SHARE

COMMUNICATION FRAMEWORK

SUPPORTING PHYSICIANS IN SHARED DECISION-MAKING WITH PATIENTS TREATED FOR METASTATIC CASTRATION RESISTANT PROSTATE CANCER (mCRPC)

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INTRODUCTION

- Hello and welcome on behalf of GU CONNECT
- My name is Tanya Dorff and together with Alicia Morgans from the USA and David Pfister from Germany we will now take you through how the SHARE approach, developed by the CONNECTS, can be successfully applied in the area of GU Oncology
- SHARE is a communication framework to help you have even better conversations with your patients, engaging them in the shared decision-making process with the ultimate aim of having a positive impact on treatment outcomes
- SHARE aims to improve the quality of interactions between physicians and patients with metastatic castration resistant prostate cancer (mCRPC), but the principles can be more widely applied to other treatment areas too

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GU, genitourinary; mCRPC, metastatic castration resistant prostate cancer; USA, United States of America.

INTRODUCING THE SCIENTIFIC COMMITTEE

TANYA DORFF, Associate Professor
City of Hope Comprehensive Cancer Center, USA

- Head of GU group within the Department of Medical Oncology at the City of Hope Comprehensive Cancer Center
- Authored more than 45 peer-reviewed articles and 35 review articles/ commentaries
- Associate editor for Clinical Genitourinary Cancer and Seminars in Urologic Oncology
- Lectured on prostate and bladder cancer treatment nationally and internationally, and presented research at national meetings
- Principal investigator for more than a dozen clinical trials, involving targeted therapy and immunotherapy, for genitourinary cancers

ALICIA MORGANS, Associate Professor
Robert H. Lurie Cancer Center, North Western University, USA

- GU medical oncologist and outcomes researcher in the Division of Hematology/ Oncology at Northwestern University's Robert H. Lurie Cancer Center
- Completed medical school and residency at the University of Pennsylvania School of Medicine. Fellowship in Hematology/ Oncology from Dana Farber Cancer Institute and Massachusetts General Hospital Cancer Center in Boston; Master of Public Health from Vanderbilt University
- Multiple federal and foundation grants to study treatment decision-making and QoL outcomes in advanced prostate cancer

DAVID PFISTER, Professor and Deputy Director of Department of Urology, University Hospital of Cologne, Germany

- Associate Professor for medical oncologic treatment in urological tumours
- Completed medical residencies in the urological department of the University of Cologne, Weiden Oberpfalz and University of Aachen, Germany
- Commissionary Leader of the Urologic Department of the University of Aachen
- Deputy Director of the Department of Urology, Uro-oncology and Robot Assisted Surgery, University Hospital of Cologne

GU, genitourinary; QoL, quality of life; USA, United States of America.

WHAT WILL YOU LEARN?

1. **Know** the different treatment options and associated clinical data suitable for patients with mCRPC

2. Be able to **explain** the advantages and disadvantages of these treatment options to a mCRPC patient in a way that aligns to the patient's goals of treatment

3. **Understand** how to apply the SHARE communication framework during interactions with mCRPC patients and how to apply the principles more broadly during interactions with patients across the disease spectrum

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mCRPC, metastatic castration resistant prostate cancer

CONTENTS

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INTRODUCING SHARE

- This programme aims to support physicians with the quality of their interactions with mCRPC patients particularly at difficult points during the treatment journey, such as disease progression
- SHARE's five letters each represent a crucial communication point in your conversations with patients
  - **S**: Success criteria and aim of treatment
  - **H**: How the treatments work
  - **A**: Advantages and disadvantages of each treatment option
  - **R**: Risks and effective management of side effects
  - **E**: Expectation for treatment success
- In each step, we will address:
  - What you need to **know**
  - What you should **explain** to the patient
  - How you should **interact** with the patient
  - We will also suggest what to avoid in patient conversations

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mCRPC, metastatic castration resistant prostate cancer

WHAT IS THE SHARE COMMUNICATION FRAMEWORK?

SHARE is a 5-step communication framework to enable shared decision-making in physician–patient interactions, that recommends the following communication points:

Success criteria and aim of treatment **S**

How the treatments work **H**

Advantages and disadvantages of each treatment option **A**

Risks and effective management of side effects **R**

Expectation for treatment success **E**

In each step, we will address:

- What you need to **know**
- What you should **explain** to the patient
- How you should **interact** with the patient

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THE **SHARE COMMUNICATION FRAMEWORK** FOR SHARED DECISION-MAKING WITH PATIENTS TREATED FOR METASTATIC CASTRATION RESISTANT PROSTATE CANCER (mCRPC)

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PRINCIPLES AND INTRODUCTION

In this section and before you progress into the 5-Steps of the **SHARE communication framework** we will briefly introduce you to:

- The 4 recognised types of typical physician–patient interaction[1]
- An overview of the **SHARE communication framework**
- The approach taken in this educational programme to help bring shared decision-making to life through the use of a case study and video role play

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1. van Laarhoven HW, et al. Oncologist. 2014;19:433-6.

THE SHARE COMMUNICATION FRAMEWORK

WHY IS A COMMUNICATION FRAMEWORK NEEDED?

The physician–patient relationship is important as evidence suggests:

- Patients prefer:[1]
  - Individualised and realistic discussions
  - Being given information about prognosis
  - A chance to ask questions
  - A check of their understanding
- Patients and their families derive more hope from physician communications when detailed prognostic information is given[2]
- Positive physician–patient discussions are associated with improved perceptions of the patients' relationship with their physician[3]

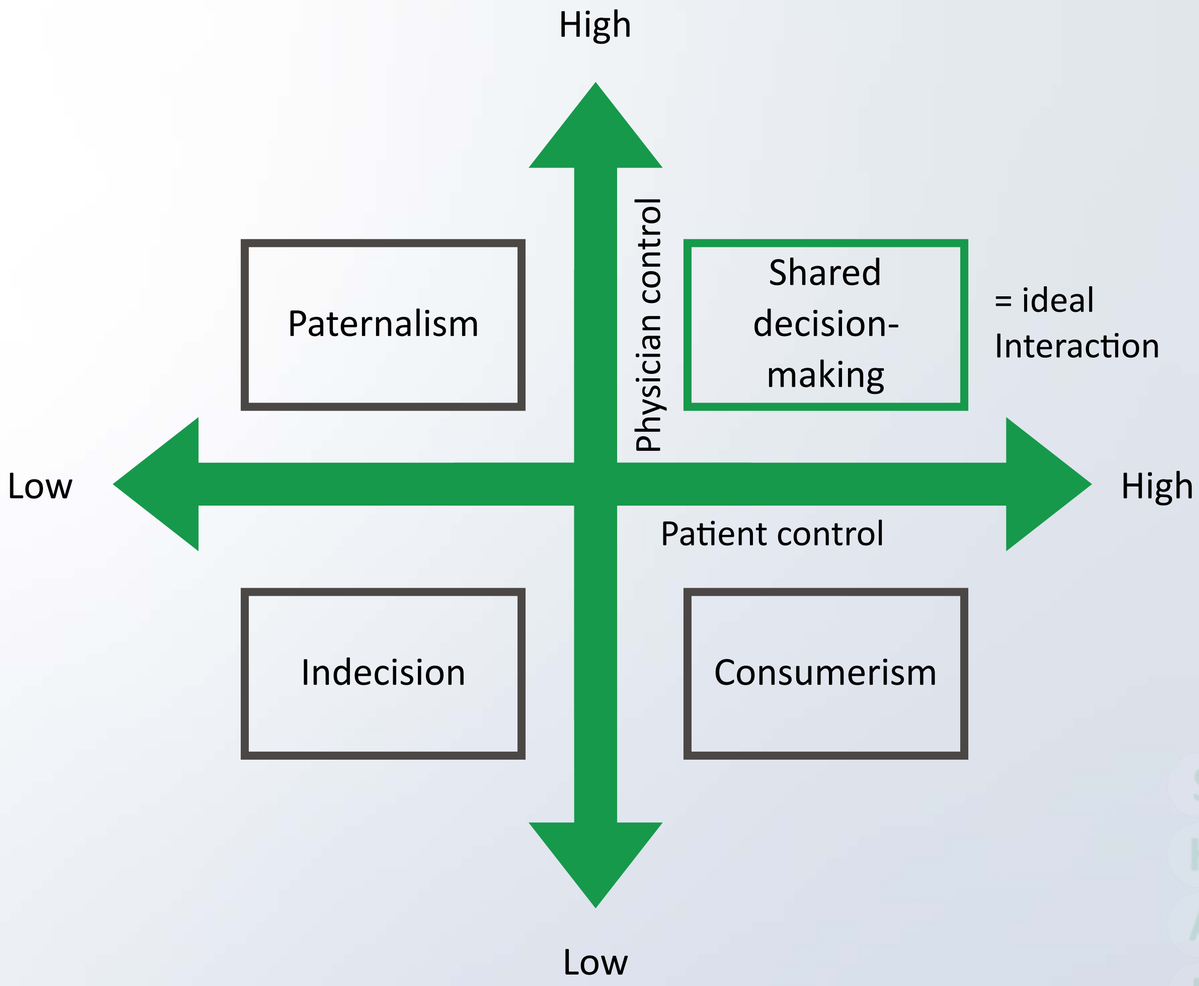
S H A R E

1. Hagerty RG, et al. J Clin Oncol. 2005;23:1278-88; 2. Mack JW, et al. J Clin Oncol. 2007;25:5636-42; 3. Fenton JJ, et al. J Clin Oncol. 2018;36:225-30.

THE FOUR TYPES OF
PHYSICIAN-PATIENT INTERACTION

Shared decision-making as best practice

- Decisions are shared jointly
- Patients understand that there may be multiple options, one of which may be preferred for the individual
- Physicians provide appropriate guidance based on their expertise
- Patient's values and preferences are accounted for



Control And Decision-Making In Physician–Patient Interactions

Used with permission from: van Laarhoven HW, et al. Oncologist. 2014;19:433-6

WHAT IS THE SHARE COMMUNICATION FRAMEWORK?

SHARE is a 5-step communication framework to enable shared decision-making in physician–patient interactions, that recommends the following communication points:

Success criteria and aim of treatment **S**

How the treatments work **H**

Advantages and disadvantages of each treatment option **A**

Risks and effective management of side effects **R**

Expectation for treatment success **E**

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PRINCIPLES AND USE OF THE
SHARE COMMUNICATION FRAMEWORK

HOW COULD YOU USE **SHARE?**

- Include each step into your conversation with a patient with mCRPC
- Consider the need to incorporate the communication framework over a series of patient conversations
- Apply principles to communication with family or caregivers
- Encourage your team to complete this training and follow the steps consistently

PRINCIPLES OF **SHARE**

- Reflects the increasing autonomy of patients and their desire to be more involved in their health and medical decision-making
- Ultimate goal is to improve outcomes through enhanced patient engagement, understanding and outlook
- The communication framework may be delivered over a number of interactions and should always be applied as a guide and adapted depending on patient needs
- The role of the caregiver in the discussion must also be considered so they feel engaged appropriately

CONSIDERATIONS FOR CAREGIVERS

- Recognise that in some interactions the caregiver may be very active in researching, learning and challenging decision-making on behalf of the patient
- Provide the caregiver with reassurance that decisions are shared between the patient and physician
- Where possible, avoid allowing the caregiver to undertake decision-making on behalf of the patient
- Respect the patient’s wishes regarding how much information is shared with the caregiver

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mCRPC, metastatic castration resistant prostate cancer

SUMMARY OF
THE SHARE COMMUNICATION FRAMEWORK

WHY IS A COMMUNICATION FRAMEWORK NEEDED?

- Shared decision-making is regarded as the best practice model for a physician–patient interaction
- Delivering the right messages to the patient at the right time can make the patient involved in their treatment decisions, facilitate honest and positive conversations, and engage the patient in order to provide a better chance of success

THE SHARE COMMUNICATION FRAMEWORK

- A 5-step communication framework to encourage shared decision-making in physician–patient interactions
- Includes a memory aid – SHARE
- Reflects patient autonomy and involvement in medical decision-making, with the ultimate goal of improving outcomes
- May be delivered over a number of interactions and should always be applied as a guide and adapted depending on patient needs

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INTRODUCING
PETER HUGHES

Peter will be used as a fictional case study throughout this educational programme

68 years old

Disease history and previous treatment:

- Patient previously underwent a radical prostatectomy and adjuvant radiotherapy
- Patient previously received Androgen Deprivation Therapy (ADT) leuprolide plus abiraterone
  - PSA was initially undetectable on this treatment approx. 0.5 ng/mL
- After 2 years treatment the PSA has started to rise to 20 ng/mL
- He now has progression of disease and two new metastases in his bones, one of which in the right hip which is becoming painful
- Peter now has newly diagnosed progressive disease (mCRPC), Gleason score 8, ECOG 1/KPS 70

Treatment aims

- Peter's daughter is getting married in 3 months and he wants to be able to walk his daughter down the aisle at her wedding
- Peter is retired but still very active. He wants to continue to play golf and enjoy his walking holidays

ADT, androgen deprivation therapy; CT, computerised tomography; ECOG, eastern cooperative oncology group; KPS, Karnofsky performance status; mCRPC, metastatic castration resistant prostate cancer; PSA, prostate specific antigen.

