Chemotherapy Protocol

Acute Myeloid Leukaemia

GILTERITINIB

Regimen

- AML - Gilteritinib

Indication

Gilteritinib for treating relapsed/refractory FLT3 mutation positive myeloid leukaemia in adults where;

- the patient has a proven diagnosis of acute myeloid leukaemia.
- the patient has a FMS-like tyrosine kinase 3 (FLT3) mutation (internal tandem duplication (ITD) or tyrosine kinase domain (TKD) as determined by a validated test.
- the patient has relapsed/refractory FLT3 positive acute myeloid leukaemia.
- the patient has not received previous systemic therapy with other FLT3 inhibitors (with the exception of sorafenib or midostaurin used in first-line therapy or in clinical trials in 1st line therapy).
- the patient has an ECOG performance status of 0, 1 or 2.
- gilteritinib will be used as monotherapy.
- gilteritinib will be continued until disease progression, unacceptable toxicity or at the time at which the patient is considered to be cured or until the patient receives a haematopoietic stem cell transplant whichever occurs first.

Toxicity

Drug	Adverse Effect
Gilteritinib	Dizziness, QT prolongation, pericardial effusion, hypotension, cough, dyspnoea, differentiation syndrome, diarrhoea, nausea, constipation, increased transaminases, blood creatine phosphokinase increase, blood alkaline phosphatase increase, pain in extremity, arthralgia, myalgia, fatigue, peripheral oedema, asthenia, pancreatitis, posterior reversible encephalopathy syndrome (PRES), foetal toxicity

The adverse effects listed are not exhaustive. Please refer to the relevant Summary of Product Characteristics for full details.

Monitoring

- FBC, U&Es and LFTS prior to each cycle (including magnesium).
- Baseline ECG prior to starting treatment, on day 8 and day 15 of cycle 1 and prior to the start of the next three subsequent months of treatment.
- Creatine phosphokinase level prior to initiation of treatment, on cycle one day fifteen and monthly afterwards.
- For woman of child bearing potential a negative pregnancy test prior to starting treatment. Barrier methods of contraception are recommended.

Dose Modifications

The dose modifications listed are for haematological, liver and renal function and drug specific toxicities only. Dose adjustments may be necessary for other toxicities as well.

Please discuss all dose reductions / delays with the relevant consultant before prescribing, if appropriate. The approach may be different depending on the clinical circumstances.

Haematological

No dose reduction is required for disease related abnormal haematological counts.

Consider blood transfusion or the use of erythropoietin according to NICE TA323 if patient symptomatic of anaemia or where the haemoglobin is less than 8g/dL.

Hepatic Impairment

No dose adjustment is required for patients with mild (Child-Pugh class A) or moderate (Child-Pugh class B) hepatic impairment. Gilteritinib is not recommended in patients with severe hepatic impairment (Child-Pugh class C) as safety and efficacy have not evaluated in this patient population.

Renal Impairment

No dose adjustment is necessary in patients with mild or moderate renal impairment. There is no clinical experience in patients with severe renal impairment.

Other adverse effects

Criteria	Gilteritinib dosing
Differentiation syndrome	• If differentiation syndrome is suspected, administer corticosteroids and initiate hemodynamic monitoring. • Interrupt gilteritinib if severe signs and/or symptoms persist for more than 48 hours after initiation of corticosteroids. • Resume Gilteritinib at the same dose when signs and symptoms improve to grade 2a or lower.
Posterior reversible encephalopathy syndrome	• Discontinue gilteritinib
QTcF interval >500 msec	• Interrupt gilteritinib • Resume gilteritinib at a reduced dose (80mg or 120mg) when QTcF interval returns to within 30 msec of baseline or less than or equal to 480msec.
QTcF interval increased by >30 msec in ECG on D8 of cycle 1	• Confirm with ECG on day 9. • If confirmed, consider a dose reduction to 80mg.
Pancreatitis	• Interrupt gilteritinib until pancreatitis resolved.

	• Resume treatment with gilteritinib at reduced dose (80mg or 120mg).
Other grade 3 or higher toxicity related to treatment	• Interrupt gilteritinib until toxicity resolves or improves to grade 1. • Resume treatment with gilteritinib at a reduced dose (80mg or 120mg).

Regimen

28 day cycle until disease progression, cure, haematopoietic stem cell transplant or intolerance (12 cycles will be set in Aria)

Drug	Dose	Days	Administration
Gilteritinib	120mg once a day*	1-28 (inclusive)	Oral

*In the absence of response (patient did not achieve a composite complete remission after 4 weeks of treatment, the dose can be increased to 200mg once daily, if tolerated or clinically warranted.

Dose Information

- Gilteritinib is available as 40mg film-coated tablets.

Administration Information

- Gilteritinib should be administered at about the same time each day.
- Gilteritinib tablets can be taken with or without food. They should be swallowed whole with water (tablets should not be broken or crushed).
- If a dose is missed or not taken at the usual time, the dose should be administered as soon as possible on the same day, and the patients should return to the normal schedule the following day.
- If the patient vomits after dosing, patients should not take another dose but should return to the normal schedule the following day.

Additional Information

- The National Patient Safety Alert on oral chemotherapy (NPSA/2008/RRR001) must be followed in relation to gilteritinib.
- It must be made clear to all staff, including those in the community, that gilteritinib should only be prescribed under the supervision of a consultant haematologist.
- Gilteritinib interacts with many other agents. Always check for drug interactions. Gilteritinib interacts with Azole antifungals – additional toxicity monitoring may be required (including ECG monitoring).
- Gilteritinib has minor influence on the ability to drive and operate machinery. Dizziness has been reported in patients taking gilteritinib.

References

1. Astellas Pharma Ltd (2021). Xospata 40mg film-coated tablets summary of product characteristics. Available from www.medicines.org.uk. Accessed 11/07/2022.
2. Perl et al. Gilteritinib or chemotherapy for relapsed or refractory FLT3-mutated AML. New Engl J Med (2019); 381: 1728-1740.

REGIMEN SUMMARY

Gilteritinib

Cycle 1 onwards

Day 1-28

1. Gilteritinib 120mg once a day oral
   Administration Information
   Oral SACT
   Swallow whole, do not crush or chew.

DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
1	July 2022	None	Alexandra Pritchard Pharmacist	Dr Deborah Richardson Consultant

This chemotherapy protocol has been developed as part of the chemotherapy electronic prescribing project. This was and remains a collaborative project that originated from the former CSCCN. These documents have been approved on behalf of the following Trusts;

Hampshire Hospitals NHS Foundation Trust
NHS Isle of Wight
Portsmouth Hospitals NHS Trust
Salisbury NHS Foundation Trust
University Hospital Southampton NHS Foundation Trust
Western Sussex Hospitals NHS Foundation Trust

All actions have been taken to ensure these protocols are correct. However, no responsibility can be taken for errors that occur as a result of following these guidelines.