Prostate Cancer Clinical Practice Guidelines Update

Selected updates relevant to ADT and LHRH antagonist use: NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) Clinical Practice Guidelines for Prostate Cancer

Selected updates adapted from v4.2023 (Sept 7, 2023) to v3.2024 (Mar 8, 2024)

Sumitomo Pharma | Pfizer Oncology

MED-Rel-US-2809 3/24

Table of Contents

Principles of Androgen Deprivation Therapy

KEY CHANGES

N0 or M0 *Clinically Localized*	N1 or M0 *Regional*	N1 Pathological (pN1)	M0 CSPC *PSA Recurrent After RP or RT*	M0 CSPC *Post Maximal Pelvic Therapy*	M1 CSPC	M0 or M1 CRPC *Secondary Hormone Therapy*	Optimal ADT

- Neoadjuvant ADT for RP is strongly discouraged outside of a clinical trial
- ADT should not be used as monotherapy for clinically localized PC unless there is a contraindication to definitive local therapy
- Giving ADT before, during, and/or after radiation prolongs survival in selected patients treated with radiation
  - For short-term ADT with prostate-only RT, concurrent/adjuvant ADT is preferred over neoadjuvant ADT

ADT Options for N0 or M0 Clinically Localized
LHRH agonist alone
Goserelin, leuprolide, or triptorelin
LHRH agonist (as above) + first generation antiandrogen
Nilutamide, flutamide, or bicalutamide
LHRH antagonist
Degarelix or **relugolix**
LHRH agonist or antagonist with abiraterone (very high risk only)

All recommendations are category 2A unless otherwise indicated.
Highlighted content has been updated with v3.2024.

What's changed?

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MED-Rel-US-2809 3/24

Principles of Androgen Deprivation Therapy

KEY CHANGES

N0 or M0 *Clinically Localized*	**N1 or M0** ***Regional***	N1 Pathological (pN1)	M0 CSPC *PSA Recurrent After RP or RT*	M0 CSPC *Post Maximal Pelvic Therapy*	M1 CSPC	M0 or M1 CRPC *Secondary Hormone Therapy*	Optimal ADT

- Patients with N1,M0 prostate cancer and a life expectancy >5 years or who are symptomatic can be treated with:
  - EBRT and neoadjuvant, concurrent, and/or adjuvant ADT as for patients with N0,M0 disease without abiraterone
  - EBRT and neoadjuvant, concurrent, and/or adjuvant LHRH agonist or antagonist with abiraterone
  - ADT alone or with abiraterone
- Abiraterone with ADT should be considered for a total of 2 years for those patients with N1 disease who are treated with radiation to the prostate and pelvic nodes
- Patients with regional disease and life expectancy ≤5 years who chose ADT can receive: LHRH agonist, LHRH antagonist, or orchiectomy

ADT Options for N1 or M0 Regional
Orchiectomy
LHRH agonist alone
Goserelin, leuprolide, or triptorelin
LHRH agonist (as above) + first generation antiandrogen
Nilutamide, flutamide, or bicalutamide
LHRH antagonist
Degarelix or **relugolix**
Orchiectomy + abiraterone
LHRH agonist (as above) + abiraterone
LHRH antagonist + abiraterone

All recommendations are category 2A unless otherwise indicated.
Highlighted content has been updated with v3.2024.

What's changed?

Principles of Androgen Deprivation Therapy

KEY CHANGES

N0 or M0 *Clinically Localized*	N1 or M0 *Regional*	**N1 Pathological (pN1)**	M0 CSPC *PSA Recurrent After RP or RT*	M0 CSPC *Post Maximal Pelvic Therapy*	M1 CSPC	M0 or M1 CRPC *Secondary Hormone Therapy*	Optimal ADT

- In one randomized trial, immediate and continuous use of ADT in patients with positive nodes following RP resulted in significantly improved OS compared to patients who received delayed ADT
- EBRT may be added (category 2B), in which case the ADT options are as for neoadjuvant, concurrent, and/or adjuvant ADT for clinically localized disease (see N0 or M0 Localized)
- Many of the side effects of continuous ADT are cumulative over time on ADT

ADT Options for N1 Pathological (pN1)
Immediate LHRH agonist
Goserelin, leuprolide, or triptorelin
Immediate LHRH antagonist
Degarelix or **relugolix**
Immediate Orchiectomy

All recommendations are category 2A unless otherwise indicated.

See prior slides for relevant updates with v3.2024.

