Castration-Resistant Prostate Cancer (CRPC): Evaluation of the Quality of Care and Disease Management in Real-Life Setting

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ARCC Canadian Centre for Applied Research in Cancer Control

Presentation outline

- Background
- Objectives
- Methodology
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- Conclusion
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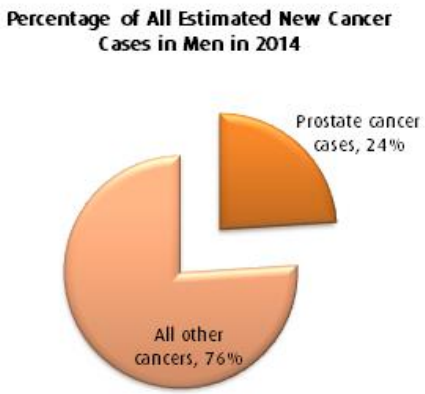
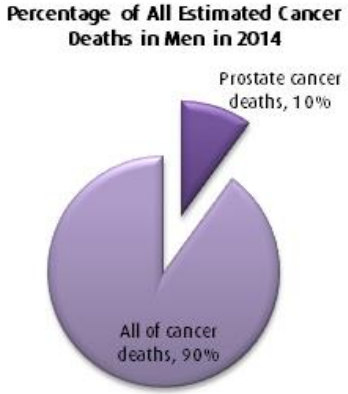
- Thanks
- References

Background

Prostate cancer (PCa)



