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| **ALL IC 2002 BFM** | **standard-risk group** | **intermediate-risk group** | **high-risk group** |
| **induction therapy** | Protocol I  prednisone/prednisolone 60 mg/m2/d (days 1-28),  vincristine 1.5 mg/m2, max. 2 mg (days: 8, 15, 22, 29),  daunorubicin 30 mg/m2 (days 8, 15, 22, 29 – SRG ALL-T and IRG or days 8, 15 – SRG ALL-BCP)  E. coli, l-asparaginase 5,000 IU/m2/d (days 12, 15, 18, 21, 24, 27, 30, 33),  cyclophosphamide 1,000 mg/m2/d (days 36, 64),  6-mercaptopurine 60 mg/m2/d (days 36-63), cytarabine 75 mg/m2/d (days 38-41, 45-48, 52-55, 59-62),  intrathecal methotrexate, age-adjusted dosage, max. 12 mg/d (days 1, 12, 33, 45, 59), if CNS positive or traumatic LP additional doses on days 18, 27) | Protocol I  prednisone/prednisolone 60 mg/m2/d (days 1-28),  vincristine 1.5 mg/m2, max. 2 mg (days: 8, 15, 22, 29),  daunorubicin 30 mg/m2 (days 8, 15, 22, 29),  E. coli, l-asparaginase 5,000 IU/m2/d (days 12, 15, 18, 21, 24, 27, 30, 33),  cyclophosphamide 1,000 mg/m2/d (days 36, 64),  6-mercaptopurine 60 mg/m2/d (days 36-63), cytarabine 75 mg/m2/d (days 38-41, 45-48, 52-55, 59-62),  intrathecal methotrexate, age-adjusted dosage, max. 12 mg/d (days 1, 12, 33, 45, 59), if CNS positive or traumatic LP additional doses on days 18, 27) | Protocol I  prednisone/prednisolone 60 mg/m2/d (days 1-28),  vincristine 1.5 mg/m2, max. 2 mg (days 8, 15, 22, 29),  daunorubicin 30 mg/m2 (days 8, 15, 22, 29),  E. coli, l-asparaginase 5,000 IU/m2/d (days 12, 15, 18, 21, 24, 27, 30, 33),  cyclophosphamide 1,000 mg/m2/d (days 36, 64),  6-mercaptopurine 60 mg/m2/d (days 36-63), cytarabine 75 mg/m2/d (days 38-41, 45-48, 52-55, 59-62),  intrathecal methotrexate, age-adjusted dosage, max. 12 mg/d (days 1, 12, 33, 45, 59), if CNS positive or traumatic LP additional doses on days 18, 27) |
| **consolidation therapy** | Protocol M  6-mercaptopurine 25 mg/m2/d (days 1-56),  methotrexate 2,000 mg/m2 (days 8, 22, 36, 50) – SRG ALL-BCP or 5,000 mg/m2 (days 8, 22, 36, 50) – SRG ALL-T  intrathecal methotrexate, age-adjusted dosage, max. 12 mg/d (days 8, 22, 36, 50) | Protocol M  6-mercaptopurine 25 mg/m2/d (days 1-56),  methotrexate 2,000 mg/m2 (days 8, 22, 36, 50) – IRG ALL-BCP or 5,000 mg/m2 (days 8, 22, 36, 50) – IRG ALL-T  intrathecal methotrexate, age-adjusted dosage, max. 12 mg/d (days 8, 22, 36, 50) | Protocol HR1, HR2, HR3  dexamethasone 20 mg/m2/d (days 1-5 prot. HR1, HR2, HR3)  vincristine 1,5 mg/m2/d, max. 2 mg (days 1, 6 prot. HR1),  methotrexate 5,000 (day 1 prot. HR1, HR2),  cyclophosphamide 200 mg/m2/d (5 doses on days 2, 3, 4 prot. HR1),  cytarabine 2,000 mg/m2/d (2 doses on day 5 prot. HR1, 4 doses on days 1-2 prot. HR3),  l-asparaginase 25,000 IU/m2/d (days 6, 11 prot. HR1, HR2, HR3),  vindesine 3 mg/m2/d, max. 5 mg (days 1, 6 prot. HR2),  ifosfamide 800 mg/m2/d (5 doses on days 2, 3, 4 prot. HR2),  daunorubicin 30 mg/m2/d (day 5 prot. HR2),  etoposide 100 mg/m2/d (5 doses on days 3, 4, 5 prot. HR3),  intrathecal methotrexate+cytarabine+prednizolone, age-adjusted dosage, max. 12+30+10 mg/d (day 1 prot. HR1, HR2, HR3) |