STEP 1

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SUCCESS CRITERIA
AND AIM OF TREATMENT

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LEARNING OBJECTIVE

STEP 1: SUCCESS CRITERIA AND AIM OF TREATMENT

WHAT
WILL YOU LEARN?

The importance of understanding what success looks like from the patient's perspective, whilst also communicating what you consider to be the most appropriate aim of treatment

WHY
IS THIS IMPORTANT?

Gaining insight into the patient's goals of treatment and concerns will enable you to discuss and engage them in the most relevant treatment strategies for the patient

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WHAT THE PHYSICIAN
NEEDS TO KNOW

- Before engaging in a conversation with a patient, it is essential for the physician to know

That mCRPC is an incurable stage of prostate cancer[1,2]

The current treatment guidelines for mCRPC

The appropriate treatments for mCRPC patients

The patient's disease factors and treatment history

- It is key at this stage to **recognise the emotional impact** on a patient when they are informed their disease has progressed
    - It is crucial at this point to recognise the potentially low morale of the patient and how it may limit the amount of information they can retain as well as affect their decision-making

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mCRPC, metastatic castration resistant prostate cancer

1. Dong L et al. Asian J Urol 2019; 6: 26-41; 2. Cook L et al. https://www.gotoper.com/publications/ajho/2016/2016august/targeting-bone-metastatic-castration-resistant-prostate-cancer. Accessed 10 Dec 2019

CASTRATION RESISTANT PROSTATE CANCER (CRPC)
IS AN INCURABLE STAGE OF PROSTATE CANCER

- More than 80% of patients with mCRPC develop bone metastases that result in a significant increase in the risk of morbidity[1]
- Most patients are clinically asymptomatic[2]
  - Those with symptoms may experience acute pain due to fractures, compression of the spine and other skeletal symptoms
- Skeletal pain is generally the most common form of cancer-related pain[2]
  - It can be severe and cause invalidity and have a negative effect on Quality of Life (QoL) and mobility
- Prostate cancer deaths are typically the result of mCRPC
  - Historically the median survival for men with mCRPC has been less than two years[3]

S H A R E

CRPC, castration resistant prostate cancer; mCRPC, metastatic castration resistant prostate cancer; QoL, quality of life

1. Bubendorf L, et al. Hum Pathol. 2000;31(5):578–583; 2. Kirby M, et al. Int J Clin Pract. 2011;65:1180-92; 3. The American Urological Association. Castration-resistant prostate cancer: AUA guideline 2018. Retrieved from: https://www.auanet.org/guidelines/prostate-cancer-castration-resistant-guideline#x1929/Access. Access date: 03 May 2019.

THE CURRENT GUIDELINES
FOR mCRPC

The choice of therapy for mCRPC is dependent on the patient's disease factors and treatment history

Physicians should refer to the most appropriate treatment guidelines for their country & institution

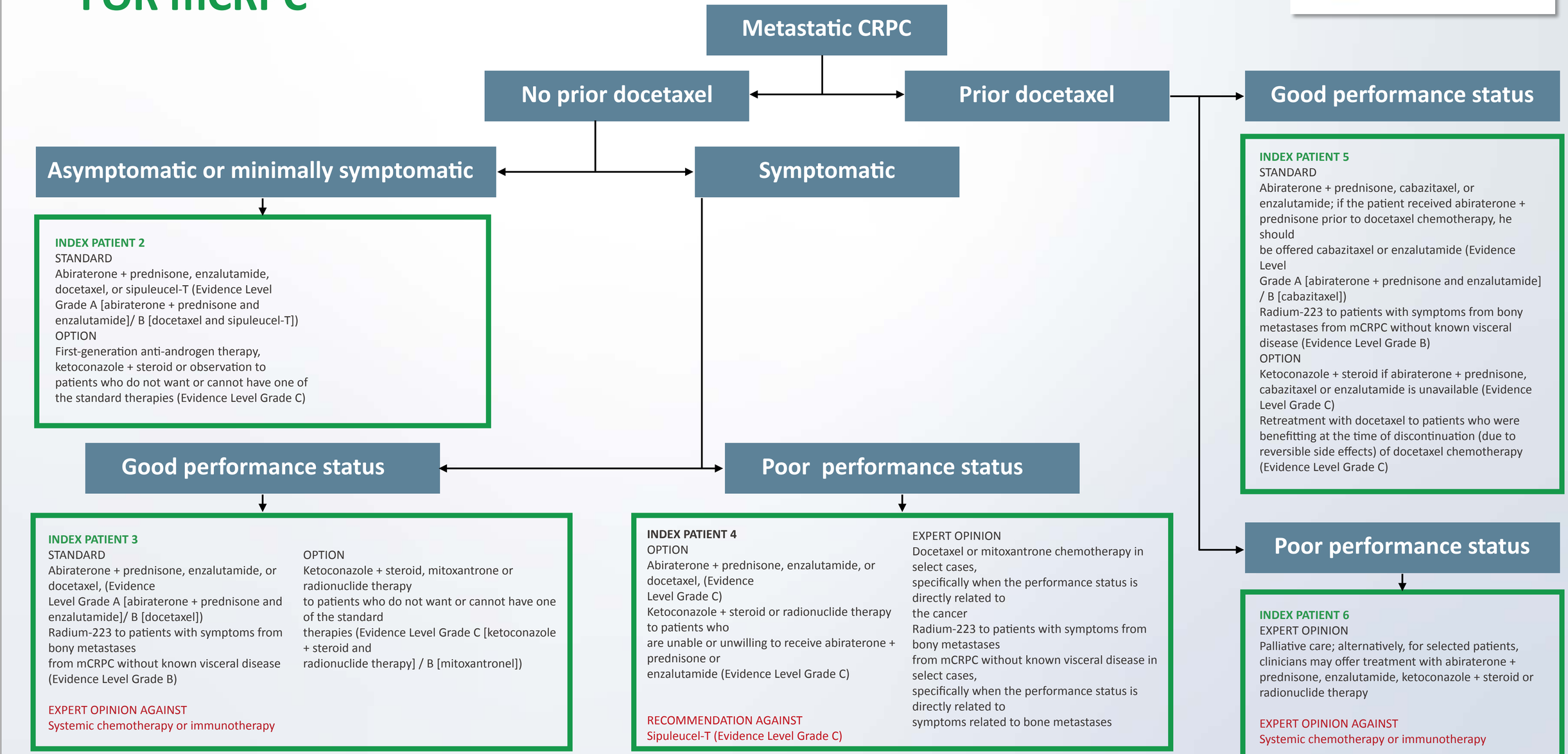
American Urological Association

European Association of Urology

NCCN National Comprehensive Cancer Network®

AUA, American Urological Association; EAU, European Association of Urology; mCRPC, metastatic castration resistant prostate cancer; NCCN, National Comprehensive Cancer Network

AUA TREATMENT GUIDELINES
FOR mCRPC



AUA, American Urological Association; CRPC, castration resistant prostate cancer; mCRPC, metastatic castration resistant prostate cancer.

The American Urological Association. Castration-resistant prostate cancer: AUA guideline 2018. Retrieved from: https://www.auanet.org/guidelines/prostate-cancer-castration-resistant-guideline#x1929/Access. Access date: 03 May 2019.

EAU TREATMENT GUIDELINES
FOR mCRPC

European Association of Urology

Recommendations for castration-resistant prostate cancer	LE	GR
Ensure testosterone levels are confirmed to be < 50 ng/ml before diagnosing CRPC	4	A
Do not treat patients for nmCRPC outside of a clinical trial	3	A
Counsel, manage and treat patients with mCRPC in a MDT	3	A
In men treated with maximal androgen blockade, stop androgen therapy once PSA progression is documented. At 4-6 weeks after discontinuation of flutamide or bicalutamide, an eventual antiandrogen withdrawal effect will be apparent	2a	A
Treat patients with mCRPC with life-prolonging agents. Base the choice of first line treatment on the PS, symptoms, comorbidities, and extent of disease (alphabetical order: abiraterone, cabazitaxel, docetaxel, enzalutamide, Ra-223, sipuleucel-T)	1b	A
Offer patients with mCRPC who are candidates for cytotoxic therapy, docetaxel 75 mg/m^2 every 3 weeks	1a	A
Base second-line treatment decisions of mCRPC on pretreatment PS, comorbidities and extent of disease	1a	B
Offer bone-protective agents to patients with skeletal metastases to prevent osseous complications; however, the benefit must be balanced against the toxicity of these agents, and jaw necrosis in particular must be avoided	1b	B
Offer calcium and vitamin D supplementation when prescribing denosumab or bisphosphonates	1b	A
Treat painful bone metastases early on with palliative measures such as EBRT, radionuclides and adequate use of analgesics	1a	B
In patients with spinal cord compression, start immediate high-dose corticosteroids and assess for spinal surgery followed by irradiation. Offer radiation therapy alone if surgery not appropriate	1b	A

S H A R E

CRPC, castration resistant prostate cancer; EBRT, external beam radiotherapy; EAU, European Association of Urology; GR, grade; LE, level of evidence; mCRPC, metastatic castrate resistant prostate cancer; MDT, multidisciplinary team; nmCRPC, non metastatic castrate resistant prostate cancer PS, performance statusRa-223, radium-223

Cornford P et al. European Urology 2017; 71: 630-642

NCCN TREATMENT GUIDELINES

FOR mCRPC

National Comprehensive Cancer Network®

First-line treatment

FIRST-LINE TREATMENT
- Abiraterone with prednisone
- Docetaxel
- Enzalutamide
- Radium-223 for symptomatic bone metastases
- Abiraterone with methylprednisolone
- Clinical trial
- Other secondary hormone therapy

Prior therapy Abiraterone/Enzalutamide

Prior therapy Docetaxel

Second-line treatment

SECOND-LINE TREATMENT
- Docetaxel
- Radium-223 for symptomatic bone metastases
- Pembrolizumab for MSI-H or dMMR
- If not previously received:
  - Abiraterone with prednisone
  - Abiraterone with methylprednisolone
  - Enzalutamide
  - Sipuleucel-T
  - Clinical trial
  - Other secondary hormone therapy
- Best supportive care

Second-line treatment

SECOND-LINE TREATMENT
- Abiraterone with prednisone
- Cabazitaxel
- Enzalutamide
- Radium-223 for symptomatic bone metastases
- Abiraterone with methylprednisolone
- Pembrolizumab for MSI-H or dMMR
- If not previously received:
  - Sipuleucel-T
  - Clinical trial
  - Consider docetaxel rechallenge
  - Mitoxantrone with prednisone
  - Other secondary hormone therapy
  - Best supportive care

Subsequent treatment

SUBSEQUENT TREATMENT

At progression
- If not previously received:
  - Abiraterone with prednisone
  - Enzalutamide
  - Cabazitaxel
  - Radium-223 for symptomatic bone metastases
  - Abiraterone with methylprednisolone
  - Mitoxantrone with prednisone
  - Pembrolizumab for MSI-H or dMMR
- Clinical trial
- Docetaxel rechallenge
- Other secondary hormone therapy
- Best supportive care

CRPC, castrate resistant prostate cancer; dMMR, mismatch repair deficient; M, metastasis; mCRPC, metastatic castrate resistant prostate cancer; MSI-H, microsatellite instability-high; NCCN, national comprehensive cancer network.

NCCN Clinical Practice Guidelines in Oncology (Prostate Cancer) Version 4, Aug 2019. Retrieved from: https://www.nccn.org/professionals/physician_gls/pdf/prostate.pdf. Access date: 03 Dec 2019.

First-line treatment | Second-line treatment | Subsequent treatment

POTENTIAL TREATMENTS
FOR mCRPC

REVIEW RECENT DATA ON CABAZITAXEL
when you see this symbol in Step 1

According to available treatment guidelines[1-3], the following may be potential treatment options for symptomatic mCRPC patients like Peter *(depending on prior therapy)* in addition to continuing treatment with ADT:

- Abiraterone + prednisone
- Enzalutamide
- Radium-223 (if bone metastases detected)
- Docetaxel
- Sipuleucel-T for asymptomatic/minimally symptomatic men
- Cabazitaxel for men who have progressed on docetaxel
    - Peter has not received docetaxel previously so this option will not be discussed further as a treatment option for Peter.
- Clinical trial

NOTE: Treatment options may vary per country depending on available licensed products and local treatment guidelines

S H A R E

ADT, androgen deprivation therapy; mCRPC, metastatic castration resistant prostate cancer.