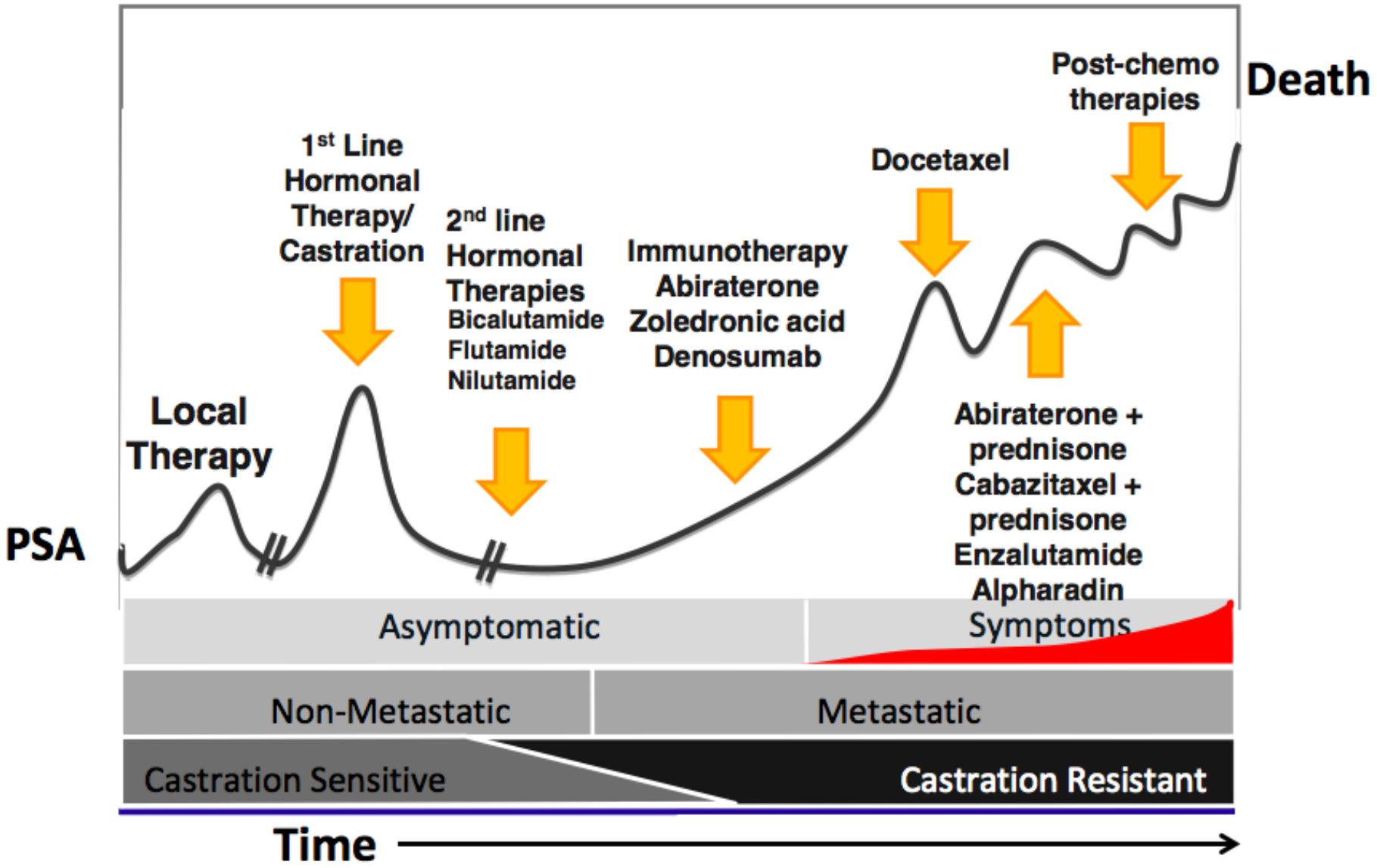


New cases	23,600
Incidence rate (for every 100,000 people)*	101
Deaths	4,000
Death rate (for every 100,000 people)*	17
5-year survival (estimates for 2006–2008)	96%

* Age-standardized to the 1991 Canadian Standard Population. Age-standardization is a statistical method that removes the effect of age on the calculated rate. It allows rates to be compared over time or across provinces and territories.

Canadian Cancer Society's Advisory Committee on Cancer Statistics. Canadian Cancer Statistics 2014. Toronto, ON: Canadian Cancer Society; 2014

PCa treatment landscape



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What is CRPC?

- Castration-Resistant Prostate Cancer
- 10 – 20% of patients with PCa progress to CRPC

- Canadian Urology Association's (CUA) definition

  - «*Castration-resistant prostate cancer (CRPC) is defined by* ***disease progression despite castrate levels of testosterone*** *and may present as either* ***a continuous rise in serum prostate-specific antigen*** *(PSA) levels, the* ***progression of preexisting disease****, and/or the* ***appearance of new metastases***»

