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Managing castration resistant prostate cancer: real life snapshot from a multicenter cohort

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Materials and Methods (1)

We prospectively collected data on chemo-naïve CRPC patients treated with Abiraterone Acetat (AA) or Enzalutamide (EZ).

Primary outcomes:

- **PSA response**
- **oncologic outcomes**
- **toxicity profile.**

The Kaplan-Meier method was used to compare differences in terms of progression-free survival (PFS) between:

- **AA vs EZ**
- **high-volume vs low-volume**

Materials and Methods (2)

- Survival probabilities were computed at 12, 24, 36 months.

- Univariable and multivariable Cox regression analyses were performed to identify predictors of PFS.

- Toxicity, PSA-response rates and oncologic outcomes on second-line were compared with those observed on first-line.

Results (1)

Table 1 Clinical features of the whole cohort

Clinical features	Median or *N* (IQR or %)
Age (years)	76 (71–82)
ECOG	
0	93 (67.9)
1	44 (32.1)
ISUP grade group (%)	
NA	6 (4.4)
1	6 (4.4)
2	18 (13.1)
3	38 (27.7)
4	34 (24.8)
5	35 (25.5)
Baseline staging PCa (%)	
cT	
x	48 (35)
T1	4 (2.9)
T2	22 (16.1)
T3	63 (46)
cN	
0	113 (82.5)
1	24 (17.5)
cM	
0	102 (74.5)
1	35 (25.5)
Local treatment (%)	
Radical prostatectomy	27 (19.7)
Radiation therapy	35 (25.5)
None	48 (35)
Both	27 (19.7)
ADT length (mo)	27 (9–65)
ADT lines (*N*)	2 (2–2)
Time to CRPC (years)	5 (2–9)
PSA CRPC (ng/dl)	9.7 (3.5–29.7)
cN CRPC (%)	
Nx	33 (24.1)
N0	49 (35.8)
N1	55 (40.1)
High-volume disease (%)	44 (32.1)
Follow-up (mo)	17 (10–27)

Table 2 First line treatment – Clinical Features

Clinical features	Mean or *N* (SD or %)		
	Enzalutamide (*N* = 49)	Abiraterone (*N* = 88)	*p* value
Age (years)	74.2 (9.1)	76.8 (7.3)	0.065
ECOG			0.70
0	32 (65.3)	61 (69.3)	
1	17 (34.7)	27 (30.7)	
CCI	4 (1.4)	3 (1.2)	0.62
ISUP grade group (%)			0.40
NA	4 (8.2)	2 (2.3)	
1	3 (6.1)	3 (3.4)	
2	5 (10.2)	13 (14.8)	
3	14 (28.6)	24 (27.3)	
4	9 (18.4)	25 (28.4)	
5	14 (28.6)	21 (23.9)	
Baseline staging PCa (%)			
cT			0.33
x	18 (36.7)	30 (34.1)	
T1	3 (6.1)	1 (1.1)	
T2	6 (12.2)	16 (18.2)	
T3	22 (44.9)	41 (46.6)	
cN			0.16
0	37 (75.5)	76 (86.4)	
1	12 (24.5)	12 (13.6)	
cM			0.41
0	39 (79.6)	63 (71.6)	
1	10 (20.4)	25 (28.4)	
Local treatment (%)			<0.001
Radical prostatectomy	7 (14.3)	20 (22.7)	
Radiation therapy	16 (32.7)	19 (21.6)	
None	14 (28.6)	34 (38.6)	
Both	12 (24.5)	15 (17)	
ADT length (mo)	60.2 (55.4)	37.9 (46.3)	0.017
ADT lines (*N*)	2.1 (0.4)	2.1 (0.4)	0.70
Time to CRPC (years)	5.9 (5.1)	5.9 (4.9)	0.98
PSA CRPC (ng/dl)	8 (3–21.9)	9.8 (3.5–34)	0.59
cN CRPC (%)			0.02
Nx	18 (36.7)	15 (17)	
N0	9 (18.4)	40 (45.5)	
N1	22 (44.9)	33 (37.5)	
High-volume disease (%)	19 (38.8)	21 (23.9)	<0.001
Follow-up (mo)	19.7 (16.8)	19.5 (11)	0.935

Results (2)

Table 3 First-line treatment—adverse events

Variable *N* (%)	Enza-lutamide (*N* = 49)	Abiraterone (*N* = 88)	*p* value
Adverse events	8 (16.3)	9 (10.2)	0.437
Any grade ≥ 3 adverse event	1 (2)	0	0.232
Most common adverse events			0.156
Hypertension	2 (4.1)	3 (3.4)	
New onset	1 (2.05)	1 (1.1)	
Worsening	1 (2.05)	2 (2.3)	
Fatigue	4 (8.2)	0	
Osteoporotic fracture	1 (2)	0	
Hepatic impairment	1 (2)	2 (2.3)	
Nausea	0	1 (1.1)	
Headache	0	1 (1.1)	
Thrombocytopenia	0	2 (2.3)	

On first-line:

- EZ significantly higher PSA-response than AA (95.9%vs67%, p<0.001),
- comparable toxicity rate (10.2%vs16.3%, p=0.437)
- Comparable PFS probabilities (p=0.145)

Baseline PSA, **metastatic CRPC** and **high-volume disease** were predictors of lower PFS probabilities at univariable analysis (p=0.027, 0.044 and p=0.007, respectively).

