PROTOCOL

Systemic Anti Cancer Therapy Protocol

# Olaparib
# Prostate Cancer

PROTOCOL REF: MPHAOPC
(Version No.: 1.1)

## Approved for use:

Olaparib monotherapy for metastatic castration-resistant prostate (mCRPC) cancer bearing germline and/or somatic BRCA 1 or 2 mutations in patients who have progressed following previous treatment with an androgen receptor targeted agent (enzalutamide or apalutamide or darolutamide or abiraterone) AND:

- HAVE ALSO BEEN TREATED WITH DOCETAXEL. (OLAP7 blueteq form).

OR

- HAVE NOT BEEN PREVIOUSLY TREATED WITH DOCETAXEL (OLAP8 blueteq form).

Previous treatment with PARP inhibitor NOT permitted.

Treatment with ADT to continue unless patient has undergone surgical castration.

ECOG performance status of 0 to 2.

****Blueteq Form to be completed****

## Dosage:

| Drug | Dosage | Route | Frequency |
|---|---|---|---|
| Olaparib | 300mg | PO | Twice daily, continuously until disease progression |

Four weeks supply will be issued at each SACT treatment visit.

NOTE: Medical castration with luteinising hormone releasing hormone (LHRH) analogue should be continued during treatment in patients not surgically castrated.

## Patient Counselling Points:

Olaparib is available as 100mg and 150 mg film-coated tablets. It should be swallowed whole and not chewed, crushed, dissolved or divided irrespective of food intake at roughly the same time each day.

If a patient misses a dose of olaparib, they should take their next normal dose at its scheduled time.

Male patients should use a condom if in a sexual relationship with woman of childbearing potential, even if she is pregnant (potential risk of harm to foetus), for the durations of treatment and 3 months after receiving the last dose of olaparib. PLEASE NOTE: The efficacy of some hormonal contraceptives may be reduced if co-administered with olaparib.

Patients should avoid any food or drink containing grapefruit and grapefruit juice, Seville oranges, or pomelos within 7 days prior to start of treatment and until treatment discontinuation, as these have the potential to interact with olaparib.

Olaparib has a moderate effect on the ability to drive and operate heavy machinery due to fatigue, physical/genralised weakness or dizziness. Caution is advised when when driving or using machines.

## Emetogenic risk:

Mildly emetogenic.

## Supportive treatments:

Metoclopramide 10mg orally up to three times a day when required for nausea and vomiting for maximum duration of 5 consecutive days.

## Dosing in renal and hepatic impairment:

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| **Renal** | GFR > 50 ml/min: no dose adjustment<br>GFR 30-50 ml/min- recommended dose is 200mg BD<br>GFR < 30 ml/min or haemodialysis- not studied. Use with caution. Consult with clinical team. Consider dose reduction to 150mg BD. |

**Hepatic**

Child-Pugh A and B: no dose adjustment is needed
Child-Pugh C: not studied. Use with caution. Consult with clinical team. consider starting dose 150mg BD.

| Parameters | 1 point | 2 points | 3 points |
|---|---|---|---|
| Total bilirubin (µmol/L) | < 34 | 34–50 | > 50 |
| Serum albumin (g/L) | > 35 | 28–35 | < 28 |
| Prothrombin time, prolongation (s)<br>*Or*<br>INR | < 4<br><br>< 1.7 | 4–6<br><br>1.7-2.3 | > 6<br><br>>2.3 |
| Ascites | None | Mild to Moderate (diuretic responsive) | Severe (diuretic refractory) |
| Hepatic encephalopathy | None | Grade I–II (or suppressed with medication) | Grade III–IV (or refractory to medication) |

INR: International Normalised Ratio.
Child-Pugh Class A = 5-6 points
Child-Pugh Class B = 7-9 points
Child-Pugh Class C = 10 or more points
**Please note**: assessment of Child-Pugh Class is to help guide clinical teams when prescribing and pharmacists when screening.