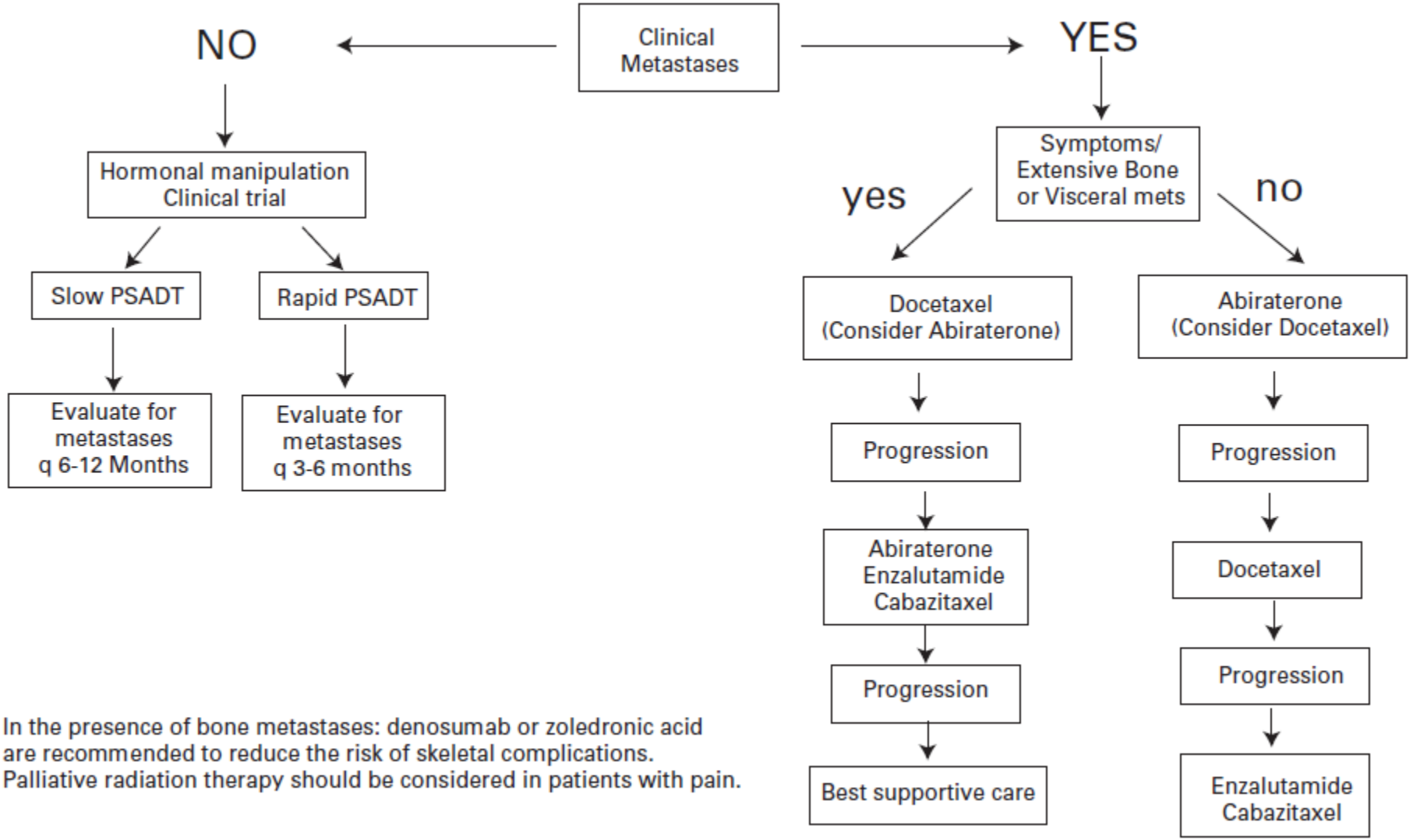
What is CRPC?

- Mestastasis
  - M_0 CRPC = clinically localized
  - mCRPC
  - Bone metastases (90%)
  - Lymph Nodes (>10% at time of diagnosis)
  - Visceral metastases (lung/liver)

Worsening survival

- Life expectancy
  - 5-year survival for mCRPC = 28%

CUA Guidelines - 2013



In the presence of bone metastases: denosumab or zoledronic acid are recommended to reduce the risk of skeletal complications. Palliative radiation therapy should be considered in patients with pain.

Can Urol Assoc J 2013:7(7-8):213-7

Objectives

Objectives

- Analyze quality of care and healthcare services utilization in the real-life setting for patients with CRPC by measuring
  - Adherence to Canadian clinical guidelines for the management of CRPC
    - Including treatment sequences
  - Other quality of care indicators

Methodology

Study design

- A retrospective cohort study design
- Patients treated for PCa at
  - The McGill University Health Center (MUHC)
  - Jewish General Hospital (JGH)
  - St-Mary Hospital Center (SMHC)
- From January 2010 to June 2014
- All patients of 40 years and older which have CRPC were selected

Collected data

- Individual information were collected from the patients' electronic and/or hardcopy files
  - Medications
  - Imaging
  - Laboratory tests
  - Histopathology results
  - Comorbidities
  - Medical visits
  - Interventions
  - Emergency visits
  - Hospitalisations

Quality of care assessment

- Assessed by evaluating clinicians' adherence to Canadian clinical guidelines for CRPC management
  - Canadian Urological Association
  - Updated in 2013