| **reinduction therapy** | Protocol II  dexamethasone 10 mg/m2/d (days 1-21),  vincristine 1.5 mg/m2/d, max. 2 mg (days 8, 15, 22, 29),  doxorubicin 30 g/m2/d (days 8, 15, 22, 29),  E. coli L-asparaginase 10,000 IU/m2/d (days 8, 11, 15, 18),  cyclophosphamide 1,000 mg/m2/d (day 36),  6-thioguanine 60 mg/m2/d (days 36-49),  cytarabine 75 mg/m2/d (days 38-41, 45-48),  intrathecal methotrexate, age-adjusted dosage, max. 12 mg/d (days 38, 45), if CNS positive or traumatic LP additional doses on days 1, 18) | Protocol II  dexamethasone 10 mg/m2/d (days 1-21),  vincristine 1.5 mg/m2/d, max. 2 mg (days 8, 15, 22, 29),  doxorubicin 30 g/m2/d (days 8, 15, 22, 29),  E. coli L-asparaginase 10,000 IU/m2/d (days 8, 11, 15, 18),  cyclophosphamide 1,000 mg/m2/d (day 36),  6-thioguanine 60 mg/m2/d (days 36-49),  cytarabine 75 mg/m2/d (days 38-41, 45-48),  intrathecal methotrexate, age-adjusted dosage, max. 12 mg/d (days 38, 45), if CNS positive or traumatic LP additional doses on days 1, 18) | Protocol II  dexamethasone 10 mg/m2/d (days 1-21),  vincristine 1.5 mg/m2/d, max. 2 mg (days 8, 15, 22, 29),  doxorubicin 30 g/m2/d (days 8, 15, 22, 29),  E. coli L-asparaginase 10,000 IU/m2/d (days 8, 11, 15, 18),  cyclophosphamide 1,000 mg/m2/d (day 36),  6-thioguanine 60 mg/m2/d (days 36-49),  cytarabine 75 mg/m2/d (days 38-41, 45-48),  intrathecal methotrexate, age-adjusted dosage, max. 12 mg/d (days 38, 45), if CNS positive or traumatic LP additional doses on days 1, 18)  Interim Maintenance - 4 weeks  methotrexate 20 mg/m2 (once per week),  6-mercaptopurine 50 mg/m2/d (once per day),  Protocol II’ as protocol II |
| maintenance therapy | methotrexate 20 mg/m2 (once per week),  6-mercaptopurine 50 mg/m2/d (once per day),  intrathecal methotrexate, age-adjusted dosage, max. 12 mg/d (every 4 weeks, 2-4 doses in selected groups of patients); no MTX i.th. if CRT indicated | methotrexate 20 mg/m2 (once per week),  6-mercaptopurine 50 mg/m2/d (once per day),  intrathecal methotrexate, age-adjusted dosage, max. 12 mg/d (every 4 weeks, 2-4 doses in selected groups of patients) ; no MTX i.th. if CRT indicated | methotrexate 20 mg/m2 (once per week),  6-mercaptopurine 50 mg/m2/d (once per day),  therapeutic or prophylactic CRT |
| Cumulative asparaginase dose | 80 000 u/m2 | 80 000 u/m2 | 270 000 u/m2 |

Supplementary table 1. Treatment for standard-, intermediate- and high-risk groups according to ALL IC BFM 2002 protocol.

