



Monitoring

Viral screening is required before starting treatment including Hepatitis B surface antigen, core antibody and HIV status.

FBC, U&Es (including potassium, serum bicarbonate, blood urea nitrogen, phosphate, LDH, creatinine, adjusted calcium and uric acid) and LFTs should be measured prior to starting therapy and pre-existing electrolyte abnormalities corrected. There is a risk of tumour lysis syndrome (TLS) hence it is necessary to monitor potassium, uric acid, phosphate, adjusted calcium, LDH and creatinine at 6 to 8 hours and at 24 hours after the first dose and during each dose increase of venetoclax. Electrolyte abnormalities should be corrected promptly. The next venetoclax dose should not be administered until the 24 hour blood chemistry results have been evaluated (see section on TLS below).

Dose Modifications

The dose modifications listed are for haematological, liver and renal function and drug





Assess blood chemistry (potassium, uric acid, phosphorus, calcium and creatinine) and correct pre-existing abnormalities prior to initiation of treatment with venetoclax

Monitor blood chemistries for TLS at pre-dose, 6 to 8 hours after each new dose during titration and 24 hours after reaching final dose

For patients with risk factors for TLS (e.g. circulating blasts, high burden of leukaemia involvement in bone marrow, elevated pre-treatment LDH or reduced renal function) additional measures should be considered, including increased laboratory monitoring and reducing venetoclax starting dose

Table 1 - Tumour lysis syndrome (TLS) management whilst on venetoclax

| Abnormality | Dose modification and management |
|--|--|
| Hyperkalaemia | |
| Potassium more than or equal to 0.5mmol/l increase from prior value (and within upper limit of normal (ULN)) | Hold venetoclax until resolution. Recheck calcium, creatinine, phosphate, potassium and uric acid in 1 hour. If further 0.2mmol/l or less rise in potassium do an ECG and consider calcium gluconate and calcium resonium in line with local hyperkalaemia policy. Continue to monitor for TLS every 2 hours. Resume protocol testing if change in potassium is less than 0.2mmol/l and no other evidence of TLS resume venetoclax |
| Potassium more than ULN but less than 6.0mmol/l | Hold venetoclax until resolution. Do an ECG and consider calcium gluconate and calcium resonium in line with local hyperkalaemia policy. Recheck calcium, creatinine, phosphate, potassium and uric acid in 1 hour. If potassium less than ULN continue to monitor for TLS 2 and 4 hours later. |
| Potassium more than or equal to 6.0mmol/l and/or symptomatic (e.g. muscle cramps, weakness, paraesthesia, nausea, vomiting or diarrhoea) | Hold venetoclax until resolution. Refer to local hyperkalaemia guideline and seek advice from renal team. Recheck calcium, creatinine, phosphate, potassium and uric acid every hour. |





4. Wei AG et al (2020). Venetoclax plus IDAC for newly diagnosed AML ineligible for intensive chemotherapy: a phase 3 randomized placebo-controlled trial. *Blood* 2020 June; 135(24): 2137-2145





9 Cytarabine 20mg/m² subcutaneous bolus.

Administration Instruction

Administer into the thigh or abdomen. Rotate injection sites.

Ensure adequate provision is in place to allow administration in the community. Pharmacy if this is to be given in the community please label accordingly.

If this is being given in an out-patient setting please record the administration in the patients journal on ARIA.

10 Warning - Check hydration status

Administration Instruction

Patients should be adequately hydrated during the dose titration phase to reduce the risk of TLS. Patients should be instructed to drink plenty of water daily starting 2 days before and throughout the dose titration phase. Patients should be particularly instructed to drink 1.5 to 2L of water daily, 2 days prior to and the days of dosing at initiation and each subsequent dose increase. Intravenous fluids should be administered as indicated based on overall risk of TLS or for those who cannot maintain an adequate level of oral hydration.

11. Venetoclax 300mg once a day for 1 day oral

Administration Instruction

Take with or just after food, orally. Take with 8-16 oz of water. Q 1lt .5t ttid

12 Cytarabine 20mg/m² subcutaneous bolus.

Administration Instruction

Administer into the thigh or abdomen. Rotate injection sites.

Ensure adequate provision is in place to allow administration in the community. Pharmacy if this is to be given in the community please label accordingly.

If this is being given in an out-patient setting please record the administration in the patients journal on ARIA.

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Patients should be adequately hydrated during the dose titration phase to reduce the risk of TLS. Patients should be instructed to drink plenty of water daily starting 2 days before and throughout the dose titration phase. Patients



