
GU
connect®
POWERED BY COR2ED

mCSPC – OPTIMISING PATIENT SELECTION AND TREATMENT

Dr. Fabio Schutz, MD
Medical Oncologist
A Beneficência Portuguesa de São Paulo,
São Paulo, Brazil

JUNE 2021

mCSPC, metastatic castration-sensitive prostate cancer

DISCLAIMER AND DISCLOSURES

Please note: The views expressed within this presentation are the personal opinions of the author. They do not necessarily represent the views of the author's academic institution or the rest of the GU CONNECT group.

This content is supported by an Independent Educational Grant from Bayer.

Dr. Fabio Schutz has received financial support/sponsorship for research support, consultation, or speaker fees from the following companies:

- Astellas, AstraZeneca, Bayer, BMS, Janssen, MSD, Roche

INTRODUCTION

- Androgen deprivation therapy (ADT) has been the backbone of treatment for metastatic castration-sensitive prostate cancer (mCSPC) for many years, but this approach has limitations when used as monotherapy
- The addition of docetaxel or an androgen axis-targeting agent to ADT has demonstrated improved outcomes, and represents the new standard of care for patients with mCSPC
- Multiple treatment options are now available for mCSPC
  - Treatment decisions require consideration of all available options, including androgen receptor (AR)-directed therapies and chemotherapy
  - Clinical considerations and patient preferences should be taken into account to match the right treatment with an individual patient

Hahn A, et al. Am Soc Clin Oncol Educ Book. 2018;38:363-71

mCSPC – DOCETAXEL TRIALS

Trial	Comparator	Phase; size	Primary endpoint	Results (docetaxel vs comparator)	Febrile neutropenia	Steroids?
GETUG-15 2013[1]	ADT	3; 385	OS	mOS 58.9 vs 54.2 months HR 1.01, NS	8% (↓ with G-CSF)	Corticosteroids for 3 days
CHAARTED 2015[2]	ADT	3; 790	OS	mOS 57.6 vs 44.0 months HR 0.61, p<0.001	6.2%	Dexamethasone 3 doses
STAMPEDE 2016[3]	ADT (+ zoledronate)	3; 1,776 (2 arms)	OS	mOS 81 vs 71 months HR 0.78, p=0.006	15%	Prednisolone 10 mg/day + premedication

ADT, androgen deprivation therapy; G-CSF, granulocyte colony-stimulating factor; HR, hazard ratio; mCSPC, metastatic castration-sensitive prostate cancer; (m)OS, (median) overall survival; NS, non-significant

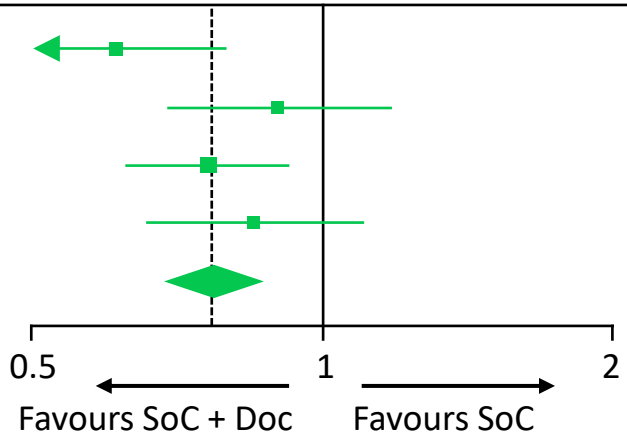
1. Gravis G, et al. Lancet Oncol. 2013;14:149-58; 2. Sweeney C, et al. N Engl J Med. 2015;373:737-46; 3. James N, et al. Lancet. 2016;387:1163-77

mCSPC – DOCETAXEL TRIALS META-ANALYSIS

OS

	Control	Treatment	HR (95% CI)
CHAARTED	136/393	101/397	0.61 (0.47-0.80)
GETUG-15	NA/193	NA/192	0.90 (0.69-1.81)
STAMPEDE (SoC ± Doc)	350/724	144/362	0.76 (0.62-0.93)
STAMPEDE (SoC + ZA ± Doc)	170/366	158/365	0.85 (0.65-1.10)
Overall			**0.77 (0.68-0.87)**

