Acute Lymphoblastic Leukemia (ALL) Treatment Regimens

Clinical Trials: The NCCN recommends cancer patient participation in clinical trials as the gold standard for treatment. Cancer therapy selection, dosing, administration, and the management of related adverse events can be a complex process that should be handled by an experienced healthcare team. Clinicians must choose and verify treatment options based on the individual patient; drug dose modifications and supportive care interventions should be administered accordingly. The cancer treatment regimens below may include both U.S. Food and Drug Administration-approved and unapproved indications/regimens. These regimens are only provided to supplement the latest treatment strategies. These Guidelines are a work in progress that may be refined as often as new significant data becomes available. The National Comprehensive Cancer Network Guidelines® are a consensus statement of its authors regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult any NCCN Guidelines® is expected to use independent medical judgment in the context of individual clinical circumstances to determine any patient’s care or treatment. The NCCN makes no warranties of any kind whatsoever regarding their content, use, or application and disclaims any responsibility for their application or use in any way.

Note: All recommendations are category 2A unless otherwise indicated.

CNS Prophylaxis\(^1\,\^a\)

<table>
<thead>
<tr>
<th>PROTOCOL(^1,^b)</th>
<th>REGIMEN and DOSING</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intrathecal (IT) Cytarabine(^2,^4)</td>
<td>Day 1: Cytarabine 50-100mg intrathecal with or without 50mg Hydrocortisone (preservative free). Note: Frequency and duration are dependent on CNS disease status and risk of CNS relapse.</td>
</tr>
<tr>
<td>IT Cytarabine/Methotrexate/Hydrocortisone(^2,^4)</td>
<td>Day 1: Cytarabine 50-100mg intrathecal, with: Day 1: Methotrexate 12-15mg intrathecal, with: Day 1: Hydrocortisone 50-100mg (preservative-free) intrathecal. Note: Frequency and duration are dependent on CNS disease status and risk of CNS relapse.</td>
</tr>
<tr>
<td>IT Methotrexate(^2,^4)</td>
<td>Day 1: Methotrexate 12-15mg intrathecal with or without 50mg Hydrocortisone (preservative-free). Note: Frequency and duration are dependent on CNS disease status and risk of CNS relapse.</td>
</tr>
</tbody>
</table>

Newly-diagnosed ALL\(^1,\^a\)

Adolescents and Young Adults (AYA) (15-39 years)\(^b\)

Philadelphia Chromosome-Positive [Ph (+)] Disease\(^d\)

Other Recommended Regimens

CALGB 10701\(^1,\^a\)

| Course I (First Induction): | Days 1-7: Dasatinib 140 mg orally daily Days 1-7: Dexamethasone 10mg/m\(^2\) orally or IV. Course II (If ≤20% lymphoblasts in marrow at Day 15): | Days 1-7: Dasatinib 140 mg orally daily Days 1-7: Dexamethasone 10mg/m\(^2\) orally or IV. Course II (If ≥20% lymphoblasts in marrow at Day 15): | Days 1-7: Dasatinib 140 mg orally daily Days 1-7: Dexamethasone 10mg/m\(^2\) orally or IV. Vincristine and Daunorubicin also administered. Course III (Second Induction for patients not in complete remission (CR) or CR with incomplete hematologic recovery (CHR)): | Patients received Dasatinib, Cyclophosphamide, Vincristine, Daunorubicin, Dexamethasone. Course IV (CNS Prophylaxis): | Patients received Dasatinib, IV Vincristine, and IV, oral, and intrathecal Methotrexate. Course V: | Patients treated with stem cell transplantation or chemotherapy. Course VI (Maintenance): | Dasatinib: Starting on Day 30 of Course V and continued for 12 months and until 2 consecutive negative BCR-ABL1 RT-PCR assays 3 months apart or relapse. |

Corticosteroids + TKI\(^6,\^3,\^a\)

- **Dasatinib + Prednisone**
  - **PrePhase:** Days (-7-1): Prednisone 10-60mg/m\(^2\) in increasing doses.
  - **Induction Therapy:** Dasatinib 70mg twice daily for 84 days Prednisone 60mg/m\(^2\) daily (capped at 120mg daily) administered until Day 24 and then tapered and stopped at Day 32. Days 22,43: Methotrexate intrathecal.
- **Imatinib + Prednisone**
  - **PrePhase:** Days (-7-1): Prednisone 10-40mg/m\(^2\) in increasing doses.
  - **Induction Therapy:** Days 1-48: Imatinib 800mg orally Days 1-48: Prednisone 40mg/m\(^2\)

Note: Induction Therapy with Corticosteroid + Nilotinib is also a recommended regimen.

Note: These regimens are used for induction therapy and additional therapy is needed.

Note: These regimens are used for induction therapy and additional therapy is needed.

continued
## Acute Lymphoblastic Leukemia (ALL) Treatment Regimens

**Newly-diagnosed ALL**\(^{1, a}\) (continued)

<table>
<thead>
<tr>
<th>PROTOCOL(^{b})</th>
<th>REGIMEN and DOSING</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Adolescents and Young Adults (AYA) (15-39 years)</strong> (^{1, a}) (continued)</td>
<td></td>
</tr>
<tr>
<td><strong>Philadelphia Chromosome-Positive [Ph (+)] Disease</strong> (^{d}) (continued)</td>
<td></td>
</tr>
<tr>
<td><strong>Other Recommended Regimens</strong> (continued)</td>
<td></td>
</tr>
</tbody>
</table>

---

**EsPhALL Regimen:** TKI and a backbone of the Berlin-Frankfurt-Munster regimen\(^{8, 9, e}\)

- **Imatinib-Based Therapy**
  - **Protocol IB:**
    - **Day 1,28:** Cyclophosphamide 1000mg/m\(^2\) IV
    - **Days 1-28:** 6-Mercaptopurine 60mg/m\(^2\) orally
    - **Days 3-6, 10-13, 17-20, 24-27:** Cytarabine 75mg/m\(^2\) subcutaneous
    - **Days 3,7:** Methotrexate 12mg intrathecal
    - **Days 1-28:** Imatinib 300mg/m\(^2\) orally.
  - **Consolidation Block HR1:**
    - **Days 1-5:** Dexamethasone 20mg/m\(^2\) oral or IV
    - **Days 1,6:** Vincristine 1.5mg/m\(^2\) IV
    - **Day 1:** Methotrexate 5000mg/m\(^2\) IV
    - **Day 5:** Cytarabine 2000mg/m\(^2\) IV
    - **Day 6:** L-Asparaginase 25,000 IU/m\(^2\) IM
    - **Day 2-4:** Cyclophosphamide 200mg/m\(^2\) IV
    - **Day 1:** Methotrexate 12mg intrathecal
    - **Day 1:** Cytarabine 30mg intrathecal
    - **Day 1:** Prednisone 10mg intrathecal
    - **Days 6-20:** Imatinib 300mg/m\(^2\) orally.
  - **Consolidation Block HR2:**
    - **Day 1-5:** Dexamethasone 20mg/m\(^2\) oral or IV
    - **Days 1,6:** Vindesine 3mg/m\(^2\) IV
    - **Day 1:** Methotrexate 5000mg/m\(^2\) IV
    - **Days 2-4:** Ifosfamide 800mg/m\(^2\) IV
    - **Days 6:** L-Asparaginase 25,000 IU/m\(^2\) IM
    - **Day 5:** Daunorubicin 30mg/m\(^2\) IV
    - **Day 1:** Methotrexate 12mg intrathecal
    - **Day 1:** Cytarabine 30mg intrathecal
    - **Day 1:** Prednisone 10mg intrathecal
    - **Days 6-20:** Imatinib 300mg/m\(^2\) orally.
  - **Consolidation Block HR3:**
    - **Days 1-5:** Dexamethasone 20mg/m\(^2\) oral or IV
    - **Days 1,2:** Cytarabine 2,000mg/m\(^2\) IV
    - **Days 3-5:** Vepeside 100mg/m\(^2\) IV
    - **Day 6:** L-Asparaginase 25,000 IU/m\(^2\) IM
    - **Day 1:** Methotrexate 12mg intrathecal
    - **Day 1:** Cytarabine 30mg intrathecal
    - **Day 1:** Prednisone 10mg intrathecal
    - **Days 6-20:** Imatinib 300mg/m\(^2\) orally.

- **Reinducion Protocol II:**
  - **Days 1-21 + tapering:** Dexamethasone 10mg/m\(^2\) orally
  - **Days 8,15,22,29:** Vincristine 1.5mg/m\(^2\) IV
  - **Days 8,15,22,29:** Doxorubicin 25mg/m\(^2\) IV
  - **Days 8,11,15,18:** L-Asparaginase 10,000 IU/m\(^2\) IM
  - **Day 36:** Cyclophosphamide 1,000 mg/m\(^2\) IV
  - **Days 36-49:** 6-Thioguanine 60mg/m\(^2\) orally
  - **Days 38,41, 45-48:** Cytarabine 75mg/m\(^2\) subcutaneous
  - **Days 38,45:** Methotrexate 12mg intrathecal
  - **Days 36-63:** Imatinib 300mg/m\(^2\) orally.

- **Interim Maintenance:**
  - **Days 1-29:** 6-Mercaptopurine 50mg/m\(^2\) orally
  - **Days 8,15,22,29:** Methotrexate 20mg/m\(^2\) orally
  - With cranial irradiation.

---

\(^{1}\) CancerTherapyAdvisor.com
Acute Lymphoblastic Leukemia (ALL) Treatment Regimens

**Newly-diagnosed ALL**

<table>
<thead>
<tr>
<th>PROTOCOL</th>
<th>REGIMEN and DOSSING</th>
</tr>
</thead>
</table>
| **Adolescents and Young Adults (AYA) (15-39 years)**
| Philadelphia Chromosome-Positive [Ph (+)] Disease |

**EsPhALL Regimen:** TKI and a backbone of the Berlin-Frankfurt-Munster regimen (continued)

- **Imatinib-Based Therapy**
  - **Reinduction Protocol II:**
    - Days 1-21 + tapering: Dexamethasone 10mg/m² orally
    - Days 8,15,22,29: Vincristine 1.5mg/m² IV
    - Days 8,15,22,29: Doxorubicin 25mg/m² IV
    - Days 8,11,15,18: L-Asparaginase 10,000 IU/m² IM
    - Days 36: Cyclophosphamide 1,000 mg/m² IV
    - Days 36-49: 6-Thioguanine 60mg/m² orally
    - Days 38-41, 45-48: Cytarabine 75mg/m² subcutaneous
    - Days 36-63: Imatinib 300mg/m² orally.

  - **Continuation Therapy Maintenance:**
    - 6-Mercaptopurine 50mg/m² orally daily until Day +728 from diagnosis
    - Methotrexate 20mg/m² orally weekly until day +728 from diagnosis.

  - **Note:** This regimen has also been studied in combination with Dasatinib.

**Hyper CVAD with TKI and High-Dose Methotrexate, Cytarabine**

- **Dasatinib-based Therapy**
  - **Cycle A:**
    - Days 1-3: Cyclophosphamide 300mg/m² over 3 hours every 12 hours for 6 doses
    - Days 1-3: Mesna 600mg/m² IV continuous infusion over 24 hours starting 15 minutes before the first dose of Cyclophosphamide and completing 12 hours after the last dose of Cyclophosphamide is started.
    - Day 4: Doxorubicin 50mg/m² IV push OR IV continuous infusion over 24 hours
    - Days 4, 11: Vincristine 2mg IV over 5-10 minutes
    - Days 1-4, 11-14: Dexamethasone 40mg IV OR orally daily
    - Day 2: Methotrexate 12mg intrathecal
    - Day 7: Cytarabine 100mg intrathecal.
    - Days 1-14: Dasatinib 100mg orally daily.

  - **Repeat cycle every 3 weeks for 4 cycles alternating with Cycle B.**

  - **Cycle B:**
    - Day 1: Methotrexate 200mg/m² IV over 2 hours, then 800mg/m² IV continuous infusion over 22 hours. (Alkaline hydration is required pre- and post-administration of high-dose Methotrexate.)
    - Day 2: Leucovorin 50mg IV over 15 minutes administered 12 hours after completion of 22-hour Methotrexate infusion, then 15mg IV over 15 minutes OR orally every 6 hours for at least 8 doses (until Methotrexate serum concentration is <0.05 micromol/L)
    - Days 2-3: Cytarabine (age <60 years) 3,000mg/m² IV over 3 hours every 12 hours for 4 doses OR Cytarabine (age ≥60 years) 1,000 mg/m² IV over 3 hours every 12 hours for 4 doses
    - Day 2: Methotrexate 12mg intrathecal
    - Day 7: Cytarabine 100mg intrathecal.
    - Days 1-14: Dasatinib 100mg orally daily.

  - **Repeat cycle every 3 weeks for 4 cycles alternating with Cycle A.**

- **Imatinib-Based Therapy**
  - **Cycle A:**
    - Days 1-3: Cyclophosphamide 300mg/m² over 3 hours every 12 hours for 6 doses
    - Days 1-3: Mesna 600mg/m² IV continuous infusion over 24 hours starting 15 minutes before the first dose of Cyclophosphamide and completing 12 hours after the last dose of Cyclophosphamide is started.
    - Day 4: Doxorubicin 50mg/m² IV push OR IV continuous infusion over 24 hours
    - Days 4, 11: Vincristine 2mg IV over 5-10 minutes
    - Days 1-4, 11-14: Dexamethasone 40mg IV OR orally daily
    - Day 2: Methotrexate 12mg intrathecal
    - Day 7: Cytarabine 100mg intrathecal.
    - Days 1-14: Imatinib 400mg orally daily.

  - **Repeat cycle every 3 weeks for 4 cycles alternating with Cycle B.**

**continued**
Acute Lymphoblastic Leukemia (ALL) Treatment Regimens

**Newly-diagnosed ALL**

### PROTOCOL REGIMEN and DOSING

<table>
<thead>
<tr>
<th>Adolescents and Young Adults (AYA) (15-39 years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Philadelphia Chromosome-Positive [Ph (+)] Disease</td>
</tr>
<tr>
<td>Other Recommended Regimens (continued)</td>
</tr>
</tbody>
</table>

**Hyper CVAD with TKI and High-Dose Methotrexate, Cytarabine**

- **Imatinib-Based Therapy** (continued)
  - **Cycle B:**
    - **Day 1:** Methotrexate 200mg/m² IV over 2 hours, then 800mg/m² IV continuous infusion over 22 hours. (Alkaline hydration is required pre- and post-administration of high-dose Methotrexate.)
    - **Day 2:** Leucovorin 50mg IV over 15 minutes administered 12 hours after completion of 22-hour Methotrexate infusion, then 15mg IV over 15 minutes OR orally every 6 hours for at least 8 doses (until Methotrexate serum concentration is <0.05 micromol/L)
    - **Days 2-3:** Cytarabine (age <60 years) 3,000mg/m² IV over 3 hours every 12 hours for 4 doses OR Cytarabine (age ≥60 years) 1,000 mg/m² IV over 3 hours every 12 hours for 4 doses
    - **Day 2:** Methotrexate 12mg intrathecal
    - **Day 7:** Cytarabine 100mg intrathecal
    - **Days 1-14:** Imatinib 400mg orally daily. Repeat cycle every 3 weeks for 4 cycles alternating with Cycle A.

- **Ponatinib-Based Therapy**
  - **Cycle A:**
    - **Days 1-3:** Clophosphamide 300mg/m² over 3 hours every 12 hours for 6 doses
    - **Days 1-3:** Mesna 600mg/m² IV continuous infusion over 24 hours daily starting 15 minutes before the first dose of Clophosphamide and completing 12 hours after the last dose of Clophosphamide is started.
    - **Day 4:** Doxorubicin 50mg/m² IV push OR IV continuous infusion over 24 hours
    - **Days 4 and 11:** Vincristine 2mg IV over 5-10 minutes
    - **Days 4, 11-14:** Dexmethylasone 40mg IV OR orally daily
    - **Day 2:** Methotrexate 12mg intrathecal
    - **Day 7:** Cytarabine 100mg intrathecal
    - **Days 1-14:** Ponatinib 45mg orally daily (cycle 1), **followed by:**
    - **Days 1-21:** Ponatinib 30mg orally daily (cycles 2-4).
  - Repeat cycle every 3 weeks for 4 weeks alternating with Cycle B.
  - **Cycle B:**
    - **Day 1:** Methotrexate 200mg/m² IV over 2 hours, then 800mg/m² IV continuous infusion over 22 hours. (Alkaline hydration is required pre- and post-administration of high-dose Methotrexate.)
    - **Day 2:** Leucovorin 50mg IV over 15 minutes administered 12 hours after completion of 22-hour Methotrexate infusion, then 15mg IV over 15 minutes OR orally every 6 hours for at least 8 doses (until Methotrexate serum concentration is <0.05 micromol/L)
    - **Days 2-3:** Cytarabine (age <60 years) 3,000mg/m² IV over 3 hours every 12 hours for 4 doses OR Cytarabine (age ≥60 years) 1,000 mg/m² IV over 3 hours every 12 hours for 4 doses
    - **Day 2:** Methotrexate 12mg intrathecal
    - **Day 7:** Cytarabine 100mg intrathecal
    - **Days 1-21:** Ponatinib 30mg orally. Repeat cycle every 3 weeks for 4 cycles alternating with Cycle A.

**Multiagent Chemotherapy** (Daunorubicin, Vincristine, Prednisone, Dexamethasone) + TKI

- **Dasatinib-Based Therapy**
  - **Induction Therapy:**
    - **Weeks 1-2:** All patient received the first 2 weeks of Induction Therapy on a frontline COG or DCFI ALL trial
    - **Weeks 3-4:**
      - **Days 1.8 of AALL0622 regimen or Days 15.22 of induction regimen:** Vincristine 1.5mg/m² IV/dose (maximum dose: 2mg)
      - **Days 1.8 of AALL0622 regimen or Days 15.22 of induction regimen:** Daunorubicin 25mg/m² IV/dose
      - **Days 15 of AALL0622 regimen or Day 29 of induction therapy:** Triple intrathecal therapy
  - **Note:** Patients who were CNS3 also received triple intrathecal therapy on Days 1.8 of AALL0622 regimen or Days 15 and 22 of induction regimen
  - **Days 1-14 or 1-21:** Dasatinib 60mg/m² orally twice daily.

- **Consolidation Therapy - Block I (weeks 6-8)**
  - **Days 1-5:** Etoposide 100mg/m² IV
  - **Days 1-5:** Ifosfamide 1800mg/m² with Mesna
  - **Day 1:** Triple intrathecal therapy
  - **Note:** Prior to study amendment, all patients received dose of triple intrathecal therapy on Day 1, which is Day 36 of protocol therapy. After study amendment, patients did not receive triple intrathecal therapy on Day 1 of consolidation. Patients who were classified as CNS 2a, 2b, or 2c and those with traumatic taps who did not receive 2 triple intrathecal doses in induction also received doses on Days 8,15.
**Acute Lymphoblastic Leukemia (ALL) Treatment Regimens**

### Newly-diagnosed ALL\(^1\)\(^a\) (continued)

<table>
<thead>
<tr>
<th>PROTOCOL(^b)</th>
<th>REGIMEN and DOSING</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Adolescents and Young Adults (AYA) (15-39 years)(^c)</strong> (continued)</td>
<td></td>
</tr>
<tr>
<td>Philadelphia Chromosome-Positive [Ph (+)] Disease(^d) (continued)</td>
<td></td>
</tr>
<tr>
<td>Other Recommended Regimens (continued)</td>
<td></td>
</tr>
</tbody>
</table>

Multiagent Chemotherapy (Daunorubicin, Vincristine, Prednisone, Dexamethasone) + TKI\(^e\)\(^f\) (continued)

#### Representative Regimens (continued)

- **Dasatinib-Based Therapy** (continued)

**Consolidation Therapy - Block II**

- **Day 1:** High-dose Methotrexate 500mg/m\(^2\) over 30 minutes, then 4,500mg/m\(^2\) over remainder of 24 hours
- **Day 1:** Triple intrathecal therapy (see note above)
- **Days 2-3:** Cytarabine 3,000mg/m\(^2\)/dose IV over 3 hours every 12 hours x 4 doses
- **Beginning on Day 4:** Filgrastim (G-CSF) 5mcg/kg dose subcutaneous/IV continued until ANC >1,500/uL.
- **Days 1-14 or 1-21:** Dasatinib 60mg/m\(^2\) orally twice daily.

- **Re-Induction Therapy – Block I (weeks 12-14; patients not proceeding to HSCT):**
  - **Days 1, 2:** Daunorubicin 45mg/m\(^2\)
  - **Days 3, 4:** Cyclophosphamide 250mg/m\(^2\) IV every 12 hours x 4 doses
  - **Day 4:** PEG-Asparaginase 2,500 IU/m\(^2\) IM or IV
  - **Day 1, 15:** Triple intrathecal therapy
  - **Days 1-15-21:** Dexamethasone 6mg/m\(^2\) orally divided twice daily
  - **Day 5:** Filgrastim (G-CSF): 5mcg/kg dose subcutaneous or IV and continued until ANC >1,500/uL
  - **Days 1-14 or 1-21:** Dasatinib 60mg/m\(^2\) orally twice daily.

- **Intensification Therapy – Block I (weeks 15-23; patients not proceeding to HSCT):**
  - **Days 1, 2:** High-dose Methotrexate 500mg/m\(^2\) IV over 30 minutes, then 4,500mg/m\(^2\) over remainder of 24 hours
  - **Day 1, 15:** Triple intrathecal therapy
  - **Days 2-26:** Etoposide 100mg/m\(^2\) over 1 hour
  - **Days 2-26:** Cyclophosphamide 300mg/m\(^2\) IV over 1 hour* with Mesna
  - **Day 27:** Filgrastim (G-CSF) 5mcg/kg dose subcutaneous or IV and continued until ANC >1,500/uL
  - **Days 43, 44:** Cytarabine 3,000 mg/m\(^2\) IV every 12 hours × 4 doses
  - **Day 44:** L-Asparaginase 6,000 IU/m\(^2\) administered 6 hours after completion of Cytarabine
  - **Days 1-14, 22-35, 43-56 or Days 1-63:** Dasatinib 60mg/m\(^2\) orally twice daily.

