Chemotherapy Protocol

LYMPHOMA

LONCASTUXIMAB TESIRINE

Regimen

- Diffuse Large B-Cell Lymphoma (DLBCL) / High Grade B-Cell Lymphoma (HGBL) - Loncastuximab Tesirine Monotherapy

Indication

- Adult patients with relapsed or refractory DLBCL or HGBL, who received two or more lines of systemic therapy, which included anti-CD20, anthracycline and polatuzumab vedotin (unless contraindicated), and who are not candidates for future CAR T cell therapy

Toxicity

Drug	Adverse Effect
Loncastuximab Tesirine	Increased transaminases, neutropenia, fatigue, anaemia, thrombocytopenia, nausea, peripheral oedema, rash, photosensitivity, pleural effusion

The adverse effects listed are not exhaustive. Please refer to the relevant summary of product characteristics for further details.

Monitoring

Regimen

- FBC, LFTs, including AST and GGT, and U&Es prior each cycle.
- LDH, ESR, urate, magnesium, calcium, glucose, coagulation screen, Immunoglobulins, B2-microglobulin, Hep B core Ab, Hep B surface Ag, Hep C Ab, HIV 1+2 prior cycle 1
- ECG +/- ECHO if clinically indicated prior cycle 1.

Dose Modifications

The dose modifications listed are for haematological, liver and renal dysfunction and drug specific toxicities only. Dose adjustments may be necessary for other toxicities as well.

In principle all dose reductions due to adverse drug reactions should not be re-escalated in subsequent cycles without consultant approval. It is also a general rule for chemotherapy that if a third dose reduction is necessary treatment should be stopped.

Please discuss all dose reductions / delays with the relevant consultant before prescribing. The approach may be different depending on the clinical circumstances.

Haematological

Consider blood transfusion or erythropoietin if patient symptomatic of anaemia or has a haemoglobin of less than 8g/dL (80g/L)
All dose reductions and delays should be discussed with the relevant consultant. Treatment should re-start as soon as these haematological parameters are met. Dose delays rather than dose reductions are recommended.

Neutrophils (x10^9/L)	**Dosage Modification**
1 or greater	100%
Less than 1	Withhold until neutrophil count returns to 1 x 10^9/L or higher
Adverse Reaction	**Dosage Modification**
Platelet count more than 50,000/mcL	100%
Platelet count less than 50,000/mcL	Withhold until platelet count returns to 50,000/mcL or higher

Hepatic Impairment

No dose adjustment is recommended for patients with mild hepatic impairment.

Loncastuximab Tesirine has not been studied in patients with moderate or severe hepatic impairment (total bilirubin</= ULN and AST> ULN, or total bilirubin >1.5 × ULN and any AST).

In patients with hepatic impairment, monitoring for adverse reactions is recommended.

Kidney Impairment

No dose adjustment of Loncastuximab Tesirine is required for patients with mild to moderate renal impairment.

Loncastuximab Tesirine has not been studied in patients with severe renal impairment (CrCl 15 to 29 mL/min). The effect of severe renal impairment, and end-stage renal disease is unknown.

Other toxicities

Adverse reaction	Severity	Dose modification
Oedema or effusion	NCI-CTC Grade 2 or higher	Withhold until the toxicity resolves to Grade 1 or less
Others (e.g. Photosensitivity)	NCI-CTC Grade 3 or higher	Withhold until the toxicity resolves to Grade 1 or less

If treatment is delayed by more than 3 weeks due to toxicity related to Loncastuximab Tesirine, subsequent doses should be reduced by 50%. If toxicity requires dose reduction following the second dose of 0.15 mg/kg (Cycle 2), the patient should receive the dose of 0.075 mg/kg for Cycle 3.

If toxicity reoccurs after two dose reductions following an adverse reaction, permanent discontinuation of to Loncastuximab Tesirine should be considered.

