Olaparib

Indication

Maintenance treatment of BRCA mutation-positive advanced ovarian, fallopian tube or peritoneal cancer after response to platinum-based chemotherapy who:

1. are in response following platinum-based FIRST line chemotherapy (OLAP1a) or
2. have a recent first relapse of platinum-sensitive disease and are now in response following a SECOND platinum-based chemotherapy (OLAP2) or
3. have a recent second or subsequent relapse of platinum-sensitive disease and are now in response following a THIRD or subsequent platinum-based chemotherapy (OLAP3)

Adjuvant treatment of high-risk BRCA-mutated, HER2-negative early breast cancer which has previously been treated with surgery and neoadjuvant or adjuvant chemotherapy (as defined by OlympiA trial entry criteria)

Treatment of BRCA mutation-positive HER2-negative metastatic breast cancer after chemotherapy

Hormone-relapsed metastatic prostate cancer with BRCA1 or BRCA2 mutations that has progressed after a newer hormonal treatment (such as abiraterone or enzalutamide)

Regimen details

Olaparib tablets 300mg BD
Gynae: Treatment should start no later than 8 weeks after completion of final dose of platinum-containing regimen.
Breast (adjuvant): treatment should start least 2 weeks after completion of last treatment (surgery, chemotherapy or radiotherapy) but ideally no later than 12 weeks
Prostate: continue LHRHa therapy during treatment with olaparib

Cycle frequency

28 days

Number of cycles

Gynae, prostate and metastatic breast: Continue until disease progression, or unacceptable toxicity.
For maintenance treatment following first line chemotherapy (gynae), if the patient is in complete remission at the end of 2 years, maintenance olaparib can continue if the treating clinician considers that the patient will derive further benefit (must complete Blueteq form OLAP1b)
Adjuvant breast: 12 months

Administration

Take with or without food. Grapefruit and grapefruit juice should be avoided while on olaparib.

Additional supportive medication

Nil regular

Investigations – pre first cycle

Investigation	Validity period
BRCA mutation status	
FBC	14 days
U+E (including creatinine)	14 days
LFT (including AST)	14 days
Hep B and C screen	28 days
Pregnancy test (if pre-menopausal women who has not already undergone hysterectomy/BSO)	28 days
ECG	

Investigations –pre subsequent cycles

FBC, U+E (including creatinine), LFT (including AST)

Standard limits for administration to go ahead

If blood results not within range, authorisation to administer **must** be given by prescriber/ consultant.

Investigation	Limit
Neutrophil count	≥ 1.0 x 10^9/L
Platelet count	≥ 100 x 10^9/L
Hb	>90
Creatinine clearance	>30mL/min (Not recommended for use in patients with severe renal impairment or end-stage renal disease)
ECG (pre cycle 1)	QTc<470 msec

Delay one week if:

- Neuts <1.0
- Platelets <100
- Hb < 90

repeat FBC, if not recovered, delay one week more and contact consultant for clinic review and dose reduction

Dose modifications

Can be administered to patients with mild renal impairment (CrCl > 50)
For patients with moderate renal impairment (creatinine clearance 31 to 50 ml/min) the recommended dose of olaparib tablets is 200 mg (two 100 mg tablets) twice daily (equivalent to a total daily dose of 400 mg)

Not recommended in patients with hepatic impairment (bilirubin > 1.5 x ULN)

Treatment should be interrupted to manage adverse events. If required, reduce dose to 250 mg twice daily in the first instance, then 200 mg twice daily if further reduction required

Adverse effects –

for full details consult product literature/ reference texts

Reduced appetite, altered taste sensation, headache, dizziness, nausea, vomiting, diarrhoea, dyspepsia, stomatitis, upper abdominal pain, fatigue, anaemia, neutropenia, thrombocytopenia

Myelodysplastic syndrome/Acute myeloid leukaemia: < 1.5%

Pneumonitis, including events with a fatal outcome, has been reported in <1.0%

Significant drug interactions

Elimination of olaparib is mainly through hepatic metabolism, with CYP3A4 being the major enzyme involved.

Concomitant use of strong or moderate CYP3A inducers (eg phenytoin, rifampicin, carbamazepine, St John's Wort) with olaparib should be avoided as this may increase the risk of therapeutic failure.

Co-administration with strong or moderate CYP3A inhibitors (eg itraconazole, clarithromycin) should also be avoided. If this is not possible the recommended olaparib dose reduction is to 100mg twice daily with a strong CYP3A inhibitor or 150mg twice daily with a moderate CYP3A inhibitor (eg fluconazole).

Caution should be exercised if olaparib is administered in combination with any statin, as it cannot be excluded that olaparib may increase exposure to statins.

Additional comments

Women of childbearing potential who are sexually active must agree, with their partners, to the use of two highly effective forms of contraception in combination. This should be started from the signing of the informed consent and continue, throughout the period of taking olaparib and for at least 1 month after the last dose of olaparib, or they must totally/truly abstain from any form of sexual intercourse

Male patients must use a condom during treatment and for 3 months after last dose of olaparib when having sexual intercourse with a pregnant woman or with a woman of childbearing potential. Female partners of male patients should also use a highly effective form of contraception if they are of childbearing potential

References

Moore, K et al NEJM 2018; 379 :2495-2505
Tutt, AN et al N Engl J Med 2021; 384:2394-2405
De Bono et al N Engl J Med 2020; 382:2091-2102

THIS PROTOCOL HAS BEEN DIRECTED BY DR EATON, CONSULTANT MEDICAL ONCOLOGIST

RESPONSIBILITY FOR THIS PROTOCOL LIES WITH THE HEAD OF SERVICE

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