- **Re-Induction Therapy – Block II (weeks 24-26; patients not proceeding to HSCT):**
  - **Days 1, 2:** High-dose Methotrexate 500mg/m\(^2\) IV over 30 minutes, then 4,500mg/m\(^2\) over remainder of 24 hours
  - **Day 1, 2:** Triple intrathecal therapy
  - **Days 22-26:** Etoposide 100mg/m\(^2\) over 1 hour
  - **Days 22-26:** Cyclophosphamide 300mg/m\(^2\) IV over 1 hour* with Mesna
  - **Day 27:** Filgrastim (G-CSF) 5mcg/kg dose subcutaneous or IV and continued until ANC >1,500/uL
  - **Days 43, 44:** Cytarabine 3,000 mg/m\(^2\) IV every 12 hours × 4 doses
  - **Day 44:** L-Asparaginase 6,000 IU/m\(^2\) IM given 6 hours after completion of Cytarabine
  - **Days 1-14, 22-35, 43-56 or Days 1-63:** Dasatinib 60mg/m\(^2\) orally twice daily.

- **Consolidation Therapy - Block II**

  - **Beginning on Day 34:**
    - **Days 29-33:** Filgrastim (G-CSF) 5mcg/kg dose subcutaneous or IV administered 6 hours after completion of Cytarabine
    - **Days 1-14, 22-35, 43-56 or Days 1-63:** Dasatinib 60mg/m\(^2\) orally twice daily.
Acute Lymphoblastic Leukemia (ALL) Treatment Regimens

NEWLY-DIAGNOSED ALL\(^1,a\) (continued)

**PROTOCOL\(^{b}\)**

**REGIMEN and DOSING**

**Adolescents and Young Adults (AYA) (15-39 years)**

**Philadelphia Chromosome-Positive [Ph (+)] Disease**

**Other Recommended Regimens**

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Representative Regimens</strong></td>
<td>(continued)</td>
</tr>
<tr>
<td><strong>Dasatinib-Based Therapy</strong></td>
<td>(continued)</td>
</tr>
<tr>
<td><strong>Maintenance Therapy – Cycle 5 (weeks 68-75; patients not proceeding to HSCT)</strong></td>
<td></td>
</tr>
<tr>
<td>Days 1,29:</td>
<td>Vincristine 1.5mg/m(^2) IV (maximum dose: 2mg)</td>
</tr>
<tr>
<td>Days 1-5, 29-33:</td>
<td>Dexamethasone 6mg/m(^2) orally divided twice daily</td>
</tr>
<tr>
<td><strong>First Day after Cranial Irradiation Completion:</strong></td>
<td>Mercaptopurine 75mg/m(^2) orally daily</td>
</tr>
<tr>
<td>Days 8,15,22,29,36,43,50:</td>
<td>Methotrexate 20mg/m(^2) orally</td>
</tr>
<tr>
<td>Days 1-14, 29-42 or Days 1-49:</td>
<td>Dasatinib 60mg/m(^2) orally twice daily.</td>
</tr>
<tr>
<td><strong>Maintenance Therapy – Cycles 6-12 (weeks 76-131; patients not proceeding to HSCT)</strong></td>
<td></td>
</tr>
<tr>
<td>Days 1,29:</td>
<td>Vincristine 1.5mg/m(^2) IV (maximum dose: 2mg)</td>
</tr>
<tr>
<td>Days 1-5, 29-33:</td>
<td>Dexamethasone 6mg/m(^2) orally divided twice daily</td>
</tr>
<tr>
<td>Days 1-56:</td>
<td>Mercaptopurine 75mg/m(^2) orally given on an empty stomach</td>
</tr>
<tr>
<td>Days 1,8,15,22,29,36,43,50:</td>
<td>Methotrexate 20mg/m(^2) orally</td>
</tr>
<tr>
<td>Days 1-14, 29-42 or Days 1-49 or 1-21:</td>
<td>Dasatinib 60mg/m(^2) orally twice daily.</td>
</tr>
<tr>
<td><strong>Imatinib-Based Therapy</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Induction Therapy:</strong></td>
<td></td>
</tr>
<tr>
<td>Day 1:</td>
<td>Cyclophosphamide 1,200mg/m(^2) IV over 3 hours(^6)</td>
</tr>
<tr>
<td>Days 1-3:</td>
<td>Daunorubicin 60mg/m(^2) IV over 1 hour</td>
</tr>
<tr>
<td>Days 1,8,15,22:</td>
<td>Vincristine 1.3mg/m(^2) IV bolus</td>
</tr>
<tr>
<td>Days 1-21:</td>
<td>Prednisolone 60mg/m(^2) orally</td>
</tr>
<tr>
<td>Days 8-63:</td>
<td>Imatinib 600mg orally</td>
</tr>
<tr>
<td>Day 29:</td>
<td>Methotrexate 15mg intrathecal</td>
</tr>
<tr>
<td>Day 29:</td>
<td>Cytarabine 40mg intrathecal</td>
</tr>
<tr>
<td>Day 29:</td>
<td>Dexamethasone 4mg intrathecal.</td>
</tr>
<tr>
<td><strong>Consolidation Therapy – Cycle I:</strong></td>
<td></td>
</tr>
<tr>
<td>Day 1:</td>
<td>Methotrexate 1,000mg/m(^2) IV over 24 hours</td>
</tr>
<tr>
<td>Days 2.3:</td>
<td>Cytarabine 2,000/m(^2) over 3 hours × 2</td>
</tr>
<tr>
<td>Days 1-3:</td>
<td>Methylprednisolone 50mg IV over 1 hour × 2</td>
</tr>
<tr>
<td>Day 1:</td>
<td>Methotrexate 15mg intrathecal</td>
</tr>
<tr>
<td>Day 1:</td>
<td>Cytarabine 40mg intrathecal</td>
</tr>
<tr>
<td>Day 1:</td>
<td>Dexamethasone 4mg intrathecal.</td>
</tr>
<tr>
<td>Administer for 4 cycles alternating with Cycle II.</td>
<td></td>
</tr>
<tr>
<td><strong>Consolidation Therapy – Cycle II:</strong></td>
<td></td>
</tr>
<tr>
<td>Days 1-28:</td>
<td>Imatinib 600mg orally</td>
</tr>
<tr>
<td>Day 1:</td>
<td>Methotrexate 15mg intrathecal</td>
</tr>
<tr>
<td>Day 1:</td>
<td>Cytarabine 40mg intrathecal</td>
</tr>
<tr>
<td>Day 1:</td>
<td>Dexamethasone 4mg intrathecal.</td>
</tr>
<tr>
<td>Administer for 4 cycles alternating with Cycle I.</td>
<td></td>
</tr>
<tr>
<td><strong>Maintenance Therapy:</strong></td>
<td></td>
</tr>
<tr>
<td>Day 1:</td>
<td>Vincristine 1.3mg/m(^2) IV (bolus) (2mg maximum)</td>
</tr>
<tr>
<td>Days 1-5:</td>
<td>Prednisolone 60mg/m(^2) orally</td>
</tr>
<tr>
<td>Days 1-28:</td>
<td>Imatinib 600mg orally.</td>
</tr>
<tr>
<td>Maintenance therapy administered every 4 weeks up to 2 years from the date of CR.</td>
<td></td>
</tr>
<tr>
<td><strong>Nilotinib-Based Therapy</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Induction Therapy:</strong></td>
<td></td>
</tr>
<tr>
<td>Days 1-3:</td>
<td>Daunorubicin 90mg/m(^2) IV continuous 24 hour infusion</td>
</tr>
<tr>
<td>Days 1,8:</td>
<td>Vincristine 2mg IV push</td>
</tr>
<tr>
<td>Days 1,3:</td>
<td>Prednisolone 60mg/m(^2) orally or 48mg/m(^2) IV</td>
</tr>
<tr>
<td><strong>Day 8 to start of conditioning for allo-HCT or until the end of 2 years of maintenance therapy:</strong></td>
<td>Nilotinib 400mg orally twice daily.</td>
</tr>
<tr>
<td><strong>Consolidation – Cycle A:</strong></td>
<td></td>
</tr>
<tr>
<td>Days 1-2:</td>
<td>Daunorubicin 45mg/m(^2) IV continuous 24-hour infusion</td>
</tr>
<tr>
<td>Days 1-8:</td>
<td>Vincristine 2mg IV push</td>
</tr>
<tr>
<td>Day 1-7:</td>
<td>Prednisolone 60mg/m(^2) orally</td>
</tr>
<tr>
<td>Nilotinib 400mg orally twice daily.</td>
<td></td>
</tr>
<tr>
<td>Administer for 1 cycle.</td>
<td></td>
</tr>
</tbody>
</table>
# Acute Lymphoblastic Leukemia (ALL) Treatment Regimens

## Newly-diagnosed ALL\(^1\text{a}\) (continued)

<table>
<thead>
<tr>
<th>PROTOCOL(^1\text{b})</th>
<th>REGIMEN and DOSING</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Adolescents and Young Adults (AYA) (15-39 years)</strong>(^3) (continued)</td>
<td></td>
</tr>
<tr>
<td>Philadelphia Chromosome-Positive [Ph (+)] Disease(^4) (continued)</td>
<td></td>
</tr>
<tr>
<td>Other Recommended Regimens (continued)</td>
<td></td>
</tr>
</tbody>
</table>

### Multiagent Chemotherapy (Daunorubicin, Vincristine, Prednisone, Dexamethasone) + TKI\(^6\text{a},\text{b}\) (continued)

### Representative Regimens (continued)

- **Nilotinib-Based Therapy** (continued)
  - **Consolidation – Cycle B:**
    - Days 1-4: Cytarabine 2000mg/m\(^2\) IV over 2 hours
    - Days 1-4: Etoposide 150mg/m\(^2\) IV over 3 hours
    - Nilotinib 400mg orally twice daily.
    - Administer for 2 cycles alternating with Cycle C.
  - **Consolidation – Cycle C:**
    - Days 1-2, 15-16: Methotrexate 220mg/m\(^2\) IV bolus, then 60mg/m\(^2\) per hour for 36 hours
    - Leucovorin, followed immediately by 50mg/m\(^2\) IV every 6 hours for 3 doses; then Leucovorin orally until serum Methotrexate <0.05 micromol/L
    - Nilotinib 400mg orally twice daily.
    - Administer for 2 cycles alternating with Cycle B.
  - **Maintenance Therapy:**
    - Nilotinib 400mg orally twice daily for 2 years.
  - **CNS Prophylaxis:**
    - Up to 10 doses of Methotrexate 15mg intrathecal, with: Hydrocortisone 50mg during or after Induction Therapy.

### Vincristine + Dexamethasone + TKI\(^5\)

### PrePhase Therapy:

- Days (-7)(-1):
  - Prednisone 60mg/m\(^2\) orally
- Between Days (-7)(-1):
  - Methotrexate 15mg intrathecal

- **Imatinib-Based Regimen**

### Induction Therapy:

- Days 1.8,15,22: Vincristine 2mg IV
- Days 1-2, 8-9, 15-16, 22-23: Dexamethasone 40mg orally
- Days 1-28: Imatinib 400mg orally twice daily

**Note:** Induction Therapy with Vincristine + Dexamethasone + Dasatinib and Vincristine + Dexamethasone + Nilotinib are also recommended regimens.

**Note:** These regimens are used for induction therapy and additional therapy is needed.

### Ph (-) Disease\(^h\)

### Preferred Regimens

**CALGB 10403 (for patients <40 years)\(^3\)**

### Induction Therapy:

- Allopurinol 300mg daily (unless allergic) should be administered until peripheral blasts and extramedullary disease are reduced.
- **Day 1:** Cytarabine 70mg intrathecal
- Days 1-28: Prednisone 60mg/m\(^2\) daily orally or IV in 2 divided doses
- Days 1.8,15,22: Vincristine 1.5mg/m\(^2\) IV (maximum dose 2mg)
- Days 1.8,15,22: Daunorubicin 25mg/m\(^2\) IV
- **Day 4:** Pegylated Asparaginase 2,500 IU/m\(^2\) IM or IV
- Days 8,29 (also administered on Days 15, 22 for patients with CNS3): Methotrexate 15mg intrathecal

### Extended Remission Induction Therapy (if required):

- Days 1-14: Prednisone 60mg/m\(^2\) daily orally or IV in 2 divided doses
- **Day 1:** Daunorubicin 25mg/m\(^2\) IV
- **Day 1:** Vincristine 1.5mg/m\(^2\) (maximum dose 2mg) IV
- **Day 4:** Pegylated Asparaginase 2,500 IU/m\(^2\) IM or IV

### Remission Consolidation Therapy:

- Days 1.29: Cyclophosphamide 1000mg/m\(^2\) IV
- Days 1.4,8,11,29-32,36-39: Cytarabine 75mg/m\(^2\) IV or SC
- Days 1.14,29-42: E-Mercaptopurine 60mg/m\(^2\) orally
- Days 1.15,22,43,50: Vincristine 1.5mg/m\(^2\) (maximum 2mg) IV
- Days 1.15,43: Pegylated Asparaginase 2,500 IU/m\(^2\) IM or IV
- Days 1.8,15,22 (omit doses on Days 15 and 22 for patients with CNS3): Methotrexate 15mg intrathecal.

---

\(^1\text{a}\): Adolescents and Young Adults (AYA) (15-39 years)

\(^2\text{b}\): Philadelphia Chromosome-Positive [Ph (+)] Disease

\(^3\text{c}\): Other Recommended Regimens

\(^4\text{d}\): Multiagent Chemotherapy (Daunorubicin, Vincristine, Prednisone, Dexamethasone) + TKI

\(^5\text{e}\): Representative Regimens

\(^6\text{f}\): Consolidation – Cycle B:

\(^7\text{g}\): Consolidation – Cycle C:

\(^8\text{h}\): CNS Prophylaxis:

\(^9\text{i}\): Vincristine + Dexamethasone + TKI
Acute Lymphoblastic Leukemia (ALL) Treatment Regimens

**Newly-diagnosed ALL\(^1\)**

<table>
<thead>
<tr>
<th>PROTOCOL(^b)</th>
<th>REGIMEN and DOSING</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adolescents and Young Adults (AYA) (15-39 years)(^1)** (continued)</td>
<td></td>
</tr>
<tr>
<td>Ph (-) Disease(^h) (continued)</td>
<td></td>
</tr>
<tr>
<td>Preferred Regimens (continued)</td>
<td></td>
</tr>
</tbody>
</table>
| CALGB 10403 (for patients <40 years)\(^{18, i}\) (continued) | **Interim Maintenance Therapy:**
| Days 1,11,21,31,41: Methotrexate at a starting dose of 100mg/m\(^2\) IV escalated by 50mg/m\(^2\)/dose | |
| Days 1,11,21,31,41: Vincristine 1.5mg/m\(^2\) IV (maximum dose 2mg) | |
| Days 2,22: Pegylated Asparaginase 2,500 IU/m\(^2\) IM or IV | |
| Days 1,33: Methotrexate 15mg intrathecal. | |
| **Delayed Intensification Therapy:**
| Days 1,8,15,43,50: Vincristine 1.5mg/m\(^2\) (maximum dose 2mg) | |
| Days 1,7-15-21: Dexamethasone 10mg/m\(^2\) orally or IV administered in 2 divided doses | |
| Days 1,8,15: Doxorubicin 25mg/m\(^2\) IV | |
| Days 4 (or Day 5 or Day 6), 43: Pegylated Asparaginase 2,500 IU/m\(^2\) IM or IV | |
| Day 29: Cytarabine 1,000mg/m\(^2\) IV | |
| Days 29-32, 36-39: Cytarabine 75mg/m\(^2\) IV or SC | |
| Days 29-42: 6-Thioguanine 60mg/m\(^2\) orally daily | |
| Days 1,29,36: Methotrexate 15mg intrathecal. | |
| **Maintenance Therapy:**
| Days 1,29,57: Vincristine 1.5mg/m\(^2\) (maximum dose 2mg) IV | |
| Days 1-5,29-33,57-61: Dexamethasone 6mg/m\(^2\) orally daily in 2 divided doses | |
| Days 1-84: 6-Mercaptopurine 75mg/m\(^2\) orally daily | |
| Day 1,29: Methotrexate 15mg intrathecal. | |
| Days 1,29: Methotrexate 15mg intrathecal. | |
| Days 1,29,57, 8,15,22,29,36,43,50,61: Methotrexate 15mg intrathecal | |
| Days 8,15,22,29,36,43,50,57,64,71,78 (held on Day 29 of the first 4 courses of maintenance with intrathecal Methotrexate is given): Methotrexate 20mg/m\(^2\) orally weekly. | |
| Days 1,29,57: Methotrexate 15mg intrathecal. | |
| Days 1,29: Methotrexate 15mg intrathecal. | |
| Days 1,29,57: Methotrexate 15mg intrathecal. | |
| Days 1,29: Methotrexate 15mg intrathecal. | |
| Days 1,29: Methotrexate 15mg intrathecal. | |
| Days 1,29,57, 8,15,22,29,36,43,50,61: Methotrexate 15mg intrathecal | |
| Days 8,15,22,29,36,43,50,57,64,71,78 (held on Day 29 of the first 4 courses of maintenance with intrathecal Methotrexate is given): Methotrexate 20mg/m\(^2\) orally weekly. | |
| Days 1,29,57: Methotrexate 15mg intrathecal. | |
| Days 1,29: Methotrexate 15mg intrathecal. | |
| Days 1,29,57: Methotrexate 15mg intrathecal. | |
| Days 1,29: Methotrexate 15mg intrathecal. | |
| Days 1,29,57, 8,15,22,29,36,43,50,61: Methotrexate 15mg intrathecal | |
| Days 8,15,22,29,36,43,50,57,64,71,78 (held on Day 29 of the first 4 courses of maintenance with intrathecal Methotrexate is given): Methotrexate 20mg/m\(^2\) orally weekly. | |
# Acute Lymphoblastic Leukemia (ALL) Treatment Regimens

## Newly-diagnosed ALL\(^1,a\) (continued)

<table>
<thead>
<tr>
<th>PROTOKOL(^b)</th>
<th>REGIMEN and DOSING</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adolescents and Young Adults (AYA) (15-39 years)(^4) (continued)</td>
<td>Ph (-) Disease(^h) (continued)</td>
</tr>
</tbody>
</table>
| Preferred Regimens (continued) | |}

### COG AALL0232 (for patients ≤21 years)\(^{19,20,i}\) (continued)

**Interim Maintenance II:**
- Days 1,11,21,31,41: Vincristine 1.5mg/m\(^2\) IV
- Days 1,11,21,31,41: Methotrexate 100mg/m\(^2\) IV
- Days 2,22: Pegaspargase 2,500mg/m\(^2\) IM\(^i\)
- Days 1,31: Methotrexate 15mg intrathecal.

**Delayed Intensification II:**
Same regimen as Delayed Intensification I.

**Maintenance Therapy:**
- Days 1,29,57: Vincristine 1.5mg/m\(^2\) (2mg maximum) IV
- Days 1-5, 29-33, 57-61: Prednisone 20mg/m\(^2\) twice daily
- Daily: Mercaptopurine 75mg/m\(^2\) orally
- Weekly: Methotrexate 20mg/m\(^2\) orally
- Days 1 (and 29 first 4 cycles): Methotrexate 15mg intrathecal

### COG AALL0434 (with Nelarabine added to Consolidation Regimen)\(^{21,22,i}\) (for patients with T-ALL)

**Induction Therapy:**
At diagnostic lumbar puncture or Day 1: Cytarabine 15mg intrathecal
- Days 1,8,15,22: Vincristine 1.5mg/m\(^2\) IV (2 mg maximum)
- Days 1-28: Prednisone 30mg/m\(^2\) IV twice daily
- Days 1,8,16,22: Daunorubicin 25mg/m\(^2\) IV
- Days 4, 5, or 6: Pegaspargase 2,500 U/m\(^2\) IM\(^i\)
- Days 8,29 (CNS3\(^g\) + Days 15,22): Methotrexate 15mg intrathecal

**Consolidation Therapy With Nelarabine:**
- Days 8,50: Cyclophosphamide 1,000mg/m\(^2\) IV
- Days 8-11, 15-18, 50-53, 57-60: Cytarabine 75mg/m\(^2\)
- Days 8-21, 50-63: Mercaptopurine 60mg/m\(^2\)
- Days 22,29,64,71: Vincristine 1.5mg/m\(^2\) IV (2mg maximum)
- Days 22,64: Pegaspargase 2,500 U/m\(^2\) IM\(^i\)
- Days 15,22,57,64 (omit Day 22 for CNS3\(^g\)): Methotrexate 15mg intrathecal
- Days 1-5, 43-47: Nelarabine 650mg/m\(^2\) IV, with: Cranial radiation therapy and testicular radiation therapy.

**Interim Maintenance:**
- Days 1,11,21,31,41 (every 10 days x 5 doses): Vincristine 1.5mg/m\(^2\) IV (2 mg maximum)
- Days 1,11,21,31,41 (every 10 days x 5 doses): Methotrexate 100mg/m\(^2\) IV
- Days 2,22: Pegaspargase 2,500 U/m\(^2\) IM\(^i\)
- Days 1,31: Methotrexate 15mg intrathecal.

