Idelalisib Rituximab

INDICATION: Chronic lymphocytic leukaemia-in CLL patients who have had at least 1 prior line of therapy

Not to be initiated as first line in CLL patients with a 17p deletion or TP53 mutation

Prior to a course of treatment

- If appropriate discuss possibility of pregnancy with female patients. Women of childbearing potential should use highly effective contraception while taking idelalisib and for 1 month after stopping treatment. Women using hormonal contraceptives should add a barrier method
- Patients should be informed about the risk of serious and/or fatal infections
- Idelalisib should not be initiated in patients with any evidence of ongoing systemic,bacterial,fungal or viral infection
- Patients should be advised to promptly report any new respiratory symptoms
- Written consent for course
- Check FBC, U&Es, LFTs
- Check hepatitis B & C serology
- Regular screening for CMV should be conducted-discontinue in patients with evidence of infection or viraemia
- Check concurrent medications – idelalisib should not be co-administered with potent CYP3A inducers such as rifampicin, phenytoin, St John's wort or carbamazepine as these may reduce idelalisib exposure

Prior to each dose

- Medical review of fitness for chemotherapy – exclude active infection, major changes in organ function
- Monitor for respiratory signs and symptoms throughout treatment
- Check FBC, U&Es, creat, LFTs - neuts must be >1.0 and plats > 100
- Monitor neutrophils every 2 weeks for the first 6 months of treatment and at least weekly if neutrophil count is less than 1.0

Rituximab:

Cycle	Day	Rituximab Dose	Volume
1	1	50mg/m^2	100ml 0.9% sodium chloride
	2	325mg/m^2	500ml 0.9% sodium chloride
	15	500mg/m^2	500ml 0.9% sodium chloride
2	1	500mg/m^2	500ml 0.9% sodium chloride
	15	500mg/m^2	500ml 0.9% sodium chloride
3-6	1	500mg/m^2	500ml 0.9% sodium chloride

Cycle length is 28 days

Rapid infusion is <u>not</u> appropriate for this regimen

Idelalisib: 150mg orally twice daily from start of treatment and continued until disease progression or unacceptable toxicity

Rituximab pre-medication	Paracetamol 1g orally, Chlorphenamine 10mg IV, Hydrocortisone 100mg IV 30 minutes before each infusion
Other medications	Antimicrobials as per local policy (including PCP prophylaxis) Loperamide as required

Dose modifications

Reduced neutrophil count

Neutrophils 1.0-1.5	Maintain dosing
Neutrophils 1.0-0.5	Maintain dosing-monitor neutrophils at least weekly
Neutrophils <0.5	Interrupt treatment Monitor at least weekly until neutrophils >0.5 and then restart at 100mg bd
Elevated liver transaminases	Withold idelalisib if ALT or AST > 5 x ULN. Resume treatment at 100mg twice daily once values have returned to < 3 x ULN
Diarrhoea/Colitis	Withold idelalisib if grade 3 or 4 diarrhoea/colitis. Resume treatment at 100mg twice daily once resolved
Pneumonitis	Withold idelalisib in the event of suspected pneumonitis. Resume treatment at 100mg twice daily if appropriate when resolved
Rash	Withold idelalisib in the event of grade 3 or 4 rash. Resume treatment at 100mg twice daily if appropriate. If rash does not recur, re-escalate dose to 150mg twice daily
Renal impairment	No dose modification required
Hepatic impairment	No dose modification required. Use with caution in patients with severe hepatic impairment

Adverse events	
Infections	Neutropenia
Pneumonitis	Raised liver transaminases
Rash	Pyrexia
Diarrhoea/colitis	Neutropenia
Cytokine release syndrome/tumour lysis syndrome	Hepatitis B reactivation
Lymphocytosis	Infusion related reactions
Hypotension	Posterior reversible encephalopathy syndrome
Reversible posterior leukoencephalopathy syndrome	

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