- Other quality of care indicators
  - Psychological assistance
  - Pivot / oncological nurse
  - Initial evaluation of general health status
    - Initial Dental test
    - Performance status evaluation

Statistical analysis

- Percentages, medians, means (SD) were obtained, when applicable, for
  - Patients characteristics
  - Primary disease characteristics
  - Initial PCa treatments
  - First-line CRPC treatments
  - Treatments sequence
    - Only the first two treatments are presented here
  - Other quality of care indicators

Preliminary Results

Patients characteristics

Patients characteristics		**(n = 159)**
Age at CRPC, median (Mean ± SD)		74.1 (73.4±8.8)
Other characteristics		**%**
Insurance (n = 157)	Public	**78.3**
	Private	2.6
	Both	19.1
Comorbidities (n = 152)	Overall	**69.1**
	Combination	40.1
	HTA	14.5
	Db	6.6
	RF	4.6
	DLP	2.6
	MI	0.7

Primary disease characteristics

Primary disease characteristics		**(n = 118)**
Initial PSA (ng/ml), median (mean ± SD)		25.0 (**146.8** ± 471.8)
Initial parameters		**%**
Initial PSA (n = 118)	< 10 ng/ml	24.6
	10 – 20 ng/ml	21.2
	20 – 100 ng/ml	33.9
	> 100 ng/ml	20.3
Initial Gleason score (n = 73)	5-6	6.9
	7	28.8
	8-10	**64.4**
Initial metastases (n = 169)		**29.0**
Initial bone metastases (n = 133)	Low volume	15.0
	High volume	12.8

Initial PCa treatments

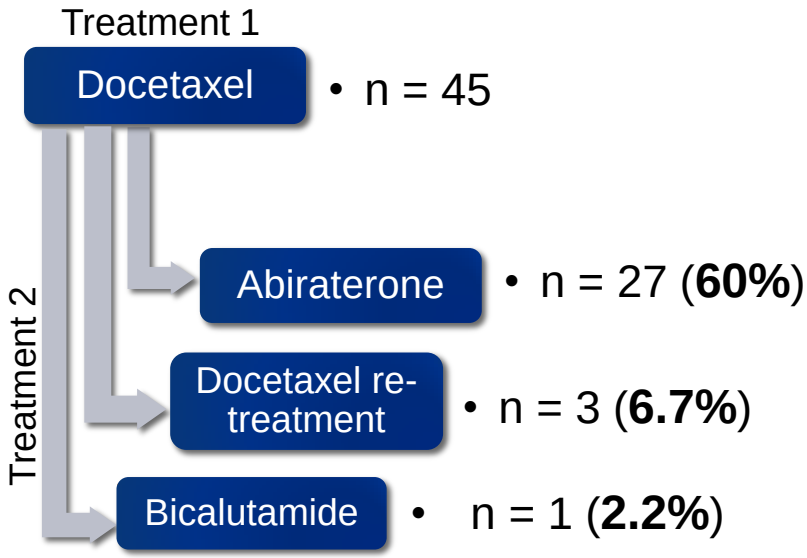
Initial PCa treatments		(n = 171)	N	%
Observation			5	2.9
Surgical treatments		Radical prostatectomy (RP)	35	**20.5**
		RP combined with hormonal therapy	5	2.9
Radiotherapy (RT)		RT alone	17	9.9
		RT combined with hormonal therapy	40	**23.4**
Hormonal therapy	ADT	Alone	35	**20.5**
	AAs	Alone	2	1.2
	TAB		34	**19.9**
Docetaxel chemotherapy			2	1.2