Principles of Androgen Deprivation Therapy

KEY CHANGES

N0 or M0 *Clinically Localized*	N1 or M0 *Regional*	N1 Pathological (pN1)	M0 CSPC *PSA Recurrent After RP or RT*	M0 CSPC *Post Maximal Pelvic Therapy*	M1 CSPC	M0 or M1 CRPC *Secondary Hormone Therapy*	Optimal ADT

- The timing of ADT for patients whose only evidence of cancer after definitive treatment is an increasing PSA is influenced by PSA velocity, patient anxiety, the short- and long-term side effects of ADT, and the underlying comorbidities of the patient
- Earlier ADT may be better than delayed ADT, although the definitions of early and late (what level of PSA) are controversial. Since the benefit of early ADT is not clear, treatment should be individualized until definitive studies are done. Patients with a shorter PSADT (or a rapid PSA velocity) and an otherwise long life expectancy should be encouraged to consider ADT earlier
- Patients with prolonged PSADTs (>12 months) and who are older are candidates for observation
- Patients who choose ADT should consider intermittent ADT

ADT Options for PSA Recurrent CSPC Post RP
EBRT +/- neoadjuvant, concurrent and/or adjuvant ADT
EBRT + LHRH agonist or antagonist with abiraterone (studies positive for pelvic nodal recurrence only)

ADT Options for PSA Recurrent CSPC Post RT
Orchiectomy
LHRH agonist alone
Goserelin, leuprolide, or triptorelin
LHRH agonist (as above) + first generation antiandrogen
Nilutamide, flutamide, or bicalutamide
LHRH antagonist
Degarelix or **relugolix**
Orchiectomy, LHRH agonist (as above), or LHRH antagonist plus abiraterone (studies positive for pelvic nodal recurrence only)

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MED-Rel-US-2809 3/24

Principles of Androgen Deprivation Therapy

KEY CHANGES

N0 or M0 *Clinically Localized*	N1 or M0 *Regional*	N1 Pathological (pN1)	M0 CSPC *PSA Recurrent After RP or RT*	**M0 CSPC** *Post Maximal Pelvic Therapy*	M1 CSPC	M0 or M1 CRPC *Secondary Hormone Therapy*	Optimal ADT

- Monitoring until diagnosis of metastatic disease is preferred for patients with non-metastatic castration-sensitive disease who are not candidates for pelvic therapy
- PSADT and Grade Group should be considered when deciding whether to begin ADT for patients with M0 disease
- ADT monotherapy is an option for these patients, and intermittent ADT can be considered to reduce toxicity
- Enzalutamide with or without leuprolide is an option for patients who have the following high-risk criteria:
  - M0 by conventional imaging;
  - PSADT ≤9 months;
  - PSA ≥2 ng/mL above nadir after RT or ≥1 ng/mL after RP with or without postoperative RT;
  - Not considered a candidate for pelvic-directed therapy

ADT Options for M0 CSPC Post Maximal Pelvic Therapy
Orchiectomy
LHRH agonist alone
Goserelin, leuprolide, or triptorelin
LHRH agonist (as above) + first generation antiandrogen
Nilutamide, flutamide, or bicalutamide
LHRH antagonist
Degarelix or **relugolix**
Orchiectomy, LHRH agonist (as above), or LHRH antagonist plus abiraterone (studies positive for pelvic nodal recurrence only)

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Principles of Androgen Deprivation Therapy

KEY CHANGES

N0 or M0 *Clinically Localized*	N1 or M0 *Regional*	N1 Pathological (pN1)	M0 CSPC *PSA Recurrent After RP or RT*	M0 CSPC *Post Maximal Pelvic Therapy*	M1 CSPC	M0 or M1 CRPC *Secondary Hormone Therapy*	Optimal ADT

- ADT with treatment intensification is strongly recommended for most patients with metastatic prostate cancer. The use of ADT monotherapy in metastatic castration-sensitive disease is discouraged unless there are clear contraindications to combination therapy. If ADT monotherapy is given, intermittent ADT can be considered to reduce toxicity
- In addition, three meta-analyses of randomized controlled trials did not show a difference in survival between intermittent and continuous ADT
- Close monitoring of PSA and testosterone levels and possibly imaging is required when using intermittent ADT, especially during off-treatment periods, and patients may need to switch to continuous ADT upon signs of disease progression