1. The American Urological Association. Castration-resistant prostate cancer: AUA guideline 2018. Retrieved from: https://www.auanet.org/guidelines/prostate-cancer-castration-resistant-guideline#x1929/Access. Access date: 03 May 2019; 2. NCCN Clinical Practice Guidelines in Oncology (Prostate Cancer) Version 4, Aug 2019. Retrieved from: https://www.nccn.org/professionals/physician_gls/pdf/prostate.pdf. Access date: 03 Dec 2019. 3. Cornford P et al. European Urology 2017; 71: 630-642

CARD
STUDY DESIGN

PATIENTS WITH mCRPC WHO PROGRESSED ≤12 MONTHS ON PRIOR ALTERNATIVE ARTA (BEFORE OR AFTER DOCETAXEL)
N=255

1:1 Randomisation

Cabazitaxel (25 mg/m² Q3W) + prednisone + G-CSF
n=129

Abiraterone (1000 mg QD) + prednisone
OR
Enzalutamide (160 mg QD)
n=126

Endpoints Primary: rPFS
Key secondary: OS, PFS, PSA response, tumour response
Other secondary: Pain response, time to symptomatic skeletal event, safety, HRQoL, biomarkers

Multicenter, randomized, open-label study
Enrollment: Nov 2015 – Nov 2018
Median follow-up: 9.2 months

Stratification factors:
ECOG PS (0/1 vs 2)
Time to progression on prior alternative ARTA (0–6 vs >6–12 months)
Timing of ARTA (before vs after docetaxel)

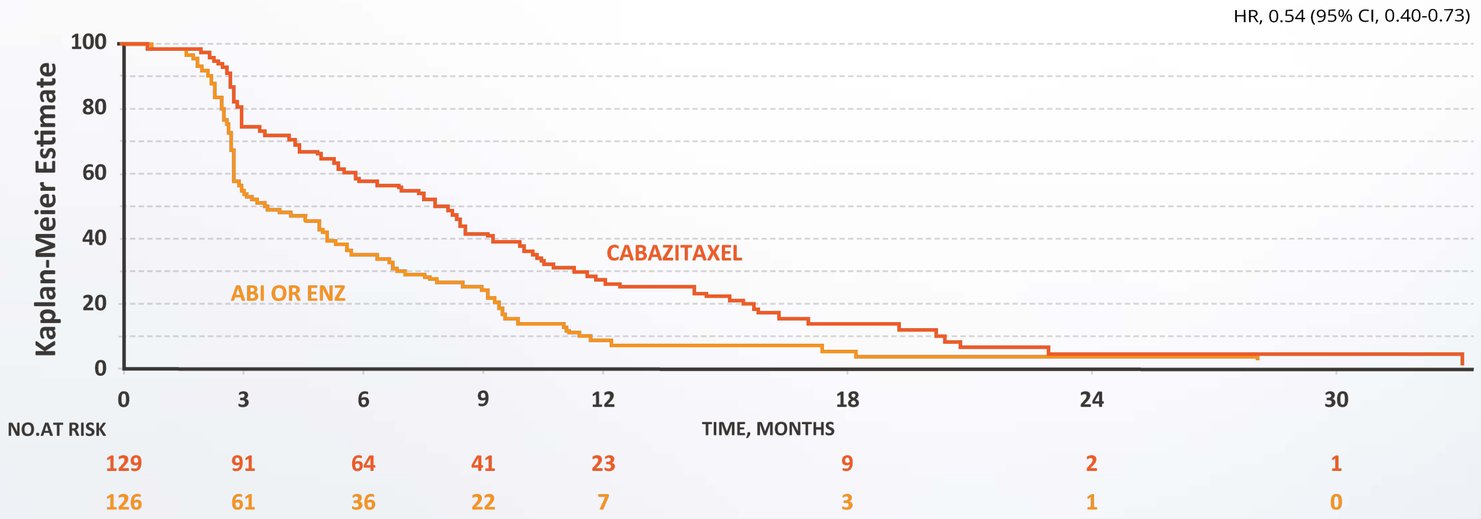
ARTA, androgen receptor-targeted agents; ECOG PS, eastern cooperative oncology group performance status; G-CSF, granulocyte colony stimulating factor; HRQoL, health related quality of life; mCRPC, metastatic castration resistant prostate cancer; OS, overall survival; Q3W, every three weeks; QD, once daily; (r)PFS, (radiographic)progression free survival; PSA, prostate specific antigen

de Wit,R, et al. ESMO 2019 Abstract #LBA13; de Wit R, et al; NEJM 2019: DOI: 10.1056/NEJMoa1911206.

CARD STUDY

PRIMARY ENDPOINT

RADIOGRAPHIC PFS (Investigator assessed)



	cabazitaxel (N=129)	abi/enza (N=126)
Median rPFS (months) (95% CI)	8.0 (5.7-9.2)	3.7 (2.8-5.1)
Hazard ratio (95% CI)	0.54	
	(0.40-0.73)	
	P<0.0001	

rPFS benefit observed for cabazitaxel compared to abi/enz was consistent across key subgroups, especially timing of ART with respect to receipt of docetaxel, as well as time from ART initiation to progression

Abi, abiraterone; CI, confidence interval; enza, enzalutamide; PCWG2, prostate cancer working group 2; RECIST, response evaluation criteria in solid tumours; (r)PFS, (radiographic) progression free survival
de Wit,R, et al. ESMO 2019 Abstract #LBA13; de Wit R, et al; NEJM 2019: DOI: 10.1056/NEJMoa1911206.

CARD STUDY
SUMMARY

- **The CARD trial addresses an unmet clinical need regarding sequencing of 3rd line treatments for progressive mCRPC patients**
- The current treatment landscape should be for fit patients to receive docetaxel and abiraterone or enzalutamide at some stage (+/- radium-223)
- The results of the **CARD trial** are in agreement with those of previous studies that have **shown poor outcomes with a second androgen signaling–targeted inhibitor**[1-5]
- Based on information presented in the CARD trial, **cabazitaxel is a new standard of care for 3rd line patients with progressive disease on prior novel androgen signaling inhibitors therapy ≤12 months of initiating therapy, and with prior docetaxel therapy**

mCRPC, metastatic castration resistant prostate cancer

1. Attard G, et al. JCO. 2018;36(25):2639-46; 2. Khalaf D, et al. JCO. 2018;36(15):5015; 3. Smith MR, et al. Eur Urol. 2017;72(1):10-13; 4. Zhang T, et al. Clin Genitourin Cancer. 2015;13:392-9; 5. Azad AA, et al. Eur Urol. 2015;67:23-9; 6. de Wit R, et al. ESMO 2019 Abstract #LBA13;
7. de Wit R, et al. NEJM 2019: DOI: 10.1056/NEJMoa1911206.

WHAT THE PATIENT
NEEDS TO UNDERSTAND

The main treatment aim is to **control/stabilise the disease** and that further treatment of mCRPC is **not curative**[1,2]

All patients are different and that it is important to find the right treatment for them as an individual. **They are instrumental in the treatment decision**

The **treatment can be adjusted** to manage side effects and QoL

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mCRPC, metastatic castration resistant prostate cancer; QoL, quality of life.

1. Dong L et al. Asian J Urol 2019; 6: 26-41; 2. Cook L et al. https://www.gotoper.com/publications/ajho/2016/2016august/targeting-bone-metastatic-castration-resistant-prostate-cancer. Accessed 10 Dec 2019

HOW TO BEST INTERACT
WITH THE PATIENT

- **Listen to the patient's concerns** and **provides reassurance. Determine** what is important to the patient in terms of the **goals of treatment** and any personal milestones he wants to achieve
- **Determine the relationship of the caregiver to the patient and** ensure **that** both the patient and caregiver understand the purpose of the discussion

- **Seek to** ensure **the patient and caregiver's** understanding of the current disease state and treatment objectives
- **Highlight the patient's current state of well-being** and that the objective is to maintain a good QoL over the coming months
- Prepare the patient for what they might expect in the coming months
- **Seek the patient's understanding** (and that of the caregiver) of the situation **before moving on to potential options**

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QoL, quality of life

STEP 1 - SUMMARY
SUCCESS CRITERIA AND AIM OF TREATMENT

WHAT TO DO

- Give the patient a warm welcome and introduction. Ask questions to demonstrate an ongoing relationship, interest and empathy
- Manage patient expectations that you will be controlling NOT curing the disease
- Ask the patient and caregiver if they have any questions and continually seek confirmation that the patient understands
- Allow time for the patient to digest and assimilate information
- Highlight any positives such as patient's current state of well-being
- Reassure the patient that everyone is different and the need to find the right treatment for them as an individual
- Understand the patient's treatment objectives – what does success looks like for them?

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STEP 1 - SUMMARY
SUCCESS CRITERIA AND AIM OF TREATMENT

WHAT TO AVOID

- Failing to make a ‘connection’ with the patient at the start – short introduction and straight into the consultation
- Talking too much and interrupting
- Failing to engage and respond to others in the room
- Being insensitive to the emotional response of the patient
- Moving very quickly on to treatment options without establishing with the patient why they should be considered in the first place
- Not giving the patients time to absorb the news that their disease is not under control
- Not allowing the patient opportunity to give direction on their treatment aims
- Not checking that the patient understands or allowing the patient the opportunity to ask questions

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STEP 2

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HOW THE TREATMENTS WORK?

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LEARNING OBJECTIVE

STEP 2: HOW THE TREATMENTS WORK?

WHAT
WILL YOU LEARN?

The need to explain to the patient 'How the treatments work', how they may differ from treatments they have received previously and the differing methods of administration and mechanisms of action

WHY
IS THIS IMPORTANT?

If the patient is clear how the treatments work and what this means, the patient can feel part of the shared decision process

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WHAT THE PHYSICIAN
NEEDS TO KNOW

LEARN MORE ABOUT THE OTHER POTENTIAL TREATMENT OPTIONS
when you see this symbol

- **Clinical background and data** are essential for the physician to know at this stage in the conversation to enable discussion as to mechanism of action (MOA) and methods of administration with the patient
- **The basic health literacy of the patient** before engaging in a discussion that leans towards more ‘scientific’ content

The **SHARE framework** recommends the physician selects the 3 most appropriate treatment options to discuss in detail with the patient. Based on Peter’s disease status, treatment goals and prior treatment the most relevant treatment options are:

DOCETAXEL

RADIUM-233

CLINICAL TRIAL

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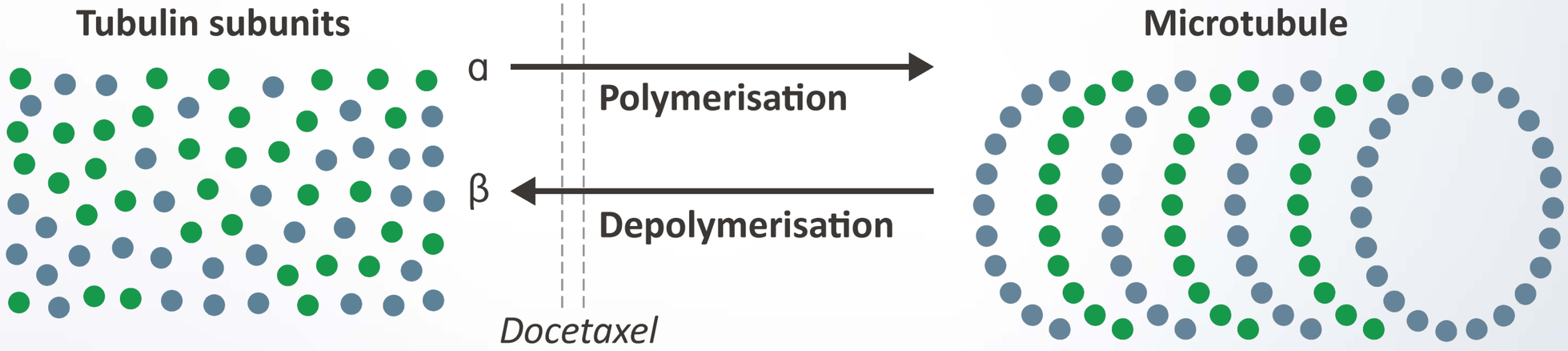
DOCETAXEL MECHANISM OF ACTION (MOA)



- **Antineoplastic agent** which acts by **promoting the assembly of tubulin into stable microtubules** and inhibits their disassembly which leads to a marked decrease of free tubulin
- Microtubules are critical for cell division, as cancer cells are dividing more rapidly than normal cells, they suffer more damage. However normal cells will also have some damage due to the mechanism of action of docetaxel

