North of Scotland Clinical Management Guideline (CMG): Prostate Cancer Last Updated 27/04/2023

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For symptoms of suspected urological cancers, please refer to the Scottish Referral Guidelines for Suspected Cancer

General Principles

- All patients referred with a suspicion of prostate cancer need to be treated equally whether referred as USC, Urgent or Routine by referral GP / HCP / other speciality.
- All patients must be discussed at MDT meeting throughout their patient journey as required.
- Patients should be vetted in accordance with the Scottish Referral Guidelines for Suspected Cancer.
- Where available, clinical trials should always be considered as an option for all eligible patients and consideration given to referral to other Scottish boards.
- Patients must be involved in decision-making relating to their care with informed consent required for patients undergoing treatment.
- All patients should be referred to or made aware of the Clinical Nurse Specialist services available in the North of Scotland, for assessment and ongoing advice, education, support and coordination.
- The wishes of the patients must influence decision-making with respect to treatment choices within this CMG.
- A list of SACT regimens is provided (page 12).
- Full regional SACT Protocols will be developed and linked to from this document.

Initial Evaluation

- Symptoms – IPSS
- Urine flow – Qmax and PVR
- Prostate examination including accurate sizing
- Co-morbidities / life expectancy / ECOG performance status
- PSA density and PSA trend
- Clinical T stage
  (see page 13 for TNM classifications)
- Use nomograms to aide patient discussion

Contents

Diagnosis and Staging – multi-parametric MRI

If after initial assessment, patient wants to consider further investigations all patients with suspected clinically localised prostate cancer who would be suitable for and agreeable to radical treatment should have a pre-biopsy multi-parametric MR (unless an MR is contraindicated).

MR Scans with PI-RADS 3-5 should proceed with biopsy.

MR Scans with PI-RADS 1-2 but high clinical suspicion of prostate cancer should proceed with biopsy, after discussion with patient.

MR Scans with PI-RADS 1-2 but low clinical suspicion of prostate cancer should be discussed with patient and decision regarding follow-up made.

Diagnosis and Staging – biopsy

Transrectal biopsy is considered the standard approach in the North of Scotland. However, transperineal biopsies should also be considered due to the reduced risk of infection. The NCA Urology Pathway Board supports the use of transperineal biopsies.

A minimum of 10 cores should be taken with specific cores from suspicious lesions visible on MR, for suspected T2 disease or less (less biopsies required for patients with advanced disease).

Hospitals with image-guided techniques can use these to aid targeted biopsies, however standard peripheral zone biopsies should still be performed.

North of Scotland Clinical Management Guideline (CMG): Prostate Cancer evaluation Last Updated 27/04/2023

Radiological Staging	MDT	Risk Stratification

MR should be part of initial evaluation of all patients unless high risk of metastases

↓

<u>Cross-sectional imaging with CT (chest abdomen & pelvis) if MRI is contraindicated</u>

*Patient has metastatic disease on bone scan

*If very high risk patients with high suspicion of metastatic disease

↓

<u>Isotope bone scan if:</u>

*PSA≥ 20

*Grade group ≥ 3, or other aggressive feature on pathology

*Suspicion of bony metastases, T3 disease or N1 disease on MR or raised alkaline phosphatase or metastatic symptoms

Note: If available, Whole Body Diffusion MR can be used as additional investigation

All patients discussed at Urology MDT prior to definitive treatment

→ **<u>Localised Disease (N0 M0)</u>**

Low risk
Clinical / radiological / pathological T1 / T2a and PSA <10 and Gleason score =6

Intermediate risk
All others

High risk
Clinical / radiological / pathological T3a+ or PSA>20 or Gleason score >= 8

→ *See Page 4*

→ **<u>Pelvic nodal metastases</u>**
Tany N1 M0

→ **<u>Distant metastases</u>**
Tany Nany M1

→ *See Pages 6 & 7*

Treatment

See page 3 for risk categorisation

Low risk disease

- Active surveillance
- Brachytherapy (see page 12)
- Radical Radiotherapy
- Robitically-assisted Radical Prostatectomy
- Watchful waiting

