Destaques ASCO GU 2018

A Beneficência
Portuguesa
de São Paulo

-- Câncer de Próstata Avançado Hormonio Sensível --

Fabio Kater

Addition of docetaxel to first-line long-term hormone therapy in prostate cancer (STAMPEDE): long-term survival, quality-adjusted survival and cost-effectiveness analysis.

Nicholas James
on behalf of
Beth Woods, Eleftherios Sideris, Matthew Sydes,
Melissa Spears, Mark Sculpher and the STAMPEDE Investigators

Addition of docetaxel to first-line long-term hormone therapy in prostate cancer (STAMPEDE): long-term survival, quality-adjusted survival and cost-effectiveness analysis

Overview

- Objective: establish whether adding docetaxel to standard of care represents a cost-effective use of healthcare resources in M0 and M1 patients
  - Requires estimates of lifetime costs and quality-adjusted life years (QALYs) for each treatment
  - Model-based approach used to allow extrapolation and incorporation of external data
- Policy context
  - Docetaxel widely available in M1 first line
  - Role in M0 first line less clear

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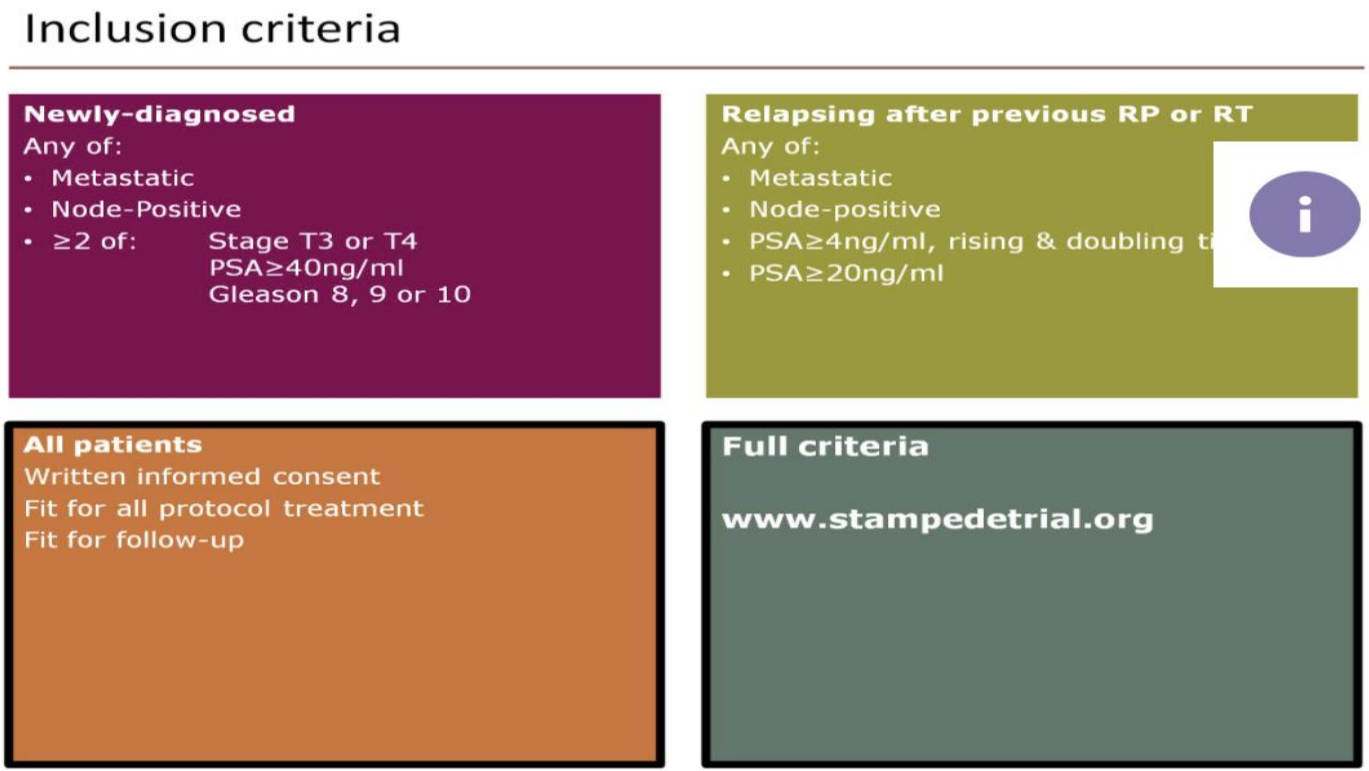

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Outcome measures

Primary outcome measure
Overall survival

Secondary outcome measures
Failure-free survival (FFS)
Progression-free survival (PFS)
Metastatic progression-free survival (MPFS)
Skeletal-related events (SRE)
Toxicity
Cost effectiveness
Quality of life (EQ5D)

This presentation

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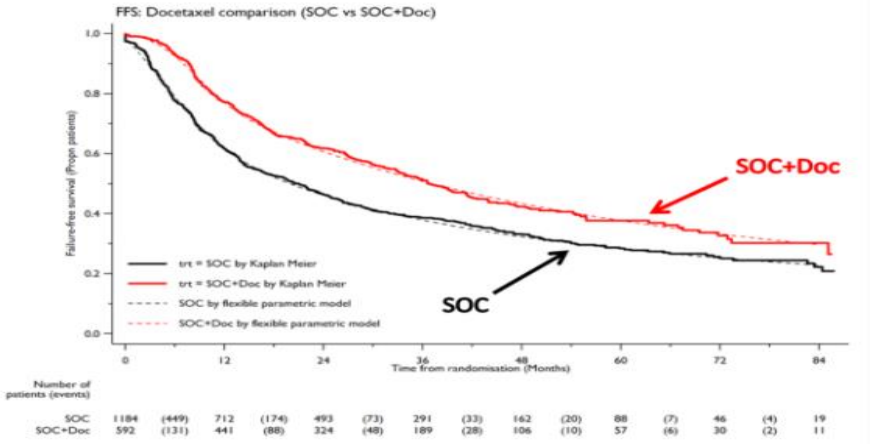
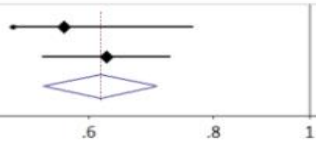
Docetaxel: Failure-free survival



HR (95%CI) 0.61 (0.53, 0.70)
P-value $0.413*10^{-12}$

Non-PH p-value <0.0001

Mets status	FFS events	No. pts	Haz. Ratio (95% CI)
M0	229	689	0.57 (0.42, 0.76)
M1	832	1087	0.62 (0.54, 0.73)
Overall	1061	1776	0.62 (0.54, 0.70)



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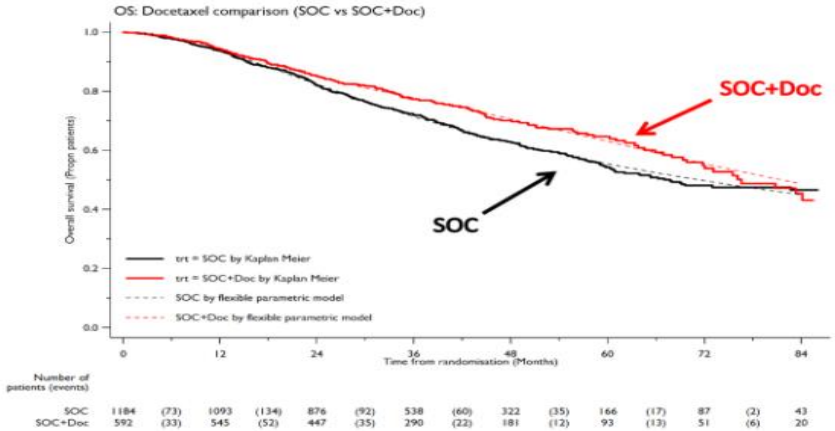
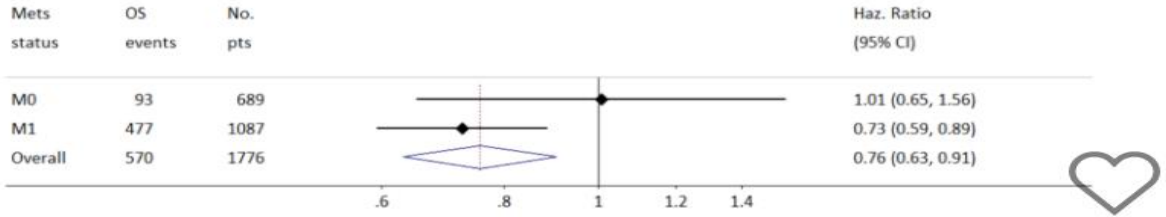
Docetaxel: Survival



HR (95%CI) **0.78** (0.66, 0.93)
P-value **0.006**

Non-PH p-value 0.87



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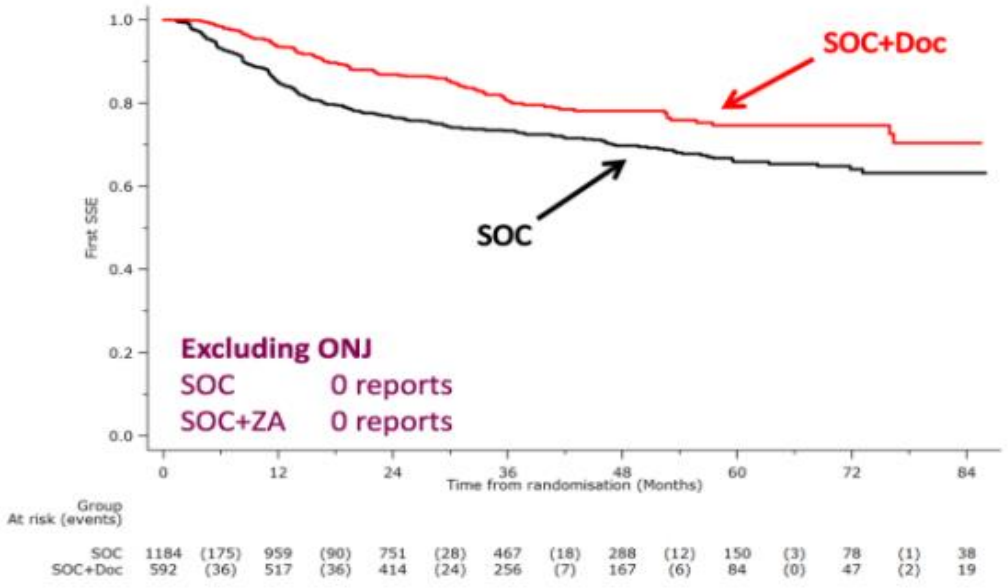
Docetaxel: Skeletal events (All patients)



