

Darolutamide (Nubeqa) – Hope for men with high-risk non-metastatic hormone resistant prostate cancer

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In March this year, Australia's Therapeutic Goods administration approved darolutamide (Nubeqa) for the treatment of high-risk non-metastatic hormone (castrate) resistant prostate cancer. This is great news for men who have a rising PSA despite hormone therapy, with darolutamide shown to slow tumour progression, delaying metastases and extending overall survival. However, for many men the treatment is unaffordable, and an application is currently being considered for subsidisation of the drug under the Pharmaceutical Benefits Scheme (PBS). In this blog we examine the evidence and invite consumers to send their comments to the PBS committee about the importance of darolutamide to Australian men impacted by prostate cancer.

What is non-metastatic castrate resistant prostate cancer?

Testosterone and related male hormones known collectively as androgens, can stimulate prostate cancer cells to grow. Blocking the effects of androgens using various forms of androgen deprivation therapy (ADT) can slow the growth of these cancers. However, prostate cancer cells are good at adapting and finding ways around androgen deprivation so they can continue to grow.

Non-metastatic castrate resistant prostate cancer (nmCRPC) is a form of advanced prostate cancer. Men with nmCRPC have rising PSA levels suggesting that ADT is no longer effective, but scans don't show evidence of tumour spread to other parts of the body (metastasis).

A diagnosis of nmCRPC can be a little confusing. These men will have had their prostate tumours removed and only occasionally will prostate cancer cells re-grow in the area known as the prostate bed, where the prostate used to be. So, if PSA levels are rising, it must be because prostate cancer cells have spread to other parts of the body and started to grow. However, if these tumours are very small, they will not be detected by CT scans and the man will receive a diagnosis of nmCRPC. But with the increased use of highly sensitive PSMA-PET scans in Australia, tiny

metastatic tumours are more easily detected so that some of these men might be diagnosed with metastatic disease instead.

Treatments for non-metastatic castrate resistant prostate cancer.

Currently, there are few treatment options for nmCRPC in Australia. Once the disease progresses and becomes metastatic, there are several options for treating the now visible tumour growths including chemotherapy, radiotherapy and new therapies like Enzalutamide and Apalutamide.

There is evidence, however, that Enzalutamide and Apalutamide can be of benefit for men with nmCRPC and Apalutamide, but not Enzalutamide, has been approved by the TGA for treating this type of the disease. However, before these medications can be practically used to treat prostate cancer, they need both TGA approval to say that they are safe and effective treatments for nmCRPC and Pharmaceutical Benefit Scheme (PBS) listing so that they are affordable.

In February last year we published a detailed [blog](#) describing the results of the ARAMIS clinical trial. This trial was testing the effectiveness of a new drug called Darolutamide for the treatment of nmCRPC. Darolutamide is a new type of anti-androgen drug that was found to be effective in slowing prostate cancer progression in men with metastatic castration resistant prostate cancer. Based on these findings, the ARAMIS trial was conducted to see if Darolutamide might also be effective in non-metastatic castrate resistant prostate cancer.

Results from the ARAMIS trial have been published in [The New England Journal of Medicine](#). ARAMIS is a multicentre randomized, double-blind, placebo-controlled, phase 3 clinical trial. The trial recruited 1509 men with nmCRPC and PSA levels of at least 2 ng/ml with a doubling time of 10 months or less. These men were at high risk of developing metastatic disease. The men were randomly assigned to receive darolutamide (955 men) or a placebo (554 men).

Strikingly, Darolutamide was found to improve metastasis-free survival time. The average metastasis-free survival time was 40.4 months in the Darolutamide group, compared with 18.4 months for men taking the placebo. That means that it took longer for men taking Darolutamide to develop tumours (metastases) that could be detected by a scan.

The Darolutamide treatment also:

- increased the average amount of time before significant pain was experienced (40.3 months for the Darolutamide group compared to 25.4 months for placebo)

- prolonged the time before chemotherapy was needed
- was associated with a lower risk of death, within the trial time period
- increased time before PSA levels rapidly rose (33.2 months for the Darolutamide group compared to 7.3 months for placebo)

In terms of safety and side effects, Darolutamide was similar to placebo.

The ARAMIS trial has provided evidence that Darolutamide can slow prostate cancer progression in men with non-metastatic castration resistant prostate cancer, with reasonable safety in terms of side effects.

TGA approval and PBS listing of Darolutamide

The impressive results of the ARAMIS trial have led to [approval](#) from the Australian Therapeutic Goods Administration (TGA) for Darolutamide to be used to treat men with non-metastatic castrate resistant prostate cancer. The drug is sold under the tradename Nubeca. However, for this medicine to be an affordable treatment option, it will need to be listed with the Pharmaceutical Benefits Scheme (PBS) so that its cost can be subsidised by the government.

For a new medicine to be listed on the PBS it must be approved by the PBS Advisory Committee. This is a lengthy process to assess the clinical effectiveness, safety and cost effectiveness of the medicine compared to other therapies already available. During the process, numerous stakeholders including patients, carers, members of the public, health professionals and members of consumer interest groups are invited to provide their thoughts and comments on whether a medicine should be listed.

From now until 10 June 2020, you can have your say on whether Darolutamide (Nubeca) should be listed on the PBS, have a look at this link [here](#).