Post-Prostatectomy Prostate Cancer Treated with Radiation Therapy: Adverse Features and ADT Use in a Statewide Consortium

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Abstract

Background: The 2024 AUA/ASTRO/SUO guidelines recommend early salvage radiation (RT) for biochemical recurrence after radical prostatectomy and androgen deprivation therapy (ADT) for high-risk features. Increasingly, men with high-risk disease are undergoing radical prostatectomy. We therefore characterized contemporary RT and ADT practices within the Michigan Radiation Oncology Quality Consortium (MROQC) and Michigan Urological Surgery Improvement Collaborative (MUSIC).

Methods: Patients receiving post-prostatectomy RT from 06/09/20–09/18/24 were eligible. Prospectively collected data included surgical pathology and radiation/ADT details. RT was adjuvant (pre-RT PSA <0.1ng/mL), consolidative (persistent PSA ≥0.1), or salvage (all others). Multivariable analyses evaluated associations between clinicopathologic features and ADT use.

Results: Among 345 patients across 26 centers, 56% had ≥1 high-risk feature: pT3b/T4 (24%), pN1 (6%), Grade Group (GG) 4/5 (30%), pre-RT PSA >0.5 ng/mL (27%). Radiation was adjuvant (10%), consolidative (28%), or salvage (62%), initiated at median PSA of 0.07 (IQR:0.03-0.09), 0.5 (IQR:0.3-1.5), and 0.3 ng/mL (IQR:0.2-0.5), respectively. Median time to RT was 8, 6, and 29 months.

ADT was intended in 60%; commonly ≤6-month duration (65%), with a minority recommended ≥24 months (17%) or AR-pathway inhibitors (5%). On MVA, ADT was associated with: pT3b/T4 (OR=2.77 [1.34–5.93]), pN1 (OR=6.22 [1.35–47.57]), GG 4/5 (OR=2.87 [1.51–5.56]), pre-RT PSA >0.5 (OR=2.11 [1.17–3.91]).

Conclusions: Within MROQC, over half who received post-prostatectomy radiation had high-risk features; nearly 30% required consolidation for persistently positive PSA. ADT was associated with high-risk features, but few received ADT intensification. Studies are needed to personalize ADT, especially for those with persistent PSA, who are frequently treated yet under-represented in trials.

Introduction

The 2024 AUA-ASTRO-SUO consensus statements provide guidelines on salvage therapies for biochemical recurrence after radical prostatectomy.[1–3] These include both the appropriate use of early salvage radiotherapy at a PSA ≤0.5 ng/mL and the addition of androgen deprivation therapy (ADT) for patients with high-risk pathologic features.[1,2] The ARTISTIC meta-analysis supports an early salvage approach over adjuvant radiation, sparing up to 60% of men from potential toxicities while maintaining event-free survival.[4] However, men with adverse pathologic features (e.g., Grade Group 4/5, pT3/4, pN1, persistently elevated post-operative PSA) were under-represented in the contemporary trials included in ARTISTIC,[5–7] and retrospective studies suggest they may derive greater benefit from adjuvant therapy.[8,9] Patients with persistently positive post-operative PSA represent a particularly high-risk subset that may benefit from "consolidative" treatment targeting immediately detectable residual disease, a distinct clinical entity from both the adjuvant and early salvage radiation.[10]

The optimal use of ADT with post-operative radiotherapy (PORT) remains uncertain. Short-course ADT at a minimum improves biochemical control and progression free survival.[11–13] In higher risk populations, ADT intensification, whether through prolonged adjuvant duration or the addition of androgen receptor pathway inhibitors (ARPI), may improve metastasis-free survival (MFS).[14,15] The recent DADSPORT meta-analysis suggests that any duration of ADT confers a small but statistically significant improvement in MFS, without an overall survival benefit.[16] Whether the persistently positive PSA subgroup could benefit from ADT intensification is currently unclear.

Recent analysis of a prospective trial of men with high-risk prostate cancer treated with radical prostatectomy found nearly 70% received either adjuvant or salvage radiation.[17] As more

men with high-risk disease undergo primary RP,[18] the rate of men with adverse pathologic features referred for PORT will increase. The prevalence of these patients and their management in the context of contemporary randomized evidence and national guidelines remain unclear, including the use of consolidative radiation. We aimed to characterize RT and ADT use in a prospective cohort from the Michigan Radiation Oncology Quality Consortium (MROQC) and the Michigan Urological Surgery Improvement Collaborative (MUSIC).

