AMÂNAȚI PROGRESIA.
PRELUNGIȚI SUPRAVIEȚUIREA.[4,5]

Erleada®
(apalutamidă) comprimate filmate

Eficacitatea opțiunilor de tratament ulterioare tratamentului cu ERLEADA® (apalutamidă) + ADT

Congresul de cancer genito-urinar ASCO-GU 2023 ACTUALIZARE

Erleada®
(apalutamidă) comprimate filmate

Context:

Pentru a obține indicii privind tratamentul ulterior optim după progresia pacienților aflați pe tratament cu ERLEADA® + ADT, a fost evaluată pentru prima dată eficacitatea comparativă a tratamentelor de primă linie pentru pacienții cu mCRPC, într-o analiză post-hoc* a studiului SPARTAN[†1-3]

Metodă/modelul studiului:*[1]

Această analiză *post-hoc* a studiului SPARTAN a evaluat mediana supraviețuirii globale ulterioare (subsecvente) (sOS) pentru tratamentele ulterioare administrate după tratamentul cu ERLEADA® + ADT, care au inclus:

- acetat de abirateronă + prednison/prednisolon
- docetaxel
- enzalutamidă
- alte tratamente

sOS=mediana supraviețuiri globale ulterioare (subsecvente) în cazul primului tratament pentru mCPRC inițiat după progresia pe tratament cu ERLEADA® + ADT[1]

Mediana supraviețuiri globale ulterioare (subsecvente) (sOS) în cazul primului tratament pentru mCPRC inițiat după progresia pe tratament cu ERLEADA® + ADT[1]

sOS ulterioară (subsecventă) tratamentului cu ERLEADA® + ADT (luni) la pacienții cu nmCRPC

enzalutamidă	docetaxel	acetat de abirateronă +prednison/ prednisolon	alte tratamente	global
(n=20)	(n=29)	(n=241)	(n=21)	(N=311)
17.0	**18.2**	**20.2**	**21.6**	**20.0**

Deoarece acesta a fost un studiu descriptiv, nu au fost efectuate comparații statistice formale.
Adaptat după Oudard S, *et al.* 2023[1]

Concluzie: Tratamentul cu ERLEADA® + ADT determină întârzierea semnificativă a progresiei către mCRPC comparativ cu placebo + ADT.[2,3] Administrarea ERLEADA® + ADT determină întârzierea semnificativă a progresiei către mCRPC comparativ cu placebo + ADT.[2,3] După progresie, tratamentele de primă linie pentru mCRPC oferă rezultate de sOS comparabile - **menținând deschise toate opțiunile de tratament ulterioare ale dumneavoastră și ale pacienților dumneavoastră**[1]

Tratamentul cu ERLEADA® + ADT a prezentat un profil de siguranță gestionabil la pacienții cu nmCRPC care au avut o perioadă mediană de urmărire de >4 ani

Pentru informații suplimentare, consultați posterul original.

ADT, terapie de deprivare androgenică; mCRPC, cancer de prostată metastatic rezistent la castrare; nmHSPC, cancer de prostată non metastatic rezistent la castrare; sOS, supraviețuire globală ulterioară (subsecventă)
*Pacienții incluși în această analiză au dezvoltat mCRPC în timpul tratamentului cu ERLEADA® + ADT și au primit un prim tratament ulterior pentru mCRPC ("Cohorta următoare"). Data index a fost data inițierii primei terapii ulterioare. Caracteristicile inițiale ale "Cohortei următoare" au fost comparate cu cele ale populației ITT ERLEADA® + ADT din studiul SPARTAN[2].
Analiza Kaplan-Meier a fost utilizată pentru a calcula sOS de la data indexului.[1]
†SPARTAN a fost un studiu de fază III, dublu-orb, controlat cu placebo, care a inclus bărbați cu cancer de prostată non-metastatic rezistent la castrare și un timp de dublare a PSA de ≤10 luni (N=1207). În contextul unui nivel de castrare al testosteronului fără dovezi de metastaze pe imagistică convențională. Pacienții au fost repartizați aleatoriu, într-un raport 2:1, pentru a primi fie tratament cu ERLEADA® (240 mg pe zi) + ADT, fie tratament cu placebo + ADT. Toți pacienții au continuat să primească ADT [2]

ERLEADA® este indicat:[5] În tratamentul cancerului de prostată non-metastatic rezistent la castrare (nmCRPC, nonmetastatic castration-resistant prostate cancer) la bărbați adulți, care prezintă un risc crescut de a dezvolta boală metastatică; în tratamentul cancerului de prostată metastatic sensibil la terapie hormonală (mHSPC, metastatic hormone sensitive prostate cancer) la bărbați adulți, în asociere cu o terapie de deprivare androgenică (ADT, androgen deprivation therapy)

▼Acest medicament face obiectul unei monitorizări suplimentare. Acest lucru va permite identificarea rapidă de noi informații referitoare la siguranță. Profesioniștii din domeniul sănătății sunt rugați să raporteze orice reacții adverse suspectate. Consultați Rezumatul Caracteristicilor Produsului pentru detalii referitoare la modul de raportare a reacțiilor adverse.