SOC	**328 SSE events**
SOC+Doc	**112 SSE events**
HR (95%CI)	**0.60** (0.48, 0.74)
P-value	**0.00000127**

Non-PH p-value 0.0001

Restricted mean SSE time

SOC	61.4m
SOC+Doc	68.0m
Diff (95%CI)	6.6m (3.6, 9.6m)

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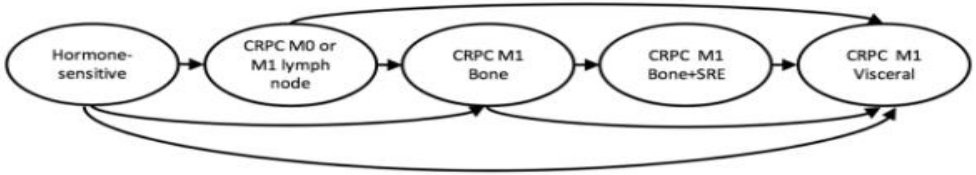
Methods

- State transition model used to reflect natural history of patients entering STAMPEDE



- Rate of progression determined from STAMPEDE clinical data
  - M1 data used in M0 patients once experience M1 CRPC (due to immaturity of OS data)
- Quality of life estimated from STAMPEDE EQ-5D data collection
- Costs from literature and STAMPEDE

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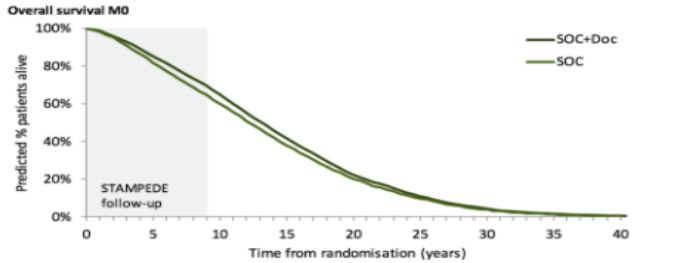
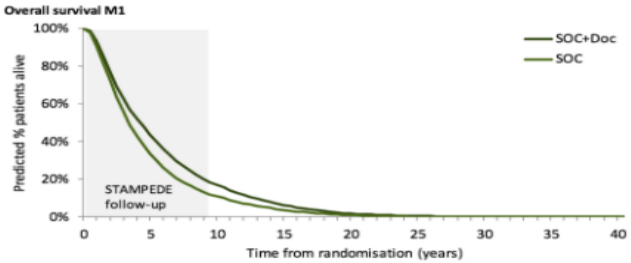
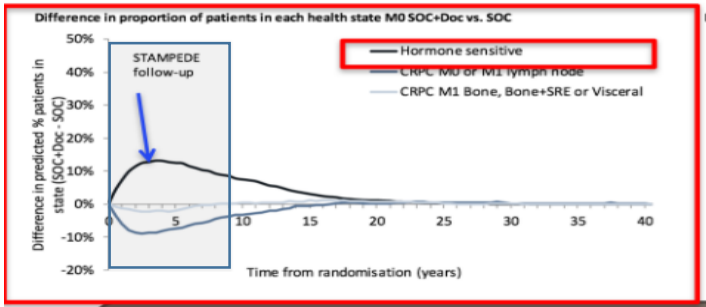
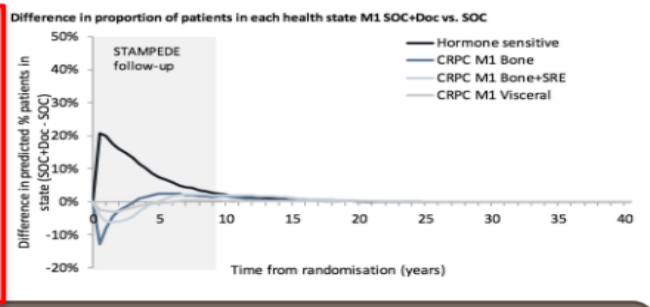
Results – state membership over time









Patients receiving docetaxel spend more time in the hormone sensitive state (without treatment failure) and **less time with CRPC – particularly M0 patients**

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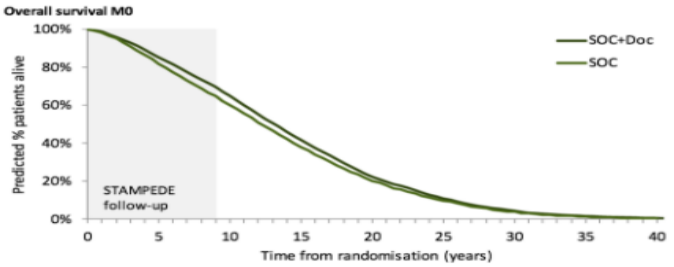

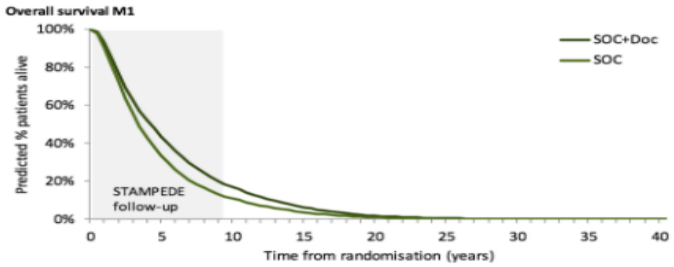

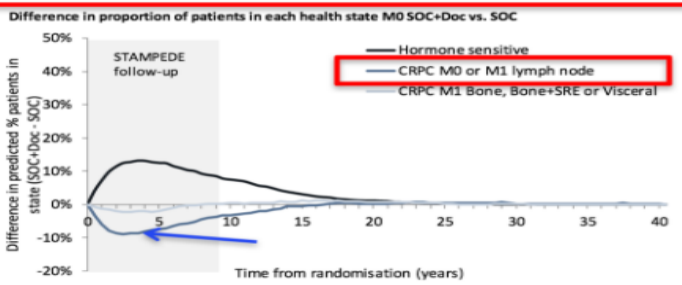

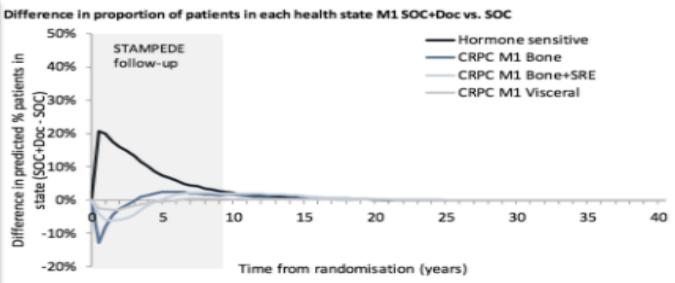

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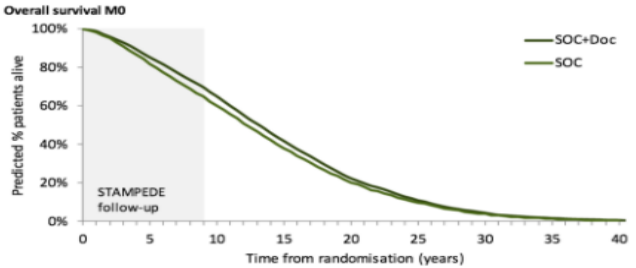

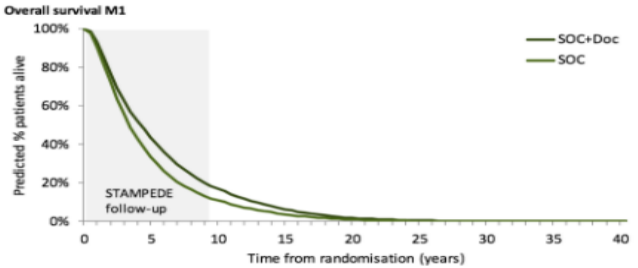

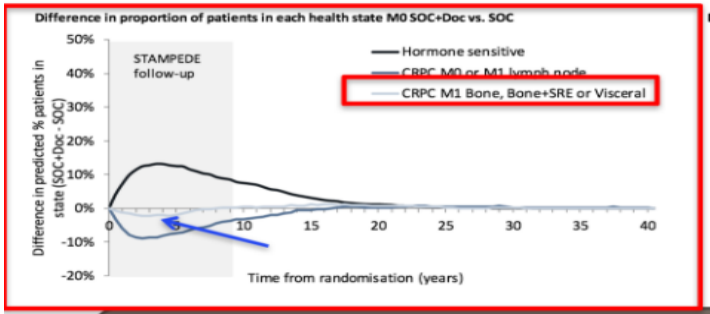

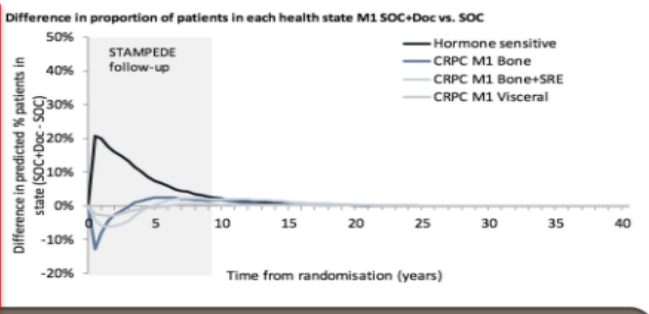

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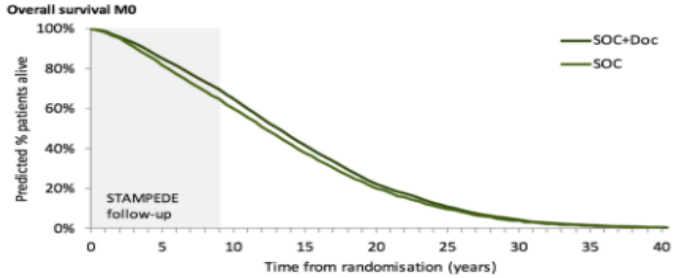

