# ALL CONSOLIDATION- Cycle 2 (25-60 years)

## INDICATION

Adult Acute Lymphoblastic Leukaemia (ALL) in remission not eligible for allogeneic transplantation

**This protocol is suitable for patients aged 25-60 years. It may sometimes be used in older patients ≤ 65 years or in patients ≥ 19 years with Philadelphia Chromosome positive acute lymphoblastic leukaemia. Follow MDT recommendation.**

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## TREATMENT INTENT

Curative or to maximize remission

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## PRE-ASSESSMENT:

Ensure all previous pre-assessments as per induction 1 have been completed, also:

1. Blood tests - FBC, creatinine, LFTs
2. Urine pregnancy test - before cycle 1 of each new chemotherapy course in women aged 12 – 55 years of age unless they have been sterilised or undergone a hysterectomy
3. Record performance status (WHO/ECOG)
4. Record height and weight (also needed to calculate CrCl)
5. 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. Patients must be consented for consolidation cycles 1-4 as a single programme of treatment i.e. “ALL consolidation.” Obtain written consent on the day of treatment.
6. Treatment should be agreed in the relevant MDT

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## DRUG REGIMEN / CYCLE 2

To commence 3 weeks from Consolidation Cycle 1 Day 1 or when ANC > 0.75 x $10^9$/L and Plt > 75 x $10^9$/L

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|---|---|
| **Days 1 to 5** | **CYTARABINE** 75mg/$m^2$ slow IV bolus (concentration 20mg/ml). |
| **Days 1 to 5** | **ETOPOSIDE** 100mg/$m^2$ in 500ml 0.9% Sodium Chloride (final concentration 0.2 to 0.4mg/ml) IVI over 60 minutes. |
| **Day 1** | **METHOTREXATE** 12.5mg INTRATHECAL. |
| **Continuous** | **IMATINIB** 600mg PO once daily.<br>**** ONLY for Philadelphia Positive patients ****. |

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## DOSE MODIFICATIONS

**Haematological toxicity:**
Cycle 2 consolidation starts 3 weeks from Consolidation Cycle 1 Day 1 or when ANC > 0.75 x $10^9$/L and Plt > 75 x $10^9$/L.
Do NOT dose reduce on basis of blood count.

**Renal/hepatic Impairment:**

**CYTARABINE- Discuss with consultant**

| Renal impairment | Hepatic impairment |
|---|---|
| No dose reduction necessary | **Hyperbilirubinaemia**<br>Bilirubin < 50 full dose<br>Bilirubin ≥ 50 but < 90 : 50% dose<br>Bilirubin ≥ 90 but < 120 : 25% dose<br>Bilirubin ≥ 120 omit dose<br>Check LFT's only if patient jaundiced. Do not alter dose for abnormal transaminases. |

**ETOPOSIDE- Discuss with consultant**

| Renal impairment | Hepatic impairment |
|---|---|
| GFR (ml/min) Dose<br>> 50 100%<br>15-50 75%<br>< 15 50%<br>Subsequent doses should be based on clinical response.<br><br>**Dialysis**<br>Start at reduced dose and increase according to clinical response. | Arguments for and against dose reduction.<br><br>Bilirubin 26-51micromol/L or AST 60-180u/L<br>- 50% dose<br>Bilirubin >51micromol/L or AST >180u/L<br>- clinical decision |

**IMATINIB- Discuss with consultant**
**Any severe non-haematological** toxicity- Withhold treatment until resolved.
Resume treatment depending on the initial severity of the event.

| Renal impairment | Hepatic impairment |
|---|---|
| Use with caution.<br>400mg minimum dose.<br>Reduce if not tolerated.<br>Increase dose for lack of efficacy. | 400mg minimum dose with any impairment.<br>Reduce if not tolerated.<br><br>If Bilirubin > 3 x ULN or Liver transaminases > 5 x ULN, withhold until Bilirubin < 1.5 x ULN and Liver transaminase < 2.5 x ULN. Resume at reduced dose: 400mg to 300mg; 600mg to 400mg |

## INVESTIGATIONS

- FBC, Coagulation screen.
- Creatinine, U&Es, LFTs

## CONCURRENT MEDICATION

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|---|---|
| **Aciclovir** | 200mg three times a day continuous |
| **PJP Prophylaxis** | Co-trimoxazole 960mg PO twice a day for 2 days each week;<br>If allergic or unable to tolerate co-trimoxazole, then monthly pentamidine 4mg/kg (max 300mg) in 100ml 0.9% Sodium Chloride IVI over 60 minutes. |
| **FLUCONAZOLE** | 50mg PO once daily continuous |
| **Proton pump inhibitor** | As per local formulary |
| **Norethisterone** | 5-10mg PO TDS until platelets >100x $10^9$/L with recovery (menstruating women only) |

## ANTI-EMETICS

| | |
|---|---|
| Days 1 to 5 | Low-Moderate emesis risk |
| Day 6 onwards | Low emesis risk |

## ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS

Note: Patients must be consented for consolidation cycles 1-4 as a single programme of treatment i.e. “ALL consolidation.”

Main side effects experienced during consolidation include: nausea and vomiting, myelosuppression, infections, liver toxicity and hair loss, nerve damage (including confusion, constipation, pins-and-needles in hands and feet, weakness leading to difficulty in flexing ankle). The neurological problems are usually related to vincristine which appears in Consolidation 3. **Imatinib:** Neutropenia, thrombocytopenia, anaemia, hepatotoxicity, headache, nausea, diarrhoea, vomiting, dyspepsia, abdominal pain, fluid retention, dermatitis, muscle spasm and cramps, musculoskeletal pain. Reactivation of HBV has also been reported.

**Further detailed information on managing specific adverse events can be found on UKALL14 trial protocol.**

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## MORTALITY

Treatment related risk for overall ALL consolidation for patients in remission is approximately 1%

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## REFERENCES

1. UKALL14. A randomized trial for adults with newly diagnosed acute lymphoblastic leukaemia. Eudract No: 2009-012717-22. Version 12.0, 26.06.2018.
2. The North London Cancer Network Dosage Adjustment for Cytotoxics in Renal Impairment. UCLH Version 3 updated January 2009.
3. The North London Cancer Network Dosage Adjustment for Cytotoxics in Hepatic Impairment. UCLH Version 3 updated January 2009.
4. London Cancer Alliance North and South. Haemato-Oncology Clinical Guidelines, Acute Leukaemias and Myeloid Neoplasms Part 1: Acute Lymphoblastic Leukaemia. April 2015.
5. Imatinib (Glivec). Summary of product characteristics. Last Updated on eMC Updated 20-May-2019.

**Review**

| Name | Revision | Date | Version | Review date |
|---|---|---|---|---|
| Julia Wong<br>Nadjoua Maouche<br>Dr Andy Peniket | New protocol | April 2017 | 1.0 | April 2019 |
| Cheuk-kie Cheung | General formatting | May 2017 | 1.1 | April 2019 |
| Jon Barrett<br>Haematology Pharmacist.<br>NSSG Myeloid Group | Annual Protocol meeting | October 2019 | 1.2 | October 2021 |