PROTOCOL

Systemic Anti Cancer Therapy Protocol

Olaparib
Prostate Cancer (Private Use Only)

PROTOCOL REF: MPHAOPC
(Version No.: 1.0)

Approved for use:

For the treatment of adult patients with metastatic castration-resistant prostate cancer with *BRCA1/*2-mutations (germline and/or somatic) and associated homologous recombination repair (HRR) gene-mutations in patients who have progressed following prior therapy with enzalutamide or abiraterone.

Private funded patients patient only

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.

Administration:

Olaparib is available as 50mg, 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 Lynparza, they should take their next normal dose at its scheduled time.

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

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:

Renal	GFR > 50 ml/min: no dose adjustment GFR 30-50 ml/min- recommended starting dose 200mg BD GFR <30 ml/min or haemodialysis- not studied. Use with caution. consider starting dose 150mg BD.

Hepatic	Child-Pugh A and B: no dose adjustment is needed Child-Pugh C: 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) *Or* INR	< 4 < 1.7	4–6 1.7-2.3	> 6 >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

Phenobarbital, phenytoin, rifampicin, rifabutin, rifapentine, carbamazepine, nevirapine and St John's Wort.

Increased exposure to the following medicines may also occur: digoxin, dabigatran, colchicine, methotrexate, rosuvastatin and sulfasalazine, glibenclamide, repaglinide, statins, and valsartan, metformin, cyclosporin, ergot alkaloids, fentanyl, pimozide, tacrolimus and quetiapine

Main toxicities:

Olaparib	
Haematological toxicity	Very common - Anaemia, neutropenia, thrombocytopenia and lymphopenia
Gastrointestinal disorders	Very common- Nausea, Vomiting, Diarrhoea, Dyspepsia Common - Upper abdominal pain, Stomatitis
General disorders	Very common Fatigue (including asthenia), Decreased appetite, Headache, Dizziness, taste disturbance
Pneumonitis	Reported in a small number of patients, monitor patients for new or worsening respiratory symptoms such as dyspnoea, cough and fever
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. 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
Full Observations	x	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 indicative pneumonitis (e.g. shortness of breath, cough, and fever.

Dose Modifications and Toxicity Management:

Dose adjustments	
Initial dose	300mg twice daily
First dose reduction	250mg twice daily
Second dose reduction	200mg twice daily

Haematological toxicity:

Proceed on day 1 if:-

ANC ≥ 1.0 x 10^9/L	Platelets ≥ 100 x 10^9/L

Delay 1 week on day 1 if:-

ANC ≤ 0.9 x 10^9/L	Platelets ≤ 99 x 10^9/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 Oncologist

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:

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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 03/01/2022

Circulation/Dissemination

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Version History

Date	Version	Author name and designation	Summary of main changes
March 2022	1.0	**Rachel Pritchard**	V1.0 New Regimen Protocol