Methods

Data Collection

MROQC and MUSIC are statewide collaborations across the state of Michigan, established through a partnership with Blue Cross Blue Shield of Michigan (BCBSM), aimed at improving the quality of care in Radiation Oncology and Urology practices, respectively. Patient and treatment-related data for patients with prostate adenocarcinoma treated within participating centers are collected prospectively. MROQC captures androgen deprivation therapy (ADT) intent, type, and duration using standardized physician-completed forms prior to treatment. In this study, eligible patients were those treated at an MROQC site with definitive-intent post-operative radiotherapy after prior radical prostatectomy (RP) for localized prostate adenocarcinoma. Patients with distant metastases or prior radiotherapy were excluded. MUSIC contributed additional prospectively collected data including surgical pathology and PSA values. Patient race is self-reported, and when analyzing data, “Other” includes Asian, American Indian, Alaskan Native, and Unknown/Not Reported. This study was institutional review board exempt as a quality improvement initiative. Both MROQC and MUSIC received financial support from

BCBSM and the Blue Care Network of Michigan as part of the BCBSM Value Partnerships Program.

Statistical Analysis

The primary outcomes of the study were the intended ADT use and intensity with PORT and the setting in which PORT (adjuvant, salvage, consolidative) was delivered. PSA persistence was defined as an initial post-operative PSA (drawn ≥28 days to 6 months post-RP) ≥0.1 ng/mL, while PSA <0.1 ng/mL was considered undetectable. Adjuvant radiotherapy was defined as radiation initiated in patients without a detectable post-operative PSA ≥0.1 ng/mL at any timepoint post-RP. Consolidative radiotherapy was defined as radiation initiated in patients with persistently positive post-operative PSA ≥0.1. Finally, salvage radiotherapy was defined as radiation initiated in patients with an initially undetectable PSA who subsequently experienced a rise to ≥0.1 ng/mL prior to receiving radiation.

Associations between patient and treatment-related variables and ADT intent were evaluated with univariable and multivariable analyses. Logistic regression analysis was utilized to test associations between established high-risk features (defined as grade group [GG] 4/5, pT3b/T4, pN1, pre-PORT PSA >0.5 ng/mL, and PORT setting) and ADT intent. A pre-PORT PSA >0.5 ng/mL was chosen based on analysis from RTOG 9601, DADSPORT and FORMULA 509; sensitivity analyses evaluated PSA as a continuous variable and ADT intent. Subset analyses were performed to evaluate factors associated with planned ADT duration, and ADT intent among patients staged with molecular PET imaging. Additional analyses examined associations between clinicopathologic variables and pelvic nodal irradiation. A two-sided p-value <0.05 was considered statistically significant. All analyses were performed in SAS (version 9.4).

Results

Patient and Treatment Characteristics

Between June 9, 2020, and September 18, 2024, 345 patients across 26 MROQC centers received PORT. Baseline demographics and surgical pathology data are described in Table 1. The majority of patients pre-prostatectomy were either unfavorable intermediate risk (43%) or high risk (35%) by National Comprehensive Cancer Network (NCCN) criteria. Post-prostatectomy, most patients (56%) had at least one high-risk factor (pT3b/T4, pN1, Grade Group 4/5, and/or a pre-RT PSA >0.5 ng/mL). Approximately 60% of patients underwent molecular PET imaging (prostate specific membrane antigen [PSMA] or Fluciclovine F18).

PORT was categorized as adjuvant in 10% (n = 35), consolidative in 28% (n = 95), and salvage in 62% (n = 215). Patients receiving consolidative PORT had statistically significantly more aggressive pathologic features compared to salvage patients, including higher rates of pT3b (37% vs. 16%), pN1 (10% vs. 2%), GG 4/5 (45% vs. 25%), and median pre-RT PSA (0.5 vs. 0.3 ng/mL). Table 2 compares the pathologic characteristics within the MROQC prospective cohort with those reported in large, randomized trials evaluating ADT with post-prostatectomy radiotherapy.

The median time from RP to radiation initiation was 19 months (interquartile range [IQR]: 7 – 40 months), varying by PORT setting: 8 months for adjuvant, 6 months for consolidative, and 29 months for salvage (Table 3). Most patients received either conventional fractionation (>28 fractions; 63%) or moderate hypofractionation (20 – 28 fractions; 31%). The majority (71%) received both prostate bed and pelvic nodal irradiation. The median pre-radiation PSA for the entire cohort was 0.30 ng/mL (IQR: 0.20 – 0.60), drawn at a median time of 61 days

prior to the start of radiation. There were statistically significant differences in pre-treatment PSA between PORT treatment settings: 0.07 ng/mL in adjuvant, 0.50 ng/mL in consolidative, and 0.30 ng/mL in salvage patients (p = 0.006; Table 1).