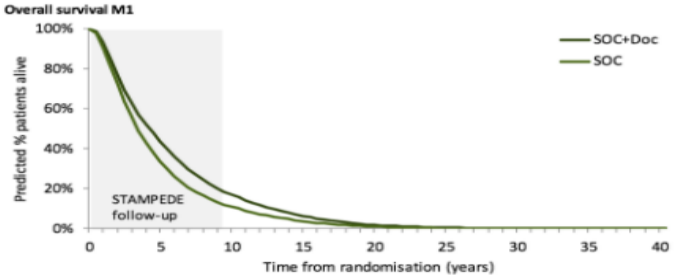

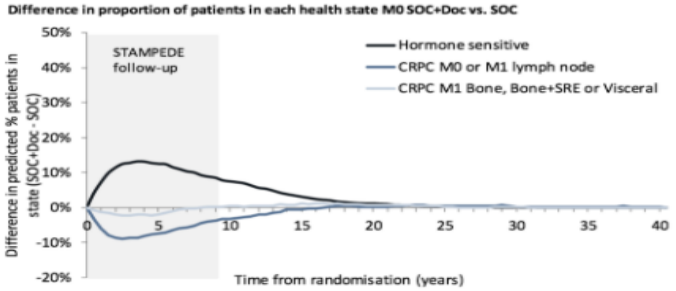

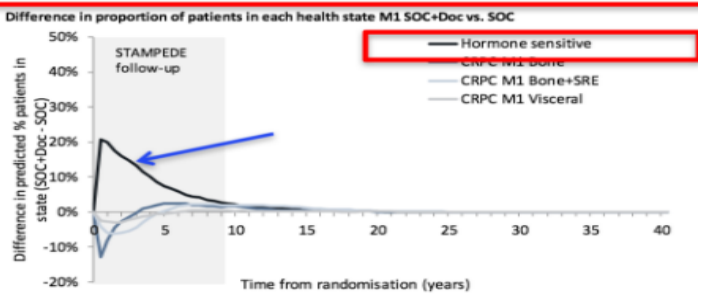

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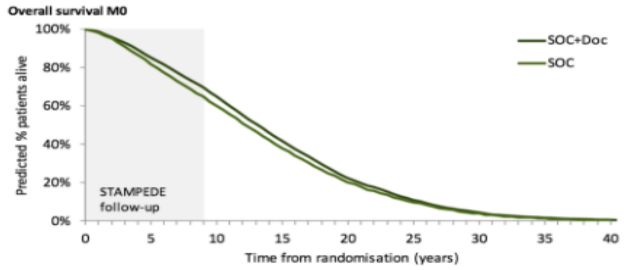

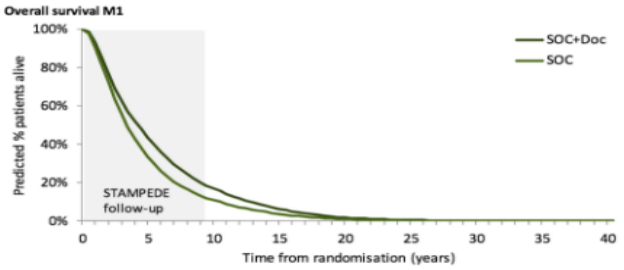

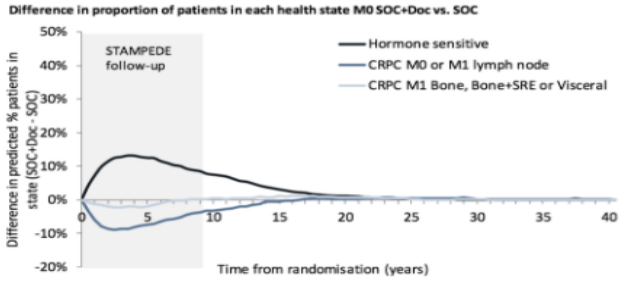

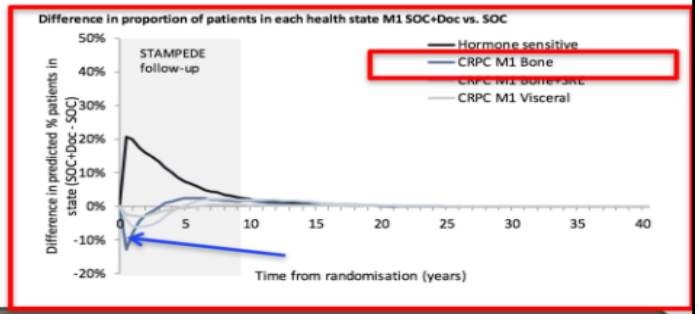

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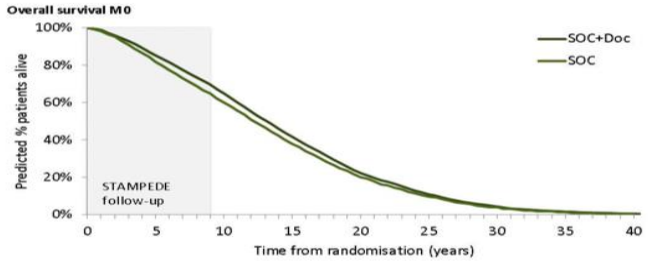

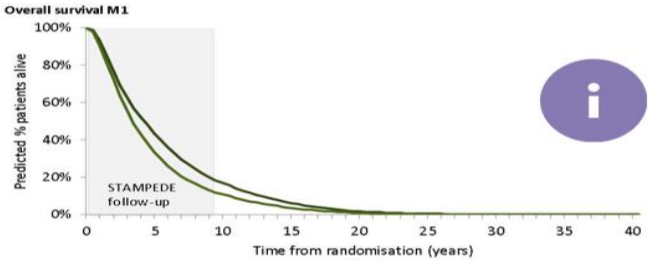

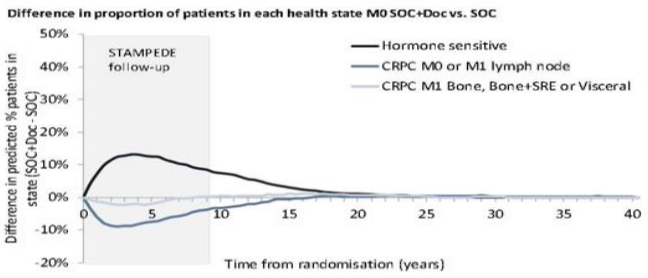

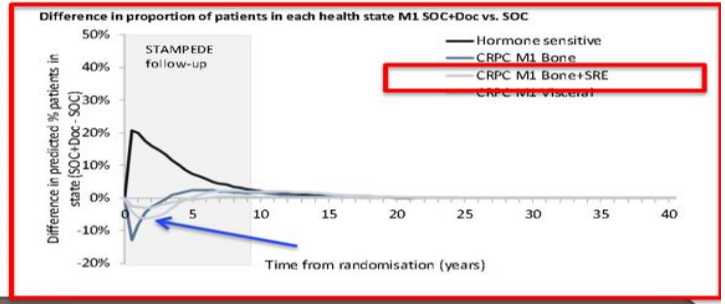

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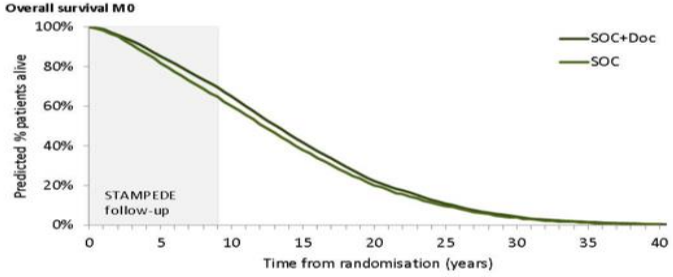

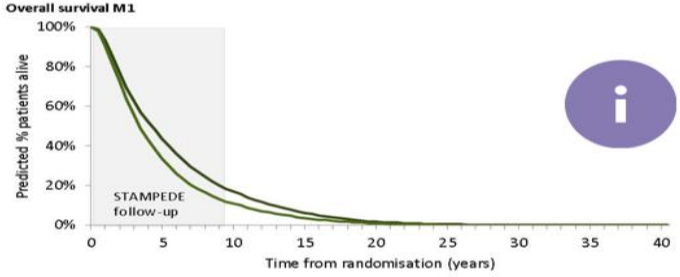

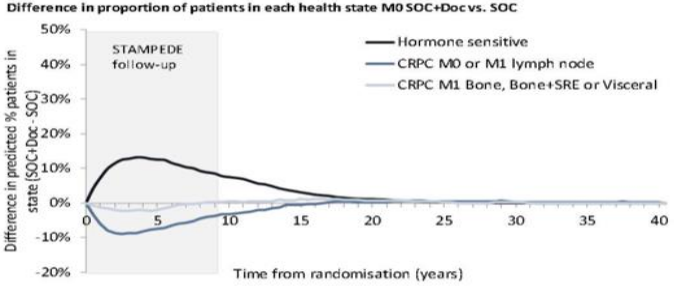

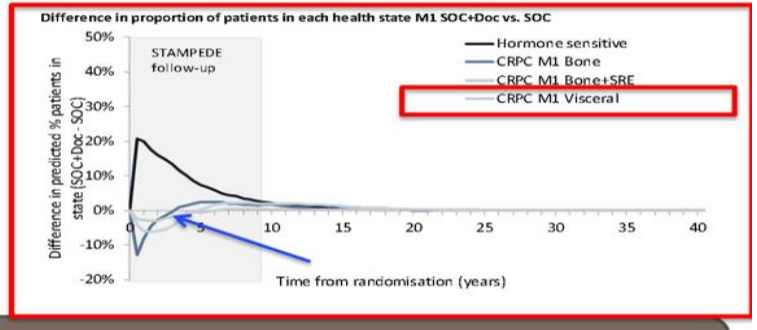

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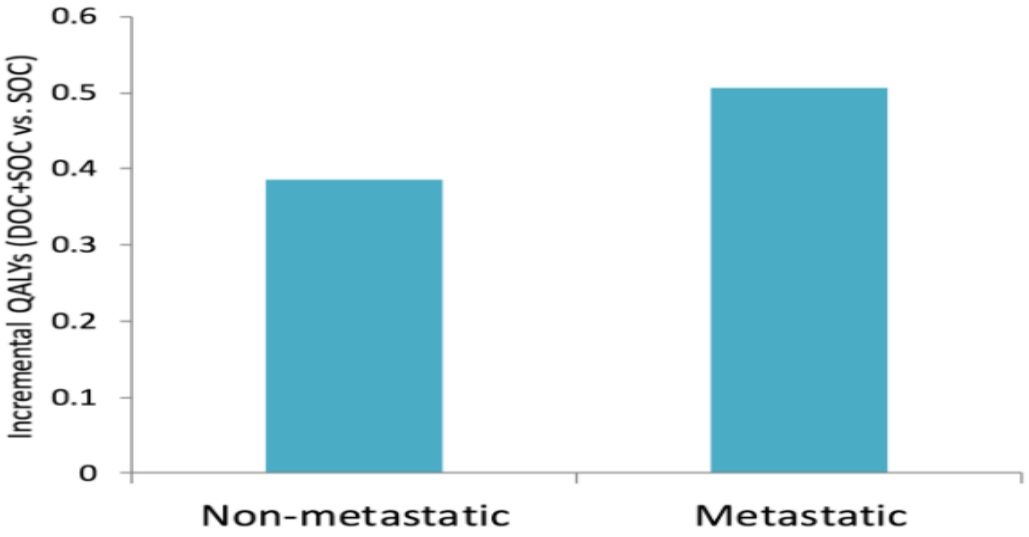
Impact of docetaxel on Quality Adjusted Life Years (QALYs)