Regimen

21-day cycle

Cycle 1 and 2

Drug	Dose	Days	Administration
Loncastuximab Tesirine	0.15mg/kg	1	Intravenous infusion in 50mL glucose 5% over 30mins.

From cycle 3 onwards

Drug	Dose	Days	Administration
Loncastuximab Tesirine	0.075mg/kg	1	Intravenous infusion in 50mL glucose 5% over 30mins.

Dose Information

- Loncastuximab Tesirine will be dose banded according to the national dose bands (5mg/mL)
- Patient with BMI> 35 kg/m2 or more should be dosed using Adjusted Body Weight

Administration Information

- Give via a dedicated infusion line with a sterile, non-pyrogenic, low-protein binding inline or add-on filter (0.2 or 0.22 micrometre pore size) and catheter.

Extravasation

- Irritant with vesicant-like properties

Additional Therapy

- Premedication

Dexamethasone 4 mg is to be administered orally or intravenously twice daily for 3 days, beginning the day before the administration of Loncastuximab Tesirine

- No antiemetics are required.

- Tumour lysis syndrome (TLS) prophylaxis should be prescribed according to the individual patient TLS risk and at consultant discretion.

- Anti-infective prophylaxis:

  - Aciclovir 400mg oral twice a day

  - Co-trimoxazole 960mg once a day on Monday, Wednesday and Friday oral

Additional Information

- Patients should avoid prolonged exposure of skin to sunlight due to reports of light-sensitive skin rashes.

- Patients should be advised to minimise or avoid exposure to direct natural or artificial sunlight including exposure through glass windows. Patients should be instructed to protect skin by wearing sun-protective clothing and/or the use of sunscreen products. If a skin reaction or rash develops, dermatologic consultation should be considered.

- Missed dose: If a planned dose is missed, it should be administered as soon as possible, and the schedule of administration should be adjusted to maintain a 21-day interval between doses

References

1. *Zynlonta, 10mg, powder for concentrate for solution for infusion - summary of product characteristics (SmPC) - (EMC)*. Available at: https://www.medicines.org.uk/emc/product/14786/smpc#gref (Accessed: 20 December 2024).
2. *NICE*. NICE. Loncastuximab tesirine for treating relapsed or refractory diffuse large B-cell lymphoma and highgrade B-cell lymphoma after 2 or more systemic treatments [TA947].Available at: https://www.nice.org.uk/guidance/ta947 (Accessed: 20 December 2024).
3. *Loncastuximab tesirine in relapsed/refractory high-grade B-cell lymphoma: A subgroup analysis from the lotis-2 study | blood advances | american Society of Hematology*. Available at: https://ashpublications.org/bloodadvances/article/6/16/4736/485791/Loncastuximab-tesirine-in-relapsed-refractory-high (Accessed: 20 December 2024).

REGIMEN SUMMARY

LONCASTUXIMAB TESIRINE

Cycle 1

Day 1

1. Warning- Photosensitivity
   Patients should be advised to minimise or avoid exposure to direct natural or artificial sunlight including exposure through glass windows. Patients should be instructed to protect skin by wearing sun-protective clothing and/or the use of sunscreen products. If a skin reaction or rash develops, dermatologic consultation should be considered.

2. Warning – check dexamethasone has been taken
   Administration instruction
   If dexamethasone administration does not begin the day before, oral or intravenous dexamethasone 4mg should begin at least 2 hours prior to administration of Loncastuximab Tesirine.

3. Loncastuximab Tesirine 0.15mg/kg in 50mL glucose 5% intravenous infusion over 30mins.
   Administration instruction
   Give via a dedicated infusion line with a sterile, non-pyrogenic, low-protein binding inline or add-on filter (0.2 or 0.22 micrometre pore size) and catheter.

Take home medicines

4. Dexamethasone 4mg oral TWICE a day for 3 days
   Administration Instructions
   Take 4mg in the evening of day 1 and then twice a day for 2 days. Please supply 5 doses.