## Interactions:

Olaparib under goes extensive metabolism by CYP3A4/5 and P-gp therefore inducers or inhibitors of this isoenzymes should be avoided. Olaparib may also induce several hepatic CYP metabolic pathways potentially reducing efficacy of hormonal contraceptives.

This list is not exhaustive, for full list of interactions please refer to SmPC or consult with a member of the pharmacy team.

**CYP3A Inhibitors**

Strong- itraconazole, telithromycin, clarithromycin, protease inhibitors boosted with ritonavir or cobicistat, boceprevir, telaprevir
Moderate- erythromycin, diltiazem, fluconazole, verapamil

**Concomitant use of:**

- **Strong or moderate CYP3A inhibitors is not recommended and alternative agents should be considered.** If a strong CYP3A inhibitor must be co-administered, the recommended **olaparib dose reduction is to 100 mg taken twice daily.**
- **If a moderate CYP3A inhibitor must be co-administered, the recommended olaparib dose reduction is to 150 mg taken twice.**

**CYP3A Inducers**

Co-administration of CYP3A  strong inducers (Phenobarbital, phenytoin, rifampicin, rifabutin, rifapentine, carbamazepine, nevirapine and St John's Wort) with olaparib have is NOT RECOMMENDED as this been shown to decrease significantly olaparib levels.

Increased exposure to the following medicines may also occur when co-administered with olaparib:

- Medication with narrow therapeutic index (digoxin, simvastatin, cisapride, cyclosporine, ergot alkaloids, fentanyl, pimozide, sirolimus, tacrolimus and quetiapine)- Appropriate clinical monitoring is recommended
- Other medication (dabigatran, colchicine, methotrexate, rosuvastatin, rosuvastatin, sulfasalazine, bosentan, glibenclamide, repaglinide, statins, valsartan, metformin, fentanyl, pimozide.

## Main toxicities:

| **Olaparib**<br>Most common (≥ 10%) adverse effects (any grade)- nausea, fatigue/asthenia, anaemia, vomiting, diarrhoea, decreased appetite, headache, neutropenia, dysgeusia, cough, leukopenia, dizziness, dyspnoea and dyspepsia.<br>Grade ≥ 3 adverse reactions occurring in > 2% of patients- anaemia (15%), neutropenia (5%), fatigue/asthenia (4%), leukopenia (3%) and thrombocytopenia (2%). | |
|---|---|
| Haematological toxicity | Very common - Anaemia, neutropenia, thrombocytopenia and lymphopenia |
| Gastrointestinal disorders | Very common- Nausea, Vomiting, Decreased appetite, Diarrhoea, Dyspepsia<br>Common - Upper abdominal pain, Stomatitis |
| Respiratory | Very common- Cough, SOB |
| CNS | Very common Fatigue (including asthenia), Headache, Taste Disturbance, Dizziness. |
| Pneumonitis | Reported in a small number of patients, monitor patients for new or worsening respiratory symptoms such as dyspnoea, cough and fever |
| Investigations | Common- Blood creatinine increased, VTE (predominantly PE) |
| Embryofoetal toxicity | Olaparib should not be used during pregnancy. Women of childbearing potential must use two forms of reliable contraception before starting Lynparza treatment, during therapy and for 1 month after receiving the last dose. Two highly effective and complementary forms of contraception are recommended. |

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|---|---|
| | Male patients and their female partners of childbearing potential should use reliable contraception during therapy and for 3 months after receiving the last dose. |

