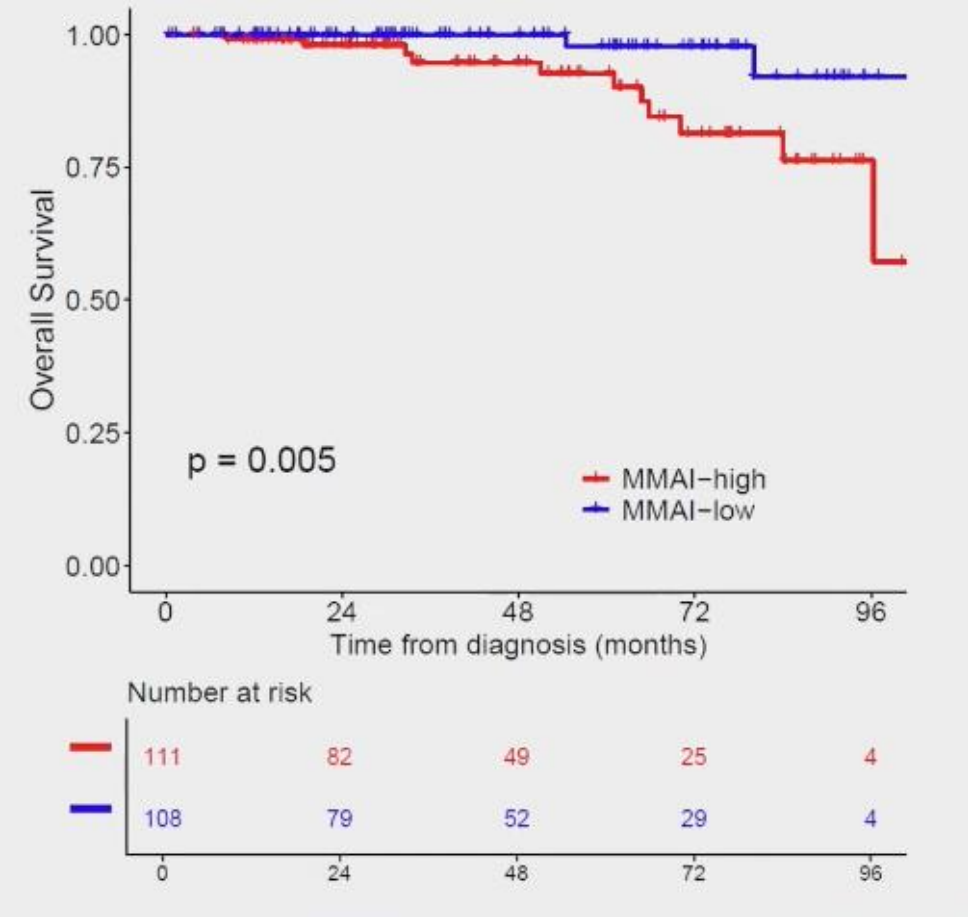
Sutera et al ASTRO Annual Meeting 2024

AI for Prognostication

omCSPC

Retrospective group

- Higher MMAI:
  - Higher PSA at dx (5.95 vs 9.61)
  - Higher PSA at mets (3 vs 5.35)
  - More GG4+ disease (39.6% vs 69.4%),
  - More patients with de novo disease (8.1% vs 28.8%)
  - More bone metastasis (39.6% vs 55.5%)



