Key Opinion Leader Flashcard

NUBEQA® (darolutamide) *TREATMENT GUIDELINES*

NUBEQA® is an androgen receptor inhibitor indicated for the treatment of adult patients with:

- Non-metastatic castration-resistant prostate cancer (nmCRPC)
- Metastatic castration-sensitive prostate cancer (mCSPC)
- Metastatic castration-sensitive prostate cancer (mCSPC) in combination with docetaxel

NCCN CLINICAL PRACTICE GUIDELINES IN ONCOLOGY (NCCN GUIDELINES®)[1]

mCSPC DAROLUTAMIDE (NUBEQA) WITH ADT + DOCETAXEL	mCSPC DAROLUTAMIDE (NUBEQA) WITH ADT	nmCRPC DAROLUTAMIDE (NUBEQA) WITH ADT
AN NCCN CATEGORY 1 PREFERRED OPTION[a,b] for appropriate patients with high-volume synchronous or metachronous metastases	**AN NCCN CATEGORY 2A OPTION[c]** for appropriate patients with high-volume synchronous or metachronous metastases	**AN NCCN CATEGORY 1 PREFERRED OPTION[a,b]** for patients with PSADT ≤10 months
AN NCCN CATEGORY 2B OPTION[d] for appropriate patients with low-volume synchronous metastases	**AN NCCN CATEGORY 2B OPTION[d]** for appropriate patients with low-volume synchronous metastases or low-volume metachronous metastases	

The use of docetaxel + ADT alone is NOT RECOMMENDED in mCSPC

AMERICAN UROLOGICAL ASSOCIATION
(AUA/ASTRO/SUO Guidelines)[2]

mCSPC: Strong Recommendation[e]; Evidence Level Grade B[f]
Darolutamide (NUBEQA) with ADT + docetaxel in selected patients with de novo mCSPC

nmCRPC: Strong recommendation[e]; Evidence Level Grade A[g]
Darolutamide (NUBEQA) with ADT for men at high risk of developing metastasis with a PSADT ≤10 months

EUROPEAN ASSOCIATION OF UROLOGY
(EAU/EANM/ESTRO/ESUR/SIOG Guidelines)[3]

mCSPC: Strong Recommendation
Darolutamide (NUBEQA) with ADT + docetaxel in men with mCSPC who fit for docetaxel

nmCRPC: Strong recommendation
Darolutamide (NUBEQA) with ADT for men at high risk of developing metastasis with a PSADT <10 months

ADT, androgen deprivation therapy; ASTRO, American Society for Radiation Oncology; AUA, American Urological Association; CRPC, castration-resistant prostate cancer; EANM, European Association of Nuclear Medicine; EAU, European Association of Urology; ESTRO, European Society for Radiotherapy and Oncology; ESUR, European Society of Urogenital Radiology; M0, no metastases; NCCN, National Comprehensive Cancer Network; PSADT, prostate specific-antigen doubling time; SIOG, International Society of Geriatric Oncology; SUO, Society of Urologic Oncology.

"Daroluatmide® (NUBEQA) is supported across all of the major guidelines, but the Category 1, Preferred Option in the NCCN Guidelines for both mCSPC[a,b] (for appropriate patients with high-volume synchronous or metachronous metastases) and nmCRPC[a,b] is significant for NUBEQA."
—Zachary Klaassen, MD, MSc

[a]Category 1: Based upon high-level evidence (≥1 randomized phase 3 trials or high-quality, robust meta-analyses), there is uniform NCCN consensus (≥85% support of the Panel) that the intervention is appropriate.
[b]Preferred option: Interventions that are based on superior efficacy, safety, and evidence; and, when appropriate, affordability.[1]
[c]Category 2A: Based upon lower-level evidence, there is uniform NCCN consensus (≥85% support of the Panel) that the intervention is appropriate.[1]
[d]Category 2B: Based upon lower-level evidence, there is NCCN consensus (≥50%, but <85% support of the Panel) that the intervention is appropriate.[1]
[e]Strong recommendation: Directive statement that an action should be undertaken because net benefit is substantial.[1]
[f]Evidence Grade B: The statement can be applied to most patients in most circumstances; better evidence could change confidence.
[g]Evidence Grade A: The statement can be applied to most patients in most circumstances; future research is unlikely to change confidence.