MOA, mechanism of action

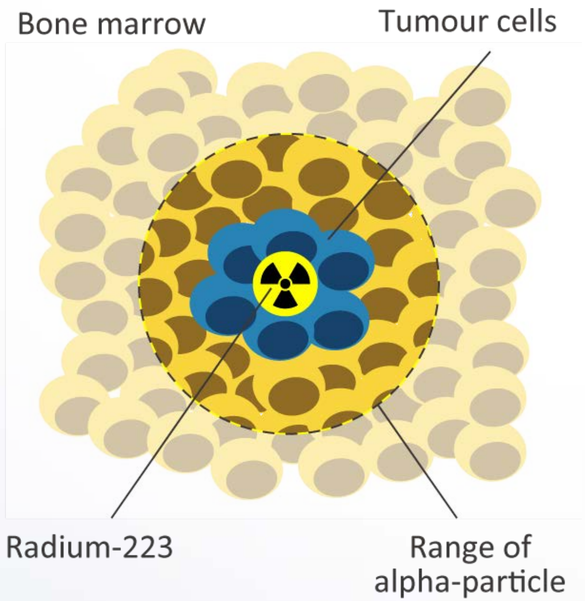
DOCETAXEL ADMINISTRATION & DOSE

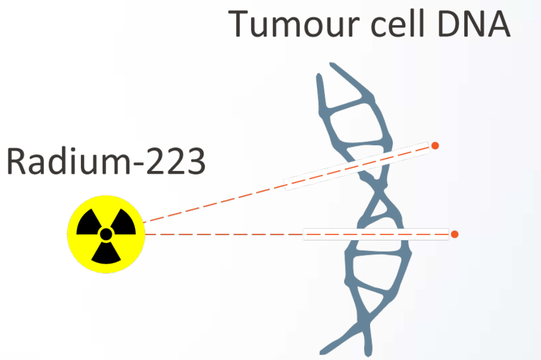
- 75 mg/m^2 docetaxel administered as intravenous infusion (IV) over one hour every 3 weeks
  - Usually given until disease progression or intolerable side effects up to 10 cycles
- 8 mg dexamethasone to be administered orally: 12 hours, 3 hours and 1 hour before Docetaxel infusion
  - Reduces incidence and severity of fluid retention and hypersensitivity reaction
- 5 mg of prednisone (prednisolone) may also be given twice daily continuously whilst the patient is receiving chemotherapy
- Patient receives treatment in an outpatient clinic or hospital setting and goes home after treatment

V, intravenous.

Docetaxel Prescribing Information Jun 2019; Mackler N, et al. Nat Rev Urol 2005: 2, 92–100
Docetaxel Prescribing Information Jun 2019; Tannock IF, et al. NEJM. 2004;351:1502-12

RADIUM-223 MOA IN BONE METASTASES





Action of α particles on DNAα

Nonreparable DNA double strand breaks and tumour cell death

- Alpha particle-emitting isotope **radium-223** (as radium Ra 223 dichloride), **mimics calcium and forms complexes with the bone mineral** hydroxyapatite at areas of increased bone turnover, such as bone metastases
- The high linear energy transfer of alpha emitters (80 keV/micrometer) leads to a high frequency of double-strand DNA breaks in adjacent cells, resulting in an anti-tumor effect on bone metastases
- The **alpha particle range from radium-223** dichloride is **less than 100 micrometers** (less than 10 cell diameters) which **limits damage to the surrounding normal tissue**

keV, kiloelectron volt; mCRPC, metastatic castration resistant prostate cancer; MOA, mechanism of action; Ra-223, radium-223.

Radium-223 Prescribing Information Aug 2018.

Figure adapted from: Deshayes E et al. Drug Design, Development and Therapy, 2017 Volume 11, 2643–2651

RADIUM-223 ABSORBED RADIATION

DOSES PER ADMINISTERED ACTIVITY

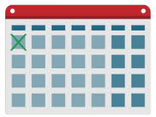
Organ	Mean (mGy/MBq)	Mean (rad/mCi)	Coefficient of Variation (%)	Organ	Mean (mGy/MBq)	Mean (rad/mCi)	Coefficient of Variation (%)
Osteogenic cells	1152	4263	41	**Gallbladder wall**	0.23	0.85	14
Red marrow	139	514	41	**Stomach wall**	0.14	0.51	22
LLI wall*	46	172	83	**Adrenals**	0.12	0.44	56
Colon*	38	142	56	**Muscle**	0.12	0.44	41
ULI wall*	32	120	50	**Pancreas**	0.11	0.41	43
Small intestine wall	7.3	27	45	**Brain**	0.10	0.37	80
Urinary bladder wall	4.0	15	63	**Spleen**	0.09	0.33	54
Kidneys	3.2	12	36	**Testes**	0.08	0.31	59
Liver	3.0	11	36	**Skin**	0.07	0.27	49
Heart wall	1.7	6.4	42	**Thyroid**	0.07	0.26	96
Lungs	1.2	4.5	48	**Thymus**	0.06	0.21	109
Ovaries	0.49	1.8	40	**Breasts**	0.05	0.18	120
Uterus	0.26	0.94	28	**Whole body**	23	86	16

*LLI:, lower large intestine; ULI, upper large intestine; Colon dose = 0.43 x LLI dose[2]
mGY: milligray; MBq, megabequerel; mCI, microcurie
Radium-223 Prescribing Information Aug 2018

RADIUM-223 ADMINISTRATION & DOSE

- Ra-223 must be administered by a radiation oncologist or nuclear medicine physician in a designated clinical setting, including a licensed practice or a hospital outpatient setting.

1 MINUTE INJECTION



EVERY **4 WEEKS**

6 INJECTIONS TOTAL

Treatment may be completed in 5 months

- The patient-ready dose is 1.49 microcurie (55 kBq) per kg body weight

The volume to be administered to a given patient is calculated as follows:

$$\text{Volume to be administered (mL)} = \frac{\text{Body weight in kg} \times \text{v } 55 \text{ kBq/kg body weight}}{\text{Decay factor} \times 1100 \text{ kBq/mL}} \quad \textbf{OR} \quad \frac{\text{Body weight in kg} \times 1.49 \text{ mCi/kg body weight}}{\text{Decay factor} \times 30 \text{ mCi/mL}}$$

- The shelf life of Ra-223 in the patient-ready syringe is 96 hours
- Ra-223 is a ready-to-use solution and should not be diluted or mixed with any other solutions
- Patient goes home after treatment

kBq, kilobecquerel

Radium-223 Prescribing Information Aug 2018; https://hcp.xofigo-us.com/administer-xofigo/dosing-and-administration/dosing-information/ Accessed 08 Aug 2019.

CLINICAL TRIAL

- Clinical trials bring life extending and curative new treatments to cancer patients and play a vital role in moving new treatments to patients who need them most
- NCCN believe that the best management for any patient with cancer is in a clinical trial[1]
- The MOA and administration of drugs in clinical trials depends on the treatments under study

Visit www.clinicaltrials.gov for a full listing of available studies

- Currently > 140 Phase III drug trials & > 650 Phase I/II trials in progress for prostate cancer in the United States alone.[2]
- Those that are approved will join the 9 new drugs approved for men with advanced metastatic disease since 2010:
  - Cabazitaxel, sipuleucel-T, denusomab, radium 223 dichloride, enzalutamide, abiraterone, apalutamide, pembrolizumab, darolutamide

MOA, mechanism of action; NA, north America; NCCN, national comprehensive cancer network.

1. NCCN Framework for Resource Stratification of NCCN Guidelines (NCCN Framework™). Basic Resources (Prostate Cancer) Version 2, 2019. Retrieved from: https://www.nccn.org/professionals/physician_gls/pdf/prostate_basic.pdf. Accessed 08 Aug 2019;
2. https://www.pcf.org/patient-resources/patient-navigation/prostate-cancer-clinical-trials/. Accessed 05 Nov 2019.

OTHER POTENTIAL TREATMENT OPTIONS

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ABIRATERONE
ADMINISTRATION & DOSE

1000 mg
ABIRATERONE ACETATE
ONCE DAILY*

+

5 mg
PREDNISONE
TWICE DAILY

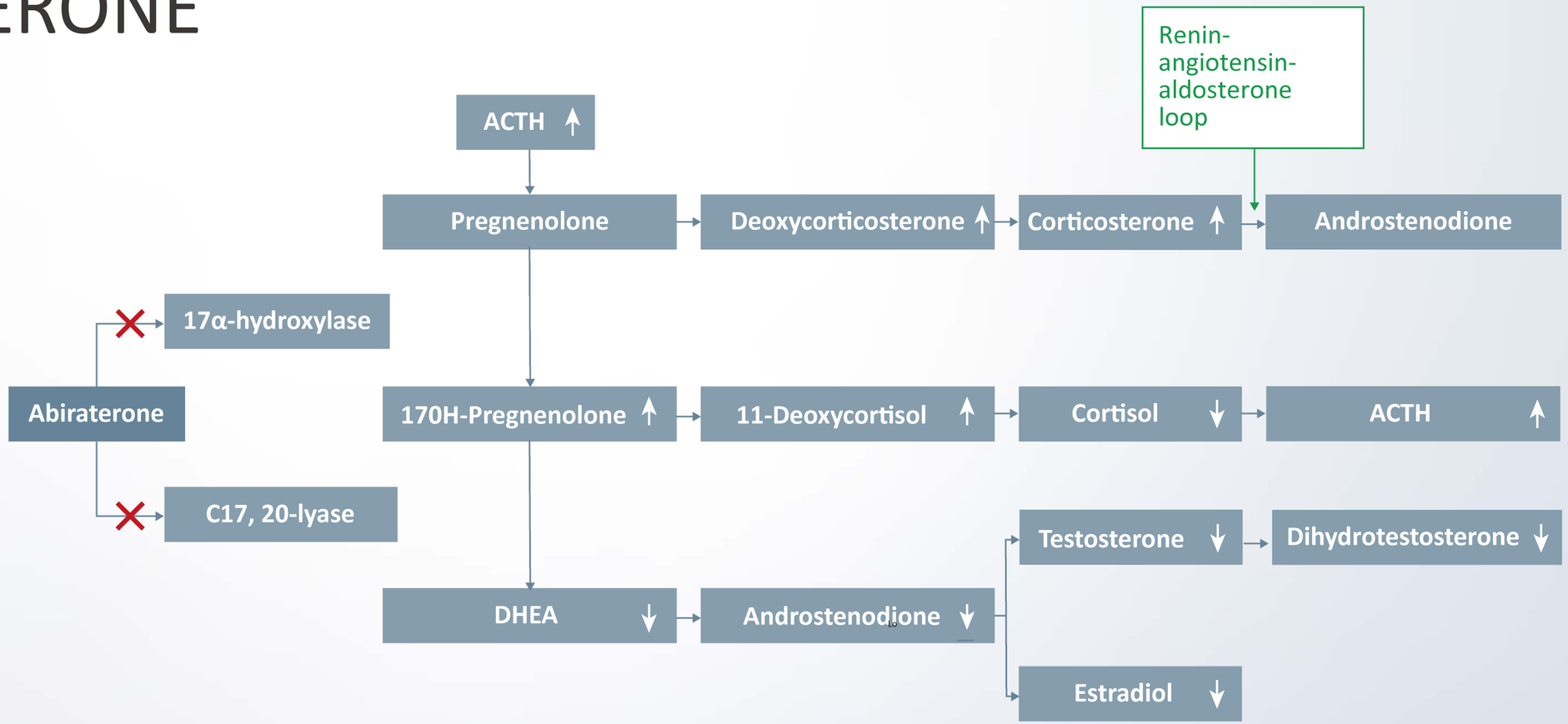
Taken Orally at home

*other formulations of abiraterone may have different pill doses

https://www.drugs.com/zytiga-images.html. Accessed 11 Dec 2019; Abiraterone Prescribing Information Jun 2019

ABIRATERONE

MOA



- A steroidal CYP17 inhibitor
- Abiraterone acetate is converted in vivo to Abiraterone, an androgen biosynthesis inhibitor, that inhibits 17 α-hydroxylase/C17, 20-lyase (CYP17)
- This enzyme is expressed in testicular, adrenal, and prostatic tumour tissues and is required for androgen biosynthesis
- Glucocorticoid production is suppressed by abiraterone, thus prednisone is generally given as a replacement

ACTH, adrenocorticotropic hormone; CYP, cytochrome; DHEA, dehydroepiandrostenedione; MOA, mechanism of action.