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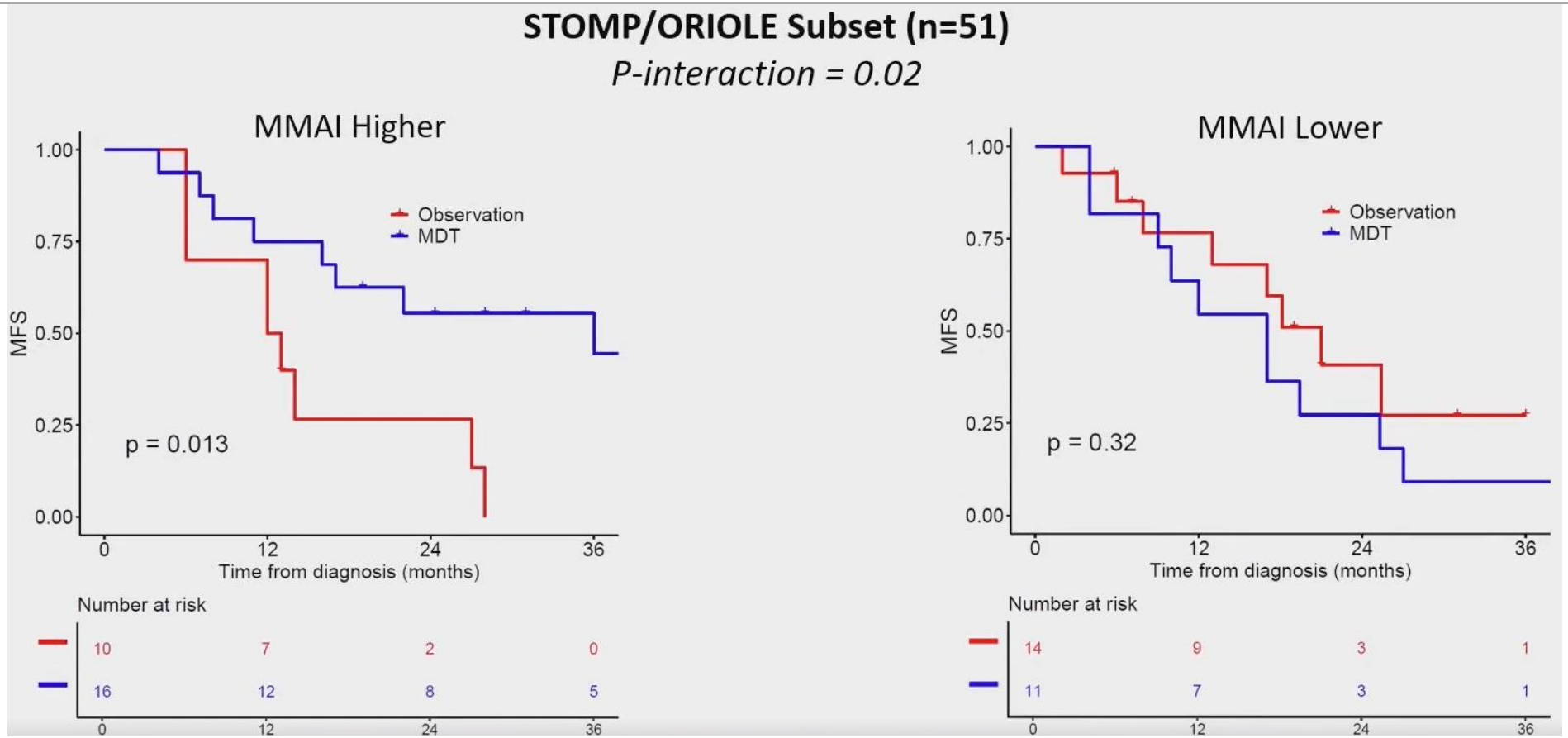
AI for Prognostication

omCSPC



Sutera et al ASTRO Annual Meeting 2024

Phase 3 Proton Study - PARTIQoL

Protons for prostate cancer

Goal: Examine differences in toxicity and QoL between proton and photon (IMRT) for definitive prostate radiotherapy

Enrolled intermediate or low risk randomized to PBT or IMRT without hormone therapy and stratified for age, institution, dose/fractions (79.2 Gy/44 vs 70 Gy/28 fx)

Followed bowel, urinary, and sexual function at multiple time points for 60 months after RT

Endpoint: Compare changes in baseline QoL using software score (0-100) specifically bowel function

Phase 3 Proton Study - PARTIQoL

Protons for prostate cancer

450 patients from 30 recruiting centers

- Median age 68 years
- 59% intermediate risk disease
- 51% completed shorter course of radiation
- 48% rectal spacer