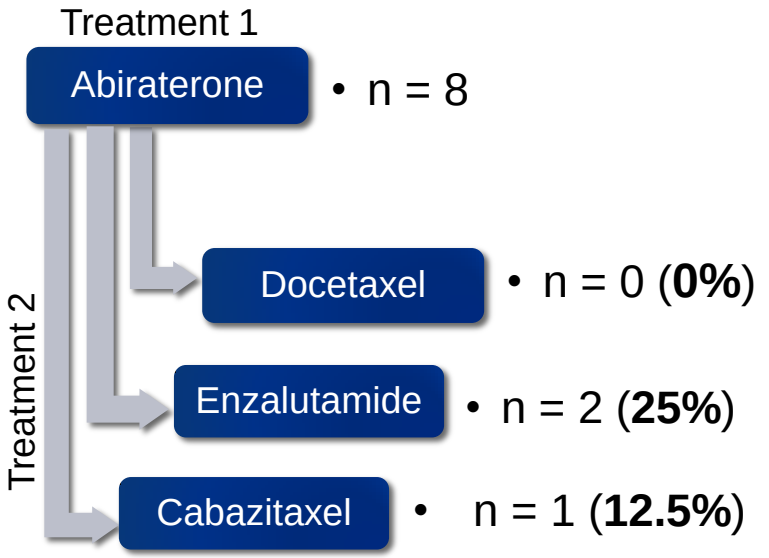
First-line CRPC treatment and duration

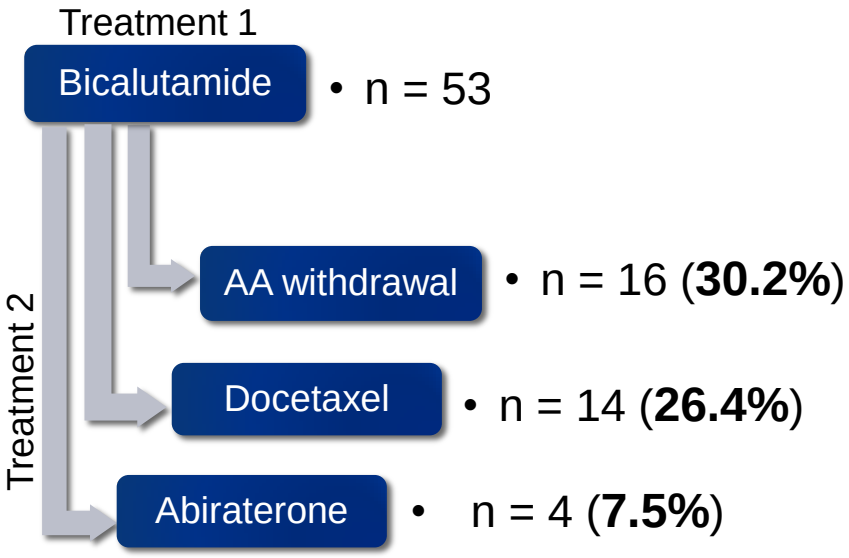
Variable		Patients		Duration (months)	
		N	%	Median	Mean (SD)
Drug prescribed (n = 98)	**Abiraterone**	5	**5.1**	5.0	6.5 (5.0)
	Docetaxel	42	**42.9**	3.5	3.6 (1.5)
	Antiandrogens (AAs)	34	**34.7**	8.4	15.4 (19.9)
	AAs withdrawal	8	**8.1**	4.0	7.6 (10.5)
	Others*	9	9.2	6.4	9.4 (9.7)
Number of docetaxel cycles (n = 42)	Median	6			
	Mean (SD)	5.8 (2.1)			