SOC Standard of care
DOC Docetaxel

>0 favours Docetaxel

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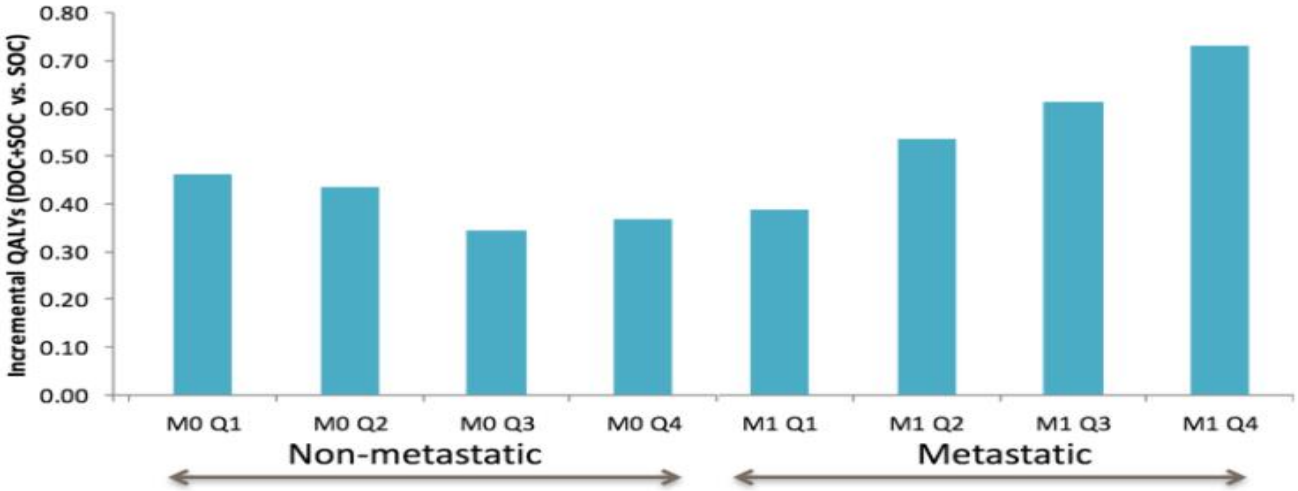

- Gains in M1 vary considerably by quartile
- Gains in M0 more homogeneous and lower than in M1
- All groups show a QALY gain

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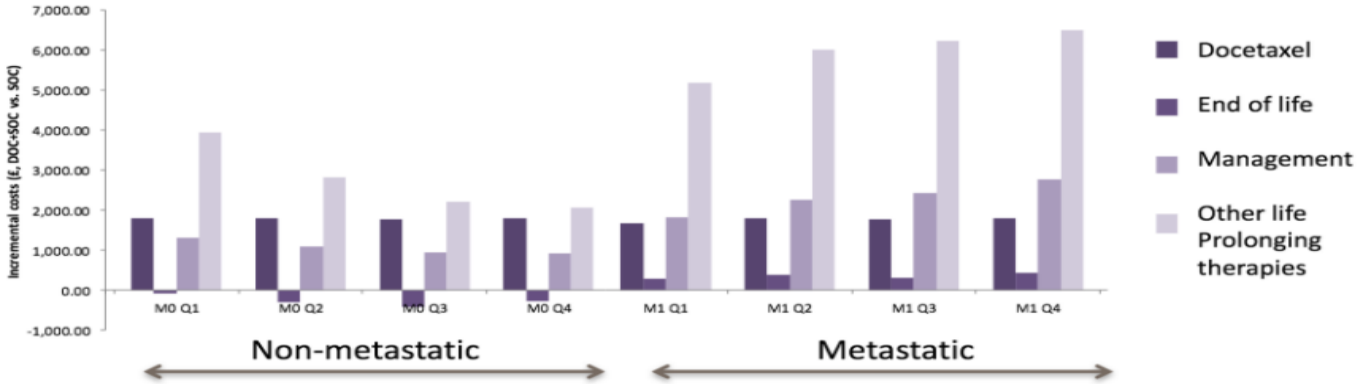
Incremental cost breakdown



- Incremental management costs attributable to extensions to life
  - Lower for M0 due to shorter extension to life and less intense management
- Incremental life extending therapy costs attributable to higher use of AR-pathway inhibitors in docetaxel arm
  - Lower for M0 due to less time spent in M1 CRPC health states

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Reflecting current treatment in M1 CRPC

- AR-pathway inhibitors approved during STAMPEDE for the post-chemotherapy then pre-chemotherapy settings
- Current treatment involves earlier use of abiraterone/enzalutamide for M1 CRPC patients[1]
- Broadly what was seen in STAMPEDE docetaxel arm as all patients technically "post-chemotherapy"
- Standard of care arm costs and QALYs adjusted within model

[1] Gillessen S, Attard G, Beer TM, et al: Management of Patients with Advanced Prostate Cancer: The Report of the Advanced Prostate Cancer Consensus Conference APCCC 2017. Eur Urol, 2017

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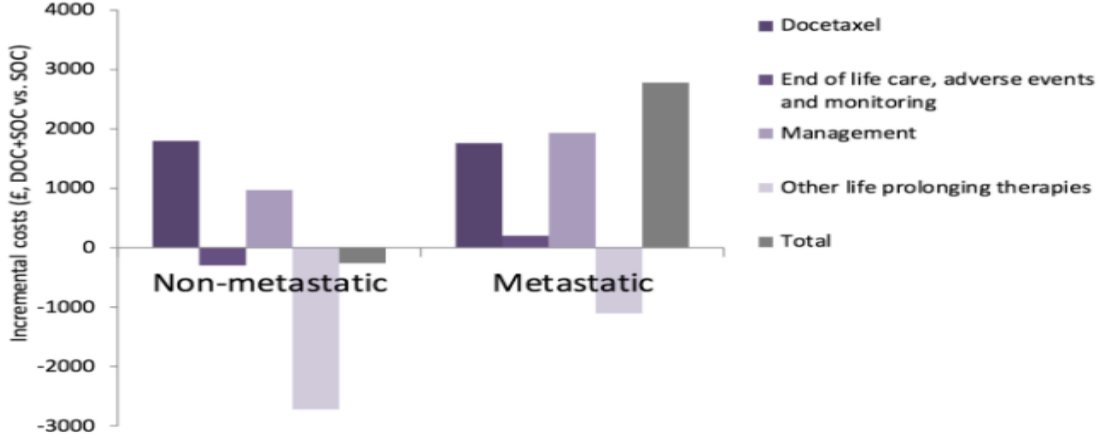
Incremental cost breakdown – modelled to current practice



- Savings in life extending therapies due to shorter period of time spent in CRPC states for patients on DOC+SOC
- Much greater for M0 patients as patients allocated to docetaxel arm spend a much shorter period in CRPC
  - (i.e. extensions to FFS do not fully translate to increased OS)

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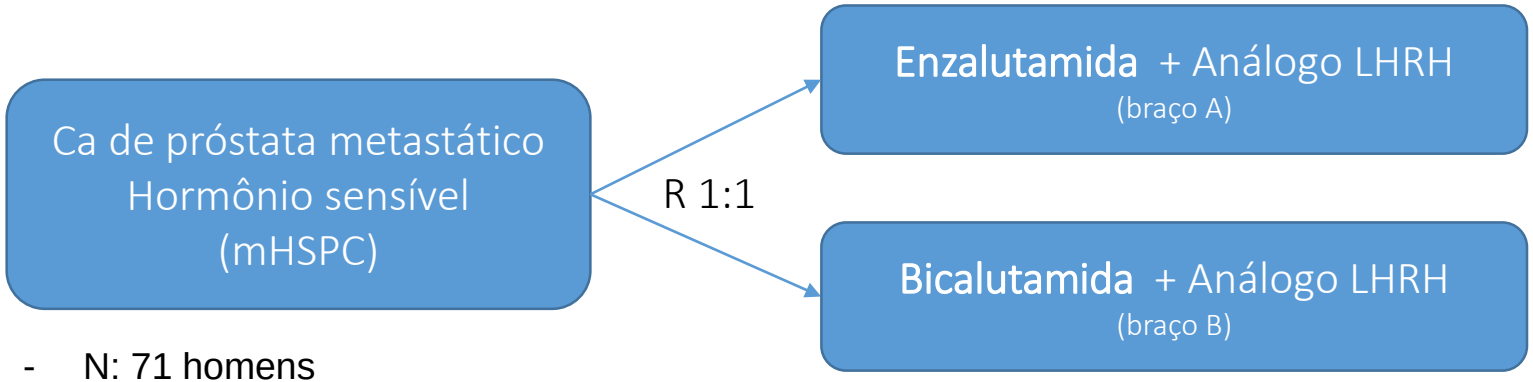
Key messages

