Abstract 26-3126

IP73-12: Real-world darolutamide safety and effectiveness in patients with nonmetastatic castration-resistant prostate cancer (nmCRPC) with comorbidities and concomitant medications: *Post hoc* analyses at DAROL interim analysis 4 (IA4)

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In real-world settings, darolutamide can be considered as a standard-of-care treatment option for patients with nmCRPC, regardless of comorbidity status

SUMMARY

- Darolutamide is a standard-of-care treatment for men with nmCRPC
- The real-world DAROL study included 799 patients, most of whom were elderly with other health conditions and were taking additional medications. About one-third had low to moderate comorbidities, whereas two-thirds had high comorbidities
- Patients with high comorbidities experienced more medical problems, especially fatigue, but most of these problems were of low severity, and few patients had to stop treatment as a result. Treatment effectiveness, including PSA response, was generally similar between comorbidity levels. Quality of life was generally good at treatment start and remained stable for up to 3 years in both subgroups
- Overall, these results show that darolutamide is effective and well-tolerated in real-world patients with nmCRPC, including those with multiple comorbidities

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Footnotes
*Safety analysis set includes all patients enrolled in the study who have taken ≥1 dose of darolutamide (according to the investigator's routine clinical practice) and completed ≥12 months of treatment or discontinued treatment.
†Medical history is listed by system organ class with a cut-off of >10% of patients.
‡Prior and concomitant therapies are listed by medication class with a cut-off of >10% of patients.
§Excluding prostate cancer therapy. Concomitant medications started before darolutamide and were ongoing at darolutamide initiation.
¶Including calcium homeostasis, corticosteroids for systemic use, pituitary and hypothalamic hormones and analogs, and thyroid therapy. Excluding sex hormones and insulins.
**Including antineoplastic agents, endocrine therapy, immunostimulants, and immunosuppressants.
††TEAEs include all events, including those not deemed by the investigator to be related to darolutamide.
‡‡Some patients had more than one action taken.
§§Two patients had fatigue with no grade specified in the high comorbidities subgroup.
¶¶One patient had asthenia with no grade specified in the high comorbidities subgroup.
***Full analysis set includes patients who received ≥1 dose of darolutamide (according to the investigator's routine clinical practice), met inclusion/exclusion criteria, and had ≥1 post-baseline assessment after receiving darolutamide.
†††Cox regression models adjusted by IPTW used the baseline covariates of age, race, region, Gleason score, ECOG PS, cancer stage, local/regional lymph nodes, previous ADT use, bone health agents use, log transformation of PSA level, PSADT, time from initial diagnosis to castration resistance, alanine aminotransferase, bilirubin, alkaline phosphatase, lactate dehydrogenase, hemoglobin, and neutrophil:lymphocyte ratio. For all covariates with missing values >20%, the multiple imputation method was used to impute the missing values.
‡‡‡Death was treated as a competing risk.
§§§The survey may not be collected exactly at the specified treatment timelines. In that case, the closest collected survey date to the timeline is reported.
¶¶¶Minimally important change, required for reporting a difference in the health status, defined as ± 0.1 variation in the EQ-5D-3L index score.[4]
****Excludes patients with missing observations at that timepoint.
††††Deterioration is determined by a decrease in the EQ-5D-3L index score, with a patient reporting a higher level of problems in one or more of the five dimensions (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression) over time.
‡‡‡‡Stable/improvement is determined by no change or an increase in the EQ-5D-3L index score, with a patient reporting the same or a lower level of problems in one or more of the five dimensions over time.

Abbreviations
ADT, androgen deprivation therapy; **CCI**, Charlson Comorbidity Index; **CI**, confidence interval; **ECOG PS**, Eastern Cooperative Oncology Group performance status; **EQ-5D-3L**, EuroQol 5 dimensions 3 levels; **HRQoL**, health-related quality of life; **IA4**, interim analysis 4; **IPTW**, inverse probability of treatment weighting; **IQR**, interquartile range; **MFS**, metastasis-free survival; **nmCRPC**, nonmetastatic castration-resistant prostate cancer; **PSA**, prostate-specific antigen; **PSA ≥50**, ≥50% reduction in PSA from baseline; **PSA ≥90**, ≥90% reduction in PSA from baseline; **PSADT**, PSA doubling time; **TEAE**, treatment-emergent adverse event.