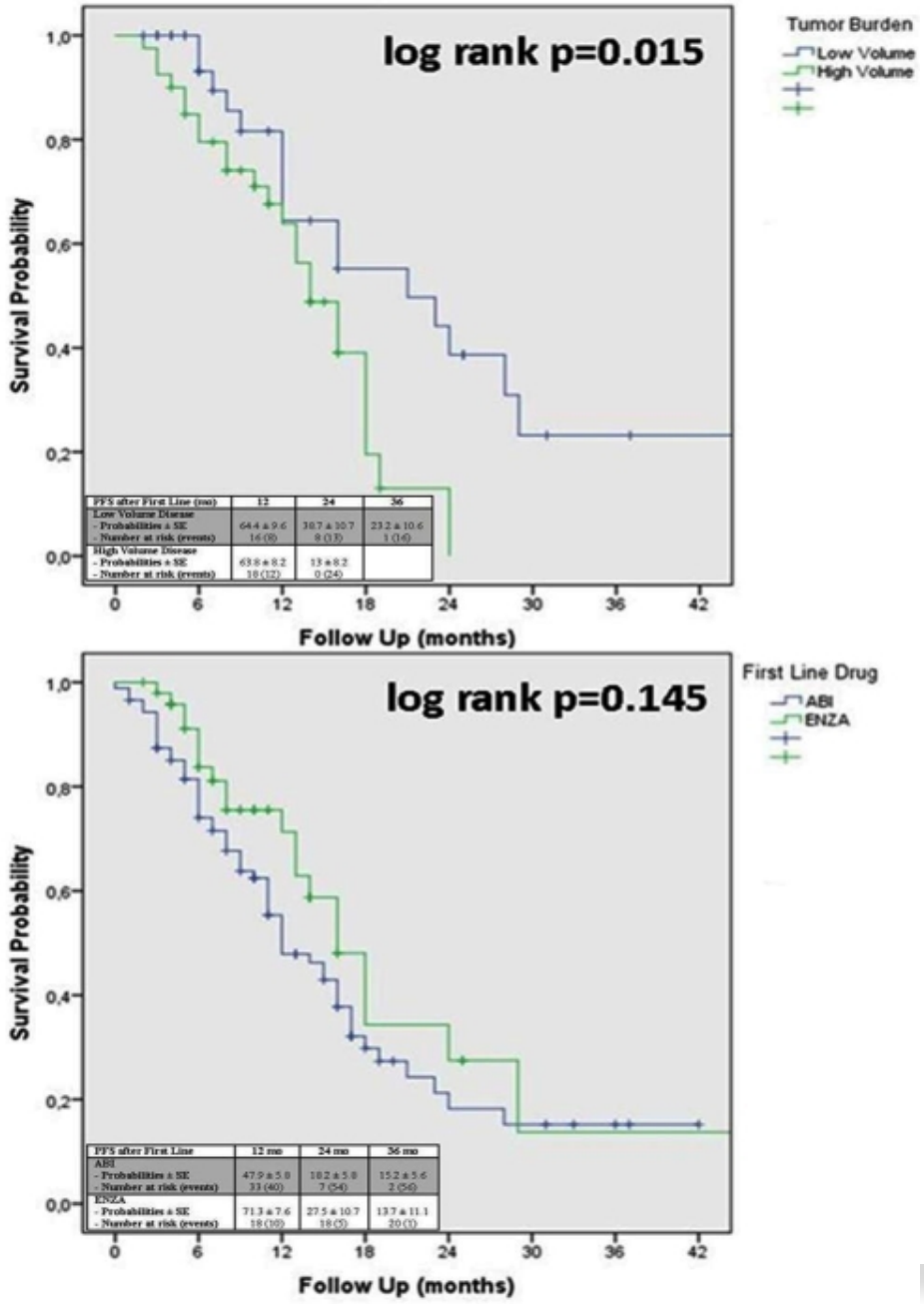


Fig. 1 Kaplan–Meier curves showing progression-free survival (PFS) probability in first-line therapy

Results (3)

Results (4)

