Real-world treatment patterns in patients with biochemical recurrence after local therapy for prostate cancer: A retrospective analysis of a large US database

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INTRODUCTION

- Despite the frequent success of radical prostatectomy (RP) and radiation therapy (RT), 20–50% of patients with prostate cancer (PC) will eventually develop biochemical recurrence (BCR) within 10 years of primary localized therapy[1,2]
- BCR is characterized by rising prostate-specific antigen (PSA), represents disease progression, and is associated with an increased risk of metastasis and mortality[1,2]
- Patients with BCR who have short PSA doubling time (PSADT) are at increased risk of morbidity and mortality[2]
- Identification of BCR and stratification of patients with high- or low-risk BCR progression are important for informing disease prognosis and tailoring treatment choice, which in turn may influence clinical outcomes[2]
- However, the current landscape of treatments being used after BCR is unknown

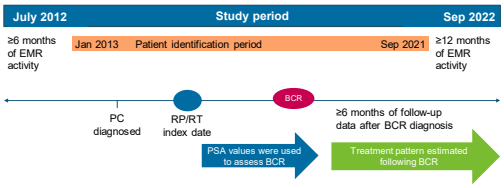
OBJECTIVE

- This study describes real-world treatment patterns for anti-cancer hormonal therapy (including androgen-deprivation therapy [ADT] and androgen receptor inhibitor [ARI] therapy) and RT among patients with PC who developed BCR after primary therapy, stratified by their PSADT (or risk status) before BCR

METHODS

- This retrospective cohort study used the Optum© Electronic Medical Records (EMR) database – a longitudinal nationally representative database containing multiple large healthcare provider organizations across the USA that covers >97 million patients
- Data used in this study spanned July 2012 to September 2022 (Figure 1)
- Eligible patients were adults (aged ≥18 years) with PC who developed BCR after RP or RT and had ≥6 months of follow-up data after BCR diagnosis to analyze treatment received
  - Patients with other cancers or metastatic PC before or within 3 months of primary therapy were excluded
- BCR was defined as:
  - PSA ≥0.2 ng/mL ≥6 weeks after RP (American Urology Association recommendation)[3]
  - PSA ≥nadir (lowest PSA value within 6 weeks to 18 months after RT) + 2 ng/mL after RT (Phoenix recommendation)[4] or ≥5 ng/mL
- Risk status was defined using PSADT before BCR
  - PSADT of <12 months or ≥12 months was used to define high- or low-risk BCR, respectively
  - In a sensitivity analysis, high- or low-risk status was defined using the cutoff of ≤9 months or >9 months, respectively

Figure 1. Study design



BCR, biochemical recurrence; EMR, Electronic Medical Record; PC, prostate cancer; PSA, prostate-specific antigen; RP, radical prostatectomy; RT, radiotherapy.

RESULTS

Table 1. Baseline characteristics of patients with BCR by risk status*

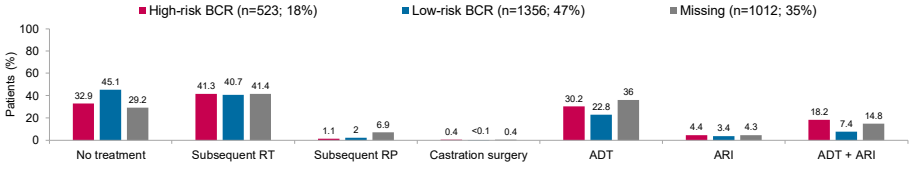
	RP cohort (n=2891)			RT cohort (n=697)		
	High-risk BCR (n=523; 18%)	Low-risk BCR (n=1356; 47%)	Missing (n=1012; 35%)	High-risk BCR (n=498; 71%)	Low-risk BCR (n=122; 18%)	Missing (n=77; 11%)
Age at first RP/RT date, years						
Median (Q1–Q3)	66 (61–70)	64 (59–69)	66 (60–71)	68 (62–75)	68 (62–74)	68 (63–75)
Age at BCR diagnosis, years						
Median (Q1–Q3)	67 (62–71)	66 (61–71)	66 (60–71)	70 (64–78)	71 (64–76)	71 (65–76)
Race, n (%)						
African American	61 (11.7)	174 (12.8)	131 (12.9)	82 (16.5)	24 (19.7)	13 (16.9)
Caucasian	438 (83.7)	1133 (83.6)	840 (83.0)	402 (80.7)	93 (76.2)	61 (79.2)
Other	24 (4.6)	49 (3.6)	41 (4.1)	14 (2.8)	5 (4.1)	3 (3.9)
Insurance type, n (%)						
Commercial	206 (39.4)	579 (42.7)	368 (36.4)	179 (35.9)	45 (36.9)	31 (40.3)
Public insurance	124 (23.7)	286 (21.1)	277 (27.4)	159 (31.9)	29 (23.8)	25 (32.5)
Other	125 (23.9)	309 (22.8)	234 (23.1)	127 (25.5)	36 (29.5)	17 (22.1)
Unknown	68 (13.0)	182 (13.4)	133 (13.1)	33 (6.6)	12 (9.8)	4 (5.2)
PSA value before BCR						
Median (Q1–Q3)	0.43 (0.31–0.75)	0.21 (0.20–0.27)	0.80 (0.32–2.99)	4.20 (2.94–6.20)	4.95 (3.36–6.52)	8.10 (5.70–17.50)
Follow-up (BCR to last active date), months						
Median (Q1–Q3)	30.2 (18.9–50.6)	31.9 (18.3–51.2)	35.9 (21.2–57.5)	23.3 (14.2–39.6)	24.0 (13.3–44.0)	22.3 (12.8–46.3)