**Delayed Intensification without Nelarabine:**
- Days 1,8,15,43,50: Vincristine 1.5mg/m\(^2\) IV (2mg maximum)
- Days 4 or 5 or 6, 43: Pegaspargase 2,500 U/m\(^2\) IM\(^i\)
- Days 1-7,15-21: Dexamethasone 5mg/m\(^2\) twice daily
- Days 1,8,15: Doxorubicin 25mg/m\(^2\) IV
- Days 29-32, 36-39: Cytarabine 75mg/m\(^2\)
- Day 29: 1,000mg Cyclophosphamide 1,000mg/m\(^2\) IV\(^i\)
- Days 29-42 (omit for patients receiving cranial irradiation therapy): Thioguanine 60mg/m\(^2\)
- Days 1,29,36: Methotrexate 15mg intrathecal.

**Delayed Intensification with Nelarabine:**
- Days 1,8,15,50: Vincristine 1.5mg/m\(^2\) IV (2mg maximum)
- Days 4 or 5 or 6 and 50: Pegaspargase 2,500 U/m\(^2\) IM\(^i\)
- Days 1,7,15-21: Dexamethasone 5mg/m\(^2\) twice daily
- Days 1,8,15: Doxorubicin 25mg/m\(^2\) IV
- Days 36-39, 43-46: Cytarabine 75mg/m\(^2\) IV
- Day 36: Cyclophosphamide 1,000 mg/m\(^2\) IV\(^i\)
- Days 36-49 (omit for patients receiving cranial irradiation therapy): Thioguanine 60mg/m\(^2\) IV
- Days 1,36,43: Methotrexate 15mg intrathecal
- (Days 29-33: Nelarabine 650 mg/m\(^2\) IV), with: Cranial irradiation therapy.

---

\(^{9}\) CancerTherapyAdvisor.com
## Acute Lymphoblastic Leukemia (ALL) Treatment Regimens

**Newly-diagnosed ALL**

### Adolescents and Young Adults (AYA) (15-39 years)

**Ph (-) Disease**

**Preferred Regimens**

<table>
<thead>
<tr>
<th>PROTOCOL</th>
<th>REGIMEN and DOSING</th>
</tr>
</thead>
</table>
| **COG AALL0434 (with Nelarabine added to Consolidation Regimen)** | Maintenance Therapy without Nelarabine (12-week cycles):  
- Days 1,29,57: Vincristine 1.5mg/m² IV (2mg maximum)  
- Days 1-5, 29-33, 57-61: Prednisone 20mg/m² twice daily  
- Days 1-84: Mercaptopurine 75mg/m² orally daily  
- Days 8,15,22,36,43,50,52,64,71: Methotrexate 20mg/m² orally  
- Day 1 (and Day 29 first 4 cycles; low-risk only): Methotrexate 15mg intrathecal.  
Maintenance Therapy with Nelarabine (12-week cycles):  
- Days 1,57: Vincristine 1.5mg/m² IV (2mg maximum)  
- Days 1-5, 29-33, 57-61: Prednisone 20mg/m² twice daily  
- Days 1-28, 36-84: Mercaptopurine 75mg/m² orally daily  
- Day 1: Methotrexate 15mg intrathecal  
- Days 29-33 (first 3 cycles): Nelarabine 650mg/m² IV |
| **DFCI ALL (study performed in patients <50 years)** | Induction Therapy (4 weeks):  
- Days 1,8,15,22: Vincristine 2mg IV  
- Days 1-28: Prednisone 40mg/m²  
- Days 1,2: Doxorubicin 30mg/m² IV  
- Day 3: Methotrexate 4g/m² (8-24 hours after Doxorubicin) with Leucovorin rescue  
- Day 5: E. coli L-Asparaginase 25,000 IU/m² IM  
- Day 0: Cytarabine 50mg intrathecal (prior to initiation of systemic therapy)  
- Days 15,29: Methotrexate 12mg intrathecal  
- Days 15,29: Cytarabine 40mg intrathecal  
- Days 15,29: Hydrocortisone 50mg intrathecal.  
CNS Therapy (3 Weeks):  
- Vincristine 2mg IV x 1 dose  
- 6-Mercaptopurine 50mg/m² orally x 14 consecutive days  
- Doxorubicin 30mg/m² IV x 1 dose  
- Methotrexate 12mg intrathecal twice weekly x 4 doses  
- Cytarabine 40mg intrathecal twice weekly x 4 doses. **with:** Cranial irradiation.  
Intensification (30 weeks; every 3-week cycles):  
- Day 1: Vincristine 2mg IV  
- Days 1-5: Dexamethasone 18mg/m²/day orally twice daily  
- Day 1 of each cycle to a cumulative dose of 300mg/m²  
- Day 1: Doxorubicin 30mg/m² IV  
- 6-Mercaptopurine 50mg/m²/day orally x 14 consecutive days  
- E. coli Asparaginase: Individualized dosing; 12,500 IU/m²/dose (starting dose)  
- Methotrexate 30mg/m² IV or IM weekly, 1 day after asparaginase (no weekly Methotrexate until Doxorubicin completed)  
- At start of cycle: Methotrexate 12mg intrathecal; Cytarabine 40mg intrathecal; Hydrocortisone 50mg intrathecal every 18 weeks.  
**Note:** Intrathecal therapy of Methotrexate/Cytarabine at start of cycle every 18 weeks.  
Continuation Therapy (74 weeks; every 3-week cycles):  
- Same as intensification except no Asparaginase and Dexamethasone dose reduced to 6mg/m²/day. |
| **GRAALL-2005 (for patients <60 years, with Rituximab for CD20-positive disease)** | Rituximab (375mg/m² IV):  
- Days 1,7: First induction course  
- Days 1,7: Salvage Reinduction (if needed)  
- Days 1,29: Consolidation Phase I, II, III  
- Days 1,7: Late Intensification  
Day 1 of Months 1,3,5,7,9,11 of Maintenance Therapy  
Prephase Treatment:  
- Days (-7)–(-1): Prednisone 60mg/m² orally  
**Between Days (-7) and (-4): Methotrexate 15mg intrathecal.** |

---

**Note:**

- **GRAALL-2005:** Patients ≥60 years or >20% blasts in BM can receive 74 weeks of therapy.
- **GRAALL-2005 (for patients <60 years, with Rituximab for CD20-positive disease):** Rituximab (375mg/m² IV) days 1,7,14.

---

**Continued...**
Acute Lymphoblastic Leukemia (ALL) Treatment Regimens

Newly-diagnosed ALL\textsuperscript{1,\text{a}} (continued)

<table>
<thead>
<tr>
<th>PROTOCOL\textsuperscript{1,\text{b}}</th>
<th>REGIMEN and DOSING</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Adolescents and Young Adults (AYA) (15-39 years)</strong>\textsuperscript{(continued)}</td>
<td></td>
</tr>
<tr>
<td><strong>Ph (-) Disease</strong>\textsuperscript{h} (continued)</td>
<td></td>
</tr>
<tr>
<td><strong>Other Recommended Regimens</strong> (continued)</td>
<td></td>
</tr>
<tr>
<td><strong>GRAALL-2005 (for patients &lt;60 years, with Rituximab for CD20-positive disease)</strong>\textsuperscript{24} (continued)</td>
<td></td>
</tr>
<tr>
<td><strong>Induction Therapy:</strong></td>
<td></td>
</tr>
<tr>
<td>Days 1-14: Prednisone 60mg/m\textsuperscript{2} orally</td>
<td></td>
</tr>
<tr>
<td>Days 1,8,15,22: Vincristine 2 mg IV</td>
<td></td>
</tr>
<tr>
<td>Days 1-3: Daunorubicin 50mg/m\textsuperscript{2} IV</td>
<td></td>
</tr>
<tr>
<td>Days 15,16: Daunorubicin 30mg/m\textsuperscript{2} IV</td>
<td></td>
</tr>
<tr>
<td>Days 8,10,12, L-Asparaginase 6,000 IU/m\textsuperscript{2} daily IV over 1 hour (not done if CNS involvement), then,</td>
<td></td>
</tr>
<tr>
<td>Days 20,22,24,26,28: L-Asparaginase 6,000 IU/m\textsuperscript{2} daily IV over 1 hour</td>
<td></td>
</tr>
<tr>
<td>Day 1: Cyclophosphamide 750mg/m\textsuperscript{2} IV over 3 hours'</td>
<td></td>
</tr>
<tr>
<td>Day 15: Cyclophosphamide 750mg/m\textsuperscript{2} IV over 3 hours (1 infusion) OR Days 15-17: Cyclophosphamide 300mg/m\textsuperscript{2} over 3 hours every 12 hours (6 infusions')</td>
<td></td>
</tr>
<tr>
<td>Day 18 to neutrophil recovery: Lenograstim 263 mcg/day subcutaneous or IV.</td>
<td></td>
</tr>
<tr>
<td><strong>Salvage Reintroduction Therapy:</strong></td>
<td></td>
</tr>
<tr>
<td>Days 1-3: Idarubicin 12mg/m\textsuperscript{2} IV over 1 hour</td>
<td></td>
</tr>
<tr>
<td>Days 1-4 (8 infusions): Cytarabine 2,000mg/m\textsuperscript{2} IV over 2 hours every 12 hours</td>
<td></td>
</tr>
<tr>
<td>Day 9 to neutrophil recovery: Lenograstim 263 mcg subcutaneous or IV daily.</td>
<td></td>
</tr>
<tr>
<td><strong>Interphase-1 Therapy:</strong></td>
<td></td>
</tr>
<tr>
<td>Day 1: Vincristine 2mg IV</td>
<td></td>
</tr>
<tr>
<td>Day 1: Dexamethasone 40mg orally daily.</td>
<td></td>
</tr>
<tr>
<td><strong>Consolidation Therapy I – Block 1:</strong></td>
<td></td>
</tr>
<tr>
<td>Days 1 (4 infusions): Cytarabine 2,000mg/m\textsuperscript{2} IV over 2 hours every 12 hours</td>
<td></td>
</tr>
<tr>
<td>Days 1.2: Dexamethasone 10mg orally every 12 hours</td>
<td></td>
</tr>
<tr>
<td>Days 3: L-Asparaginase (E coli): 10,000 IU/m\textsuperscript{2} IV over 1 hour</td>
<td></td>
</tr>
<tr>
<td>Days 9-13: Lenograstim 263 mcg orally or IV</td>
<td></td>
</tr>
<tr>
<td><strong>Consolidation Therapy I – Block 2:</strong></td>
<td></td>
</tr>
<tr>
<td>Day 15: Vincristine 2mg IV</td>
<td></td>
</tr>
<tr>
<td>Day 15: Methotrexate 3,000 mg/m\textsuperscript{2} continuous IV over 24 hours</td>
<td></td>
</tr>
<tr>
<td>Day 16: L-Asparaginase 10,000 IU/m\textsuperscript{2} IV over 1 hour</td>
<td></td>
</tr>
<tr>
<td>Days 15-21: 6-Methotrexate 60mg/m\textsuperscript{2} orally</td>
<td></td>
</tr>
<tr>
<td>Days 23-27: Lenograstim 263 mcg SC or IV daily</td>
<td></td>
</tr>
<tr>
<td><strong>Consolidation Therapy I – Block 3:</strong></td>
<td></td>
</tr>
<tr>
<td>Day 29: Methotrexate 25mg/m\textsuperscript{2} IV</td>
<td></td>
</tr>
<tr>
<td>Days 29,30: Cytosine arabinoside 500mg/m\textsuperscript{2} IV daily over 3 hours'</td>
<td></td>
</tr>
<tr>
<td>Days 28,30: Etoposide 75mg/m\textsuperscript{2} IV over 1 hour.</td>
<td></td>
</tr>
<tr>
<td>Day 31 to neutrophil recovery: Lenograstim 263mcg SC or IV daily.</td>
<td></td>
</tr>
<tr>
<td><strong>Consolidation Therapy II:</strong></td>
<td></td>
</tr>
<tr>
<td>Block 4 – identical to Block 1</td>
<td></td>
</tr>
<tr>
<td>Block 5 – identical to Block 2</td>
<td></td>
</tr>
<tr>
<td>Block 6 – identical to Block 3</td>
<td></td>
</tr>
<tr>
<td><strong>Late Intensification Therapy (if CR after 1st course):</strong></td>
<td></td>
</tr>
<tr>
<td>Day 1: Prednisone 60mg/m\textsuperscript{2} orally</td>
<td></td>
</tr>
<tr>
<td>Day 1,8,15,22: Vincristine 2mg IV</td>
<td></td>
</tr>
<tr>
<td>Day 1-3,15,16: Daunorubicin 30mg/m\textsuperscript{2} IV</td>
<td></td>
</tr>
<tr>
<td>Days 8,10,12,20,22,24,26,28: L-Asparaginase 6,000 IU/m\textsuperscript{2} IV over 1 hour</td>
<td></td>
</tr>
<tr>
<td>Day 1: Cyclophosphamide 750mg/m\textsuperscript{2} IV over 3 hours, then,</td>
<td></td>
</tr>
<tr>
<td>Day 15 (1 infusion): Cyclophosphamide 750mg/m\textsuperscript{2} over 3 hours OR Days 15-17 (6 infusions): 300mg/m\textsuperscript{2} over 3 hours every 12 hours</td>
<td></td>
</tr>
<tr>
<td>Day 18 to neutrophil recovery: Lenograstim 263mcg subcutaneous or IV daily.</td>
<td></td>
</tr>
<tr>
<td><strong>Late Intensification Therapy (if late CR):</strong></td>
<td></td>
</tr>
<tr>
<td>Days 1-3: Idarubicin 9mg/m\textsuperscript{2} IV over 1 hour daily</td>
<td></td>
</tr>
<tr>
<td>Days 1-4 (8 infusions): Cytarabine 2,000mg/m\textsuperscript{2} IV over 2 hours every 12 hours</td>
<td></td>
</tr>
<tr>
<td>Day 9 to neutrophil recovery: Lenograstim 263mcg SC or IV daily.</td>
<td></td>
</tr>
<tr>
<td><strong>Consolidation Therapy III:</strong></td>
<td></td>
</tr>
<tr>
<td>Repeat Consolidation Therapy I Blocks 1-3.</td>
<td></td>
</tr>
<tr>
<td><strong>Maintenance Therapy</strong></td>
<td></td>
</tr>
<tr>
<td>Day 1 (month 1-12): Vincristine 2mg IV</td>
<td></td>
</tr>
<tr>
<td>Days 1-7 (month 1-12): Prednisone 40mg/m\textsuperscript{2} orally daily</td>
<td></td>
</tr>
<tr>
<td>Months 1-24: 6-Mercaptopurine 60mg/m\textsuperscript{2} orally daily</td>
<td></td>
</tr>
<tr>
<td>Months 1-24: Methotrexate 25mg/m\textsuperscript{2} orally weekly.</td>
<td></td>
</tr>
</tbody>
</table>
Acute Lymphoblastic Leukemia (ALL) Treatment Regimens

Newly-diagnosed ALL\textsuperscript{1,2} (continued)

<table>
<thead>
<tr>
<th>PROTOCOL\textsuperscript{b}</th>
<th>REGIMEN and DOSING</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Adolescents and Young Adults (AYA) (15-39 years)</strong> (continued)</td>
<td></td>
</tr>
<tr>
<td><strong>Ph (-) Disease</strong> (continued)</td>
<td></td>
</tr>
<tr>
<td><strong>Other Recommended Regimens</strong> (continued)</td>
<td></td>
</tr>
</tbody>
</table>

**Hyper CVAD high-dose Methotrexate/Cytarabine\textsuperscript{10,11}**

| Cycle A: | |
| Days 1-3: Cyclophosphamide 300mg/m\textsuperscript{2} over 3 hours every 12 hours for 6 doses\textsuperscript{1} | |
| Days 1-3: Mesna 600mg/m\textsuperscript{2} IV continuous infusion over 24 hours daily starting 15 minutes before the first dose of Cyclophosphamide and completing 12 hours after the last dose of Cyclophosphamide is started | |
| Day 4: Doxorubicin 50mg/m\textsuperscript{2} IV push OR IV continuous infusion over 24 hours | |
| Days 4 and 11: Vincristine 2mg IV over 5-10 minutes | |
| Days 1-4, 11-14: Dexamethasone 40mg IV OR orally daily | |
| Day 2: Methotrexate 12mg intrathecal | |
| Day 7: Cytarabine 100mg intrathecal | |

**Cycle B:**

| Day 1: Methotrexate 200mg/m\textsuperscript{2} IV over 2 hours, then 800mg/m\textsuperscript{2} IV continuous infusion over 22 hours. (Alkaline hydration is required pre- and post-administration of high-dose Methotrexate.) | |
| Day 2: Leucovorin 50mg IV over 15 minutes administered 12 hours after completion of 22-hour Methotrexate infusion, then 15mg IV over 15 minutes OR orally every 6 hours for at least 8 doses (until Methotrexate serum concentration is <0.05micromol/L) | |
| Days 2-3: Cytarabine (age <60 years) 3,000mg/m\textsuperscript{2} IV over 3 hours every 12 hours for 4 doses OR Cytarabine (age ≥60 years) 1,000 mg/m\textsuperscript{2} IV over 3 hours every 12 hours for 4 doses | |
| Day 2: Methotrexate 12mg intrathecal | |
| Day 7: Cytarabine 100mg intrathecal | |

Repeat every 3 weeks for 4 cycles alternating with Cycle A.

**Hyper CVAD + Rituximab – high dose Methotrexate/Cytarabine** (for patients with CD20-positive disease)\textsuperscript{10,11}

| Cycle A: | |
| Day 1: Rituximab 375mg/m\textsuperscript{2} IV | |
| Days 1-3: Cyclophosphamide 300mg/m\textsuperscript{2} over 3 hours every 12 hours for 6 doses\textsuperscript{1} | |
| Days 1-3: Mesna 600mg/m\textsuperscript{2} IV continuous infusion over 24 hours daily starting 15 minutes before the first dose of Cyclophosphamide and completing 12 hours after the last dose of Cyclophosphamide is started. | |
| Day 4: Doxorubicin 50mg/m\textsuperscript{2} IV push OR IV continuous infusion over 24 hours | |
| Days 4, 11: Vincristine 2mg IV over 5-10 minutes | |
| Days 1-4, 11-14: Dexamethasone 40mg IV OR orally daily | |
| Day 2: Methotrexate 12mg intrathecal | |
| Day 7: Cytarabine 100mg intrathecal. | |

Repeat every 3 weeks for 4 cycles alternating with Cycle B.

**Cycle B:**

| Day 1: Rituximab 375mg/m\textsuperscript{2} IV | |
| Day 1: Methotrexate 200mg/m\textsuperscript{2} IV over 2 hours, then 800mg/m\textsuperscript{2} IV continuous infusion over 22 hours. (Alkaline hydration is required pre- and post-administration of high-dose Methotrexate.) | |
| Day 2: Leucovorin 50mg IV over 15 minutes administered 12 hours after completion of 22-hour Methotrexate infusion, then 15mg IV over 15 minutes OR orally every 6 hours for at least 8 doses (until Methotrexate serum concentration is <0.05micromol/L) | |
| Days 2-3: Cytarabine (age <60 years) 3,000mg/m\textsuperscript{2} IV over 3 hours every 12 hours for 4 doses OR Cytarabine (age ≥60 years) 1,000 mg/m\textsuperscript{2} IV over 3 hours every 12 hours for 4 doses | |
| Day 2: Methotrexate 12mg intrathecal | |
| Day 7: Cytarabine 100mg intrathecal | |

Repeat every 3 weeks for 4 cycles alternating with Cycle A.

**Linker Regimen\textsuperscript{26,27}**

**Induction Therapy (1A):**

| Days 1-3: Daunorubicin 60mg/m\textsuperscript{2} IV push, followed by: | |
| Day 15: Daunorubicin 60mg/m\textsuperscript{2} IV push (only if Day 14 bone marrow has residual leukemia) | |
| Days 1.8,15.22: Vincristine 1.4mg/m\textsuperscript{2} IV (maximum 2mg if age >40 years) over 5-10 minutes | |
| Days 1-28: Prednisone 60mg/m\textsuperscript{2} orally | |
| Days 1-4, 15-18: Dexamethasone 9mg/m\textsuperscript{2} orally twice daily | |
| Day 15: Pegaspargase 2,000 international units/m\textsuperscript{2} (maximum 3,750 international units, rounded to vial size) IV over 1 hour | |
| Day 1: Methotrexate 12mg intrathecal. | |

Administer for one 4-week cycle, followed by:

**Consolidation Therapy (1B):**

| Days 1-4: Cytarabine 2,000 mg/m\textsuperscript{2} IV over 2 hours | |
| Days 1-4: Etoposide 500mg/m\textsuperscript{2} IV over 3 hours | |
| Days 1,8,15: Methotrexate 12mg intrathecal. | |

Administer for one 4-week cycle, followed by:

continued
### Newly-diagnosed ALL\(^1,a\) (continued)

#### PROTOCOL\(^b\) REGIMEN and DOSING

<table>
<thead>
<tr>
<th>Adolescents and Young Adults (AYA) (15-39 years)(^\d) (continued)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ph (-) Disease(^h)</strong> (continued)</td>
</tr>
<tr>
<td><strong>Other Recommended Regimens</strong> (continued)</td>
</tr>
</tbody>
</table>

#### Linker Regimen\(^{26,27}\) (continued)

- **Consolidation Therapy (1C):**
  - **Days 1,15:** Methotrexate 220mg/m\(^2\) IV over 15 minutes, then immediately followed by 60mg/m\(^2\)/hour IV continuous infusion over 36 hours (Alkaline hydration required for high-dose Methotrexate.)
  - **Days 2, 16:** Leucovorin 50mg/m\(^2\) IV over 15 minutes every 6 hours for 3 doses starting immediately after completion of 36-hour Methotrexate infusion on days 2 and 16, then, Leucovorin 25mg IV over 15 minutes or orally every 6 hours (until Methotrexate serum concentration is <0.05micromol.)
  - **Days 1-28:** Mercaptopurine 75mg/m\(^2\) orally daily
  - **Days 1, 8:** Methotrexate 12mg intrathecal (after adequate clearance of serum Methotrexate). Administer for one 4-week cycle, followed by:
    - **Consolidation Therapy (2A):**
      - **Days 1-3:** Daunorubicin 60mg/m\(^2\) IV push
      - **Days 1,8,15:** Prednisone 60mg/m\(^2\) orally daily OR Days 1-4,15-18: Dexamethasone 9mg/m\(^2\) orally twice daily
      - **Day 4:** Pegaspargase 2,000 international units/m\(^2\), followed by:
    - **Consolidation Therapy (2B):**
      - **Days 1-4:** Cytarabine 2,000 mg/m\(^2\) IV over 2 hours
      - **Days 1-4:** Etoposide 500mg/m\(^2\) IV over 3 hours
      - **Days 1,8,15:** Methotrexate 12mg intrathecal. Administer for one 4-week cycle, followed by:
    - **Consolidation Therapy (2C):**
      - **Days 1,15:** Methotrexate 220mg/m\(^2\) IV over 15 minutes, then immediately followed by 60mg/m\(^2\)/hour IV continuous infusion over 36 hours (Alkaline hydration required for high-dose Methotrexate.)
      - **Days 2, 16:** Leucovorin 50mg/m\(^2\) IV over 15 minutes every 6 hours for 3 doses starting immediately after completion of 36-hour Methotrexate infusion on days 2 and 16, then, Leucovorin 25mg IV over 15 minutes or orally every 6 hours (until Methotrexate serum concentration is <0.05micromol.)
      - **Days 1-28:** Mercaptopurine 75mg/m\(^2\) orally daily.
      - **Day 4:** Pegaspargase 2,000 international units/m\(^2\), followed by:
    - **Maintenance Therapy:**
      - **Days 1-28:** Mercaptopurine 75mg/m\(^2\) orally
      - **Days 1,8,15,22:** Methotrexate 20mg/m\(^2\) orally.
      - Repeat cycle every 4 weeks until patient is in complete remission for 30 months.

