Darolutamide

Prioritizing survival and quality of life in men with non-metastatic prostate cancer

Darolutamide is an approved therapy for men with non-metastatic castration-resistant prostate cancer (nmCRPC) that delays metastases and extends survival while limiting the burdensome side effects of therapy – allowing patients to continue their active lifestyle without disruption.[1]

Addressing unmet medical needs for men with nmCRPC...

Men diagnosed with nmCRPC are typically active and often have no cancer-related symptoms. Therefore, the goals of treatment are to:

Extend survival

Improving overall survival is as vital for men with nmCRPC as at all stages of the prostate cancer continuum[2,3]

Delay disease progression

nmCRPC is a critical point in the disease progression. About **one-third of men with nmCRPC go on to develop metastases, within two years,**[3,4] associated with reduced quality of life and increased morbidity and healthcare costs

Preserve quality of life

Treatment side effects can compromise quality of life, overall well-being, and compliance with the prostate cancer treatment. Co-medications for other diseases frequently found in elderly men may be affected as well[5,6,7]

Darolutamide...

is an oral androgen receptor inhibitor (ARi) with a **distinct chemical structure** that inhibits the growth of prostate cancer, while **limiting the burden of side effects** on patients' everyday lives, including **central nervous system-related adverse events** such as fatigue and cognitive impairment[2]

has been investigated in two Phase III clinical trials:

- **ARAMIS** in nmCRPC (results published)[2]
- **ARASENS** in metastatic hormone sensitive prostate cancer (mHSPC) (ongoing)[8]

has been shown to:

- **Significantly delay metastasis-free survival** (MFS)[2]
- **Significantly improve overall survival** (OS) and delay onset of cancer-associated morbidity[9]
- Have a **favorable safety profile, even with a longer duration of treatment,** allowing men with nmCRPC to maintain their lifestyle without disruption[1,7,9]

Darolutamide (Nubeqa™) is approved in the U.S., Australia, Brazil, Canada, Japan, China and the European Union. It is under review with other health authorities worldwide.

Forward-Looking Statements
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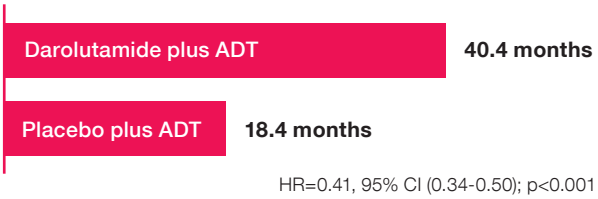
Phase III clinical trial data supporting use of darolutamide in nmCRPC

Delaying disease progression and extending life...

Highly significant improvement in MFS[2]

Darolutamide plus androgen deprivation therapy (ADT) showed a statistically **significant improvement in MFS** compared to placebo plus ADT



HR=0.41, 95% CI (0.34-0.50); p<0.001

Significant improvement in OS and delay in onset of cancer associated morbidity[9]

At the final pre-specified OS analysis of ARAMIS, darolutamide plus ADT demonstrated the following compared to placebo plus ADT:

31% **reduction in the risk of death**

HR=0.69, 95% CI 0.53-0.88; p=0.003

And a significant delay in:

- **Time to pain progression**
- **Time to first initiation of cytotoxic chemotherapy**
- **Time to first symptomatic skeletal event (SSE)**

...While maintaining mens' lifestyles

Maintained quality of life[10]

Darolutamide plus ADT **maintained quality of life** in men with nmCRPC beyond end of study treatment with scores similar to placebo plus ADT

Low potential for clinically relevant Drug-Drug Interactions (DDIs)[11]

Darolutamide is an AR-targeting therapy that has demonstrated a **low potential for clinically relevant DDIs** in men with nmCRPC treated with darolutamide and other types of medications typically used in this patient population for conditions such as hypertension, diabetes or cardiovascular disease

Reduced impact of cognitive impairment and other central nervous system (CNS) effects[1,2]

- Overall **low incidence of CNS-related adverse events** seen in men receiving darolutamide plus ADT may be explained by results seen in preclinical studies and in healthy humans, which demonstrated **a low blood-brain barrier penetration** by darolutamide[12,13]
- In a study investigating drug-induced changes in cerebral blood flow relevant to cognitive function, it was shown that darolutamide did not significantly impact the cerebral blood flow compared with placebo[13]

Favorable safety profile

Darolutamide plus ADT has demonstrated a **favorable safety profile**, even with a longer treatment duration, as shown in the final pre-specified OS analysis of ARAMIS. The frequency of adverse events (AEs) in men receiving darolutamide plus ADT is **overall comparable to ADT alone with no clinically relevant increases in rates of hypertension, falls or cognitive impairment.**[1,7]

The most frequent adverse reactions in the darolutamide plus ADT arm that occurred with an absolute increase in frequency of ≥2% compared to placebo plus ADT, were fatigue/asthenic conditions, pain in extremity, and rash. Discontinuation due to adverse events occurred in 9% of patients in both arms of the study.

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