ADT Options for M1 CSPC
ADT alone (orchiectomy, LHRH agonist, LHRH agonist plus first-generation antiandrogen*, or LHRH antagonist)
Orchiectomy plus abiraterone, enzalutamide, or apalutamide
Orchiectomy plus docetaxel and abiraterone or darolutamide
LHRH agonist plus abiraterone, enzalutamide, or apalutamide
LHRH agonist plus docetaxel and abiraterone or darolutamide
LHRH antagonist plus abiraterone, enzalutamide, or apalutamide
LHRH antagonist plus docetaxel and abiraterone or darolutamide
EBRT given with ADT in low metastatic burden
Orchiectomy alone or with abiraterone or docetaxel
LHRH agonist alone or with abiraterone or docetaxel
LHRH antagonist alone or with abiraterone or docetaxel

*A first-generation antiandrogen must be given with LHRH agonist for ≥7 days to prevent testosterone flare if metastases are present in weightbearing bone

All recommendations are category 2A unless otherwise indicated.

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What's changed?

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Principles of Androgen Deprivation Therapy

N0 or M0 *Clinically Localized*	N1 or M0 *Regional*	N1 Pathological (pN1)	M0 CSPC *PSA Recurrent After RP or RT*	M0 CSPC *Post Maximal Pelvic Therapy*	M1 CSPC	M0 or M1 CRPC *Secondary Hormone Therapy*	KEY CHANGES: Optimal ADT

NCCN Guidelines v4.2023

Androgen receptor activation and autocrine/paracrine androgen synthesis are potential mechanisms of recurrence of prostate cancer during ADT (CRPC). Thus, castrate levels of testosterone (<50 ng/dL) should be maintained by continuing LHRH agonist or degarelix while additional therapies are applied.

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NCCN Guidelines v3.2024

Androgen receptor activation and autocrine/paracrine androgen synthesis are potential mechanisms of recurrence of prostate cancer during ADT (CRPC). Thus, castrate levels of testosterone (<50 ng/dL) should be maintained by continuing LHRH agonist or antagonist while additional therapies are applied.

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MED-Rel-US-2809 3/24

Principles of Androgen Deprivation Therapy

N0 or M0 *Clinically Localized*	N1 or M0 *Regional*	N1 Pathological (pN1)	M0 CSPC *PSA Recurrent After RP or RT*	M0 CSPC *Post Maximal Pelvic Therapy*	M1 CSPC	M0 or M1 CRPC *Secondary Hormone Therapy*	KEY CHANGES: Optimal ADT

- Medical castration (ie, LHRH agonist or **antagonist**) and surgical castration (ie, bilateral orchiectomy) are equally effective.
- Combined androgen blockade (medical or surgical castration combined with an antiandrogen) provides modest to no benefit over castration alone in patients with metastatic disease.
- Antiandrogen therapy should precede or be coadministered with LHRH agonist and be continued in combination for at least 7 days for patients with overt metastases who are at risk of developing symptoms associated with the flare in testosterone with initial LHRH agonist alone.
- Antiandrogen monotherapy appears to be less effective than medical or surgical castration and is not recommended.
- No clinical data support the use of finasteride or dutasteride with combined androgen blockade.
- Patients who do not achieve adequate suppression of serum testosterone (<50 ng/dL) with medical or surgical castration can be considered for additional hormonal manipulations (with antiandrogens, LHRH antagonists, or steroids), although the clinical benefit remains uncertain. Consider monitoring testosterone levels 12 weeks after first dose of LHRH therapy, then upon increase in PSA. The optimal level of serum testosterone to affect “castration” has yet to be determined.

<Contextual statements regarding relugolix combination therapies have been removed in the latest guidelines>

- Data are limited on long-term adherence to **oral relugolix** and the potential effects on optimal ADT. Ongoing monitoring for sustained suppression of testosterone (<50 ng/dL) can be considered, and relugolix may not be a preferred agent if adherence to the prescribed regimen is uncertain

All recommendations are category 2A unless otherwise indicated.
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MED-Rel-US-2809 3/24

Appendix

Selected updates relevant to ADT and LHRH antagonist use: NCCN Guidelines® for Prostate Cancer

Selected updates adapted from v4.2023 (Sept 7, 2023) to v3.2024 (Mar 8, 2024)