- Upfront docetaxel results in a robust gain in quality adjusted life years in all subgroups.
- Results support healthcare policy in metastatic patients
- Results supports use of docetaxel in high-risk non-metastatic patients:
  - At the patient level: it provides overall quality of life benefits
  - The model also predicts an eventual survival gain
  - At the provider level it represents a cost-effective use of resources

Randomized Phase II Screening Trial Of Enzalutamide Versus Bicalutamide In Combination With Androgen Deprivation In Metastatic Hormone Sensitive Prostate Cancer: A Prostate Cancer Clinical Trials Consortium Trial

Ulka Vaishampayan[1], Sreenivasa Chinni[1], Lance Heilbrun[1], Paul Monk[2], Sheila Tejwani[3], Guru Sonpavde[4], Daryn Smith[1], Pallavi Jasti[1], Kimberlee Dobson[1], Michael Cher[1], Elisabeth Heath[1], Joseph Fontana[1].
1 Karmanos Cancer Institute/Wayne State University, Detroit MI, 2 Ohio State University, Columbus OH, 3 Henry Ford Hospital, Detroit MI, 4 University of Alabama at Birmingham, AL



- N: 71 homens

- *Endpoint* primário: nadir PSA < 4 ng/ml após 7 meses de tratamento
- *Endpoints* secundários: toxicidade, SLP bioquímica, SLP radiológica e SG

→ Estudo interrompido quando Abiraterona precoce mostrou benefício de SG em mHSPC

J Clin Oncol 36, 2018 (suppl 6S; abstr 190)

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1 Karmanos Cancer Institute/Wayne State University, Detroit MI, 2 Ohio State University, Columbus OH, 3 Henry Ford Hospital, Detroit MI, 4 University of Alabama at Birmingham, AL

- POPULAÇÃO:

- N: 71 homens
  - 29 afro-descendentes; 41 brancos; 1 asiático
  - Idade mediana: 67 anos (46 – 87 anos)
  - PSA mediano: 56,3 ng/ml (braço A) e 60 ng/ml (braço B)
  - 27 pts (38,5%) com dor óssea e 13 pts com metástase visceral

Characteristic	Enzalutamide N=36	Bicalutamide N=35
Median age	66 years	63 years
Race AA patients	15 (41.2%)	14 (40%)
Bone pain (yes) Bone Pain (No)	14 (38.8%) 22 (61.2%)	12 (34.2%) 23 (65.8%)
Lung/Liver mets	1 (2.7%)	2 (6%)
Performance Status 0/1	16 (44%)/20 (56%)	16 (46%)/19 (54%)
Bone mets	31(86%)	28 (80%)
Extensive (> 4 bone lesions) Limited Disease (≤4 bone lesions)	20 (55%) 16(44%)	17 (48.5%) 18 (51.5%)
Late induction	26 (72%)	22 (62.8%)
Measurable disease	17 (47%)	17 (48.5%)
Current Status Deaths	4 (11%)	13 (37.1%)
Current Status On Treatment	16 (44.44)	8 (22.8%)

J Clin Oncol 36, 2018 (suppl 6S; abstr 190)

Randomized Phase II Screening Trial Of Enzalutamide Versus Bicalutamide In Combination With Androgen Deprivation In Metastatic Hormone Sensitive Prostate Cancer: A Prostate Cancer Clinical Trials Consortium Trial

Ulka Vaishampayan[1], Sreenivasa Chinni[1], Lance Heilbrun[1], Paul Monk[2], Sheila Tejwani[3], Guru Sonpavde[4], Daryn Smith[1], Pallavi Jasti[1], Kimberlee Dobson[1], Michael Cher[1], Elisabeth Heath[1], Joseph Fontana[1].
1 Karmanos Cancer Institute/Wayne State University, Detroit MI, 2 Ohio State University, Columbus OH, 3 Henry Ford Hospital, Detroit MI, 4 University of Alabama at Birmingham, AL

- RESULTADOS:
  - EAs grau 3 →

Toxicities	Enzalutamide N=36	Bicalutamide N=35
Syncope	3 (8.3%)	0 (0%)
Diarrhea	0 (0%)	1 (2.8%)
Hypertension	4 (11%)	6 (17%)
Fall	1 (2.7%)	0 (0%)
Hot Flashes	0 (0%)	1 (2.8%)
Urinary Tract Infection	2(5.6%)	1 (2.8%)
Second Malignancies	2 (5.6%)	2 (5.6%)
Fatigue	0 (0%)	2 (5.6%)
Anemia	1 (2.7%)	1 (2.8%)
Myocardial Infarction	0 (0%)	1 (2.8%)
GI bleed	1 (2.7%)	0 (0%)

- PSA < 4 ng/ml

Enzalutamida + aLHRH	Bicalutamida + aLHRH
96,3% dos pacientes	66,7% dos pacientes

- Duração Taxas de Remissão PSA em 6 meses após o 7º mês

Enzalutamida + aLHRH	Bicalutamida + aLHRH
86%	79%

A Beneficência Portuguesa de São Paulo

J Clin Oncol 36, 2018 (suppl 6S; abstr 190)

Randomized Phase II Screening Trial Of Enzalutamide Versus Bicalutamide In Combination With Androgen Deprivation In Metastatic Hormone Sensitive Prostate Cancer: A Prostate Cancer Clinical Trials Consortium Trial

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- CONCLUSÃO:

→ O uso precoce de Enzalutamida em mHSPC tem potencial para aumentar as taxas de remissão de PSA e, consequentemente, melhorar as taxas de SLP e SG

J Clin Oncol 36, 2018 (suppl 6S; abstr 190)

Abstract 251: Co-targeting AR Signaling and Cell Cycle: A Randomized Phase II Study of Androgen Deprivation Therapy with or without Palbociclib in RB-positive Metastatic Hormone Sensitive Prostate Cancer (mHSPC)

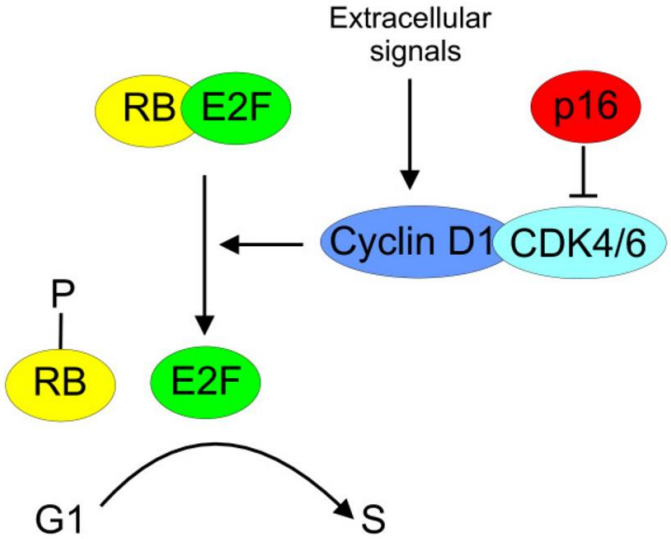
Phillip L. Palmbos[1*], Scott A. Tomlins[1], Neeraj Agarwal[2], Przemyslaw Twardowski[3], Alicia K. Morgans[4], Wm Kevin Kelly[5], Vivek K. Arora[6], Emmanuel S. Antonarakis[7], Javed Siddiqui[1], Stephanie Daignault[1], Felix Y. Feng[8], Karen E. Knudsen[5], Maha Hussain[9].

COMPREHENSIVE CANCER CENTER MICHIGAN MEDICINE

[1]Michigan Medicine Comprehensive Cancer Center, Ann Arbor, MI. [2]Huntsman Cancer Institute, University of Utah, Salt Lake City, UT. [3]City of Hope Cancer Center, Duarte, CA. [4]Vanderbilt-Ingram Cancer Center, Nashville, TN. [5]Thomas Jefferson University, Philadelphia, PA. [6]Washington University in St. Louis, St. Lous, MO. [7]Sidney Kimmel Comprehensive Cancer Center at John Hopkins, Baltimore, MD. [8]University of California at San Francisco, San Francisco, CA. [9]Northwestern University/Robert H. Lurie Comprehensive Cancer Center, Chicago, IL.

*Email Contact: ppalmbos@umich.edu

- Background



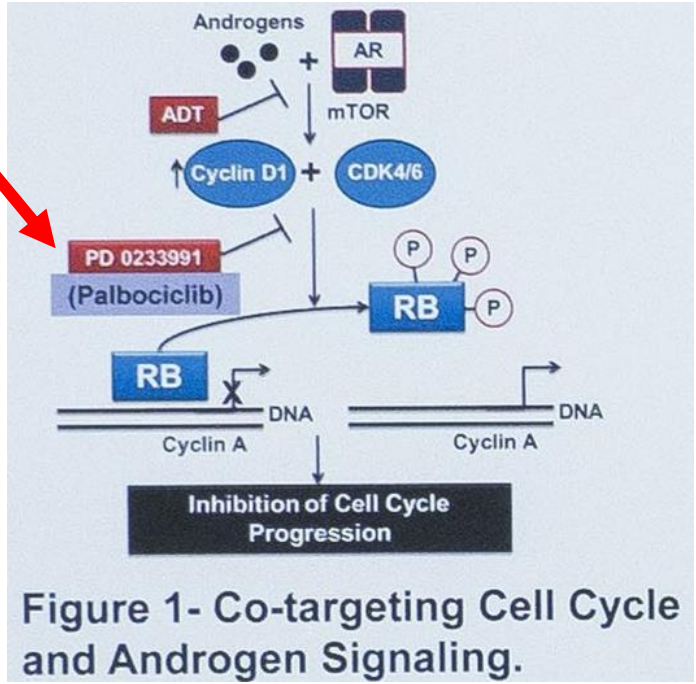


Figure 1- Co-targeting Cell Cycle and Androgen Signaling.