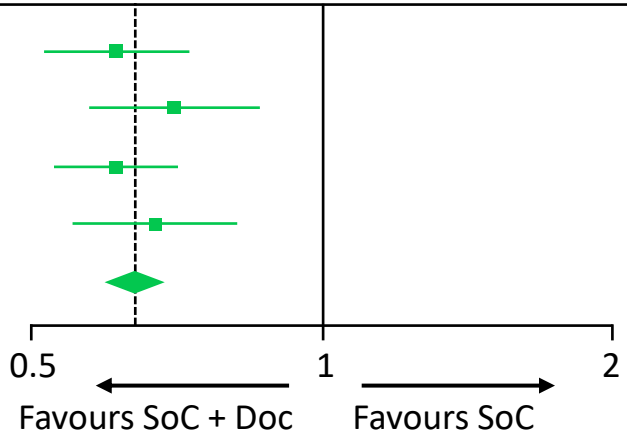
Heterogeneity: χ^2=4.80; df=3; p=0.187; I^2=37.5%



FFS

	Control	Treatment	HR (95% CI)
CHAARTED	NA/393	NA/397	0.61 (0.51-0.73)
GETUG-15	158/193	143/192	0.70 (0.57-0.86)
STAMPEDE (SoC ± Doc)	585/724	252/362	0.61 (0.53-0.71)
STAMPEDE (SoC + ZA ± Doc)	286/366	255/365	0.67 (0.55-0.82)
Overall			**0.64 (0.58-0.70)**

Heterogeneity: χ^2=1.66; df=3; p=0.646; I^2=0%



CI, confidence interval; Doc, docetaxel; FFS, failure-free survival; HR, hazard ratio; mCSPC, metastatic castration-sensitive prostate cancer; OS, overall survival; SoC, standard of care; ZA, zoledronate

Vale CL, et al. Lancet Oncol. 2016;17:243-56

LIMITED REAL-WORLD USE OF DOCETAXEL

- According to data from Optum (2007-2018) and SEER Medicare (2007-2016) databases, only 3.8% of patients with mCSPC received docetaxel + ADT ± bicalutamide since 2014
- Majority of patients receive less than the recommended dose of 6 cycles

Baseline characteristics of docetaxel-treated patients with mCSPC

Characteristic	N	Mean (SD)	Median (IQR)
Age at mCSPC, years	192	68.5 (8.8)	69 (64-75)
Baseline PSA, ng/mL	73	431.2 (882.4)	93.1 (10.9-449.3)
Docetaxel treatment duration, days	192	115 (84.2)	118 (55-149)
Characteristic	**N**	**n (%)**	
De novo	192	168 (87.5)	
Prior RP/RT	192	11 (6)	
Visceral metastasis at mCSPC	192	34 (18)	

ADT, androgen deprivation therapy; IQR, interquartile range; mCSPC, metastatic castration-sensitive prostate cancer; PSA, prostate-specific antigen; RP, radical prostatectomy; RT, radiotherapy; SD, standard deviation; SEER, Surveillance, Epidemiology, and End Results

Agarwal N, et al. J Clin Oncol. 2020;38 suppl 15:e19322

mCSPC – NEW HORMONAL AGENTS

Treatment	Trial publication year	Population	Comparator	Phase; study size	Primary endpoint	Treatment vs control	Serious adverse events
Abiraterone acetate with prednisone	LATITUDE 2017	mCSPC	ADT + placebo	3; 1,199	OS	53.3 vs 36.5 months (HR: 0.66 [95% CI: 0.56-0.78], p<0.0001)	Elevated AST Elevated ALT Hypokalaemia Hypertension Cardiac disorder
	STAMPEDE 2017	mCSPC and locally advanced prostate cancer	ADT alone	3; 1,917	OS	Estimated 83% vs 73% alive at 3 years (HR: 0.63 [95% CI: 0.52-0.76], p<0.001)	
Enzalutamide	ENZAMET 2019	mCSPC	ADT + non-steroidal AR-directed therapy	3; 1,125	OS	Estimated 80% vs 72% alive at 3 years (HR: 0.67 [95% CI: 0.52-0.86], p=0.002)	Fatigue Falls Seizures Ischaemic heart disease
	ARCHES 2019	mCSPC-stratified by CHAARTED criteria	ADT + placebo	3; 1,150	rPFS or death	NR vs 19 months (HR: 0.39 [95% CI: 0.3-0.5], p<0.001)	
Apalutamide	TITAN 2019	mCSPC	ADT + placebo	3; 1,052	rPFS or death	68.2% vs 47.5% at 24 months (HR: 0.48 [95% CI: 0.39-0.60], p<0.001)	Rash Fractures Hypothyroidism Seizure
					OS	82.4% vs 73.5% alive at 24 months (HR: 0.67 [95% CI: 0.51-0.89], p=0.005)	

ADT, androgen deprivation therapy; ALT, alanine aminotransferase; ART, androgen receptor; AST, aspartate aminotransferase; CI, confidence interval; HR, hazard ratio; mCSPC, metastatic castration-sensitive prostate cancer; NR, not reached; OS, overall survival; rPFS, radiographic progression-free survival

