Vinblastine-based therapy for LCH

Induction and maintenance treatment for multisystem Langerhans cell histiocytosis

Drugs/Dosage:

Week 1 – 6

Vinblastine	6mg/m^2 (no "cap")	IV	once weekly for 6 weeks
Prednisolone	40mg/m^2	PO	once daily for 4 weeks, then taper over 2 weeks

Week 7 - 52

Vinblastine	6mg/m^2 (no "cap")	IV	Day 1 every 3 weeks
Prednisolone	40mg/m^2	PO	Day 1 to Day 5 every 3 weeks
Mercaptopurine	50mg/m^2	PO	once daily continuous from week 7 to week 52

Administration: Vinblastine diluted in 50ml 0.9% sodium chloride and infused over 5 - 10 minutes
Prednisolone tablets to be taken in the morning with or after food
Mercaptopurine tablets (available as 50mg tablets, which may be halved) to be swallowed with plenty of water. They may be taken with food (not dairy) or on an empty stomach, but patients should standardise the timing of administration in relation to food. The dose should be taken at least 1 hour before, or 2 hours after, milk or dairy products.

Other drugs: Omeprazole or H_2 receptor antagonist (e.g. ranitidine) is recommended whilst treating with steroids
Co-trimoxazole 480mg od as PCP prophylaxis

Frequency: a one year course; involving a 6 week induction, followed by maintenance therapy (maximum 15 x 3 week cycles if no delays) to complete one year

Main Toxicities: myelosuppression; infections; hepatotoxicity; constipation; neuropathy; stomatitis; alopecia; steroid side effects; ovarian failure; infertility

Anti – emetics: mildly emetogenic

Extravasation: vinblastine is a vesicant

Regular Investigations:	FBC	before each dose of vinblastine (weekly for 6 weeks, then every 3 weeks)
	LFTs	before each dose of vinblastine, and also watch closely when mercaptopurine initiated
	U&Es	baseline, then monthly throughout

Dose Modifications

Haematological Toxicity: If neutrophils < 1.0 x 10^9/l or platelets < 100 x 10^9/l, defer vinblastine dose until recovered
And also, during continuation therapy with mercaptopurine:
interrupt mercaptopurine treatment until recovery above these levels, and then resume as tolerated.
If neutrophils < 0.5 x 10^9/l or platelets < 50 x 10^9/l on more than 2 occasions, consider discontinuation of co-trimoxazole. Pentamidine or dapsone can be used as alternative prophylaxis for PCP.

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Hepatic toxicity to 6MP: If bilirubin > 50 µmol/l, omit mercaptopurine until bilirubin < 20 µmol/l and then re-start at 50% of previous dose.
Escalate to 75%, then 100% dose at 10 day intervals provided hyperbilirubinaemia does not recur.
Do not dose adjust for elevated transaminases.

Hepatic Impairment:

ALT/AST		Bilirubin (µmol/l)	Vinblastine Dose
60 – 180	**or**	26 –51	Give 50% dose
Normal	**and**	> 51	Give 50% dose
> 180	**and**	> 51	Discontinue

Renal Impairment: If CrCl 10 – 50ml/min, consider increasing mercaptopurine dosing interval to every 48 hours (alternate days).

Neuropathy: If Grade 2 neuropathy develops, reduce dose of vinblastine to 3mg/m^2

Patient Information: Macmillan or CRUK leaflets for vinblastine and mercaptopurine

Reference: Gadner, H et al; Blood 2013; 121 (25): 5006 - 5014