Baseline Characteristics

Characteristic, N (%)	Proton Beam Therapy (n=221)	Intensity Modulated Radiotherapy (n=216)
Followup, mo, median (range)	60.8 (4.1-123.9)	58.9 (3.1-135.1)
Age, y, median (range)	68 (46-89)	68 (48-84)
Race		
White	181 (82%)	170 (79%)
Black	27 (12%)	29 (13%)
Other	13 (6%)	17 (8%)
ECOG performance status 0	213 (96%)	208 (96%)
Low risk	91 (41%)	89 (41%)
Intermediate favorable risk	96 (43%)	102 (47%)
Intermediate unfavorable risk	34 (15%)	25 (12%)
PSA, ng/mL, median (range)	6.4 (1.6-18.9)	6.1 (1.1-17.5)

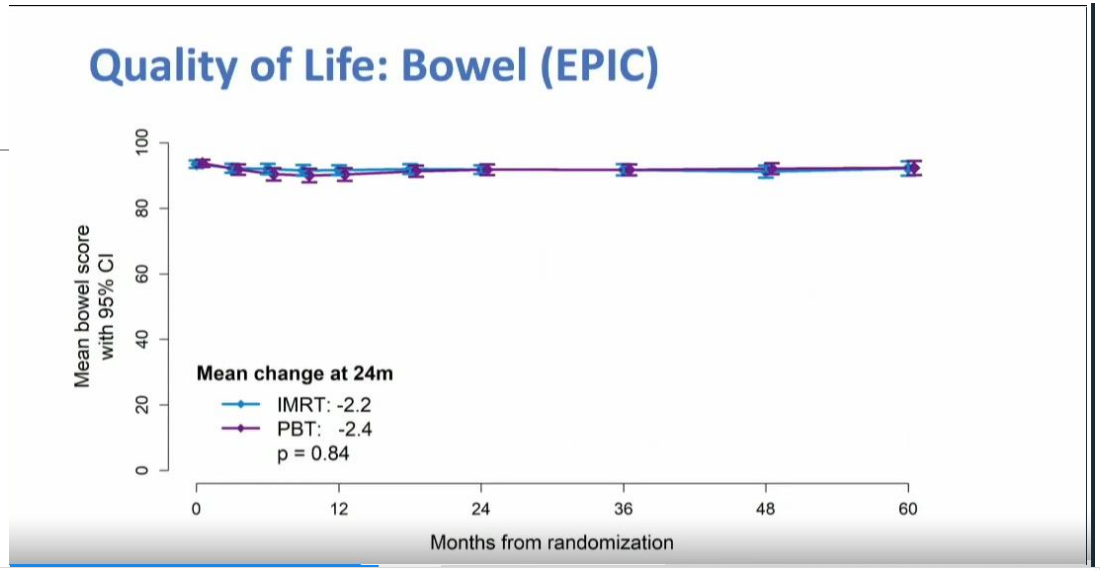
Efstathiou ASTRO Annual Meeting 2024

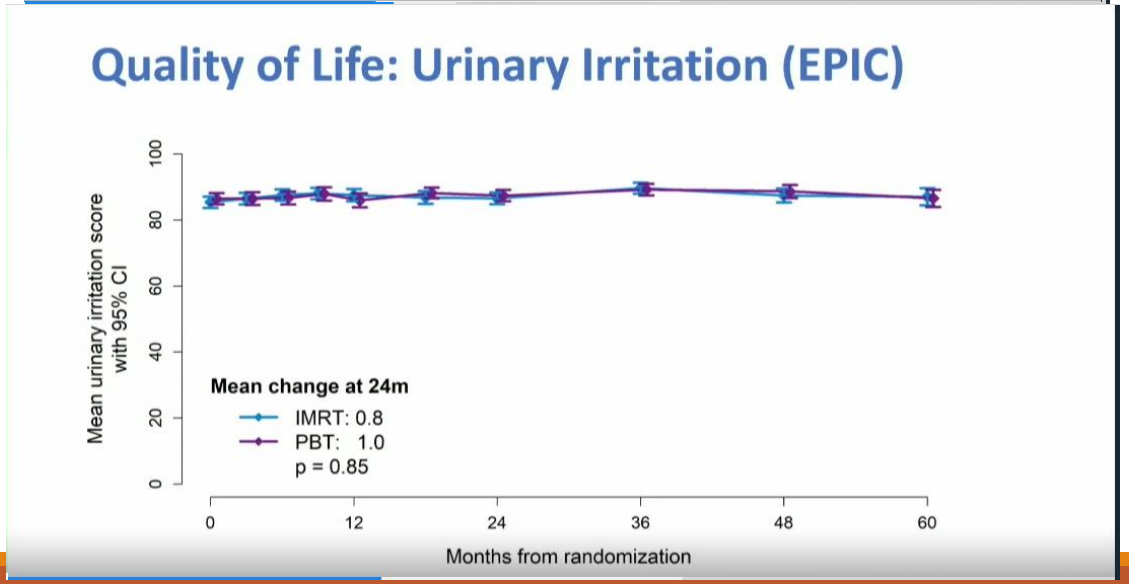
Phase 3 Proton Study - PARTIQoL

Protons for prostate cancer

No differences found

- Bowel, urinary, or sexual function
- PFS (93.4% vs 93.7%)





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Are Protons Out for Prostate?

- Prior negative proton studies for toxicity
  - Vapiwala et al IJROBP 2021: Multi-instituition
  - Yu et al JCO 2024: SEER-Medicare Study
- Technology Improvements?
- SBRT?
- High risk prostate cancer?
- Younger patients with secondary malignancy?

Results

The final sample included 772 PBT patients matched to 1,544 IMRT patients. The frequency of GI toxicity for IMRT versus PBT was 3.5% versus 2.5% at 6 months (*P* = .18), 9.5% versus 10.2% at 12 months (*P* = .18), and 20.5% versus 23.4% at 24 months (*P* = .11). The frequency of only procedure codes indicative of GI toxicity for IMRT versus PBT was too low to be reported and not significantly