

Chemotherapy agents used during treatment:

Induction:

- dexamethasone 6mg/m²/day orally for 28 days (maximum single dose 10mg/day)
- vincristine 1.5mg/m² IV weekly for 2 weeks, starting on day 2 (maximum single dose 2mg)
- daunorubicin 25mg/m² IV on days 2, 9, 16, 23
- pegaspargase 1000iu/m² IM day 4 and 18
- methotrexate 12mg intrathecal on days 1, 8, 29
- mercaptopurine 60mg/m²/day orally from day 29 to day 28 of consolidation.

Standard BFM consolidation:

- cyclophosphamide 1000mg/m² IV days 1 and 15
- cytarabine 75mg/m²/day IV or subcutaneous. 4 consecutive days in weeks 6,7,8,9
- mercaptopurine 60mg/m²/day orally until day 28 of consolidation
- methotrexate 12mg intrathecal days 1, 8, 15

Augmented BFM consolidation:

- cyclophosphamide 1000mg/m² IV days 1, 29
- cytarabine 75mg/m² IV or subcutaneous. 4 consecutive days in weeks 6,7,10 and 11
- mercaptopurine 60mg/m²/day for 21 days starting week 5 of induction, and again for 14 days on days 29-42
- vincristine 1.5mg/m² IV days 16, 23, 44, 51 (maximum single dose 2mg)
- pegaspargase 1000 units/m² intramuscular days 16, 44
- methotrexate 12mg intrathecal days 1, 8, 22

Standard interim maintenance:

- dexamethasone 6mg/m²/day orally days 1-5 and days 29-33
- vincristine 1.5mg/m² IV day 1, 29 (maximum single dose 2mg)
- mercaptopurine 75mg/m²/day orally days 1056
- methotrexate 20mg/m² orally once/week on week 11, 12, 14, 15, 16, 18, 19
- methotrexate 12mg intrathecal days 15, 43

Protocol M

- mercaptopurine 25mg/m²/day orally days 1-56
- methotrexate 5g/m² IV days 8, 22, 36, 50
- folinic acid 15mg/m² IV 42,48 and 54 hours after start of methotrexate infusion
- methotrexate 12mg intrathecal days 8, 22, 36, 50

Capizzi interim maintenance:

- vincristine 1.5mg/m² IV days 2, 12, 22, 32, 42 (maximum single dose 2mg)
- methotrexate 100mg/m² IV day 2. Escalating subsequent doses as tolerated on days 12, 22, 32, 42
- pegaspargase 1000 units/m² IM days 3, 23
- methotrexate 12mg intrathecal day 1, 31

Protocol M-A:

- mercaptopurine 25mg/m²/day orally days 1-49
- methotrexate 5g/m² IV days 1, 15, 29, 43

- folinic acid 15mg/m² IV 42,48 and 54 hours after start of methotrexate infusion
- methotrexate 12mg intrathecal days 1, 15, 29, 43
- pegaspargase 1000 units/m² IM days 2, 23

Delayed intensification:

- dexamethasone 10mg/m²/day orally for 7 days week 20 and 22
- vincristine 1.5mg/m² IV days 2,9,16 (maximum single dose 2mg)
- doxorubicin 25mg/m² IV days 2,9,16
- pegaspargase 1000iu/m² IM day 4
- methotrexate 12mg intrathecal day 1
- cyclophosphamide 1000mg/m² IV day 29
- mercaptopurine 60mg/m²/day orally day 29-42
- cytarabine 75mg/m²/day IV or subcutaneous. 4 consecutive days weeks 24,25

If delayed intensification is in regimen C the dexamethasone is given days 2-5 and 16-22, cytarabine is given in weeks 28 and 29, and vincristine given on days 2, 9, 16, 43 and 50. Intrathecal methotrexate is also given on days 29 and 36, and pegaspargase is also given on day 43.

Maintenance:

- mercaptopurine 75mg/m²/day orally throughout maintenance
- methotrexate 20mg/m² orally days 1, 8, 22, 29, 36, 43, 50, 57, 64, 71, 78

If a patient has been randomised to pulses during maintenance they also receive:

- dexamethasone 6mg/m²/day orally days 1-5, 29-33, 57-61
- vincristine 1.5mg/m² IV days 1, 29 and 57 (maximum single dose 2mg)

If patient was randomised to standard or Capizzi interim maintenance they will also receive 12mg of intrathecal methotrexate on day 15 of each cycle, as will T-ALL patients presenting with a white cell count of >100x10⁹/L.

All patients are also to receive co-trimoxazole prophylaxis for PCP throughout treatment (except during protocol M and M-A) with dose depending on body surface area.