Schulte B, et al. Am Soc Clin Oncol Educ Book. 2020;40:198-207

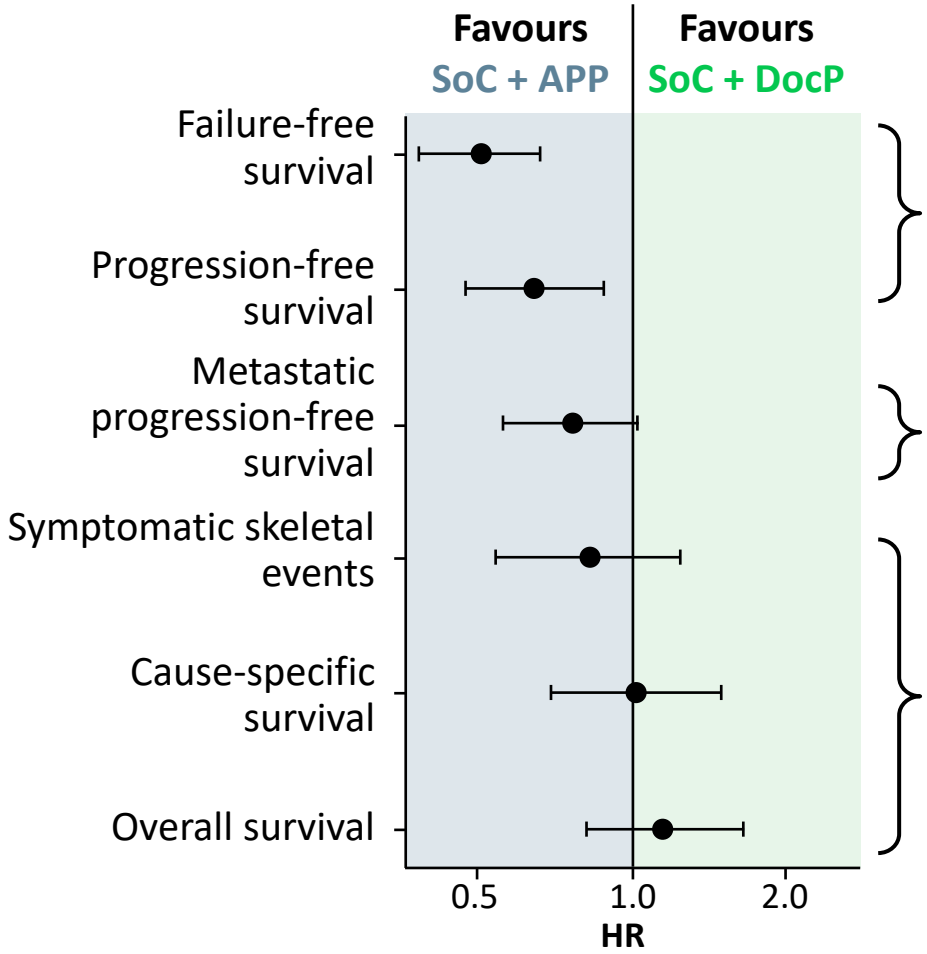
mCSPC – ENZALUTAMIDE/APALUTAMIDE TRIALS DESIGN AND POPULATION

		ARCHES[1] (double-blind)	ENZAMET[2] (open-label)	TITAN[3] (double-blind)
Treatment		**Enzalutamide + ADT (N=574) vs placebo + ADT (N=576)**	**Enzalutamide + ADT (N=563) vs NSAA + ADT (N=562)**	**Apalutamide + ADT (N=525) vs placebo + ADT (N=527)**
Key inclusion criteria	**Metastasis**	Bone or soft tissue	Bone or soft tissue	≥1 bone lesion, patients EXCLUDED if visceral metastases only
	Prior ADT	Allowed	Allowed	Allowed
	Prior docetaxel	Allowed (18%)	Not allowed	Allowed (11%)
	Early concomitant docetaxel	Not allowed	Allowed (45%)	Not allowed
Average duration of therapy		14 months	34 months	23 months

ADT, androgen deprivation therapy; mCSPC, metastatic castration-sensitive prostate cancer; NSAA, non-steroidal anti-androgen

1. Armstrong AJ, et al. J Clin Oncol. 2019;37:2974-86; 2. Davis ID, et al. N Engl J Med. 2019;381:121-31; 3. Chi K, et al. N Engl J Med. 2019;381:13-24

STAMPEDE TRIAL
ABIRATERONE ACETATE VS DOCETAXEL



Summary

Head-to-head data in 566 patients (Nov. 2011 to Mar. 2013)

