PROTOCOL

The Clatterbridge Cancer Centre NHS Foundation Trust

Systemic Anti Cancer Therapy Protocol

THALIDOMIDE AND PREDNISOLONE MYELOFIBROSIS

PROTOCOL REF: MPHATPM
(Version No. 1.0)

Approved for use in:

Single patient diagnosed with myelofibrosis who is transfusion dependent and has not responded to and not eligible for ruxolitinib, hydroxycarbamide and pegylated interferon under the care of Dr Nauman Butt.

Dosage:

Drug	Dose	Route	Frequency
Thalidomide	**50mg nocte**	Oral	Continuous
Prednisolone	**0.5mg/kg/day mane**	oral	Days 1 to 28 of cycle 1
Prednisolone	**0.25mg/kg/day mane**	oral	Days 1 to 28 of cycle 2
Prednisolone	**0.125mg/kg/day mane**	oral	Days 1 to 28 of cycle 3 and then stop

Maximum number of cycles: treatment can be extended past 6 months in patients that have responded to treatment after discussion of the case at the MPN/CML MDT.

Administration:

- Thalidomide is teratogenic and all patients need to be counselled concerning this risk and Celgene's Pregnancy Prevention Program must be followed.
- Thalidomide is pro-thrombotic and patients must have their VTE risk assessed prior to treatment and regularly throughout treatment and prophylactic dose dalteparin or treatment

dose dalteparin prescribed. NB platelets must be greater than 50 x 10^9/L for dalteparin to be prescribed.

- Thalidomide can cause drowsiness and should be taken at night
- Prednisolone should be taken with or after food in the morning.
- Capsules should not be opened or crushed

Emetogenic risk:

Mildly emetogenic.

Supportive treatments:

- VTE prophylaxis (dalteparin 5000 units s/c OD) *if platelets are greater than 50 x 10^9/L*
- Omeprazole PO 20mg OD whilst on steroids (if the patient is on another PPI from primary care then this can be continued)
- Allopurinol PO 300mg OD (100mg OD if CrCl <30ml/min) for first cycle only
- Consider metoclopramide PO 10mg TDS PRN

Interactions:

Thalidomide

Thalidomide has sedative properties, thus may enhance the sedation induced by anxiolytics, hypnotics, antipsychotics, H1 antihistamines, opiate derivatives, barbiturates and alcohol. Caution should be used when thalidomide is given in combination with medicinal products that cause drowsiness.

Due to thalidomide's potential to induce bradycardia, caution should be exercised with medicinal products having the same pharmacodynamic effect such as active substances known to induce torsade de pointes, beta blockers or anticholinesterase agents.

Medicinal products known to be associated with peripheral neuropathy (e.g. vincristine and bortezomib) should be used with caution in patients receiving thalidomide.

Combined hormonal contraceptives are not recommended due to the increased risk of venous thromboembolic disease.

For more detailed interactions please refer to the SPC

Treatment schedule:

Cycle 1:

Day	Drug	Dose	Route	
1 to 28	**Prednisolone**	**0.5mg/kg/day**	**PO**	Mane with food
	Thalidomide	**50mg**	**PO**	Nocte

Cycle 2:

Day	Drug	Dose	Route	
1 to 28	**Prednisolone**	**0.25mg/kg/day**	**PO**	Mane with food
	Thalidomide	**50mg**	**PO**	Nocte

Cycle 3:

Day	Drug	Dose	Route	
1 to 28	**Prednisolone**	**0.125mg/kg/day**	**PO**	Mane with food
	Thalidomide	**50mg**	**PO**	Nocte

Cycle 4 onwards:

Day	Drug	Dose	Route	
1 to 28	**Thalidomide**	**50mg**	**PO**	Nocte

Main toxicities:

Thrombocytopenia, neutropenia, anaemia, nausea, vomiting, diarrhoea, VTEs and peripheral neuropathy.

Investigations and treatment plan:

	Pre	Cycle 1	Cycle 2	Cycle 3	Ongoing
Informed Consent	x				
Clinical Assessment	x	x	x	x	As clinically indicated or at the end of treatment
Pregnancy Authorisation Form	X	X	X	X	Prior to every cycle of thalidomide
SACT Assessment (to include PS and toxicities)	x	x	x	x	Every cycle
On treatment review					
FBC	x	x	x	x	Every cycle
U&E & LFTs & Magnesium	x	x	x	x	Every Cycle
CrCl (Cockcroft and Gault)	x				
Hepatitis B core antibody and surface antigens & Hep C & HIV 1+2	x				
Clinical exam of spleen size or ultrasound spleen if not palpable.	x				If clinically indicated
Bone marrow biopsy	x				Only if clinically indicated
ECG					If clinically indicated
Blood pressure measurement	x				Repeat if clinically indicated
Respiratory Rate					If clinically indicated
Weight recorded	x	x	x	x	Every cycle
Blood glucose	x				Repeat if clinically indicated
Pregnancy test	x	x	x	x	Prior to every cycle for WCBP as per PPP

Dose Modifications and Toxicity Management:

Haematological toxicity:

Cycle 1 should proceed despite any cytopenias. If blood counts deteriorate during treatment or fail to improve then the haematology consultant should be consulted.

These haematological guidelines assume that patients are well with good performance status, that other acute toxicities have resolved and the patient has not had a previous episode of neutropenic sepsis.

Non- Haematological toxicity:

Dosing in renal and hepatic impairment:

Renal and Hepatic	Thalidomide	Thalidomide capsules have not formally been studied in patients with impaired renal or hepatic function. No specific dose recommendations for these patient populations are available. Patients with severe organ impairment should be carefully monitored for adverse reactions

Peripheral Neuropathy	Thalidomide	Grade 1 (paraesthesia, weakness and/or loss of reflexes) with no loss of function	Continue to monitor the patient with clinical examination. Consider stopping if symptoms worsen.
		Grade 2 (interfering with function but not with activities of daily living)	Interrupt treatment and continue to monitor the patient with clinical and neurological examination. If the neuropathy resolves to Grade 1 or better, the treatment may be restarted, if the benefit/risk is favourable.

		Grade 3 (interfering with activities of daily living)	Discontinue treatment
		Grade 4 (neuropathy which is disabling)	Discontinue treatment

References:

1. https://www.medicines.org.uk/emc Thalidomide. Updated Aug 2021. Accessed 18/11/21.
2. Mesna et al. A phase 2 trial of combination low-dose thalidomide and prednisone for the treatment of myelofibrosis with myeloid metaplasia. Blood, 1 April 2003; Volum 101, Number 7.

Circulation/Dissemination

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Version History

Date	Version	Author name and designation	Summary of main changes
		Aileen McCaughey **Advanced Pharmacist Haemato-oncology**	New Regimen Protocol V1.0