#### PETFEMA ALL-96 (patients aged <30 years)\(^{2k}\)

- **Remission Induction Therapy:**
  - **Days 1,8,15,22:** Vincristine 2mg IV
  - **Days 1,8,15,22:** Daunorubicin 30mg/m\(^2\) IV
  - **Days 1-27:** Prednisone 60mg/m\(^2\) IV or orally daily
  - **Days 28-35:** Prednisone 30mg/m\(^2\) IV or orally daily
  - **Days 10-12, 17-19, 24-26:** Asparaginase 10,000 U/m\(^2\) IV
  - **Day 36:** Cyclophosphamide 1,000mg/m\(^2\) IV
  - **Days 1,29:** Methotrexate 15mg intrathecal
  - **Days 1,29:** Cytarabine 30mg intrathecal
  - **Days 1,29:** Hydrocortisone 20mg intrathecal

- **Consolidation Therapy I:**
  - **Days 1-7:** Mercaptopurine 50mg/m\(^2\) orally
  - **Days 1,28,56:** Methotrexate 3.000mg/m\(^2\) (with folic acid rescue, beginning 12 hours after the end of Methotrexate infusion) IV over 24 hours
  - **Days 14,42:** Teniposide 150mg/m\(^2\) IV every 12 hours
  - **Days 14-15,42-43:** Cytarabine 500mg/m\(^2\) every 12 hours
  - **Days 1,28,56:** Methotrexate 15mg intrathecal
  - **Days 1,28,56:** Cytarabine 30mg intrathecal
  - **Days 1,28,56:** Hydrocortisone 20mg intrathecal

---

\(^{1}\) CancerTherapyAdvisor.com
### New-diagnosed ALL<sup>1,a</sup> (continued)

<table>
<thead>
<tr>
<th>PROTOCOL&lt;sup&gt;b&lt;/sup&gt;</th>
<th>REGIMEN and DOSING</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Adolescents and Young Adults (AYA) (15-39 years)</strong>&lt;sup&gt;c&lt;/sup&gt; (continued)</td>
<td><strong>Ph (-) Disease</strong>&lt;sup&gt;h&lt;/sup&gt; (continued)</td>
</tr>
<tr>
<td><strong>Other Recommended Regimens</strong> (continued)</td>
<td><strong>PETHEMA ALL-96 (patients aged &lt;30 years)</strong>&lt;sup&gt;f&lt;/sup&gt; (continued)</td>
</tr>
<tr>
<td><strong>Consolidation Therapy II/Reinduction:</strong></td>
<td><strong>Induction Therapy I:</strong></td>
</tr>
<tr>
<td>Days 1-14: Dexamethasone 10mg/m&lt;sup&gt;2&lt;/sup&gt; orally or IV daily</td>
<td>Days 1-3: Daunorubicin 60mg/m&lt;sup&gt;2&lt;/sup&gt; IV</td>
</tr>
<tr>
<td>Days 15-21: Dexamethasone 5mg/m&lt;sup&gt;2&lt;/sup&gt; orally or IV daily</td>
<td>Days 1,8,15, 22: Vincristine 1.4mg/m&lt;sup&gt;2&lt;/sup&gt; IV (maximum, 2mg)</td>
</tr>
<tr>
<td>Days 1,2,8,15: Daunorubicin 30mg/m&lt;sup&gt;2&lt;/sup&gt; IV</td>
<td>Days 15: Pegaspargase 2,000 IU/m&lt;sup&gt;2&lt;/sup&gt; IV</td>
</tr>
<tr>
<td>Days 1,15: Cyclophosphamide 600mg/m&lt;sup&gt;2&lt;/sup&gt; IV daily&lt;sup&gt;l&lt;/sup&gt;</td>
<td>Days 1-3, 15-17: Asparaginase 10,000 U/m&lt;sup&gt;2&lt;/sup&gt; IM or IV</td>
</tr>
<tr>
<td>Days 1,15: Methotrexate 15mg intrathecal</td>
<td>Days 1,15: Cytarabine 30mg intrathecal</td>
</tr>
<tr>
<td>Days 1,15: Cytarabine 30mg intrathecal</td>
<td>Days 1,15: Hydrocortisone 20mg intrathecal</td>
</tr>
<tr>
<td>Maintenance Therapy I (+ Reinductions until week 52):</td>
<td><strong>Reinductions (every 4 weeks):</strong></td>
</tr>
<tr>
<td>Methotrexate 20mg/m&lt;sup&gt;2&lt;/sup&gt; IM weekly</td>
<td>Day 1: Vincristine 1.5 mg/m&lt;sup&gt;2&lt;/sup&gt; IV (maximum, 2mg)</td>
</tr>
<tr>
<td>Mercaptopurine 50mg/m&lt;sup&gt;2&lt;/sup&gt; orally daily.</td>
<td>Days 1-7: Prednisone 60mg/m&lt;sup&gt;2&lt;/sup&gt; IV or orally daily</td>
</tr>
<tr>
<td><strong>Maintenance Therapy II (weeks 53-104):</strong></td>
<td>Day 1: Asparaginase 20,000 U/m&lt;sup&gt;2&lt;/sup&gt; IV</td>
</tr>
<tr>
<td>Methotrexate 20mg/m&lt;sup&gt;2&lt;/sup&gt; IM weekly</td>
<td>Day 1: Methotrexate 12mg intrathecal.</td>
</tr>
<tr>
<td>Mercaptopurine 50mg/m&lt;sup&gt;2&lt;/sup&gt; orally daily.</td>
<td><strong>Induction Therapy II:</strong></td>
</tr>
<tr>
<td><strong>USC ALL Based on CCG-1882 (for patients aged 18-57 years)</strong>&lt;sup&gt;j&lt;/sup&gt;</td>
<td>Days 1,8,15,22: Vincristine 1.4mg/m&lt;sup&gt;2&lt;/sup&gt; IV (maximum, 2mg)</td>
</tr>
<tr>
<td><strong>Induction Therapy I:</strong></td>
<td>Days 15: Pegaspargase 2,000 IU/m&lt;sup&gt;2&lt;/sup&gt; IV</td>
</tr>
<tr>
<td>Days 1,8,15,22: Vincristine 1.4mg/m&lt;sup&gt;2&lt;/sup&gt; IV (maximum, 2mg)</td>
<td>Days 1-28: Prednisone 60mg/m&lt;sup&gt;2&lt;/sup&gt; orally</td>
</tr>
<tr>
<td>Days 15,22,43,50: Vincristine 1.4mg/m&lt;sup&gt;2&lt;/sup&gt; IV (maximum, 2mg)</td>
<td>Days 1-8,15: Methotrexate 12mg intrathecal.</td>
</tr>
<tr>
<td><strong>Induction Therapy II:</strong></td>
<td><strong>Intensification Therapy:</strong></td>
</tr>
<tr>
<td>Days 1,29: Cyclophosphamide 1,000mg/m&lt;sup&gt;2&lt;/sup&gt; IV</td>
<td>Days 1,15: Methotrexate 1,000mg/m&lt;sup&gt;2&lt;/sup&gt; IV (T-cell ALL, 2,500mg/m&lt;sup&gt;2&lt;/sup&gt; IV), with Leucovorin 15mg</td>
</tr>
<tr>
<td>Days 1-4, 8-11, 29-32, 36-39: Cytarabine 75mg/m&lt;sup&gt;2&lt;/sup&gt; IV</td>
<td>every 6 hours IV starting 36 hours from start of Methotrexate</td>
</tr>
<tr>
<td>Days 15,22,43,50: Vincristine 1.4mg/m&lt;sup&gt;2&lt;/sup&gt; IV (maximum, 2mg)</td>
<td>Day 16: Pegaspargase 2,000 IU/m&lt;sup&gt;2&lt;/sup&gt; IV</td>
</tr>
<tr>
<td>Days 15: Pegaspargase 2,000 IU/m&lt;sup&gt;2&lt;/sup&gt; IV</td>
<td>Days 16-30: Prednisone 20mg/m&lt;sup&gt;2&lt;/sup&gt; orally.</td>
</tr>
<tr>
<td>Days 15-29: Prednisone 20mg/m&lt;sup&gt;2&lt;/sup&gt; orally</td>
<td><strong>Consolidation Therapy:</strong></td>
</tr>
<tr>
<td>Days 1-14, 29-43: Mercaptopurine 60mg/m&lt;sup&gt;2&lt;/sup&gt; orally</td>
<td>Days 1-5: Cytarabine 75mg/m&lt;sup&gt;2&lt;/sup&gt; IV</td>
</tr>
<tr>
<td>Days 1,8,15,22: Methotrexate 12mg intrathecal.</td>
<td>Days 1-5: Teniposide 60mg/m&lt;sup&gt;2&lt;/sup&gt; IV.</td>
</tr>
<tr>
<td><strong>Intensification Therapy:</strong></td>
<td><strong>Delayed Reinduction Therapy:</strong></td>
</tr>
<tr>
<td>Days 1,15: Methotrexate 1,000mg/m&lt;sup&gt;2&lt;/sup&gt; IV (T-cell ALL, 2,500mg/m&lt;sup&gt;2&lt;/sup&gt; IV), with Leucovorin 15mg</td>
<td>Days 1,8,15,22: Daunorubicin 25mg/m&lt;sup&gt;2&lt;/sup&gt; IV</td>
</tr>
<tr>
<td>every 6 hours IV starting 36 hours from start of Methotrexate</td>
<td>Days 1,8,15,43,50: Vincristine 1.4mg/m&lt;sup&gt;2&lt;/sup&gt; IV (maximum, 2mg)</td>
</tr>
<tr>
<td>Day 16: Pegaspargase 2,000 IU/m&lt;sup&gt;2&lt;/sup&gt; IV</td>
<td>Days 15-22, 43-50: Dexamethasone 10mg/m&lt;sup&gt;2&lt;/sup&gt; orally</td>
</tr>
<tr>
<td>Days 16-30: Prednisone 20mg/m&lt;sup&gt;2&lt;/sup&gt; orally.</td>
<td>Day 15: Pegaspargase 2,000 IU/m&lt;sup&gt;2&lt;/sup&gt; IV</td>
</tr>
<tr>
<td><strong>Consolidation Therapy:</strong></td>
<td>Day 29: Cyclophosphamide 1,000mg/m&lt;sup&gt;2&lt;/sup&gt; IV</td>
</tr>
<tr>
<td>Days 1-5: Cytarabine 75mg/m&lt;sup&gt;2&lt;/sup&gt; IV</td>
<td>Days 29-32, 36-39: Cytarabine 75mg/m&lt;sup&gt;2&lt;/sup&gt; IV</td>
</tr>
<tr>
<td>Days 1-5: Teniposide 60mg/m&lt;sup&gt;2&lt;/sup&gt; IV.</td>
<td>Days 26-42: Thioguanine 60mg/m&lt;sup&gt;2&lt;/sup&gt; orally</td>
</tr>
<tr>
<td><strong>Delayed Reinduction Therapy:</strong></td>
<td>Days 1,29,36: Methotrexate 12mg intrathecal.</td>
</tr>
<tr>
<td>Days 1,8,15,22: Daunorubicin 25mg/m&lt;sup&gt;2&lt;/sup&gt; IV</td>
<td>continued</td>
</tr>
</tbody>
</table>
### New-diagnosed ALL (continued)

#### Adolescents and Young Adults (AYA) (15-39 years) (continued)

**Ph (-) Disease** (continued)

**USC ALL Based on CCG-1882 (for patients aged 18-57 years)**

<table>
<thead>
<tr>
<th>REGIMEN and DOSING</th>
<th>Maintenance Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Days 1-5 (year 1, monthly; year 2, every 2 months):</td>
<td>Prednisone 60mg/m(^2) IV orally</td>
</tr>
<tr>
<td>Day 1 (year 1, monthly; year 2, every 2 months):</td>
<td>Vincristine 1.4mg/m(^2) IV (maximum, 2mg)</td>
</tr>
<tr>
<td>Days 1-28:</td>
<td>Mercaptopurine 60mg/m(^2) orally</td>
</tr>
<tr>
<td>Days 1,8,15,22:</td>
<td>Methotrexate 20mg/m(^2) orally</td>
</tr>
<tr>
<td>Once every 3 months (year 1):</td>
<td>Methotrexate 12mg intrathecal.</td>
</tr>
</tbody>
</table>

**Ph (+) Disease**

**Other Recommended Regimens**

**CALGB 10701**

**Course I (First Induction):**
- Days 1-7: Dasatinib 140mg orally daily
- Days 1-7: Dexamethasone 10mg/m\(^2\) orally or IV

**Course II (If ≤20% lymphoblasts in marrow at Day 15):**
- Days 1-7: Dasatinib 140mg orally daily
- Days 1-7: Dexamethasone 10mg/m\(^2\) orally or IV.

**Course II (If >20% lymphoblasts in marrow at Day 15):**
- Days 1-7: Dasatinib 140mg orally daily
- Days 1-7: Dexamethasone 10mg/m\(^2\) orally or IV.

Vincristine and Daunorubicin also administered.

**Course III (Second Induction for patients not in CR/CRi):**
Patients received Dasatinib, Cyclophosphamide, Vincristine, Daunorubicin, Dexamethasone.

**Course IV (CNS Prophylaxis):**
Patients received Dasatinib, IV Vincristine, and IV, oral, and intrathecal Methotrexate.

**Course V:**
Patients treated with stem cell transplantation or chemotherapy.

**Course VI (Maintenance):**
Dasatinib
- Starting on Day 30 of Course V and continued for 12 months and until 2 consecutive negative BCR-ABL1 RT-PCR assays 3 months apart or relapse.

**Corticosteroids + TKI**

- **Dasatinib + Prednisone**
  **PrePhase:**
  - Days (-7 to -1): Prednisone 10-60mg/m\(^2\) in increasing doses.

  **Induction Therapy:**
  - Dasatinib 70mg twice daily for 84 days
  - Prednisone 50mg/m\(^2\) daily (capped at 120mg daily) administered until Day 24 and then tapered and stopped at Day 32.
  - Days 22,43: Methotrexate intrathecal.

- **Imatinib + Prednisone**
  **PrePhase:**
  - Days (-7 to -1): Prednisone 10-40mg/m\(^2\) in increasing doses from 10-40mg/m\(^2\).

  **Induction Therapy:**
  - Days 1-45: Imatinib 800mg orally
  - Days 1-45: Prednisone 40mg/m\(^2\)

**Note:** Induction Therapy with Corticosteroid + Nilotinib is also a recommended regimen.

**Note:** These regimens are used for induction therapy and additional therapy is needed.

**Hyper CVAD with TKI and High-Dose Methotrexate/Cytarabine**

- **Dasatinib-based Therapy**
  **Cycle A:**
  - Days 1-3: Cyclophosphamide 300mg/m\(^2\) over 3 hours every 12 hours for 6 doses
  - Days 1-3: Mesna 60mg/m\(^2\) IV continuous infusion over 24 hours daily starting 15 minutes before the first dose of Cyclophosphamide and completing 12 hours after the last dose of Cyclophosphamide is started
  - Day 4: Doxorubicin 50mg/m\(^2\) IV push OR IV continuous infusion over 24 hours
  - Days 4 and 11: Vincristine 2mg IV over 5-10 minutes
  - Days 1-4, 11-14: Dexamethasone 40mg IV OR orally daily
  - Day 2: Methotrexate 12mg intrathecal
  - Day 7: Cytarabine 100mg intrathecal.
  - Days 1-14: Dasatinib 100mg orally daily.
  - Repeat cycle every 3 weeks for 4 cycles alternating with Cycle B.

**Note:** These cycles are used for induction therapy and additional therapy is needed.
Newly-diagnosed ALL\textsuperscript{1,a} (continued)

- **Dasatinib-based Therapy** (continued)

  **Cycle B:**
  
  **Day 1:** Methotrexate 200mg/m\textsuperscript{2} IV over 2 hours, then 800mg/m\textsuperscript{2} IV continuous infusion over 22 hours. (Alkaline hydration is required pre- and post-administration of high-dose Methotrexate.)
  
  **Day 2:** Leucovorin 50mg IV over 15 minutes administered 12 hours after completion of 22-hour Methotrexate infusion, then 15mg IV over 15 minutes OR orally every 6 hours for at least 8 doses (until Methotrexate serum concentration is <0.05micromol/L)
  
  **Days 2-3:** Cytarabine (age <60 years) 3,000mg/m\textsuperscript{2} IV over 3 hours every 12 hours for 4 doses OR Cytarabine (age ≥60 years) 1,000 mg/m\textsuperscript{2} IV over 3 hours every 12 hours for 4 doses
  
  **Day 2:** Methotrexate 12mg intrathecal
  
  **Day 7:** Cytarabine 100mg intrathecal
  
  **Days 1-14:** Dasatinib 100mg orally daily.
  
  Repeat cycle every 3 weeks for 4 cycles alternating with Cycle A.

- **Imatinib-based Therapy**

  **Cycle A:**
  
  **Days 1-3:** Cyclophosphamide 300mg/m\textsuperscript{2} over 3 hours every 12 hours for 6 doses
  
  **Days 1-3:** Mesna 600mg/m\textsuperscript{2} IV continuous infusion over 24 hours daily starting 15 minutes before the first dose of Cyclophosphamide and completing 12 hours after the last dose of Cyclophosphamide is started.
  
  **Day 4:** Doxorubicin 50mg/m\textsuperscript{2} IV push OR IV continuous infusion over 24 hours
  
  **Days 4 and 11:** Vincristine 2mg IV over 5-10 minutes
  
  **Days 1-4, 11-14:** Dexamethasone 40mg IV OR orally daily
  
  **Day 2:** Methotrexate 12mg intrathecal
  
  **Day 7:** Cytarabine 100mg intrathecal
  
  **Days 1-14:** Imatinib 400mg orally daily.
  
  Repeat cycle every 3 weeks for 4 cycles alternating with Cycle B.

  **Cycle B:**
  
  **Day 1:** Methotrexate 200mg/m\textsuperscript{2} IV over 2 hours, then 800mg/m\textsuperscript{2} IV continuous infusion over 22 hours. (Alkaline hydration is required pre- and post-administration of high-dose Methotrexate.)
  
  **Day 2:** Leucovorin 50mg IV over 15 minutes administered 12 hours after completion of 22-hour Methotrexate infusion, then 15mg IV over 15 minutes OR orally every 6 hours for at least 8 doses (until Methotrexate serum concentration is <0.05micromol/L)
  
  **Days 2-3:** Cytarabine (age <60 years) 3,000mg/m\textsuperscript{2} IV over 3 hours every 12 hours for 4 doses OR Cytarabine (age ≥60 years) 1,000 mg/m\textsuperscript{2} IV over 3 hours every 12 hours for 4 doses
  
  **Day 2:** Methotrexate 12mg intrathecal
  
  **Day 7:** Cytarabine 100mg intrathecal
  
  **Days 1-14:** Imatinib 400mg orally daily.
  
  Repeat cycle every 3 weeks for 4 cycles alternating with Cycle A.

- **Ponatinib-based Therapy**

  **Cycle A:**
  
  **Days 1-3:** Cyclophosphamide 300mg/m\textsuperscript{2} over 3 hours every 12 hours for 6 doses
  
  **Days 1-3:** Mesna 600mg/m\textsuperscript{2} IV continuous infusion over 24 hours daily starting 15 minutes before the first dose of Cyclophosphamide and completing 12 hours after the last dose of Cyclophosphamide is started.
  
