# Loncastuximab Tesirine - Zynlonta® (Lymphoma)

**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

Relapsed or refractory diffuse large B-cell lymphoma (DLBCL) and high-grade B-cell lymphoma (HGBL) after 2 or more systemic treatments only if they have previously had polatuzumab vedotin or if polatuzumab vedotin is contraindicated or not tolerated.

(NICE TA947)

**Response Rates**

Phase 2 LOTIS-2 trial

- Single arm study – 145 patients
- ORR: 48.3%
- Median PFS: 4.9 months

**Treatment related mortality**

1-2%

## Regimen details

**Cycles 1 & 2**

| Day | Drug | Dose | Route |
|---|---|---|---|
| 1 | Loncastuximab tesirine (Zynlonta®) | 0.15mg/kg* | IV infusion |

**Cycle 3 onwards**

| Day | Drug | Dose | Route |
|---|---|---|---|
| 1 | Loncastuximab tesirine (Zynlonta®) | 0.075mg/kg* | IV infusion |

* For patients with BMI > 35kg/m2, consider dosing at adjusted body weight ($35kg/m^2$ x (height in metres)$^2$)

### Cycle frequency
21 days

### Number of cycles
Until disease progression or unacceptable toxicity.

### Pre-medication
Dexamethasone 4mg PO or IV BD for 3 days starting the day before administration
If dexamethasone administration does not begin the day before treatment, oral or intravenous dexamethasone should begin at least 2 hours prior to locastuximab tesirine administration.

### Supportive medication
Tumour lysis syndrome (TLS) prophylaxis -risk stratification before cycle 1. Management as per local policy, typically with oral hydration and oral allopurinol, unless high risk.
Proton-pump inhibitor or H2 antagonist with steroid treatment as per local policy
Antiviral prophylaxis e.g. acyclovir, dose as per local policy
PCP prophylaxis e.g. co-trimoxazole, dose as per local policy
Antifungal prophylaxis e.g. fluconazole, dose as per local policy.

Consider GCSF as secondary prophylaxis as indicated

### Emetogenicity
This regimen has low emetic potential – refer to local policy

### Administration
Loncastuximab tesirine (Zynlonta®) is administered as an IV infusion in 50mL glucose 5% over 30 minutes via a sterile, non-pyrogenic low protein binding in-line 0.22 micron in-line filter.

Patients should be monitored (blood pressure, temperature, pulse and respiratory rate) before the start and at the end of the infusion.

### Extravasation
Irritant (group 3)

## Mandatory investigations – pre first cycle

| Investigation | Validity period |
|---|---|
| FBC | 14 days |
| U&E (including creatinine) | 14 days |
| LFT (including AST and GGT) | 14 days |

## Additional investigations advised pre-first cycle

- Calcium
- LDH
- TLS risk assessment
- Glucose
- HIV, hepatitis B and C serology

## Investigations – pre subsequent cycles

| Investigation | Validity period |
|---|---|
| FBC | 96 hours |
| U&E (including creatinine) | 7 days |
| LFT (including AST and GGT) | 7 days |

## Additional investigations advised pre subsequent cycles

- Glucose, as required.

## 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 |
| Creatinine clearance (CrCl) | ≥ 30mL/min |
| Bilirubin | < 1.5 x ULN |
| ALT/AST | < ULN |
| GGT | < 5 x ULN |

## Dose modifications

If dosing is delayed by more than 3 weeks due to toxicity, subsequent doses should be reduced by 50%. If toxicity following the second dose of 0.15mg/kg (i.e. cycle 2), the patient should receive the standard dose of 0.075mg/kg for cycle 3.

### Haematological toxicity

| Toxicity | Action |
|---|---|
| Neutrophils < 1.0 x $10^9$/L | Withhold treatment until neutrophil count ≥ 1.0 x $10^9$/L<br>Consider GCSF<br>If > 3-week delay in dosing, reduce dose by 50%. |
| Platelets < 50 x $10^9$/L | Withhold treatment until neutrophil count ≥ 50 x $10^9$/L<br>If > 3-week delay in dosing, reduce dose by 50%. |

### Renal impairment

No dose adjustment is required for mild or moderate renal impairment (CrCl ≥ 30mL/min). The effect of severe renal impairment, end stage renal disease or haemodialysis on loncastuximab tesirine pharmacokinetics is unknown. Additional monitoring for adverse reactions in these patients is recommended.

### Hepatic impairment

No dose adjustment is recommended for patients with mild hepatic impairment (bilirubin < 1.5 x ULN and any ALT/AST). Loncastuximab tesirine has not been studied in moderate or severe hepatic impairment (bilirubin > 1.5 x ULN and any ALT/AST). Additional monitoring for adverse reactions is recommended in patients with hepatic impairment.