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MED-Rel-US-2809 3/24

NCCN Guideline Revisions Relevant to Relugolix

N0 or M0 Clinically Localized

Back to previous

NCCN Guidelines v4.2023

ADT for Clinically Localized (N0,M0) Disease

- Neoadjuvant ADT for RP is strongly discouraged outside of a clinical trial.
- ADT should not be used as monotherapy in clinically localized prostate cancer unless there is a contraindication to definitive local therapy such as life expectancy ≤5 years and comorbidities. Under those circumstances, ADT may be used [see ADT for Patients on Observation Who Require Treatment and Those with Life Expectancy ≤5 Years (PROS-I].
- Giving ADT before, during, and/or after radiation (neoadjuvant, concurrent, and/or adjuvant ADT) prolongs survival in selected radiation-managed patients. Options are:
- LHRH agonist alone
  - Goserelin, leuprolide, or triptorelin
- LHRH agonist (as above) plus first-generation antiandrogen
  - Nilutamide, flutamide, or bicalutamide
- LHRH antagonist
  - Degarelix or relugolix
- LHRH agonist or degarelix with abiraterone (very high risk only)

NCCN Guidelines v3.2024

ADT for Clinically Localized (N0,M0) Disease

- Neoadjuvant ADT for RP is strongly discouraged outside of a clinical trial.
- ADT should not be used as monotherapy in clinically localized prostate cancer unless there is a contraindication to definitive local therapy such as life expectancy ≤5 years and comorbidities. Under those circumstances, ADT may be used [see ADT for Patients on Observation Who Require Treatment and Those with Life Expectancy ≤5 Years (PROS-G)].
- Giving ADT before, during, and/or after radiation (neoadjuvant, concurrent, and/or adjuvant ADT) prolongs survival in selected patients treated with radiation. For short-term ADT with prostate-only RT, concurrent/adjuvant ADT is preferred over neoadjuvant ADT. Options are:
- Luteinizing hormone-releasing hormone (LHRH) agonist alone
  - Goserelin, leuprolide, or triptorelin
- LHRH agonist (as above) plus first-generation antiandrogen
  - Nilutamide, flutamide, or bicalutamide
- LHRH antagonist
  - Degarelix or relugolix
- LHRH agonist or antagonist with abiraterone (very high risk only)

NCCN Guideline Revisions Relevant to Relugolix

N1 or M0 Regional

Back to previous

NCCN Guidelines v4.2023

ADT for Regional (N1,M0) Disease

- Patients with N1,M0 prostate cancer and a life expectancy >5 years can be treated with:
  - EBRT and neoadjuvant, concurrent, and/or adjuvant ADT as for patients with N0,M0 disease (see above) without abiraterone
  - EBRT and neoadjuvant, concurrent, and/or adjuvant LHRH agonist or antagonist with abiraterone
  - ADT alone or with abiraterone (see below)
- Abiraterone should be given with concurrent steroid:
  - Prednisone 5 mg PO once daily for the standard formulation
  - Methylprednisolone 4 mg PO twice daily for the fine-particle formulation (category 2B)
  - Abiraterone with ADT should be considered for a total of 2 years for those patients with N1 disease who are treated with radiation to the prostate and pelvic nodes.
- Options for ADT are:
  - Orchiectomy
  - LHRH agonist alone
    - Goserelin, leuprolide, or triptorelin
  - LHRH agonist (as above) plus first-generation antiandrogen
    - Nilutamide, flutamide, or bicalutamide
  - LHRH antagonist
    - Degarelix or relugolix
  - Orchiectomy plus abiraterone
  - LHRH agonist (as above) plus abiraterone
  - Degarelix plus abiraterone
- Patients with regional disease and life expectancy ≤5 years who chose ADT can receive LHRH agonist, LHRH antagonist, or orchiectomy.

NCCN Guidelines v3.2024

ADT for Regional (N1,M0) Disease

- Patients with N1,M0 prostate cancer and a life expectancy >5 years or who are symptomatic can be treated with:
  - EBRT and neoadjuvant, concurrent, and/or adjuvant ADT as for patients with N0,M0 disease (see above) without abiraterone
  - EBRT and neoadjuvant, concurrent, and/or adjuvant LHRH agonist or antagonist with abiraterone
  - ADT alone or with abiraterone (see below)
- Abiraterone should be given with concurrent steroid:
  - Prednisone 5 mg PO once daily for the standard formulation
  - Methylprednisolone 4 mg PO twice daily for the fine-particle formulation (category 2B)
  - Abiraterone with ADT should be considered for a total of 2 years for those patients with N1 disease who are treated with radiation to the prostate and pelvic nodes.
- Options for ADT are:
  - Orchiectomy
  - LHRH agonist alone
    - Goserelin, leuprolide, or triptorelin
  - LHRH agonist (as above) plus first-generation antiandrogen
    - Nilutamide, flutamide, or bicalutamide
  - LHRH antagonist
    - Degarelix or relugolix
  - Orchiectomy plus abiraterone
  - LHRH agonist (as above) plus abiraterone
  - LHRH antagonist plus abiraterone
- The use of ADT plus abiraterone in patients with N1 M0 prostate cancer is based on the STAMPEDE trial, which demonstrated improved OS of the combination compared with ADT alone
- Patients with regional disease and life expectancy ≤5 years who chose ADT can receive LHRH agonist, LHRH antagonist, or orchiectomy.