  **Day 4:** Doxorubicin 50mg/m\textsuperscript{2} IV push OR IV continuous infusion over 24 hours
  
  **Days 4 and 11:** Vincristine 2mg IV over 5-10 minutes
  
  **Days 1-4, 11-14:** Dexamethasone 40mg IV OR orally daily
  
  **Day 2:** Methotrexate 12mg intrathecal
  
  **Day 7:** Cytarabine 100mg intrathecal
  
  **Days 1-14:** Ponatinib 45mg orally daily (cycle 1), followed by:
  
  **Days 1-21:** Ponatinib 30mg orally daily (cycles 2-4).
  
  Repeat cycle every 3 weeks for 4 weeks alternating with Cycle B.
### Newly-diagnosed ALL\(^1\)\(^a\) (continued)

<table>
<thead>
<tr>
<th>PROTOCOL(^1)(^b)</th>
<th>REGIMEN and DOSING</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adults (age 40-64 years, unless otherwise specified)(^1) (continued)</td>
<td></td>
</tr>
<tr>
<td><strong>Ph (+) Disease(^a)</strong> (continued)</td>
<td></td>
</tr>
</tbody>
</table>

#### Other Recommended Regimens (continued)

<table>
<thead>
<tr>
<th>Hyper CVAD with TKI and High-Dose Methotrexate/Cytarabine(^2)(^3)(^4) (continued)</th>
<th>• <strong>Ponatinib-Based Therapy</strong> (continued)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cycle B: Day 1: Methotrexate 200mg/m(^2) IV over 2 hours, then 800mg/m(^2) IV continuous infusion over 22 hours (Alkaline hydration is required pre- and post-administration of high-dose Methotrexate.)</td>
<td></td>
</tr>
<tr>
<td>Day 2: Leucovorin 50mg IV over 15 minutes administered 12 hours after completion of 22-hour Methotrexate infusion, then 15mg IV over 15 minutes OR orally every 6 hours for at least 8 doses (until Methotrexate serum concentration is &lt;0.05 micromol/L)</td>
<td></td>
</tr>
<tr>
<td>Days 2-3: Cytarabine (age &lt;60 years) 3,000mg/m(^2) IV every 12 hours for 4 doses OR Cytarabine (age ≥60 years) 1,000mg/m(^2) IV every 12 hours for 4 doses</td>
<td></td>
</tr>
<tr>
<td>Day 2: Methotrexate 12mg intrathecal</td>
<td></td>
</tr>
<tr>
<td>Day 7: Cytarabine 100mg intrathecal</td>
<td></td>
</tr>
<tr>
<td>Days 1-21: Ponatinib 30mg orally.</td>
<td></td>
</tr>
<tr>
<td>Repeat cycle every 3 weeks for 4 cycles alternating with Cycle A.</td>
<td></td>
</tr>
</tbody>
</table>

#### Multiagent Chemotherapy (Daunorubicin, Vincristine, Prednisone, Dexamethasone) + TKI\(^2\)\(^3\)\(^4\) (continued)

**Representative Regimens**

• **Dasatinib-Based Therapy**

**Induction Therapy:**

- **Weeks 1-2:** All patient received the first 2 weeks of Induction Therapy on a frontline COG or DCFI ALL trial
- **Weeks 3-6:**
  - Days 1.8 of AALL0622 regimen OR Days 15,22 of induction regimen: Vincristine 1.5mg/m\(^2\) IV/dose (maximum dose: 2mg)

**Consolidation Therapy - Block I (weeks 6-8)**

- Days 1-5: Etoposide 100mg/m\(^2\) IV
- Days 1-5: Ifosfamide 1800mg/m\(^2\) with Mesna
- Day 1: Triple intrathecal therapy

**Consolidation Therapy - Block II**

- Days 1,15: High-dose Methotrexate 500mg/m\(^2\) over 30 minutes, then 4,500mg/m\(^2\) every remainder of 24 hours
- Day 1: Triple intrathecal therapy (see note above)
- Days 2,3: Cytarabine 3,000mg/m\(^2\)/dose IV over 3 hours every 12 hours × 4 doses

**Re-Induction Therapy – Block I (weeks 12-14; patients not proceeding to HSCT):**

- Days 1,8,15: Vincristine 1.5mg/m\(^2\) IV (maximum dose: 2mg)
- Days 1,2: Daunorubicin 45mg/m\(^2\) IV
- Days 3,4: Cyclophosphamide 250mg/m\(^2\) IV every 12 hours
- Day 4: PEG-Asparaginase 2,500 IU/m\(^2\) IM or IV
- Day 1,15: Triple intrathecal therapy
- Days 1,7,15-21: Dexamethasone 6mg/m\(^2\) orally divided twice daily
- Day 5: Filgrastim (G-CSF): 5mcg/kg subcutaneous/IV continued until ANC >1,500/uL
- Days 1,14 or 1,21: Dasatinib 60mg/m\(^2\) orally twice daily

**Intensification Therapy – Block I (weeks 15-23; patients not proceeding to HSCT):**

- Days 1,115: High-dose Methotrexate 500mg/m\(^2\) IV over 30 minutes, then 4,500mg/m\(^2\) every remainder of 24 hours
- Day 1,22: Triple intrathecal therapy
- Days 22-26: Etoposide 100mg/m\(^2\) over 1 hour
- Days 22-26: Cyclophosphamide 300mg/m\(^2\) IV over 1 hour with Mesna
- Day 27: Filgrastim (G-CSF) 5mcg/kg subcutaneous or IV and continued until ANC >1500/uL
- Days 43,44: Cytarabine 3,000mg/m\(^2\) IV every 12 hours × 4 doses
- Day 44: l-Asparaginase 6,000 IU/m\(^2\) administered 6 hours after completion of Cytarabine

*continued*
Acute Lymphoblastic Leukemia (ALL) Treatment Regimens

<table>
<thead>
<tr>
<th>PROTOCOL</th>
<th>REGIMEN and DOSING</th>
</tr>
</thead>
</table>
| **Adults (age 40-64 years, unless otherwise specified)**

**Ph (+) Disease**

**Other Recommended Regimens**

**Representative Regimens**

- **Dasatinib-Based Therapy**

**Re-induction Therapy – Block II (weeks 24-26; patients not proceeding to HSCT):**

- Days 1,8,15: Vincristine 1.5mg/m² IV (maximum dose: 2mg)
- Days 1,2: Daunorubicin 45mg/m² IV
- Days 3,4: Cyclophosphamide 250mg/m² IV every 12 hours × 4 doses
- Day 4: PEG-Asparaginase 2,500 IU/m² IM after last dose of Cyclophosphamide
- Days 1,15: Triple intrathecal therapy
- Days 1,7,15-21: Dexamethasone 6mg/m² orally divided twice daily
- Beginning on Day 5: Filgrastim (G-CSF) 5mcg/kg subcutaneous or IV
- Days 1-14 or 1-21: Dasatinib 60mg/m² orally twice daily.

**Intensification Therapy – Block II (weeks 27-35; patients not proceeding to HSCT):**

- Days 1,15: High-dose Methotrexate 500mg/m² IV over 30 minutes, then 4,500mg/m² IV over remainder of 24 hours
- Day 1,22: Triple intrathecal therapy
- Days 22-26: Etoposide 100mg/m² IV over 1 hour
- Days 22-26: Cyclophosphamide 300mg/m² IV over 1 hour with Mesna
- Beginning Day 27: Filgrastim (G-CSF) 5mcg/kg subcutaneous or IV
- Days 43,44: Cytarabine 3,000mg/m² IV every 12 hours × 4 doses
- Day 44: L-Asparaginase 6,000 IU/m² IM given 6 hours after completion of Cytarabine
- Days 1,14,22-35,43-56 or Days 1-63: Dasatinib 60mg/m² orally twice daily.

**Maintenance Therapy – Cycles 1-4 (weeks 36-67; patients not proceeding to HSCT):**

- Day 1: High-Dose Methotrexate 500mg/m² IV over 30 minutes, then 4,500mg/m² IV over remainder of 24 hours
- Day 1,29: Triple intrathecal therapy
- Days 1,29: Vincristine 1.5mg/m² IV (maximum dose: 2mg)
- Days 1-5,29-33: Dexamethasone 6mg/m² orally divided twice daily
- Days 8-28: Mercaptopurine 75mg/m² orally
- Days 8,15,22: Methotrexate 20mg/m² orally on an empty stomach
- Days 29-33: Etoposide 100mg/m² IV over 1 hour
- Days 29-33: Cyclophosphamide 300mg/m² IV given immediately following Etoposide with Mesna
- Beginning Day 34: Filgrastim (G-CSF) 5mcg/kg subcutaneous or IV and continued until ANC >1,500/uL
- Days 1,14,29-42 or Days 1-49: Dasatinib 60mg/m² orally twice daily.

**Maintenance Therapy – Cycle 5 (weeks 68-75; patients not proceeding to HSCT):**

- Beginning on Day 1: Cranial irradiation
- Days 1,29: Vincristine 1.5mg/m² IV (maximum dose: 2mg)
- Days 1-5,29-33: Dexamethasone 6mg/m² orally divided twice daily
- First Day after Cranial Irradiation Completion: Mercaptopurine 75mg/m² orally daily
- Day 8,15,22,29,36,43,50: Methotrexate 20mg/m² orally
- Days 1-14, 29-42 or Days 1-49: Dasatinib 60mg/m² orally twice daily.

**Maintenance Therapy – Cycles 6-12 (weeks 76-131; patients not proceeding to HSCT):**

- Days 1,29: Vincristine 1.5mg/m² IV (maximum dose: 2mg)
- Days 1-5,29-33: Dexamethasone 6mg/m² orally divided twice daily
- Days 8,15,22,29,36,43,50: Methotrexate 20mg/m² orally
- Days 1-14, 29-42 or Days 1-49 or 1-21: Dasatinib 60mg/m² orally twice daily.

- **Imatinib-Based Therapy**

**Induction Therapy:**

- Day 1: Cyclophosphamide 1,200mg/m² IV over 3 hours
- Days 1-3: Daunorubicin 60mg/m² IV over 1 hour
- Days 1,8,15,22: Vincristine 1.3mg/m² IV bolus
- Days 1-21: Prednisolone 60mg/m² orally
- Days 8-63: Imatinib 600mg orally
- Day 29: Methotrexate 15mg intrathecal
- Day 29: Cytarabine 40mg intrathecal
- Day 29: Dexamethasone 4mg intrathecal.
### Newly-diagnosed ALL

#### PROTOCOL

<table>
<thead>
<tr>
<th>REGIMEN and DOSING</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adults (age 40-64 years, unless otherwise specified)</td>
</tr>
<tr>
<td>Ph (+) Disease</td>
</tr>
</tbody>
</table>

#### Other Recommended Regimens

**Multiagent Chemotherapy** *(Daunorubicin, Vincristine, Prednisone, Dexamethasone) + TKI* *(continued)*

<table>
<thead>
<tr>
<th>Representative Regimens</th>
<th>(continued)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Imatinib-Based Therapy</strong></td>
<td>(continued)</td>
</tr>
</tbody>
</table>

### Consolidation Therapy – Cycle I:

- **Day 1:** Methotrexate 1,000mg/m² IV over 24 hours
- **Days 2,3:** Cytarabine 2,000/m² over 3 hours × 2
- **Days 1-3:** Methylprednisolone 50mg IV over 1 hour × 2
- **Day 1:** Methotrexate 15mg intrathecal
- **Day 1:** Cytarabine 40mg intrathecal
- **Day 1:** Dexamethasone 4mg intrathecal.
  - Administer for 4 cycles alternating with Cycle II.

### Consolidation Therapy – Cycle II:

- **Days 1-28:** Imatinib 600mg orally
- **Day 1:** Methotrexate 15mg intrathecal
- **Day 1:** Cytarabine 40mg intrathecal
- **Day 1:** Dexamethasone 4mg intrathecal.
  - Administer for 4 cycles alternating with Cycle I.

### Maintenance Therapy:

- **Day 1:** Vincristine 1.3mg/m² IV (bolus) (2mg maximum)
- **Days 1-5:** Prednisolone 60mg/m² orally
- **Days 1-28:** Imatinib 600mg orally.
  - Maintenance therapy administered every 4 weeks up to 2 years from the date of CR.

#### Nilotinib-Based Therapy

### Induction Therapy:

- **Days 1-3:** Daunorubicin 90mg/m² IV continuous 24 hour infusion
- **Days 1-8:** Vincristine 2mg IV push
- **Days 1-14:** Prednisolone 60mg/m² orally or 48mg/m² IV
- **Day 8 to start of conditioning for allo-HCT or until the end of 2 years**
  - of maintenance therapy: Nilotinib 400mg orally twice daily.

### Consolidation – Cycle A:

- **Days 1-2:** Daunorubicin 45mg/m² IV continuous 24-hour infusion
- **Days 1-8:** Vincristine 2mg IV push
- **Days 1-14:** Prednisolone 60mg/m² orally
  - Nilotinib 400mg orally twice daily.
  - Administer for 1 cycle.

### Consolidation – Cycle B:

- **Days 1-4:** Cytarabine 2000mg/m² IV over 2 hours
- **Days 1-4:** Etoposide 150mg/m² IV over 3 hours
  - Nilotinib 400mg orally twice daily.
  - Administer for 2 cycles alternating with Cycle C.

### Consolidation – Cycle C:

- **Days 1-2, 15-16:** Methotrexate 220mg/m² IV bolus, then 60mg/m² per hour for 36 hours
  - Leucovorin, followed immediately by 50mg/m² IV every 6 hours for 3 doses; then Leucovorin orally until serum Methotrexate <0.05micromol/L
  - Nilotinib 400mg orally twice daily.
  - Administer for 2 cycles alternating with Cycle B.

### Maintenance Therapy:

- Nilotinib 400mg orally twice daily for 2 years.

### CNS Prophylaxis:

- Up to 10 doses of Methotrexate 15mg intrathecal, with:
  - Hydrocortisone 50mg during or after Induction Therapy.

---

*Continued*
### New-diagnosed ALL\(^1\text{a}\) (continued)

**PROTOCOL\(^1\text{b}\)**

<table>
<thead>
<tr>
<th>REGIMEN and DOSING</th>
<th>Adults (age 40-64 years, unless otherwise specified)(^1\text{b}) (continued)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ph (+) Disease</strong></td>
<td>(continued)</td>
</tr>
</tbody>
</table>
| Vincristine + Dexamethasone + TKI\(^1\text{c},d\) | PrePhase Therapy:  
Days (-7)(-1): Prednisone 60mg/m\(^2\) orally  
Between Days (-7)(-1): Methotrexate 15mg intrathecal  
- Imatinib-Based Regimen  
  **Induction Therapy:**  
  Days 1,8,15,22: Vincristine 2mg IV  
  Days 1,8,15,22: Dexamethasone 40mg orally  
  Days 1,28: Imatinib 400mg orally twice daily  
  **Note:** Induction Therapy with Vincristine + Dexamethasone + Dasatinib and Vincristine + Dexamethasone + Nilotinib are also recommended regimens.  
  **Note:** These regimens are used for induction therapy and additional therapy is needed. |

<table>
<thead>
<tr>
<th>Ph (-) Disease(^h)</th>
<th>Other Recommended Regimens</th>
</tr>
</thead>
</table>
| **CALGB 8811 Larson Regimen\(^2,29\)** | Induction Therapy (patients age <60 years):  
  Day 1: Cyclophosphamide 1,200mg/m\(^2\) IV over 30 minutes'  
  Days 1-3: Daunorubicin 45mg/m\(^2\) IV push  
  Days 1,8,15,22: Vincristine 2mg IV over 5-10 minutes  
  Days 1-21: Prednisone 60mg/m\(^2\) orally daily  
  Day 5: Pegaspargase 2,000 international units/m\(^2\) (maximum 3,750 international units, rounded to vial size) IV over 1 hour. Administer for one 4-week cycle.  
  **OR**  
  Induction Therapy (patients ≥60 years):  
  Day 1: Cyclophosphamide 800mg/m\(^2\) IV over 30 minutes'  
  Days 1-3: Daunorubicin 30mg/m\(^2\) IV push  
  Days 1,8,15,22: Vincristine 2mg IV over 5-10 minutes  
  Days 1-7: Prednisone 60mg/m\(^2\) orally daily  
  Day 5: Pegaspargase 2,000 international units/m\(^2\) (maximum 3,750 international units, rounded to vial size) IV over 1 hour. Administer for one 4-week cycle, followed by:  
  **Early Intensification:**  
  Days 1: Cyclophosphamide 1,000mg/m\(^2\) IV over 30 minutes'  
  Days 1-14: Mercaptopurine 60mg/m\(^2\) orally daily  
  Days 1-4, 8-11: Cytarabine 75mg/m\(^2\) subcutaneous  
  Day 1: Methotrexate 15mg intrathecal  
  Days 15,22: Vincristine 2mg IV over 5-10 minutes  
  Day 5: Pegaspargase 2,000 international units/m\(^2\) (maximum 3,750 international units, rounded to vial size) IV over 1 hour. Repeat every 4 weeks for 2 cycles, followed by:  
  **CNS Prophylaxis and Interim Maintenance:**  
  Days 1,8,15,22,29: Methotrexate 15mg intrathecal  
  Days 1-70: Mercaptopurine 60mg/m\(^2\) orally daily  
  Days 36,43,50,57,64: Methotrexate 20mg/m\(^2\) orally daily  
  Administer for one 84-day cycle with cranial irradiation on days 1-12, followed by:  
  **Late Intensification:**  
  Days 1,8,15: Doxorubicin 30mg/m\(^2\) IV push  
  Days 1,8,15: Vincristine 2mg IV over 5-10 minutes  
  Days 1-14: Dexamethasone 10mg/m\(^2\) orally daily  
  Days 29: Cyclophosphamide 1,000mg/m\(^2\) IV over 30 minutes'  
  Days 29-42: Thio guanine 60mg/m\(^2\) orally daily  
  Days 29-32, 36-39: Cytarabine 75mg/m\(^2\) subcutaneous daily.  
  Administer for one 56-day cycle, followed by:  
  **Prolonged Maintenance:**  
  Day 1: Vincristine 2mg IV over 5-10 minutes  
  Days 1-5: Prednisone 60mg/m\(^2\) orally daily  
  Days 1,8,15,22: Methotrexate 20mg/m\(^2\) orally daily  
  Days 1-28: Mercaptopurine 60mg/m\(^2\) orally daily.  
  Repeat cycle every 4 weeks until 24 months from diagnosis.  
  **Note:** For Patients aged 60 years or older, reduced doses of Cyclophosphamide, Daunorubicin, and Prednisone. |
Newly-diagnosed ALL\textsuperscript{1,a} (continued)

<table>
<thead>
<tr>
<th>PROTOCOL\textsuperscript{b}</th>
<th>REGIMEN and DOSING</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adults (age 40-64 years, unless otherwise specified)\textsuperscript{l} (continued)</td>
<td></td>
</tr>
<tr>
<td>Ph (-) Disease\textsuperscript{h} (continued)</td>
<td></td>
</tr>
<tr>
<td>Other Recommended Regimens (continued)</td>
<td></td>
</tr>
</tbody>
</table>

**GRAALL-2005 (with Rituximab for CD20-Positive Disease) – for patients aged <60 years\textsuperscript{m}**

**Rituximab (375mg/m\textsuperscript{2} IV):**
- Days 1,7: First induction course
- Days 1,7: Salvage Reinduction (if needed)
- Days 1,29: Consolidation Phase I, II, III
- Days 1,7: Late Intensification
- Day 1 of Months 1,3,5,7,9,11 of Maintenance Therapy

**Prephase Treatment:**
- Days (-7)–(-1): Prednisone 60mg/m\textsuperscript{2} orally
- Between Days (-7) and (-4): Methotrexate 15mg intrathecal.

**Induction Therapy:**
- Days 1-14: Prednisone 60mg/m\textsuperscript{2} orally
- Days 1,8,15,22: Vincristine 2 mg IV
- Days 1-3: Daunorubicin 50mg/m\textsuperscript{2} IV
- Days 15,16: Daunorubicin 30mg/m\textsuperscript{2} IV
- Days 8,10,12: L-Asparaginase 6,000 IU/m\textsuperscript{2} daily IV over 1 hour (not done if CNS involvement), then,
- Days 20,22,24,26,28: L-Asparaginase 6,000 IU/m\textsuperscript{2} daily IV over 1 hour
- Day 1: Cyclophosphamide 750mg/m\textsuperscript{2} IV over 3 hours\textsuperscript{i}
- Day 15: Cyclophosphamide 750mg/m\textsuperscript{2} IV over 3 hours (1 infusion) OR Days 15-17: Cyclophosphamide 300mg/m\textsuperscript{2} over 3 hours every 12 hours (6 infusions)\textsuperscript{i}
- Day 18 to neutrophil recovery: Lenograstim 263 mcg/day subcutaneous or IV.

**Salvage Reintroduction Therapy:**
- Days 1-3: Idarubicin 12mg/m\textsuperscript{2} IV over 1 hour
- Days 1-4 (8 infusions): Cytarabine 2,000mg/m\textsuperscript{2} IV over 2 hours every 12 hours
- Day 9 to neutrophil recovery: Lenograstim 263 mcg subcutaneous or IV daily.

**Interphase-1 Therapy:**
- Day 1: Vincristine 2mg IV
- Day 1: Dexamethasone 40mg orally daily.

**Consolidation Therapy I – Block 1:**
- Days 1,2: Cytarabine 2,000mg/m\textsuperscript{2} IV over 2 hours every 12 hours
- Days 1,2: Dexamethasone 10mg orally every 12 hours
- Day 3: L-Asparaginase (\textit{E coli}): 10,000 IU/m\textsuperscript{2} IV over 1 hour
- Days 9-13: Lenograstim 263 mcg orally or IV

**Consolidation Therapy I – Block 2:**
- Day 15: Vincristine 2mg IV
- Day 15: Methotrexate 3,000 mg/m\textsuperscript{2} continuous IV over 24 hours
- Day 16: L-Asparaginase 10,000 IU/m\textsuperscript{2} IV over 1 hour
- Day 15-21: 6-Methotrexate 60mg/m\textsuperscript{2} orally
- Days 23-27: Lenograstim 263 mcg SC or IV daily

**Consolidation Therapy I – Block 3:**
- Day 29: Methotrexate 25mg/m\textsuperscript{2} IV
- Days 29,30: Cyclophosphamide 500mg/m\textsuperscript{2} IV daily over 3 hours\textsuperscript{i}
- Days 28,30: Etoposide 75mg/m\textsuperscript{2} IV over 1 hour.
- Day 31 to neutrophil recovery: Lenograstim 263 mcg SC or IV daily.