Figure 1 illustrates the distribution of pre-radiation PSA values and timing of PORT initiation after RP, highlighting that most adjuvant or consolidative patients received RT within one year post-RP. Most salvage patients received RT beyond one year, at PSAs between 0.2 and 0.5 ng/mL, consistent with early salvage treatment. The rate of each type of PORT type varied across MROQC, with salvage RT representing 20% to 81% of all PORT cases treated at that MRQOC site (Supplemental Figure 1).

Associations with Androgen Deprivation Therapy and Pelvic Nodal Irradiation

Approximately 60% (n=204) patients were recommended by their treating physician to receive androgen deprivation therapy (ADT) with radiotherapy. Among them, the most common recommended ADT duration was short-term (≤6 months; 67%), while 17% were recommended long-term ADT (≥24 months). Among long-term ADT recipients, 41% were consolidative patients, and 50% were salvage. Approximately 45% of ADT courses included a neoadjuvant component, typically ≤3 months (Supplemental Table 1). Only 5% (n = 10) of patients received an ARPI (abiraterone, enzalutamide, apalutamide, or darolutamide). Additional ADT details by type of PORT are described in Supplemental Table 1, and percent of patients receiving ADT by pre-RT PSA level is illustrated in Supplemental Figure 2.

Univariate analysis (UVA) of intended ADT use is detailed in Supplemental Table 2. As illustrated in Figure 2, multivariate analysis (MVA) identified several statistically significant positive associations with ADT use including GG 4/5 disease, pT3b/T4, pN1, and pre-radiation

PSA of >0.5 ng/mL. Conversely, adjuvant radiation was associated with a lower likelihood of intended ADT use. Analysis excluding PORT type as a covariate found similar associations for GG 4/5 disease, pT3b/T4, and pre-radiation PSA >0.5 ng/mL (Supplemental Table 3). Additional analysis using pre-radiation PSA as a continuous variable found associations similar to that seen in the primary analysis between ADT use and GG 4/5 disease, pT3b/T4, pN1, and adjuvant radiation. However, pre-RT PSA as a continuous variable was not associated with ADT use (Supplemental Table 4). While PET imaging findings were statistically significantly associated with ADT use on UVA, a subset analysis of PET-staged patients showed no significant association with ADT use on MVA (Supplemental Table 5). Factors associated with an intended ADT duration ≥12 months were explored in a second subset UVA (Supplemental Table 6) and MVA (Supplemental Table 7). Only GG 4/5 disease and pN1 were statistically significantly associated with a planned ADT duration ≥12 months on MVA.

Approximately 71% of patients received pelvic nodal irradiation (PLNRT), most of whom also received ADT, while patients receiving prostate bed irradiation with ADT constituted only 6% of the study population (Table 3). Clinicopathologic details of pN1 subgroup are listed in Supplemental Table 8. The same UVA and MVA were performed to evaluate associations of clinical factors with PLNRT. Receipt of PLNRT was statistically significantly associated with pT3a (OR = 1.81 [95% CI: 1.02 = 3.23]), pT3b/T4 (OR = 3.91 [95% CI: 1.88 – 8.59]), and pre-RT PSA of >0.5 ng/mL (OR = 2.18 [95% CI: 1.18 – 4.22]), but not Grade Group, PORT setting, nor pathologic nodal stage (Supplemental Table 9). In the subset of PET-staged patients, PET imaging findings were not associated with receipt of PLNRT (Supplemental Table 10).

Discussion

Our study demonstrates that within a real-world prospective cohort, patients receiving post-prostatectomy radiation are enriched for high-risk pathologic features. Notably, while adjuvant radiation was utilized in only 10% of the cohort, nearly 30% had persistently detectable PSA requiring consolidative radiation, a subgroup that has been poorly represented in prospective trials. Androgen deprivation therapy was associated with known adverse characteristics, and only a small minority receive ADT intensification.

The optimal duration and intensity of ADT in the post-operative setting remains unclear. Several trials have prospectively evaluated the addition of ADT to salvage radiation after radical prostatectomy.[11–13,15,19] In this study, multivariate analysis confirmed that adverse pathologic features (e.g., pT3b/T4, pN1, grade group 4/5) were associated with increased likelihood of intended ADT use within MROQC. Short-term ADT given with salvage radiation has consistently been shown to improve biochemical control and decrease progression.[11–13] While the majority of patients within MROQC receiving ADT had an intended duration ≤6 months, a minority received therapy intensification, either with longer duration (≥24 months, 17% of patients) or with ARPI therapies (5%).