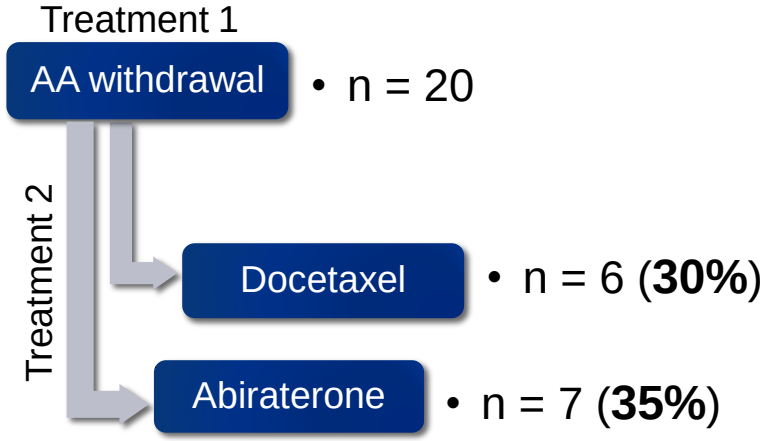
*Others: ketoconazole, palliative care, estramustine, vinblastine

Two first treatments after diagnosis









First-line mCRPC treatment

Variable		mCRPC	
		Yes (%)	**No** (%)
Drug prescribed as first-line treatment (n = 140)	Abiraterone	12 (11.9)	4 (**10.3**)
	Docetaxel	31 (**30.7**)	8 (**20.6**)
	Antiandrogens (AAs)	31 (**30.1**)	19 (**48.7**)
	AAs withdrawal	14 (13.9)	4 (10.3)
	Others*	10 (9.9)	3 (7.7)
	None	3 (3.0)	1 (2.6)
	Total	101	39

*Others: ketoconazole, palliative care, estramustine, vinblastine

Overall docetaxel and abiraterone use

Docetaxel and abiraterone use (n = 181)		N	%
Abiraterone	At any time point	96	**53.1**
	Pre-docetaxel	2	1.1
	Post-docetaxel	64	35.4
	Only (never doc)	30	**16.6**
Docetaxel	At any time point	100	**55.2**
	Only (never abi)	34	18.8
Abiraterone or docetaxel		130	71.8

Supportive care
Bone-targeted therapy

BTTx type, (n = 122)	N	%
None	38	**31.2**
Denosumab	56	**45.9**
Zoledronic acid	20	**16.4**
Denosumab and Zoledronic acid	7	5.7
Others (pamidronate)	1	0.8

Other quality of care indicators

Other quality of care indicators		N	%
Participation in clinical trials (n = 163)		17	10.4
Dental exam before bone-targeted therapy (n = 128)		53	**41.4**
Pivot oncological nurse during the first month of treatment (n = 146)		24	**16.4**
Pivot nurse during the initial CRPC treatment (n = 122)	During the first month, or	45	36.9
	During the second month, or	54	44.3
	During the third month	60	**49.1**
Emergency visit during the first month of initial CRPC treatment (n = 159)		6	3.8
Psychosocial assistance during the CRPC phase (n = 157)		35	**22.3**

Conclusion
Future outlook

Conclusion

- Current management of CRPC patients in the MUHC seems to differ from the recommendations of Canadian clinical guidelines for CRPC
  - 10.3 % of non metastatic patients received abiraterone
  - 20.6% of non metastatic patients received docetaxel
  - Only 10.3% of non metastatic patients had AAs withdrawal
  - 30.1 % of patients with metastatic disease received AAs as first-line treatment
  - Only 30.7 % of patients with metastatic disease received docetaxel
  - 3.0% of patients with metastatic disease didn’t receive any treatment
  - 31.2% of patients did not received bone-targeted therapy at all

Future Outlook

- Continue data collection
  - Jewish General Hospital (JGH)
  - St-Mary Hospital Center (SMHC)

- Further analyses with a complete database will allow identifying factors that might explain the difference in practice patterns for the management of patients with CRPC.

Thanks

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- ROSSY Cancer Network
- Prostate Cancer Canada

Thank you for your attention!