*PSADT of <12 months or ≥12 months was used to define high- or low-risk BCR, respectively.
BCR, biochemical recurrence; PSA, prostate-specific antigen; PSADT, prostate-specific antigen doubling time; Q, quartile; RP, radical prostatectomy; RT, radiation therapy.

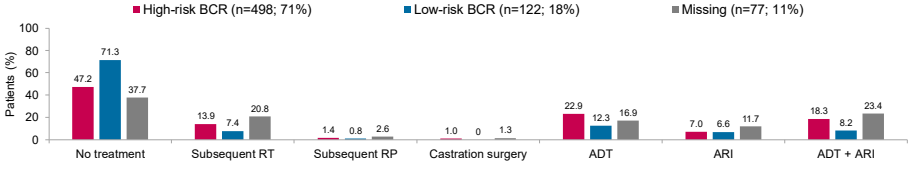
- A total of 3588 patients with BCR (RP cohort: n=2891; RT cohort: n=697) were included in the study (Table 1)
  - Median (Q1–Q3) age at BCR diagnosis was 67 (61–72) years
  - Most patients were Caucasian (82.7%)
  - Median (Q1–Q3) follow-up was 30.8 (18.1–50.8) months
- Of the 3588 patients, 28.5% (n=1021) and 41.2% (n=1478) had high- or low-risk BCR, respectively; 30.4% (n=1089) had missing PSADT or undetermined risk status

Figure 2. Treatment patterns after BCR† by risk status‡

(A) RP cohort (n=2891)



(B) RT cohort (n=697)



Treatment patterns estimated from ≥6 months of follow-up data after BCR diagnosis.
†BCR was defined as PSA ≥0.2 ng/mL after RP and PSA ≥nadir + 2 ng/mL after RT;
‡PSADT of <12 months or ≥12 months was used to define high- or low-risk BCR, respectively.
ADT, androgen-deprivation therapy; ARI, androgen receptor inhibitor; BCR, biochemical recurrence; PSA, prostate-specific antigen; PSADT, prostate-specific antigen doubling time; RP, radical prostatectomy; RT, radiation therapy.

- Many patients did not receive any treatment, including those with high-risk BCR (Figure 2)
- RP cohort: the most common treatments for high- and low-risk BCR were RT, ADT monotherapy, and ADT + ARI (Figure 2)
- RT cohort: the most common treatments for high- and low-risk BCR were ADT monotherapy and ADT + ARI (Figure 2)
- Bicalutamide was the most common ARI monotherapy (data no shown)
- Similar findings were observed in the sensitivity analyses (PSADT of ≤9 months or >9 months; data not shown)
- In both cohorts, patients with missing PSADT had a similar treatment profile to high-risk BCR patients (data not shown)

LIMITATIONS

- Retrospective studies are subject to possible selection bias and unknown potential confounders
- People with a low income or without insurance may be under-represented in the EMR data, and the study may underestimate true prescription use in clinical practice

CONCLUSIONS

- This real-world retrospective study evaluated treatment patterns in patients with PC with BCR from a large US EMR database, with a median follow-up of 31 months
- Even within the high-risk BCR population (PSADT of <12 months or ≤9 months), many patients did not receive any treatment following BCR
  - After RP, the most common treatments were subsequent RT followed by ADT monotherapy and ADT + ARI
  - After RT, the most common treatments were ADT monotherapy and ADT + ARI
- Future studies should assess differences in outcomes for treated and non-treated patients
- Physicians should discuss available treatment options with patients and caregivers at the first sign of BCR in PC

