Key Opinion Leader Flashcard

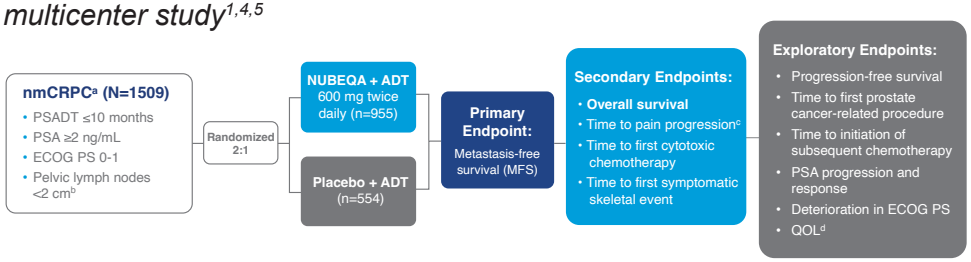
NUBEQA® (darolutamide)
ARAMIS ROLLOVER STUDY DESIGN

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

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

ARAMIS Study Design[1-3]

Double-blind (DB), placebo-controlled, international, multicenter study[1,4,5]

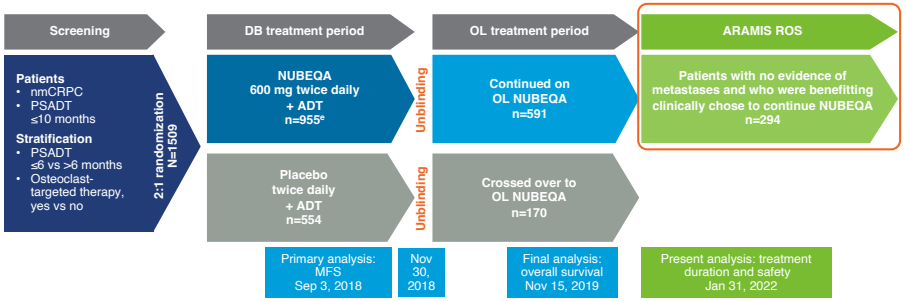


- Treatment continued until radiographic disease progression as assessed by conventional imaging (CT, MRI, 99mTc bone scan) by blinded independent central review, discontinuation due to adverse reactions, or withdrawal of consent

> *"Following the primary analysis of the ARAMIS study, the trial was unblinded, enabling patients in both treatment arms to receive open-label NUBEQA. Upon study completion, patients without evidence of metastases who were experiencing clinical benefits were allowed to continue NUBEQA treatment under the ARAMIS ROS Design.[4,5,6]"*
>
> *—Neal Shore, MD, FACS*

ARAMIS Rollover Study (ROS) Design[6]

DB, placebo-controlled, international, multicenter study[1,4,5]



- In the ARAMIS study after the primary analysis, the study was unblinded, and patients in both treatment groups could receive open-label NUBEQA
- After study completion, patients with no evidence of metastases who were benefitting clinically could continue on NUBEQA in the ARAMIS ROS Design

[a]All patients received concurrent ADT (treatment with GnRH analog or previous bilateral orchiectomy).
[b]Lymph nodes located below the aortic bifurcation as measured by the short axis.
[c]Time to pain progression was defined as at least a 2-point worsening from baseline of pain score on BPI-SF (a validated health-related QOL instrument) or initiation of opioids and reported in 28% of all patients on study.
[d]Tools used to prespecify QOL exploratory endpoints are the EQ-5D-3L, a preference-based instrument, and the FACT-P, BPI-SF, and EORTC-QLQ-PR25 prostate-specific questionnaires.
[e]One patient initially randomized to receive NUBEQA did not receive treatment and is not included in the analyses presented here.

ADT; androgen deprivation therapy; BPI-SF, Brief Pain Inventory Short Form; CT, Computed tomography; ECOG PS, Eastern Cooperative Oncology Group performance status; EORTC-QLQ-PR25, European Organization for Research and Treatment of Cancer quality of life questionnaire, a 25-item questionnaire; EQ-5D-3L, EuroQol Group 5-dimension 3-level; FACT-P, Functional Assessment of Cancer Therapy-Prostate; GnRH, gonadotropin-releasing hormone; MRI, magnetic resonance imaging; OL, open label; OS, overall survival; PSA, prostate-specific antigen; PSADT, prostate-specific antigen doubling time; QOL, quality of life; rPFS, radiographic progression-free survival.