The MROQC cohort has a higher proportion of patients with adverse features (e.g., Gleason 8-10, pT3b, pN1) compared to GETUG-AFU-16, RTOG 0534, and the RADICALS-HD short-term ADT studies. By contrast, the cohort more closely resembles the patient population from the RADICALS-HD short vs. long-term ADT study.[15] This trial demonstrated an approximately 6% absolute improvement in metastasis-free survival (MFS) at 10 years with 24 months of ADT compared to 6 months.[15] A long-term update of RTOG 9601 reported significant improvements in 18-year distant metastases, prostate cancer death, and overall survival with two years of anti-androgen therapy (bicalutamide) versus placebo, albeit in a more historic patient

population with higher pre-RT PSA values.[20] Conversely, the recent DADSPORT meta-analysis reported that any duration of ADT improves 8-year MFS, with incrementally more benefit in patients with adverse prognostic features (e.g., pT3b, pre-RT PSA), but no additional benefit to prolonging duration.[16] Given the low rates of ADT intensification within the MROQC cohort despite being enriched for patients with aggressive pathologic features, our study suggests that some patients in real-world practices across Michigan may be undertreated. It is important to note, however, that 60% of patients in the MROQC cohort underwent PSMA imaging prior to radiation therapy to exclude clinically evident distant metastasis. By doing so, physicians and patients may be more comfortable with shorter durations of ADT given mutual concerns about potential toxicity. Additionally, intensification via ARPI therapy is not a standard of care in this patient population, likely contributing to provider hesitancy. Further studies are needed to risk stratify patients and elucidate the optimal setting, if any, for long-term ADT.

A secondary analysis of RTOG 9601 found that the subset of patients with a pre-RT PSA >0.6 ng/mL derived a survival benefit from two years of bicalutamide.[21] Similarly, the FORMULA 509 trial demonstrated that of patients with unfavorable pathologic features and a pre-RT PSA >0.5 ng/mL, intensification of short-term ADT with apalutamide may improve MFS.[14] And while RADICALS-HD did not find a differential benefit with ADT prolongation in a pre-specified analysis of pre-RT PSA level, long-term ADT was favored in patients with a pre-RT PSA >0.5 ng/mL with a HR for MFS of 0.67 (95% CI: 0.45 – 1.00).[15] However, the DADSPORT meta-analysis did not find a differential effect of the addition of ADT across a variety of PSA ranges (e.g., PSA >0.5 – 1.5 ng/mL versus ≤0.3 ng/mL).[16] We were interested in also evaluating a threshold of >0.5 ng/mL to mirror these contemporary studies and based on our analysis, providers within MROQC may be using pre-RT PSA as a guide for recommending

ADT. Whether a PSA threshold or PSA doubling time (PSA-DT) can guide ADT use is an ongoing area of research.

Pelvic nodal irradiation improves biochemical control in addition to short-term ADT, at the expense of increased acute toxicities.[11] We demonstrate that while similar pathologic characteristics are associated with both ADT and PLNRT (i.e., pT stage, pre-RT PSA), these populations are not overlapping, and some patients received only one of either modality. In the MROQC cohort, approximately 25% of those who received PLNRT did not receive ADT, an approach that was not evaluated in RTOG 0534.[11]

Consolidative radiation is distinguished from "true" adjuvant radiotherapy based on the presence of detectable post-prostatectomy PSA, as this represents detectable residual disease requiring further treatment.[10] Persistently detectable PSA is recognized as an adverse prognostic feature,[1] and a recent population-based study found men with PSA persistence had a 10 year risk of prostate-cancer specific mortality of 12%, compared to 2% in low-risk relapsed patients (Gleason 6/7, PSA-DT >12 months).[22] Another recent large retrospective cohort study suggested PSA persistence is associated with worse all-cause mortality and prostate cancer specific mortality in men with a pre-RP PSA ≤20 ng/mL, but cautioned that some of those with pre-RP PSA >20 ng/mL may be incorrectly diagnosed with PSA persistence by premature post-RP PSA evaluation.[23] Both RTOG 3506 and NRG-GU002 are evaluating therapy intensification with enzalutamide and docetaxel, respectively, in patients with PSA persistence, recognizing this as an adverse prognostic feature.[24,25] Other retrospective evidence suggests that PSA persistence may only be associated with worse oncologic outcomes in patients with additional "high-risk" features (pT3b, GG4/5, pre-RP PSA <20 ng/mL, pN1) and not "low risk" patients (pT2, GG1, PSA <10 ng/mL, pNx).[26] In this real-world prospective dataset, men receiving consolidative