Strong evidence favouring AAP

Weak evidence favouring AAP

No good evidence of a difference

→ Proportionately different time spent in each disease state

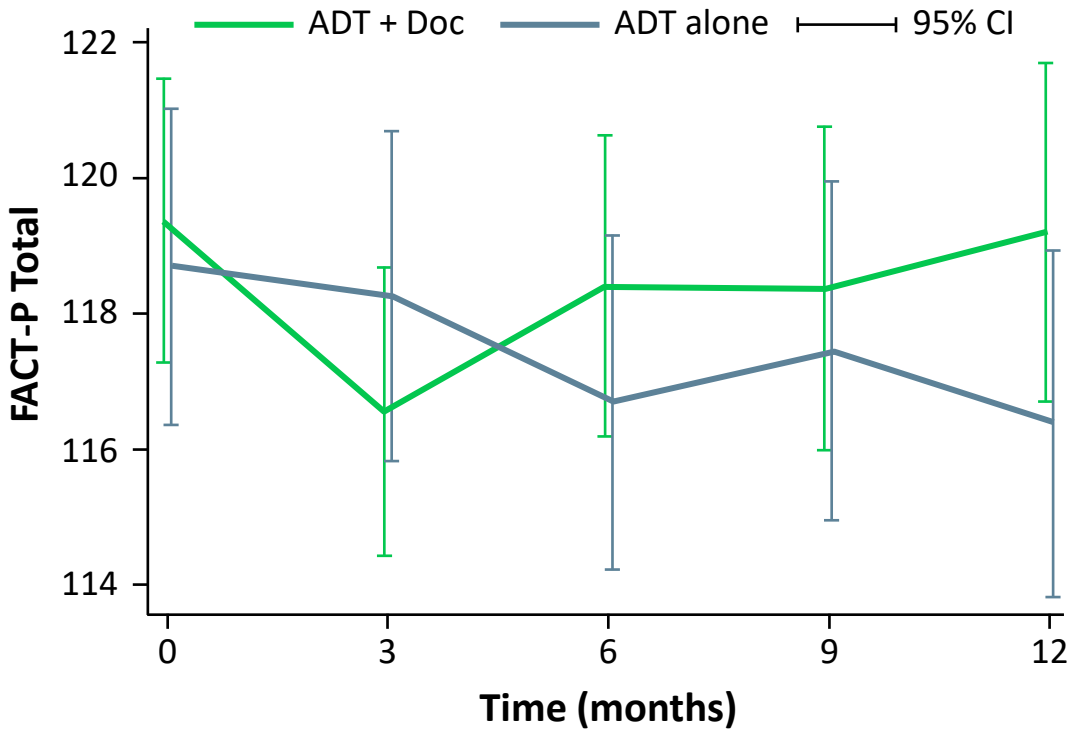
Toxicity profiles quite different and well known

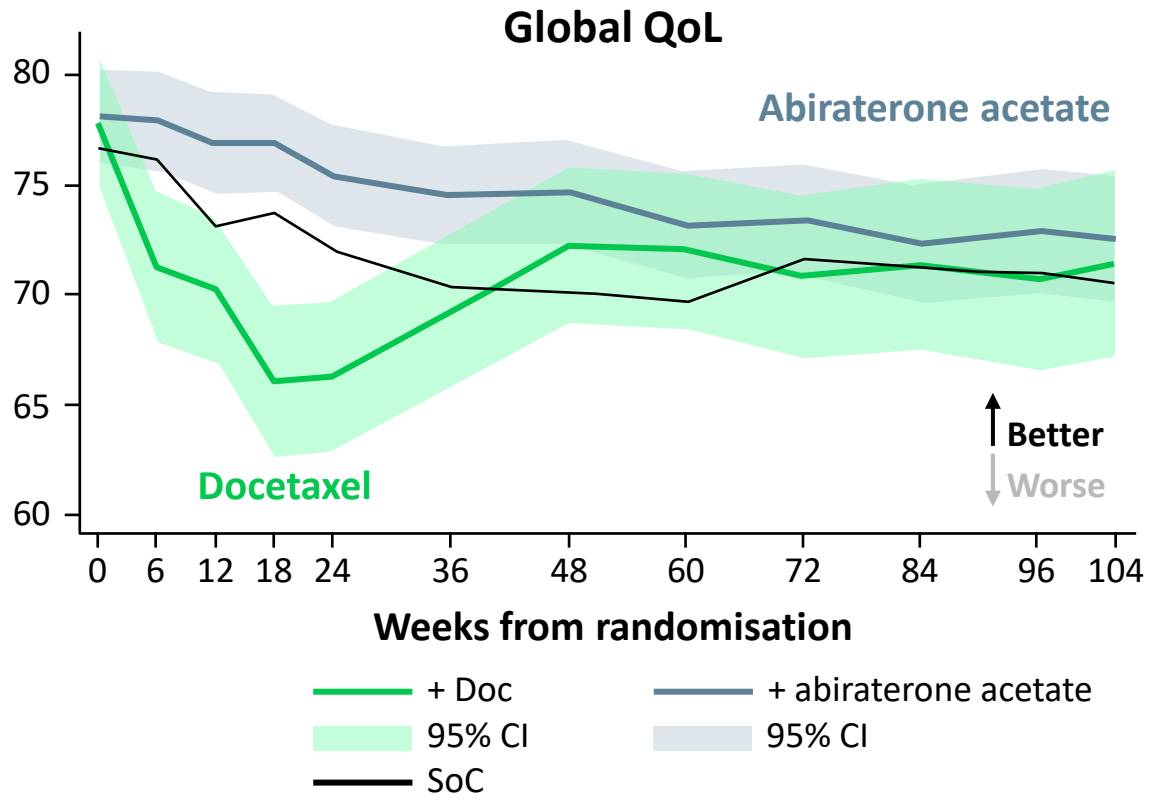
AAP, abiraterone acetate with prednisolone; DocP, docetaxel with prednisolone; HR, hazard ratio; SoC, standard of care