Intermediate risk disease including T2c

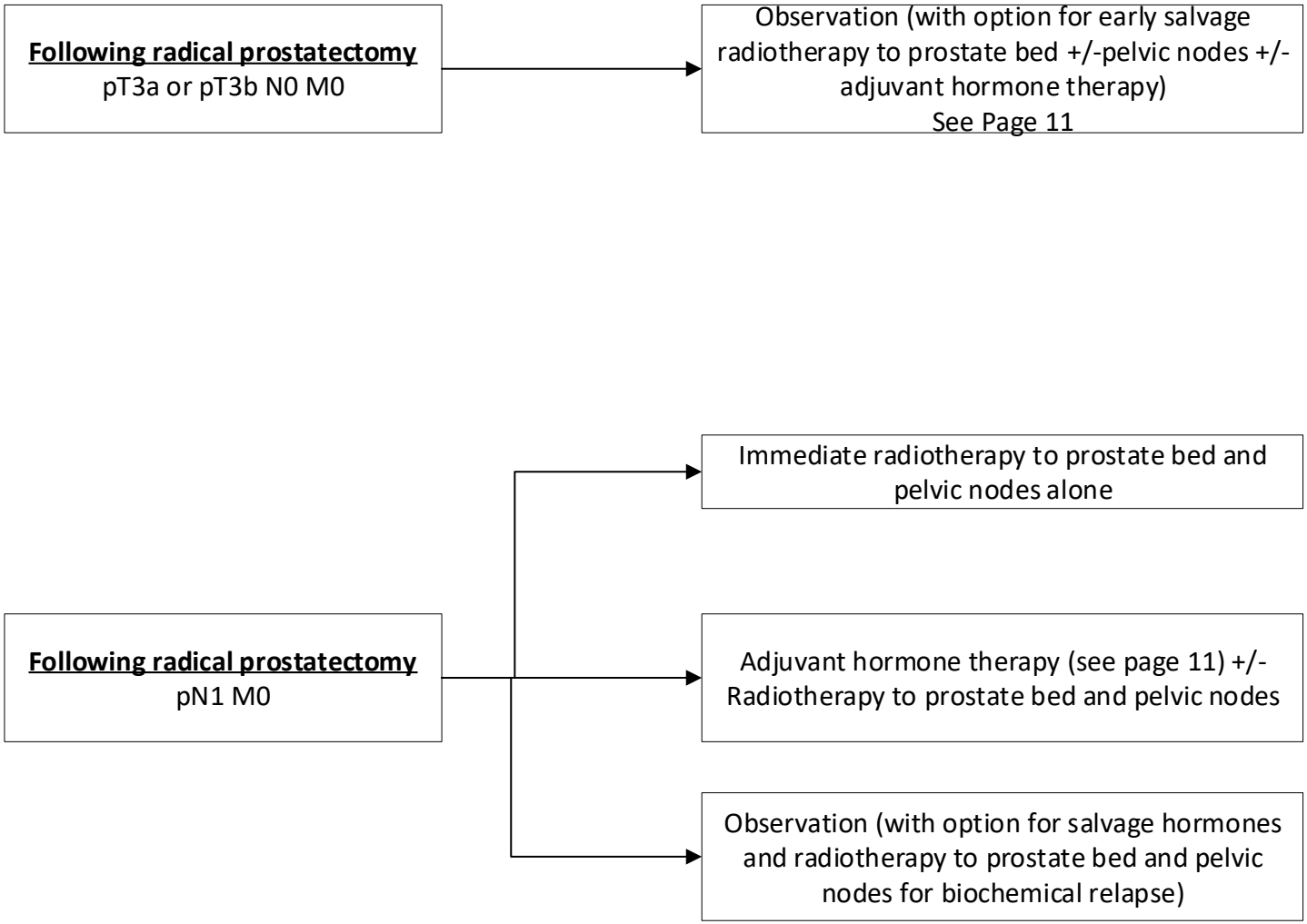
- Active surveillance (in selected patients)
- Brachytherapy (see page 12)
- Radical Radiotherapy
- Robitically-assisted Radical Prostatectomy
- Watchful waiting
- Hormone therapy for 6 months (see page 11) + radical radiotherapy