References
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Disclosures
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OBJECTIVE

- The aim of the international DAROL study (NCT04122976) is to assess real-world safety and effectiveness of darolutamide in patients with nmCRPC and to support the phase 3 ARAMIS trial[1,2]
- In this elderly population, many patients have comorbidities and are receiving concomitant medication. We report real-world outcomes in patients treated with darolutamide with comorbidities and concomitant medications classified by CCI score

COMORBIDITIES AND CONCOMITANT MEDICATIONS

- Most patients in DAROL IA4 had at least one ongoing comorbidity, most commonly vascular and metabolic disorders and/or were receiving at least one concomitant medication at study entry
- At DAROL IA4 (n=799*), a CCI score of 5 was used as the cut-off to define the CCI subgroups:[3]
  - CCI score ≤5: 34% of patients had low to moderate comorbidities
  - CCI score >5: 66% of patients had high comorbidities

System organ class, %†	Low to moderate comorbidities (N=269)*		High comorbidities (N=530)*	
	Ongoing at study start	Occurring after study start	Ongoing at study start	Occurring after study start
All	92.4	7.6	93.2	6.8
Vascular	60.2	5.3	71.0	5.0
Metabolism and nutrition	49.7	1.2	59.6	3.9
Musculoskeletal	18.1	0	33.1	1.1
Cardiac	9.9	0.6	32.9	6.3
Renal and urinary	12.9	2.9	31.5	3.4
Gastrointestinal	14.0	4.1	26.1	3.6
Reproductive system	19.3	2.3	21.5	2.9
Respiratory	5.3	2.9	20.0	2.3
Nervous system	7.0	1.8	17.5	4.1
Psychiatric	9.4	1.2	15.9	0.7
Blood and lymphatic system	4.1	0.6	10.4	0.7

Medication class, %‡	Low to moderate comorbidities (N=269)*		High comorbidities (N=530)*	
	Prior medication	Concomitant medication§	Prior medication	Concomitant medication§
Any	61.0	69.9	79.2	82.6
Cardiovascular system	46.5	52.4	65.3	68.3
Alimentary tract and metabolism	35.3	47.6	60.6	65.5
Nervous system	25.3	31.6	48.1	54.0
Blood and blood-forming organs	23.8	27.1	45.3	48.7
Musculoskeletal system	21.6	28.3	38.1	42.8
Genitourinary system and sex hormones	17.5	25.7	34.3	39.2
Dermatologicals	12.3	20.8	22.5	31.9
Sensory organs	8.9	17.5	22.1	30.4
Respiratory system	9.7	15.6	17.9	24.9
Systemic hormonal preparations¶	10.4	13.4	17.9	22.5
Anti-infectives for systemic use	3.3	12.3	5.8	17.2
Antineoplastic and immunomodulating agents**	7.1	7.8	10.9	12.6

BASELINE CHARACTERISTICS

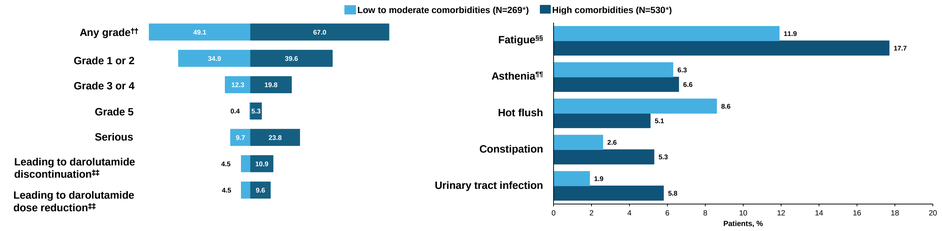
- In the low to moderate comorbidities subgroup, there were proportionally more younger patients and more patients with ECOG PS 0 than in the high comorbidities subgroup
- Gleason score, baseline PSA, and PSADT were generally balanced between subgroups