Ang JE, et al. Br J Cancer. 2009;100:671-675; Abiraterone Prescribing Information June 2019

S H A R E

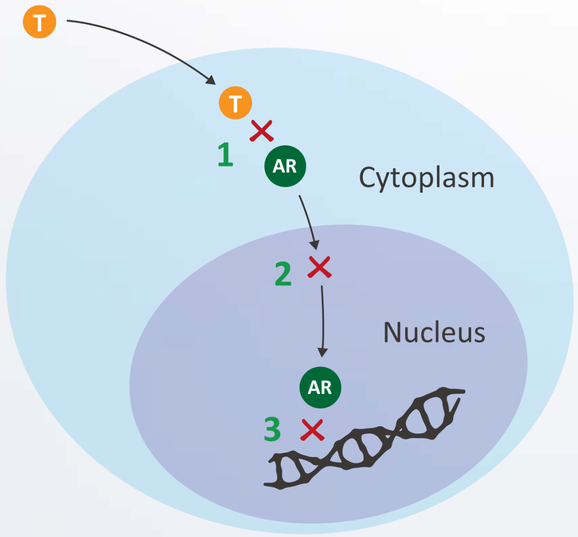
ENZALUTAMIDE

ADMINISTRATION & DOSE

160MG 1X DAILY
ENZALUTAMIDE

4 x 40mg
Taken Orally

MECHANISM OF ACTION (MOA)

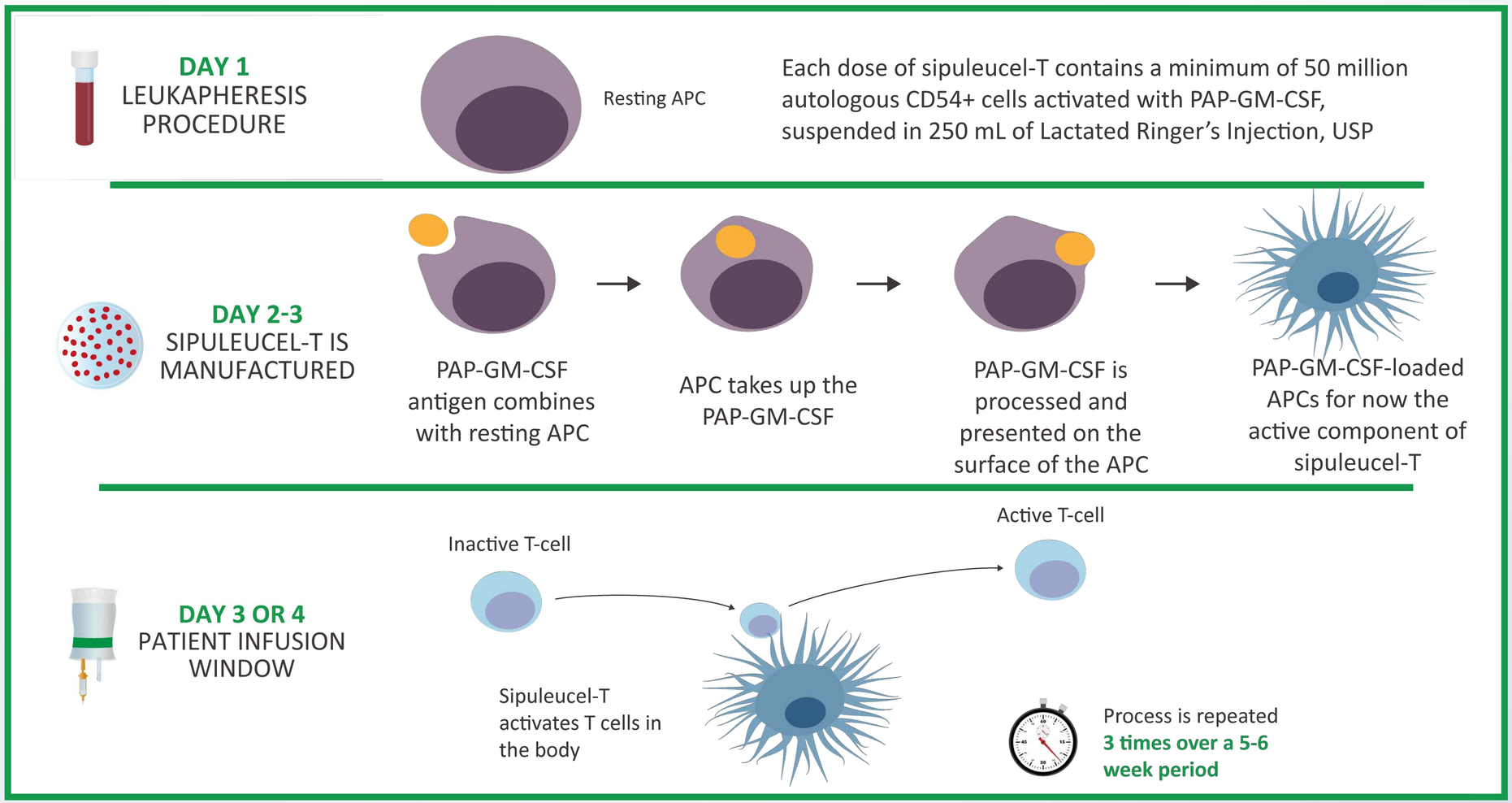


- Enzalutamide is an androgen receptor (AR) signalling inhibitor
- Inhibits androgen receptor nuclear translocation, DNA binding, and coactivator recruitment, reducing androgen receptor signalling

AR, androgen receptor; T, testosterone; MOA, mechanism of action.
Enzalutamide Prescribing Information July 2018; Tran C et al. Science 2009; 324: 787-790

SIPULEUCEL–T (IMMUNOTHERAPY)

- Treatment is given as an intravenous infusion
- Visits occur at 2 different sites
  - leukapheresis at a Red Cross or Haemacare facility
  - infusion at the physician's clinic or hospital
- Patients go home after treatment



- Autologous activated cellular immunotherapy designed to induce an immune response targeted against prostatic acid phosphatase (PAP), an antigen expressed in prostate cancer tissues
- Involves leukapheresis to collect dendritic cells which are incubated with a recombinant human protein, PAP-GM-CSF
- During ex vivo culture APCs take up and process the recombinant target antigen into small peptides that are then displayed on the APC surface
- The activated cells are then infused into the same patient from whom they were taken

APC, antigen presenting cell; CD, cluster of differentiation; GM-CSF, granulocyte-macrophage colony-stimulating factor; PAP, prostatic acid phosphatase.

Sipuleucel-T Prescribing Information July 2017; https://www.provenge.com. Accessed 05Dec2019

WHAT NEEDS TO BE EXPLAINED
TO THE PATIENT

Treatment guidelines in EU & USA recommend **several therapies for mCRPC**

The **available therapies** have **different molecular targets** and **mechanisms of action**

The **treatment chosen** at this stage will be the **first in a series** of treatments given over time. The choice at this stage will **affect future treatment options**

The **different methods** of **administration and frequency** of administration for each treatment

In addition to the systemic treatments, the patient will also receive localised radiotherapy to the painful bony metastasis in the right hip

Treatment with ADT (LHRH agonist or antagonist) must continue for the rest of the patient's life

ADT, androgen deprivation therapy; EU, Europe; LHRH, luteinizing hormone releasing hormone; mCRPC, metastatic castration resistant prostate cancer; USA, United States of America.

S H A R E

HOW BEST TO INTERACT
WITH THE PATIENT

- Explain options in **non-technical language** using **visuals and handouts** to support
- **Highlight** the **impact** the treatments may have **on the patient's everyday life**
- **Ask the patient** whether they would like **more or less information** about the mechanisms of action (MoA) of the available treatment options

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MoA, mechanism of action

STEP 2 - SUMMARY
HOW DO THE TREATMENTS WORK?

WHAT TO DO

- Explain equivalent treatment options
- Explain in patient-friendly terms, avoiding language that is too technical
- Tailor the level of detail to the interest and health literacy of the patient
- Include how the different drugs impact the patient in terms of how often they will need to take them, how they are administered and where they will be taken (home vs hospital)

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STEP 2 - SUMMARY
HOW DO THE TREATMENTS WORK?

WHAT TO AVOID

- Fast explanation without recognising options
- Overwhelming the patient with too much information
- Using extensive technical language
- No pause to check for understanding
- Inappropriate reference to data – lack of relevance for the patient
- Lack of clear background upon which to base any form of decision-making

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STEP 3

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ADVANTAGES AND DISADVANTAGES OF EACH TREATMENT OPTION

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LEARNING OBJECTIVE

STEP 3: ADVANTAGES AND DISADVANTAGES OF EACH TREATMENT OPTION

WHAT
WILL YOU LEARN?

You will learn about the 'Advantages and disadvantages of each treatment option' in terms of clinical benefit for the patient

WHY
IS THIS IMPORTANT?

To highlight to the patient that there are choices available whilst temporarily postponing the discussion around safety and side effects

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WHAT THE PHYSICIAN
NEEDS TO KNOW

LEARN MORE ABOUT THE OTHER POTENTIAL TREATMENT OPTIONS
when you see this symbol

- Clinical background and data are essential for the physician to know at this stage in the conversation so that the physician can **convey the clinical benefit** of the appropriate treatment options to the patient
- Patients with **mCRPC** have a poor prognosis and a **predicted survival rate of less than 2 years** from the initial time of progression[1, 2]
- **All treatment options provide clinical benefit** to the patient
  - In clinical trials, these treatments have been compared either to placebo or outdated comparators[3-10]
  - The treatments have not been compared head-to-head **therefore direct comparison cannot be made**

DOCETAXEL | **RADIUM-223** | **CLINICAL TRIAL**

S H A R E

mCRPC, metastatic castration resistant prostate cancer.

1. Frieling J et al. Cancer Control 2015; 22: 109-120; 2. American Cancer Society. http://www.cancer.org/cancer/prostate-cancer/detection-diagnosis-staging/survival-rates.html.. Accessed 06 May 2019; 3. Tannock IF, et al. NEJM. 2004;351:1502-12; 4. Parker C, et al. NEJM. 2013;369:213-23; 5. Ryan CJ, et al. NEJM. 2013;368:138-48; 6. De Bono JS, et al. NEJM. 2011;364:1995-2005; 7. Ryan CJ, et al. Lancet Oncol. 2015;16(2): 152-60; 8. Beer TM, et al. NEJM. 2014;371:424-33; 9. Scher HI, et al. NEJM. 2012;367:1187-97; 10. Kantoff PW, et al. NEJM 2010;363:411-22

EFFICACY OF PREFERRED TREATMENT OPTIONS

	Docetaxel**		Radium-223	
Patient population	mCRPC patients receiving primary androgen-ablation therapy as maintenance therapy		mCRPC patients with symptomatic bone metastases (inc. patients who had received docetaxel, were not healthy enough to receive, had declined docetaxel or it was not available)	
Trial	TAX327[1]		ALSYMPCA[2, 3]	
	Docetaxel	Mitoxantrone	Radium-223	Placebo
OS (median)	18.9 mo	16.5 mo	14.9 mo	11.3 mo
	HR 0.76; p=0.009		HR 0.70; p<0.001	
Time to PSA progression (median)	7.7 mo	7.8 mo	3.6 mo	3.4 mo
	p=NS		HR 0.64; p<0.001	
PSA response rate‡	45%	32%	16%	6%
	p<0.001		p<0.001	
Objective response rate	12%	7%	NR	NR
	p=0.11			
Time to first symptomatic skeletal event (median)	NR	NR	15.6 mo	9.8 mo
			HR 0.66; p<0.001	
QoL (FACT-P)	16-point improvement: 22%	16-point improvement: 13%	≥10 point improvement: 25%	≥10 point improvement: 16%
	p=0.009		p=0.02	
QoL (other)	2-point reduction PPI: 35%	2-point reduction PPI: 22%	EQ-5D: 29.2%	EQ-5D: 18.5%
	p=0.01		P=0.004	

Green cells – statistically significant effect shown.

**3-weekly cycle of docetaxel; ‡TAX327 study patients with a ≥ 50% decline in PSA and ALSYMPCA study patients with a ≥ 30% decline;
EQ-5D, EuroQol-5D; FACT-P, Functional Assessment of Cancer Therapy–Prostate; HR, hazard ratio; mCRPC, metastatic castration resistant prostate cancer; mo, months; NR, not reported; OS, overall survival; PPI, present pain intensity; PSA, prostate specific antigen.

1. Tannock IF, et al. NEJM. 2004;351:1502-12; 2. Parker C, et al. NEJM. 2013;369:213-23; 3. Nilsson S et al. Ann Oncol 2016; 27: 868-874

CLINICAL TRIAL

- The physician should determine the patient's suitability for a clinical trial based on:
  - Available clinical trials: https://clinicaltrials.gov/
  - Patient's disease status and prior treatment history

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EFFICACY OF ADDITIONAL TREATMENT OPTIONS

	Abiraterone Acetate			
Patient population	mCRPC patients chemotherapy naïve*		mCRPC patients previously treated with docetaxel*	
Trial	COU-AA-302[1, 3]		COU-AA-301[2]	
	Abiraterone	Placebo	Abiraterone	Placebo
OS (median)	34.7 mo	30.3 mo	14.8 mo	10.9 mo
	HR 0.81; P=0.0033		HR 0.65; P< 0.001	
rPFS (median)	16.5 mo	8.3 mo	5.6 mo	3.6 mo
	HR 0.53; P<0.001		HR 0.67; P<0.001	
Time to PSA progression (median)	11.1 mo	5.6 mo	10.2 mo	6.6 mo
	HR 0.49; P<0.001		HR 0.58; P<0.001	
PSA response rate	62%‡	24%‡	29%	5.5%
	RR 2.59; P<0.001		P<0.001	
Objective response rate	36%	16%	14%	2.8%
	RR 2.27 P<0.001		P<0.001	
Time to first symptomatic skeletal event	NR	NR	Time to 25% patients having a skeletal event:	
			9.9 mo	4.9 mo
Time to initiation of cytotoxic chemotherapy	25.2 mo	16.8 mo	NA	NA
	HR 0.58; P<0.001			
QoL	Decline in FACT-P score†:		Improved pain palliation:	
	12.7 mo	8.3 mo	44%	27%
	HR 0.78; P=0.003		P=0.002	

Green cells – statistically significant effect shown.