High risk disease

- Hormone therapy for 24-36 months (see page 11) and radical radiotherapy and consider Docetaxel in patients with grade group 5
- Watchful waiting
- Robotically-assisted Radical Prostatectomy + pelvic nodes with discussion re: possibility of adjuvant / salvage radiotherapy

National Cancer Medicines Advisory Group (NCMAG102) Advice (12 Jan 2023)
Abiraterone plus prednisolone in addition to androgen deprivation therapy for adults with high-risk hormone-sensitive non-metastatic prostate cancer. Off-label use is support for generic abiraterone acetate products.
For access to the full advice document, see the NCMAG webpage link from the NCA webpage.

Clinical Scenario	Adjuvant Treatment



North of Scotland Clinical Management Guideline (CMG): Prostate Cancer – Castrate Resistant - Non-Metastatic Disease

Last Updated 27/04/2023

Evaluation	Treatment

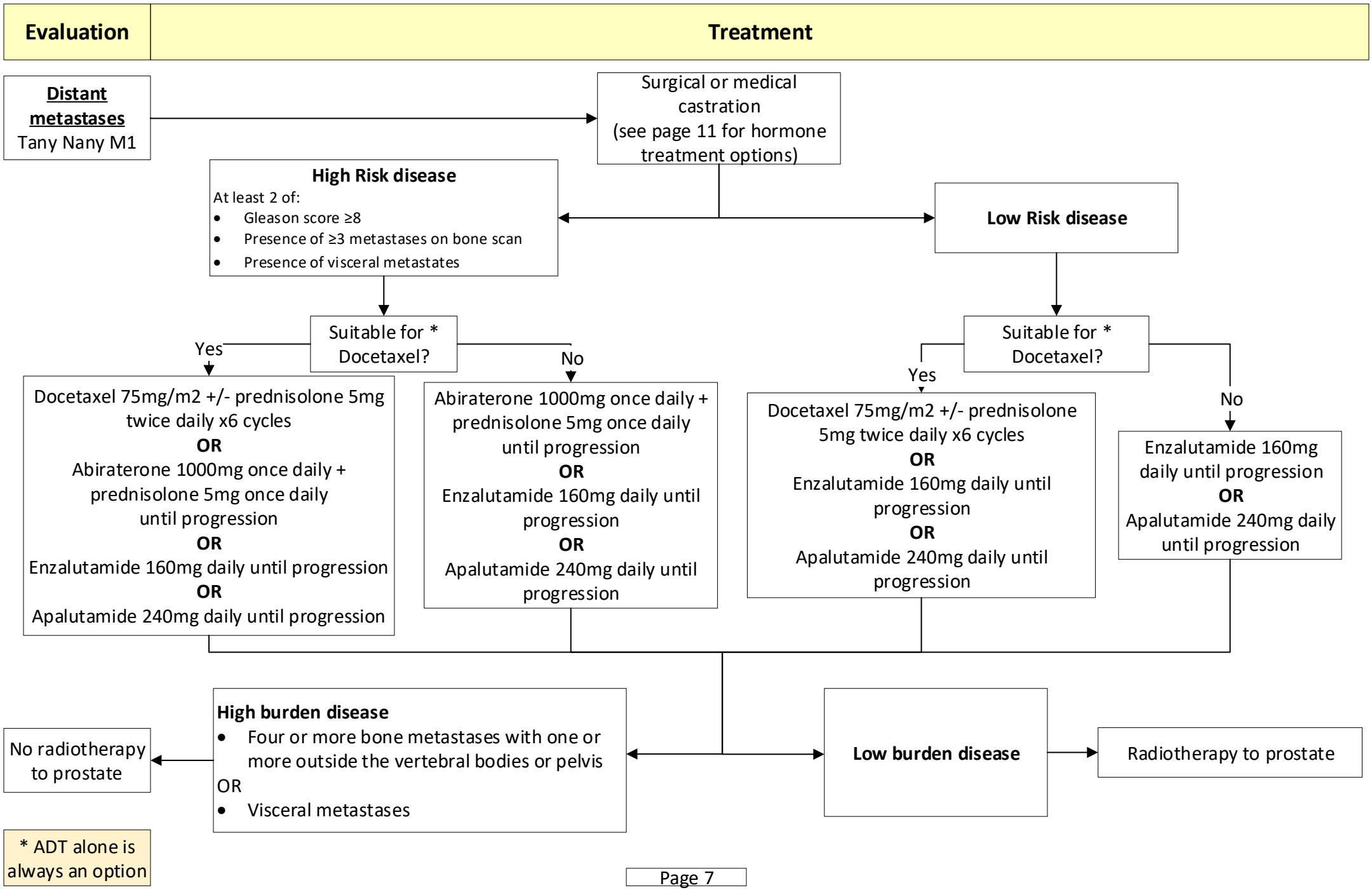
Stage
Tany Nany M0

→ PSA ≥2ngl/mL (with doubling time <10months*)
Calculated based on ≥3 recent PSAs

→ Darolutamide 600mg twice daily with food

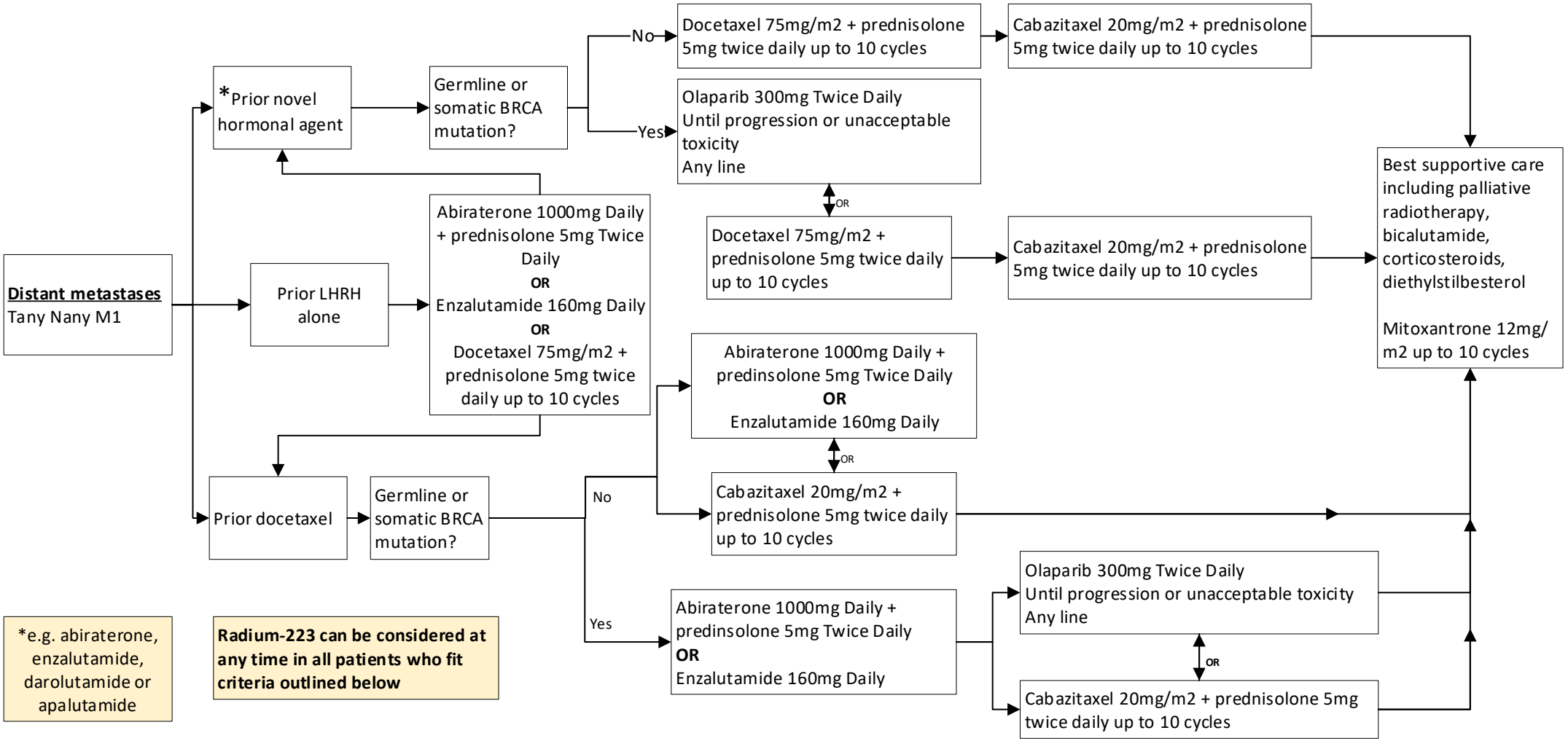
Doubling time should be calculated based on at least 3 recent PSA readings