## Investigations and treatment plan:

| | Pre | Cycle 1 | Cycle 2 | Cycle 3 | Cycle 4 | Ongoing |
|---|---|---|---|---|---|---|
| Informed Consent | x | | | | | |
| Clinical Assessment | x | | x | | | As clinically indicated or every 3 months |
| SACT Assessment (to include PS and toxicities*) | x | x | x | x | x | Every cycle |
| FBC | x | x | x | x | x | Every cycle |
| LFTs (ALT, AST and Bilirubin) | x | x | x | x | x | Every cycle |
| U&E & renal profile | x | x | x | x | x | Every Cycle |
| CrCl (Cockcroft and Gault) | x | x | x | x | x | Every cycle |
| CT scan | x | | | | x | Every 3 months or as clinically indicated |
| PSA | x | x | x | x | x | Every cycle<br>(do not defer if PSA not recorded- to be added for next cycle) |
| Full Observations (*BP, heart rate, temperature, respiratory rate and $O_2$ sats*) | | x | | | | At baseline then as clinically indicated |
| Weight recorded | x | x | x | x | x | Every cycle |
| Height | x | | | | | |

* Monitor patients for new or worsening pulmonary symptoms e.g. shortness of breath, cough, and fever) indicative pneumonitis or pulmonary embolism.

## Dose Modifications and Toxicity Management:

| Dose adjustments | |
|---|---|
| Initial dose | 300mg twice daily |
| First dose reduction | 250mg twice daily |
| Second dose reduction | 200mg twice daily |
| Third dose reduction if GFR < 30ml/min ( refer to 'Dosing in renal and hepatic impairment') | 150mg twice daily |

## Haematological toxicity:

**Anaemia** was the most common CTCAE grade ≥3 adverse reaction reported in clinical studies. Median time to first onset of anaemia was approximately 4 weeks (approximately 7 weeks for CTCAE grade ≥3 events). Anaemia was managed with blood transfusions, dose interruptions and dose reductions as appropriate.

Proceed on day 1 if:-

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| ANC ≥ 1.0 x $10^9$/L | Platelets ≥ 100 x $10^9$/L | Hb ≥ 80 g/L |

Delay 1 week on day 1 if:-

| | | |
|---|---|---|
| ANC ≤ 0.9 x $10^9$/L | Platelets ≤ 99 x $10^9$/L | Hb < 80 g/L |

If platelets or ANC still below required levels for treatment at week 2, delay treatment again and patient will need assessed and chemotherapy dose reduction by clinical team.

If the blood parameters remain clinically abnormal after 4 weeks of olaparib dose interruption, bone marrow analysis and/or blood cytogenetic analysis are recommended due to risk of myelodysplastic syndrome/acute myeloid leukaemia (MDS/AML).

## Non- Haematological toxicity:

Treatment must be interrupted for any patient who experiences an intolerable grade 2 or any grade 3 or 4 adverse event, treatment can be restarted at a reduced dose when the toxicity returns to grade 1 or less.

## References:

De Bono, J., Mateo, J., Fizazi, K., Saad, F., Shore, N., Sandhu, S., Chi, K.N., Sartor, O., Agarwal, N., Olmos, D. and Thiery-Vuillemin, A., 2020. Olaparib for metastatic castration-resistant prostate cancer. *New England Journal of Medicine*, *382*(22), pp.2091-2102.

Krens S D, Lassche, Jansman G F G A, et al. Dose recommendations for anticancer drugs in patients with renal or hepatic impairment. Lancet Oncol 2019; 20: e201–08.

Lynparza 150mg tablets, Summary of Product Characteristics, AstraZeneca UK, United Kingdom. Available from www.medicines.org.uk/emc/medicine. Last Updated 20/4/23

NICE Technology appraisal guidance (TA887): Olaparib for previously treated BRCA mutation-positive hormone-relapsed metastatic prostate cancer. Published: 10 May 2023

## Circulation/Dissemination

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|---|---|
| Date added into Q-Pulse | 20th October 2023 |
| Date document posted on the Intranet | N/A |

## Version History

| Date | Version | Author name and designation | Summary of main changes |
|---|---|---|---|
| March 2022 | 1.0 | **Rachel Pritchard** | V1.0<br>New Regimen Protocol (private patients only) |
| May 2023 | 1.1 | **Rachel Pritchard**<br>**Urology SRG Pharmacist** | **V1.1**<br>**Update in-line with NHSE commissioning** |
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