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| **ALL IC 2009 BFM** | **standard-risk group** | **intermediate-risk group** | **high-risk group** |
| **induction therapy** | Protocol I  prednisone/prednisolone 60 mg/m2/d (days 1-28),  vincristine 1.5 mg/m2, max. 2 mg (days 8, 15, 22, 29),  daunorubicin 30 mg/m2 (days 8, 15, 22, 29 – SRG ALL-T or days 8, 15 only – SRG ALL-BCP)  E. coli, l-asparaginase 5,000 IU/m2/d (days 12, 15, 18, 21, 24, 27,  30, 33), cyclophosphamide 1,000 mg/m2/d (days 36, 64),  6-mercaptopurine 60 mg/m2/d (days 36-63),  cytarabine 75 mg/m2/d (days 38-41, 45-48, 52-55, 59-62),  intrathecal methotrexate, age-adjusted dosage, max. 12 mg/d (days 1, 12, 33, 45, 59, if CNS positive or traumatic LP additional doses on days 18, 27) | Protocol I  prednisone/prednisolone 60 mg/m2/d (days 1-28),  vincristine 1.5 mg/m2, max. 2 mg (days 8, 15, 22, 29),  daunorubicin 30 mg/m2 (days 8, 15, 22, 29),  E. coli, l-asparaginase 5,000 IU/m2/d (days 12, 15, 18, 21, 24, 27,  30, 33), cyclophosphamide 1,000 mg/m2/d (days 36, 64),  6-mercaptopurine 60 mg/m2/d (days 36-63),  cytarabine 75 mg/m2/d (days 38-41, 45-48, 52-55, 59-62),  intrathecal methotrexate, age-adjusted dosage, max. 12 mg/d (days 1, 12, 33, 45, 59, if CNS positive or traumatic LP additional doses on days 18, 27) | Protocol I  prednisone/prednisolone 60 mg/m2/d (days 1-28),  vincristine 1.5 mg/m2, max. 2 mg (days 8, 15, 22, 29, 50, 57, 78, 85),  daunorubicin 30 mg/m2 (days 8, 15, 22, 29),  E. coli, l-asparaginase 5,000 IU/m2/d (days 12, 15, 18, 21, 24, 27,  30, 33, 50, 52, 54, 57, 59, 61, 78, 80, 82, 85, 87, 89),  cyclophosphamide 1,000 mg/m2/d (days 36, 64),  6-mercaptopurine 60 mg/m2/d (days 36-49, 64-77),  cytarabine 75 mg/m2/d (days 37-40, 43-46, 65-68, 72-75),  intrathecal methotrexate, age-adjusted dosage, max. 12 mg/d (days 1, 12, 33, 37, 44, 51, 58, if CNS positive or traumatic LP additional doses on days 18, 27) |
| **consolidation therapy** | Protocol M  6-mercaptopurine 25 mg/m2/d (days 1-56),  methotrexate 2,000 mg/m2 (days 8, 22, 36, 50) – SRG ALL-BCP or 5,000 mg/m2 (days 8, 22, 36, 50) – SRG ALL-T  intrathecal methotrexate, age-adjusted dosage, max. 12 mg/d (days 8, 22, 36, 50) | Protocol M  6-mercaptopurine 25 mg/m2/d (days 1-56),  methotrexate 5,000 mg/m2/d (days 8, 22, 36, 50),  intrathecal methotrexate, age-adjusted dosage, max. 12 mg/d (days 8, 22, 36, 50) | Protocol HR1, HR2, HR3  dexamethasone 20 mg/m2/d (days 1-5 prot. HR1, HR2, HR3)  vincristine 1,5 mg/m2/d, max. 2 mg (days 1, 6 prot. HR1),  methotrexate 5,000 mg/m2/d (day 1 prot. HR1, HR2),  cyclophosphamide 200 mg/m2/d (5 doses on days 2, 3, 4 prot. HR1),  cytarabine 2,000 mg/m2/d (2 doses on day 5 prot. HR1, 4 doses on days 1 and 2 prot. HR3),  