Lenalidomide - Rituximab (Subcutaneous)

Healthier Lancashire & South Cumbria | Cancer Alliance

Indication

Previously treated follicular lymphoma (grade 1 to 3A) in adults-NICE- [TA 627]
Interim treatment option during the COVID-19 pandemic, endorsed by NHS England (NG-161), Bluteq required

Regimen details

Table 1 – Treatment regimen details

DRUG	DOSE	DILUENT	ROUTE	FREQUENCY/DURATION
Cycle 1				
Rituximab	375mg/m^2	500mL Sodium Chloride 0.9%	Intravenous Infusion (see protocol for rituximab infusion)	Day 1, 8, 15 & 22
Lenalidomide	20mg		PO	OD Days 1-21
Cycle 2-5				
Rituximab	1400mg		Subcutaneous injection	Day 1
Lenalidomide	20mg		PO	OD Days 1-21
Cycle 6-12				
Lenalidomide	20mg		PO	OD Days 1-21

Cycle frequency

Repeat cycle every 28 days

Number of cycles

12 cycles

Administration

Intravenous Rituximab should be administered as per local protocol. Second and subsequent doses may be given by rapid infusion if patient meets local criteria.

Subcutaneous Rituximab to be given over 5 minutes

Pre-medication

Chlorphenamine 4mg PO 30 minutes prior to rituximab
Paracetamol 1g PO 30 minutes prior to rituximab

Emetogenicity – consult anti-emetic policy for full details

Minimum Risk (Category D)

Additional supportive medication

Table 2 – Additional supportive medication

Table 2: Adjuvant medications for use with FVD		
Allopurinol	300mg po od	Cycle 1 only (Consider use of Rasburicase if high risk for Tumour Lysis Syndrome)
LMWH Prophylaxis	As per local policy	Continuous throughout Lenalidomide treatment. May substitute with low dose aspirin in low risk patients

Extravasation

Table 3 – Extravasation Risk Category for each intravenous drug in the regimen

Rituximab	Non-Vesicant

Investigations – pre first cycle

NOTE – Lenalidomide is renally excreted. Check U&E, LFT and Thyroid Function prior to start – if abnormal discuss with consultant and see dose modification.

- Check FBC
  - Patient should have adequate bone marrow reserve, i.e neutrophils > 1.0, platelets >75 unless cytopaenia is due to disease, e.g marrow infiltration, splenomegaly - if not discuss with consultant
- Check hepatitis B and C serology
- Pregnancy Test
  - If appropriate discuss possibility of pregnancy with female patients and need for contraception with both male and female patients. Note whether Lenalidomide causes infertility is unknown – offer semen cryopreservation to males.
- Note that Lenalidomide is contraindicated if there is a history of hypersensitivity or desquamating rash with thalidomide
- Assess for neuropathy – do not use Lenalidomide if there is grade 3 neuropathy (sensory loss or paraesthesia interfering with activities of daily living or causing disability) or higher
- Assess risk of tumour lysis syndrome – consider Rasburicase and monitoring for tumour lysis syndrome

Table 4 - Standard Investigations prior to first cycle

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

Investigations –pre subsequent cycles

Medical review of fitness for chemotherapy

- Exclude active infection, major changes in organ function.

Reassess for treatment related toxicity

FBC, U+E (including creatinine), LFT (including AST)

Review necessary measures in the Lenalidomide risk management programme.

Standard limits for administration to go ahead

If blood results not within range, authorisation to administer **must** be given by prescriber/ consultant.

Table 5 – Standard test result limits for each administration to go ahead

Investigation	Limit
Neutrophil count	≥ 1.0 x 10^9/L
Platelet count	≥ 50 x 10^9/L (see dose modification)
Creatinine clearance	≥ 60 mL/min
Bilirubin	≤ 1.5 x ULN
AST	< 1.5 x ULN

Dose modifications

Table 6 – Lenalidomide dose reduction steps

Dose level 1	20mg od for 21 days
Dose level 2	15mg od for 21 days
Dose level 3	10mg od for 21 days
Dose level 4	5mg od for 21 days

Table 7- Dose modification for Neutropenia (unless due to disease)

Neutropenia Grade on day of treatment	Modification of dose/schedule
Grade 3 or 4 (neuts <1.0 x10^9/L)	Hold treatment and monitor FBC, restart Lenalidomide at next lower dose level when neutrophils >1.0x10^9/L or consider the same dose with GCSF support

Table 8 - Dose modification due to thrombocytopenia (unless due to disease)

Thrombocytopenia Grade on day of treatment	Modification of dose/schedule
Grade 3 or 4 (plts <50x10^9/L)	Hold treatment and monitor FBC, restart Lenalidomide at next lower dose level when platelets > 50

Table 9 - Dose modification due to renal function

Creatinine Clearance (estimated using Cockroft & Gault)	Modification of dose/schedule
30-59mL/min	Reduce Lenalidomide to 10mg OD days 1-21
<30mL//min (not requiring dialysis)	Reduce Lenalidomide to 15mg OD alternate days on days 1-21 or 7.5mg OD days 1-21. Can be increased to 10mg OD if patient is not responding
<30mL//min (requiring dialysis)	Lenalidomide 5mg OD days 1-21, On days of dialysis take Lenalidomide after dialysis

Table 10 - Dose modification due to liver function

Liver Function	Modification of dose/schedule
AST/ALT increased > 5x ULN Or Bilirubin > 1x ULN	Stop Lenalidomide; if returned to baseline in <14 days resume at same dose, if >14 days resume at next lower dose level

Table 11 - Dose modification due to Rash

Grade of Rash	Modification of dose/schedule
Grade 3-4 non-desquamating or non-blistering rash	Stop Lenalidomide; restart if resolved to ≤ grade 1
Grade 4 rash or any desquamating or blistering rash	Stop Lenalidomide permanently

Table 12 - Dose modification due to Peripheral Neuropathy

Grade of Neuropathy	Modification of dose/schedule
Grade 3 neuropathy i.e sensory alteration and symptoms interfering with function	Stop Lenalidomide; restart if resolved to ≤ grade 1 i.e asymptomatic, paraesthesia, loss of deep tendon reflexes
Grade 4 neuropathy i.e life threatening, urgent intervention required	Stop Lenalidomide permanently

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

- **Serious side effects**
  - Tumour lysis syndrome with 1st cycle
  - Severe and life-threatening infection
  - Infusion reactions – fever, rigors, hypotension, pruritus
  - Severe mucocutaneous reactions (Stevens-Johnson syndrome)
  - Reactivation of hepatitis B and C infection
  - Peripheral neuropathy

- **Frequently occurring side effects**
  - Neutropenia Thrombocytopenia[^,◊,] Anaemia
  - Nausea & vomiting
  - Fatigue
  - Diarrhoea, Constipation, Abdominal pain
  - Paraesthesia
  - Abnormal liver function tests
  - Abnormal liver function tests
  - Muscle spasms
  - Fatigue, Asthenia

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

Digoxin toxicity

References

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