Adapted from Sydes M, et al. Ann Oncol. 2018;29:1235-48

mCSPC – DOCETAXEL VS ABIRATERONE ACETATE (QoL)

- Docetaxel usually associated with more “acute” adverse events and worse QoL in both CHAARTED (vs ADT alone) and STAMPEDE (vs abiraterone acetate)



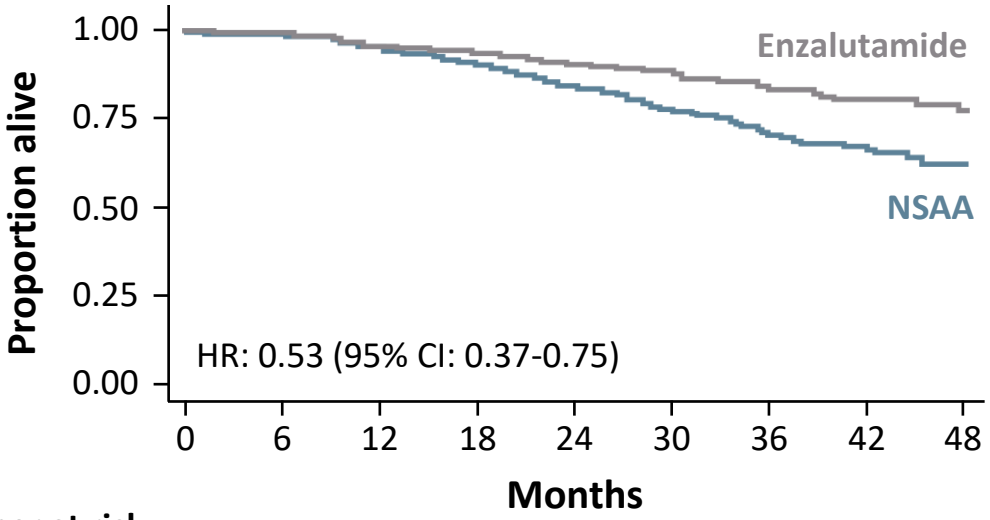


ADT, androgen deprivation therapy; CI, confidence interval; Doc , docetaxel; FACT-P, Functional Assessment of Cancer Therapy-Prostate; mCSPC, metastatic castration-sensitive prostate cancer; QoL, quality of life; SoC, standard of care

Adapted from Morgans A, et al. J Clin Oncol. 2018;36:1088-95; Rush H, et al. J Clin Oncol. 2020;38 suppl 6:14 (oral presentation)

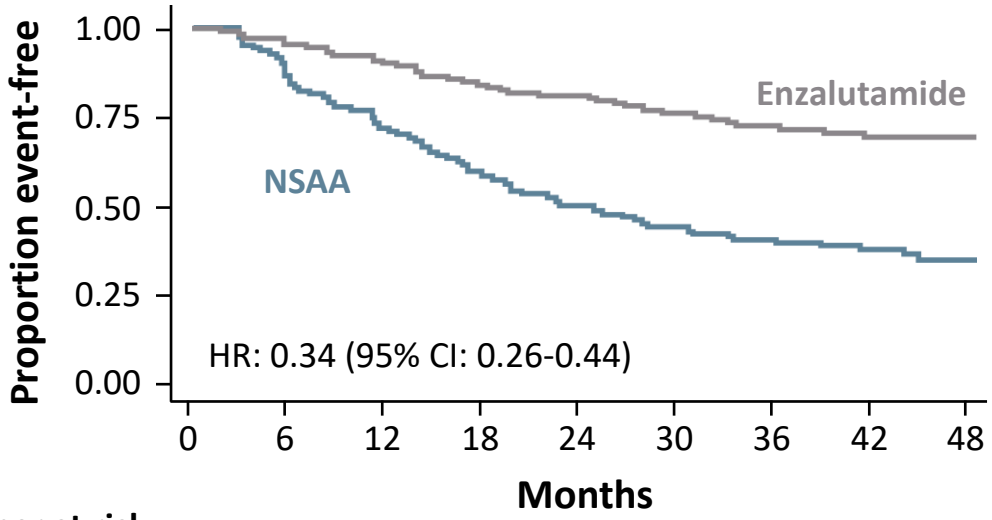
mCSPC – ENZAMET: NO CONCURRENT DOCETAXEL

