POPULATION-BASED ANALYSIS OF RATES OF USE OF NOVEL HORMONAL AGENTS AT THE END-OF-LIFE IN MEN WITH CASTRATION-RESISTANT PROSTATE CANCER

Centre universitaire de santé McGill – Institut de recherche | McGill University Health Centre – Research Institute

Hu J[1], Aprikian A[1,3,4], Vanhuyse M[2,4], Dragomir A[1]

[1]Division of Urology, McGill University; [2]Division of Medical Oncology, McGill University; [3]Department of Urology, McGill University Health Centre; [4]Department of Oncology, McGill University Health Centre.

McGill

INTRODUCTION

- Prostate cancer (PCa) is the third deadliest cancer in Canadian men
- Metastatic castration-resistant prostate cancer (mCRPC) is the last phase of PCa
  - Incurable
  - Median survival of from onset of castration-resistance: 2-3 years

Several drug therapies currently available for management of advanced PCa :

- Maintenance of *hormone therapy/androgen deprivation therapy*:
  - Medical castration – (Luteinizing hormone-releasing hormone [LHRH] agonist/antagonist)
  - Anti-androgens (AA)
- **Approved drug therapies for mCRPC**
  - Docetaxel (approved in 2005) – Intravenous chemotherapy
  - **Novel hormonal agents (NHAs)**
    - Abiraterone (approved in 2012 in Quebec) - Oral drug
    - Enzalutamide (approved in 2014 in Quebec) - Oral drug
- **Use of systemic cancer therapy at the end-of-life is a recognized indicator of overaggressive end-of-life cancer care**
- **Abundance of cancer drugs available, especially oral drugs, may lead to overuse at the end-of-life period**
- **Very little is known about contemporary end-of-life care in men dying of mCRPC, in particular regarding the use of NHAs**

OBJECTIVE

The objective of the current study is to report the use of NHAs in the last 30 days of life in men dying of mCRPC in the province of Quebec.

METHODS

Design :

- Retrospective, observational cohort

Data sources : Quebec public healthcare administrative databases

- Régie de l'assurance maladie du Québec (RAMQ) and MED-ECHO

Cohort definition :

- Died between 2012-2016
- Treated with an NHA (abiraterone or enzalutamide)
- Registered to provincial drug plan

Primary outcome: Use of NHA in the last 30 days of life

Secondary outcomes:

- Use of NHA in last 90 and 60 days of life
- First/new use of NHA in 30 days of life

Statistical Analysis:

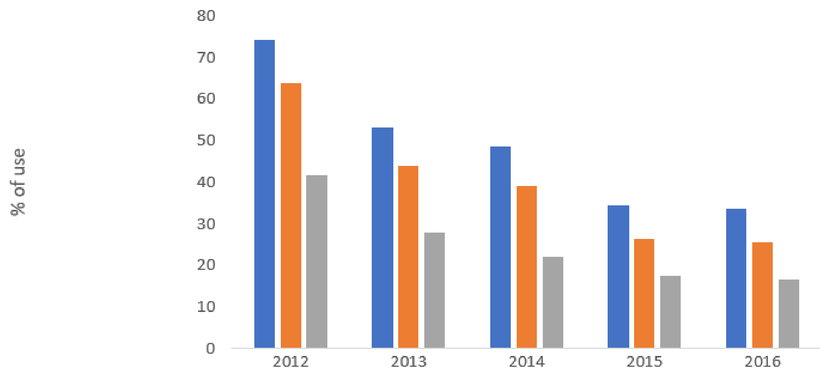
- Multivariable logistic regression to identify factors associated with use of an NHA in last 30 days of life
- All tests 2-sided with significance level set at 0.05

RESULTS

Table 1: Cohort characteristics

Variables	Total n=1,347
Age at death	
Median (Q1-Q3)	78.0 (72.0-84.0)
≤65	109 (8.1)
66-75	408 (30.3)
76-85	589 (43.7)
>85	241 (17.9)
Charlson comorbidity score, n(%)	
0-1	621 (46.1)
2-3	445 (33.0)
≥4	281 (20.9)
Residence area, n (%)	
Rural	429 (31.9)
Localized treatment, n (%)	
None	830 (61.6)
Year of death, n (%)	
2012	108 (8.0)
2013	205 (15.2)
2014	300 (22.3)
2015	343 (25.5)
2016	391 (29.0)
Time from PCa diagnosis to death	
≤ 5 years	466 (34.6)
> 5 years	881 (65.4)
Time from ADT start to death, n (%)	
≤ 24 months	80 (5.9)
> 24 months	1,268 (94.1)
mCRPC drug therapy at any time before death, n (%)	
Chemotherapy	634 (47.1)
Abiraterone	1,214 (90.1)
Enzalutamide	246 (18.3)

Figure 1: NHA use in last 90, 60 and 30 days of life by year of death



	2012	2013	2014	2015	2016	
NHA 90 days before death	74.1	53.2	48.7	34.4	33.5	*p<0.001**
NHA 60 days before death	63.9	43.9	39.0	26.5	25.6	*p<0.001**
NHA 30 days before death	41.7	27.8	22.0	17.5	16.6	*p<0.001**

*p-values from Cochran-Armitage test for yearly trend

Table 2: Characteristics of NHA use in last 30 days of life

	n	% (/295)	% (/1347)
NHA use 30 days before death	295	100.0	21.9
Abiraterone	237	80.9	17.6
Enzalutamide	56	19.1	4.2
First prescription of any NHA	50	17.1	3.7
First prescription of an NHA not used before	56	19.0	4.2

Table 3: Multivariable logistic regression analysis of NHA use in last 30 days of life

Factor	Multivariable OR	95%CI		p-value
Year of death (ref: 2012)				
2013	0.47	0.28	0.79	0.004
2014	0.32	0.19	0.52	<0.001
2015	0.24	0.15	0.40	<0.001
2016	0.23	0.14	0.38	<0.001
Age at death (ref: ≤65)				
66-75	2.02	1.04	3.94	0.038
76-85	3.26	1.71	6.19	0.000
>85	3.43	1.72	6.83	0.001
Charlson comorbidity score (ref: 0-1)				
2-3	1.42	1.04	1.95	0.028
≥4	1.68	1.18	2.38	0.004
Rural residence (ref: No)				
Yes	1.11	0.83	1.49	0.492
Prior localized treatment (ref: No)				
Yes	0.85	0.63	1.15	0.299
Time from ADT start to death (ref: >24 months)				
≤24 months	2.82	1.55	5.13	0.001

LIMITATIONS

- Administrative data:
  - Lacks patient, clinical, and disease variables (performance status, treatment response, patient preferences, etc.)
- No linkage to death registry: Could not identify patients who died suddenly of non-mCRPC causes
- No specific ICD code for mCRPC exists
  - However, drug therapy extracted from RAMQ is appropriate indirect evidence of mCRPC
- Record of prescription filling is only surrogate for patient intake

CONCLUSION

- Usage of NHA in the last 30 days of life were high initially but decreased from 2012 to 2016
- Further monitoring of this metric is warranted to examine if trend will be maintained given recent approvals of even more oral NHAs
- Regardless, future mCRPC clinical guidelines should advise on the appropriate use of drug therapies, especially oral drugs, at the end-of-life to curtail potential overuse

ACKNOWLEDGEMENTS

Coté-Sharp Family Foundation
Prostate Cancer Discovery Grant
Rossy Cancer Network
Fonds de recherche Santé -Québec

TWENTY YEARS | Prostate Cancer Canada | Réseau de cancérologie Rossy – Rossy Cancer Network | Fonds de recherche Santé Québec