North of Scotland Clinical Management Guideline (CMG): Metastatic Hormone Sensitive Prostate Cancer Last Updated 27/04/2023



North of Scotland Clinical Management Guideline (CMG): Metastatic – Castrate Resistant Prostate Cancer Last Updated 27/04/2023

Evaluation	Treatment



Notes 1. Palliative radiotherapy available at any point in the pathway; 2. Docetaxel may be initiated in patients who are symptomatic or asymptomatic; 3. Radium-223 is not permitted for patients with non-lymph node visceral disease; 4. Radium-223 is only permitted with symptomatic bone metastases; 5. Radium-223 should not be used simultaneously with abiraterone or enzalutamide. In particular combination with abiraterone may be unsafe; 6. Radium-223 should only be used in progression after at least two prior lines of systemic therapy for mCRPC (other than LHRH analogues) or if ineligible for any available systemic mCRPC treatment; 7. Radium should not be considered for patients with only a low number of bone metastases; 8. Patients may move to best supportive care at any point in the pathway; 9. Abiraterone / enzalutamide should only be used if no prior darolutamide (or similar) in the non metastatic setting. 10. Olaparib monotherapy indicated for the treatment of adult patients with metastatic castration-resistant prostate cancer and BRCA 1/2 mutations (germline and/or somatic) who have progressed following prior therapy that included new hormonal agent. 11. Determination of BRCA mutational status will be subject to availability of routine testing.

North of Scotland Clinical Management Guideline (CMG): Prostate Cancer local relapse Last Updated 27/04/2023

Clinical Scenario	Evaluation	Management options

Following radical prostatectomy
Rising PSA on 2 occasions with second rise reaching minimum of 0.1ng/l

Following brachytherapy relapse defined as:
At least 2 consecutive PSA rises reaching a minimum of nadir PSA+ 2
(be aware of the possibility of PSA bounce)

Following radiotherapy
Relapse defined as: at least 2 consecutive PSA rises, reaching a minimum of nadir PSA +2.

→ **Assess:**
*patient fitness for salvage therapy
*chance of prostate bed only relapse

Increasing chance:
+ve margins
Gleason score 6-7
No SV or nodal involvement
Nadir PSA <0.1
Increased time to relapse slow rising PSA

→ MDT

→ Discussion with patient re: relative risks of systemic vs. prostate bed relapse and consider staging MRI/CT and bone scan if clinically appropriate

PSMA PET-CT scan can be used where available

→ Salvage Radiotherapy to prostate bed (+/- pelvic nodes) +/- neoadjuvant hormone therapy (see page 11)

→ Consider hormone therapy alone (consider intermittent androgen ablation) (see page 11)

→ Watchful Waiting

→ MDT

→ Consider restaging MRI +/- bone scan with biopsy if required

PMSA PET-CT scan can be used where available

→ Watchful Waiting

→ Salvage prostatectomy

→ Salvage cryotherapy

→ Salvage brachytherapy

Eligibility

Men diagnosed with localised prostate cancer who are fit for radical therapy and;
- have stage T1c (ie all patients must have had a needle biopsy (not TURP alone) or clinical T2a disease
- PSA <10ng/ml
- Gleason score 3+3=6, consider low volume 3+4
- no greater than 50% of any core involved by tumour
- less than or equal to 3 cores (of 10) involved with tumour
- PSA density <=0.2 (based on TRUS biopsy prostate size)
- MRI prostate shows no adverse features (large volume, likely undersampling on biopsy, extracapsular disease, SV invasion)
- willing to pursue active surveillance, and willing to receive radical therapy if indicated

