Impact of treatment sequence on survival outcome in patients with a 2nd treatment line for mCRPC: A new-user design in the French nationwide claims database

NH. Thurin[1], M. Rouyer[1], M. Gross-Goupil[2], T. Haaser[2], X. Rébillard[3], M. Soulié[4], G. de Pouvourville[5], F. Messaoudi[6], H. Stitou El Amine Demnati[6], E. Bignon[1], J. Jové[1], S. Lamarque[1], C. Droz-Perroteau[1], N. Moore[1], P. Blin[1]

[1] Bordeaux PharmacoEpi, INSERM CIC1401, Université de Bordeaux, Bordeaux, France, [2] CHU de Bordeaux, Bordeaux, France
[3] Clinique Beau Soleil, Montpellier, France, [4] CHU de Toulouse, Toulouse, France, [5] ESSEC, Cergy-Pontoise, France, [6] Janssen, Issy les Moulineaux, France

Background

Abiraterone acetate in association with prednisone/prednisolone, and docetaxel can both be used as 1st or 2nd line treatments for metastatic castration-resistant prostate cancer (mCRPC). Is it better to start with an abiraterone acetate 1st-line followed by a docetaxel 2nd-line (ABI-DOCE sequence) or to use the inverse sequence DOCE-ABI ?

Methods

Patients selection

- mCRPC patients were identified in the French National Healthcare System database (SNDS) using a validated algorithm*.
- SNDS covers the French population from birth to death and includes out- and inpatients information.
- To be included, patients had:
  - ✓ To be aged ≥40 and covered by the *Régime Général* health insurance (86% of the French population),
  - ✓ To have initiated in 2014 an abiraterone acetate 1st-line followed by a docetaxel 2nd-line (ABI-DOCE sequence) or a docetaxel 1st-line followed by an abiraterone acetate 2nd-line (DOCE-ABI sequence), all drugs presumed to be used according to the Summary of Product Characteristics,
  - ✓ To have a 3-year follow-up and 5-year history with no gap >1 year.

**Thurin NH, Rouyer M, Gross-Goupil M, et al. Epidemiology of metastatic castration-resistant prostate cancer: A first estimate of incidence and prevalence using the French nationwide healthcare database. Cancer Epidemiol. 2020;69:101833.*

Comparative analyses

- A high dimensional propensity score (hdPS), was calculated for each patient of each cohort: estimation of the probability for a patient to be treated by ABI-DOCE sequence *versus* DOCE-ABI sequence based on forced and empirically selected variables from 5 dimensions:

Forced variables	*Dimensions for variable empirical selection*
• Age at index date • Cancer stage prior to mCRPC status • Charlson comorbidity index	• Long term disease registration • Hospital discharge diagnoses • Dispensed drugs • Performed laboratory tests • Performed medical procedures

- Patients were 1:1 matched on hdPS (+/- 0.01), cancer stage prior to mCRPC (mHSPC NDx = hormonosensitive prostate cancer with synchronous metastases, progressive mHSPC = HSPC with metachronous metastases, nmCRPC = resistant and non-metastatic prostate cancer, nmHSPC = hormonosensitive and non-metastatic prostate cancer), and date of initial diagnosis (+/- 1 year).
- After matching, standardized differences were estimated for 367 variables to check for potential residual confusion bias, and those significantly linked to the outcome were use for adjustment in survival analyses.
- Cox proportional hazards risk model were used to compare:
  - ✓ The 36-month overall survival (death),
  - ✓ The 36-month discontinuation-free survival (treatment switch or death).

Results

Patients

- In 2014, 3 949 mCRPC patients initiated a 1st-line treatment : 1 162 died during 1st-line treatment, and 2 283 had a 2nd-line treatment. Among them :
  - ✓ 693 patients received the ABI-DOCE sequence,
  - ✓ 354 patients received the DOCE-ABI sequence.

hdPS matching

- After trimming and matching: 159 patients per group.