IMPORTANT SAFETY INFORMATION

Warnings & Precautions

Ischemic Heart Disease – Ischemic heart disease, including fatal cases, occurred in patients receiving NUBEQA.

In a pooled analysis of ARAMIS and ARANOTE, ischemic heart disease occurred in 3.4% of patients receiving NUBEQA and 2.2% receiving placebo, including Grade 3-4 events in 1.4% and 0.3%, respectively. Ischemic events led to death in 0.4% of patients receiving NUBEQA and 0.4% receiving placebo.

In ARASENS, ischemic heart disease occurred in 3.2% of patients receiving NUBEQA with docetaxel and 2% receiving placebo with docetaxel, including Grade 3-4 events in 1.3% and 1.1%, respectively. Ischemic events led to death in 0.3% of patients receiving NUBEQA with docetaxel and 0% receiving placebo with docetaxel.

Monitor for signs and symptoms of ischemic heart disease. Optimize management of cardiovascular risk factors, such as hypertension, diabetes, or dyslipidemia. Discontinue NUBEQA for Grade 3-4 ischemic heart disease.

Please see additional Important Safety Information on reverse side. For full Prescribing Information, please visit NUBEQA PI.

NUBEQA® (darolutamide) 300 mg tablets

Additional
IMPORTANT SAFETY INFORMATION

Warnings & Precautions (cont.)

Seizure – Seizure occurred in patients receiving NUBEQA.

In a pooled analysis of ARAMIS and ARANOTE, Grade 1-3 seizure occurred in 0.2% of patients receiving NUBEQA. Seizure occurred from 261 to 665 days after initiation of NUBEQA.

In ARASENS, seizure occurred in 0.8% of patients receiving NUBEQA with docetaxel, including two Grade 3 events. Seizure occurred from 38 to 1754 days after initiation of NUBEQA.

It is unknown whether anti-epileptic medications will prevent seizures with NUBEQA. Advise patients of the risk of developing a seizure while receiving NUBEQA and of engaging in any activity where sudden loss of consciousness could cause harm to themselves or others. Consider discontinuation of NUBEQA in patients who develop a seizure during treatment.

Embryo-Fetal Toxicity – The safety and efficacy of NUBEQA have not been established in females. NUBEQA can cause fetal harm and loss of pregnancy. Advise males with female partners of reproductive potential to use effective contraception during treatment with NUBEQA and for 1 week after the last dose.

Adverse Reactions

In ARAMIS, serious adverse reactions occurred in 25% of patients receiving NUBEQA and in 20% of patients receiving placebo. Serious adverse reactions in ≥1% of patients who received NUBEQA included urinary retention, pneumonia, and hematuria. Fatal adverse reactions occurred in 3.9% of patients receiving NUBEQA and 3.2% of patients receiving placebo. Fatal adverse reactions that occurred in ≥2 patients who received NUBEQA included death (0.4%), cardiac failure (0.3%), cardiac arrest (0.2%), general physical health deterioration (0.2%), and pulmonary embolism (0.2%). The most common (>2% with a ≥2% increase compared to placebo) adverse reactions, including laboratory test abnormalities, were increased AST (23%), decreased neutrophil count (20%), fatigue (16%), increased bilirubin (16%), pain in extremity (6%), and rash (4%). Clinically relevant adverse reactions occurring in 2% or more of patients treated with NUBEQA included ischemic heart disease (4%) and heart failure (2.1%).