Certain men with higher risk disease may wish to pursue active surveillance and may do so, although it may not be recommended by MDT

NICE National Institute for Health and Care Excellence

Timing	Tests [a]
Year 1 of active surveillance	Every 3 to 4 months: measure prostate-specific antigen (PSA)[b] Throughout active surveillance: monitor PSA kinetics[c] At 12 months: digital rectal examination (DRE)[d] At 12 to 18 months: multiparametric MRI
Year 2 and every year thereafter until active surveillance ends	Every 6 months: measure PSA[b] Throughout active surveillance: monitor PSA kinetics[c] Every 12 months: DRE[d]

[a] If there is concern about clinical or PSA changes at any time during active surveillance, reassess with multiparametric MRI and/or re-biopsy.

[b] Could be carried out in primary care if there are agreed shared-care protocols and recall systems.

[c] Could include PSA density and velocity.

[d] Should be performed by a healthcare professional with expertise and confidence in performing DRE. In a large UK trial that informed this protocol, DREs were carried out by a urologist or a nurse specialist.

This guideline updates and replaces NICE guideline CG175 (January 2014) and NICE diagnostics guidance 17 (June 2015).

Indications for further investigation

Any concerning changes in PSA characteristics should indicate repeat MRI. Repeat biopsies indicated if progression on MRI. If there is no progression on MRI but PSA continues to rise, then DRE +/- biopsies should be considered.

Indications for continued active surveillance

- No clinical progression on DRE or other examination
- PSAdt>10 years
- No changes on 12month MR

Indications for discontinuing active surveillance

- Patient preference for radical therapy
- Gleason grade 4 on biopsy
- PSAdt<3years
- Increasing volume of disease

If any of the above apply, then patient referred for surgery, radiotherapy or brachytherapy as appropriate

- Patient no longer fit for radical therapy – **adopt watching waiting**
- Development of metastatic disease – **see pages 6 & 7**

*SACT Regimen	Treatment Intent
Abiraterone (hormone sensitive - HS)	Non-curable
Abiraterone (castrate resistant - CR)	Non-curable
Abiraterone (hormone sensitive - HS) - non-metastatic	Curable
Apalutamide (hormone sensitive - HS)	Non- curable
Cabazitaxel (castrate resistant - CR)	Non-curable
Darolutamide (castrate resistant - CR) - non-metastatic disease	Non-curable
Docetaxel 75mg/m^2 3 weekly (hormone sensitive - HS) - metastatic	Non-curable
Docetaxel 75mg/m^2 3 weekly (hormone sensitive - HS) - non-metastatic	Curable
Docetaxel 75mg/m^2 3 weekly (castrate resistant - CR)	Non-curable
Docetaxel 25mg/m^2 weekly (castrate resistant - CR)	Non-curable
Enzalutamide (castrate resistant - CR)	Non-curable
Enzalutamide (hormone sensitive - HS)	Non-curable
Mitoxantrone	Non-curable
Olaparib	Non-curable
Radium 223	Non-curable

*Until Regional SACT Protocols are developed, full details of each agreed SACT Regimen may be found on the Bladder Cancer SACT Regimen Spreadsheet, hosted on the NCA website

LHRH analogues and anti-androgen therapy

Selection and availability of these agents depends on local formulary status, patient factors and national contracts.

Brachytherapy services for prostate cancer are delivered by referral to either the Western General Hospital, Edinburgh, or the Beatson Cancer Centre, Glasgow. Eligibility criteria as below.

Edinburgh Cancer Centre

Real-time USS guided LDR brachytherapy using radioactive Iodine^{125} seeds. In ECC, we use stranded seeds. Our local audit shows a 5-year PSA relapse free survival of 94% (low risk), 81% (intermediate risk).

