Patient-Reported Burden of Disease Across Treatment Regimens in Metastatic Castration-Resistant Prostate Cancer: An Analysis of the IRONMAN Registry

Divyan Chopra[1], Emma C. Martin[2], Katie Frampton[2], Mike Greenwood[2], Kim Cocks[2], Jake Vinson[3], Daniel George[4], Philip W. Kantoff[5], Lorelei Mucci[6], Joaquin Mateo Valderrama[7], Kim Chi[8], Deborah Enting[9], Ian D. Davis[10], Anders Bjartell[11], Aurelius Omlin[12], Kjell Russnes[13], Ray McDermott[14], Andrey Fay[15], Charles Waihenya[16], Ademola Popoola[17], Simone Badal[18], John Lazarus[19], Camille Ragin[20], Folakemi Odedina[21], Natalie Greaves[22], Simon Anderson[23], and Bjoern Stollenwerk[24]

Affiliations: [1]Amgen, Thousand Oaks, CA, USA; [2]Adelphi Values, Bollington, UK; [3]Prostate Cancer Clinical Trials Consortium, New York, NY, USA; [4]Duke Cancer Institute, Durham, NC, USA; [5]Convergent Therapeutics, Cambridge, MA, USA; [6]Harvard T.H. Chan School of Public Health, Boston, MA, USA; [7]Vall d'Hebron Barcelona Hospital Campus, Barcelona, Spain; [8]BC Cancer – Vancouver Centre, University of British Columbia, Vancouver, BC, Canada; [9]Guy's and St Thomas' NHS Foundation Trust, London, UK; [10]Monash University and Eastern Health Clinical School, Melbourne, Australia; [11]Skåne University Hospital, Malmö, Sweden; [12]Onkozentrum Zürich, University of Zurich, Zurich, Switzerland; [13]Oslo University Hospital, Oslo, Norway; [14]St. Vincent's University Hospital and University College Dublin, Dublin, Ireland; [15]PUCRS School of Medicine, Porto Alegre, Brazil; [16]University of Nairobi, Nairobi, Kenya; [17]University of Ilorin Teaching Hospital, Ilorin, Nigeria; [18]The University of the West Indies, Kingston, Jamaica; [19]University of Cape Town, Cape Town, South Africa; [20]Fox Chase Cancer Center, Philadelphia, PA, USA; [21]Mayo Clinic Comprehensive Cancer Center, Rochester, MN, USA; [22]The University of the West Indies, Cave Hill, Barbados; [23]The University of the West Indies, Cave Hill, Barbados; [24]Amgen (Europe) GmbH, Rotkreuz, Switzerland.

BACKGROUND

Prostate cancer is the second most diagnosed cancer among men globally, and accounts for 14% of cancer diagnoses globally and 7% of cancer-related deaths in 2020 (1). Although most patients initially respond to androgen deprivation therapy (ADT), resistance eventually develops, leading to castration-resistant prostate cancer (CRPC), a more aggressive and treatment-refractory disease state (2).

Up to 20% of prostate cancer cases metastasize to lymph nodes, bones, or distant organs (3). Patients diagnosed with metastatic CRPC (mCRPC), recently termed androgen pathway modulation-resistant (APMR) prostate cancer by PCWG4 (4), have poor prognosis with a five-year survival rate of 34% (5,6).

Patients with mCRPC experience a substantial symptom burden (7), as well as impaired health-related quality of life (HRQoL) (8). While the impact of mCRPC treatment on HRQoL has been assessed in a number of clinical trials (9,10), these were restricted to a single treatment class or country. To gain a more complete understanding of the impact of real-world clinical practice, the aim of this study was to assess how different treatment classes impact patient HRQoL, using data from a large, multinational cohort of patients with mCRPC.

OBJECTIVE

The objective of this study was to provide real-world patients' insights into the HRQoL and symptom burden in patients with mCRPC, using patient-reported outcome (PRO) data collected in the International Registry for Men with Advanced Prostate Cancer (IRONMAN) including:

- Characterising HRQoL over time by treatments received (taxane chemotherapy, ARPI) post-enrolment in the IRONMAN Registry
- Summarising HRQoL stratified by exposure to taxane chemotherapy prior to enrolment.

METHODS

Data Source

The IRONMAN Registry began enrolment in 2017 to collect information about patients with prostate cancer across 15 countries*, including treatments received and side effects experienced by patients. Treatment data and patient enrolment characteristics are collected from medical records, pathology reports, questionnaires, blood biospecimens, and physician questionnaires (11).

PROs were collected at enrolment, then every 3 months, including European Organization for Research and Treatment of Cancer Quality of Life Questionnaire – Core 30 (EORTC QLQ-C30) and Brief Pain Inventory – Short Form (BPI-SF) (Q3 & Q5). The IRONMAN data collected until 30 September 2024 was used for these analyses.

