



Chemotherapy Protocol

Acute Myeloid Leukaemia

AZACITIDINE (SC) - VENETOCLAX

Regimen

AML – Azacitidine (SC) - Venetoclax

Indication

Newly diagnosed acute myeloid leukaemia (AML).

Patient has had/is having molecular analysis performed

Patient has de novo AML or secondary AML.

The most recent bone marrow blast count shows more than 30% blasts.

Standard intensive chemotherapy is unsuitable due to age, fitness or the presence of significant comorbidities

Patient has been prospectively assessed for the risk of development of tumour lysis syndrome with venetoclax and that appropriate risk mitigation strategies have been put in place.



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).

If known cardiovascular or pulmonary disease patients should undergo a full cardiopulmonary assessment before and during treatment with azacitidine.

Dose Modifications





Dose Information

Azacitidine will be dose banded according to the national dose bands (25mg/m²).

Venetoclax is available as 10mg 50mg and 100mg filmcoated tablets.

Administration Information

Before administration the contents of the azacitidine syringe must be re-suspended by inverting the syringe 2-3 times and vigorously rolling the syringe between the palms for 30 seconds.

Azacitidine should be administered by subcutaneous injection into the upper arm, thigh or abdomen. Injection sites should be rotated. New injections should be given at least 2.5cms from the previous sites and never into areas where the site is tender;



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

Hydrocortisone 1% cream apply to the injection site for the relief of inflammation up to four times a day, topical

Sema 15mg at night when required for the relief of constipation oral

Aciclovir 400mg twice a day

Antifungal prophylaxis

- Posaconazole tablets 300mg twice a day on D4, then 300mg once a day thereafter
- Voriconazole tablets 400mg twice a day on D4, then 200mg twice a day thereafter

Additional Information

The National Patient Safety Alert on oral chemotherapy (NPSA/2008/RRR001) must be followed in relation to venetoclax

It must be made clear to all staff, including those in the community, that venetoclax must only be prescribed under the supervision of a consultant haematologist

There are many drug interactions associated with venetoclax. Always check for drug interactions.

References

1. DiNardo et al (2018) Safety and preliminary efficacy of venetoclax with decitabine or azacitidine in elderly patients with previously untreated acute myeloid leukaemia: a non-randomised open-label, phase 1b study. *Lancet Oncol* 19: 216-228
2. DiNardo et al (2019) Venetoclax combined with decitabine or azacitidine in treatment-naïve, elderly patients with acute myeloid leukaemia. *Blood* 133(1):7-17
3. Agarwal SK et al (2017) Management of Venetoclax-Posaconazole Interaction in Acute Myeloid Leukemia Patients: Evaluation of Dose Adjustments. *Clin Ther*: 2017 Feb;39(2):359-367
4. Abbvie. Venclyxto® Summary of Product Characteristics. Updated 25/02/22. Accessed on 13/06/22 via <http://www.medicines.org.uk/emc>.
5. Bristol Myers Squibb Pharmaceuticals Limited. Venclyxto® Summary of Product Characteristics. Updated 30/05/2022. Accessed on 14/06/2022 via <http://www.medicines.org.uk/emc>



Day 2



Day 4

18 Ondansetron 8mg oral or intravenous

19 Azacitidine 75mg/m² in water for injection over one minute subcutaneous injection

Administration instructions:

Before administration the contents of the syringe must be re-suspended by inverting the syringe 2-3 times and vigorously rolling the syringe between the palms for 30 seconds.

Azacitidine should be administered by subcutaneous injection into the upper arm, thigh or abdomen. Injection sites should be rotated. New injections should be given at least 2.5 cm from the previous site and never into areas where the site is tender, bruised, red, or hardened.

Doses of greater than 100mg (4mL) should be injected into two separate sites.

Day one of the cycle should be a Monday

Take home Day 4

20 Warning – Check hydration status

Administration instructions

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.

21. Warning – Check Venetoclax Dose

Administration Instructions

If $CrCl < 1$ mL/min, do not start and consider increasing the dose of venetoclax to



Cycle 2 onwards

Day 1, 2, 3, 4, 5, 8, 9

26 Ondansetron 8mg oral or intravenous

27. Azacitidine 75mg/m² in water for injection over one minute subcutaneous injection

Administration instructions:

Before administration the contents of the syringe must be re-suspended by inserting the syringe 2-3 times and vigorously rolling the syringe between the palms for 30 seconds.

Azacitidine should be administered by subcutaneous injection into the upper arm, thigh or abdomen. Injection sites should be rotated. New injections should be given at least 2.5 cm from the previous site and never into areas where the site is tender, bruised, red, or hardened.

Doses of greater than 100mg (4mL) should be injected into two separate sites.
Day one of the cycle should be a Monday

Take home Day 1

28 Venetoclax 100mg once a day for 28 days oral

Administration Information

Take with or just after food, or a meal. Take with a full glass of water.

29 Metoclopramide 10mg three times a day when required for the relief of nausea oral

Administration Instructions

Please supply 28 tablets or nearest equivalent pack size

30 Hydrocortisone 1% cream apply to the injection site for the relief of inflammation up to four times a day, topical

Administration instructions

Please supply 30g or nearest equivalent original pack

31. Senna 15mg at night when required for the relief of constipation, oral

Administration instructions:

Please supply 28 tablets or nearest equivalent

32 Antifungal prophylaxis

Administration instructions

The choice of antifungal prophylaxis is dependent on local formulary and may include:

- Posaconazole tablets 300mg once a day for 28 days.
- Voriconazole tablets 200mg twice a day for 28 days.

33 Aciclovir 400mg twice a day for 28 days

