Guidelines for Antifungal Prophylaxis in Haematological Malignancy

The table below should be used as a guide to identify haematology patients at risk of fungal disease with suggested antifungal prophylaxis.

Risk Classification	Clinical examples	Regime Examples	Prophylaxis and duration	Additional Information
HIGH	AML –patients undergoing intensive chemotherapy MDS – patients receiving AML like chemotherapy	DA 3+8 DA 3+10 High dose cytarabine FLAG-IDA	From Day 1 of chemotherapy until neutropenia resolves (neutrophils above 0.5 for 7 days) Posaconazole **tablets** 300mg BD on day 1 then 300mg daily OR Posaconazole **liquid** 200mg TDS with meals. Where possible tablets should be used in preference due to better bioavailability	Posaconazole liquid and tablets are dosed very differently ensure that the correct dose is prescribed with the formulation stated. -Azoles inhibit cytochrome P450 isoenzymes that may lead to impaired clearance of other drugs. -Reversible liver enzyme abnormalities are observed with azoles. Pre-existing abnormal liver function tests are not a contra-indication to azoles but patients should be monitored carefully and azoles discontinued if there is associated progressive hepatotoxicity. -If patient develops diarrhoea or vomiting lasting for 48 hours or longer discuss with a pharmacist as there may be a decrease in therapeutic drug levels.
	Patients with a history of suspected or confirmed invasive fungal disease having further chemotherapy		Posaconazole as above (except for those who developed an invasive fungal infection on posaconazole prophylaxis. An alternative agent will need to be considered on an individual basis)	
	Significant GVHD		Continue antifungal initiated by tertiary centre	
	Allogeneic HSCT		Continue antifungal initiated by tertiary centre	
	ALL - patients undergoing intensive chemotherapy	UKALL protocols	From Day 1 of chemotherapy until neutropenia resolves (neutrophils above 0.5 for 7 days) Ambisome 2mg/kg three time per week	-Test dose required prior to first dose being given -Can cause hypokalaemia and hypomagnesaemia -For those with mild infusion related reaction increase infusion time to 2 hours

Risk Classification	Clinical examples	Regime Examples	Prophylaxis and duration	Additional Information
INTERMEDIATE	Lymphoma -patients receiving intensive/dose-escalated therapy	Maxi-CHOP RCHOP+HDMTX R-IVE Ferreri Protocol R-ESHAP DA-EPOCH-R	From Day 1 of chemotherapy Fluconazole 50mg OD for the duration of treatment If patients are experiencing long periods of neutropenia (neutrophils less than 1 for 10 days or more) discuss with a pharmacist	
		R-CODOX-M/R-IVAC	Ambisome 2mg/kg 3 times per week during the neutropenic phase only	-Test dose required prior to first dose being given -Can cause hypokalaemia and hypomagnesaemia -For those with mild infusion related reaction increase infusion time to 2 hours
	MDS –patients with neutropenia	Azacitidine	From Day 1 of chemotherapy Itraconazole liquid 200mg BD for the duration of treatment and until neutropenia resolves	-Azoles inhibit cytochrome P450 isoenzymes that may lead to impaired clearance of other drugs. -Reversible liver enzyme abnormalities are observed with azoles. Pre-existing abnormal liver function tests are not a contra-indication to azoles but patients should be monitored carefully and azoles discontinued if there is associated progressive hepatotoxicity. -If patient develops diarrhoea or vomiting lasting for 48 hours or longer discuss with a pharmacist as there may be a decrease in therapeutic drug levels.
	AML-patients receiving low dose chemotherapy	Low dose cytarabine		
	CLL-patients receiving Alemtuzumab	Alemtuzumab		
	Autologous HSCT		Continue antifungal initiated by tertiary centre	

Risk Classification	Clinical examples	Regime Examples	Prophylaxis and duration	Additional Information
LOW	Myeloma-patients receiving steroids within chemotherapy regime	CTD/CTDa MPT Lenalidomide +Dex Pomalidomide+Dex VCD VTD Bendamustine VDT-PACE	From Day 1 of chemotherapy Fluconazole 50mg OD for the duration of treatment	-Azoles inhibit cytochrome P450 isoenzymes that may lead to impaired clearance of other drugs. -Reversible liver enzyme abnormalities are observed with azoles. Pre-existing abnormal liver function tests are not a contra-indication to azoles but patients should be monitored carefully and azoles discontinued if there is associated progressive hepatotoxicity.
	CLL-patients on more intensive chemotherapy	FCR High dose Methylprednisolone R-Bendamustine	From Day 1 of chemotherapy Fluconazole 50mg OD for the duration of treatment	
	Lymphoma – patients receiving standard intensity chemotherapy	RCHOP RCVP ABVD	Nil unless HIV positive use Fluconazole 50mg OD for the duration of treatment Nystatn 1ml QDS can be considered	
		Bendamustine	From Day 1 of chemotherapy Fluconazole 50mg OD for the duration of treatment	
VERY LOW	CML	All regimes	Nil	
	CLL- patient on low risk treatment	R-Idelalisib Ibrutinib	Nil	
	Other myeloproliferative neoplasms	Ruxolitinib Hydroxycarbamide Anagrelide Busulphan	Nil	

References:
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2.Chau, MM., Kong, DC.,van Hal, SJ. et al. Consensus guidelines for optimising antifungal drug delivery and monitoring to avoid toxicity and improve outcomes in patients with haematological malignancy, 2014. *Intern Med J* 2014; Dec;44(12b):1364-88
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