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CP-378213 Data pregătirii: martie 2023

Efficacy of subsequent treatments in patients who progressed to mCRPC following treatment with apalutamide for nonmetastatic castration-resistant prostate cancer (nmCRPC): A post-hoc analysis of the SPARTAN phase III trial.

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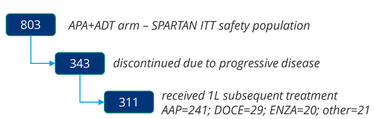
INTRODUCTION

- Apalutamide (APA) delays the onset of metastases and extends survival in high-risk (HR, defined as PSADT≤10 months) nmCRPC[1]
- The relative benefit of subsequent therapies for metastatic castration resistant prostate cancer (mCRPC) is inadequately explored
- We conducted a *post hoc* analysis of the SPARTAN (NCT01946204) trial to describe the relative efficacy of subsequent therapies in mCRPC for those patients who progressed following initial treatment with APA plus ADT

METHODS

- Included patients were those randomized to APA who experienced progressive disease and then received a first subsequent therapy for mCRPC (the "Next Cohort"); patients who discontinued therapy for any other reason were excluded
- The index date was the initiation of first subsequent treatment for mCRPC, however baseline characteristics are reported from the time of initial randomization (as they could not be derived at the index date)
- Subsequent progression-free survival per physician assessment (sPFS) and subsequent overall survival (sOS) were calculated from the index date using Kaplan-Meier survival curve estimates
- To compare sPFS and sOS between subsequent therapies, hazard ratios (HR) and 95% confidence intervals (CI) were estimated using multivariable proportional hazards regression analyses
- Analyses were adjusted for imbalances in prognostic baseline characteristics, including age, ECOG PS, Gleason score at baseline, baseline PSA, PSADT, prior hormonal therapy, loco-regional disease, use of bone-sparing agent, and time to progressive disease after initiation of APA

FIGURE 1: Patients included in the Next Cohort



PROSTATE CANCER

RESULTS

The Next Cohort

- At SPARTAN study completion, 237 patients remained on APA without progression, while 311 were included in the Next Cohort (Figure 1)

TABLE 1: Selected baseline characteristics at initial randomization (SPARTAN ITT v Next Cohort)

	SPARTAN ITT (N=806)	Next Cohort (N=311)
Age		
≥ 75 years	48.8%	50.5%
Prior hormonal therapy		
1	19.4%	19%
≥ 2	80%	80.4%
PSA value at baseline		
Above median	Median PSA at study entry 7.78ng/ml	59.2%
PSA doubling time		
≤ 6 months	71.5%	79.1%

- Compared to the APA ITT group in SPARTAN[1,2,3], the Next Cohort:
  - had a higher PSA value and proportion of patients with PSADT ≤6 months at the point of randomization (Table 1)
  - experienced poorer deep PSA response to APA in terms of undetectable PSA and PSA90 (Figure 2), and had poorer outcomes in terms of median MFS and OS from randomization (Table 2)

FIGURE 2: Overall PSA response to APA (SPARTAN ITT v Next Cohort)

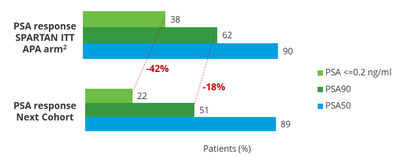
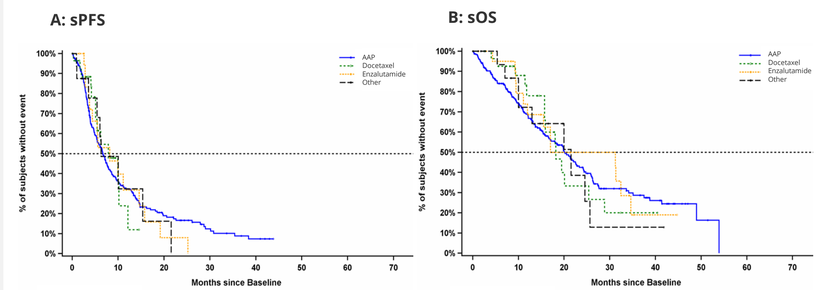


