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

N. 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, 2], P. Blin[1]

[1] Bordeaux PharmacoEpi, INSERM CIC1401, Univ. Bordeaux, Bordeaux, France; [2] CHU Bordeaux, Bordeaux, France; [3] Clinique Beau Soleil, Montpellier, France; [4] CHU Toulouse, Toulouse, France; [5] ESSEC, Cergy-Pontoise, France; [6] Janssen, Issy-Les-Moulineaux, France

BACKGROUND & OBJECTIVE

- 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).
- This work aims at assessing weather starting with an abiraterone acetate 1st-line followed by a docetaxel 2nd-line (ABI-DOCE sequence) or to use the inverse sequence DOCE-ABI has an impact on survival outcome in mCRPC patients in real life.

METHODS

Patient 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

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 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 first line 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**

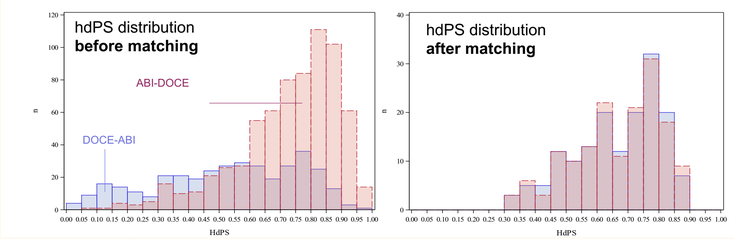

Figure 1. *hdPS distribution before and after matching*

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; 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*

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*

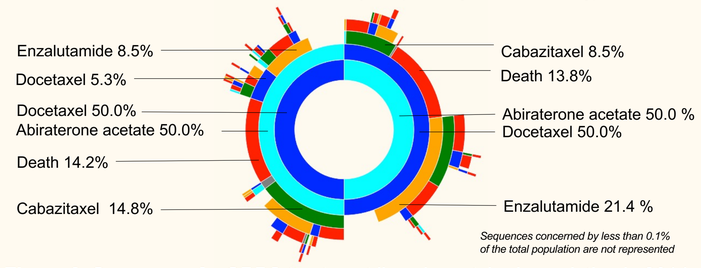

Figure 2. *Sequence of mCRPC treatment lines in matched population in 2014*

Survival outcomes

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]	

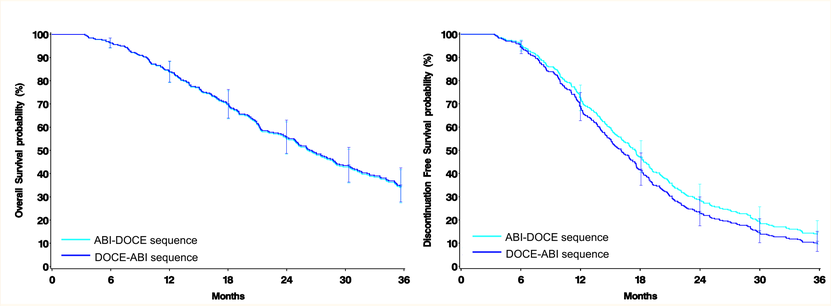

Figure 2. *Adjusted overall survival (left) and discontinuation-free survival (right) probability according to the mCRPC treatment sequence after trimming and matching (Cox model)*

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.

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*nicolas.thurin@u-bordeaux.fr

Declaration of interest statement: *the CAMERRA study is carried out by the Bordeaux PharmacoEpi platform in collaboration with Janssen® company, and supervised by a Scientific Committee.*

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