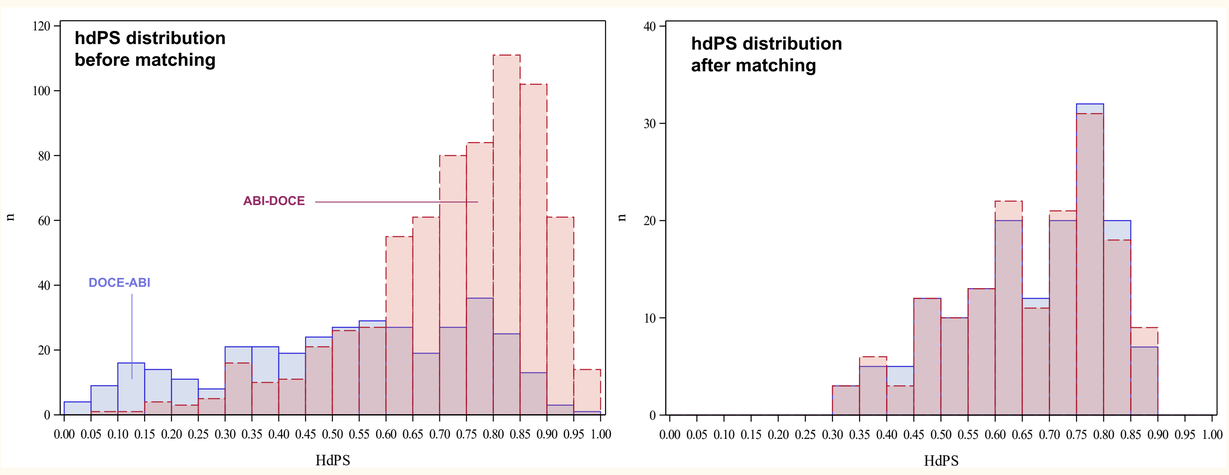


Figure 1. hdPS distribution before and after matching

Demographics and treatment lines

Table 1. Baseline characteristics at index date before and after matching

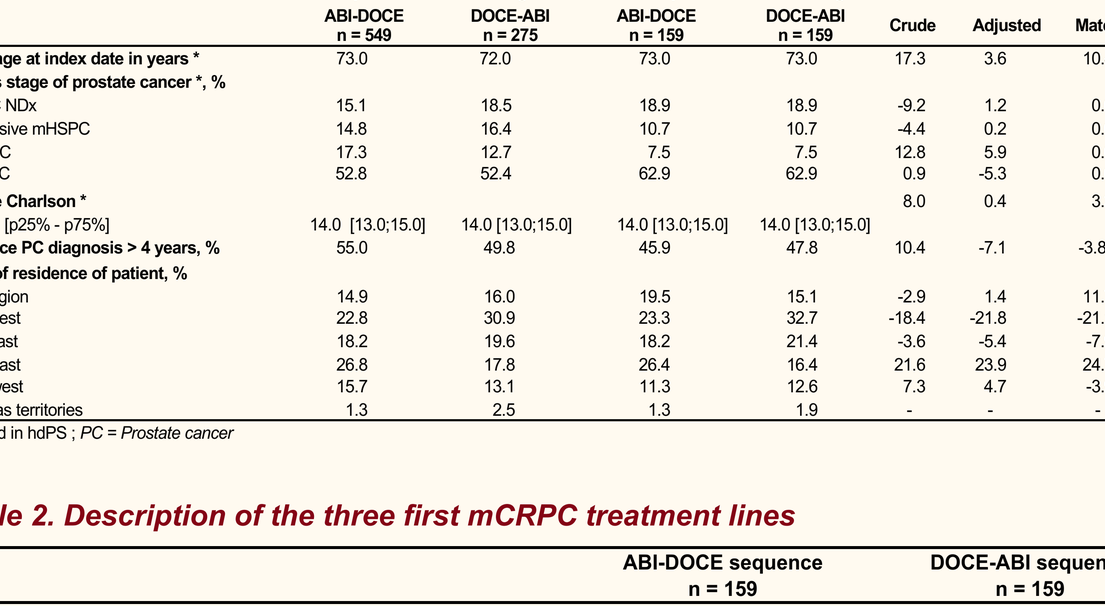
	All patients after trimming		Matched patients after trimming		Standardized difference %		
	ABI-DOCE n = 549	DOCE-ABI n = 275	ABI-DOCE n = 159	DOCE-ABI n = 159	Crude	Adjusted	Matched
Median age at index date in years *	73.0	72.0	73.0	73.0	17.3	3.6	10.4
Previous stage of prostate cancer *, %							
mHSPC NDx	15.1	18.5	18.9	18.9	-9.2	1.2	0.0
Progressive mHSPC	14.8	16.4	10.7	10.7	-4.4	0.2	0.0
nmCRPC	17.3	12.7	7.5	7.5	12.8	5.9	0.0
nmHSPC	52.8	52.4	62.9	62.9	0.9	-5.3	0.0
Score de Charlson *					8.0	0.4	3.3
Median [p25% - p75%]	14.0 [13.0;15.0]	14.0 [13.0;15.0]	14.0 [13.0;15.0]	14.0 [13.0;15.0]			
Time since PC diagnosis > 4 years, %	55.0	49.8	45.9	47.8	10.4	-7.1	-3.8
Region of residence of patient, %							
Paris region	14.9	16.0	19.5	15.1	-2.9	1.4	11.7
North-west	22.8	30.9	23.3	32.7	-18.4	-21.8	-21.1
North-east	18.2	19.6	18.2	21.4	-3.6	-5.4	-7.9
South-east	26.8	17.8	26.4	16.4	21.6	23.9	24.7
South-west	15.7	13.1	11.3	12.6	7.3	4.7	-3.9
Overseas territories	1.3	2.5	1.3	1.9	-	-	-