*All patients received either prednisone or prednisolone; ‡ patients with a ≥ 50% decline in PSA; †Decline in functional status defined as decline of ≥ 10 points in FACT-P total score at any visit. FACT-P, Functional Assessment of Cancer Therapy–Prostate; HR, hazard ratio; mCRPC, metastatic castration resistant prostate cancer; mo, months; NA, not applicable; NR, not reported; OS, overall survival; PSA, prostate specific antigen; QoL, quality of life; rPFS, radiographic progression-free survival; RR, relative risk.

1. Ryan CJ, et al. NEJM. 2013;368:138-48; 2. De Bono JS, et al. NEJM. 2011;364:1995-2005; 3. Ryan CJ, et al. Lancet Oncol. 2015;16(2):152-60.

S H A R E

EFFICACY OF ADDITIONAL TREATMENT OPTIONS

	Enzalutamide			
Patient population	mCRPC patients chemotherapy naive		mCRPC patients previously treated with docetaxel	
Trial	PREVAIL[1]		AFFIRM[2]	
	enzalutamide	placebo	enzalutamide	placebo
OS (median)	32.4 mo	30.2 mo	18.4 mo	13.6 mo
	HR 0.71; P<0.001		HR 0.63; P<0.001	
rPFS (median)	Not reached	3.9 mo	8.3 mo	2.9 mo
	HR 0.19; P<0.001		HR 0.40; P<0.001	
Time to PSA progression (median)	11.2 mo	2.8 mo	8.3 mo	3.0 mo
	HR 0.17; P<0.001		HR 0.25; P<0.001	
PSA response rate (Pts with a ≥ 50% decline in PSA)	78%	3%	54%	2%
	P<0.001		P<0.001	
Objective response rate	59%	5%	29%	4%
	P<0.001		P<0.001	
Time to first symptomatic skeletal event (median)	31.1 mo	31.3 mo	16.7 mo	13.3 mo
	HR 0.72; P<0.001		HR 0.69; P<0.001	
Time to initiation of cytotoxic chemotherapy	28.0 mo	10.8 mo	NA	NA
	HR 0.35; P<0.001			
QoL	Median time until decline in FACT-P score*:-		10 point improvement in FACT-P:	
	11.3 mo	5.6 mo	43%	18%
	HR 0.63; P<0.001		P<0.001	

Green cells – statistically significant effect shown.

*The time to degradation of the FACT-P global score was defined as time from randomization to first assessment with at least a 10-point decrease from baseline in the total FACT-P score. FACT-P, Functional Assessment of Cancer Therapy–Prostate; HR, hazard ratio; mCRPC, metastatic castration resistant prostate cancer; mo, months; NA, not applicable; OS, overall survival; PSA, prostate specific antigen; Pts, patients; QoL, quality of life; rPFS, radiographic progression-free survival.1. Beer TM, et al. NEJM. 2014;371:424-33; 2. Scher HI, et al. NEJM. 2012;367:1187-97.

S H A R E

ENZALUTAMIDE IN mCRPC PATIENTS PREVIOUSLY TREATED WITH ABIRATERONE

- PSA response rate was much lower than that observed in abiraterone-naïve men with mCRPC in previous studies[2,3]

Effects of enzalutamide following abiraterone treatment[1]	
N	214
Trial	9785-CL-0410
	Single arm trial of 160 mg enzalutamide after ≥ 24 weeks of abiraterone acetate treatment plus prednisone
rPFS (median)	8.1 mo 95% CI: 6.1-8.3
OS (median)	Not Reached
Time to PSA progression (median)	5.7 mo 95% CI: 5.6-5.8
PSA response rate (Pts with a ≥ 50% decline in PSA)	27.0% 95% CI: 20-34

CI, confidence interval; mCRPC, metastatic castration resistant prostate cancer; mo, months; OS, overall survival; PSA, prostate specific antigen; Pts, patients; rPFS, radiographic progression-free survival.

1. de Bono JS, et al. Eur Urol. 2018;74:37-45; 2. Beer TM, et al. NEJM. 2014;371:424-33; 3. Scher HI, et al. NEJM 2012;367:1187-97.

EFFICACY OF ADDITIONAL TREATMENT OPTIONS

	Sipuleucel-T	
Patient population	mCRPC patients who had undergone ≤ 2 chemotherapy regimens	
Trial	IMPACT	
	Sipuleucel-T	Placebo
OS (median)	25.8 mo	21.7 mo
	HR 0.78; P=0.03	
Objective disease progression (median)	3.7 mo	3.6 mo
	HR 0.95; P=0.63	
Time to PSA progression (median)	NR	
PSA response rate (Pts with a ≥ 50% decline in PSA)	2.6%	1.3%
Objective response rate	NR	
Time to first symptomatic skeletal event (median)	NR	
Time to initiation of cytotoxic chemotherapy	NR	
QoL	NR	

Green cells – statistically significant effect shown.

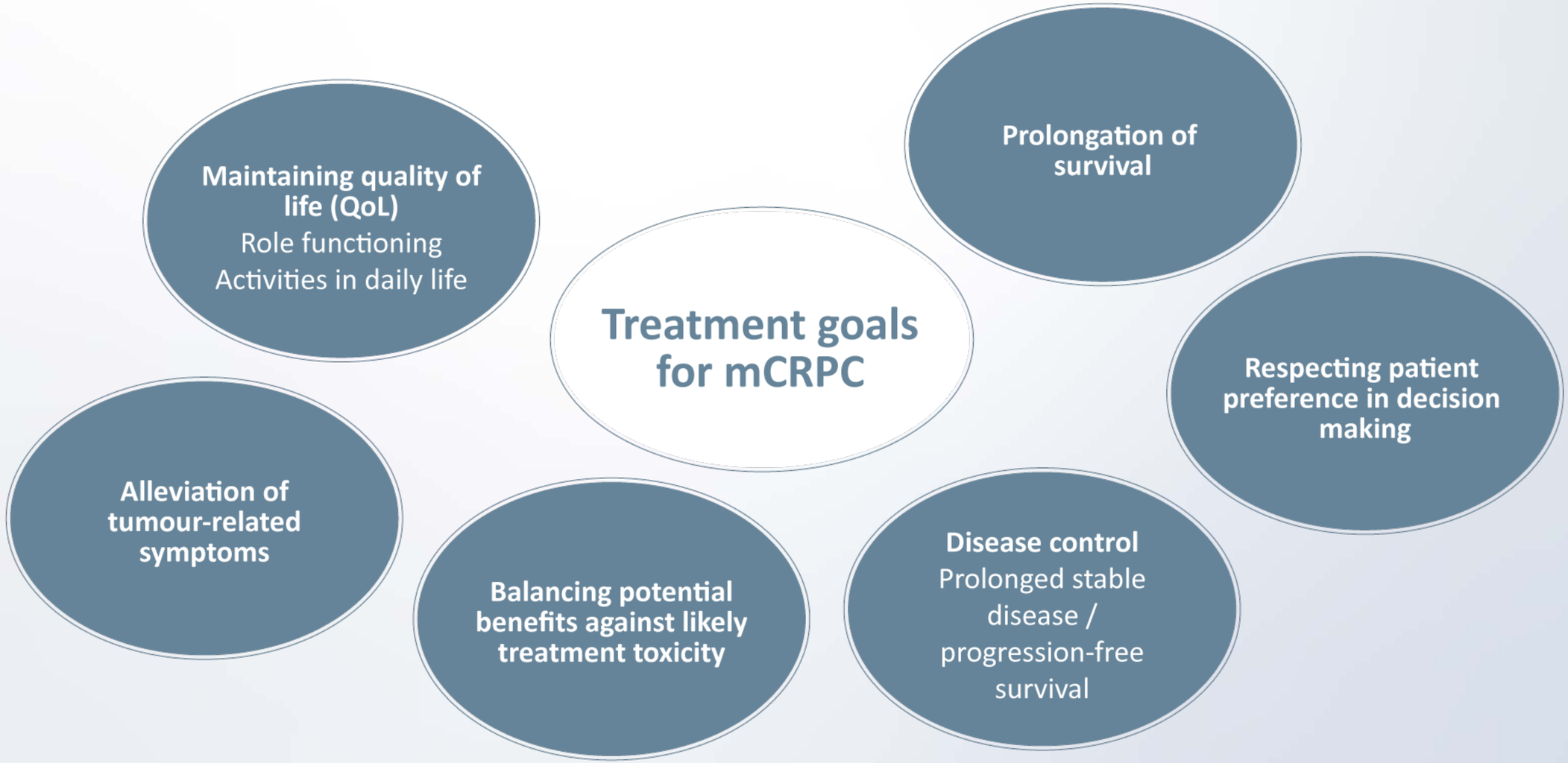
HR, hazard ratio; mCRPC, metastatic castration resistant prostate cancer; mo, months; NA, not applicable; NR, not reported; OS, overall survival; PSA, prostate specific antigen; Pts, patients; QoL, quality of life.

Kantoff PW, et al. NEJM 2010;363:411-22.

S H A R E

WHAT THE PHYSICIAN NEEDS TO KNOW

TREATMENT GOALS AND OPTIONS



mCRPC, metastatic castration resistant prostate cancer; QoL, quality of life.

WHAT NEEDS TO BE EXPLAINED
TO THE PATIENT

2-3 treatment options should be recommended based on patient's needs

The available treatments have been shown to **prolong survival by 2.2 to 4.8 months** in clinical trials compared to placebo or other active treatments[1-8]

Clinical trial options: the benefit the patient may derive from a clinical trial **depends on the treatments being compared**

Chemotherapy is not necessarily the **last treatment option** for a patient[9,10]

Explain **costs** of different treatments
(not relevant in all healthcare systems)

The treatment **recommendations** are proposed based on the **patient's disease status and preferences**[11]

The treatment recommendation for Peter is Radium-223

S H A R E

1. Tannock IF, et al. NEJM. 2004;351:1502-12; 2. Parker C, et al. NEJM. 2013;369:213-23; 3. Ryan CJ, et al. NEJM. 2013;368:138-48; 4. De Bono JS, et al. NEJM. 2011;364:1995-2005; 5. Ryan CJ, et al. Lancet Oncol. 2015;16(2):152-60; 6. Beer TM, et al. NEJM. 2014;371:424-33; 7. Scher HI, et al. NEJM. 2012;367:1187-97; 8. Kantoff PW, et al. NEJM 2010;363:411-22; 9. NCCN Clinical Practice Guidelines in Oncology (Prostate Cancer) Version 4, Aug 2019. Retrieved from: https://www.nccn.org/professionals/physician_gls/pdf/prostate.pdf. Access date: 03 Dec 2019; 10. de Wit R et al. NEJM 2019; 381: 2506-2518; 11. Caffo O et al. Clin Interv Aging 2017; 12: 19-28

HOW BEST TO INTERACT
WITH THE PATIENT

- Provide **fact-based** and **clear information**
- Explain the different options available
- **Remind the patient** that their **opinions are important**
- Communicate the **efficacy expectations** of the treatment options and **link these back to the patient's goals of therapy**

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STEP 3 - SUMMARY

ADVANTAGES AND DISADVANTAGES OF EACH TREATMENT OPTION

WHAT TO DO

- Share appropriate information that is fact-based and not misleading
- Physician to make a steer to one treatment, whilst maintaining a balanced view of alternatives
- Ensure plenty of pauses to allow the patient to consider and ask questions
- Physician to actively seek confirmation that the patient understands and to provide the opportunity for questions to be raised
- Physician to emphasise that patient’s opinions are valuable to them
- Focus on efficacy data at this point, postponing side effects until the different options, their relative benefits, and a potential treatment recommendation have been presented

STEP 3 - SUMMARY

ADVANTAGES AND DISADVANTAGES OF EACH TREATMENT OPTION

WHAT TO AVOID

- Avoid presenting so many ‘cons’ that patients will be reluctant to use particular treatments at a later stage of the disease. Painting a poor picture of medicines that the patient will need in the future will make later discussions for treatment more challenging
- Avoid making one treatment sound significantly better or worse based on the physician’s preferences. Patient preferences are what matter
- Avoid a monologue going into extensive technical detail
- Lack of patient involvement in the discussion with the patient having no ability or opportunity to ask questions or consider alternatives
- No insistence or reassurance from the physician that the patient’s opinions are equally valid

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STEP 4

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RISKS AND EFFECTIVE MANAGEMENT OF SIDE EFFECTS

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LEARNING OBJECTIVE

STEP 4: RISKS AND EFFECTIVE MANAGEMENT OF SIDE EFFECTS

WHAT
WILL YOU LEARN?

