Acute Lymphoblastic Leukaemia: BFM 2000[1] Schema

Induction Protocol 1A: (course duration: 35 days); initial 7 days of prephase with prednisolone and intrathecal methotrexate is included here. Patients to receive: All risk groups			
Prednisolone	PO	60 mg/m^2	Day 1 to 28 then taper over 10 days and cease
Methotrexate*	IT	12 mg	Days 1, 12, 33
DAUNOrubicin	IV	30 mg/m^2	Days 8, 15, 22, 29
vinCRISTine	IV	1.5 mg/m^2 (cap at 2 mg)	Days 8, 15, 22, 29
L-asparaginase (Colaspase)	IV	5000 IU/m^2	Days 12, 15, 18, 21, 24, 27, 30, 33
***Patients with CNS involvement receive additional therapy on day 18 and 27 i.e. total of 5 intrathecal doses**			
NOTE: A bone marrow aspirate is required for MRD testing on day 15 and day 33('Timepoint 1') of Protocol IA			
Consolidation Protocol 1B: (course duration: 29 days); ideally day 1 of Protocol IB commences on day 36 from the start of Protocol 1A). Patients to receive: All risk groups.			
CYCLOPHOSPHamide	IV	1000 mg/m^2	Days 1 and 29
Mesna	IV	400 mg/m^2 at 0, 4 and 8 hours post each cyclophosphamide dose	Days 1 and 29
Mercaptopurine	PO	60 mg/m^2	Days 1 to 28
Cytarabine	SC	75 mg/m^2	Days 3 to 6, 10 to 13, 17 to 20 and 24 to 27
Intrathecal methotrexate	IT	12 mg	Days 10 and 24
Protocol M: (course duration: 56 days); ideally day 1 of Protocol M commences on day 79 after the start of Protocol 1A (2 weeks after the last dose of cyclophosphamide in Protocol 1B). Patients to receive: Standard Risk (SR) and Medium Risk (MR) groups.			
Mercaptopurine	PO	25 mg/m^2	Days 1 to 56
Methotrexate	IV	500 mg/m^2	Days 8, 22, 36, 50
Methotrexate	IV	4500 mg/m^2	Days 8, 22, 36, 50
Methotrexate	IT	12 mg	Days 8, 22, 36, 50
Calcium folinate*	IV	15 mg/m^2 every 6 hours	Days 9, 23, 37, 51
***Commence 36 hours after start of methotrexate infusion, continue until methotrexate level is less than 0.05 micromol/L**			
NOTE: A bone marrow aspirate is required for MRD testing on day 1 of Protocol M (i.e. day 79 from the start of Protocol IA) ('Timepoint 2'). If result identifies patient as high risk, then convert to HR blocks after first high dose methotrexate.			
Reinduction Protocol II: (course duration: 50 days), ideally day 1 of Protocol II commences 2 weeks after the end of Protocol M for SR and MR patients i.e. on day 70 after the start of Protocol M. For HR patients (and VHR not proceeding to transplantation) Protocol II begins 3 weeks after the end of the 6th HR block (i.e. Protocol II begins on day 57 after the start of HR block 6). Patients to receive: All risk groups.			
Dexamethasone	PO	10 mg/m^2	Days 1 to 21 then taper and cease
DOXOrubicin	IV	30 mg/m^2	Days 8, 15, 22, 29
vinCRISTine	IV	1.5 mg/m^2 (cap at 2 mg)	Days 8, 15, 22, 29
L-asparaginase (Colaspase)	IV	10,000 IU/m^2	Days 8, 11, 15, 18
Thioguanine	PO	60 mg/m^2	Days 36 to 49
CYCLOPHOSPHamide	IV	1000 mg/m^2	Day 36
Mesna	IV	400 mg/m^2 at 0, 4 and 8 hours post each cyclophosphamide dose	Day 36
Cytarabine	SC	75 mg/m^2	Days 38 to 41 and 45 to 48
Methotrexate*	IT	12 mg	Days 38 and 45
***Patients with CNS involvement receive additional intrathecal therapy on day 1 and 18 i.e. total of 4 intrathecal doses**			
NOTE: Cranial irradiation should be considered for patients with initial CNS involvement; as prophylaxis treatment for all HR and VHR patients not undergoing allogeneic stem cell transplant; and in T-ALL patients (other than low risk patients) especially those with initial WCC > 100 x 10^9/L. Cranial irradiation is usually administered on day 38 of Protocol II depending on patient's clinical condition.			
NOTE: A bone marrow aspirate is required for MRD testing prior to Protocol II.			