5. Dexamethasone 4mg oral Twice a day for 3 days starting the day before Loncastuximab Tesirine infusion.
   Administration instructions: This is the supply for the next cycle

6. Aciclovir 400mg twice a day oral for 21 days
   Administration Instructions
   Please supply 21 days or the nearest original pack size

7. Co-trimoxazole 960mg once a day on Monday, Wednesday and Friday oral for 21 days
   Administration Instructions: This may be administered as 480mg twice a day according to local practice

Cycle 2

Day 1

8. Warning- Photosensitivity
   Patients should be advised to minimise or avoid exposure to direct natural or artificial sunlight including exposure through glass windows. Patients should be instructed to protect skin by wearing sun-protective clothing and/or the use of sunscreen products. If a skin reaction or rash develops, dermatologic consultation should be considered.

9. Warning – check dexamethasone has been taken
   Administration instruction
   If dexamethasone administration does not begin the day before, oral or intravenous dexamethasone 4mg should begin at least 2 hours prior to administration of Loncastuximab Tesirine.

10. Loncastuximab Tesirine 0.15mg/kg in 50mL glucose 5% intravenous infusion over 30mins.
    Administration instruction
    Give via a dedicated infusion line with a sterile, non-pyrogenic, low-protein binding inline or add-on filter (0.2 or 0.22 micrometre pore size) and catheter.

Take home medicines

11. Dexamethasone 4mg oral Twice a day for 3 days starting the day before Loncastuximab Tesirine infusion.
    Administration instructions: This is the supply for the next cycle

12. Aciclovir 400mg twice a day oral for 21 days
    Administration Instructions
    Please supply 21 days or the nearest original pack size

13. Co-trimoxazole 960mg once a day on Monday, Wednesday and Friday oral for 21 days
    Administration Instructions: This may be administered as 480mg twice a day according to local practice

Cycle 3 onwards

Day 1

14. Warning- Photosensitivity
    Patients should be advised to minimise or avoid exposure to direct natural or artificial sunlight including exposure through glass windows. Patients should be instructed to protect skin by wearing sun-protective clothing and/or the use of sunscreen products. If a skin reaction or rash develops, dermatologic consultation should be considered.

15. Warning -check patient has taken dexamethasone.
    Administration instruction
    If dexamethasone administration does not begin the day before, oral or intravenous 4mg dexamethasone should begin at least 2 hours prior to administration of Loncastuximab Tesirine.

16. Loncastuximab Tesirine 0.075mg/kg in 50mL glucose 5% intravenous infusion over 30mins.
    Administration instruction
    Give via a dedicated infusion line with a sterile, non-pyrogenic, low-protein binding inline or add-on filter (0.2 or 0.22 micrometre pore size) and catheter.

Take home medicines

17. Dexamethasone 4mg oral Twice a day for 3 days starting the day before Loncastuximab Tesirine infusion.
    Administration instructions: This is the supply for the next cycle

18. Aciclovir 400mg twice a day oral for 21 days
    Administration Instructions
    Please supply 21 days or the nearest original pack size

19. Co-trimoxazole 960mg once a day on Monday, Wednesday and Friday oral for 21 days
    Administration Instructions This may be administered as 480mg twice a day according to local practice.

DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
1	Dec 2024	New Document	Rafael Jimenez Lazaro Pharmacist	Dr Vivek Radhakrishnan Consultant

This chemotherapy protocol has been developed as part of the chemotherapy electronic prescribing project. This was and remains a collaborative project that originated from the former CSCCN. These documents have been approved on behalf of the following Trusts;

Hampshire Hospitals NHS Foundation Trust
NHS Isle of Wight
Portsmouth Hospitals NHS Trust
Salisbury Hospital NHS Foundation Trust
University Hospital Southampton NHS Foundation Trust
Western Sussex Hospitals NHS Foundation Trust

All actions have been taken to ensure these protocols are correct. However, no responsibility can be taken for errors that occur as a result of following these guidelines.