In ARANOTE, serious adverse reactions occurred in 24% of patients receiving NUBEQA. Serious adverse reactions in ≥1% of patients who received NUBEQA included pneumonia (2%), urinary tract infection (1.8%), musculoskeletal pain (1.6%), hemorrhage (1.6%), arrhythmias (1.3%), and spinal cord compression (1.1%). Fatal adverse reactions occurred in 4.7% of patients receiving NUBEQA and those that occurred in ≥2 patients included sepsis (1.1%), craniocerebral injury (0.4%), and myocardial infarction (0.4%). The most common (≥10% with a ≥2% increase compared to placebo) adverse reaction is urinary tract infection (12%). The most common laboratory test abnormalities (≥15% with a ≥5% increase over placebo) are increased AST (32%), increased ALT (28%), increased bilirubin (17%), and decreased neutrophil count (16%). Clinically relevant adverse reactions in <10% of patients who received NUBEQA included arrhythmia (8.8%), pneumonia (3.6%), and myocardial infarction (0.7%).

In ARASENS, serious adverse reactions occurred in 45% of patients receiving NUBEQA with docetaxel. Serious adverse reactions in ≥2% of patients who received NUBEQA with docetaxel included febrile neutropenia (6%), neutrophil count decreased (2.8%), musculoskeletal pain (2.6%) and pneumonia (2.6%). Fatal adverse reactions occurred in 4% of patients receiving NUBEQA with docetaxel. Fatal adverse reactions in ≥2 patients who received NUBEQA included COVID-19/COVID-19 pneumonia (0.8%), myocardial infarction (0.3%), and sudden death (0.3%). The most common (≥10% with a ≥2% increase over placebo with docetaxel) adverse reactions are constipation (23%), rash (20%), decreased appetite (19%), hemorrhage (18%), increased weight (18%), and hypertension (14%). The most common laboratory test abnormalities (≥30%) are anemia (72%), hyperglycemia (57%), decreased lymphocyte count (52%), decreased neutrophil count (49%), increased AST (40%), increased ALT (37%), and hypocalcemia (31%). Clinically relevant adverse reactions in <10% of patients who received NUBEQA with docetaxel included fractures (8%), ischemic heart disease (3.2%), seizures (0.6%), and drug-induced liver injury (0.3%).

Drug Interactions

Effect of Other Drugs on NUBEQA – Concomitant use of NUBEQA with a combined P-gp and strong or moderate CYP3A4 inducer decreases darolutamide exposure which may decrease NUBEQA activity. Avoid concomitant use of NUBEQA with combined P-gp and strong or moderate CYP3A4 inducers.

Concomitant use of NUBEQA with a combined P-gp and strong CYP3A4 inhibitor increases darolutamide exposure which may increase the risk of NUBEQA adverse reactions. Monitor patients more frequently for NUBEQA adverse reactions and modify NUBEQA dosage as needed.

Effects of NUBEQA on Other Drugs – NUBEQA is an inhibitor of BCRP transporter. Concomitant use of NUBEQA increases the AUC and C_{max} of BCRP substrates, which may increase the risk of BCRP substrate-related toxicities. Avoid concomitant use with drugs that are BCRP substrates where possible. If used together, monitor patients more frequently for adverse reactions, and consider dose reduction of the BCRP substrate drug.

NUBEQA is an inhibitor of OATP1B1 and OATP1B3 transporters. Concomitant use of NUBEQA may increase the plasma concentrations of OATP1B1 or OATP1B3 substrates. Monitor patients more frequently for adverse reactions of these drugs and consider dose reduction while patients are taking NUBEQA.

Review the Prescribing Information of drugs that are BCRP, OATP1B1, and OATP1B3 substrates when used concomitantly with NUBEQA.

You are encouraged to report side effects or quality complaints of products to the FDA by visiting **www.fda.gov/medwatch** or calling 1-800-FDA-1088.

References: 1. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Prostate Cancer V.2.2025. © National Comprehensive Network, Inc. 2025. All rights reserved. Accessed June 6, 2025. To view the most recent and complete version of the guideline, go online to NCCN.org warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way. **2.** Lowrance W et al. Advanced prostate cancer: AUA/ASTRO/SUO guideline. American Urological Association; 2023. *J Urol*. 2023;209(6):10.1097/JU.0000000000003452. **3.** Mottet N et al. EAU-EANM-ESTRO-ESUR-SIOG guidelines on prostate cancer. European Association of Urology; 2023. https://uroweb.org/guidelines/prostate-cancer/chapter/treatment. Accessed August 19, 2023.

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