**Consolidation Therapy II:**
- Block 4 – identical to Block 1
- Block 5 – identical to Block 2
- Block 6 – identical to Block 3

**Late Intensification Therapy (if CR after 1st course):**
- Day 1,4: Prednisone 60mg/m\textsuperscript{2} orally
- Day 1,8,15,22: Vincristine 2mg IV
- Day 1-3,15,16: Daunorubicin 30mg/m\textsuperscript{2} IV
- Day 8,10,12,20,22,24,26,28: L-Asparaginase 6,000 IU/m\textsuperscript{2} IV over 1 hour
- Day 15 (1 infusion): Cyclophosphamide 750mg/m\textsuperscript{2} IV over 3 hours, then,
- Days 15-17 (6 infusions): 300mg/m\textsuperscript{2} over 3 hours every 12 hours\textsuperscript{i}
- Day 18 to neutrophil recovery: Lenograstim 263mcg subcutaneous or IV daily.
Newly-diagnosed ALL\(^1\)\(^\text{a}\) (continued)

<table>
<thead>
<tr>
<th>PROTOCOL(^1)(^b)</th>
<th>REGIMEN and DOSING</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adults (age 40-64 years, unless otherwise specified)(^1) (continued)</td>
<td></td>
</tr>
<tr>
<td>Ph (-) Disease(^b) (continued)</td>
<td></td>
</tr>
<tr>
<td>Other Recommended Regimens (continued)</td>
<td></td>
</tr>
</tbody>
</table>

### GRAALL-2005 (with Rituximab for CD20-Positive Disease) – for patients aged <60 years\(^2\)^4 (continued)

**Late Intensification Therapy (if late CR):**

- **Days 1-3:** Idarubicin 9mg/m\(^2\) IV over 1 hour daily
- **Days 1-4 (8 infusions):** Cytarabine 2,000mg/m\(^2\) IV over 2 hours every 12 hours
- **Day 9 to neutrophil recovery:** Lenograstim 263mcg SC or IV daily.

**Consolidation Therapy III:**

Repeat Consolidation Therapy I Blocks 1-3.

**Maintenance Therapy**

- **Day 1 (month 1-12):** Vincristine 2mg IV
- **Days 1-7 (month 1-12):** Prednisone 40mg/m\(^2\) orally daily
- **Months 1-24:** 6-Mercaptopurine 60mg/m\(^2\) orally daily
- **Months 1-24:** Methotrexate 25mg/m\(^2\) orally weekly.

### Hyper CVAD high-dose Methotrexate/Cytarabine\(^10,11\)

**Cycle A:**

- **Days 1-3:** Cyclophosphamide 300mg/m\(^2\) IV over 3 hours every 12 hours for 6 doses\(^1\)
- **Days 1-3:** Mesna 600mg/m\(^2\) IV continuous infusion over 24 hours daily starting 15 minutes before the first dose of Cyclophosphamide and completing 12 hours after the last dose of Cyclophosphamide is started.
- **Day 4:** Doxorubicin 50mg/m\(^2\) IV push OR IV continuous infusion over 24 hours
- **Days 4 and 11:** Vincristine 2mg IV over 5-10 minutes
- **Days 1-4, 11-14:** Dexamethasone 40mg IV OR orally daily
- **Day 2:** Methotrexate 12mg intrathecal
- **Day 7:** Cytarabine 100mg intrathecal.

Repeat every 3 weeks for 4 cycles alternating with Cycle B.

**Cycle B:**

- **Day 1:** Methotrexate 200mg/m\(^2\) IV over 2 hours, then 800mg/m\(^2\) IV continuous infusion over 22 hours. (Alkaline hydration is required pre- and post-administration of high-dose Methotrexate.)
- **Day 2:** Leucovorin 50mg IV over 15 minutes administered 12 hours after completion of 22-hour Methotrexate infusion, then 15mg IV over 3 minutes OR orally every 6 hours for at least 8 doses (until Methotrexate serum concentration is <0.05micromol/L)
- **Days 2-3:** Cytarabine (age <60 years) 3,000mg/m\(^2\) IV over 3 hours every 12 hours for 4 doses OR Cytarabine (age ≥60 years) 1,000mg/m\(^2\) IV over 3 hours every 12 hours for 4 doses
- **Day 2:** Methotrexate 12mg intrathecal
- **Day 7:** Cytarabine 100mg intrathecal.

Repeat every 3 weeks for 4 cycles alternating with Cycle A.

### Hyper CVAD + Rituximab – high dose Methotrexate/Cytarabine\(^10,11\) for patients with CD20-positive disease\(^2\)^11

**Cycle A:**

- **Day 1:** Rituximab 375mg/m\(^2\) IV
- **Days 1-3:** Cyclophosphamide 300mg/m\(^2\) IV over 3 hours every 12 hours for 6 doses\(^1\)
- **Days 1-3:** Mesna 600mg/m\(^2\) IV continuous infusion over 24 hours daily starting 15 minutes before the first dose of Cyclophosphamide and completing 12 hours after the last dose of Cyclophosphamide is started.
- **Day 4:** Doxorubicin 50mg/m\(^2\) IV push OR IV continuous infusion over 24 hours
- **Days 4 and 11:** Vincristine 2mg IV over 5-10 minutes
- **Days 1-4, 11-14:** Dexamethasone 40mg IV OR orally daily
- **Day 2:** Methotrexate 12mg intrathecal
- **Day 7:** Cytarabine 100mg intrathecal.

Repeat every 3 weeks for 4 cycles alternating with Cycle B.

**Cycle B:**

- **Day 1:** Methotrexate 375mg/m\(^2\) IV
- **Day 1:** Rituximab 375mg/m\(^2\) IV over 2 hours, then 800mg/m\(^2\) IV continuous infusion over 22 hours. (Alkaline hydration is required pre- and post-administration of high-dose Methotrexate.)
- **Day 2:** Leucovorin 50mg IV over 15 minutes administered 12 hours after completion of 22-hour Methotrexate infusion, then 15mg IV over 3 minutes OR orally every 6 hours for at least 8 doses (until Methotrexate serum concentration is <0.05 micromol/L)
- **Days 2-3:** Cytarabine (age <60 years) 3,000mg/m\(^2\) IV over 3 hours every 12 hours for 4 doses OR Cytarabine (age ≥60 years) 1,000mg/m\(^2\) IV over 3 hours every 12 hours for 4 doses
- **Day 2:** Methotrexate 12mg intrathecal
- **Day 7:** Cytarabine 100mg intrathecal.

Repeat every 3 weeks for 4 cycles alternating with Cycle A.
### Acute Lymphoblastic Leukemia (ALL) Treatment Regimens

**Newly-diagnosed ALL\(^{1,a}\) (continued)**

<table>
<thead>
<tr>
<th>PROTOCOL(^{lb})</th>
<th>REGIMEN and DOSING</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Adults (age 40-64 years, unless otherwise specified)(^{1})</strong> (continued)</td>
<td></td>
</tr>
<tr>
<td><strong>Ph (-) Disease(^{h})</strong> (continued)</td>
<td></td>
</tr>
<tr>
<td><strong>Other Recommended Regimens</strong> (continued)</td>
<td></td>
</tr>
</tbody>
</table>

**Linker Regimen (for patients aged <60 years)**\(^{26,27}\)

**Induction Therapy (1A):**
- **Days 1-3:** Daunorubicin 60mg/m\(^2\) IV push, **followed by:**
- **Day 15:** Daunorubicin 60mg/m\(^2\) IV push (only if Day 14 bone marrow has residual leukemia)
- **Days 1,8,15,22:** Vincristine 1.4mg/m\(^2\) IV (maximum 2mg if age >40 years) over 5-10 minutes
- **Days 1-28:** Prednisone 60mg/m\(^2\) orally
- **Day 1:** Methotrexate 12mg intrathecal.
  - Administer for one 4-week cycle, **followed by:**

**Consolidation Therapy (1B):**
- **Days 1-4:** Cytarabine 2,000 mg/m\(^2\) IV over 2 hours
- **Days 1-4:** Etoposide 500mg/m\(^2\) IV over 3 hours
- **Days 1,8,15:** Methotrexate 12mg intrathecal.
  - Administer for one 4-week cycle, **followed by:**

**Consolidation Therapy (1C):**
- **Days 1,15:** Methotrexate 220mg/m\(^2\) IV over 15 minutes, then immediately **followed by** 60mg/m\(^2\)/hour IV continuous infusion over 36 hours (Alkaline hydration required for high-dose Methotrexate.)
- **Days 2,16:** Leucovorin 50mg/m\(^2\) IV over 15 minutes every 6 hours for 3 doses starting immediately after completion of 36-hour Methotrexate infusion on days 2 and 16, then,
  - Leucovorin 25mg IV over 15 minutes or orally every 6 hours (until Methotrexate serum concentration is <0.05 micromol.)
- **Days 1-28:** Mercaptopurine 75mg/m\(^2\) orally daily
- **Days 1,15:** Methotrexate 12mg intrathecal (after adequate clearance of serum Methotrexate).
  - Administer for one 4-week cycle, **followed by:**

**Consolidation Therapy (2A):**
- **Days 1-3:** Daunorubicin 60mg/m\(^2\) IV push
- **Days 1,8,15:** Vincristine 1.4mg/m\(^2\) (maximum 2mg if age >40 years) IV over 5-10 minutes
- **Days 1-21:** Prednisone 60mg/m\(^2\) orally daily OR **Days 1-4,15-18:** Dexamethasone 9mg/m\(^2\) orally twice daily)
- **Day 4:** Pegasparagse 2,000 international units/m\(^2\) (maximum 3,750 international units, rounded to vial size) IV over 1 hour
  - Day 1: Methotrexate 12mg intrathecal.
- Administer for one 4-week cycle, **followed by:**

**Consolidation Therapy (2B):**
- **Days 1-4:** Cytarabine 2,000 mg/m\(^2\) IV over 2 hours
- **Days 1-4:** Etoposide 500mg/m\(^2\) IV over 3 hours
- **Days 1,8,15:** Methotrexate 12mg intrathecal.
  - Administer for one 4-week cycle, **followed by:**

**Consolidation Therapy (2C):**
- **Days 1,15:** Methotrexate 220mg/m\(^2\) IV over 15 minutes, then immediately **followed by** 60mg/m\(^2\)/hour IV continuous infusion over 36 hours (Alkaline hydration required for high-dose Methotrexate.)
- **Days 2,16:** Leucovorin 50mg/m\(^2\) IV over 15 minutes every 6 hours for 3 doses starting immediately after completion of 36-hour Methotrexate infusion on days 2 and 16, then,
  - Leucovorin 25mg IV over 15 minutes or orally every 6 hours (until Methotrexate serum concentration is <0.05 micromol.)
- **Days 1-28:** Mercaptopurine 75mg/m\(^2\) orally daily.
  - Administer for one 4-week cycle, **followed by:**

**Consolidation Therapy (3C):**
- **Days 1,15:** Methotrexate 220mg/m\(^2\) IV over 15 minutes, then immediately **followed by** 60mg/m\(^2\)/hour IV continuous infusion over 36 hours (Alkaline hydration required for high-dose Methotrexate.)
- **Days 2,16:** Leucovorin 50mg/m\(^2\) IV over 15 minutes every 6 hours for 3 doses starting immediately after completion of 36-hour Methotrexate infusion on days 2 and 16, then,
  - Leucovorin 25mg IV over 15 minutes or orally every 6 hours (until Methotrexate serum concentration is <0.05 micromol.)
- **Days 1-28:** Mercaptopurine 75mg/m\(^2\) orally daily.
  - Administer for one 4-week cycle, **followed by:**

**Maintenance Therapy:**
- **Days 1-28:** Mercaptopurine 75mg/m\(^2\) orally
- **Days 1,8,15,22:** Methotrexate 20mg/m\(^2\) orally.

Repeat cycle every 4 weeks until patient is in complete remission for 30 months.

**Note:** Rituximab can be administered with this regimen for patients with CD20-positive disease. Refer to GRAALL-2005 regimen for timing and frequency of administration.

Note:
- Rituximab can be administered with this regimen for patients with CD20-positive disease.
- Refer to GRAALL-2005 regimen for timing and frequency of administration.
## Acute Lymphoblastic Leukemia (ALL) Treatment Regimens

**Newly-diagnosed ALL**

### PROTOCOL

<table>
<thead>
<tr>
<th>REGIMEN and DOSING</th>
<th>Adults (age 40-64 years, unless otherwise specified)</th>
<th>Ph (-) Disease</th>
<th>Other Recommended Regimens</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>MRC UKALLXII/ECOG2993</strong></td>
<td><strong>Induction Therapy:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Phase 1, weeks 1-4:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Days 1,8,15,22: Daunorubicin 60mg/m² IV</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Days 1,8,15,22: Vincristine 1.4mg/m² IV</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Days 17-28: L-Asparaginase 10,000 U IV or IM</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Days 1-28: Prednisone 60mg/m² orally daily</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Day 15: Methotrexate 12.5mg intrathecal.</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Phase 2, weeks 5-8:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Days 1,15,29: Cyclophosphamide 650mg/m² IV</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Days 1-4,8,11,15,18,22-25: Cytarabine 75mg/m² IV</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Days 1-28: 6-Mercaptopurine 6mg/m² orally</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Days 1,8,15,22: Methotrexate 12.5mg intrathecal.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Older Adults (age ≥65 years, unless otherwise specified)

#### Ph (+) Disease

**Low-Intensity**

- **Corticosteroids + TKI**
  
  **PrePhase:**
  Days (-7)-(1): Prednisone in increasing doses from 10-40mg/m².

  **Induction Therapy:**
  Dasatinib 70mg twice daily for 84 days
  Prednisone 60mg/m² daily (capped at 120mg daily) administered until Day 24 and then tapered and stopped at Day 32.
  Days 22,43: Methotrexate intrathecal.

- **Imatinib + Prednisone**
  
  **PrePhase:**
  Days (-7)-(1): Prednisone in increasing doses from 10-40mg/m².

  **Induction Therapy:**
  Days 1-45: Imatinib 800mg orally
  Days 1-45: Prednisone 40mg/m²

  **Note:** Induction Therapy with Corticosteroid + Nilotinib is also a recommended regimen.

**Note:** These regimens are used for induction therapy and additional therapy is needed.

#### Vincristine + Dexamethasone + TKI

**PrePhase Therapy:**
Days (-7)-(1): Prednisone 60mg/m² orally
Between Days (-7)-(1): Methotrexate 15mg intrathecal

- **Imatinib-Based Regimen**

  **Induction Therapy:**
  Days 1,8,15,22: Vincristine 2mg IV
  Days 1-2, 8-9, 15-16, 22-23: Dexamethasone 40mg orally
  Days 1-28: Imatinib 400mg orally twice daily

  **Note:** Induction Therapy with Vincristine + Dexamethasone + Dasatinib and Vincristine + Dexamethasone + Nilotinib are also recommended regimens.

  **Note:** These regimens are used for induction therapy and additional therapy is needed.

### Moderate Intensity

**CALGB 10701**

**Course I (First Induction):**
Days 1-7: Dasatinib 140 mg orally daily
Days 1-7: Dexamethasone 10mg/m² orally or IV

**Course II (If ≤20% lymphoblasts in marrow at Day 15):**
Days 1-7: Dasatinib 140 mg orally daily
Days 1-7: Dexamethasone 10mg/m² orally or IV.

**Course II (If >20% lymphoblasts in marrow at Day 15):**
Days 1-7: Dasatinib 140 mg orally daily
Days 1-7: Dexamethasone 10mg/m² orally or IV.
Vincristine and Daunorubicin also administered.

### Continued
Acute Lymphoblastic Leukemia (ALL) Treatment Regimens

**Newly-diagnosed ALL**

PROTOCOL**1,b** REGIMEN and DOSING

Older Adults (age ≥65 years, unless otherwise specified)**1** (continued)

**Ph (+) Disease** (continued)

**Moderate Intensity** (continued)

**CALGB 10701**  (continued)

-Course III (Second Induction for patients not in CR/CRI):
- Patients received Dasatinib, Cyclophosphamide, Vincristine, Daunarubicin, Dexamethasone.

-Course IV (CNS Prophylaxis):
- Patients received Dasatinib, IV Vincristine, and IV, oral, and intrathecal Methotrexate.

-Course V:
- Patients treated with stem cell transplantation or chemotherapy.

-Course VI (Maintenance):
- Dasatinib
- Starting on Day 30 of Course V and continued for 12 months and until 2 consecutive negative BCR-ABL1 RT-PCR assays 3 months apart or relapse.

**EWALL**  (continued)

- **· EWALL + Dasatinib (EWALL-Ph-001)**
  - Prephase Period
    - Days (-7)-(-3): Dexamethasone 10mg daily
    - Methotrexate 15mg intrathecal administered once.
  - Induction Therapy:
    - Days 1-7: TKI (Dasatinib 140mg orally once daily [100mg for patients >70 years]). Administer for 4 weeks, with:
      - Day 1: Vincristine 2mg IV (1mg for patients >70 years) with:
      - Days 1-2: Dexamethasone 40mg (20mg for patients >70 years).
  - Consolidation Therapy – Cycle A:
    - Day 1: TKI (Dasatinib 100mg orally once daily), followed by:
      - Day 1: Methotrexate 10000mg/m² IV (5000mg/m² for patients >70 years)
      - Day 2: Asparaginase 10,000 IU/m² IM (5,000 IU/m² IM for patients >70 years).
    - Repeat every 4 weeks for 3 cycles alternating with Consolidation Therapy Cycle B.
  - Consolidation Therapy – Cycle B:
    - Days 1,3,5: Cytarabine 1000mg/m² IV (500mg/m² IV for patients >70 years) every 12 hours.
    - Repeat every 4 weeks for 3 cycles with Consolidation Therapy Cycle A.
  - Maintenance Therapy – Cycle A:
    - Days 1-28: TKI (Dasatinib 100mg orally once daily).
    - Repeat cycle every 4 weeks alternating with Maintenance Therapy – Cycle B until 24 months from diagnosis.
  - Maintenance Therapy – Cycle B:
    - Days 1-28: 6-Mercaptopurine 60mg/m²
    - Days 1: Methotrexate 35mg/m² orally weekly.
    - Repeat cycle every 4 weeks alternating with Maintenance Therapy – Cycle A until 24 months from diagnosis.
  - Maintenance Therapy – Cycle C:
    - Day 1: Vincristine 2mg IV (1mg for patients >70 years)
    - Days 1-2: Dexamethasone 40mg (20mg for patients >70 years).
    - Administer every 3 months during Maintenance Therapy until 24 months from diagnosis.

- **· EWALL + Nilotinib (EWALL-Ph-002)**
  - Nilotinib administered at 400mg twice daily during induction and then continuously through consolidation and maintenance therapy.

**High Intensity**

Hyper CVAD with TKI alternating with High-Dose Methotrexate/Cytarabine (with dose-reduced Cytarabine to 1000mg/m²)**2,3**

- **· Dasatinib-based Therapy**
  - **Cycle A**:
    - Days 1-3: Cyclophosphamide 300mg/m² over 3 hours every 12 hours for 6 doses’
    - Days 1-3: Mesna 600mg/m² IV continuous infusion over 24 hours daily starting 15 minutes before the first dose of Cyclophosphamide and completing 12 hours after the last dose of Cyclophosphamide is started.
    - Day 4: Doxorubicin 50mg/m² IV push OR IV continuous infusion over 24 hours
    - Days 4 and 11: Vincristine 2mg IV over 5-10 minutes
    - Days 1-4, 11-14: Dexamethasone 40mg IV OR orally daily
    - Day 2: Methotrexate 12mg intrathecal
    - Day 7: Cytarabine 100mg intrathecal.
    - Days 1-14: Dasatinib 100mg orally daily.
    - Repeat cycle every 3 weeks for 4 cycles alternating with Cycle B.