different. The frequency of GU toxicity for IMRT versus PBT was 6.8% versus 5.7% (*P* = .30), 14.3% versus 12.2% (*P* = .13), and 28.2% versus 25.8% (*P* = .21) at 6, 12, and 24 months, respectively. When looking only at procedure codes, the frequency of GU toxicity for IMRT was 1.0% at 6 months, whereas it was too infrequent to report for PBT (*P* = .64). GU toxicity for IMRT versus PBT was 3.3% versus 2.1% (*P* = .10), and 8.7% versus 6.7% (*P* = .10) at 12 and 24 months, respectively.

Conclusion

In this observational study, there were no statistically significant differences between PBT and IMRT in terms of GI or GU toxicity.

Bladder Adjuvant RT (BART) Phase 3 Trial

Adjuvant Bladder

Goal: Demonstrate safety of adjuvant bladder irradiation for higher risk patients

Enrolled

- M0 MIBC with 1+ high risk feature: pT3-4, pN1-3, nodal yield < 10, + margin, neoadjuvant chemo for ≥ cT3 disease
- Intervention: 5.5 weeks of daily radiation to cystectomy bed and pelvic nodal irradiation

Endpoint: 2-yr LRFS (but not released this session), initial results focused on toxicity

BART Phase 3 Trial

Adjuvant Bladder

153 patients enrolled

- Median age 57

Obs: 76, RT: 77 pts

- 49% pN+, 4.5% R1, 28% with variant histology
- Chemo: 70.6% received neoadjuvant, 19.6% adjuvant (no adj IO)

63/77 complete radiation plan

- 8 defaulted RT, 4 progressed before RT, 2 because of cystectomy complications

Murthy ASTRO Annual Meeting 2024

BART Phase 3 Trial

Adjuvant Bladder

Acute Grade 2+ toxicity

19.1% vs 5.6% (p = 0.02)