IMPORTANT SAFETY INFORMATION

Warnings & Precautions

Ischemic Heart Disease – In a study of patients with nmCRPC (ARAMIS), ischemic heart disease occurred in 3.2% of patients receiving NUBEQA versus 2.5% receiving placebo, including Grade 3-4 events in 1.7% vs. 0.4%, respectively. Ischemic events led to death in 0.3% of patients receiving NUBEQA vs. 0.2% receiving placebo. In a study of patients with mHSPC (ARASENS), ischemic heart disease occurred in 3.2% of patients receiving NUBEQA with docetaxel vs. 2% receiving placebo with docetaxel, including Grade 3-4 events in 1.3% vs. 1.1%, respectively. Ischemic events led to death in 0.3% of patients receiving NUBEQA with docetaxel vs. 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 – In ARAMIS, Grade 1-2 seizure occurred in 0.2% of patients receiving NUBEQA vs. 0.2% receiving placebo. Seizure occurred 261 and 456 days after initiation of NUBEQA. In ARASENS, seizure occurred in 0.6% of patients receiving NUBEQA with docetaxel, including one Grade 3 event, vs. 0.2% receiving placebo with docetaxel. Seizure occurred 38 to 340 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 – 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 vs. 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 vs. 3.2% of patients receiving placebo. Fatal adverse reactions in 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 adverse reactions (>2% with a ≥2% increase over placebo), including laboratory test abnormalities, were increased AST, decreased neutrophil count, fatigue, increased bilirubin, pain in extremity, and rash. Clinically relevant adverse reactions occurring in ≥2% of patients treated with NUBEQA included ischemic heart disease and heart failure.

In ARASENS, serious adverse reactions occurred in 45% of patients receiving NUBEQA with docetaxel vs. 42% of patients receiving placebo with docetaxel. Serious adverse reactions in ≥2% of patients who received NUBEQA with docetaxel included febrile neutropenia (6%), decreased neutrophil count (2.8%), musculoskeletal pain (2.6%), and pneumonia (2.6%). Fatal adverse reactions occurred in 4% of patients receiving NUBEQA with docetaxel vs. 4% of patients receiving placebo with docetaxel. Fatal adverse reactions in patients who received NUBEQA included COVID-19/COVID-19 pneumonia (0.8%), myocardial infarction (0.3%), and sudden death (0.3%). The most common adverse reactions (≥10% with a ≥2% increase over placebo with docetaxel) were constipation, rash, decreased appetite, hemorrhage, increased weight, and hypertension. The most common laboratory test abnormalities (≥30%) were anemia, hyperglycemia, decreased lymphocyte count, decreased neutrophil count, increased AST, increased ALT, and hypocalcemia. Clinically relevant adverse reactions in <10% of patients who received NUBEQA with docetaxel included fractures, ischemic heart disease, seizures, and drug-induced liver injury.

Drug Interactions

Effect of Other Drugs on NUBEQA – Combined P-gp and strong or moderate CYP3A4 inducers decrease NUBEQA exposure, which may decrease NUBEQA activity. Avoid concomitant use.

Combined P-gp and strong CYP3A4 inhibitors increase NUBEQA exposure, which may increase the risk of NUBEQA adverse reactions. Monitor more frequently and modify NUBEQA dose as needed.

Effects of NUBEQA on Other Drugs – NUBEQA inhibits breast cancer resistance protein (BCRP) transporter. Concomitant use increases exposure (AUC) and maximal concentration of BCRP substrates, which may increase the risk of BCRP substrate-related toxicities. Avoid concomitant use where possible. If used together, monitor more frequently for adverse reactions, and consider dose reduction of the BCRP substrate.

NUBEQA inhibits OATP1B1 and OATP1B3 transporters. Concomitant use may increase plasma concentrations of OATP1B1 or OATP1B3 substrates. Monitor more frequently for adverse reactions and consider dose reduction of these substrates.

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. NUBEQA® (darolutamide) [prescribing information]. Whippany, NJ: Bayer HealthCare Pharmaceuticals Inc; October 2023. **2.** Erleada® (apalutamide) [prescribing information]. Horsham, PA: Janssen Products, LP; April 2022. **3.** Xtandi® (enzalutamide) [prescribing information]. Northbrook, IL: Astellas Pharma US, Inc.; January 2022. **4.** Fizazi K et al. *N Engl J Med*. 2019;380(13):1235-1246. **5.** Fizazi K et al. *N Engl J Med*. 2020;383(11):1040-1049. **6.** Shore ND et al. Treatment duration and long-term safety and tolerability of darolutamide in nonmetastatic castration-resistant prostate cancer (nmCRPC): ARAMIS Rollover Study. Poster presented at: AUA Annual Meeting; April 28-May 1, 2023; Chicago, IL.

Please see additional Important Safety Information on reverse side.
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