**Australia, Barbados, Brazil, Canada, Jamaica, Kenya, Ireland, Nigeria, Norway, South Africa, Spain, Sweden, Switzerland, UK and the USA.*

Study cohort

Treatment cohorts were defined by the first treatment initiated following enrolment in the IRONMAN registry. HRQoL was summarised in treatment cohorts with sufficient data (>50 patients), which included:

- taxane chemotherapy [TC]
- androgen receptor pathway inhibitor [ARPI]

HRQoL was summarised descriptively over time in each treatment cohort using mean scores. PRO assessments were assigned to 3-week windows post- treatment initiation.

Analyses were repeated stratified by treatment with taxane chemotherapy prior to enrolment (prior-taxane and taxane-naïve).

RESULTS

1151 patients with mCRPC at enrolment were identified, with 1084 included in the analysis, of these 620 patients received new treatments post-enrolment; 91 initiated TC and 167 initiated ARPI with evaluable baseline and follow-up HRQoL assessments (Figure 1).

In the mCRPC population, baseline characteristics were similar across the treatment cohorts (TC, ARPI) and when stratified by prior taxane and prior taxane-naïve groups(Table 1).

HRQoL and pain score trajectories were similar between the two treatment groups at treatment start (Table 2, Figure 2) and remained relatively stable during the 6-month follow-up (Figure 3). Stratification by prior TC exposure also showed similar PRO trajectories (Figure 4).

Table 1: Sample characteristics

	All mCRPC		Prior Taxane Chemotherapy		Prior Taxane-Naïve	
	Taxane chemotherapy (N=158)	ARPI (N=273)	Taxane chemotherapy (N=58)	ARPI (N=69)	Taxane chemotherapy (N=100)	ARPI (N=204)
Age						
< 65 Years	43 (27.2%)	56 (20.5%)	18 (31.0%)	22 (31.9%)	25 (25.0%)	34 (16.7%)
65-74 Years	68 (43.0%)	99 (36.3%)	25 (43.1%)	33 (47.8%)	43 (43.0%)	66 (32.4%)
≥ 75 Years	47 (29.7%)	118 (43.2%)	15 (25.9%)	14 (20.3%)	32 (32.0%)	104 (51.0%)
Region						
USA	35 (22.2%)	107 (39.2%)	11 (19.0%)	19 (27.5%)	24 (24.0%)	88 (43.1%)
Europe	92 (58.2%)	88 (32.2%)	37 (63.8%)	32 (46.4%)	55 (55.0%)	56 (27.5%)
Rest of World	31 (19.6%)	78 (28.6%)	10 (17.2%)	18 (26.1%)	21 (21.0%)	60 (29.4%)
Race						
White / Caucasian	122 (77.2%)	196 (71.8%)	49 (84.5%)	51 (73.9%)	73 (73.0%)	145 (71.1%)
Other / Missing	36 (22.8%)	77 (28.2%)	9 (15.5%)	18 (26.1%)	27 (27.0%)	59 (28.9%)
ECOG PS						
Grade 0	69 (43.7%)	136 (49.8%)	22 (37.9%)	31 (44.9%)	47 (47.0%)	105 (51.5%)
Grade 1	48 (30.4%)	72 (26.4%)	19 (32.8%)	18 (26.1%)	29 (29.0%)	54 (26.5%)
Grade 2+	7 (4.4%)	19 (7.0%)	3 (5.2%)	7 (10.1%)	4 (4.0%)	12 (5.9%)

