Talazoparib (Breast)

Please note this protocol has been produced in a new format that is currently being piloted. Any feedback on this new format should be sent to SSGMeetings@uhbw.nhs.uk

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Indication

HER2-negative locally advanced or metastatic breast cancer in patients with germline BRCA1 or BRCA2 mutations who have previously been treated with:

- an anthracycline or a taxane or both, unless these treatments are not suitable
- endocrine therapy if hormone receptor-positive breast cancer unless this is not suitable

(NICE TA 952)

Response Rates

Phase 3 open label EMBRACA trial
Talazoparib (n=287) vs standard single agent physician's choice of chemotherapy (n=144)
Median PFS: 8.6 months vs 5.6 months
ORR: 62.6% vs 27.2%

Treatment related mortality

<1%

Regimen details

Drug	Dose	Route
Talazoparib	1mg OD*	Oral

* Dose reductions may be required due to drug interactions. See drug interactions section for details.

Cycle frequency
28 days (continuous)

Number of cycles
Until disease progression or unacceptable toxicity.

Pre-medication
Nil

Supportive medication
Antiemetics if required

Emetogenicity
This regimen has mild emetic potential

Administration
Talazoparib is available as 1mg and 0.25mg capsules. The capsules should be swallowed whole and must not be opened or dissolved and may be taken with or without food. If the patient vomits or misses a dose of talazoparib, an additional dose should not be taken and the next dose should be taken at the usual time.

Mandatory investigations – pre first cycle

Investigation	Validity period
FBC	14 days
U&E (including creatinine)	14 days
LFT	14 days

Investigations – pre subsequent cycles

Investigation	Validity period
FBC	96 hours
U&E (including creatinine)	7 days
LFT	7 days

Standard limits for administration to go ahead

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

Investigation	Limit
Neutrophils	≥ 1.0 x 10^9/L
Platelets	≥ 50 x 10^9/L
Haemoglobin	≥ 8g/dL
Creatinine clearance (CrCl)	≥ 60 mL/min

Dose modifications

Dose level	Talazoparib dose
Recommended starting dose	1mg OD
First dose reduction	0.75mg OD
Second dose reduction	0.5mg OD
Third dose reduction	0.25mg OD

Haematological toxicity

Toxicity	Action
Neutrophils < 1.0 x 10^9/L	Withhold talazoparib until neutrophils ≥ 1.5 x 10^9/L Resume at next lower dose level
Platelets < 50 x 10^9/L	Withhold talazoparib until platelets ≥ 75 x 10^9/L Resume at next lower dose level
Haemoglobin < 8g/dL	Withhold talazoparib until haemoglobin ≥ 9g/dL Resume at next lower dose level

Renal impairment

Creatinine clearance	Dose
≥ 60 mL/min	1mg OD
30-59mL/min	0.75mg OD
15-29mL/min	0.5mg OD
<15 mL/min or haemodialysis	Contraindicated

Hepatic impairment

Talazoparib undergoes minimal hepatic metabolism. No dose adjustment is required for any grade of hepatic impairment.

Other toxicities

Toxicity	Definition	Action/Dose adjustment
Non-haematological adverse reaction	Grade 3 or 4	Withhold talazoparib until improved to ≤ grade 1. Consider restarting at next lower dose level or discontinuing treatment.

Side Effects

EMBRACA study:

Toxicity		Any grade (%)	Grade 3 or 4 (%)
Haematological	Anaemia	52.8	39.2
	Neutropenia	34.6	20.9
	Thrombocytopenia	26.9	18.5
	Febrile neutropenia	0.3	0
Non-haematological	Fatigue	50.3	1.7
	Nausea	48.6	0.3
	Headache	32.5	1.7
	Alopecia	25.2	NA
	Vomiting	24.8	2.4
	Diarrhoea	22.0	0.7
	Constipation	22.0	0.3
	Decreased appetite	21.3	0.3
	Back pain	21.0	2.4
	Dyspnoea	17.5	2.4
	Pleural effusion	2.1	1.7
	Palmar-plantar erythrodysaesthesia	1.4	0.3

Specific drug related side effects:

Common (>10%)	Uncommon (1-10%)	Rare (<1%)
Anaemia	Dysgeusia	Myelodysplastic syndrome/ acute myeloid leukaemia
Thrombocytopenia	Dyspepsia	
Neutropenia		
Fatigue		
Nausea		
Decreased appetite		

Myelodysplastic syndrome/Acute myeloid leukaemia

Myelodysplastic syndrome/acute myeloid leukaemia (MDS/AML) have been reported in patients who received PARP inhibitors, including talazoparib. Overall MDS/AML has been reported in <1% of solid tumour patients treated with talazoparib in clinical studies. Potential contributing factors for the development of MDS/AML include previous platinum containing chemotherapy, other DNA damaging agents or radiotherapy. FBC should be checked at baseline and monitored regularly for signs of haematological toxicity during treatment. If MDS/AML is confirmed, talazoparib should be discontinued.

Additional information

A highly effective method of contraception is required for female patients during treatment with talazoparib and for at least 7 months after completing treatment. Male patients with female partners of reproductive potential should be advised to use effective contraception during treatment with talazoparib and for at least 4 months after the final dose.

Significant drug interactions – for full details consult product literature/ reference texts

Strong P-gp inhibitors (e.g. itraconazole, amiodarone, carvedilol, clarithromycin, cobicistat, darunavir, dronedarone, erythromycin, indinavir, itraconazole, ketoconazole, lapatinib, lopinavir, propafenone, quinidine, ranolazine, saquinavir, telaprevir, tipranavir, verapamil): concomitant use should be avoided, but if co-administration is unavoidable talazoparib should be reduced to the next lower dose level.
P-gp inducers (e.g. carbamazepine, phenytoin and St John's Wort) may decrease talazoparib exposure
Strong BCRP inhibitors (e.g. ciclosporin and curcumin): concomitant use should be avoided. If co-administration is unavoidable monitor for increased adverse reactions.

References

- Summary of Product Characteristics Talazoparib (Pfizer) accessed 21st November 2024 via www.medicines.org.uk
- National Institute for Clinical Excellence (TA952) accessed 21st November 2024 via www.nice.org.uk
- Litton, J.K. et al. Talazoparib in patients with advanced breast cancer and germline BRCA mutations. N Engl J Med 2018;379:753-63

Version	Issue date	Review date	Revision	Written/Checked/Authorised
1	Nov 2024	Nov 2027	New protocol	Written/reviewed: Dr C Comins (Consultant Oncologist, UHBW NHS Trust), A Pearce (Trainee ANP, UHBW NHS Trust) Checked: Kate Gregory (Lead Pharmacist for SACT protocols, SWAG Cancer Alliance) Authorised: Dr J Braybrooke (Consultant Oncologist, UHBW NHS Trust and SWAG Cancer Alliance)

Schedule of investigations and treatment plan

Activity	Pre-tx	Cycle 1	Cycle 2	Cycle 3	Ongoing
Informed consent	x				
Clinical assessment	x	x	x	x	Every cycle
FBC	x	x	x	x	Every cycle
U&E & LFTs	x	x	x	x	Every cycle
CrCl	x	x	x	x	Every cycle
Imaging as per guidance	x				Repeat if clinically indicated
Weight recorded	x				Repeat if necessary