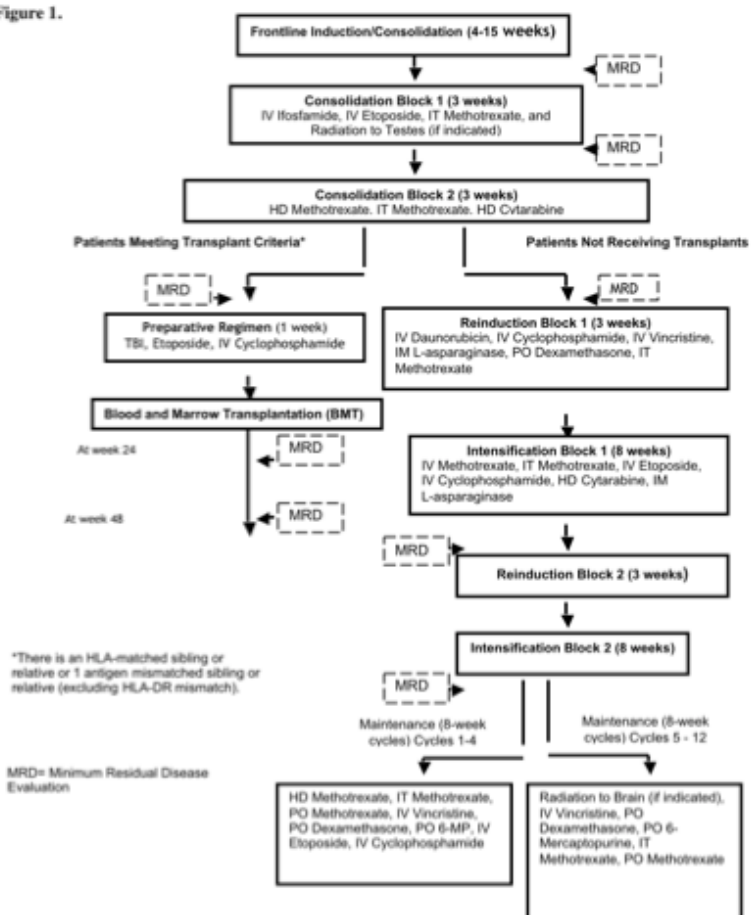
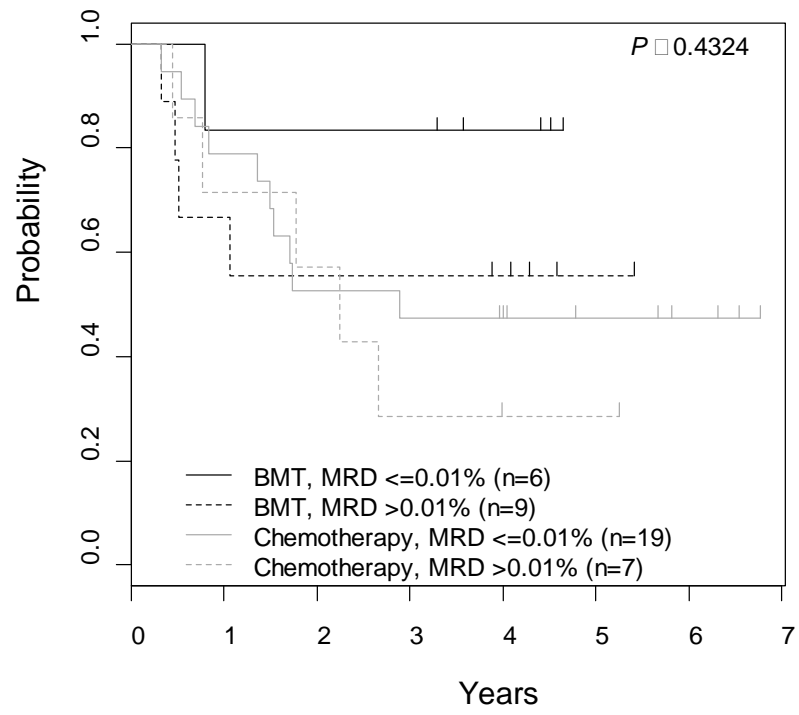


Figure 1.