You will learn the importance of discussing the possible side effects of the proposed treatments with the patient and ensuring they understand that many of these can be effectively managed

WHY
IS THIS IMPORTANT?

To ensure the patient understands the full picture of the treatments being proposed and is prepared for what to expect over the coming months

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WHAT THE PHYSICIAN
NEEDS TO KNOW

LEARN MORE ABOUT THE SIDE EFFECTS OF OTHER POTENTIAL TREATMENT OPTIONS - when you see this symbol

- Clinical background and data that are essential to know at this stage of the conversation:
  - Common side effects of proposed treatments
  - Managing side effects of proposed treatments

DOCETAXEL

RADIUM-223

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COMMON SIDE EFFECTS WITH DOCETAXEL

LEARN MORE ABOUT THE SIDE EFFECTS OF OTHER POTENTIAL TREATMENT OPTIONS - when you see this symbol

Safety profiles reported in the prescribing information for docetaxel[1]:

DOCETAXEL

The most common all-grade adverse reactions across all docetaxel indications:

- Infection
- Hypersensitivity
- Neuropathy
- Dysgeusia
- Dyspnoea
- Constipation
- Anorexia
- Nail disorders
- Fluid retention
- Asthenia
- Pain
- Nausea
- Diarrhoea
- Vomiting
- Mucositis
- Alopecia
- Skin reactions
- Myalgia
- Haematotoxicity included anaemia, neutropenia, febrile neutropenia and thrombocytopenia

Peripheral neuropathy is a long-term side effect of taxane chemotherapy that may be persistent for patients after completion of treatment[2]

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1. Docetaxel Prescribing Information Jun 2019; 2.Hilkens PH et al. Ann Oncol 1997, 8: 187-190

COMMON SIDE EFFECTS WITH
RADIUM-223

LEARN MORE ABOUT THE SIDE EFFECTS OF OTHER POTENTIAL TREATMENT OPTIONS - when you see this symbol

Safety profiles reported in the prescribing information for radium-223[1] are:

RADIUM-223

The most common all-grade adverse reactions:*

- Diarrhoea
- Nausea
- Vomiting
- Peripheral oedema
- Haematotoxicity included anaemia, lymphocytopenia, leukopenia, neutropenia and thrombocytopenia

Bone marrow suppression has been observed (2%) – should not be used in combination with chemotherapy as a result

The combination of radium-223 plus abiraterone/prednisone is not recommended as it has been associated with an increased risk of bone fractures {ERA-223 study}[2]

Bone support with bisphosphonates or denosumab has been shown to prevent excess fractures whilst patients receive radium-223, particularly in combination with hormonal therapies[3]

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*The most common adverse reactions, as reported in the corresponding prescribing information, are those occurring in ≥10% of patients from the ALYSMPCA study

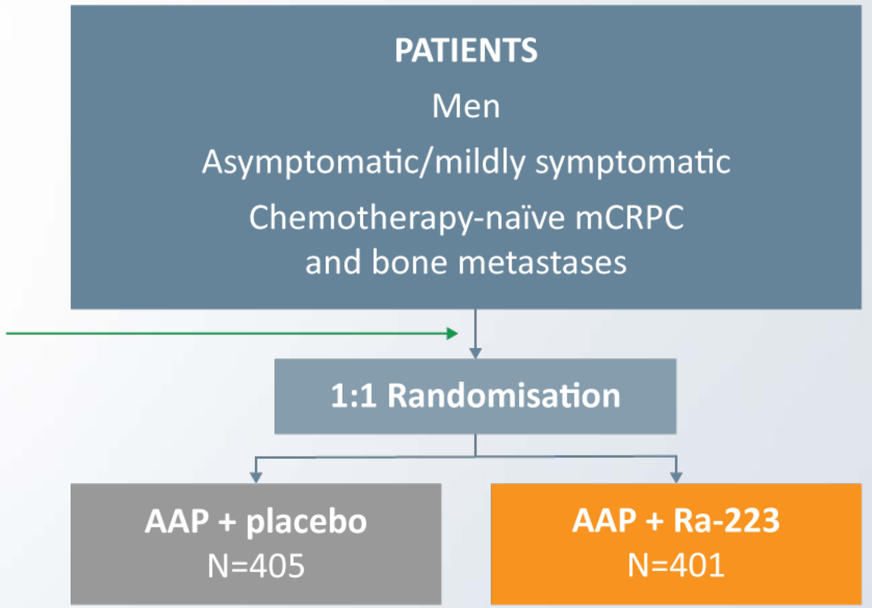
1. Radium-223 Prescribing Information Aug 2018; 2. Smith MR, et al. Lancet Oncology 2019; 408-419; 3. Tombal, B et al. JCO. 2019;37:5007

COMBINATION OF RADIUM-223 PLUS ABIRATERONE

ERA-223 STUDY

- Phase 3, double-blind, randomised
- Primary endpoint: SSE-FS

BONE HEALTH AGENTS (bisphosphonates or denosumab) were **only allowed in patients receiving them at baseline**



- The **combination of AAP + Ra-223 did not improve SSE-FS or OS compared with** AAP monotherapy[1]
  - This was unexpected, given both AAP and Ra-223 have been shown to improve OS in mCRPC[2-6]
- In addition, there **were more bone fractures with combination treatment compared with monotherapy**[1]
  - BHAs were used in less than half the patients despite them being recommended

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AAP, Abiraterone Acetate and Prednisone/Prednisolone; BHAs, Bone Health Agents; mCRPC, metastatic Castration-Resistant Prostate cancer; OS, overall survival; Ra-223, Radium-223; SSE-FS, Symptomatic Skeletal Events-Free Survival.

1. Smith MR, et al. Lancet Oncology 2019; 408-419; 2. Ryan CJ, et al. NEJM. 2013;368:138-48; 3. De Bono JS, et al. NEJM. 2011;364:1995-2005; 4. Ryan CJ, et al. Lancet Oncol. 2015;16(2):152-60; 5. Parker C, et al. NEJM. 2013;369:213-23; 6. Nilsson S et al. Ann Oncol 2016' 27: 868-874

FRACTURES
IN ERA-223

- November 2017 the IDMC recommended unblinding in November 2017 after noting more fractures and deaths in the abiraterone acetate/prednisone or prednisolone (AAP) + radium-223 arm than in the AAP arm
- 40% of the excess fractures in the AAP + Ra-223 occurred in the 6 first months
- Approx. 40% of the patients were receiving bone health agents (BHA) at entry
- In post-hoc analyses, BPA substantially impacted the rate of fracture in both arms (37% vs. 15% in Ra-223/AAP without vs. with BPA, respectively)

	AAP + radium 223	AAP + placebo
Patients with ≥1 fracture*, n	76	23
No bone metastasis at site of fracture, n	60	17
Type of fracture, n		
Pathological	19	6
Traumatic	27	13
Osteoporotic	37	4
Indeterminate	1	0

*Independent review of fractures was based on patients with fractures and available image scans: n=80 in AAP + radium-223 group, n=27 in AAP + placebo group.

AAP, abiraterone acetate and prednisone/prednisolone; BHA, bone health agents; IDMC, independent data monitoring committee;
Slide courtesy of Bertrand Tombal. Smith M, et al. Lancet Oncol. 2019;20(3):408-19

BONE FRACTURES AND CUMULATIVE INCIDENCE SAFETY POPULATION

PEACE III STUDY

Time point	Treatment and use of bone protecting agents			
	With exposure to BHA		Without exposure to BHA	
	Enza+Rad (N=39)	Enza (N=49)	Enza+Rad (N=37)	Enza (N=35)
	Cum Incidence (95% CI)*	Cum Incidence (95% CI)	Cum Incidence (95% CI)	Cum Incidence (95% CI)
3 months	0 (-)	0 (-)	0 (-)	5.7 (1.0-16.7)
6 months	0 (-)	0 (-)	5.6 (1.0-16.3)	8.8 (2.2-21.0)
9 months	0 (-)	0 (-)	22.6 (10.6-37.3)	8.8 (2.2-21.0)
12 months	**0 (-)**	**0 (-)**	**37.4 (21.8-53.1)**	**12.4 (3.9-26.2)**
15 months	0 (-)	0 (-)	43.6 (26.8-59.3)	16.6 (5.9-32.0)
18 months	0 (-)	0 (-)	43.6 (26.8-59.3)	16.6 (5.9-32.0)

* the one fracture in this group occurred at month 27

BHA, bone health agents; CI, confidence interval; Cum, cumulative; ENZA, enzalutamide; Rad, radium-223.

Tombal, B et al. JCO. 2019;37:5007.

COMMON SIDE EFFECTS OF OTHER TREATMENT OPTIONS

Abiraterone acetate[1]	Enzalutamide[2]	Sipuleucel-T[3]
The most common adverse reactions (≥10%) are fatigue, arthralgia, hypertension, nausea, oedema, hypokalaemia, hot flush, diarrhoea, vomiting, upper respiratory infection, cough, and headache.	The most common adverse reactions (≥10%) are asthenia/fatigue, decreased appetite, hot flush, arthralgia, dizziness/vertigo, hypertension, headache and decreased weight.	The most common adverse reactions reported in clinical trials (≥ 15% of patients receiving sipuleucel-T) are chills, fatigue, fever, back pain, nausea, joint ache, and headache.
The most common laboratory abnormalities (>20%) are anaemia, elevated alkaline phosphatase, hypertriglyceridaemia, lymphopenia, hypercholesterolaemia, hyperglycaemia, and hypokalaemia.	Seizure occurred in 0.4% of enzalutamide-treated patients. In patients with predisposing factors, seizures were reported in 2.2% of patients. Rare cases of posterior reversible encephalopathy syndrome (PRES) have been reported in enzalutamide-treated patients.	Most common (≥ 2%) grade 3-5 adverse events were back pains and chills.
The common adverse events (≥1%) resulting in discontinuation of abiraterone and prednisone were hepatotoxicity and cardiac disorders. Hepatotoxicity led to treatment discontinuation in 1.1% of the 2230 patients receiving abiraterone during clinical trials.	The most common adverse events resulting in discontinuation of enzalutamide in clinical trials were seizure (0.9% of patients in the AFFIRM study) and fatigue/asthenia (1% of patients in the PREVAIL study).	In clinical trials over 70% of patients experienced acute infusion reactions, such as chills, fatigue, fever, nausea, and joint ache.
		Sipuleucel-T should be used with caution in patients with risk factors for thromboembolic events.

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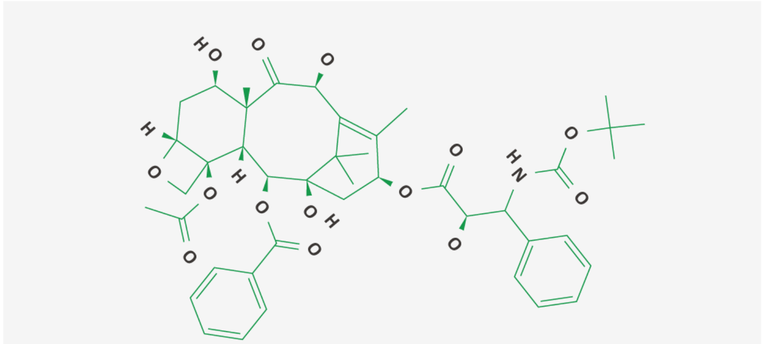
1. Abiraterone Prescribing Information June 2019; 2. Enzalutamide Prescribing Information July 2018; 3. Sipuleucel-T Prescribing Information July 2017

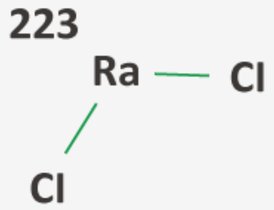
MANAGEMENT OF SIDE EFFECTS WITH
DOCETAXEL AND RADIUM-223

LEARN MORE ABOUT THE OTHER POTENTIAL TREATMENT OPTIONS
when you see this symbol

- Critical components of the effective management of side effects are:
  - Awareness of the patient's medical and treatment history
  - A close communication between the patients, caregivers and their healthcare team
  - Early identification and management of treatment-associated side effects can prevent them from worsening. Many side effects can be effectively managed with supportive measures and/or medication as well as treatment modification, thereby optimising treatment



Docetaxel Side Effects



Radium-223 Side Effects

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1. https://pubchem.ncbi.nlm.nih.gov/compound/148124. Accessed 06 Dec 2019; 2. https://www.drugs.com/ingredient/radium-223-dichloride.html. Accessed 06 Dec 2019

MANAGEMENT OF SIDE EFFECTS WITH DOCETAXEL

Management of common side effects with docetaxel[1]	
	Management
Febrile neutropenia	• Patients who experience febrile neutropenia, neutrophils < 500 cells/mm^3 for more than one week, should have the dosage reduced from 75 mg/mm^2 to 60 mg/mm^2. If patient continues to experience these symptoms at the lower dose then the treatment should be stopped.
Fluid retention and hypersensitivity reactions	• For mCRPC, given the concurrent use of prednisone, the recommended premedication regimen is oral dexamethasone 8 mg at 12 hours, 3 hours, and 1 hour before the docetaxel infusion to reduce the incidence and severity of fluid retention and hypersensitivity reactions
Oral mucositis[2]	• Prescription treatments (antifungals, antibacterials, antivirals) • Practice of good oral care • Hydration – keep mouth moist either by rinsing with water or saline • Avoid spicy foods, citric acid in foods and alcohol • Eating soothing foods
Neuropathy	• Patients who experience moderate neurosensory signs and/or symptoms should have the dosage reduced from 75 mg/mm^2 to 60 mg/mm^2. If patient continues to experience these symptoms at the lower dose then the treatment should be stopped.