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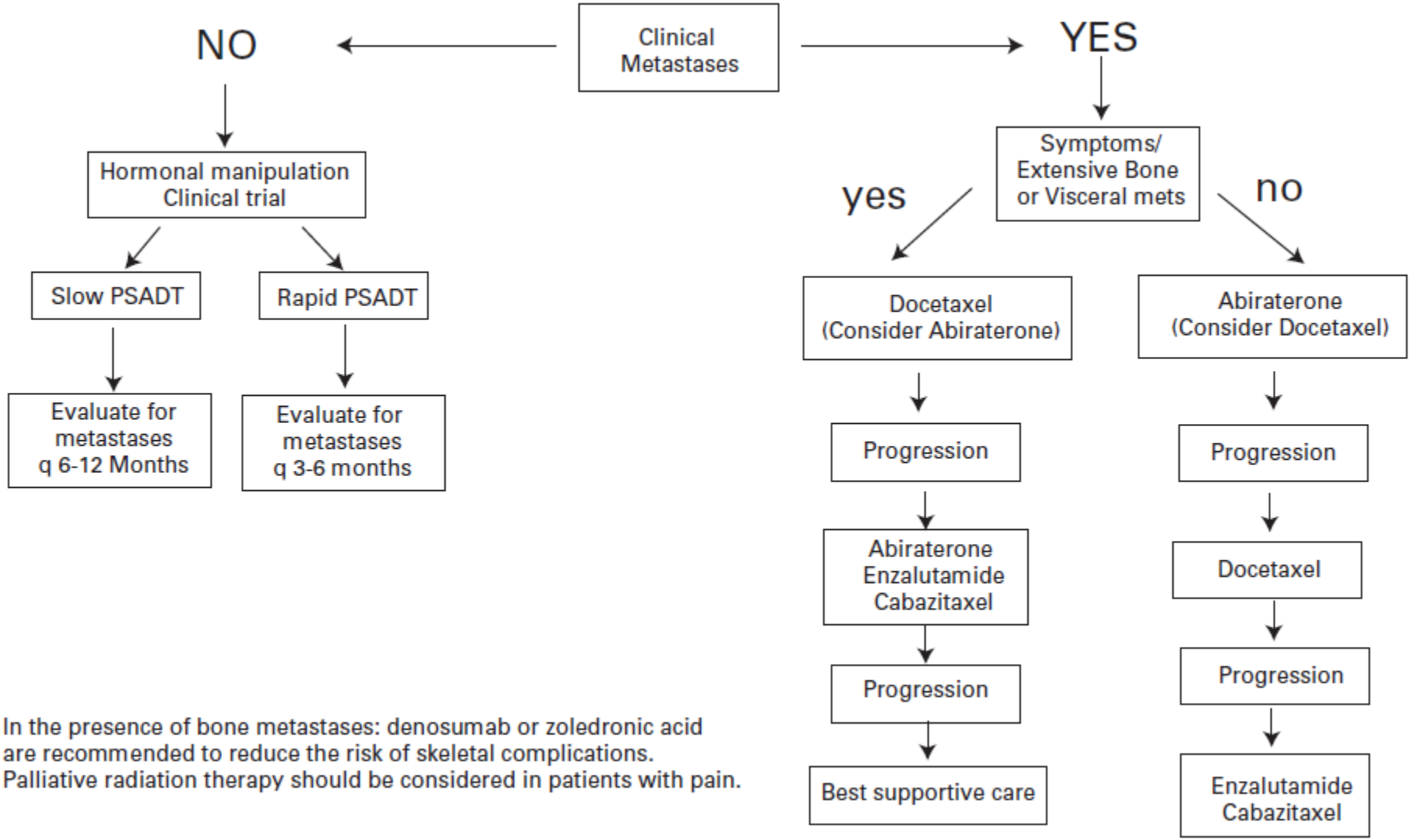
- http://www.healthline.com/health/prostate-cancer-progNsis-life-expectancy-bone-metastases#Overview1
- http://unc.org/conference/2014/OptimizingBoneHealth.pdf

BACK-UP SLIDES

CUA Guidelines - 2013



In the presence of bone metastases: denosumab or zoledronic acid are recommended to reduce the risk of skeletal complications. Palliative radiation therapy should be considered in patients with pain.

