EZ (ETOPOSIDE + IDARUBICIN)

INDICATION

Induction / Consolidation chemotherapy for AML in whom outpatient administration with oral drugs is deemed to be beneficial, particularly in terms of improving quality-of-life.

Etoposide is available as 50mg and 100mg capsules and idarubicin is available as 5mg and 10mg capsules

---

THREATMENT INTENT

Disease Modification

PRE-ASSESSMENT

1. Document patient's height and weight.
2. Ensure that patient has responded to induction chemotherapy and that there is confirmation of remission either after the first or second induction course.
3. Pregnancy Test - for all women of childbearing potential before each cycle of chemotherapy.
4. ECG +/- Echo - *if clinically indicated*.
5. Record performance status (WHO/ECOG).
6. Record height and weight.
7. Consent - ensure patient has received adequate verbal and written information regarding their disease, treatment and potential side effects. Document in medical notes all information that has been given. Obtain written consent on the day of treatment.
8. Fertility - it is very important the patient understands the potential risk of infertility, all patients should be offered fertility advice (see fertility guidelines).
9. Consider dental assessment / Advise dental check is carried out by patient's own dental practitioner before treatment starts.
10. Treatment should be agreed in the relevant MDT.
11. For patients prescribed oral chemotherapy, ensure pre-chemotherapy counselling in line with NPSA recommendation and chemotherapy measures.

DRUG REGIMEN

Days 1 to 3	**IDARUBICIN** 20 mg/m^2 PO **ONCE** daily (3 doses), rounded to closest capsule strength. Capsules to be taken with a light meal.
Days 1 to 3	**ETOPOSIDE** 60 mg/m^2 PO **TWICE** daily (6 doses), rounded to closest capsule strength. Capsules should be taken on an empty stomach.

CYCLE FREQUENCY

Patients in CR can receive 2 courses of EZ.
If the patient is defined as good- or standard-risk they should progress to Course 2 when neutrophils recover to 1 x 10^9/L and platelets to 75 x 10^9/L.
Approx. every 4-6 weeks

DOSE MODIFICATIONS - discuss with consultant.

Etoposide

Renal impairment	Hepatic impairment
GFR (mL/min) GFR >50 mL/min: 100% GFR 15-50 mL/min: 75% GFR <15ml/min: 50% HD: Not dialysed, consider 75% Subsequent doses should be based on clinical response.	Bilirubin ≤50nmicromol/L with normal albumin and renal function: 100% dose Bilirubin >50 micromol/L or decreased albumin levels: Consider 50% dose, increase if tolerated

Idarubicin

Renal impairment	Hepatic impairment
GFR ≥ 30mL/min: 100% dose GFR < 30ml/min: 67% dose	Bilirubin 45-86 micromol/L: 50% dose Bilirubin >86 micromol/L: Not recommended

Maximum cumulative dose of idarubicin by mouth: 400mg/m^2. Consider previous anthracycline usage.

INVESTIGATIONS

- FBC, Coagulation screen.
- U&E, LFT.
- Recent bone marrow aspirate - this should be evaluated cytological before proceeding with Course 2.
- Subsequent courses: Neutrophil count must be > 1 x 10^9/L and platelets > 75 x 10^9/L before the start of each course. Chemotherapy should start within 1 week of achieving these counts.

CONCURRENT MEDICATION

Drug	Dose and duration
Allopurinol	300mg OD for 14 days. (Induction only)
Fungal prophylaxis	As per local protocol
Aciclovir	200 mg three times a day for duration of treatment and for 3 months after completion
Proton pump inhibitor	As per local formulary

EMETIC RISK

Days 1-3: Moderate

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS

Idarubicin - myocardial toxicity, as manifested by potentially fatal congestive heart failure, acute life-threatening arrhythmias or other cardiomyopathies, may occur. Red discoloration of urine for 2 to 3 days after administration. Alopecia. Nausea and vomiting. Elevation of liver enzymes may occur.

Etoposide - Abdominal pain, constipation, nausea and vomiting, anorexia, hepatotoxicity, pigmentation, alopecia, hypertension, dizziness, malaise

Other- myelosuppression, Infections, mucositis,

TREATMENT RELATED MORTALITY

1-10% depending on patient factors

REFERENCES

1. Jackson GH, Taylor PR, Iqbal A, Galloway MJ, Turner G, Haynes A, Hamilton PJ, Russell N, Proctor SJ. The use of an all oral chemotherapy (idarubicin and etoposide) in the treatment of acute myeloid leukaemia in the elderly: a report of toxicity and efficacy. Leukemia. 1997 Aug;11(8):1193-6.
2. AML 97 Protocol. A randomised study comparing and oral regimen (Idarubicin and Etoposide) with an intravenous regimen (MAE) for consolidation in patients over 55 years of age with AML in first complete remission. Riverside Haematology Group. Date of production March 1998.
3. Bristol-Myers Squibb. Etoposide capsules Vepesid®. Summary of product characteristics. Updated 22/1/2021. Accessed on 3/11/2021 via http://www.medicines.org.uk
4. Pfizer. Idarubicin capsules Zavedos®. Summary of product characteristics. Updated 26/8/2020. Accessed on 3/11/2021 via http://www.medicines.org.uk
5. Krens S D et al (2019). Dose recommendations for anticancer drugs in patients with renal or hepatic impairment. *Lancet Oncol*; **20:** e201–08

REVIEW

Name	Revision	Date	Version	Review date
Prof Vyas	Mortality risk added, pre-assessment reviewed, minor changes in cycle frequency, adding treatment intent	Feb 2016	4.0	
Cheuk-kie Jackie Cheung, Haematology Pharmacist. NSSG Myeloid Group	Annual protocol meeting	Oct 2019	4.1	Oct 2021
Yen Lim, Haematology Pharmacist Andy Peniket, Consultant Haematologist NSSG Myeloid Group	Annual protocol meeting. Updated renal/hepatic dosing.	Nov 2021	1.2	Nov 2023