J Clin Oncol 36, 2018 (suppl 6S; abstr 251)

Abstract 251: Co-targeting AR Signaling and Cell Cycle: A Randomized Phase II Study of Androgen Deprivation Therapy with or without Palbociclib in RB-positive Metastatic Hormone Sensitive Prostate Cancer (mHSPC)

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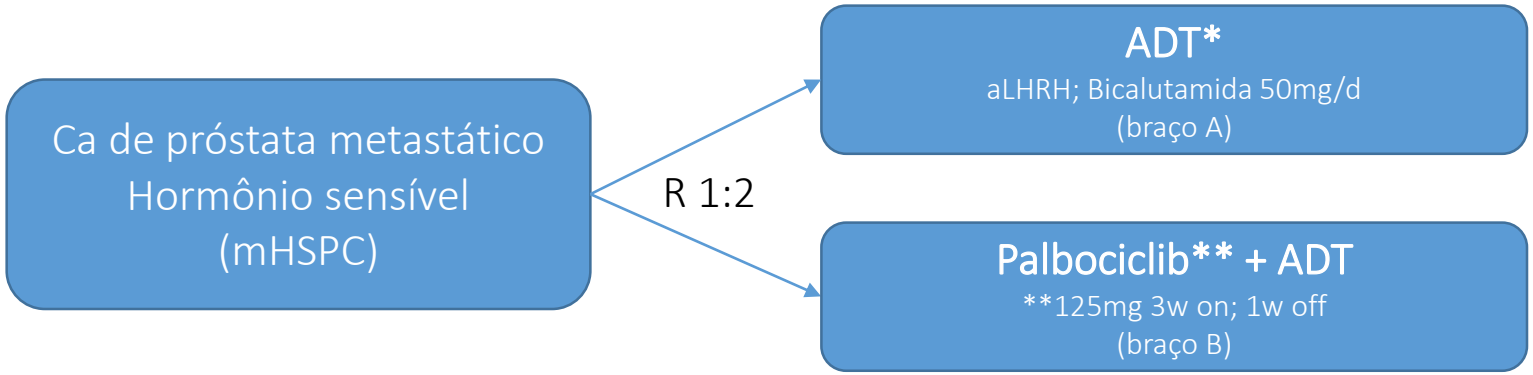

- N: 72 homens

- *Endpoint* primário: PSA RR < 4 ng/ml após 28 semanas de tratamento
- *Endpoints* secundários: segurança/tolerabilidade, SLP bioquímica, SLP clínica, RR PSA, RR radiológica

J Clin Oncol 36, 2018 (suppl 6S; abstr 251)

Abstract 251: Co-targeting AR Signaling and Cell Cycle: A Randomized Phase II Study of Androgen Deprivation Therapy with or without Palbociclib in RB-positive Metastatic Hormone Sensitive Prostate Cancer (mHSPC)

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COMPREHENSIVE CANCER CENTER
MICHIGAN MEDICINE

- POPULAÇÃO:

N: 72 homens

- 64/72 (90% pts) tinham tecido adequado p/ avaliação Rb e 62/64 (90% pts) expressavam Rb por IHQ
- 60 pcts iniciaram o tratamento (braço A: 20; braço B: 40)

	ADT Alone	PD + ADT	p-value
Median Age (Min - Max)	66.5 (44 - 81.9)	68.4 (47.4 - 87.6)	0.61
Median Baseline PSA (Min - Max)	39.9 (1.4 - 231.4)	62.6 (0.8 - 1691.6)	0.23
Primary Gleason Sum			1.00
6	0 (0%)	1 (2.5%)	
7	5 (25%)	9 (22.5%)	
8-10	11 (55%)	23 (57.5%)	
Unknown	4 (20%)	7 (17.5%)	
Prior Treatment			
Radical Prostatectomy	9 (45%)	14 (35%)	0.58
Primary Radiotherapy	2 (10%)	4 (10%)	1.00
Neoadjuvant/Adjuvant Systemic Therapy	5 (25%)	10 (25%)	1.00
Neoadjuvant/Adjuvant Radiotherapy	3 (7.5%)	2 (5%)	
Salvage Radiotherapy	3 (15%)	4 (10%)	
Other Radiotherapy	0 (0%)	5 (12.5%)	
Disease Sites at Baseline			
Visceral Mets	1 (5%)	2 (5%)	1.00
Bone Mets	14 (70%)	30 (75%)	0.76
LN Only	5 (25%)	8 (20%)	0.74
Baseline Bone Pain	5 (25%)	6 (15%)	0.48

J Clin Oncol 36, 2018 (suppl 6S; abstr 251)

- RESULTADOS:
  - Neutropenia graus 3/4

ADT	Palbociclib + ADT
0%	33%

  - PSA < 4 ng/ml (p: 0.87)

ADT	Palbociclib + ADT
80% (16/20 pts)	80% (32/40 pts)

  - Taxas de PSA indetectável na 28ª semana de tratamento (p: 0.50)

ADT	Palbociclib + ADT
50% (10/20 pts)	43% (17/40 pts)

J Clin Oncol 36, 2018 (suppl 6S; abstr 251)

Abstract 251: Co-targeting AR Signaling and Cell Cycle: A Randomized Phase II Study of Androgen Deprivation Therapy with or without Palbociclib in RB-positive Metastatic Hormone Sensitive Prostate Cancer (mHSPC)

Phillip L. Palmbos[1*], Scott A. Tomlins[1], Neeraj Agarwal[2], Przemyslaw Twardowski[3], Alicia K. Morgans[4], Wm Kevin Kelly[5], Vivek K. Arora[6], Emmanuel S. Antonarakis[7], Javed Siddiqui[1], Stephanie Daignault[1], Felix Y. Feng[8], Karen E. Knudsen[5], Maha Hussain[9].

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- RESULTADOS:

  - RR doença mensurável

ADT	Palbociclib + ADT
78%	74%

  - SLP bioquímica em 12 meses

ADT	Palbociclib + ADT
69% (95%CI: 43-85%)	74% (95%CI: 56-85%)

Figure 3. PSA Progression Free Survival.

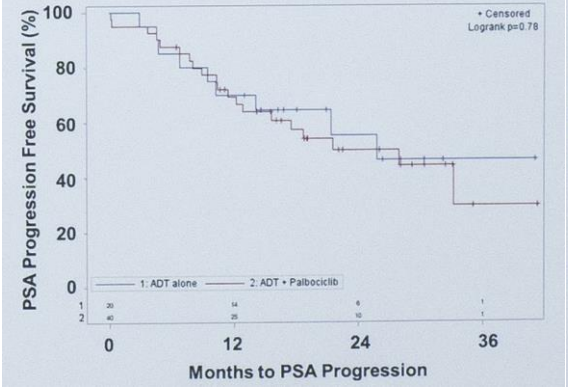
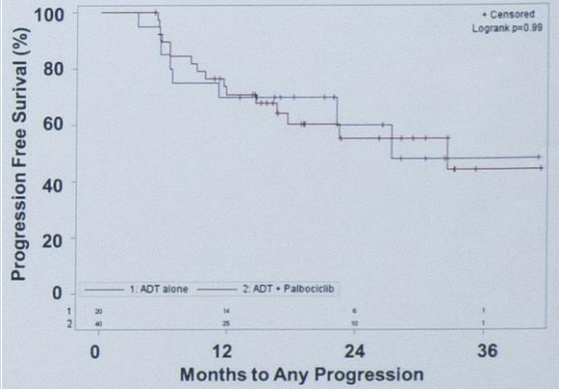


Figure 4. Progression Free Survival.



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J Clin Oncol 36, 2018 (suppl 6S; abstr 251)

- CONCLUSÃO:

→ O “duplo bloqueio” da sinalização do receptor androgênico (RA) e do ciclo celular em um estudo pré selecionado é viável em pacientes com mHSPC.

→ A perda de Rb foi rara nessa população.

→ A taxa de RR PSA a 28 semanas não foi alterada pela adição de Palbociclib

J Clin Oncol 36, 2018 (suppl 6S; abstr 251)

Phase II randomized study of Abiraterone acetate plus ADT versus Apalutamide versus Abiraterone and Apalutamide in patients with advanced prostate cancer with non-castrate testosterone levels. (LACOG 0415)

Fernando C. Maluf [1,6], Oren Smaletz [2,6], Fabio A. B. Schutz [1,6], Vinicius Carrera Souza [3,6], Andre Poisl Fay [4,6], Daniel Herchenhorn [3,6], Gustavo Werutsky [6], Telma Murias Santos [7]
1. Centro Oncológico Antônio Ermírio de Morais - BP Beneficencia Portuguesa de São Paulo, São Paulo, Brazil; 2. Hospital Israelita Albert Einstein, São Paulo, Brazil; 3. Clínica AMO, Salvador, Brazil; 4. PUCRS School of Medicine, Porto Alegre, Brazil;
2. 5. Grupo Oncologia D'Or, Rio De Janeiro, Brazil; 6. Latin American Cooperative Oncology Group (LACOG), Porto Alegre, Brazil; 7. Janssen Research and Development, LLC, Raritan, NJ

Ca de próstata Hormônio sensível avançado ou metastático (HSPC)

- Abiraterona 1000mg + PDN 5mg + ADT (braço A)
- Apalutamida 240mg (braço B)
- Abiraterona 1000mg + Apalutamida 240mg (braço C)

- ***Critérios de inclusão:***
  - 1. Adenocarcinoma de próstata confirmado histologicamente;
  - 2. Pacientes virgens de hormonioterapia com indicação para ADT nas seguintes configurações: doença loco-regional avançada não passível de terapia local curativa (T3 / 4 ou linfonodo positivo); Recidiva bioquímica após tratamento primário (cirurgia ou radioterapia) com PSA> = 4 ng / ml e aumento com tempo de duplicação de PSA inferior a 10 meses ou PSA> = 20 ng / ml ou N + ou M +;
  - 3. Doença metastática recentemente diagnosticada;
  - 4. O paciente é sintomático ou moderadamente sintomático;
  - 5. Nível de não-castração de testosterona ≥ 230 ng / dL.

A Beneficência Portuguesa de São Paulo

J Clin Oncol 36, 2018 (suppl 6S; abstr TPS404)

Phase II randomized study of Abiraterone acetate plus ADT versus Apalutamide versus Abiraterone and Apalutamide in patients with advanced prostate cancer with non-castrate testosterone levels. (LACOG 0415)

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RECRUTANDO !!!

