Chemotherapy Protocol

PROSTATE CANCER

DAROLUTAMIDE

Regimen

- Prostate - Darolutamide

Indication

- Darolutamide is recommended where the;

  - patient has a proven histological or cytological diagnosis of adenocarcinoma of the prostate without neuroendocrine differentiation or features of a small cell carcinoma.
  - patient has non-metastatic prostate cancer as defined by recent imaging with either conventional imaging with both a whole body isotope bone scan and a CT/MR scan of the chest, abdomen and pelvis or a PSMA PET-CT scan. Patients with the sole abnormality of pelvic lymph nodes measuring less than 2cm in short axis diameter and which are below the aortic bifurcation are eligible for darolutamide in this indication.
  - patient has hormone-resistant (castrate-resistant) disease as defined by 3 rising PSA levels (after the nadir PSA level) and taken at least 1 week apart during androgen deprivation therapy
  - patient's serum testosterone level is less than 1.7nmol/L on gonadotrophin releasing hormone agonist/antagonist therapy or after bilateral orchidectomy
  - current PSA level is greater than or equal to 2ng/ml.
  - the patient is at high risk of developing metastatic disease as defined by a PSA doubling time of less than or equal to 10 months.
  - patient has not received any previous 2nd generation androgen receptor inhibitors (such as enzalutamide, darolutamide, apalutamide) or CYP17 enzyme inhibitors (such as abiraterone) unless darolutamide has been accessed via a company early access scheme for this specific indication and the patient meets all the other criteria listed in this form.
  - darolutamide is being given only in combination with androgen deprivation therapy.
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  - formal medical review as to how darolutamide is being tolerated and whether treatment with darolutamide should continue or not will be scheduled to occur at least by the start of the third 4-weekly cycle of treatment.
  - a treatment break of more than 6 weeks beyond the expected 4-week cycle length is needed, a treatment break approval form will be completed before restarting treatment, including indicating as appropriate if the patient had an extended break because of COVID 19.
  - WHO performance status of 0, 1 or 2

Toxicity

Drug	Adverse Effect
Darolutamide	Fatigue/asthenia, decreased neutrophil count, raised bilirubin/AST, ischaemic heart disease, heart failure, rash, musculoskeletal pain, pain in extremities, fractures

The adverse effects listed are not exhaustive. Please refer to the relevant Summary of Product Characteristics for full details.

Monitoring

- FBC, U&Es, LFTs, PSA every four weeks for the first 12 weeks then every 8-12 weeks thereafter

Dose Modifications

The dose modifications listed are for liver and renal function and drug specific toxicities only. Dose adjustments may be necessary for other toxicities as well.

Hepatic Impairment

No dose adjustment is necessary for patients with mild hepatic impairment (Child-Pugh Class A).

Caution is advised in patients with moderate hepatic impairment (Child-Pugh Class B). For patients with moderate and severe hepatic impairment (Child-Pugh Classes B and C), the recommended starting dose is 300 mg twice daily

Renal impairment

No dose adjustment is necessary for patients with mild or moderate renal impairment.

For patients with severe renal impairment (eGFR 15-29 mL/min/1.73m^2) not receiving haemodialysis, the recommended starting dose is 300 mg twice daily.

Other

If a patient experiences NCI-CTC grade 3 or greater toxicity or an intolerable adverse reaction dosing should be withheld or reduced to 300 mg twice daily until symptoms improve. Treatment may then be resumed at a dose of 600 mg twice daily.

Dose reduction below 300 mg twice daily is not recommended, because efficacy has not been established.

Regimen

28 day cycle until disease progression (12 cycles will be set in Aria)

Drug	Dose	Days	Administration
Darolutamide	600mg twice a day	1-28 inclusive	Oral

Dose Information

- Darolutamide is available as 300mg film-coated tablets

Administration Information

- If a dose is missed, the dose should be taken as soon as the patient remembers prior to the next scheduled dose. The patient should not take two doses together to make up for a missed dose.

- Darolutamide film-coated tablets should be swallowed whole, with food and a glass of water.

Additional Information

- Darolutamide treatment should be supervised by a consultant oncologist.

- Use of strong CYP3A4 and P-gp inducers during treatment with darolutamide may decrease the plasma concentration of darolutamide and is not recommended, unless there is no therapeutic alternative. Selection of an alternate concomitant medicinal product with less potential to induce CYP3A4 or P-gp should be considered.
- Co-administration with rosuvastatin should be avoided unless there is no therapeutic alternative.
- Co-administration of darolutamide may increase the plasma concentrations of other BCRP, OATP1B1 and OATP1B3 substrates (e.g. methotrexate, sulfasalazine, fluvastatin, atorvastatin, pitavastatin). Therefore, it is recommended to monitor patients for adverse reactions of BCRP, OATP1B1 and OATP1B3 substrates. In addition, the related recommendation in the product information of these substrates should be followed when co-administered with darolutamide.

References

1. Fizazi K., Shore N., Tammela T L., Ulys A. et al., (2019). Darolutamide in Nonmetastatic, Castration-Resistant Prostate Cancer. *New England Journal of Medicine,* 380(13), pp 1235-1246
2. Bayer Plc (2020). NUBEQA 300 mg film-coated tablets Summary of Product Characteristics. Online at https://www.medicines.org.uk/emc/product/11324 last accessed 08/10/2020.

REGIMEN SUMMARY

Darolutamide

Day 1

Take Home Medicines

1. Darolutamide 600mg twice a day oral
   Administration Instructions
   Oral SACT.
   Swallow whole, with food and a glass of water.

DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
1	December 2020	None	Eleanor Taylor Oncology Pharmacist	Dr Caroline Chau Consultant Medical Oncologist

This chemotherapy protocol has been developed as part of the chemotherapy electronic prescribing project. This was and remains a collaborative project that originated from the former CSCCN. These documents have been approved on behalf of the following Trusts;

Hampshire Hospitals NHS Foundation Trust
NHS Isle of Wight
Portsmouth Hospitals NHS Trust
Salisbury NHS Foundation Trust
University Hospital Southampton NHS Foundation Trust
Western Sussex Hospitals NHS Foundation Trust

All actions have been taken to ensure these protocols are correct. However, no responsibility can be taken for errors which occur as a result of following these guidelines.