NCCN Guideline Revisions Relevant to Relugolix

M0 CSPC PSA Recurrent After RP or RT

Back to previous

NCCN Guidelines v4.2023

ADT for M0 PSA Persistence/Recurrence After RP or EBRT (ADT for M0 Castration-Sensitive Disease)

- ADT options are:
  - M0 RP PSA persistence/recurrence:
    - EBRT +/- neoadjuvant, concurrent, and/or adjuvant ADT [See ADT for Clinically Localized (N0,M0) Disease]
    - EBRT + LHRH agonist or degarelix with abiraterone (studies positive for pelvic recurrence only)
  - M0 RT recurrence, biopsy negative or M0 PSA recurrence after progression on salvage EBRT:
    - Orchiectomy
    - LHRH agonist alone
      - Goserelin, leuprolide, or triptorelin
    - LHRH agonist (as above) plus first-generation antiandrogen
      - Nilutamide, flutamide, or bicalutamide
    - LHRH antagonist
      - Degarelix or relugolix
  - Abiraterone should be given with concurrent steroid [see ADT for Regional (N1,M0) Disease].

NCCN Guidelines v3.2024

ADT for M0 PSA Persistence/Recurrence After RP or EBRT (ADT for M0 Castration-Sensitive Disease)

- ADT options are:
  - M0 RP PSA persistence/recurrence:
    - EBRT +/- neoadjuvant, concurrent, and/or adjuvant ADT [See ADT for Clinically Localized (N0,M0) Disease]
    - EBRT + LHRH agonist or antagonist with abiraterone (studies positive for pelvic nodal recurrence only)
  - M0 RT recurrence, biopsy negative or M0 PSA recurrence after progression on salvage EBRT:
    - Orchiectomy
    - LHRH agonist alone
      - Goserelin, leuprolide, or triptorelin
    - LHRH agonist (as above) plus first-generation antiandrogen
      - Nilutamide, flutamide, or bicalutamide
    - LHRH antagonist
      - Degarelix or relugolix
    - Orchiectomy, LHRH agonist (as above), or LHRH antagonist plus abiraterone (studies positive for pelvic nodal recurrence only)
  - Abiraterone should be given with concurrent steroid [see ADT for Regional (N1,M0) Disease].

NCCN Guideline Revisions Relevant to Relugolix

M1 CSPC

Back to previous

NCCN Guidelines v4.2023

ADT for Metastatic Castration-Sensitive Disease

- ADT with treatment intensification is preferred for most patients with metastatic prostate cancer. ADT alone is appropriate for some patients.
- Treatment options for patients with M1 castration-sensitive disease are:
  - ADT alone (orchiectomy, LHRH agonist, LHRH agonist plus first-generation antiandrogen, or LHRH antagonist)
    - LHRH agonists: Goserelin, leuprolide, or triptorelin
    - First-generation antiandrogens: Nilutamide, flutamide, or bicalutamide
    - A first-generation antiandrogen must be given with LHRH agonist for ≥7 days to prevent testosterone flare if metastases are present in weight-bearing bone
  - Orchiectomy plus abiraterone, enzalutamide, or apalutamide
  - Orchiectomy plus docetaxel and abiraterone or darolutamide
  - LHRH agonist (as above) plus abiraterone, enzalutamide, or apalutamide
  - LHRH agonist (as above) plus docetaxel and abiraterone or darolutamide
  - Degarelix plus abiraterone, enzalutamide, or apalutamide
  - Degarelix plus docetaxel and abiraterone or darolutamide
- Abiraterone should be given with concurrent steroid [see ADT for Regional (N1,M0) Disease].
- When EBRT to primary is given with ADT in low metastatic burden M1, the options are LHRH agonist, LHRH antagonist, and orchiectomy.