1. Docetaxel Prescribing Information Jun 2019; 2. http://chemocare.com/chemotherapy/side-effects/mouth-sores-due-to-chemotherapy.aspx. Accessed 06 Dec 2019

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MANAGEMENT OF SIDE EFFECTS WITH RADIUM-223

Management of common side effects with radium-223	
	Management
Haematological toxicity	• Haematological evaluations should be performed prior to starting radium-223 and prior to each subsequent dose • Prior to initial dose, ANC ≥1.5 x 10^9/L, platelets ≥100 x 10^9/L, haemoglobin ≥10 g/dL. Prior to subsequent doses, ANC ≥1.0 x 10^9/L, platelets ≥50 x 10^9/L • Treatment should be discontinued if haematological values do not recover within 6-8 of last treatment despite best supportive care. Monitor patients with compromised bone marrow reserve closely
Diarrhoea	• Diarrhoea is a commonly reported adverse event during treatment with radium-223 which may result in dehydration • Monitor patients' oral intake and fluid status carefully and promptly treat patients who display signs or symptoms of dehydration or hypovolemia.

ANC, absolute neutrophil count.

1. Radium-223 Prescribing Information Aug 2018.

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MANAGING SIDE EFFECTS OTHER TREATMENT OPTIONS

Abiraterone acetate[1]	Enzalutamide[2]	Sipuleucel-T[3]
For patients with baseline moderate hepatic impairment (Child-Pugh Class B), reduce the abiraterone starting dose to 250 mg once daily. No dose adjustment necessary for renal impairment.	No dose adjustment required for hepatic impairment. No dose adjustment necessary for mild to moderate renal impairment. Dosing not defined for CrCL <30 mL/min.	To manage infusion reactions, decrease the infusion rate or stop the infusion and administer appropriate medical treatment such as acetaminophen, intravenous H1 and/or H2 blockers, and low-dose intravenous meperidine
For patients who develop hepatotoxicity during treatment, hold abiraterone until recovery. Retreatment may be initiated at a reduced dose. Abiraterone should be discontinued if patients develop severe hepatotoxicity.	If a patient experiences a ≥ grade 3 toxicity or an intolerable adverse reaction, dosing should be withheld for one week or until symptoms improve to ≤ grade 2, then resumed at the same or a reduced dose (120 mg or 80 mg) if warranted	Leukapheresis using a central venous catheter is associated with an increased risk of infections and venous vascular event and this should be factored into decision making[4]

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CrCL, creatinine clearance

1. Abiraterone Prescribing Information June 2019; 2. Enzalutamide Prescribing Information July 2018; 3. Sipuleucel-T Prescribing Information July 2017; 4. Flanigan R et al. Journal of Urology 2013, 189: 521-526

WHAT NEEDS TO BE EXPLAINED
TO THE PATIENT

Which side effects they may experience from each treatment option

That they **will not get all side effects** and **not necessarily in severe form**

How the side effects can be managed and treatment adjusted to maximise their QoL whilst managing their disease

That they need to **inform the physician of the side effects** as and **when they arise**

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QoL, quality of life.

HOW BEST TO INTERACT
WITH THE PATIENT

- **Openly discuss side effects**, provide context in terms of expected frequency and **listen to patient's concerns**
- **Focus on side effect management.** Reassure patient that side effects can often be alleviated by holding or reducing the dose or adding supportive care
- Provide a reminder that **it is difficult to predict which side effects may be experienced as well as the severity of these**
- Encourage patient to **report side effects to the clinic as early as possible** as early intervention is generally more effective

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STEP 4 - SUMMARY

RISKS AND EFFECTIVE MANAGEMENT OF SIDE EFFECTS

WHAT TO DO

- Have an open discussion around side effects providing details regarding different side effects
- Listen to the patient’s concerns
- Focus on how the different side effects may be managed
- Reiterate that every patient is different to help manage expectations
- Prepare the patients for what they may expect so that they are confident and reassured that side effects can be managed

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STEP 4 - SUMMARY

RISKS AND EFFECTIVE MANAGEMENT OF SIDE EFFECTS

WHAT TO AVOID

- Avoid giving the impression that side effects are inevitable and that there is nothing we can do to reduce, prevent or reverse them
- Do not suggest any side effects take a treatment off the option list because patients will need to use most treatments in the future
- Don’t brush side effects quickly aside
- Don’t generalise side effects rather than mention them individually
- Don’t leave the patients with no idea what they may expect so they are not reassured to start treatment

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STEP 5

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EXPECTATION FOR TREATMENT SUCCESS

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LEARNING OBJECTIVE

STEP 5: EXPECTATION FOR TREATMENT SUCCESS

WHAT
WILL YOU LEARN?

You will learn the importance of discussing ‘Expectation for treatment success’ with the patient at the right point in the conversation and in the appropriate manner

WHY
IS THIS IMPORTANT?

To end the discussion with the patient on a positive note by reminding them of the treatment goal and what success could look like if the patient follows the treatment plan

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WHAT THE PHYSICIAN
NEEDS TO KNOW

- **All** available treatments will **provide clinical benefit** for mCRPC patients
- The physician needs to have sufficient knowledge of the **prescribing information and published data** as outlined in this e-learning to be able to convey these benefits to the patient in a way that aligns with the patient's personal goals

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mCRPC, metastatic castration resistant prostate cancer.

WHAT NEEDS TO BE EXPLAINED
TO THE PATIENT

Reaffirm the goal of treatment that has been decided upon – control of disease, improve survival whilst maintaining a good QoL

What to expect next, **who to contact and when**

Connect with other support groups

E.g. oncology nurse, pysch- oncologist

The patient is in control of their treatment journey, the medical team will partner with them but this is a joint decision and the patient has choices

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QoL, quality of life.

HOW BEST TO INTERACT
WITH THE PATIENT

- **End** the conversation on a **positive note** and give the patient something to aim for
- Offer **printed materials** for the patient to take away
- Return to the **patient's original goals** of treatment
- Check to **confirm** patient and caregiver's **understanding** and allow time for further questions

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STEP 5 - SUMMARY
EXPECTATION FOR TREATMENT SUCCESS

WHAT TO DO

- End the conversation on a positive note and give the patient something to ‘shoot for’
- Offer written materials for the patient to take away and consider
- Reassurance that the decision is being made jointly
- Return to the patient’s aim that has been established at the start of the discussion – attending a particular family event for example
- Checking to confirm patient understanding or allowing the opportunity for more questions – at the time or providing point of contact for after the discussion
- Not putting the patient under pressure to decide at the end of the discussion but allowing time to go away and think
- Engage with caregiver to check no additional perspective has been missed and that they understand discussion that has been held
- Setting out what the expected next steps will be

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STEP 5 - SUMMARY
EXPECTATION FOR TREATMENT SUCCESS

WHAT TO AVOID

- Pressurised decision making
- Not ending the discussion on a positive note around what success can look like - never remove hope from the patient
- Don’t be overly optimistic and give false expectations
- No reflection on the patient’s view of what successful treatment means for them
- No sense-checking that the patient fully understands or feels appropriately involved
- Decision made on a purely clinical basis
- Allowing the conversation to end with side effects as front of mind
- No access given to further reading or information
- Ambiguity about next steps

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SUMMARY & CLOSE

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BEFORE YOU GO

- **Thank you** for participating in this educational programme on the SHARE communication framework
- You should now **feel more confident** to educate and empower patients treated for mCRPC and be able to respond to a fully comprehensive range of questions
- You now **know**
  - **how to explain** the aspects of mCRPC and its treatment that are essential for the patient to understand
  - **how to optimise your support** for patients, to enhance understanding and to drive adherence
  - **and how to apply the SHARE framework** across a variety of interactions, to strengthen shared decision-making and to deliver the best possible care
- We hope you have found this useful for your daily practice

- Throughout this educational programme there are **links to additional information and resources**.
- At **www.guconnect.info** you will find the full video on the SHARE framework, as well as many other initiatives from the GU CONNECT group

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REMINDER OF THE **SHARE** COMMUNICATION FRAMEWORK

SHARE is a 5-step communication framework to enable shared decision-making in physician–patient interactions, that recommends the following communication points:

Success criteria and aim of treatment — **S**

How the treatments work — **H**

Advantages and disadvantages of each treatment option — **A**

Risks and effective management of side effects — **R**

Expectation for treatment success — **E**

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SUPPORTED BY US TOO INTERNATIONAL

Us TOO International is a nonprofit that serves the prostate cancer community by providing educational materials and resources at no charge.

Established in 1990, the organization was founded by-and continues to be governed by-people directly affected by prostate cancer. In addition to the following list of Us TOO educational resources and support services, there are more than 200 support groups throughout the U.S. and abroad that also help men and their spouses/partners and families make informed decisions about prostate cancer detection, treatment options and related side effects.

- Us TOO website (www.ustoo.org)
- Support group meetings/services & telephone support group
- Support group leader resources
- Inspire online prostate cancer communities (UsTOO.inspire.com)
- For more information or support, call 1-800-808-7866, email **ustoo@ustoo.org**, or visit www.ustoo.org including matching callers with similar survivors for peer-to-peer conversations
- Personalised connections for one-to-one support
- Monthly Hot SHEET newsletter
- Frequent 'News You Can Use' updates and articles
- Educational videos on informed decision making
- Educational content - digital and printed
- Genetics & Genomic Testing
- Educational events and presentations
- Military veterans resources - Agent Orange information
- Anxiety & depression and Prostate Cancer
- Special events like the SEA Blue Chicago Prostate Cancer Walk & Run and numerous local events across the country

More than 160,000 men are diagnosed with prostate cancer every year. While approximately 27,000 men die from the disease annually, there are nearly 3 million men living in the United States today who have been diagnosed with prostate cancer and are managing the disease. This number is estimated to reach 4.2 million men by the year 2024. These men and their spouses/partners and loved ones need information about various treatment options available for minimizing the impact of the disease while maximizing the quality of life.

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COR2ED CHECKPOINT

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ACCME ACCREDITED

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ABIM CME MOC ACCREDITED

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ABBREVIATIONS

- **AAP,** Abiraterone Acetate and Prednisone/Prednisolone
- **ACTH,** adrenocorticotropic hormone
- **ADT,** androgen deprivation therapy
- **ANC,** absolute neutrophil count
- **APC,** antigen presenting cell
- **AR,** androgen receptor
- **AUA,** American Urology Association
- **BHAs,** Bone Health Agents
- **CD,** cluster of differentiation
- **CI,** confidence interval
- **CrCL,** creatinine clearance
- **CRPC,** castration resistant prostate cancer
- **CT,** computed tomography
- **Cum**, cummulative
- **CYP**, cytochrome
- **dMMR**, mismatch repair deficient
- **DHEA**, dehydroepiandrostenedione
- **EAU**, European Association of Urology
- **ECOG**, Eastern Cooperative Oncology Group
- **Enza**, enzalutamide
- **EQ-5D**, EuroQol-5D
- **FACT-P**, Functional Assessment of Cancer Therapy–Prostate
- **GM-CSF**, granulocyte-macrophage colony-stimulating factor
- **GU**, genitourinary
- **HR,** hazard ratio
- **IDMC,** independent data monitoring committee
- **kBq,** kilobecquerel
- **keV,** kiloelectron volt
- **KPS,** Karnofsky performance status
- **LHRH,** luteinizing hormone releasing hormone
- **mCI,** microcurie
- **mCRPC,** metastatic castration resistant prostate cancer
- **MBq,** megabequerel
- **mGY,** milligray
- **MOA,** mechanism of action
- **MSI-H,** microsatellite instability-high
- **NCCN,** National Comprehensive Cancer Network
- **NR,** not reported
- **OS,** overall survival
- **PAP,** prostatic acid phosphatase
- **PFS,** progression-free survival
- **PPI,** present pain intensity
- **PS,** performance status
- **PSA,** prostate specific antigen
- **QoL,** quality of life
- **223Ra,** radium-223
- **Rad,** radium
- **rPFS,** radiographic progression-free survival
- **RR,** relative risk
- **SSE-FS,** Symptomatic Skeletal Events-Free Survival

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