radiotherapy represent a clinically meaningful subgroup of all PORT patients. Conversely, only 10% of patients in MROQC received true adjuvant therapy and most salvage patients received early treatment, at PSA levels between 0.2 and 0.5 ng/mL. This is in line with current evidence from the ARTISTIC meta-analysis,[4] though a criticism is the under-representation men with of multiple high risk features (e.g., only 20% RADICALS-RT patients had ≥2 of: Gleason 8-10, pT3b/T4, and/or positive margins).[27] The trials included in this meta-analysis have not reported on the subgroup of patients with persistently detectable post-RP PSA, and many consolidative patients in our cohort would have been excluded from these trials on the basis of post-operative PSA >0.1 ng/ mL (RAVES and GETUG-AFU 17) or >0.2 ng/mL (RADICALS-RT).[5,6,27] Caution is needed when applying these data to this particular at-risk subgroup, who may warrant therapy intensification.

One strength of this analysis is the use of prospective data collected within multicenter quality consortiums, with detailed radiation, ADT, PSA, and surgical information that is not often available in other population-based cohorts. An inherent limitation of MROQC is that the consortium only captures data on patients receiving radiation, and we are unable to characterize patients with biochemical recurrence (BCR) after radical prostatectomy who were not recommended radiotherapy. Some patients with BCR opt for observation depending on both pathologic and clinical factors, such as PSA trends and co-morbidities. These results therefore cannot be extrapolated to the overall post-prostatectomy patient population. Since the study population was restricted to only PORT patients, this introduces the risk of collider bias; both poor prognostic factors (e.g., PSA persistence) and intended ADT use could both independently influence the decision for a patient to receive PORT. However, the associations are likely to be internally valid for patients receiving PORT. Our subgroup analyses are susceptible to both Type

I and Type II errors given the multiple comparisons and relatively small patient numbers, respectively, and should be interpreted cautiously. Ultimately, these results are exploratory in nature and do not imply causal relationships between the evaluated prognostic features and intended ADT use. ADT duration in this study was based on physician's recommended duration, and not the duration completed by the patient. While some patients will not complete their planned course of ADT, intended duration is representative of physicians' practice patterns and not influenced by individual tolerability of androgen suppression. MRQOC did not collect PSA doubling time, which is part of a recently proposed risk classification tool for patients with BCR after prostatectomy,[28] thereby limiting our analysis. Detailed genomics testing data (e.g., Decipher) was currently insufficiently available in the database, which may also be influencing physician and patient decisions regarding ADT, and this will be explored within MROQC in the future. While MROQC is collecting metastasis data and patient-reported outcomes, follow-up is currently insufficient to report on these endpoints and may be a focus of future publications.

Within a prospective state-wide quality consortium, many post-prostatectomy patients receiving radiation had at least one adverse feature, with rates greater than those reported on most contemporary trials evaluating androgen deprivation therapy in this setting. ADT use was associated with known poor prognostic features, though only a minority receive ADT intensification. As more men with high-risk features undergo radical prostatectomy, prospectively defining the optimal management of these patients, especially those with post-operative PSA persistence, is paramount.

Data Availability Statement:

We are not authorized to share MROQC or MUSIC data. The data is individually owned by the member institutions of MROQC and MUSIC.

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Conflicts of Interest:

MS receives consulting fees from Innovative Analytics.

RD serves in a consulting or advisory role for Janssen Biotech.

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Table 1: Patient and Treatment Characteristics of Each Cohort