Overall survival



Number at risk									
NSAA	313	310	296	281	249	176	118	73	30
Enzalutamide	309	306	295	289	270	201	135	87	42

PSA PFS



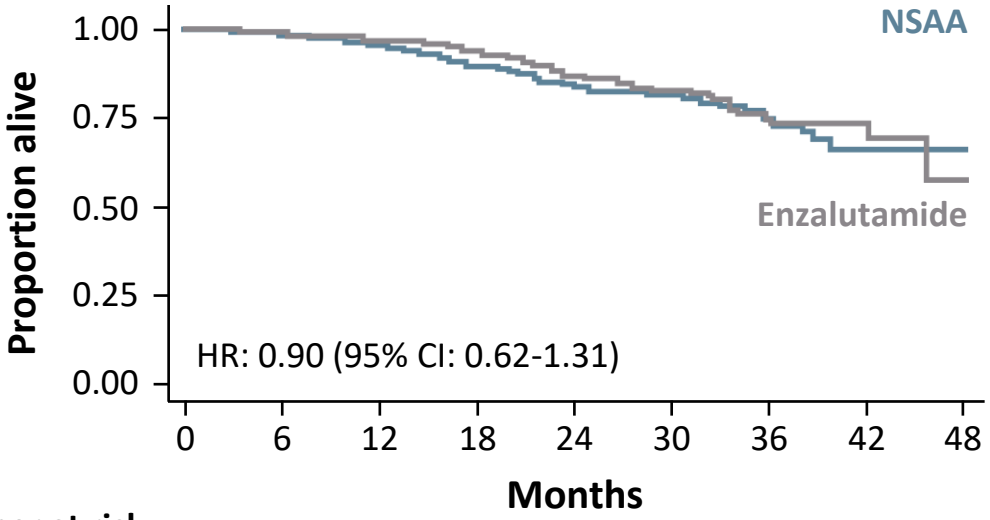
Number at risk									
NSAA	313	263	222	180	144	94	61	40	16
Enzalutamide	309	295	277	257	240	168	115	67	32

CI, confidence interval; HR, hazard ratio; mCSPC, metastatic castration-sensitive prostate cancer; NSAA, non-steroidal anti-androgen; PFS, progression-free survival; PSA, prostate-specific antigen

Sweeney C, et al. ASCO 2019, LBA2 (oral presentation)

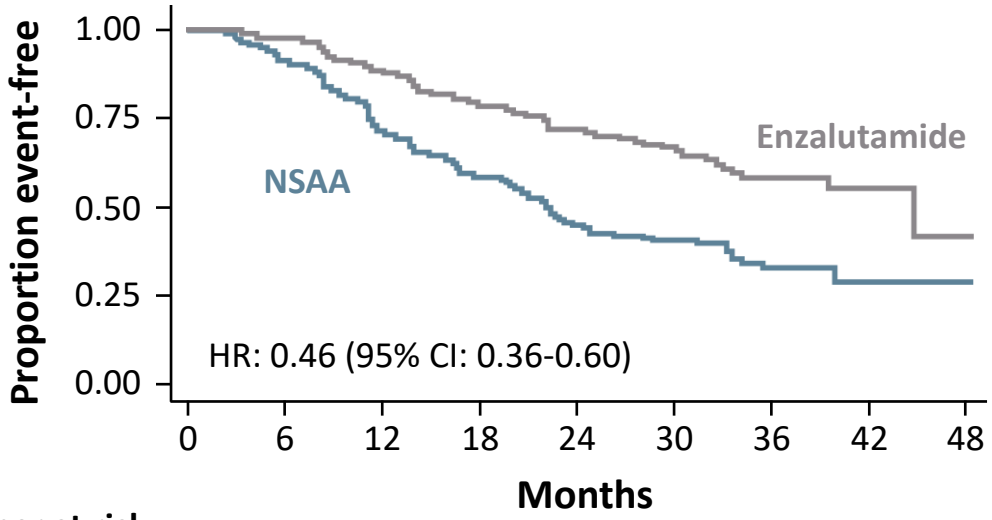
mCSPC – ENZAMET: CONCURRENT DOCETAXEL

Overall survival



Number at risk									
NSAA	249	241	235	220	203	135	56	13	2
Enzalutamide	254	252	246	238	210	139	54	19	3