Supplemental Figure 2



Supplemental Section for Supplemental Figure 1

Consolidation Block 1 (3 weeks) intrathecal [IT] methotrexate [MTX] on day 1; etoposide [VP-16] (100 mg/m²/day intravenously [IV]) and ifosfamide (3.4 g/m²/day, IV). Patients with CNS Leukemia at diagnosis received triple intrathecal therapy on days 8 and 15: MTX. Filgrastim [G-CSF] - 5 micrograms/kg per day subcutaneously [SC], was given on days 6-15. Consolidation Block 2 (3 weeks) consisted of age-adjusted intrathecal TIT on day 1; MTX (5 g/m² over 24 hours IV) on day 1; leucovorin (75 mg/m² at hour 36 post-MTX, 15 mg/m² IV or PO q6h x 6 doses on days 2 and 3; cytarabine (3 g/m²/dose IV q 12 h x 4 doses) on days 2 and 3; G-CSF - 5 micrograms/kg SC was given on days 4-13. Reinduction Block 1 (3 weeks): vincristine [VCR] (1.5 mg/m², IV) on days 1, 8, and 15; daunorubicin (45 mg/m²/day as a continuous infusion, IV) on days 1 and 2; cyclophosphamide (250 mg/m²/dose q12h x 4 doses, IV) on days 3 and 4; MESNA (125 mg/m²/dose q12h x 4 doses, IV) on days 3 and 4; L-asparaginase [L-ASP] (6000 IU/m², IM) on days 4, 6, 8, 10, 12,15, 17, 19, 21; G-CSF (5 micrograms/kg, SC) on days 5-14; MTX (age-adjusted, IT) on days 1 and 15; dexamethasone (6 mg/m²/day, PO) on days 1-21. Intensification Blocks 1 (9 weeks): MTX (5 g/m² over 24 hours, IV) on days 1 and 8 with leucovorin (as above) on days 2 and 3 and on days 9 and 10; MTX (age-adjusted, IT) on days 1 and 15; VP-16 (100 mg/ m² /day, IV) on days 15-19; cyclophosphamide (300 mg/m²/day, IV) on days 15-19; MESNA (150 mg/m²/day, IV) on days 15-19; G-CSF on days 20-29; cytarabine (3 g/m², IV) on days 36, 37, 43, and 44; L-ASP (6000 IU/m², IM) on days 37 and 44.. Reinduction Block 2 (3 weeks) and Intensification block 2 were then repeated sequentially. Maintenance (8-week cycles): Cycles 1-4 - MTX (5 g/m² over 24 hours, IV) on day 1; 75 mg/m² at hour 36, IV; 15 mg/m² IV or PO q6h x 6 doses) on days 2 and 3; MTX (age-adjusted, IT) on days 1, 29; VCR (1.5 mg/m², IV) on days 1, 29; deaxamethasone (6 mg/m²/day) on days 1-5; 29-33; 6-mercaptopurine (75 mg/m²/day) on days 8-28; MTX (20 mg/m²/wk, PO) on days 8,

15, 22; VP-16 (100 mg/m², IV) on days 36-40; cyclophosphamide (300 mg/m², IV) on days 36-40; G-CSF (5 micrograms/kg, SC) on days 41-50. Maintenance (8-week cycles) on Cycles 5-12 - MTX (age-adjusted, IT) on days 1, 29; VCR (1.5 mg/m², IV) on days 1, 29; dexamethasone (6 mg/m²/day) on days 1-5; 29-33; 6-mercaptopurine (75 mg/m²/day): days 8-28 and 36-56; MTX (20 mg/m²/wk, PO) on days 8, 15, 22, 36, 43, 50.

1 *In supplemental section:*

2 **Supplemental Figure 1: Treatment Schema for COG protocol AALL0031**

3 AALL0031 enrollment, patients had completed 4-6 weeks of 3-drug or 4-drug induction therapy
4 consistent with a frontline pediatric cooperative group (CCG or POG) regimen. The
5 chemotherapy of AALL0031 is described in the supplemental section for figure 1A.

6 Abbreviations: G-CSF=Granulocyte Colony Stimulating Factor; VP-16=Etoposide;
7 MTX=Methotrexate; SC=Subcutaneous; IT=Intrathecal; PO=Oral; Cons=Consolidation Block.
8 Reind=Reinduction Block, Inten=Intensification Block, Mtn=Maintenance.

9

10 **Supplemental Figure 2. Impact of MRD On outcomes in BMT and Chemotherapy groups**

11 Disease-free survival (DFS) curves by MRD, together with therapy given (Chemotherapy/BMT).