Talazoparib

Indication

Talazoparib is indicated as monotherapy for the treatment of adult patients with germline BRCA1/2-mutations, who have HER2-negative locally advanced or metastatic breast cancer.

Patients should have been previously treated with an anthracycline and/or a taxane in the (neo)adjuvant, locally advanced or metastatic setting unless patients were not suitable for these treatments.
Patients with hormone receptor positive breast cancer should have been treated with a prior endocrine-based therapy, or be considered unsuitable for endocrine-based therapy.

Regimen details

1 mg talazoparib once daily

Cycle frequency

4-weekly

Number of cycles

Continue until disease progression or unacceptable toxicity

Administration

Oral

Pre-medication

None

Emetogenicity

Low

Additional supportive medication

Metoclopramide prn for first cycle

Extravasation

N/A

Investigations – pre first cycle

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

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	≥ 50 x 10^9/L
Creatinine clearance	≥ 60mL/min

Dose modifications

Table 1. Dose adjustments for toxicities

	Dose level
Recommended starting dose	1 mg (one 1 mg capsule) once daily
First dose reduction	0.75 mg (three 0.25 mg capsules) once daily
Second dose reduction	0.5 mg (two 0.25 mg capsules) once daily
Third dose reduction	0.25 mg (one 0.25 mg capsule) once daily

Table 2. Dose modification and management

	Withhold talazoparib until levels resolve to	Resume Talazoparib
Haemoglobin < 80 g/L	≥ 90 g/L	Resume talazoparib at next lower dose
Platelet count < 50 x 10^9/L	≥ 75 x 10^9/L	
Neutrophil count < 1 x 10^9/L	≥ 1 x 10^9/L	
Non-haematologic adverse reaction Grade 3 or Grade 4	≤ Grade 1	Consider resuming talazoparib at next lower dose or discontinue

Renal Impairment

No adjustment required for CrCl 60mL/min and above
For patients with CrCl between 30mL/min and 60mL/min the dose should be adjusted to 0.75mg daily
For patients with severe renal impairment (CrCl between 15 to 30 mL/min), the recommended starting dose should be 0.5 mg once daily.
If renal function deteriorates during treatment, then patients should be reviewed by the clinical team

Hepatic Impairment

No adjustments required for mild hepatic impairment
Talazoparib has not been studied in patients with bilirubin above 1.5 times ULN
Withhold treatment if bilirubin increases to 2 times ULN and/or AST/ALT increases to 3 times ULN from a normal baseline result.
Ensure patient has a review with oncologist to arrange appropriate further investigations.
If AST/ALT reaches 5 times ULN from a raised baseline result, then treatment should discontinue.

Adverse effects - for full details consult product literature/ reference texts

- **Serious side effects**
  Thrombocytopenia
  Anaemia
  Neutropenia

- **Frequently occurring side effects**
  Vomiting
  Diarrhoea
  Nausea
  Abdominal pain
  Stomatitis
  Dyspepsia

- **Other side effects**
  Alopecia (grade 1/2)
  Fatigue

Dizziness
Headache
Decreased appetite

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

Strong inhibitors of P-gp may lead to increased exposure to talazoparib and therefore should be avoided

Strong inhibitors of P-gp include, but not limited to, amiodarone, carvedilol, clarithromycin, cobicistat, darunavir, dronedarone, erythromycin, indinavir, itraconazole, ketoconazole, lapatinib, lopinavir, propafenone, quinidine, ranolazine, ritonavir, saquinavir, telaprevir, tipranavir, and verapamil)

If co-administration with a strong P-gp inhibitor is unavoidable, dose of talazoparib should be reduced.

Additional comments

Appropriate contraceptive precautions must be taken, for female patients, contraceptive measures should continue for 7 months after discontinuation of talazoparib; for males patients 4 months after discontinuation

References

1. Talazoparib SPC: https://www.medicines.org.uk/emc - accessed 15/2/2024
2. Talazoparib in patients with germline BRCA mutated advanced breast cancer. Detailed safety analysis. Hurvitz et al. The Oncologist, 2019 24:1-12
3. Talazoparib in patients with advanced breast cancer and a germline BRCA mutation. Litton JK et al. NEJM 2018 379: 753-763
4. CCC protocol for talazoparib: https://www.clatterbridgecc.nhs.uk/application/files/4416/2029/7923/Talazoparib_Breast_Cancer_with_BRCA1_or_2_Mutations_Protocol_V1.0.pdf

THIS PROTOCOL HAS BEEN DIRECTED BY DR YOUNG, CONSULTANT ONCOLOGIST

RESPONSIBILITY FOR THIS PROTOCOL LIES WITH THE HEAD OF SERVICE

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