NCCN Guidelines v3.2024

ADT for Metastatic Castration-Sensitive Disease

- ADT with treatment intensification is strongly recommended for most patients with metastatic prostate cancer. The use of ADT monotherapy in metastatic castration-sensitive disease is discouraged unless there are clear contraindications to combination therapy. If ADT monotherapy is given, intermittent ADT can be considered to reduce toxicity.
- Treatment options for patients with M1 castration-sensitive disease are:
  - ADT alone (orchiectomy, LHRH agonist, LHRH agonist plus first-generation antiandrogen, or LHRH antagonist)
    - LHRH agonists: Goserelin, leuprolide, or triptorelin
    - First-generation antiandrogens:
      - Nilutamide, flutamide, or bicalutamide
    - A first-generation antiandrogen must be given with LHRH agonist for ≥7 days to prevent testosterone flare if metastases are present in weight-bearing bone
  - Orchiectomy plus abiraterone, enzalutamide, or apalutamide
  - Orchiectomy plus docetaxel and abiraterone or darolutamide
  - LHRH agonist (as above) plus abiraterone, enzalutamide, or apalutamide
  - LHRH agonist (as above) plus docetaxel and abiraterone or darolutamide
  - LHRH antagonist plus abiraterone, enzalutamide, or apalutamide
  - LHRH antagonist plus docetaxel and abiraterone or darolutamide
- Abiraterone should be given with concurrent steroid [see ADT for Regional (N1,M0) Disease, see PROS-G].
- When EBRT to primary tumor is given with ADT in low metastatic burden M1, the options for ADT are:
  - Orchiectomy alone or with abiraterone or docetaxel
  - LHRH agonist alone or with abiraterone or docetaxel
  - LHRH antagonist alone or with abiraterone or docetaxel

NCCN Guideline Revisions Relevant to Relugolix

Secondary Hormone Therapy for M0 or M1 CRPC

Back to previous

NCCN Guidelines v4.2023

Secondary Hormone Therapy for M0 or M1 CRPC

- **Androgen receptor activation and autocrine/paracrine androgen synthesis are potential mechanisms of recurrence of prostate cancer during ADT (CRPC). Thus, castrate levels of testosterone (<50 ng/dL) should be maintained by continuing LHRH agonist or degarelix while additional therapies are applied.**

NCCN Guidelines v3.2024

Secondary Hormone Therapy for M0 or M1 CRPC

- **Androgen receptor activation and autocrine/paracrine androgen synthesis are potential mechanisms of recurrence of prostate cancer during ADT (CRPC). Thus, castrate levels of testosterone (<50 ng/dL) should be maintained by continuing LHRH agonist or antagonist while additional therapies are applied.**

NCCN Guideline Revisions Relevant to Relugolix

Optimal ADT

Back to previous

NCCN Guidelines v4.2023

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Relugolix has not been adequately studied in combination with potent androgen receptor inhibitors such as enzalutamide, apalutamide, darolutamide, or abiraterone acetate, nor has it been studied in combination with docetaxel or cabazitaxel chemotherapy. Potential drug interactions include induction of cytochrome P450 enzymes and reduced concentration and efficacy of relugolix with enzalutamide or apalutamide and cardiac QTc interactions with abiraterone. Further studies of relugolix dosing and drug interactions with commonly used agents in advanced prostate cancer are needed to ensure patient safety and proper dosing.

Data are limited on long-term compliance of oral relugolix and the potential effects on optimal ADT. Ongoing monitoring for sustained suppression of testosterone (<50 ng/dL) can be considered, and relugolix may not be a preferred agent if patient compliance is uncertain.

NCCN Guidelines v3.2024

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~~*Relugolix has not been adequately studied in combination with potent androgen receptor inhibitors such as enzalutamide, apalutamide, darolutamide, or abiraterone acetate, nor has it been studied in combination with docetaxel or cabazitaxel chemotherapy. Potential drug interactions include induction of cytochrome P450 enzymes and reduced concentration and efficacy of relugolix with enzalutamide or apalutamide and cardiac QTc interactions with abiraterone. Further studies of relugolix dosing and drug interactions with commonly used agents in advanced prostate cancer are needed to ensure patient safety and proper dosing.*~~

Data are limited on long-term adherence to oral relugolix and the potential effects on optimal ADT. Ongoing monitoring for sustained suppression of testosterone (<50 ng/dL) can be considered, and relugolix may not be a preferred agent if adherence to the prescribed regimen is uncertain.