45 patients had a disease progression after first line

17 (15.7%) patients → salvage chemotherapy

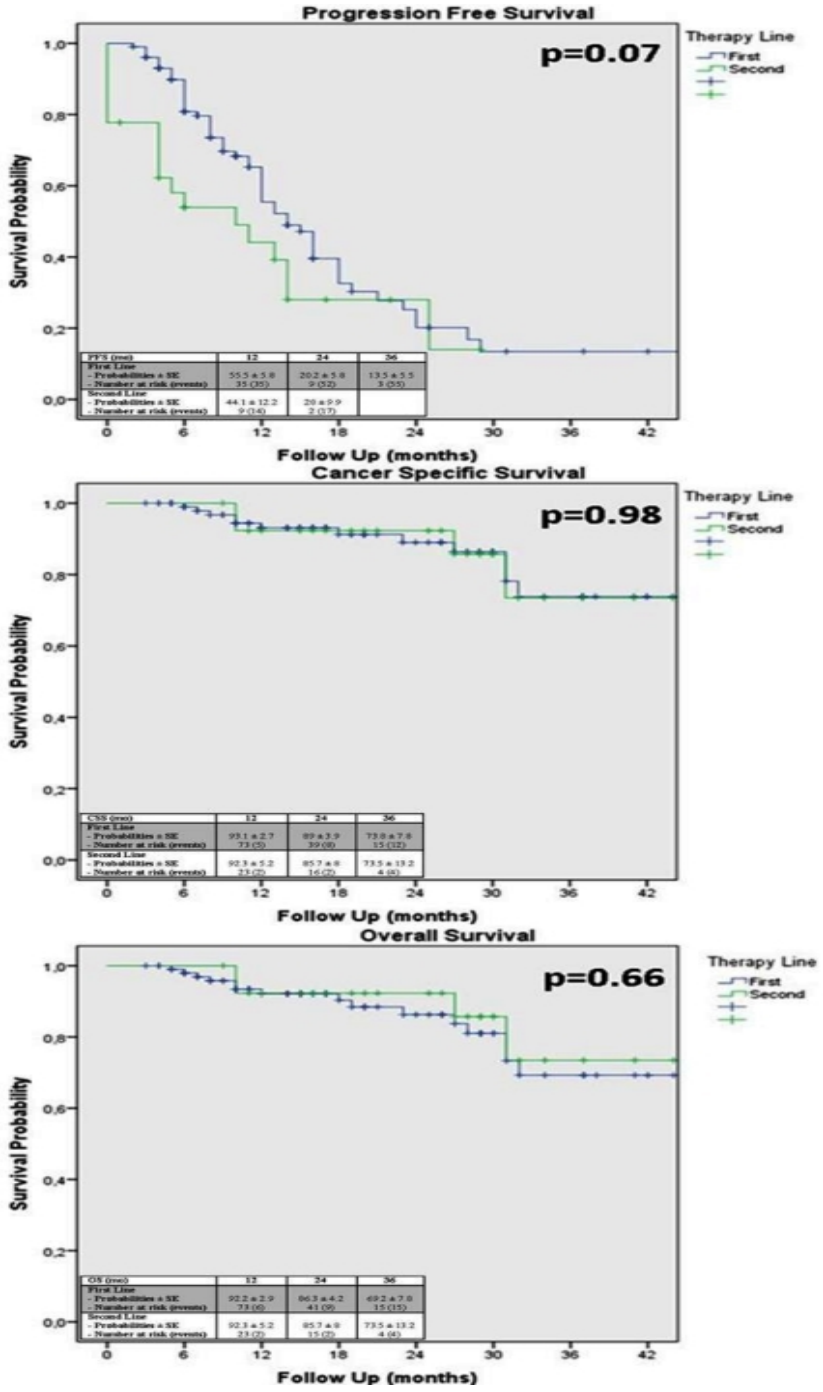
28 → **second-line** therapy:

- EZ was prescribed in 19 cases
- Radiometabolic therapy in 9 patients.

Second Line versus First Line:

- Comparable Toxicity and PSA-response rates

  (11.1%vs12.4%, p=0.77; 73.1%vs77.4%, p=0.62, respectively);



Second Line vs First Line:

comparable 2-yr PFS, CSS and OS

(12.1%vs16.2%, p=0.07; 85.7%vs86.4%, p=0.98; 71%vs80.3%, p=0.66, respectively).

Fig. 2 Kaplan–Meier curves showing progression-free survival (PFS), cancer-specific survival (CSS) and overall survival (OS) between first and second lines of therapy

Results (5)

Limitations

“Real-life” nature.

selection bias of patients: indications, choice of drug and shift to another treatment line, as well as the lack of central radiologic review for clinical staging and the lack of central laboratory test evaluation.

Most of patients represent the cohort of patients not recruited in clinical trials. (toxicity precluding adoption of a second-line treatment, or diffuse metastatic spread requiring adoption of chemotherapy schedule).

Conclusions

- Our findings support comparable **toxicity profile** and **PSA-response** rate between first-line and second-line courses.

- Patients fit for a second line treatment displayed **PFS, CSS and OS probabilities** comparable to those observed in first-line cohort.