Figure 2: HRQoL prior to initiating first post-enrolment treatment

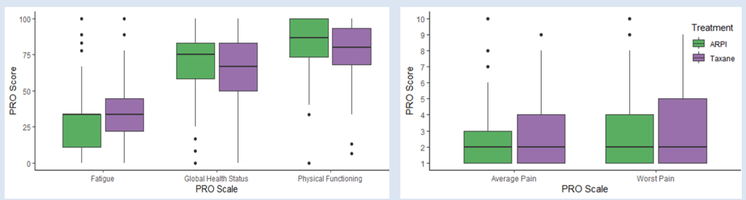


Figure 1: Patient flow

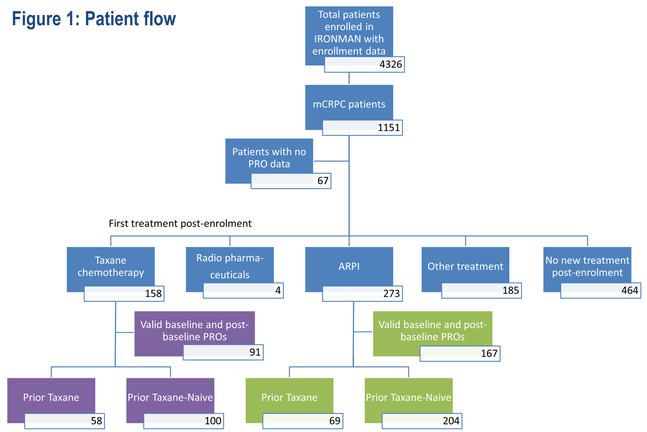
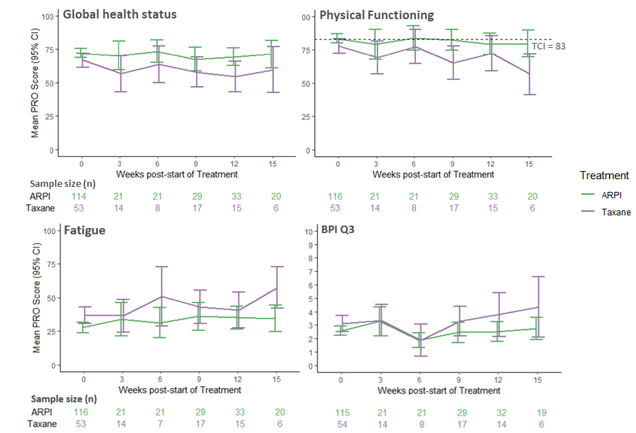


Figure 3: Mean HRQoL over time

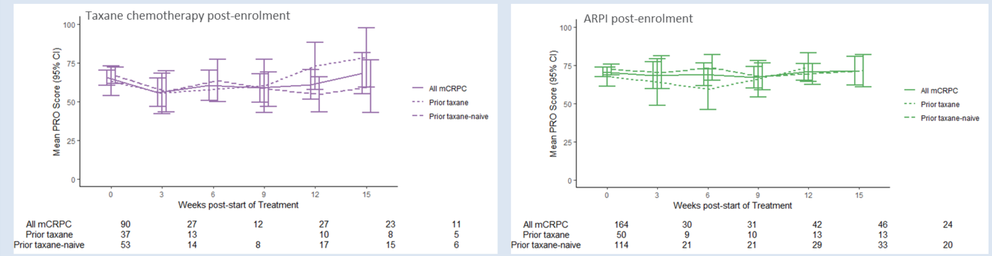


Note: for global health status and physical functioning higher scores represent better health states, for fatigue and BPI pain scores higher scores represent worse health states

Table 2: HRQoL prior to initiating first post-enrolment treatment – mean (95% CI)

	All mCRPC		Prior taxane chemotherapy		Prior taxane-naïve	
	Taxane chemotherapy N=91	ARPI N=167	Taxane chemotherapy N=37	ARPI N=50	Taxane chemotherapy N=54	ARPI N=117
Global - status	65.3 (60.3, 70.3)	70.7 (67.6, 73.8)	63.3 (53.6, 73.0)	67.5 (61.1, 73.9)	66.7 (61.3, 72.0)	72.1 (68.6, 75.6)
Physical functioning	78.4 (74.0, 83.0)	82.8 (79.8, 85.7)	79.3 (71.8, 86.8)	81.1 (75.5, 86.6)	77.9 (72.1, 83.6)	83.5 (80.0, 87.0)
Fatigue	35.2 (30.1, 40.2)	28.4 (25.2, 31.6)	33.0 (24.4, 41.7)	30.2 (23.8, 36.6)	36.7 (30.3, 43.0)	27.6 (23.9, 31.4)
Worst pain	3.35 (2.76, 3.74)	2.75 (2.41, 3.09)	3.46 (2.60, 4.32)	3.19 (2.41, 3.97)	3.11 (2.51, 3.71)	2.57 (2.21, 2.93)

Figure 4: Global Health Status mean scores over time by prior treatment



KEY TAKEAWAY

No observable improvement in key PRO domains highlight the continued burden and need for improved treatment options for patients with mCRPC.

LIMITATIONS

Incomplete PRO assessments may reflect dropout due to adverse events, disease progression or death, leading to potentially underestimating disease burden and limiting generalizability.

PRO assessment may not have been collected close to the start of treatment, which may limit interpretability.

CONCLUSIONS

In this real-world global cohort of patients with mCRPC, self-reported disease burden was considerable, surpassing thresholds for clinical importance (TCI) for physical functioning, where below 83 is considered a clinically important problem to be addressed (12).

The burden was more pronounced among those receiving taxane chemotherapy post-enrolment.

HRQoL trajectories remained stable during follow-up with no observable improvement in key domains, emphasizing the need for improved treatment options for mCRPC.

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