Haematology Cancer Clinical Guidelines

Haematology Expert Advisory Group (EAG)
on behalf of Northern Cancer Alliance

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CONTENTS

Clinical Guideline for the prophylaxis and treatment of tumour lysis syndrome in patients receiving treatment for haematological malignancies

Tumour lysis syndrome is an oncological emergency caused by massive tumour cell death causing release of potassium, phosphate and nucleic acids into the blood stream. It can occur spontaneously but is most commonly associated with initiation of chemotherapy. Sequelae include acute kidney injury, cardiac arrhythmias, seizures, neurological complications and sudden death.

Tumour lysis definition

Element	**Value**	**Change from baseline**
Laboratory Tumour lysis syndrome		
Uric acid	≥476 micromol/L	25% increase
Potassium	≥6.0 mmol/L	25% increase
Phosphorus	≥1.45 mmol/L	25% increase
Calcium	≤1.75 mmol/L	25% decrease
Clinical Tumour lysis syndrome – laboratory tumour lysis and ≥1 of the following		
Creatinine	>1.5 ULN	
Cardiac arrhythmia		
Sudden death		
Seizure		

Risk Stratification

Risk stratification should be carried out prior to initiation of first cycle of chemotherapy and used to guide the prescription of appropriate prophylactic therapy. The risk can be estimated from the disease type and presence of additional risk factors.

Risk Group	Disease Type
High	Burkitt's lymphoma/leukaemia AML and ALL with WCC ≥ 100 x 10^9/l
Intermediate	AML and ALL with WCC < 100 x 10^9/l Intermediate and high grade NHL with LDH ≥ 2 x ULN CML accelerated phase/blast crisis CLL with targeted and/or biological therapy
Low	Myeloma Other CLL Hodgkin's Lymphoma Low grade NHL CML – chronic phase Myeloproliferative disorders

Additional Risk Factors
(move up one risk group for each additional risk factor present)
Bulky disease (>10cm)
Renal Impairment
Renal involvement or urinary tract obstruction by tumour
Raised LDH (>2x ULN)
Baseline uric acid, phosphate or potassium > ULN

Modified from Cario MS et al, BJH 2010, 149, 578-586

Prevention of tumour lysis syndrome

Prophylaxis should be prescribed based on estimated risk of tumour lysis. Prophylaxis is usually only required for the first cycle of cytotoxic chemotherapy as tumour burden will be significantly reduced at the time of subsequent treatment.

Risk Group	Prophylaxis
Low	Hydration (aim for 3L day)* +/- Allopurinol 300mg od**
Intermediate	Hydration (aim for 3L day) and Allopurinol 300mg od.**
High	Hydration (aim for up to 2L/m^2) for up to 7 days following chemotherapy and Rasburicase 3mg iv. ***

*Hydration should start 24 hours before chemotherapy starts and continue for 7 days
**Allopurinol should be started no more than 12-24 hours pre chemotherapy and continued for up to 7 days. The dose of allopurinol should be reduced to 100mg od in patients with CrCl < 20ml/min. Patients with an allergy to allopurinol should be treated with hydration and monitored closely for evidence of tumour lysis.
***Rasburicase should be given immediately prior to starting chemotherapy. Repeat dose only if indicated by biochemical markers. Rasburicase should not be given to patients with G6PD. Allopurinol may partially antagonise the effect of rasburicase and should not be co-administered.

Patients at high risk of tumour lysis syndrome will usually need to be admitted for in patient monitoring following chemotherapy. IV fluids may be required if patients are unable to maintain an adequate fluid intake and fluid balance should be monitored closely. U&Es, calcium, phosphate and uric acid should be monitored twice daily for the first 72 hours (more frequently if there is evidence to suggest laboratory tumour lysis is developing). Samples for uric acid must be sent to the laboratory on ice.

Treatment of clinical tumour lysis syndrome

Increase hydration to 3L/m^2 with close attention to fluid balance aiming for a urine output of >100ml/m^2/h.

Treat hyperuricaemia with Rasburicase 0.2mg/kg repeated daily as required.

If Hyperphosphataemia and hyperkalaemia are present then the patient should be referred to ICU for consideration of renal support therapy. Standard measures to control hyperkalaemia should be used as a bridge to renal support but the effects will usually be short duration.

Asymptomatic hypocalaemia should not be treated as calcium administration can precipitate calcium phosphate precipitation in the kidneys. If the calcium is ≤1.75mmol/l or drops by ≥25% from baseline then the patient should have cardiac monitoring. Symptomatic hypocalaemia should be treated with calcium gluconate according at standard doses.