### Other toxicities

| Toxicity | Definition | Action/Dose adjustment |
|---|---|---|
| Oedema or effusion | ≥ Grade 2 | Withhold treatment until toxicity resolves to ≤ Grade 1. |
| Cutaneous reactions | ≥ Grade 3 | Withhold treatment until resolution.<br>Consider oral and topical corticosteroids and anti-pruritic therapy as indicated. |
| Any other adverse reaction | ≥ Grade 3 | Withhold treatment until toxicity resolves to ≤ Grade 1. |

## Side Effects

### LOTIS-2 study:

| Toxicity | | Any grade (%) | Grade 3 or 4 (%) |
|---|---|---|---|
| **Haematological** | Neutropenia | 40 | 26 |
| | Thrombocytopenia | 33 | 18 |
| | Anaemia | 26 | 10 |
| | Febrile neutropenia | 3 | 3 |
| **Non-haematological** | GGT increased | 40 | 16 |
| | Fatigue | 27 | 1 |
| | Nausea | 23 | 0 |
| | Cough | 22 | 1 |
| | Peripheral oedema | 20 | 1 |
| | ALP increased | 20 | 1 |
| | Pyrexia | 19 | 1 |
| | Diarrhoea | 17 | 2 |
| | ALT increased | 16 | 3 |
| | AST increased | 16 | 1 |
| | Hypophosphataemia | 16 | 6 |
| | Hypokalaemia | 15 | 4 |
| | Decreased appetite | 15 | 0 |
| | Hypomagnesaemia | 14 | 1 |
| | Vomiting | 13 | 0 |
| | Pruritis | 12 | 0 |
| | Rash | 12 | 1 |
| | Constipation | 12 | 0 |
| | Insomnia | 11 | 0 |
| | Dyspnoea | 11 | 1 |
| | Headache | 11 | 1 |
| | Erythema | 11 | 1 |
| | Abdominal pain | 11 | 3 |
| | Photosensitivity reaction | 10 | 2 |
| | Pleural effusion | 10 | 2 |

### Specific drug related side effects:

| Common (>10%) | Uncommon (1-10%) | Rare (<1%) |
|---|---|---|
| Myelosuppression | Pericarditis | Pericarditis |
| Decreased appetite | Generalised oedema | Fluid overload |
| Pleural effusion | Musculoskeletal pain | |
| Rash, pruritis, erythema | Pericardial effusion | |
| Abdominal pain, nausea, vomiting, constipation, diarrhoea | Photosensitivity reactions | |
| Peripheral oedema | Infections | |
| Fatigue, myalgia | | |
| Transaminases increased | | |

**Effusion and Oedema**
Patients should be monitored for new or worsening oedema or effusions. Diagnostic imaging should be considered in patients who develop symptoms of pleural effusion or pericardial effusion, such as new or worsened dyspnoea, chest pain and/or ascites. For grade 2 or greater toxicity withhold treatment.

**Photosensitivity and cutaneous reactions**
Patients should be monitored for new or worsening cutaneous reactions including photosensitivity. Patients should be advised to avoid exposure to direct natural or artificial sunlight including exposure through glass windows. Patients should be instructed to protect skin from exposure to sunlight by wearing sun-protective clothing and/or use of sunscreen products. If a skin reaction or rash develops consider dermatology referral.

## Additional information

Women of childbearing potential should be advised to use effective contraception during treatment and for at least 10 months after the last dose. Men with partners of childbearing potential should be advised to use effective contraception for at least 7 months after the last dose.

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

No interaction studies have been performed. No clinically important pharmacokinetic interactions are expected.

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## References


- National Institute of Health and Care Excellence TA947. Accessed 19th December 2024 via www.nice.org.uk
- Summary of Product Characteristics Loncastuximab Tesirine – Zynlonta (SOBI). Accessed 19th July 2024 via www.medicines.org.uk
- Caimi, P.F. et al. Loncastuximab tesirine in relapsed or refractory diffuse large B-cell lymphoma (LOTIS-2): a multicentre, open-label, single-arm, phase 2 trial. Lancet Oncology 2021:22(6):790-800


| Version | Issue date | Review date | Revision | Written/Checked/Authorised |
|---|---|---|---|---|
| 1 | December 2024 | December 2027 | New protocol | Written/reviewed: Dr L Lowry (Consultant Haematologist, Taunton and Somerset NHS Trust)<br>Checked: Kate Gregory (Lead Pharmacist for SACT Protocols, SWAG Cancer Alliance)<br>Authorised: Dr J Braybrooke (Consultant Oncologist, UHBW NHS Trust and SWAG Cancer Alliance) |
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