TABLE 2: Median MFS and OS from initial randomization (SPARTAN ITT v Next Cohort)

	SPARTAN ITT (N=806)	Next Cohort (N=311)
Median MFS	40.5 months[3]	25.8 months
Median OS	73.9 months[1]	52.8 months

Efficacy outcomes in 1L mCRPC after progression from APA

FIGURE 3: sPFS and sOS stratified by subsequent treatment in 1L mCRPC



	sPFS		sOS	
	Median [95% CI] (months)	HR [95% CI] vs AAP*	Median [95% CI] (months)	HR [95% CI] vs AAP*
AAP (n= 241)	6.7 (95% CI, 5.4-7.8)	1.00	20.2 (95% CI, 16.7-23.3)	1.00
Docetaxel (n=29)	7.9 (95% CI, 5.1-12.1)	1.04 [0.58;1.87]	18.2 (95% CI, 15.7-25.4)	1.14 [0.64;2.04]
Enzalutamide (n=20)	8.2 (95% CI, 3.8-14.6)	0.95 [0.54:1.66]	17.0 (95% CI, 11.1-34.6)	0.91 [0.50;1.65]
Others (n=21)	6.3 (95% CI, 3.6-15.3)	0.91 [0.45;1.86]	21.6 (95% CI, 10.0-25.7)	1.26 [0.61;2.57]
Overall (n=311)	6.8 (95% CI, 5.8-7.9)	-	20.0 (95% CI, 17.0-22.6)	-

*adjusted HR by subsequent therapy vs AAP being the largest cohort, as a reference

- Subsequent treatments cohorts were generally comparable with respect to patients' characteristics
- The analysis shows comparable outcomes between subsequent treatments, as illustrated by KM curves similar between cohorts and adjusted hazard ratios between AAP vs other treatments close to 1 (Figure 3).

DISCUSSION

- Our analysis shows no evidence of a differential efficacy between androgen-receptor signaling inhibitors (ARSI) or cytotoxic chemotherapy after progression with APA
- As compared to the ITT cohort, the Next Cohort is over-represented by patients with poor prognosis and/or poorer response to APA
- However, such a subgroup of patients is most likely the one for which the question of optimal sequencing is most urgent in clinical practice
- Limitations of this analysis include its retrospective nature and residual confounding cannot be excluded despite adjustment for differences in prognostic factors between cohorts of subsequent therapies

KEY TAKEAWAY

For patients progressing to mCRPC from APA treatment in HR nmCRPC, this *post hoc* analysis shows comparable subsequent PFS and OS in first-line mCRPC, irrespective of the choice of subsequent therapy

CONCLUSIONS

- This analysis provides, for the first time, quantitative evidence on the comparative efficacy of 1L mCRPC treatments in patients progressing after APA in HR nmCRPC
- Subsequent PFS and OS appeared similar in the Next Cohort across alternative 1L treatment options in mCRPC
- Prior treatment with APA in HR nmCRPC did not appear to influence the relative efficacy of 1L mCRPC standard of care options (ARSI or DOCE) [5,6,7]

ACKNOWLEDGMENTS

We thank StatInfo Srl for the medical writing support.

DISCLOSURES

SO has received honoraria from Pfizer, Bayer, Merck, BMS, Novartis, Eisai, Sanofi, Janssen, Astellas Pharma, MSD, Roche, Boehringer Ingelheim, IPSEN
BH has received honoraria from Lightpoint Medical, Janssen, Bayer, ABX, Astellas Pharma, Merck, Amgen, MSD, Novartis, AstraZeneca, BMS
MS has received honorarioa from Bayer, Janssen, Amgen, Pfizer, Lilly, Novartis, Astellas Pharma, ESSA, ORIC Pharmaceuticals
ES has received honoraria from Janssen, Teon Therapeutics, Fortis, Harpoon Therapeutics
LA, JD, IL, PT are employees of Janssen.
This study was funded by Janssen.

CP-378213

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Abbreviations: AAP= abiraterone acetate plus prednisone; PSADT= PSA doubling time; nmCRPC= non metastatic castration resistant prostate cancer; ITT= intent to treat; DOCE= docetaxel; ENZA= enzalutamide; MFS= metastasis free survival; OS= overall survival

Presented at ASCO GU; February 16 - 18, 2023; San Francisco, CA, USA.