PLAIN LANGUAGE SUMMARY

- Prostate cancer (PC) is the most common cancer diagnosed in men in the USA and was the second leading cause of death in 2023. Primary treatment options include radical prostatectomy (RP) and radiation therapy (RT); however, approximately 20–50% will present with rising prostate-specific antigen – a state known as biochemical recurrence (BCR)
- Patients with BCR tend to have high risk of morbidity and mortality, with approximately 24–34% of patients going on to develop metastasis. Therefore, it is important to monitor patients for BCR, identify their risk for disease progression, and tailor treatments to optimize outcomes
- In this study, we examined medical record data from a large, nationally representative US database to examine real-world treatment patterns in patients with PC who developed BCR after primary therapy
- Our analysis showed that many patients with BCR are not being treated – even those considered at high risk for disease progression. Of the patients who were treated, most received subsequent RT or androgen-deprivation therapy alone
- The findings from our study show the differences in the real-world treatment of patients with BCR and highlight a substantial treatment gap
- Patients and caregivers should discuss available treatment options and weigh individual risks and benefits at the first sign of BCR in PC

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Acknowledgments: Medical writing support was provided by Brian Jepson, PhD of Luna, OPEN Health Communications (London, UK), supported by Bayer HealthCare Pharmaceuticals (Whippany, NJ, USA), in accordance with Good Publication Practice (GPP) guidelines (www.ismpp.org/gpp-2022)..

Disclosures: **Neal D. Shore**: Consulting or advisory role: Bayer, Janssen Scientific Affairs, Dendreon, Tolmar, Ferring, Medivation/Astellas, Amgen, Pfizer, AstraZeneca, Myovant Sciences, Astellas Pharma, AbbVie, Merck, Bristol Myers Squibb/Sanofi, Clovis Oncology, Exact Imaging, FerGene, Foundation Medicine, CG Oncology, InVitae, MDxHealth, Myriad Genetics, Nymox, Propella Therapeutics, Genzyme, Sanofi, Sesen Bio, CG Oncology, Exact Sciences, Genesis Cancer Care, Pacific Edge Biotechnology, Phosphorus, UroGen Pharma, Speciality Networks, PeerView, Clarity Pharmaceuticals, Lantheus Medical Imaging, Lilly, Photocure, Sema4, Telix Pharmaceuticals, Tempus, Vaxiion; Speakers' bureau: Janssen, Bayer, Dendreon, Astellas Pharma, AstraZeneca, Clovis Oncology, Pfizer, Guardant Health, Merck, Foundation Medicine; Expert testimony: Ferring; Other relationship: Photocure, Alessa Therapeutics; Research funding: AbbVie, Amgen, Astellas Pharma, AstraZeneca, Bayer, Bristol Myers Squibb/Pfizer, Boston Scientific, Clovis Oncology, Dendreon, Exact Imaging, Ferring, Foundation Medicine, InVitae, Janssen, MDxHealth, Merck, Myovant Sciences, Myriad Genetics, Nymox, Pfizer, Sanofi, Sesen Bio, Tolmar, CG Oncology, DisperSol, FORMA Therapeutics, Guardant Health, Jiangsu Yahong Meditech, Novartis, Pacific Edge, POINT Biopharma, Propella Therapeutics, Seattle Genetics, MT Group, Theralase, Veru, Zenflow, Advantagene, Aragon Pharmaceuticals, Endocyte, Exelixis, FKD Therapies, Genentech, ISTARI Oncology, Medivation, OncoCellMDx, ORIC Pharmaceuticals, Palette Life Sciences, Plexxikon, RhoVac, Steba Biotech, UroGen Pharma, Urotronic, US Biotest, Vaxiion. **Nasreen Khan**: Employment: Bayer; Consulting or advisory role: RWE consultant (self and immediate family member); Travel, accommodations, expenses: Bayer (self and immediate family member). **Rana R. McKay**: Consulting or advisory role and/or research funding: Astellas, Medivation, AstraZeneca, Bayer, BMS, Calithera Biosciences, Caris Life Sciences, Dendreon, Exelixis, Janssen, Merck, Myovant Sciences, Novartis, Pfizer, Sanofi, Sorrento Therapeutics, Tempus, Vividion Therapeutics. **Guifang Chen, Vlasta Hlebec, Shankar Srinivasan, Zdravko Vassilev**: Employment: Bayer. **Niculae Constantinovici**: Employment: Bayer; Stock and other ownership interests: Bayer. **Daniel E. Spratt**: Honoraria: Astellas, AstraZeneca, Bayer, Blue Earth Diagnostics, Elekta, Boston Scientific, Janssen Pharmaceuticals, Myovant Sciences, Novartis, Pfizer, Varian. Consulting or advisory role: Janssen Oncology, AstraZeneca, Boston Scientific, Bayer, Blue Earth Diagnostics, Varian Medical Systems; Research funding: Janssen (Inst).

Presented at ISPOR Europe 2024, Barcelona, Spain, November 17–20, 2024

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