	All Patients (N = 345)[a]	Adjuvant (N = 35)[a]	Consolidative (N = 95)[a]	Salvage (N = 215)[a]	p-value[b]
Age, years	67 (63 – 71)	67 (60 – 70)	66 (63 – 71)	67 (62 – 71)	0.44
Race					
Black or African American	37 (10.7%)	6 (17.1%)	10 (10.5%)	21 (9.8%)	0.59
White	286 (82.9%)	28 (80.0%)	80 (84.2%)	178 (82.8%)	
Other	22 (6.4%)	1 (2.9%)	5 (5.3%)	16 (7.4%)	
Charlson Comorbidity Score					
0	253 (73.3%)	26 (74.3%)	77 (81.1%)	150 (69.8%)	0.03
1	47 (13.6%)	7 (20.0%)	10 (10.5%)	30 (14.0%)	
2+	45 (13.1%)	2 (5.7%)	8 (8.4%)	35 (16.2%)	
Pre-surgery PSA, ng/mL	7.50 (5.54 – 11.22)	6.90 (4.9 – 11.1)	8.52 (6.12 – 11.79)	7.30 (5.40 – 11.0)	0.02
Pre-RP NCCN Risk Group					
Low	16 (5.1%)	1 (3.1%)	1 (1.2%)	14 (7.0%)	0.002
Favorable Intermediate	52 (16.4%)	3 (9.4%)	10 (11.8%)	39 (19.5%)	
Unfavorable Intermediate	137 (43.2%)	18 (56.3%)	29 (34.1%)	90 (45%)	
High	112 (35.3%)	10 (31.2%)	45 (52.9%)	57 (28.5%)	
Pre-radiation PSA, ng/mL	0.30 (0.20 – 0.60)	0.07 (0.03 – 0.09)	0.50 (0.28 – 1.49)	0.30 (0.20 – 0.50)	0.006
Pathologic Grade Group					
1	32 (9.7%)	1 (3.0%)	3 (3.3%)	28 (13.5%)	<0.0001
2	100 (30.4%)	12 (37.5%)	15 (16.9%)	73 (35.1%)	
3	97 (29.5%)	11 (34.4%)	31 (34.8%)	55 (26.4%)	
4	66 (20.1%)	6 (18.8%)	29 (32.6%)	31 (14.9%)	
5	34 (10.3%)	2 (6.3%)	11 (12.4%)	21 (10.1%)	
Pathologic T Stage					
pT2	102 (31.4%)	7 (21.2%)	19 (21.4%)	76 (37.4%)	0.0005
pT3a	143 (44.0%)	14 (42.4%)	35 (39.3%)	94 (46.3%)	
pT3b	77 (23.7%)	12 (36.4%)	33 (37.1%)	32 (15.8%)	
T4	3 (0.9%)	0 (0%)	2 (2.2%)	1 (0.5%)	
Pathologic N Stage					
pN0/NX	308 (94.5%)	28 (84.9%)	80 (89.9%)	200 (98.0%)	0.0008
pN1	18 (5.5%)	5 (15.1%)	9 (10.1%)	4 (2.0%)	
Surgical Margin Status					
Negative	155 (47.7%)	11 (33.3%)	34 (38.2%)	110 (54.2%)	0.009
Positive	170 (52.3%)	22 (66.7%)	55 (61.8%)	93 (45.8%)	
≥1 High Risk Feature[d]					
No	151 (43.8%)	18 (51.4%)	19 (20%)	114 (53%)	<0.0001
Yes	194 (56.2%)	17 (48.6%)	76 (80%)	101 (47%)	
PET Results					
Not Performed	108 (34.4%)	22 (71.0%)	25 (29.1%)	61 (31.0%)	0.0002
Negative, or Prostate Bed Only	164 (52.2%)	9 (29.0%)	46 (53.5%)	109 (55.3%)	
Positive Regional Nodes	42 (13.4%)	0 (0.0%)	15 (17.4%)	27 (13.7%)	

[1] n (%) or median (IQR), total may not sum to 100% due to missingness
[b] ANOVA or chi-squared test
[c] Other includes Asian, American Indian, Alaskan Native, and Unknown/Not Reported
[d] ≥1 high risk feature, defined as pT3b/T4, pN1, Grade Group 4/5, and/or a pre-RT PSA >0.5 ng/mL

Abbreviations: PSA = prostate specific antigen, RP = Radical Prostatectomy, NCCN = National Comprehensive Cancer Network, PET = Positron Emission Tomography, IQR = Interquartile Range, ANOVA = analysis of variance

Table 2: Baseline Patient Characteristics Compared to Contemporary Prospective Trials