**continued**
# Acute Lymphoblastic Leukemia (ALL) Treatment Regimens

**Newly-diagnosed ALL**<sup>1a</sup> (continued)

<table>
<thead>
<tr>
<th>PROTOCOL&lt;sup&gt;lb&lt;/sup&gt;</th>
<th>REGIMEN and DOSING</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Older Adults (age ≥65 years, unless otherwise specified)</strong>&lt;sup&gt;1a,4&lt;/sup&gt; (continued)</td>
<td></td>
</tr>
<tr>
<td><strong>Ph (+) Disease</strong> (continued)</td>
<td></td>
</tr>
<tr>
<td><strong>High Intensity</strong> (continued)</td>
<td></td>
</tr>
<tr>
<td>Hyper CVAD with TKI alternating with High-Dose Methotrexate/ Cytarabine (with dose-reduced Cytarabine to 1000mg/m&lt;sup&gt;2&lt;/sup&gt;)&lt;sup&gt;11,12,13a&lt;/sup&gt; (continued)</td>
<td></td>
</tr>
<tr>
<td>• <strong>Dasatinib-based Therapy</strong> (continued)</td>
<td></td>
</tr>
<tr>
<td><strong>Cycle B:</strong></td>
<td></td>
</tr>
<tr>
<td>Day 1: Methotrexate 200mg/m&lt;sup&gt;2&lt;/sup&gt; IV over 2 hours, then 800mg/m&lt;sup&gt;2&lt;/sup&gt; IV continuous infusion over 22 hours. (Alkaline hydration is required pre- and post-administration of high-dose Methotrexate.)</td>
<td></td>
</tr>
<tr>
<td>Day 2: Leucovorin 50mg IV over 15 minutes administered 12 hours after completion of 22-hour Methotrexate infusion, then 15mg IV over 15 minutes OR orally every 6 hours for at least 8 doses (until Methotrexate serum concentration is &lt;0.05 micromol/L).</td>
<td></td>
</tr>
<tr>
<td>Days 2-3: Cytarabine 1000mg/m&lt;sup&gt;2&lt;/sup&gt; IV over 3 hours every 12 hours for 4 doses</td>
<td></td>
</tr>
<tr>
<td>Day 2: Methotrexate 12mg intrathecal</td>
<td></td>
</tr>
<tr>
<td>Day 7: Cytarabine 100mg intrathecal</td>
<td></td>
</tr>
<tr>
<td>Days 1-14: Dasatinib 100mg orally daily. Repeat cycle every 3 weeks for 4 cycles alternating with Cycle A.</td>
<td></td>
</tr>
<tr>
<td>• <strong>Ponatinib-Based Therapy</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Cycle A:</strong></td>
<td></td>
</tr>
<tr>
<td>Days 1-3: Cyclophosphamide 300mg/m&lt;sup&gt;2&lt;/sup&gt; over 3 hours every 12 hours for 6 doses&lt;sup&gt;f&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>Days 1-3: Mesna 600mg/m&lt;sup&gt;2&lt;/sup&gt; IV continuous infusion over 24 hours daily starting 15 minutes before the first dose of Cyclophosphamide and completing 12 hours after the last dose of Cyclophosphamide is started.</td>
<td></td>
</tr>
<tr>
<td><strong>Day 4:</strong> Doxorubicin 50mg/m&lt;sup&gt;2&lt;/sup&gt; IV push OR IV continuous infusion over 24 hours</td>
<td></td>
</tr>
<tr>
<td>Days 4 and 11: Vincristine 2mg IV over 5-10 minutes</td>
<td></td>
</tr>
<tr>
<td>Days 1-4, 11-14: Dexamethasone 40mg IV OR orally daily</td>
<td></td>
</tr>
<tr>
<td>Day 2: Methotrexate 12mg intrathecal</td>
<td></td>
</tr>
<tr>
<td>Day 7: Cytarabine 100mg intrathecal.</td>
<td></td>
</tr>
<tr>
<td>Days 1-14: Ponatinib 45mg orally daily (cycle 1), followed by:</td>
<td></td>
</tr>
<tr>
<td>Days 1-21: Ponatinib 30mg orally daily (cycles 2-4). Repeat cycle every 3 weeks for 4 weeks alternating with Cycle B.</td>
<td></td>
</tr>
<tr>
<td><strong>Cycle B:</strong></td>
<td></td>
</tr>
<tr>
<td>Day 1: Methotrexate 200mg/m&lt;sup&gt;2&lt;/sup&gt; IV over 2 hours, then 800mg/m&lt;sup&gt;2&lt;/sup&gt; IV continuous infusion over 22 hours. (Alkaline hydration is required pre- and post-administration of high-dose Methotrexate.)</td>
<td></td>
</tr>
<tr>
<td>Day 2: Leucovorin 50mg IV over 15 minutes administered 12 hours after completion of 22-hour Methotrexate infusion, then 15mg IV over 15 minutes OR orally every 6 hours for at least 8 doses (until Methotrexate serum concentration is &lt;0.05 micromol/L).</td>
<td></td>
</tr>
<tr>
<td>Days 2-3: Cytarabine 1000mg/m&lt;sup&gt;2&lt;/sup&gt; IV over 3 hours every 12 hours for 4 doses</td>
<td></td>
</tr>
<tr>
<td>Day 2: Methotrexate 12mg intrathecal</td>
<td></td>
</tr>
<tr>
<td>Day 7: Cytarabine 100mg intrathecal</td>
<td></td>
</tr>
<tr>
<td>Days 1-21: Ponatinib 30mg orally.</td>
<td></td>
</tr>
<tr>
<td>Repeat cycle every 3 weeks for 4 cycles alternating with Cycle A.</td>
<td></td>
</tr>
</tbody>
</table>

**Ph (-) Disease**

**Low Intensity**

| **Vincristine + Prednisone**<sup>34</sup> | Prednisone 60mg/m<sup>2</sup> in divided doses for 2-4 weeks and then tapered off over about another 10-14 days Vincristine 1-3.3mg/m<sup>2</sup> IV (typically within range of 1.5-2.0mg/m<sup>2</sup>) weekly in 2-4 doses. |

**POMP**<sup>10,35</sup>

| Days 1-5: Prednisone 200mg orally | |
| Days 1: Vincristine 2mg IV (maximum dose: 2mg) | |
| Days 1-5: 6-Mercaptopurine 1,000/m<sup>2</sup> IV over 1 hour | |
| Days 1-5: Methotrexate 10mg/m<sup>2</sup> IV over 1 hour. Repeat cycle every 4 weeks. | |

**Moderate Intensity**

**GMALL**<sup>32</sup>

| See Reference and NCCN Acute Lymphoblastic Leukemia Guidelines. |

**GRAALL**<sup>24</sup>

| **Prephase Treatment:** | |
| Days (-7) to (-1): Prednisone 60mg/m<sup>2</sup> orally | |
| Between Days (-7) and (-4): Methotrexate 15mg intrathecal. | |

<sup>1</sup> CancerTherapyAdvisor.com
### Newely-diagnosed ALL\(^1\)\(^{a}\) (continued)

<table>
<thead>
<tr>
<th>PROTOCOL(^1)(^{b})</th>
<th>REGIMEN and DOSING</th>
</tr>
</thead>
<tbody>
<tr>
<td>Older Adults (age ≥65 years, unless otherwise specified)(^1)(^{**}) (continued)</td>
<td></td>
</tr>
<tr>
<td>Ph (-) Disease (continued)</td>
<td></td>
</tr>
<tr>
<td>Moderate Intensity (continued)</td>
<td></td>
</tr>
</tbody>
</table>

**GRAALL\(^2\) (continued)**

**Induction Therapy:**
- Days 1-14: Prednisone 60mg/m\(^2\) orally
- Days 1,8,15,22: Vincristine 2mg IV
- Days 1-3: Daunorubicin 50mg/m\(^2\) IV
- Days 15,16: Daunorubicin 30mg/m\(^2\) IV
- Days 8,10,12: L-Asparaginase 6,000 IU/m\(^2\) daily IV over 1 hour (not done if CNS involvement), then,
- Days 20,22,24,26,28: L-Asparaginase 6,000 IU/m\(^2\) daily IV over 1 hour
- Day 1: Cyclophosphamide 750mg/m\(^2\) IV over 3 hours
- Days 15,16: Cyclophosphamide 300mg/m\(^2\) IV over 3 hours every 12 hours (6 infusions)
- **Day 18 to neutrophil recovery:** Lenograstim 263 mcg/day subcutaneous or IV.

**Salvage Reintroduction Therapy:**
- Days 1-3: Idarubicin 12mg/m\(^2\) IV over 1 hour
- Days 1-4 (8 infusions): Cytarabine 2,000mg/m\(^2\) IV over 2 hours every 12 hours
- Day 9 to neutrophil recovery: Lenograstim 263 mcg subcutaneous or IV daily.

**Interphase-1 Therapy:**
- Day 1: Vincristine 2mg IV
- Day 1: Dexamethasone 40mg orally daily.

**Consolidation Therapy I – Block 1:**
- Days 1.2 (4 infusions): Cytarabine 2,000mg/m\(^2\) IV over 2 hours every 12 hours
- Days 1.2: Dexamethasone 10mg orally every 12 hours
- Day 3: L-Asparaginase (E coli): 10,000 IU/m\(^2\) IV over 1 hour
- Days 9-13: Lenograstim 263 mcg orally or IV

**Consolidation Therapy I – Block 2:**
- Day 15: Vincristine 2mg IV
- Day 15: Methotrexate 3,000 mg/m\(^2\) continuous IV over 24 hours
- Day 16: L-Asparaginase 10,000 IU/m\(^2\) IV over 1 hour
- Days 15-21: 6-Methotrexate 60mg/m\(^2\) orally
- Days 23-27: Lenograstim 263 mcg SC or IV daily

**Consolidation Therapy I – Block 3:**
- Day 29: Methotrexate 25mg/m\(^2\) IV
- Days 29,30: Cyclophosphamide 500mg/m\(^2\) IV daily over 3 hours\(^1\)
- Days 28,30: Etoposide 75mg/m\(^2\) IV over 1 hour.
- Day 31 to neutrophil recovery: Lenograstim 263 mcg SC or IV daily.

**Consolidation Therapy II:**
- Block 4 – identical to Block 1
- Block 5 – identical to Block 2
- Block 6 – identical to Block 3

**Late Intensification Therapy (if CR after 1st course):**
- Days 1-14: Prednisone 60mg/m\(^2\) orally
- Day 1,8,15,22: Vincristine 2mg IV
- Days 1-3,15,16: Daunorubicin 30mg/m\(^2\) IV
- Days 8,10,12,20,22,24,26,28: L-Asparaginase 6,000 IU/m\(^2\) IV over 1 hour
- Day 1: Cyclophosphamide 750mg/m\(^2\) IV over 3 hours, then,\(^1\)
- Day 15 (1 infusion): Cyclophosphamide 750mg/m\(^2\) over 3 hours OR Days 15-17 (6 infusions): 300mg/m\(^2\) over 3 hours every 12 hours
- Day 18 to neutrophil recovery: Lenograstim 263mcg subcutaneous or IV daily.

**Late Intensification Therapy (if late CR):**
- Days 1-3: Idarubicin 9mg/m\(^2\) IV over 1 hour daily
- Days 1-4 (8 infusions): Cytarabine 2,000mg/m\(^2\) IV over 2 hours every 12 hours
- Day 9 to neutrophil recovery: Lenograstim 263 mcg SC or IV daily.

**Consolidation Therapy III:**
- Repeat Consolidation Therapy I Blocks 1-3.

**Maintenance Therapy**
- Day 1 (month 1-12): Vincristine 2mg IV
- Day 1-7 (month 1-12): Prednisone 40mg/m\(^2\) orally daily
- Months 1-24: 6-Mercaptopurine 60mg/m\(^2\) orally daily
- Months 1-24: Methotrexate 25mg/m\(^2\) orally weekly.

---

\(^1\) Updated February 2023
\(^{a}\) CancerTherapyAdvisor.com
## Acute Lymphoblastic Leukemia (ALL) Treatment Regimens

**PROTOCOL**

### Older Adults (age ≥65 years, unless otherwise specified)\(^{1b}\) (continued)

### Ph (-) Disease (continued)

#### Moderate Intensity (continued)

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Dosing</th>
<th>Cycle A (Cycles 1,3,5,7):</th>
</tr>
</thead>
</table>
| Inotuzumab Ozogamicin + Mini-Hyper CVD (for B-ALL)\(^{36}\) | | Days 1-3: Cyclophosphamide 150mg/m\(^2\) every 12 hours\(^{a}\)  
Days 1-4, 11\(^{14}\): Dexamethasone 20mg  
Days 1-8: Vincristine IV (2mg, flat dose)  
Repeat cycle every 4 weeks for 4 cycles alternating with Cycle B. |

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Dosing</th>
<th>Cycle B (Cycles 2,3,6,8):</th>
</tr>
</thead>
</table>
| | | Day 1: Methotrexate 250mg/m\(^2\)  
Days 2,3: Cytarabine 580mg/m\(^2\) every 12 hours  
Repeat cycle every 4 weeks for 4 cycles alternating with Cycle A. |

#### Modified DFCI 91-01\(^{17}\)

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Dosing</th>
<th>Induction Therapy (4 weeks):</th>
</tr>
</thead>
</table>
| | | Days 1-4, 9-12: Dexamethasone 40mg orally  
Days 1,2,12: Doxorubicin 30mg/m\(^2\) IV  
Days 1,8,15: Vincristine 2mg IV  
Day 3: Methotrexate 40mg/m\(^2\) IV |

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Dosing</th>
<th>Central Nervous System Therapy (3 weeks):</th>
</tr>
</thead>
</table>
| | | Day 1: Vincristine 2mg IV  
Day 1: Doxorubicin 30mg/m\(^2\) IV  
Days 1-4: 6-Mercaptopurine 50mg/m\(^2\) orally  
Days 1,4,8,11: Cytarabine 40mg/Methotrexate 12mg/Hydrocortisone 15mg intrathecal |

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Dosing</th>
<th>Intensification Therapy (21 weeks; 7 x 3 week cycles):</th>
</tr>
</thead>
</table>
| | | Days 1-5: Dexamethasone 6mg orally twice daily  
Day 1: Vincristine 2mg IV  
Day 1: Doxorubicin 30mg/m\(^2\) IV  
Days 1,4,8,11: 6-Mercaptopurine 50mg/m\(^2\) orally  
Every 18 weeks: Cytarabine 40mg/Methotrexate 12mg/Hydrocortisone 15mg intrathecal  
Days 1,8,15: Asparaginase 6,000 IU/m\(^2\) IM |

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Dosing</th>
<th>Maintenance Therapy (72 weeks: 24 x 3 week cycles):</th>
</tr>
</thead>
</table>
| | | Days 1-5: Dexamethasone 6mg orally twice daily  
Day 1: Vincristine 2mg IV  
Day 1-14: 6-Mercaptopurine 50mg/m\(^2\) orally  
Days 1,8,15: Methotrexate 30mg/m\(^2\) orally  
Every 18 weeks: Cytarabine 40mg/Methotrexate 12mg/Hydrocortisone 15mg intrathecal |

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Dosing</th>
<th>Consolidation Therapy – Cycle A:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Day 1: Methotrexate 1,000mg/m(^2) IV continuous 24 hour infusion followed by 5-FU and leucovorin rescue</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Day 2: Asparaginase (E. coli) 10,000 IU/m(^2) IV</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Dosing</th>
<th>Consolidation Therapy – Cycle B:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Days 1,3,5: Cytarabine 1,000mg/m(^2) IV</td>
</tr>
</tbody>
</table>

**Note:** Consolidation therapy consists of 6 alternating cycles of Cycle A (cycles 1,3, and 5) and Cycle B (cycles 2,4, and 6).
**Acute Lymphoblastic Leukemia (ALL) Treatment Regimens**

**Newly-diagnosed ALL\(^1\)** (continued)

<table>
<thead>
<tr>
<th>PROTOCOL(^b)</th>
<th>REGIMEN and DOSING</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Older Adults (age ≥65 years, unless otherwise specified)</strong>(^1)* (continued)</td>
<td></td>
</tr>
<tr>
<td><strong>Ph (-) Disease</strong> (^1)* (continued)</td>
<td></td>
</tr>
<tr>
<td><strong>Moderate Intensity</strong> (^1)* (continued)</td>
<td></td>
</tr>
</tbody>
</table>
| PETHEMA – Based Regimen: ALLOD07\(^1\) (continued) | Maintenance Therapy: 6-Mercaptopurine 60mg/m\(^2\) orally daily Methotrexate 25mg/m\(^2\) IM weekly.  
Reinduction Cycles:  
Days 1,2: Dexamethasone 40mg orally or IV  
Day 1: Vincristine 1mg IV.  
Administer every 3 months in the first year, and every 3 months in the second year.  
Note: Administer maintenance therapy with reinduction pulses for a total treatment duration of 2 years. |
| **High Intensity** | |
| CALGB 9111\(^1\) | Induction Therapy (4 weeks):  
Day 1: Cyclophosphamide 800mg/m\(^2\) IV  
Days 1-3: Daunorubicin 30mg/m\(^2\) IV  
Days 1-21: Prednisone 60mg/m\(^2\) orally or IV once daily  
Days 5,8,11,15,18,22: L-Asparaginase (E. coli): 6,000 IU/m\(^2\) subcutaneous or IM.  
Early Intensification (4 weeks; repeat once):  
Day 1: Methotrexate 15mg intrathecal  
Day 1: Cyclophosphamide 1000mg/m\(^2\) IV  
Days 1-14: 6-Mercaptopurine 60mg/m\(^2\) orally  
Days 1-8:11: Cytarabine 75mg/m\(^2\) subcutaneous  
Days 15,22: Vincristine 2mg IV  
Days 15,18,22,25: L-Asparaginase (E. coli): 6,000 IU/m\(^2\) subcutaneous or IM.  
CNS Prophylaxis and Interim Maintenance (12 weeks):  
Days 1,12: Cranial irradiation  
Days 1,15,22,29: Methotrexate 15 mg intrathecal  
Days 1-70: 6-Mercaptopurine 60mg/m\(^2\) orally  
Days 36,43,50,57,64: Methotrexate 20mg/m\(^2\) orally.  
Late Intensification (8 weeks):  
Days 1,8,15: Doxorubicin 30mg/m\(^2\) IV  
Days 1,8,15,20: Vincristine 2mg IV  
Days 1-14: Dexamethasone 10mg/m\(^2\) orally  
Day 29: Cyclophosphamide 1,000mg/m\(^2\) IV  
Days 29-42: 6-Thioguanine 60mg/m\(^2\) orally  
Days 29-32, 36-39: Cytarabine 75mg/m\(^2\) subcutaneous daily.  
Prolonged Maintenance (every 4 weeks until 2 years from diagnosis):  
Day 1: Vincristine 2mg IV  
Days 1-5: Prednisone 60mg/m\(^2\) orally  
Days 1-28: 6-Mercaptopurine 60mg/m\(^2\) orally  
Days 1,8,15,22: Methotrexate 20mg/m\(^2\) orally. |
| Hyper CVAD high-dose Methotrexate/Cytarabine (with Cytarabine dose reduced to 1,000mg/m\(^2\))\(^{10,11,40} \) | Cycle A:  
Days 1-3: Cyclophosphamide 300mg/m\(^2\) IV over 3 hours every 12 hours for 6 doses  
Days 1-3: Mesna 600mg/m\(^2\) IV continuous infusion over 24 hours daily starting 15 minutes before the first dose of Cyclophosphamide and completing 12 hours after the last dose of Cyclophosphamide is started.  
Day 4: Doxorubicin 50mg/m\(^2\) IV push OR IV continuous infusion over 24 hours  
Days 4 and 11: Vincristine 2mg IV over 5-10 minutes  
Days 1,4,11-14: Dexamethasone 40mg IV OR IV orally daily  
Day 2: Methotrexate 12mg intrathecal  
Day 7: Cytarabine 100mg intrathecal.  
Repeat every 3 weeks for 4 cycles alternating with Cycle B.  
Cycle B:  
Day 1: Methotrexate 200mg/m\(^2\) IV over 2 hours, then 800mg/m\(^2\) IV continuous infusion over 22 hours.  
(Alkaline hydration is required pre- and post-administration of high-dose Methotrexate.)  
Day 2: Leucovorin 50mg IV over 15 minutes administered 12 hours after completion of 22-hour Methotrexate infusion, then 15mg IV over 15 minutes OR orally every 6 hours for at least 8 doses (until Methotrexate serum concentration is <0.05 micromol/L)  
Days 2-3: Cytarabine (age ≥60 years) 1,000 mg/m\(^2\) IV over 3 hours every 12 hours for 4 doses  
Day 2: Methotrexate 12mg intrathecal  
Day 7: Cytarabine 100mg intrathecal.  
Repeat every 3 weeks for 4 cycles alternating with Cycle A.  
continued
Acute Lymphoblastic Leukemia (ALL) Treatment Regimens

Relapsed/Refractory ALL\textsuperscript{1,a,p}

**PROTOCOL**\textsuperscript{lb}  **REGENEN and DOSING**

**Ph (+) Disease**\textsuperscript{n-1}

**Other Recommended Regimens**

Blinatumomab (for B-ALL; TKI intolerant/refractory)\textsuperscript{(Category 1)}\textsuperscript{41,42}

**Prephase Therapy:** Before start of treatment until Cycle 1, induction.

**Day 1:** Dexamethasone 10mg/m\textsuperscript{2} orally or IV daily (maximum 24mg/day), followed by:

**Cycle 1 Induction Therapy:**

- **Days 1-7:** Blinatumomab 9mcg IV continuous infusion over 24 hours daily
- **Days 8-28:** Blinatumomab 28mcg IV continuous infusion over 24 hours daily

Administer for one 6-week cycle (4 weeks on followed by 2 weeks off treatment), followed by:

**Cycle 2 Induction Therapy:**

- **Days 1-28:** Blinatumomab 28mcg IV continuous infusion over 24 hours daily.

Administer for one 6-week cycle (4 weeks on followed by 2 weeks off treatment).

**Consolidation Therapy:**

- **Days 1-28:** Blinatumomab 28mcg IV continuous infusion over 24 hours daily.

Repeat cycle every 5 weeks (4 weeks on followed by 2 weeks off treatment) for 3 cycles.

**Continued Therapy:**

- **Days 1-28:** Blinatumomab 28mcg IV continuous infusion over 24 hours daily.

Administer for one 6-week cycle (4 weeks on followed by 2 weeks off treatment) for 4 cycles.

**Note:** For patients <45kg, BSA-based dosing should be used. Blinatumomab may be given up to a total of 9 cycles (2 cycles of induction followed by 3 cycles of consolidation followed by 4 cycles of continued therapy).

**Bosutinib**\textsuperscript{43,q,r}

Bosutinib 400mg twice daily or 600mg twice daily.

**Dasatinib**\textsuperscript{44,q}

Dasatinib 140mg orally once daily or 70mg orally twice daily.

**Imatinib**\textsuperscript{45,q}

Imatinib 400mg or 600mg once daily.

**Inotuzumab Ozogamicin** (for B-ALL; TKI intolerant/refractory)\textsuperscript{46}

**Day 1:** Inotuzumab Ozogamicin 0.8mg/m\textsuperscript{2} IV

**Days 8,15:** Inotuzumab Ozogamicin 0.5mg/m\textsuperscript{2} IV

Administer for one 21-day cycle, then repeat subsequent cycles every 4 weeks for up to 6 cycles. Once CR or CRi achieved, dose of Inotuzumab Ozogamicin reduced to 0.5mg/m\textsuperscript{2} IV.