Ca de próstata metastático Hormônio sensível avançado ou metastático (HSPC)

- Abiraterona 1000mg + PDN 5mg + ADT (braço A)
- Apalutamida 240mg (braço B)
- Abiraterona 1000mg + Apalutamida 240mg (braço C)

- ***Endpoint* primário:**
  - níveis de PSA indetectáveis (abaixo de 0,2 ng / mL) na semana 25
- ***Endpoints* secundários:**
  - Progressão de PSA e resposta de PSA (50% e 80%) na semana 25, sobrevida livre de progressão radiológica, segurança, qualidade de vida da vida (FACT-P) e correlação dos níveis séricos de androgênio com a resposta

A Beneficência Portuguesa de São Paulo

J Clin Oncol 36, 2018 (suppl 6S; abstr 324)

Cleveland Clinic

Treatment Patterns For Metastatic Hormone-Sensitive Prostate Cancer (mHSPC) Progressing After Up-Front Docetaxel in Combination With Androgen Deprivation Therapy (D-ADT)

Pedro C Barata[1], Hamid Emamekhoo[2], Prateek Mendiratta[1], Dharmesh Gopalakrishnan[3], Vadim Koshkin[1], Allison Tyler[1], Moshe C. Ornstein[1], Petros Grivas[1], Timothy D. Gilligan[1], Brian I Rini[1], Christos Kyriakopoulos[2], Jorge A. Garcia[1]

1. Cleveland Clinic Taussig Cancer Institute, Cleveland, OH 2. University of Wisconsin, Madison, WI 3. Hospital Medicine, Cleveland Clinic, Cleveland

- BACKGROUND:
  - D-ADT aumenta a SG em homens com mHSPC. Entretanto, pacientes progridem e desenvolvem CRPC. Pouco é sabido sobre a resposta a terapias subsequentes e seus desfechos nesse cenário
- MÉTODOS:
  - Análise retrospectiva de tratamentos consecutivos em pacientes mHSPC com ≥ 3 ciclos de D-ADT.

    (N: 146 pacientes)
  - Objetivo: descrever *baseline*, características de progressão, escolhas de tratamento, sequência e desfechos de terapia subsequentes

J Clin Oncol 36, 2018 (suppl 6S; abstr 305)

Cleveland Clinic

Treatment Patterns For Metastatic Hormone-Sensitive Prostate Cancer (mHSPC) Progressing After Up-Front Docetaxel in Combination With Androgen Deprivation Therapy (D-ADT)

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- RESULTADOS

Table 1: Baseline Patient and Disease Characteristics

Characteristics	N (%)
Median Age (Range)	65 (35-86)
ECOG	
0:	96 (71)
1:	32 (24)
2:	4 (3)
Unknown:	4 (3)
Prior cardiovascular disease	25 (19)
Gleason Score	
6:	4 (3)
7:	22 (16)
8-10	89 (65)
Unknown:	21 (15)
Neuroendocrine features	2 (1)
Prior local therapy	
None:	91 (67)
Surgery:	13 (10)
Radiation:	19 (14)
Surgery plus radiation:	11 (8)
Unknown:	2 (1)
Prior ADT	
≥ 12 months:	4 (3)
< 12 months:	21 (15)
None:	108 (79)
Unknown:	3 (2)
Median PSA at diagnosis	30.1 (0.3-5000)
Median PSA at stage IV	53.29 (1.2-4190)
Site of metastasis at stage IV	
Lymph nodes	77 (57)
Bones	117 (86)
Visceral	20 (15)
High-volume disease (per CHAARTED)	107 (79)

Table 2: Treatment with D-ADT

Characteristics	N (%)
Time from ADT to C1D1 Docetaxel, months	1.2 (0-12.6)
Number Docetaxel cycles	
3:	4 (3)
4:	3 (2)
5:	6 (4)
6:	123 (90)
Reason for not completing 6 cycles DOC	
Progressive disease	3 (2)
Treatment-related AEs	7 (5)
Other	2 (1)
Unknown	1 (1)
PSA "0"	
12 months	43 (29)
24 months	34 (23)
Median time to CRPC, months	19.6 (16.6-22.6)

Table 3: Subsequent Therapies for CRPC (n=57)

	N (%)
Number subsequent treatments	
1:	57 (100)
2:	29 (51)
3+:	12 (21)
First-line therapy for CRPC	
→ Abiraterone acetate	21 (37)
→ Enzalutamide	19 (33)
Other anti-androgen	6 (11)
Sipuleucel-T	4 (7)
Radium-223	4 (7)
QT: Docetaxel	1 (2)
QT: Cabazitaxel	2 (4)
QT: Carboplatin-based	2 (4)
Other	3 (5)

J Clin Oncol 36, 2018 (suppl 6S; abstr 305)

Cleveland Clinic

Treatment Patterns For Metastatic Hormone-Sensitive Prostate Cancer (mHSPC) Progressing After Up-Front Docetaxel in Combination With Androgen Deprivation Therapy (D-ADT)

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- RESULTADOS

Tables 4 and 5: PFS and OS for CRPC patients (n=57)

Median rPFS, months (CI 95%)	12.3 (7.5-17.1)	
HT[1] Non-HT[2]	13.3 (10.1-16.5) 3.1 (0-15.7)	*p*=0.332
[1]HT: abiraterone acetate, enzalutamide, other oral anti-androgen; [2]Sipuleucel-T excluded		

Median OS, months (CI 95%)	38.6 (27.3-49.9)	
Time to CRPC ≥ 12 months CRPC < 12 months	53.5 (30.6-76.4) 32.1 (27.8-36.4)	*p*=0.010
First subsequent treatment HT v Non-HT	47.0 (28.6-65-4) 31.4 (18.1-44.7)	*p*=0.009
Sequence of HT → HT HT → non-HT	47.0 (29.4-64.6) 31.9 (22.8-41.0)	*p*=0.152
Visceral Non-visceral	31.9 (21.1-42.7) 47.0 (32.0-61.2)	*p*=0.258

- Resposta ao tratamento foi independente do tempo de CRPC (< 12 meses *vs* ≥ 12 meses, p = 0,264)
- Tratamento de escolha foi independente do GS (GS < 8 *vs* GS ≥ 8, p = 0,513), doença visceral (p = 0,374) e tempo para CRPC (< 12 meses *vs* ≥ 12 meses, p = 0,50)

- CONCLUSÕES

  - D-ADT prévio NÃO impediu tratamentos subsequentes para pacientes com CRPC, independente do tempo para CRPC
  - A escolha da 1ª linha terapêutica para CRPC pode impactar sobrevida em favor daqueles que começarem terapia hormonal
  - Validação prospectiva é necessária

A Beneficência Portuguesa de São Paulo

J Clin Oncol 36, 2018 (suppl 6S; abstr 305)

Local ablative radiotherapy: A means to revert low volume castration-resistant prostate cancer into a hormone-sensitive status?

Tobias Hölscher [1], F. Lohaus [1], K. Zöphel [2], M. Wirth [3], M. Baumann [1, 4, 5], E.G.C. Troost [1, 4, 5]

Departments of [1]Radiation Oncology, [2]Nuclear Medicine and [3]Urology, University Hospital Carl Gustav Carus, [4]OncoRay – National Center for Radiation Research in Oncology, Medical Faculty Carl Gustav Carus, Technische Universität Dresden, [5]German Cancer Research Center (DKFZ), Heidelberg and Dresden, Germany

Universitätsklinikum Carl Gustav Carus DIE DRESDNER.

Background:

- N= 15 pacientes oligometastáticos por PET-PSMA
- Tratados Rt local
  - 25 x 2Gy
  - 3 x 10Gy
- Mantidos em ADT

Table 1: Patients' characteristics

		Mean (range)
Follow-up (months)		25.8 (12.2 – 39.9)
mean Age at PET (years)		71.8 (56.3 – 86.5)
Dose Schedule (n(%))	25*2 Gy	9 (60 %)
	3*10 Gy	6 (40 %)
Number of METs	n=1	9 (30%)
	n=2	4 (13.3%)
	n=3	2 (6.7%)
Location of METs	Bone	12 (40%)
	Lymph nodes	2 (6.7%)
	Bone and lymph nodes	1 (3.3.%)
Initial NCCN risk	Very high risk	8 (53.3%)
	High risk	6 (40 %)
	Intermediate risk	1 (6.7 %)
PSA at first diagnosis [median ng/ml] (range)		27 ng/ml (4.9 – 400)
PSA at PET-Staging [median ng/ml] (range)		3,4 ng/ml (1.3 – 14.5)
PSA-doubling time before PET [months] (range)		3.16 (0.6 - 8.7)
Duration of any ADT before PET [median months] (range)		38.5 (13.7 – 215.2)
Duration of maxADT before PET [median months] (range)		33.3 (3.6 – 91.3)

J Clin Oncol 36, 2018 (suppl 6S; abstr 188)

Local ablative radiotherapy: A means to revert low volume castration-resistant prostate cancer into a hormone-sensitive status?

Tobias Hölscher [1], F. Lohaus [1], K. Zöphel [2], M. Wirth [3], M. Baumann [1, 4, 5], E.G.C. Troost [1, 4, 5]

Departments of [1]Radiation Oncology, [2]Nuclear Medicine and [3]Urology, University Hospital Carl Gustav Carus, [4]OncoRay – National Center for Radiation Research in Oncology, Medical Faculty Carl Gustav Carus, Technische Universität Dresden, [5]German Cancer Research Center (DKFZ), Heidelberg and Dresden, Germany

Universitätsklinikum Carl Gustav Carus DIE DRESDNER.