* included in hdPS ; *PC = Prostate cancer*

Table 2. Description of the three first mCRPC treatment lines

	ABI-DOCE sequence n = 159	DOCE-ABI sequence n = 159
Median duration of 1st treatment line in months, [p25% - p75%] *	8.4 [4.9;15.4]	6.6 [4.5;9.7]
Median duration of 2nd treatment line in months, [p25% - p75%] *	6.3 [3.8;8.9]	6.5 [3.1;11.8]
3rd mCRPC treatment line, %	**61.0**	**59.7**
Enzalutamide**	70.1	28.4
Cabazitaxel**	27.8	49.5
Docetaxel**	0.0	17.9
Abiraterone acetate **	1.0	0.0
Combination**	1.0	4.2

*time between first and last infusion for docetaxel and period covered by the dispensed drug for abiraterone **among patients concerned



Sequences concerned by less than 0.1% of the total population are not represented

Figure 2. Sequence of mCRPC treatment lines in matched population in 2014

Patients

Table 3. Adjusted overall survival and discontinuation-free survival according to 1st mCRPC treatment line after trimming and matching (Cox model)

	ABI-DOCE sequence n=159	DOCE-ABI sequence n=159	*p-value*
Overall Survival			
36-month survival probability, % [95%CI]	33.8 [27.4 ; 41.7]	34.4 [27.8 ; 42.5]	0.9105
Median survival time, months [95%CI]	26.2 [22.2 ; 29.8]	26.6 [22.6 ; 30.5]	
Discontinuation-Free Survival			
36-month survival probability, % [95%CI]	13.7 [9.6 ; 19.7]	9.9 [6.4 ; 15.1]	0.1983
Median survival time, months [95%CI]	17.5 [15.4 ; 18.9]	16.1 [14.5 ; 17.6]	

