Durvalumab and Tremelimumab

Indication
Untreated advanced or unresectable hepatocellular carcinoma (HCC) in adults. Child-Pugh score A

Regimen details
Tremelimumab 300mg in 100ml 0.9% sodium chloride over 1 hour
Durvalumab 1500mg in 100ml 0.9% sodium chloride over 1 hour

For patients with body weight ≤ 30 kg, administer durvalumab 20mg/kg (until weight increases to > 30 kg)
For patients with body weight ≤ 40kg, administer tremelimumab 4mg/kg (until weight increases to >40kg)

Cycle frequency
Durvalumab given every 4 weeks
Tremelimumab cycle 1 only

Number of cycles
Treatment with durvalumab after its initial single dose in combination with tremelimumab will continue until loss of clinical benefit or unacceptable toxicity or withdrawal of patient consent, whichever occurs first

Administration
Administer tremelimumab first, followed by durvalumab

Administer the drug solution over 60 minutes using a volumetric pump through an in-line 0.2µm or 1.2µm polyethersulfone or 0.2µm positively charged nylon filter

Patients should be monitored for signs and symptoms of infusion-related reactions

The final concentration of durvalumab should be between 1mg/ml and 15mg/ml
The final concentration of tremelimumab should be between 0.1mg/ml and 10mg/ml

Pre-medication
None

Emetogenicity
Minimal

Additional supportive medication
None

Extravasation
Neutral

Investigations – pre first cycle
Standard pre-SACT tests

Investigations –pre subsequent cycles
ECOG performance status
FBC, U&Es, LFTs

TFTs – alternate doses or if abnormal at each cycle

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
Creatinine clearance	≥ 60 mL/min
Bilirubin	≤ 1.5 x ULN
AST	< 1.5 x ULN

Dose modifications

For information on treatment of Immune related side effects see:
https://www.nwcscnsenate.nhs.uk/strategic-clinical-network/our-networks/cancer/lancs-south-cumbria-chemotherapy-protocols/lsc-immune-related-toxicity-management-guidelines/

Dose Modifications/Discontinuation Criteria

Dose reductions or escalations are not recommended for either drug. Doses may be delayed or discontinued based on toxicity.
Durvalumab will be withheld for a drug-related non-hematological toxicity ≥Grade 2 (excluding fatigue).
Once the patient has recovered to Grade 0-1 the drug can be continued
Durvalumab will be permanently discontinued for any Grade 3-4, severe or life-threatening adverse reaction.
For rash / dermatitis reactions permanently discontinue only if Grade 4.
For any endocrinopathy treatment can be resumed once clinically stable.

Drug does NOT need to be delayed or discontinued for controlled endocrinopathies.

Grade 1: No action. Provide symptomatic treatment
Grade 2: May withhold durvalumab. Consider systemic corticosteroids in addition to appropriate symptomatic treatment
Grade 3 and Grade 4: Withhold durvalumab. Discontinue if unable to reduce corticosteroid dose to < 10 mg per day prednisolone equivalent within 12 weeks of toxicity.
Systemic corticosteroids are indicated in addition to appropriate symptomatic treatment. May utilize 1 to 2 mg/kg prednisolone or equivalent per day. Steroid taper should be considered once symptoms improve to Grade 1 or less and tapered over at least 4 weeks.

Infusion related Reactions.

Grade	Management	RE-Challenge
1 or 2	Stop or slow the infusion rate For durvalumab stop or slow the rate to 50%	Consider pre medication prior to subsequent infusions for durvalumab
3 or 4	Stop treatment. Mange symptoms.	Permanently discontinue (do not rechallenge)

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

- For information on treatment of Immune related side effects see: https://www.nwcscnsenate.nhs.uk/strategic-clinical-network/our-networks/cancer/lancs-south-cumbria-chemotherapy-protocols/lsc-immune-related-toxicity-management-guidelines/
- Common (25-49%) – Rash, purities (may be severed), Diarrhoea (may be severe)
- Less Common (10-24%) – Abdominal pain, fatigue, anorexia, elevated LFT's, nausea, vomiting, fever, infection (may be severe), Hypo or hyperthyroidism, Constipation, insomnia.
- Uncommon (<10%) – Myocarditis, infusion related reaction, hepatitis, nephritis, pneumonitis, pancreatitis,

adrenal insufficiency, diabetes, thyroiditis, hypophysitis, colitis, GI perforation, Guillain-Barre syndrome, Stevens-Johnson syndrome, Toxic epidermal necrolysis, encephalitis, meningitis, Immune thrombocytopenic purpura, Myasthenia, Rhabdomyolysis, Myositis, Eye disorders.

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

Corticosteroids: use of systemic corticosteroids at baseline, before starting durvalumab/tremelimumab, should be avoided because of their potential interference with the pharmacodynamic activity and efficacy of durvalumab/tremelimumab. However, systemic corticosteroids or other immunosuppressants can be used after starting durvalumab to treat immune-related adverse reactions.

References

https://www.medicines.org.uk/emc/product/9495/smpc
https://www.medicines.org.uk/emc/product/14841/smpc#gref

THIS PROTOCOL HAS BEEN DIRECTED BY DR C Mitchell, DESIGNATED LEAD CLINICIAN FOR Upper GI Cancers

RESPONSIBILITY FOR THIS PROTOCOL LIES WITH THE HEAD OF SERVICE

Date: October 2025
Review: October 2027
VERSION: 1