Acute Grade 2 Bowel toxicity

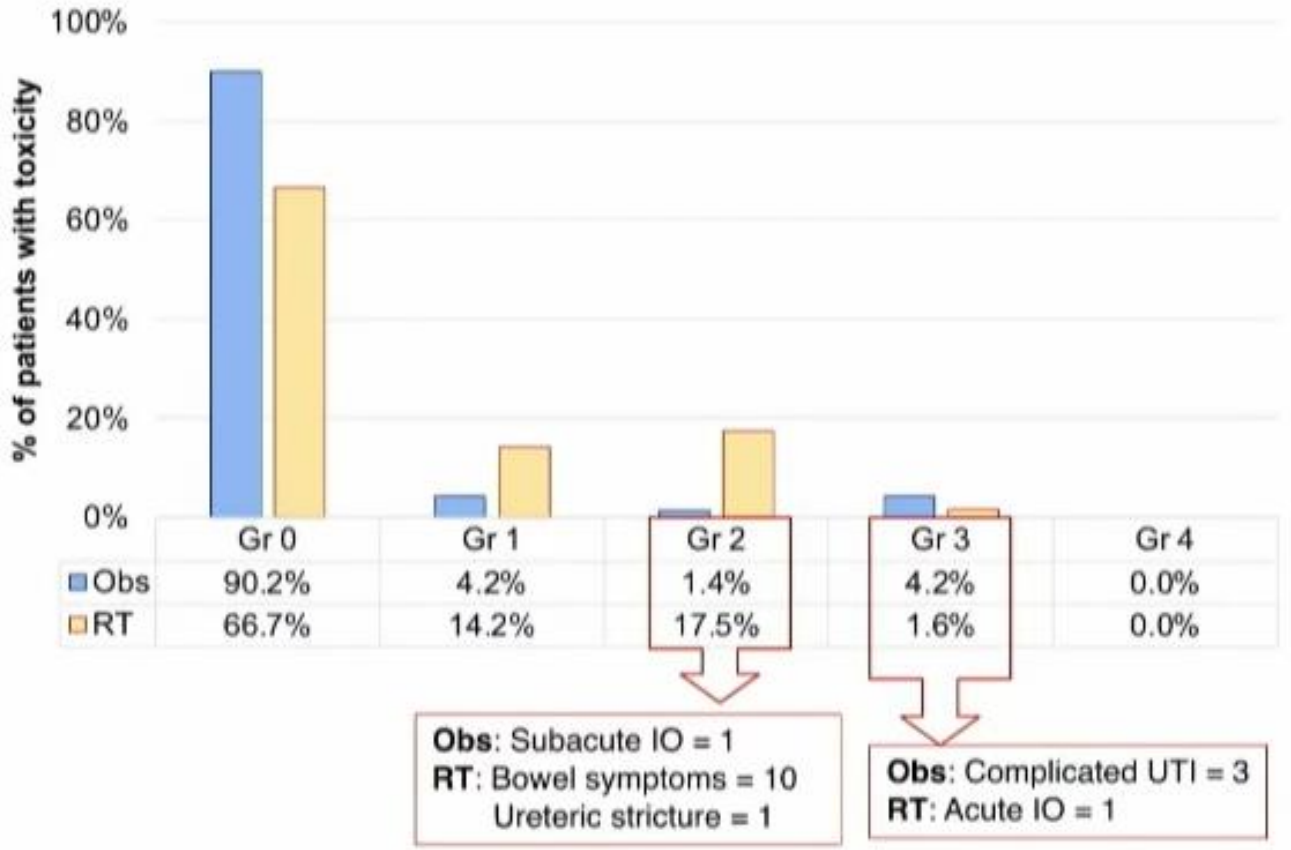
15.9% vs 8.2%

Late Grade 1-2 toxicity

10.5% vs 27.6% (p = 0.02)

Late Grade Grade 3+ Toxicity

8.2% vs 10.5% (NS)



Murthy et al ASTRO Annual Meeting 2024

My thoughts on adjuvant bladder RT

Adjuvant Bladder

Encouraging initial toxicity results….

Unclear adjuvant role

Practice not reflective of US model

- No adjuvant IO, 30% without neoadjuvant chemo

Landscape shifting towards neoadjuvant intensification

- NIAGARA

Enfortumab Vedotin & Pembro

Conclusions

Renal Cell Carcinoma

- TKI and SBRT appear safe but efficacy appears limited in op mRCC

Prostate Cancer

- Higher risk prostatectomy pts likely benefit from extended ADT duration or intensification with NHT but unclear which patient population benefits most
- MMAI has the potential to predict which patients response to MDT and its role in prostate cancer is on the horizon
- No clear role of proton therapy for localized prostate cancer

MIBC

- Adjuvant radiation appears feasible but its role/efficacy TBD in setting of ADC and IO

Thank You!

Questions?

Steven.Seyedin@ucsf.edu