High Risk Blocks 1 to 3 are administered to High Risk (HR) and Very High Risk (VHR) groups only. Commence High Risk Block 1 after completion of Consolidation Protocol IB. Patients receive the sequence of HR1, HR2, HR3, HR1, HR2, HR3, except in patients who proceed to allogeneic stem cell transplantation after the first HR2 or HR3. Patients who are not transplanted complete all of the High Risk Blocks and then commence Reinduction Protocol II followed by cranial irradiation. **High Risk Block I**: (course duration 11 days) Patients to receive: High Risk (HR) and Very High Risk (VHR) groups. NOTE: A bone marrow aspirate is required for MRD testing prior to each High Risk block.			
Dexamethasone	PO	20 mg/m^2	Day 1 to 5
vinCRISTine	IV	1.5 mg/m^2 (cap at 2 mg)	Days 1 and 6
Methotrexate	IV	500 mg/m^2	Day 1
Methotrexate	IV	4500 mg/m^2	Day 1
Methotrexate	IT	12 mg	Day 1
Cytarabine	IT	30 mg	Day 1
Hydrocortisone	IT	50 mg	Day 1
Calcium folinate*	IV	15 mg/m^2 every 6 hours	Day 2
CYCLOPHOSPHamide	IV	200 mg/m^2 every 12 hours (total 5 doses)	Day 2 to 4
Mesna	IV	70 mg/m^2 at 0, 4 and 8 hours post each cyclophosphamide dose	Day 2 to 4
Cytarabine	IV	2000 mg/m^2 TWICE daily	Day 5
L-asparaginase (Colaspase)	IV	25000 IU/m^2	Days 6 and 11
Filgrastim	SC	5 microgram/kg	Day 7 until neutrophil recovery
***Commence 36 hours after start of methotrexate infusion, continue until methotrexate level is less than 0.05 micromol/L**			
High Risk Block 2: (course duration 11 days). Patients to receive: High Risk (HR) and Very High Risk (VHR) groups			
Dexamethasone	PO	20 mg/m^2	Days 1 to 5
vinCRISTine	IV	1.5 mg/m^2 (cap at 2 mg)	Days 1 and 6
Methotrexate	IV	500 mg/m^2	Day 1
Methotrexate	IV	4500 mg/m^2	Day 1
Methotrexate**	IT	12 mg	Day 1
Cytarabine	IT	30 mg	Day 1
Hydrocortisone	IT	50 mg	Day 1
Calcium folinate***	IV	15 mg/m^2 every 6 hours	Day 2
IFOSFamide	IV	800 mg/m^2 every 12 hours (total 5 doses)	Days 2 to 4
Mesna	IV	300 mg/m^2 at 0, 4 and 8 hours post each ifosfamide dose	Days 2 to 4
DAUNOrubicin	IV	30 mg/m^2	Day 5
L-asparaginase (Colaspase)	IV	25000 IU/m^2	Days 6 and 11
Filgrastim	SC	5 microgram/kg	Day 7 until neutrophil recovery
***Not TGA registered in Australia; available via Special Access Scheme (SAS)** ****Patients with CNS involvement receive an additional therapy on day 5 i.e. total of 2 intrathecal doses** *****Commence 36 hours after start of methotrexate infusion, continue until methotrexate level is less than 0.05 micromol/L**			
High Risk Block 3: (course duration 11 days). Patients to receive: High Risk (HR) and Very High Risk (VHR) groups			
Dexamethasone	PO	20 mg/m^2	Days 1 to 5
Cytarabine	IV	2000 mg/m^2 TWICE daily	Days 1 and 2
Etoposide	IV	100 mg/m^2 every 12 hours (total 5 doses)	Days 3 to 5
Methotrexate	IT	12 mg	Day 5
Cytarabine	IT	30 mg	Day 5
Hydrocortisone	IT	50 mg	Day 5
L-asparaginase (Colaspase)	IV	25000 IU/m^2	Days 6 and 11
Filgrastim	SC	5 microgram/kg	Day 7 until neutrophil recovery
Maintenance Phase: (course duration: 24 months calculated from the start of Protocol 1); commence two weeks after the end of Protocol II depending on bone marrow recovery. Patients to receive: All risk groups (not transplanted).			
Mercaptopurine	PO	50 mg/m^2 titrated according to WCC	ONCE Daily
Methotrexate	PO	20 mg/m^2 titrated according to WCC	ONCE WEEKLY
NOTE: A bone marrow aspirate is required for MRD testing 12 months after diagnosis, then again at the completion of Maintenance Phase.			

1. Conter, V., C. R. Bartram, M. G. Valsecchi, et al. 2010. "Molecular response to treatment redefines all prognostic factors in children and adolescents with B-cell precursor acute lymphoblastic leukemia: results in 3184 patients of the AIEOP-BFM ALL 2000 study." Blood 115(16):3206-3214.