**MOpAD + TKI with and without Rituximab** (Category 2B)\textsuperscript{47}

**Days 1,15:** Methotrexate 200mg/m\textsuperscript{2} IV (reduced by 50% for creatinine clearance)

**Days 1,8,15:** Vincristine 1.4mg/m\textsuperscript{2} IV (reduced dose to 1mg for pre-existing neuropathy and/or bilirubin 2-3mg/dL; maximum dose 2mg)

**Days 2,16:** Pegylated-L-Asparaginase 2,500 IU/m\textsuperscript{2} IV (no capping of dose; decrease by 50% if direct bilirubin between 2 and 3mg/dL; hold for bilirubin >3mg/dL, especially serous pancreatitis, thrombosis not controlled with anticoagulation, or disseminated intravascular coagulation)

**Days 1-4, 15-18:** Dexamethasone 40mg IV or orally Dasatinib 70-100mg orally daily, Imatinib 400-800mg orally daily, or Nilotinib 200-400 mg orally once daily in combination with chemotherapy.

For patients with CD20-positive leukemia:

**Days 1,15:** Rituximab 375mg/m\textsuperscript{2} IV during the first 4 cycles.

**Nilotinib**\textsuperscript{48,q,r}

Nilotinib 200-400mg orally once daily.

**Ponatinib**\textsuperscript{49,q,s,t}

Ponatinib 45 mg orally once daily.

**Tisagenlecleucel** (for patients <26 years with refractory disease or \geq2 relapses and failure of 2 TKIs)\textsuperscript{50}

See NCCN Acute Lymphoblastic Leukemia Guidelines\textsuperscript{1}

**Ph (-) Disease**\textsuperscript{x}

**Preferred Regimens**

**B-ALL**

Blinatumomab (Category 1)\textsuperscript{41,42}

**Prephase Therapy:** Before start of treatment until Cycle 1, induction.

**Day 1:** Dexamethasone 10mg/m\textsuperscript{2} orally or IV daily (maximum 24mg/day), followed by:

**Cycle 1 Induction Therapy:**

- **Days 1-7:** Blinatumomab 9mcg IV continuous infusion over 24 hours daily
- **Days 8-28:** Blinatumomab 28mcg IV continuous infusion over 24 hours daily

Administer for one 6-week cycle (4 weeks on followed by 2 weeks off treatment), followed by:

**Cycle 2 Induction Therapy:**

- **Days 1-28:** Blinatumomab 28mcg IV continuous infusion over 24 hours daily.

Administer for one 6-week cycle (4 weeks on followed by 2 weeks off treatment).
**Acute Lymphoblastic Leukemia (ALL) Treatment Regimens**

## Relapsed/Refractory ALL\(^1,a,p\) (continued)

<table>
<thead>
<tr>
<th>PROTOCOL(^b)</th>
<th>REGIMEN and DOSING</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ph (-) Disease</strong>(^1,v) (continued)</td>
<td><strong>Consolidation Therapy:</strong>&lt;br&gt;Days 1-28: Blinatumomab 28mcg IV continuous infusion over 24 hours daily. Repeat cycle every 4 weeks (4 weeks on <strong>followed by</strong> 2 weeks off treatment) for 3 cycles.&lt;br&gt;&lt;br&gt;<strong>Continued Therapy:</strong>&lt;br&gt;Days 1-28: Blinatumomab 28mcg IV continuous infusion over 24 hours daily. Repeat 12-week cycle (4 weeks on <strong>followed by</strong> 8 weeks off treatment) for 4 cycles. <strong>Note:</strong> For patients &lt;45kg, BSA-based dosing should be used. Blinatumomab may be given up to a total of 9 cycles (2 cycles of induction <strong>followed by</strong> 3 cycles of consolidation <strong>followed by</strong> 4 cycles of continued therapy).</td>
</tr>
<tr>
<td><strong>Preferred Regimens</strong> (continued)</td>
<td><strong>Inotuzumab Ozogamicin</strong> (Category 1)(^46)&lt;br&gt;Day 1: Inotuzumab Ozogamicin 0.8mg/m(^2) IV&lt;br&gt;Days 8,15: Inotuzumab Ozogamicin 0.5mg/m(^2) IV&lt;br&gt;Administer for one 21-day cycle, then repeat subsequent cycles every 4 weeks for up to 6 cycles. Once CR or CRi achieved, dose of Inotuzumab Ozogamicin reduced to 0.5mg/m(^2) IV.</td>
</tr>
<tr>
<td><strong>B-ALL</strong> (continued)</td>
<td><strong>Tisagenlecleucel (patients &lt;26 years with refractory disease or ≥2 relapses)</strong>(^50) See NCCN Acute Lymphoblastic Leukemia Guidelines(^1)</td>
</tr>
</tbody>
</table>

### T-ALL

**Other Recommended Regimens**

| **Nelarabine (for T-ALL)**\(^51,52\) | Days 1.3.5: Nelarabine (age >16 years) 1,500mg/m\(^2\) IV over 2 hours. Repeat cycle every 3 weeks. OR Day 1-5: Nelarabine (age ≤21 years) 650mg/m\(^2\) IV over 60 minutes. Repeat cycle every 3 weeks. |
| **Nelarabine, Etoposide, Cyclophosphamide (for T-ALL)**\(^33,34\) | Days 1-5: Etoposide 100mg/m\(^2\) IV<br>Days 1-5: Cyclophosphamide 440mg/m\(^2\) IV\(^1\)<br>Days 7(8)-11(12): Nelarabine 650mg/m\(^2\) IV<br>Intrathecal Methotrexate or triplet intrathecal therapy (Methotrexate, Cytarabine, Hydrocortisone) typically preceding a nelarabine dose by 6 hours or following Nelarabine by 2 days. |

### B-ALL or T-ALL

**Other Recommended Regimens**

| **Alkylator Combination Regimen**\(^36\) | Days 1-5: Etoposide 100mg/m\(^2\) IV over 1.5 hours<br>Days 1-3: Mitoxantrone 8mg/m\(^2\) IV over 1 hour<br>Days 1-5: Ifosfamide 1/5mg/m\(^2\) IV over 30 minutes<br>All patients received Mesna 120mg/m\(^2\) IV immediately prior to first dose of Ifosfamide and thereafter received a continuous infusion of Mesna 1,000mg/m\(^2\) daily for 6 days. |
| **Augmented Hyper CVAD**\(^36\) | Cycle A: (every 21-35 days)<br>Days 1-3: Cyclophosphamide 300mg/m\(^2\) IV every 12 hours\(^1\), with:
  - Days 1-3: Mesna 600mg/m\(^2\) IV continuous infusion over 24 hours daily
  - Day 4: Doxorubicin 50mg/m\(^2\) IV over 24 hours
  - Days 1.8.15: Vincristine 2mg IV
  - Days 1-4, 15-18: Dexamethasone 80mg IV or orally
  - Day 1: Pegaspargase 2,500 units/m\(^2\) IV.<br>Repeat every 21-35 days for 4 cycles alternating with Cycle B.<br>Cycle B (every 21-35 days):<br>Day 1: Methotrexate 1,000mg/m\(^2\) over 24 hours<br>Days 2,3: Cytarabine 3,000mg/m\(^2\) IV every 12 hours once serum Methotrexate levels at the end of infusion reached ≤20 umole/L. IV alkalinization used to promote excretion of Methotrexate in all course. Calcium Leucovorin 50mg IV given 12 hours after completion of Methotrexate, then 15mg given every 6 hours for 8 doses or until Methotrexate levels were <0.1 umol/L. Oral Acetazolamide given for urine pH <7.0. |

---

\(^1\) Adapted from the NCCN guidelines. \(^2\) mg/m\(^2\) = milligrams per square meter. \(^3\) i.e. 1,000mg/m\(^2\) IV. \(^4\) Refer to the original source for detailed dosing instructions.

CancerTherapyAdvisor.com
Acute Lymphoblastic Leukemia (ALL) Treatment Regimens

Relapsed/Refractory ALL\textsuperscript{1,a,p} (continued)

<table>
<thead>
<tr>
<th>PROTOCOL\textsuperscript{lb}</th>
<th>REGIMEN and DOSING</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ph (-) Disease\textsuperscript{16} (continued)</td>
<td>Cycle B (every 21-35 days): (continued)</td>
</tr>
<tr>
<td>Other Recommended Regimens (continued)</td>
<td>Day 4: Doxorubicin 50mg/m\textsuperscript{2} IV over 24 hours</td>
</tr>
<tr>
<td>B-ALL or T-ALL (continued)</td>
<td>Days 1,8,15: Vincristine 2mg IV</td>
</tr>
<tr>
<td>Augmented Hyper CVAD\textsuperscript{16} (continued)</td>
<td>Days 1-4,15-18: Dexamethasone 80mg IV or orally</td>
</tr>
<tr>
<td></td>
<td>Day 5: Pegasparagase 2,500 units/m\textsuperscript{2} IV.</td>
</tr>
<tr>
<td></td>
<td>Repeat every 21-35 days for 4 cycles alternating with Cycle A.</td>
</tr>
<tr>
<td></td>
<td>Filgrastim 10mcg/kg subcutaneous daily started 24 hours after chemotherapy completion and continued until the postnadir ANC reached ≥1 x 10\textsuperscript{9}/L.</td>
</tr>
<tr>
<td></td>
<td>CNS Prophylaxis (first 2 courses; 4 treatments total):</td>
</tr>
<tr>
<td></td>
<td>Day 2: Alternating Methotrexate 12mg intrathecal</td>
</tr>
<tr>
<td></td>
<td>Day 7: Cytarabine 100mg intrathecal.</td>
</tr>
<tr>
<td></td>
<td>Maintenance Therapy (following Induction and Intensified Consolidation) (up to 12 months):</td>
</tr>
<tr>
<td></td>
<td>Mercaptopurine 50mg orally three times daily</td>
</tr>
<tr>
<td></td>
<td>Methotrexate 20mg/m\textsuperscript{2} orally weekly</td>
</tr>
<tr>
<td></td>
<td>Vincristine 2mg IV every 28-35 days</td>
</tr>
<tr>
<td></td>
<td>Days 1-5 starting with Vincristine: Prednisone 200mg orally daily.</td>
</tr>
<tr>
<td>Clofarabine\textsuperscript{27}</td>
<td>Clofarabine 52mg/m\textsuperscript{2} IV over 2 hours daily for 5 consecutive days every 2-6 weeks for up to 12 cycles.</td>
</tr>
<tr>
<td>Clofarabine-containing regimens\textsuperscript{16}</td>
<td>• Clofarabine/Cyclophosphamide/Etoposide Regimen</td>
</tr>
<tr>
<td></td>
<td>Induction Therapy:</td>
</tr>
<tr>
<td></td>
<td>Clofarabine 40mg/m\textsuperscript{2} IV over 2 hours daily, followed by:</td>
</tr>
<tr>
<td></td>
<td>Etoposide 100mg/m\textsuperscript{2} IV over 2 hours daily, with:</td>
</tr>
<tr>
<td></td>
<td>Cyclophosphamide 440mg/m\textsuperscript{2} IV over 1 hour,\textsuperscript{1}</td>
</tr>
<tr>
<td></td>
<td>Administered for 5 consecutive days as 1 or 2 induction cycles.</td>
</tr>
<tr>
<td></td>
<td>Consolidation Therapy:</td>
</tr>
<tr>
<td></td>
<td>I-3 cycles (4 days of chemotherapy).</td>
</tr>
<tr>
<td></td>
<td>Maximum of 4 cycles (induction + consolidation).</td>
</tr>
<tr>
<td></td>
<td>A daily dose of Prednisone 0.5mg/kg was administered.</td>
</tr>
<tr>
<td>Cytarabine-containing regimens\textsuperscript{19}</td>
<td>Days 1-5: Cytarabine 3,000mg/m\textsuperscript{2} IV over 3 hours</td>
</tr>
<tr>
<td></td>
<td>Day 3: Idarubicin 40mg/m\textsuperscript{2} IV rapid infusion</td>
</tr>
<tr>
<td></td>
<td>Starting on Day 7: Filgrastim (G-CSF) 5mcg/kg subcutaneous twice daily (every 12 hours) and continued until ANC &gt;5,000/uL</td>
</tr>
<tr>
<td></td>
<td>Days 2,4: Methotrexate 6mg/m\textsuperscript{2} intrathecal.</td>
</tr>
<tr>
<td>FLAG-IDA\textsuperscript{16}</td>
<td>Days 1-5: Fludarabine 30mg/m\textsuperscript{2} IV over 30 minutes</td>
</tr>
<tr>
<td></td>
<td>Days 1-5: Cytarabine 2,000mg/m\textsuperscript{2} IV over 4 hours</td>
</tr>
<tr>
<td></td>
<td>Days 1-3: Idarubicin 10mg/m\textsuperscript{2} IV</td>
</tr>
<tr>
<td></td>
<td>G-CSF 5mcg/kg subcutaneous commenced 24 hours after completion of chemotherapy and continued until neutrophils &gt;1.5 x 10\textsuperscript{9}/L.</td>
</tr>
<tr>
<td>FLAM\textsuperscript{16}</td>
<td>Days 1,2,8,9: Fludarabine 15mg/m\textsuperscript{2} over 30 minutes every 12 hours, followed by:</td>
</tr>
<tr>
<td></td>
<td>Days 1,2,8,9: Cytarabine 100mg/m\textsuperscript{2} IV over 45 minutes</td>
</tr>
<tr>
<td></td>
<td>Days 3,10: Mitoxantrone 10mg/m\textsuperscript{2} over 20 minutes.</td>
</tr>
<tr>
<td>Inotuzumab Ozogamicin + Mini-HyperCVD (for B-ALL)\textsuperscript{16}</td>
<td>Cycle A (Cycles 1,3,5,7):</td>
</tr>
<tr>
<td></td>
<td>Days 1-3: Cyclophosphamide 150mg/m\textsuperscript{2} every 12 hours\textsuperscript{1}</td>
</tr>
<tr>
<td></td>
<td>Days 1-4,11-14: Dexamethasone 20mg</td>
</tr>
<tr>
<td></td>
<td>Days 1-8: Vincristine IV (2mg, flat dose)</td>
</tr>
<tr>
<td></td>
<td>Repeat cycle every 4 weeks for 4 cycles alternating with Cycle B.</td>
</tr>
<tr>
<td></td>
<td>Cycle B (Cycles 2,3,6,8):</td>
</tr>
<tr>
<td></td>
<td>Day 1: Methotrexate 250mg/m\textsuperscript{2}</td>
</tr>
<tr>
<td></td>
<td>Days 2,3: Cytarabine 580mg/m\textsuperscript{2} every 12 hours</td>
</tr>
<tr>
<td></td>
<td>Repeat cycle every 4 weeks for 4 cycles alternating with Cycle A.</td>
</tr>
<tr>
<td></td>
<td>Note:</td>
</tr>
<tr>
<td></td>
<td>Day 3 (Cycle 1): Inotuzumab Ozogamicin 1.3mg/m\textsuperscript{2}</td>
</tr>
<tr>
<td></td>
<td>Day 3 (Cycles 2-4): Inotuzumab Ozogamicin 1.0mg/m\textsuperscript{2}</td>
</tr>
<tr>
<td></td>
<td>Note: Rituiximab administered during first 4 cycles for patients with CD-20 positive disease.</td>
</tr>
</tbody>
</table>

continued
Relapsed/Refractory ALL1,a,p (continued)

PROTOCOLb REGIMEN and DOSING

**Ph (-) Disease**1,2 (continued)

<table>
<thead>
<tr>
<th>Other Recommended Regimens (continued)</th>
<th>B-ALL or T-ALL (continued)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MOpAD Regimen47</td>
<td>Days 1,15: Methotrexate 200mg/m² IV (reduced by 50% for creatinine clearance)</td>
</tr>
<tr>
<td></td>
<td>Days 1,8,15: Vincristine 1.4mg/m² IV (reduced dose to 1mg for pre-existing neuropathy and/or bilirubin 2-3mg/dL, hold for bilirubin &gt;3mg/dL maximum dose 2mg)</td>
</tr>
<tr>
<td></td>
<td>Days 2,16: Pegylated-L-Asparaginase 2,500 IU/m² IV (no capping of dose: decrease by 50% if direct bilirubin between 2 and 3mg/dL; hold for bilirubin &gt;3mg/dL, especially serious pancreatitis, thrombosis not controlled with anticoagulation, or disseminated intravascular coagulation)</td>
</tr>
<tr>
<td></td>
<td>Days 1-4, 15-18: Dexamethasone 40mg IV or orally</td>
</tr>
<tr>
<td></td>
<td>For patients with CD20-positive ALL:</td>
</tr>
<tr>
<td></td>
<td>Days 1,15: Rituximab 375mg/m² IV during the first 4 cycles.</td>
</tr>
</tbody>
</table>

**Vincristine Sulfate Liposome Injection2** Days 1,8,15,22: Vincristine Sulfate Liposome Injection 2.25mg/m² IV over 60 minutes. Repeat cycle every 4 weeks.

- a. While these guidelines pertain primarily to patients with leukemia, patients with lymphoblastic lymphoma (LL) (B- or T-cell) also benefit from ALL-like regimens versus traditional lymphoma therapy. Such patients should be treated in a center that has experience with LL.
- b. All regimens include CNS prophylaxis with systemic therapy (eg, methotrexate, cytarabine) and/or Intrathecal (IT) therapy (eg, IT methotrexate, IT cytarabine, triple IT therapy with methotrexate, cytarabine, corticosteroid).
- c. The ALL Panel considers AYA to be within the age range of 15-39 years. However, this age is not a firm reference point because some of the recommended regimens have not been comprehensively tested across all ages.
- d. Add tyrosine kinase inhibitors (TKIs) to maintenance regimens; optimal duration is unknown. Monthly vincristine/prednisone pulses (for 2-3 years). May include weekly methotrexate + daily 6-Mercaptopurine as tolerated. For patients receiving 6-Mercaptopurine, consider testing for TPMT gene polymorphisms, particularly in patients who develop severe neutropenia after starting 6-Mercaptopurine. Dose modifications for antimetabolites in maintenance should be consistent with the chosen treatment regimen. It may be necessary to reduce dose/eliminate antimitabolite in the setting of myelosuppression and/or hepatotoxicity.
- e. TKI options include (in alphabetical order): Bosutinib, Dasatinib, Imatinib, Nilotinib, or Ponatinib. Dasatinib and Imatinib are the preferred TKIs for induction therapy; Ponatinib is also preferred for the hyper-CVAD regimen. Not all TKIs have been directly studied within the context of each specific regimen and the panel notes that there are limited data for Bosutinib in Ph+ ALL. Use of a specific TKI should account for the anticipated TKI intolerance and disease-related features.
- f. Oral hydration is strongly encouraged with cyclophosphamide; poorly hydrated patients may need supplemental IV hydration. Patients should attain combined oral and IV hydration of 2000-3000 mL/day on day of chemotherapy.
- g. CNS2 patients with white blood cell (WBC) count in CSF <5 and having no blasts in the CSF; CNS2=patients with WBC count in CSF <5 and having blasts in the CSF, CNS3=patients with WBC count in CSF >5 and having blasts in the CSF.
- h. Maintenance regimen: Weekly methotrexate + daily 6-Mercaptopurine + monthly vincristine/prednisone pulses (duration based on regimen). For patients receiving 6-Mercaptopurine, consider testing for TPMT gene polymorphisms, particularly in patients who develop severe neutropenia after starting 6-MP. Dose adjustments for antimetabolites in maintenance should be consistent with the chosen treatment regimen. It may be necessary to reduce dose/eliminate antimitabolite in the setting of myelosuppression and/or hepatotoxicity.
- k. Careful assessment of comorbid conditions, performance status, and ability to attend to activities of daily living (ADLs) and instrumental ADLs (IADLs) is important when deciding treatment intensity.
- l. Dose reduction of pegylated asparaginase (1000 IU/m²), anthracycline (50%), and/or other myelosuppressive agents may be warranted.
- m. The categorization of regimens as low, moderate, or high intensity is based on 2 factors: 1) the presence of absence of myelosuppressive and/or hepatotoxicity.
- n. All regimens should include CNS prophylaxis, antimicrobial prophylaxis, and growth factor support.
- o. For appropriate fit individuals achieving remission, consideration of autologous or reduced-intensity allogeneic SCT may be appropriate.
- p. The safety of relapsed/refractory regimens in older adults (≥65 years) has not been comprehensively tested across all ages.
- q. Ponatinib is a treatment option for patients with a T315I mutation and/or for patients for whom no other TKI is indicated.
- r. Bosutinib has minimal activity against F317L mutation. Nilotinib may be preferred over bosutinib in patients with F317L mutation.
- s. Bosutinib is contraindicated in patients with disease characterized by BCR-ABL1 mutations T315I, V299L, G250E, F317L. Dasatinib is contraindicated in patients with disease characterized by BCR-ABL1 mutations T315I/L, F317L/LV/C/L; V299L. Nilotinib is contraindicated in patients with disease characterized by BCR-ABL1 mutations IT315, V253H, E255K/V; F359V/C/L, G250E.
- t. Bosutinib has minimal activity against F317L mutation. Dasatinib may be preferred over bosutinib in patients with F317L mutation.
- u. Ponatinib is a treatment option for patients with a T315I mutation and/or for patients for whom no other TKI is indicated.
- v. Ponatinib has activity against T315I mutations and is effective in treating patients with resistant or progressive disease on multiple TKIs. However, it is associated with a high frequency of serious vascular events (eg, strokes, heart attacks, tissue ischemia). The FDA indications are for the treatment of adult patients with T315I-positive, Philadelphia chromosome-positive acute lymphoblastic leukemia (Ph+ ALL) and for the treatment of patients with Ph+ ALL for whom no other TKI therapy is indicated.
- w. The regimens for relapsed/refractory, Philadelphia-negative ALL may be considered for Philadelphia-positive ALL refractory to TKIs.
- x. For patients in late relapse (>3 years from initial diagnosis), consider treatment with the same induction regimen.

References

Acute Lymphoblastic Leukemia (ALL) Treatment Regimens

References (continued)


Acute Lymphoblastic Leukemia (ALL) Treatment Regimens

References (continued)