Background:

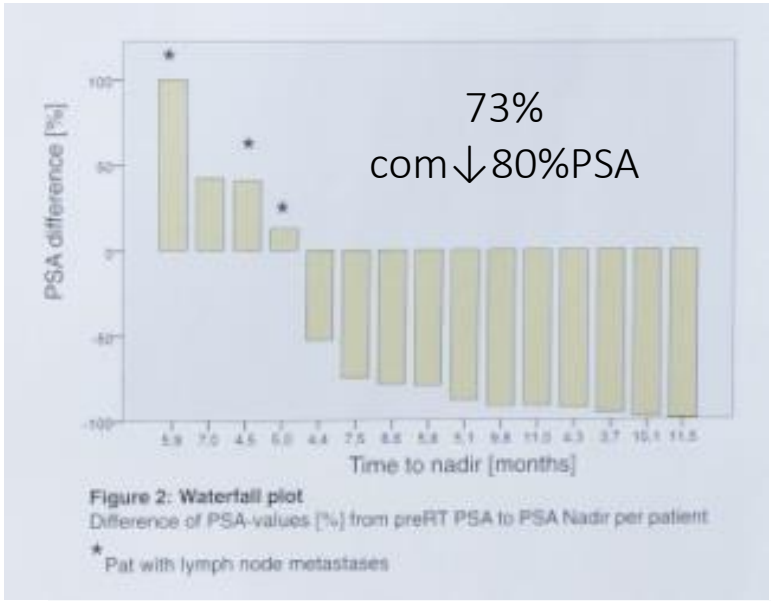

Figure 2: Waterfall plot
Difference of PSA-values [%] from preRT PSA to PSA Nadir per patient
* Pat with lymph node metastases

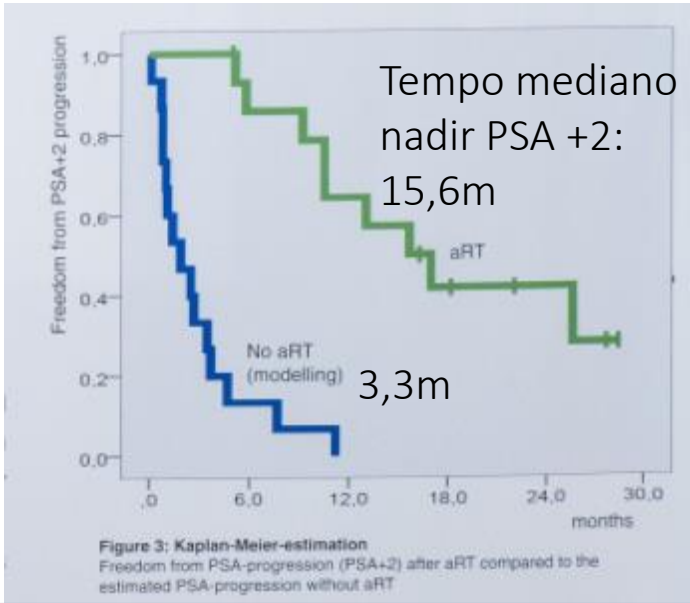

Figure 3: Kaplan-Meier-estimation
Freedom from PSA-progression (PSA+2) after aRT compared to the estimated PSA-progression without aRT

Conclusions: A relevant subset of patients with ^{68}Ga PSMA-PET-detected oligometastatic low volume CRPC had a meaningful PSA-response with aRT. They were reverted into an earlier stage of their disease again. A prospective clinical trial on this clinically highly relevant question is being prepared.

(#193) Influence of Aggressive-Variant Prostate Cancer (AVPC) Features on Outcome of Metastatic Hormone-Sensitive Prostate Cancer (mHSPC) Treated by Chemohormonal Therapy (CHT)

Kim Koczka[1], James Vanhie[2], Andrea Ibrahim[3], Nedal Bukhari[4], Neil Reaume[5], Sandeep Sehdev[5], Kylea Potvin[4], Lori Sax[4], Scott Ernst[4], Michael Vickers[5], Christina Canil[5], Eric Winquist[4], Michael Ong[5]

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- 92 pacientes
- Retrospectivo
- Ca Próstata Horm Sensível variante ANAPLÁSICA

- 90% High volume
- 95% Gleason 8-10
- 60% anaplásico

Table 1. Patient Baseline Characteristics

Characteristic	Patients (n=92)	%
Adenocarcinoma Histopathology	86	93.5%
Neuroendocrine Histopathology	2	2.2%
Gleason Score 7	4	5.5%
Gleason Score 8-10	69	94.5%
Gleason Score unknown	*19*	*20.6%*
ECOG Performance Status 0-1	76	82.6%
ECOG Performance Status 2-4	10	10.9%
ECOG Performance Status unknown	*6*	*6.5%*
Bone Pain Present	49	53.3%
Bone Metastases	83	90.2%
Lymph Node Metastases	62	67.4%
Lung Metastases	17	18.5%
Liver Metastases	7	7.6%
Other Visceral Metastases	3	3.3%

Table 2. AVPC Characteristics

AVPC Characteristic	Yes, n (%)	No, n (%)	Unavailable, n (%)
Lytic Bone Metastases	16 (17.4)	72 (78.3)	4 (4.3)
Bulky Lymph Nodes	28 (30.4)	64 (69.6)	0 (0.0)
Visceral Metastasis	21 (22.8)	71 (77.2)	0 (0.0)
Low PSA	4 (4.3)	88 (95.7)	0 (0.0)
Neuroendocrine	2 (2.2)	86 (93.5)	4 (4.3)
LDH High	*12 (13.0)*	*18 (19.6)*	*62 (67.4)*
ALP High	*40 (43.5)*	*23 (25.0)*	*29 (31.5)*
Hemoglobin Low	*29 (31.5)*	*44 (47.8)*	*19 (20.7)*
Albumin Low	*9 (9.8)*	*37 (40.2)*	*46 (50.0)*
Calcium High	*7 (7.6)*	*45 (48.9)*	*40 (43.5)*
AVPC Confirmed Score*	**47 (51.1)**	**37 (40.2)**	**8 (8.7)**
AVPC Any Score**	**55 (59.8)**	**37 (40.2)**	**Not applicable**

* Only based on first 5 characteristics (low amount of missing data, non-italicized);
** exploratory, using 'any' AVPC positive feature amongst italicized characteristics

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Table 3. %PSA Decline from ADT to Docetaxel Initiation

PSA Decline	< 50% of Baseline	50-75% of Baseline	75-90% of Baseline	>90% of Baseline
# Patients (%)	12 (13.0)	9 (9.8)	16 (17.4)	53 (58.9)
Mean Time from ADT to Docetaxel (95% CI)	40.0 days (27.3-95.4)	47.0 days (32.4-82.7)	51.5 days (41.5-93.3)	80.5 days (74.8-98.6)
Median time to CRPC (months)	9.1	10.4	16.0	16.5

Table 4. PSA Level at 6-7 Months Post-ADT

PSA Level Post 6-7 Months Docetaxel	Patients (n)	Patients (%)
PSA < 0.2 ng/ml	19	20.7%
PSA 0.2-4 ng/ml	22	22.61%
PSA > 4 ng/ml	25	27.2%

-23% progrediram para resistente à castração em < 12 meses
-Nadir de PSA em 6m bem distribuído

Table 7. Multivariable Survival Model Cox Regression Analysis

Characteristic	Hazard Ratio	p-value
AVPC** Score	15.459	0.008
PSA Fall <75% from ADT to Docetaxel	4.312	0.003

Análise multivariada para sobrevida global

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Tempo para resistência à castração

Sobrevida global

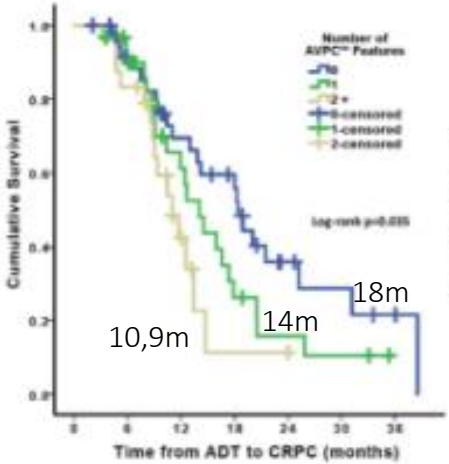

Figure 1. Number of AVPC Features and Time to CRPC**

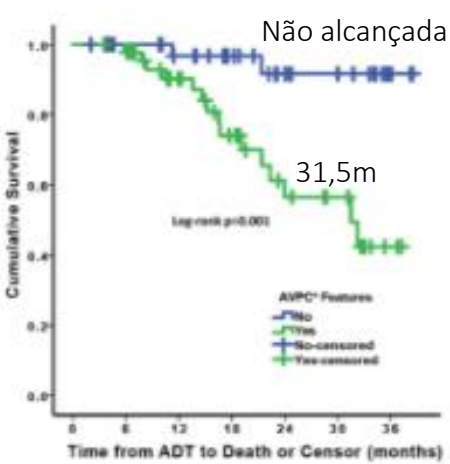

Figure 2. Presence of AVPC* Features and Overall Survival

- Median time to CRPC was 18.4, 14.0, and 10.9 mo for 0, 1, or 2+ AVPC features respectively (log-rank p=0.035) (**Figure 1**).
- Median survival time was 31.5 mo for pts with AVPC features and was not reached for pts without (log-rank p=0.001) (**Figure 2**).

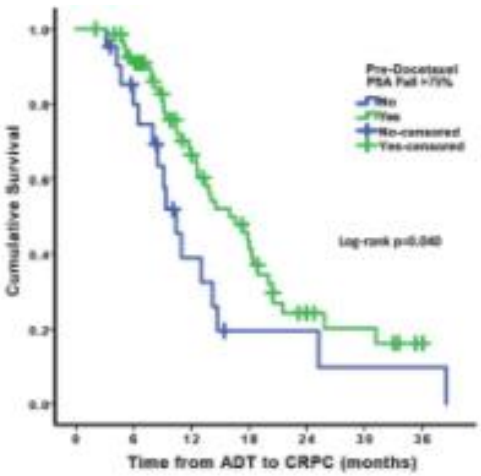

Figure 3. Pre-Docetaxel PSA Fall >75% and Time to CRPC

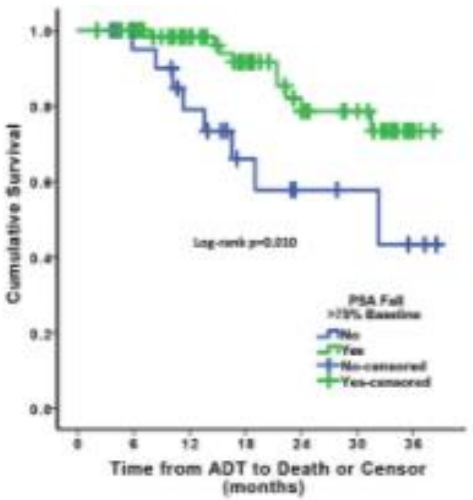

Figure 4. Pre-Docetaxel PSA Fall >75% and Overall Survival

A queda de PSA > 75% foi preditora de maior tempo para se tornar CRPC e de SG

Obrigado!

A Beneficência Portuguesa de São Paulo

fabiorkater@gmail.com