

Tucatinib, Capecitabine & Trastuzumab

Indication

Locally advanced or metastatic breast cancer after 2 or more anti-HER2 regimens.
Patients with brain metastases are eligible with new, previously treated or progressive brain disease as long as local brain directed treatment not required urgently

Regimen details

Tucatinib 300mg PO twice daily continually (with or without food)
Capecitabine 1000mg/m² PO twice daily on days 1-14 (within 30mins of food)
Trastuzumab 600mg SC on day 1

Cycle frequency

Repeat every 21 days

Number of cycles

Treatment to continue until disease progression or unacceptable toxicity

Administration

The 600 mg Trastuzumab dose should be administered as a subcutaneous injection only over 2-5 minutes. The injection site should be alternated between the left and right thigh. New injections should be given at least 2.5 cm from the old site and never into areas where the skin is red, bruised, tender, or hard. During the treatment course with Herceptin subcutaneous formulation other medicinal products for subcutaneous administration should preferably be injected at different sites.

Patients should be observed for two hours after the first injection and for 30 minutes after subsequent injections for signs or symptoms of administration-related reactions. The observation time in subsequent doses may be reduced at local clinician's discretion

Oral Tucatinib to be taken with or without food

Oral Capecitabine to be taken within 30 minutes of food

Emetogenicity

Low risk

Additional supportive medication

Oral paracetamol 30 mins pre-trastuzumab

Loperamide prn

Cyclizine prn

Extravasation

No risk

Investigations – pre first cycle

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

Bone profile	14 days
Glucose	14 days
HbA1C	14 days
Hepatitis B serology	14 days
DPYD screen	n/a
Cardiac assessment with MUGA or ECG	28 days

Investigations –pre subsequent cycles

FBC, U&Es, LFTs, Bone profile, Glucose

Cardiac assessment with MUGA or echocardiogram every 4 months

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	$\geq 1.5 \times 10^9/L$ (Discuss with consultant if 1.0 to 1.5)
Platelet count	$\geq 100 \times 10^9/L$
Creatinine clearance	≥ 50 mL/min Creatinine clearance. If CrCl 30-50 then reduce capecitabine to 75%. Contraindicated if CrCl <30)
Bilirubin	$\leq 1.5 \times ULN$ (if Gilberts syndrome then conjugated Bilirubin <1.5 x ULN)
ALT/AST	< 2.5 x ULN (or <5 x ULN if liver metastases) – for 1st cycle but see toxicity table for action with deranged LFTs whilst on treatment

Dose modifications

Tucatinib

First dose reduction – 250mg twice daily

Second dose reduction – 200mg twice daily

Third dose reduction – 150mg twice daily

If not tolerated at 150mg twice daily then permanently discontinue

Diarrhoea

Grade 1 or 2 – Treat with loperamide. No dose modification required

Grade 3 without anti-diarrhoeal treatment – initiate or intensify appropriate medical therapy. Hold tucatinib until recovery to grade 1, then resume at same dose level

Grade 3 with anti-diarrhoeal treatment – Initiate or intensify appropriate medical therapy. Hold tucatinib until recovery to grade 1, then resume at lower dose level

Grade 4 – Permanently discontinue Tucatinib

Increased ALT, AST or Bilirubin

Grade 1 Bilirubin (>ULN to 1.5 ULN) – No dose modification required

Grade 2 Bilirubin (>1.5 ULN to 3 x ULN) – Hold tucatinib until recovery to Grade 1 then resume at the same dose level

Grade 3 ALT/AST (>5 ULN to 20 x ULN) **OR** Grade 3 bilirubin (>3 ULN to 10 x ULN) – Hold tucatinib until recovery to grade 1, then resume at the next lower dose

Grade 4 ALT/AST (>20 x ULN) **OR** Grade 4 bilirubin (>10 x ULN) – Permanently discontinue Tucatinib

ALT/AST >3 x ULN **AND** Bilirubin >2 x ULN – Permanently discontinue Tucatinib

Bilirubin >3 x ULN or ALT/AST >2.5 x ULN omit Capecitabine until liver function recovers

Other adverse reactions

Grade 1 and 2 – No dose modification required

Grade 3 – Hold Tucatinib until recover to grade 1 and then resume at 1 reduced dose level

Grade 4 – Permanently discontinue Tucatinib

Toxicity due to capecitabine can be managed symptomatically and or modification of dose / dose delay

Lancashire & South Cumbria Cancer Network

Systemic Anticancer Treatment Protocol

Adverse effects –

for full details consult product literature/ reference texts

Lethargy

Diarrhoea

Nausea / vomiting

PPE

Stomatitis

Elevated AST/ALT

Elevated creatinine

Cardiac toxicity

Myelosuppression

Infusion reactions

Significant drug interactions

– for full details consult product literature/ reference texts

THIS PROTOCOL HAS BEEN DIRECTED BY DR MOON, DESIGNATED LEAD CLINICIAN FOR BREAST CANCER

RESPONSIBILITY FOR THIS PROTOCOL LIES WITH THE HEAD OF SERVICE

Date: May 2022

Review: May 2025

VERSION: 1