l-asparaginase 25,000 IU/m2/d (day 6 prot. HR1, HR2, HR3),  vindesine 3 mg/m2/d, max. 5 mg (days 1, 6 prot. HR2),  ifosfamide 800 mg/m2/d (5 doses on days 2, 3, 4 prot. HR2),  daunorubicin 30 mg/m2/d (day 5 prot. HR2),  etoposide 100 mg/m2/d (5 doses on days 3, 4, 5 prot. HR3),  intrathecal methotrexate+cytarabine+prednizolone, age-adjusted dosage, max. 12+30+10 mg/d (day 1 prot. HR1; day 1 and 5 prot. HR2, day 5 prot. HR3)  HR1’, HR2’, HR3’ as in HR |
| **reinduction therapy** | Protocol II  dexamethasone 10 mg/m2/d (days 1-21), vincristine 1.5 mg/m2/d, max. 2 mg (days 8, 15, 22, 29),  doxorubicin 30 g/m2/d (days 8, 15, 22, 29),  E. coli L-asparaginase 10,000 IU/m2/d (days 8, 11, 15, 18),  cyclophosphamide 1,000 mg/m2/d (day 36),  6-thioguanine 60 mg/m2/d (days 36-49), cytarabine 75 mg/m2/d (days 38-41, 45-48),  intrathecal methotrexate, age-adjusted dosage, max. 12 mg/d (days 38, 45), if CNS positive or traumatic LP additional doses on days 1, 18) | Protocol II  dexamethasone 10 mg/m2/d (days 1-21), vincristine 1.5 mg/m2/d, max. 2 mg (days 8, 15, 22, 29),  doxorubicin 30 g/m2/d (days 8, 15, 22, 29),  E. coli L-asparaginase 10,000 IU/m2/d (days 8, 11, 15, 18),  cyclophosphamide 1,000 mg/m2/d (day 36),  6-thioguanine 60 mg/m2/d (days 36-49), cytarabine 75 mg/m2/d (days 38-41, 45-48),  intrathecal methotrexate, age-adjusted dosage, max. 12 mg/d (days 38, 45), if CNS positive or traumatic LP additional doses on days 1, 18) | Protocol II  dexamethasone 10 mg/m2/d (days 1-21), vincristine 1.5 mg/m2/d, max. 2 mg (days 8, 15, 22, 29),  doxorubicin 30 mg/m2/d (days 8, 15, 22, 29),  E. coli L-asparaginase 10,000 IU/m2/d (days 8, 11, 15, 18),  cyclophosphamide 1,000 mg/m2/d (day 36),  6-thioguanine 60 mg/m2/d (days 36-49), cytarabine 75 mg/m2/d (days 38-41, 45-48),  intrathecal methotrexate, age-adjusted dosage, max. 12 mg/d (days 38, 45), if CNS positive or traumatic LP additional doses on days 1, 18 |
| maintenance therapy | methotrexate 20 mg/m2 (once per week),  6-mercaptopurine 50 mg/m2/d (once per day),  intrathecal methotrexate, age-adjusted dosage, max. 12 mg/d (every 4 weeks, 2-4 doses in selected groups of patients); no MTX i.th. if CRT indicated | methotrexate 20 mg/m2 (once per week),  6-mercaptopurine 50 mg/m2/d (once per day),  intrathecal methotrexate, age-adjusted dosage, max. 12 mg/d (every 4 weeks, 2-4 doses in selected groups of patients) ; no MTX i.th. if CRT indicated | methotrexate 20 mg/m2 (once per week),  6-mercaptopurine 50 mg/m2/d (once per day),  therapeutic or prophylactic CRT |
| Cumulative asparaginase dose | 80 000 u/m2 | 80 000 u/m2 | 290 000 u/m2 |

Supplementary table 2. Treatment for standard-, intermediate- and high-risk groups according to ALL IC BFM 2009 protocol.