Systemic Anti Cancer Treatment Protocol

Olaparib (EAP)
Gynaecological Cancer

PROTOCOL REF: MPHAOLGY
(Version No: 1.0)

Approved for use in:

- High grade serous epithelial ovarian, fallopian tube, or primary peritoneal cancer
- Patients with germline or somatic BRCA1 or BRCA2 mutations
- Following first line platinum based chemotherapy – must be initiated within 8 weeks of their last dose of platinum-containing regime.
- PS 0-1

Dosage:

Drug	Dosage	Route	Frequency
Olaparib tablets	300mg	PO	Twice daily, until progression

Treatment will be supplied every 28 days

Supportive treatments:

Domperidone 10mg oral tablets, up to 3 times a day or as required

Extravasation risk:

Not applicable - Oral agent

Administration:

Olaparib tablets should be swallowed whole with water and taken approximately 12 hours apart. Olaparib tablets can be taken with or without food.

For patients of child-bearing potential, ensure appropriate contraception is discussed. If a patient becomes pregnant whilst on treatment, olaparib should be discontinued immediately.

Interactions:

No other anticancer therapy (chemotherapy, immunotherapy, hormone therapy, radiotherapy, biological therapy or other novel agent) is to be permitted while the patient is receiving olaparib.

Olaparib under goes extensive metabolism by CYP3A4/5 and P-gp therefore inducers or inhibitors of this isoenzymes should be avoided where possible.

Olaparib may also induce several hepatic CYP metabolic pathways potentially reducing efficacy of hormonal contraceptives.

CYP3A Inhibitors (not exhaustive list)

Strong inhibitors (Itraconazole, telithromycin, clarithromycin, boosted protease inhibitors, indinavir, saquinavir, nelfinavir, boceprevir, telaprevir) or moderate inhibitors (ciprofloxacin, erythromycin, diltiazem, fluconazole, verapamil) should not be taken with olaparib.

If there is no alternative to the above inhibitors, then the dose of olaparib should be reduced as follows:

Strong inhibitors – reduce the dose of olaparib to 100mg twice daily for the duration of the concomitant therapy with the strong inhibitor and for 5 half-lives afterwards

Moderate inhibitors – reduce dose to 150mg twice daily for the duration of concomitant therapy with the moderate inhibitor and for 3 half-lives after.

After the washout of the inhibitor is complete, the olaparib dose can be re-escalated.

CYP3A Inducers (not exhaustive list):

Strong inducers - (Phenobarbital, phenytoin, rifampicin, rifabutin, rifapentine, carbamazepine, nevirapine and St John's Wort) and moderate inducers (bosentan, efavirenz, modafinil) should not be taken with olaparib

If the use of strong or moderate inducers is considered necessary for the patient's safety and welfare this could diminish the clinical efficacy of olaparib. If a patient requires the use of a concomitant inducer, they must be monitored carefully for any change in efficacy of olaparib.

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, Common - neutropenia, thrombocytopenia and leukopenia. Uncommon - 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. If pneumonitis is confirmed, olaparib should be discontinued.
Embryofoetal toxicity	Olaparib should not be used during pregnancy and in women of childbearing potential not using reliable contraception during therapy and for 1 month after receiving the last dose of olaparib.
MDS/AML	If patients' blood parameters remain clinically abnormal after 4 weeks of dose interruption of olaparib, bone marrow analysis is recommended. The incidence of MDS/AML in clinical trials of olaparib was <1.5% and the majority of events had a fatal outcome.

Investigations:

	Pre	Cycle 1	Cycle 2	Cycle 3	Cycle 4	Cycle 5	Cycle 6	Ongoing
Medical Assessment	X				X			Every 3 cycles or as per patients' management plan
SACT Assessment	X	X	X	X	X	X	X	Every cycle
FBC	X	X	X	X	X	X	X	Every cycle
U&E & LFT	X	X	X	X	X	X	X	Every cycle
CA125	X	X	X	X	X	X	X	Every cycle
CT scan	X							If clinically indicated
Informed Consent	X							
PS recorded	X	X	X	X	X	X	X	Every cycle
Toxicities documented	X	X	X	X	X	X	X	Every cycle
Weight recorded	X	X	X	X	X	X	X	Every cycle

Dose Modifications and Toxicity Management:

Haematological toxicity

Proceed on day 1 if:-

Hb ≥ 10g/dL	ANC ≥ 1.0 x 10^9/L	Platelets ≥ 100 x 10^9/L

Interrupt treatment for 1 week on day 1 if:-

Hb 8-10g/dL	ANC ≤ 0.9 x 10^9/L	Platelets ≤ 99 x 10^9/L

If haemoglobin, platelets or ANC still below required levels for treatment at week 2, delay treatment again and patient will need to be assessed and chemotherapy dose reduced by Oncologist

Interrupt treatment for a maximum of 4 weeks if: -

Hb ≤ 8g/dL

Upon recovery dose of olaparib should be reduced to 250mg twice daily as a first step and then to 200mg twice daily as a second step in the case of repeat Hb decrease

Non-haematological toxicities

Treatment must be interrupted for any patient who experiences an intolerable grade 2 or any grade 3 or 4 adverse event using the CTCAE V3/4, treatment can be restarted at a reduced dose when the toxicity returns to grade 1 or less.

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

Renal and hepatic impairment

Renal impairment	
Creatinine Clearance (mL/min)	Dose
>51	300mg twice daily
31-50	200mg twice daily
<31	Discontinue olaparib

Hepatic impairment
Olaparib can be administered to patients with mild or moderate hepatic impairment (Child-Pugh A or B) with no dose adjustments. Olaparib is not recommended in patients with severe hepatic impairment (Child-Pugh C).

References:

AstraZeneca Investigator's Brochure: AZD2281, Lynparza, olaparib. Edition number 15, 08 March 2018

Olaparib EAP Inclusion/Exclusion criteria

Summary of Product Charasteristics: Lymparza 100mg Film-Coated Tablets; AstraZeneca UK Limited. Last updated 09 May 2018