Demographics and baseline patient characteristics		Low to moderate comorbidities N=269*	High comorbidities N=530*
Age, years	Median (IQR) [range]	72 (67–77) [49–79]	82 (78–86) [52–98]
Age category, n (%)	<65 years	40 (14.9)	7 (1.3)
	65–74 years	128 (47.6)	72 (13.6)
	75–84 years	101 (37.5)	272 (51.3)
	≥85 years	0	179 (33.8)
Race, n (%)	White	128 (47.6)	305 (57.5)
	Asian	83 (30.9)	146 (27.5)
	Black	9 (3.3)	19 (3.6)
	Other	5 (1.9)	3 (0.6)
	Not reported	44 (16.4)	57 (10.8)
ECOG PS, n (%)	0	186 (69.1)	265 (50.0)
	1	41 (15.2)	158 (29.8)
	2/3	6 (2.2)	38 (7.2)
	Not reported	36 (13.4)	69 (13.0)

Baseline disease characteristics		Low to moderate comorbidities N=269*	High comorbidities N=530*
Gleason score at initial diagnosis, n (%)	<8	105 (39.0)	241 (45.5)
	≥8	153 (56.9)	246 (46.4)
	Missing	11 (4.1)	43 (8.1)
PSA before study entry, ng/mL	Median (IQR) [range]	3.3 (2.2–7.8) [0.0–141.0]	4.3 (2.4–10.1) [0.0–248.0]
PSA category, n (%)	<2 ng/mL	57 (21.2)	91 (17.2)
	2–10 ng/mL	161 (59.9)	303 (57.2)
	>10 ng/mL	50 (18.6)	134 (25.3)
	Missing	1 (0.4)	2 (0.4)
PSADT, months	Median (IQR) [range]	4.6 (2.7–7.7) [0.0–92.8]	5.8 (3.3–9.0) [0.0–668.4]
PSADT category, n (%)	≤6 months	129 (48.0)	196 (37.0)
	>6 months	71 (26.4)	188 (35.5)
	Missing	69 (25.7)	146 (27.5)

SAFETY OVERVIEW

- The median follow-up (time from start of treatment until data cut-off/end of observation) was similar between CCI subgroups:
  - Low to moderate comorbidities 22.2 months; high comorbidities 22.6 months
- Frequencies of any-grade TEAEs, serious TEAEs, and discontinuations due to TEAEs were higher in the high vs the low to moderate comorbidities subgroup
- Fatigue was the most frequently reported individual TEAE, with proportionally more patients with fatigue in the high than the low to moderate comorbidities subgroup



EFFECTIVENESS OUTCOMES

- Effectiveness outcomes related to darolutamide treatment were generally similar between CCI subgroups
- The proportion of patients achieving PSA responses at any time was similar between CCI subgroups

HRQoL

- A generally favorable health state is reflected by an index score of 0.8 at baseline, indicating minimal issues in mobility, self-care, usual activities, pain/discomfort, and anxiety/depression
- Patient self-rated quality of life was consistent between CCI subgroups: generally good at baseline and remained stable for up to 3 years of treatment with darolutamide, although the baseline EQ-5D-3L score was slightly lower in the high vs the low to moderate comorbidities subgroup

EQ-5D-3L index score response, n (%)	6 months (n=147****)	1 year (n=135****)	2 year (n=120****)	3 year (n=40****)
Deterioration††††	36 (24.5)	32 (23.7)	33 (27.5)	8 (20.0)
Stable/improvement‡‡‡‡	111 (75.5)	103 (76.3)	87 (72.5)	32 (80.0)

EQ-5D-3L index score response, n (%)	6 months (n=298****)	1 year (n=291****)	2 year (n=235****)	3 year (n=81****)
Deterioration††††	75 (25.2)	77 (27.4)	87 (37.0)	31 (38.3)
Stable/improvement‡‡‡‡	223 (74.8)	204 (72.6)	148 (63.0)	50 (61.7)

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