PSA PFS



Number at risk									
NSAA	249	223	173	142	105	67	17	4	1
Enzalutamide	254	248	223	198	171	101	31	10	2

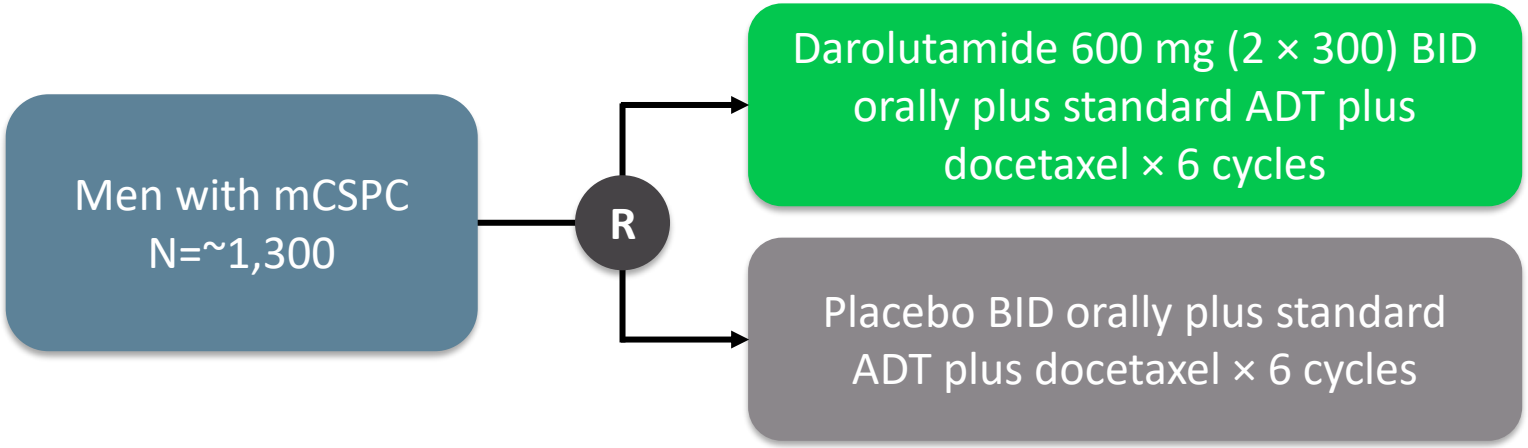
CI, confidence interval; HR, hazard ratio; mCSPC, metastatic castration-sensitive prostate cancer; NSAA, non-steroidal anti-androgen; PFS, progression-free survival; PSA, prostate-specific antigen

Sweeney C, et al. ASCO 2019, LBA2 (oral presentation)

mCSPC – ARASENS: CONCURRENT DOCETAXEL

ARASENS: RANDOMISED, DOUBLE-BLIND, PHASE 3 TRIAL OF DAROLUTAMIDE IN mCSPC[a]

- Study initiated: November 2016
- Primary endpoint: overall survival
- Approach: combining chemotherapy and AR-directed therapy



[a] ClinicalTrials.gov. NCT02799602

ADT, androgen deprivation therapy; AR, androgen receptor; BID, twice a day; mCSPC, metastatic castration-sensitive prostate cancer

mCSPC – CONCLUSIONS

- AR-directed therapies (i.e. abiraterone acetate, enzalutamide, and apalutamide) should (usually) be the preferred option in mCSPC:
  - Docetaxel is less effective than abiraterone acetate (at least in short-term endpoints)
  - Some patients with recurrent mCSPC (post RP or RT) may not need AR-directed therapies
  - Consider different adverse-events profiles, experience, and access to AR-directed therapies
- Docetaxel should (usually) be reserved for the following situations:
  - Patients with high-volume disease
  - Patients with *de novo* metastatic disease
  - Where there is no access to AR-directed therapies
  - Where docetaxel offers a cost-effective upfront strategy

mCSPC, metastatic castration-sensitive prostate cancer; RP, radical prostatectomy; RT, radiotherapy