	MROQC Cohort	RADICALS-HD (0 vs. 6 mo)	RADICALS-HD (6 mo vs. 24 mo)	GETUG-AFU-16	RTOG 0534	RTOG 9601
Publication Date	2025	2024	2024	2019	2022	2017
Number of Patients	345	1480	1523	742	1,716	760
Enrollment Period	2020 – 2024	2007 – 2015	2008 – 2015	2006 – 2010	2008 – 2015	1998 – 2003
Age, median (IQR)	67 (63 – 71)	66 (61 – 69)	65 (60 – 69)	67	64 (59 – 69)	65 (60 – 69)
Pre-radiation PSA, ng/mL	0.30 (0.20 – 0.60)	0.21 (0.11 – 0.40)	0.23 (0.10 – 0.50)	0.30 (0.20 – 0.50)	0.35 (0.20 – 0.60)	0.6 (0.2 – 1.1)
Pathologic Gleason Score						
≤6	32 (9.7%)	211 (14%)	114 (7%)	N/A	265 (15.6%)	214 (28.2%)
7						413 (54.5%)
3+4	100 (30.4%)	704 (48%)	530 (35%)	N/A	687 (40.4%)	N/A
4+3	97 (29.5%)	394 (27%)	443 (29%)	N/A	457 (26.9%)	N/A
<8				661 (89.1%)		
8-10	100 (30.4%)	169 (11%)	434 (29%)	81 (10.9%)	290 (17.1%)	131 (17.3%)
Pathologic T Stage						
pT2	102 (31.4%)	603 (41%)	421 (27.7%)	397 (53.6%)	913 (54.7%)	248 (32.6%)
pT3						512 (76.4%)
pT3a	143 (44.0%)	628 (42.7%)	636 (41.9%)	248 (33.5%)	505 (30.2%)	N/A
pT3b	77 (23.7%)	231 (15.7%)	435 (28.7%)	94 (12.7%)	252 (15.1%)	N/A
T4	3 (0.9%)	9 (0.6%)	26 (1.7%)	1 (0.2%)	0 (0%)[1]	0 (0%)[1]
Pathologic N Stage						
pN0/NX	308 (94.5%)	1,423 (97%)	1394 (92%)	742 (100%)	1,716 (100%)	758 (100%)
pN1	18 (5.5%)	50 (3%)	129 (8%)	Excluded[1]	Excluded[a]	Excluded[a]
Surgical Margin Status						
Negative	155 (47.7%)	556 (38%)	559 (37%)	371 (50%)	838 (49%)	191 (25%)
Positive	170 (52.3%)	924 (62%)	964 (63%)	371 (50%)	861 (51%)	569 (75%)

N/A = not reported or not applicable
[a] Excluded per protocol

Table 3: Treatment-related Factors for Entire Cohort

	N (%) or Median (IQR)[a]
Time from RP to PORT, mo	
Median (IQR)	19.0 (7.0 – 40.0)
<6 months from RP	57 (16.7%)
≥6 - ≤12 mo from RP	79 (23.1%)
>12 - ≤24 mo from RP	64 (18.7%)
>24 months from RP	142 (41.5%)
Initial Post-Operative PSA[b]	
Persistent (≥0.1 ng/mL)	95 (27.5%)
Undetectable (<0.1 ng/mL)	240 (69.6%)
No PSA Draw During Range	10 (2.9%)
Adjuvant Radiation	
Number (% of Total)	35 (10.2%)
Median Time to RT, mo (IQR)	8.0 (4.0 – 16.0)
Consolidative Radiation	
Number (% of Total)	95 (27.5%)
Median Time to RT, mo (IQR)	6.0 (5.0 – 11.0)
Salvage Radiation	
Number (% of Total)	215 (62.3%)
Median Time to RT, mo (IQR)	29 (16.0 – 47.0)
EBRT Fractionation	
Ultra-hypofractionation (≤7)	18 (5.6%)
Moderate Hypofractionation (20-28)	100 (31.1%)
Conventional (>28)	202 (62.7%)
Non-standard (8 – 19)	2 (0.6%)
Radiation Fields +/- ADT	
Prostate Bed Only, No ADT	73 (22.7%)
Prostate Bed Only, With ADT	21 (6.5%)
Bed + Pelvic Lymph Node Fields, No ADT	56 (17.4%)
Bed + Pelvic Lymph Node Fields, With ADT	172 (53.4%)
ADT Recommended	
Yes	204 (59.6%)
No	138 (40.4%)
Total ADT Duration Intended	
>0 – ≤6 mo	133 (67.2%)
>6 - <12 mo	5 (2.5%)
≥12 - <24 mo	26 (13.1%)
≥24 mo	34 (17.2%)
ARPI Received	
Yes	10 (4.9%)
No	194 (95.1%)

[a] Total may not sum to 100% due to missingness
[b] First draw between 4 weeks and 6 months post-prostatectomy

Figure Legends:

Figure 1: Scatter plot of pre-radiation PSA by time to initiation of post-operative radiation (adjuvant, consolidative, or salvage).

Figure 2: Multivariate analysis of ADT Receipt. *indicates a p-value <0.05 and ** indicates a p-value <0.01, and *** indicates a p-value <0.001.