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Criteria for entering into the CRPC phase

- Patient on ADT or TAB, but
  - PSA progresses
    - 3 consecutive rises of PSA
    - At least 1 week apart
    - Resulting in two 50% increases over the nadir
    - PSA increase of at least 2 ng/mL
  - Metastases develop, progress and/or spread
  - Castrate level of testosterone (<50 ng/ml)
  - Radiological progression
    - If the patient was m0CRPC before
      - Appearance of metastases (Ndal, bone or visceral)
    - If the patient was metastatic before
      - 2 new bone lesions (if he had bone metastases already before)
      - Enlargement of soft tissue lesions (if he had Ndal or visceral metastases before)

Why is testing for dental health important?

- Bone-targeted therapy is a risk factor for ONJ (Osteonecrosis of the Jaw) = BTTx-induced ONJ
  - ONJ may occur in patients taking strong antiresorptive therapies such as
    - Bisphosphonates (zoledronic acid) , RANKL inhibitors (denoumab)
  - The risk of ONJ in patients taking bisphosphonates may depend on
    - the dose of medication, the length of time it is taken and the medical condition for which the bisphosphonate is prescribed.
  - The number of ONJ cases in patients taking bisphosphonates by mouth is estimated to be between 1 in 1,000 and 1 in 100,000 for each year of exposure to the medication.
- Most cases of ONJ happen after a dental extraction.
- Prevention of ONJ
  - Good oral hygiene and regular dental care is the best way to lower the risk of ONJ
  - Conduct baseline oral exam and perform all invasive dental procedures before initiating a bone-targeted therapy

http://unc.org/conference/2014/OptimizingBoneHealth.pdf

Difference between low and high level bone metastases

- High-volume
  - more than 4 bone lesions and at least one lesion on beyond pelvis and vertebral column
- Low volume
  - bone metastases are all on pelvis and vertebral column

Treatments sequence (1st and 2nd lines)

(n= 126)	Treatment 1							
	Docetaxel		**Abiraterone**		**Bicalutamide**		**AA withdrawal**	
Treatment 2	N	%	N	%	N	%	N	%
Docetaxel	3	6.7	0	**0**	14	**26.4**	6	**30**
Abiraterone	27	**60**	0	0	4	**7.5**	7	**35.0**
Bicalutamide	1	2.2	0	0	0	0	0	0
Nilutamide	0	0	0	0	0	0	1	5.0
Flutamide	0	0	0	0	1	1.9	0	0
AA withdrawal	0	0	0	0	16	**30.2**	0	0
Enzalutamide	1	2.2	2	**25.0**	0	0	0	0
Cabazitaxel	0	0	1	**12.5**	0	0	0	0
Mitoxandrone	2	4.4	0	0	0	0	0	0
Palliative care	2	4.4	0	0	2	3.8	1	5.0
Sunitinib	2	4.4	0	0	0	0	0	0
Dexamethasone	1	2.2	0	0	0	0	0	0
Ketoconazole	0	0	0	0	3	5.7	1	5.0
Prednisone only	0	0	0	0	1	1.9	2	10
None	6	**13.3**	5	**62.5**	12	**22.6**	2	**10**
Total	**45**	100	**8**	100	**53**	100	**20**	100

ECOG

Appendix A: ECOG Performance Status

ECOG PERFORMANCE STATUS*	
Grade	**ECOG**
0	Fully active, able to carry on all pre-disease performance without restriction
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work
2	Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours
3	Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours
4	Completely disabled. Cannot carry on any selfcare. Totally confined to bed or chair
5	Dead

* As published in Am. J. Clin. Oncol.:

Oken, M.M., Creech, R.H., Tormey, D.C., Horton, J., Davis, T.E., McFadden, E.T., Carbone, P.P.: Toxicity And Response Criteria Of The Eastern Cooperative Oncology Group. Am J Clin Oncol 5:649-655, 1982.

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