REACH GU CONNECT VIA TWITTER, LINKEDIN, VIMEO & EMAIL OR VISIT THE GROUP'S WEBSITE

http://www.guconnect.info

Follow us on Twitter
@guconnectinfo

Follow the
GU CONNECT
group on LinkedIn

Watch us on the
Vimeo Channel
GU CONNECT

Email
sam.brightwell@cor2ed.com

GU connect®
POWERED BY COR2ED

GU CONNECT
Bodenackerstrasse 17
4103 Bottmingen
SWITZERLAND

Dr. Froukje Sosef MD

+31 6 2324 3636

froukje.sosef@cor2ed.com

Dr. Antoine Lacombe Pharm D, MBA

+41 79 529 42 79

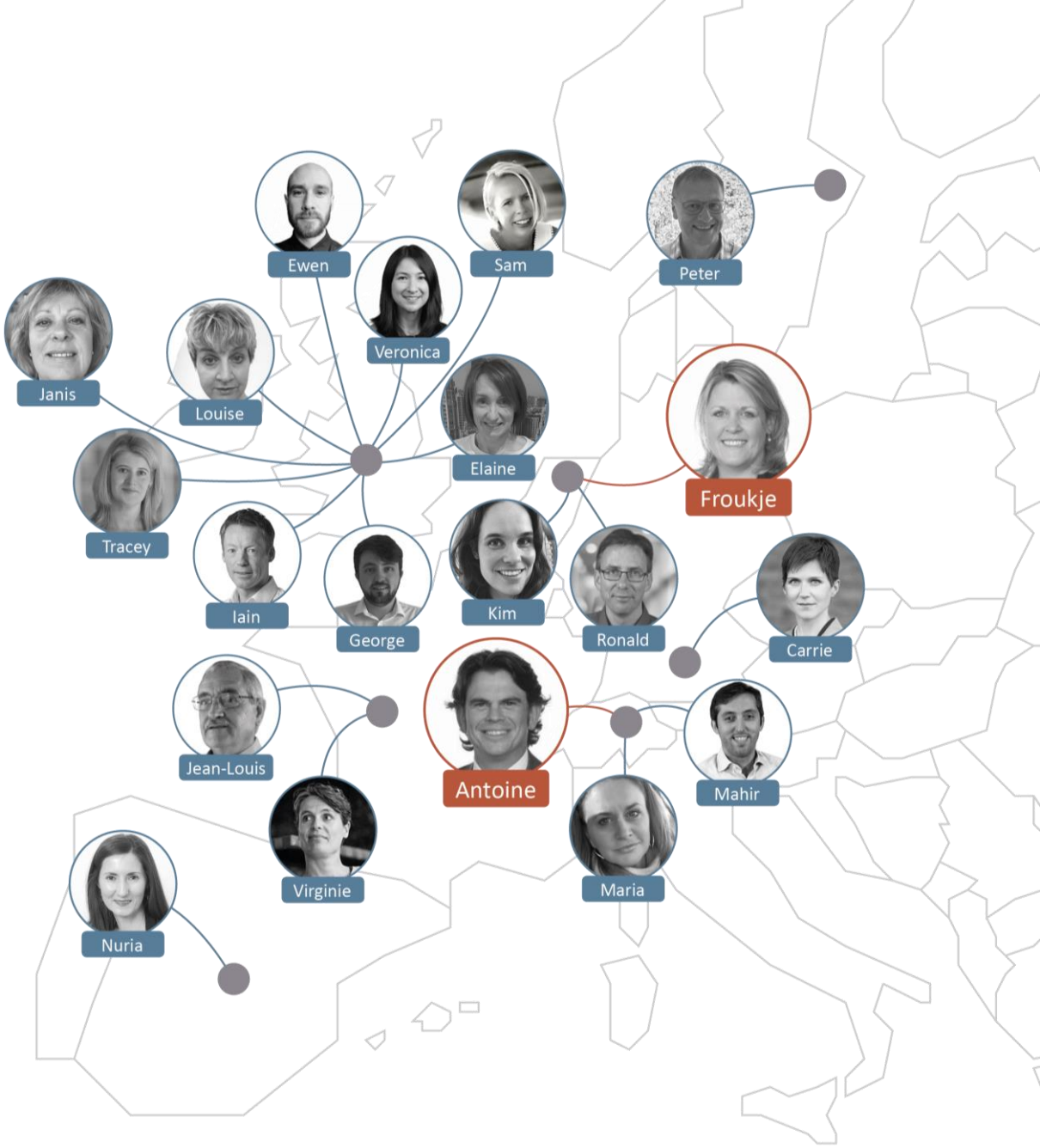
antoine.lacombe@cor2ed.com

Connect on
LinkedIn @GU CONNECT

Watch on
Vimeo @GU CONNECT

Visit us at
guconnect.info

Follow us on
Twitter @guconnectinfo



Heading to the heart of Independent Medical Education Since 2012