Figure 1

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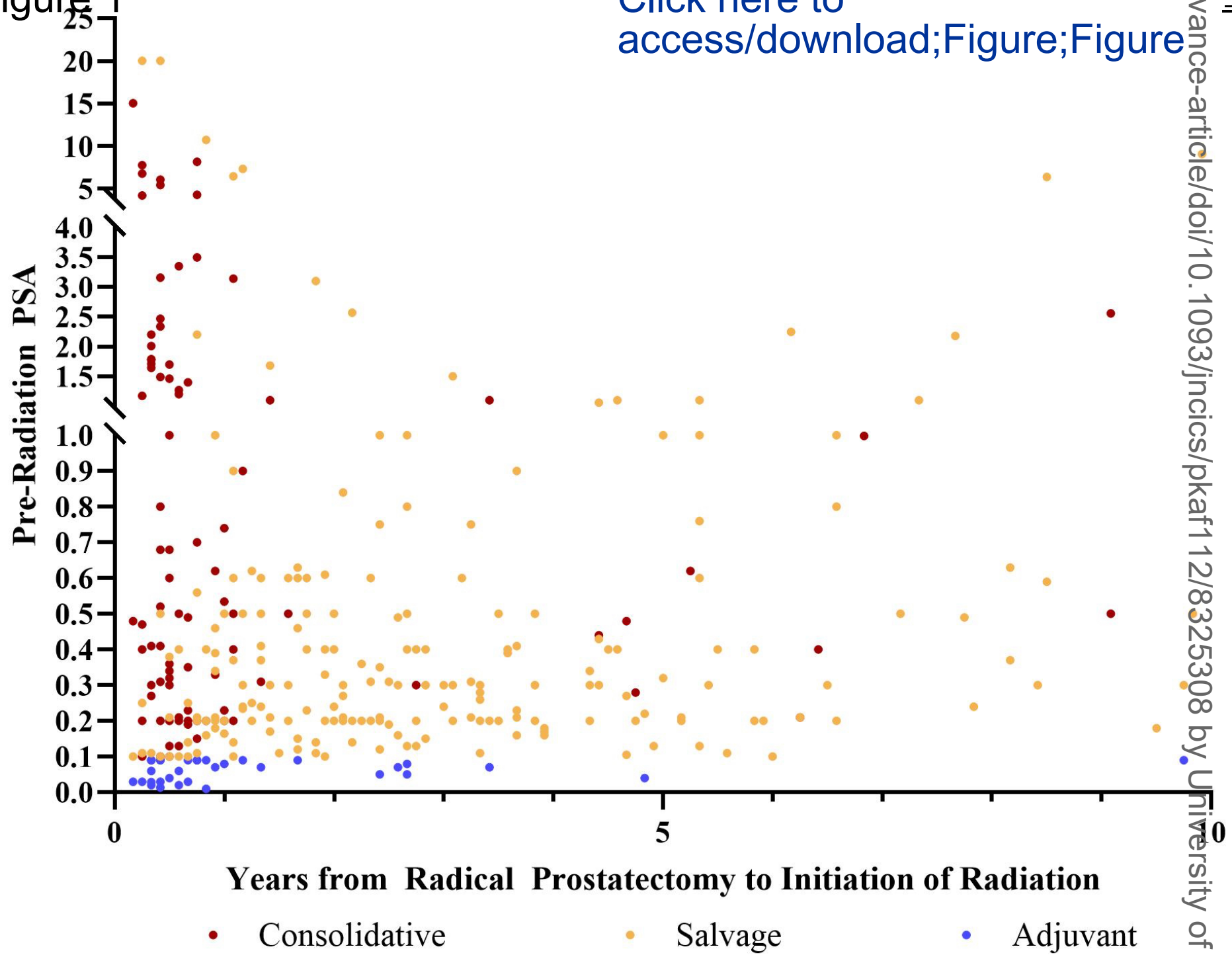

Figure 2

	ADT Receipt	
	Odds Ratio (95% CI)	**p-value**
Grade Group		
Grade Group 3 vs. 1/2	1.38 (0.76 – 2.52)	0.30
Grade Group 4/5 vs. 1/2	2.87 (1.51 – 5.56)	0.002
T Stage		
pT3a vs. pT2	1.58 (0.89 – 2.82)	0.12
pT3b/T4 vs. pT2	2.77 (1.34 – 5.93)	0.007
N Stage		
pN1 vs. pN0/NX	6.22 (1.35 – 47.57)	0.04
Maximum Pre-radiation PSA		
>0.5 ng/mL vs. ≤0.5 ng/mL	2.11 (1.17 – 3.91)	0.02
Radiation Timing		
Adjuvant vs. Salvage	0.17 (0.06 – 0.46)	<0.001
Consolidative vs. Salvage	1.18 (0.62 – 2.25)	0.62