Treatment option if:

- Low risk prostate cancer
- Selected intermediate / high risk
  (GS 6/PSA ≤ 20, GS 7/PSA ≤ 15)
- Highly selected low volume (GS 8 – 10/PSA ≤ 10)

Patient factors:

- Prostate volume ≤ 50cc (consider 3 months LHRHa if larger, up to 70cc)
- Q Max ≥10mls/second and low residual bladder volume (<150mls)
- IPSS <15 with minimal obstructive symptoms
- No previous TURP
- High number/% of prostate biopsy cores involved is a relative contraindication
- Pubic arch interference may be identified at volume study (using a 2 step procedure)

Prescribed Dose:

145Gy to prostate
≥99.5% of volume to receive 145Gy
70% of prostate volume to receive ≤150%=217.5Gy
<25% of prostate to receive 200%=290Gy
Ideally D90 dose >145 Gy

Beatson Cancer Centre

Men diagnosed with localised prostate cancer who are fit for radical therapy and have:

- Low risk disease or one low-intermediate risk feature (eg. Gleason 3+4=7 or PSA 10-15)
- No TURP within 9 months
- No significant urinay obstructive symptoms
- IPSS score <=10
- Qmax >10
- Prostate size on MRI or TRUS of <50cc (occasionally patients with prostate size upto 60cc will be accepted onto programme with prior hormone therapy)
- No suspicion of extracapsular disease or seminal vesicale invasion on MRI

TNM Staging for Prostate (ICD-O-3 C61.9) Union for International Cancer Control (8th Edition; 2017)		
Primary Tumour (T)		
Tx	TX Primary tumour cannot be assessed	
T0	No evidence of primary tumour	
	Clinically inapparent tumour that is not palpable	
T1	**T1a**	Tumour incidental histological finding in 5% or less of tissue resected
	T1b	Tumour incidental histological finding in more than 5% of tissue resected
	T1c	Tumour identified by needle biopsy (e.g., because of elevated PSA)
	Tumour that is palpable and confined within prostate	
T2	**T2a**	Tumour involves one half of one lobe or less
	T2b	Tumour involves more than half of one lobe, but not both lobes
	T2c	Tumour involves both lobes
	Tumour extends through the prostatic capsule**	
T3	**T3a**	Extracapsular extension (unilateral or bilateral) including microscopic bladder neck involvement
	T3b	Tumour invades seminal vesicle(s)
T4	Tumour is fixed or invades adjacent structures other than seminal vesicles: external sphincter, rectum, levator muscles, and/or pelvic wall	
Note	*** Invasion into the prostatic apex or into (but not beyond) the prostatic capsule is not classified as T3, but as T2.*	
Regional Lymph Nodes (N)		
Nx	Regional lymph nodes cannot be assessed	
N0	No regional lymph node metastasis	
N1	Regional lymph node metastasis	
Note	*Metastasis no larger than 0.2 cm can be designated pNmi.*	
Distant Metastasis (M)		
M0	No distant metastasis	
M1	Distant metastasis	
M1a	Non regional lymph node(s)	
M1b	Bone(s)	
M1c	Other site(s)	
Note	*When more than one site of metastasis is present, the most advanced category is used. (p)M1c is the most advanced category.*	

ADT	Androgen deprivation therapy
BRCA	Breast Cancer gene
CMG	Clinical Management Guideline
ECOG	Eastern Co-operative Oncology Group
DT	Doubling time
DRE	Digital Rectal Examination
FBC	Full Blood Count
GP	General Practitioner
GS	Gleason score
HCP	Health Care Professional
IPSS	International Prostate Symptom Score
LDR	Low dose rate
LFT	Liver Function Test
LHRH	Luteinizing hormone-releasing hormone
LUTS	Lower urinary tract symptoms
MDT	Multi-disciplinary Team
MRI	Magnetic Resonance Imaging
NCA	North Cancer Alliance
PI-RADS	Prostate Imaging Reporting and Data System
PMSA	Prostate specific membrane antigen
PSA	Prostate-Specific Antigen
PVR	Post Void Residual Volume
Qmax	Maximum urinary flow rate
SACT	Systemic Anti-Cancer Therapy
TRUS	Transrectal ultrasound scan
TURP	Transurethral resection of the prostate
U&E	Urea & Electrolytes
USS	Ultrasound scan