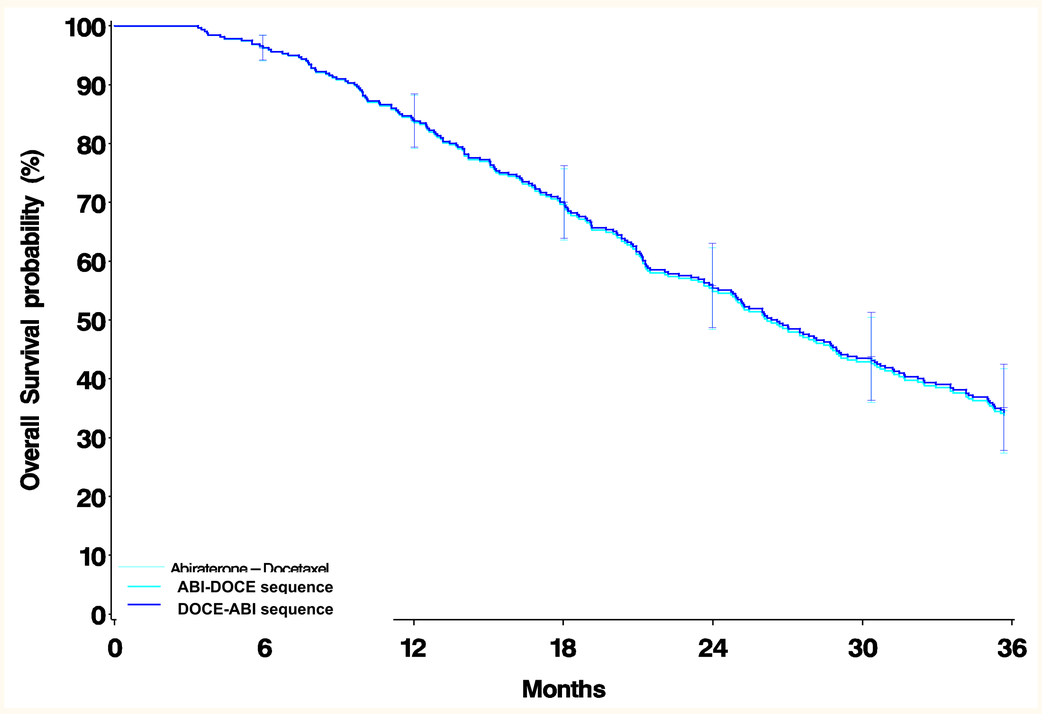


Figure 3. Adjusted overall survival probability according to mCRPC treatment sequences after trimming and matching (Cox model)

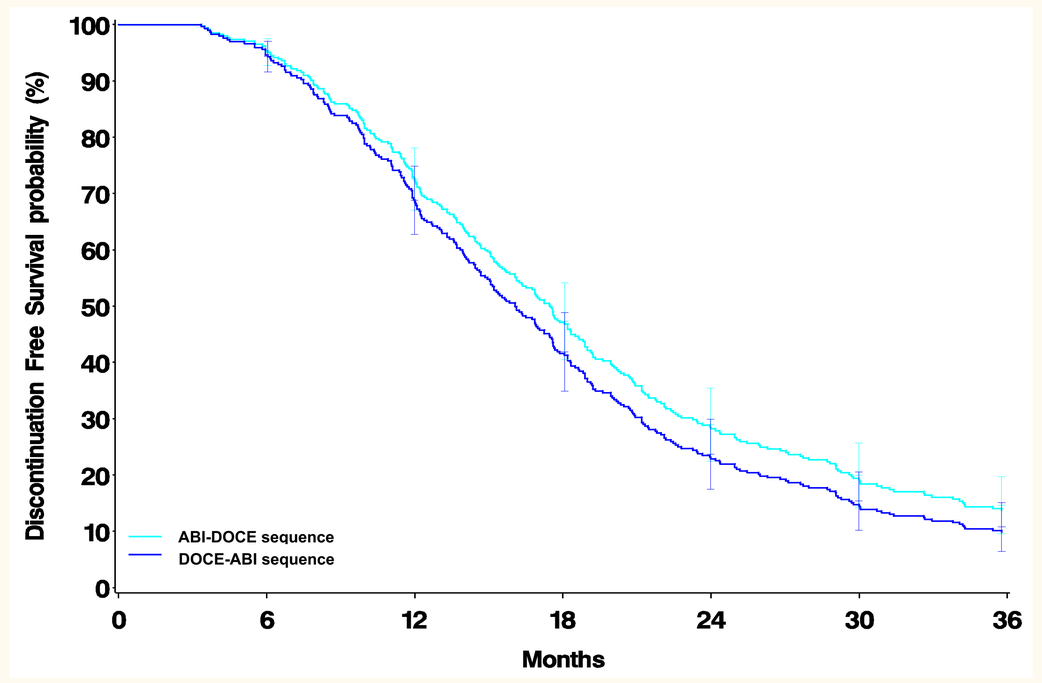


Figure 4. Adjusted Discontinuation-free survival probability according to mCRPC treatment sequences after trimming and matching (Cox model)

Conclusion

In real life settings, treatment sequences (ABI–DOCE *versus* DOCE–ABI) seem to have no differential impact on survival outcome in mCRPC patients sharing same characteristics.

www.bordeauxpharmacoepi.eu *nicolas.thurin@u-bordeaux.fr

CAMERRA study was performed by Bordeaux PharmacoEpi research platform in collaboration with Janssen, and supervised by a Scientific Committee.

Colloque Données de Santé en Vie Réelle
28 juin 2021, Paris – France