Appendix

Clinical risk classification

Participants were categorized into three groups, namely: (I) standard risk (SR, n=14); intermediate risk (IR, n=13); and high risk (HR, n=3), based on age at first diagnosis, total number of peripheral white blood cells (WBC), response to 7-day prednisone treatment, the translocation of t(4;11) and t(9;22), fusion gene detection (MLL/AF4 and BCR/ABL), and bone marrow remission status on days 15 and 33. Patients with (i) SR met the following criteria: good response to 7-day prednisone treatment; peripheral blood immature cells on day 8 <1.0 × 10^9/L; age ≥1 year and <7 years old; WBC <20 × 10^9/L; induction chemotherapy bone marrow M1 (primitive lymphocytes + naive lymphocytes) <5% or M2 (primitive lymphocytes + naive lymphocytes) between 5% and 25% on day 15; and bone marrow M1 on day 33 of induction chemotherapy. Patients with (ii) IR met the following criteria: a good prednisone response; peripheral blood immature cells <1.0 × 10^9/L on day 8; age <1 year or ≥7 years; WBC ≥20 × 10^9/L; and induction chemotherapy patients with bone marrow M3 (primitive lymphocytes + naive lymphocytes) > 25% on day 15 and M1 on day 33. Patients with (iii) HR met at least one of the following criteria: not SR or receiving induction chemotherapy; bone marrow M3 on day 15; a poor prednisone response; peripheral blood naive cells ≥1.0 × 10^9/L on day 8; bone marrow M2 or M3 on day 33; or a t(4;11) (MLL/AF4) or t(9:22) (BCR/ABL) abnormality.

Clinical treatment

Children with ALL were treated according to the German BFM2002 protocol for acute lymphoblastic leukemia (ALL) based on their risk group (SR, IR or HR). The induction therapy protocol was as follows: day 1 to day 7 prednisone test – prednisone 60 mg/(m^2.d), 3 times orally; day 8 to day 28 dexamethasone 6 mg/(m^2.d) taken orally 3 times per day. After day 29, the dose of dexamethasone was gradually reduced; it was halved every 3 days, to be taken in the morning, with the dose reduction to be completed on day 9. Vincristine (VCR): 1.5 mg/(m^2.d) (≯2 mg/time), intravenous bolus on day 8, day 15, day 22, and day 29. DNR 30 mg/(m^2.d), intravenous bolus maintenance (PI) > 1 h; for SR-ALL, DNR × 2, on day 8 and day 15; for IR-ALL, DNR × 4, on day 9, day 15, day 22, and day 29. L-ASP: 5000 U/(m^2.d), PI >1 h, on day 36 and day 64. 6-MP: 60 mg/(m^2.d), orally, on day 36 to day 63 (for 28 days total), taken at night on an empty stomach. Ara-C: 75 mg/(m^2.d), intravenous bolus, administered in 4 parts, for 4 days each time, on day 38 to day 41, on day 45 to day 48, on day 52 to day 55, and on day 59 to day 62. Consolidation treatment: 6-MP: 25 mg/(m^2.d), orally, day 1 to day 56, taken at night on an empty stomach. Medium dose methotrexate (MTX): 200 mg/(m^2.d), PI 24 h, once every 14 days, 4 times in total (day 8, day 22, day 36, and day 50); 1/10 of the total (200 mg/m^2)) to be administered for the loading dose. Intravenous drip over 30 min, 9/10 of the total (1800 mg/m^2) PI 23.5 h. Reinduction therapy: dexamethasone – 8 mg/(m^2.d), orally, 3 times, on day 1 to day 21. From day 22 onwards, the dose was gradually reduced to stop the drug; it was halved every 3 days, to be taken in the morning. VCR: 1.5 mg/(m^2.d), intravenous bolus (≯2 mg/time), on day 8, day 15, day 22, and day 29. DOX: 30 mg/(m^2.d), intravenous bolus, over 1 h, on day 8, day 15, day 22, and day 29. L-ASP: 10,000 U/(m^2.d), PI>1 h, on day 8, day 11, day 15, and day 18. CTX: 1 g/(m^2.d), PI>1 h, on day 36. Ara-C: 75 mg/(m^2.d), intravenous bolus, with 2 courses of treatment, each course for 4 days, on day 38 to day 41 and on day 45 to day 48. 6-MP: 60 mg/(m^2.d), on day 36 to day 49 (14 days), taken orally at night, in a fasted state, with milk. Consolidation treatment was mainly given through intravenous or intrathecal injection of various doses of methotrexate (IV-MTX and IT-MTX, respectively). After bone marrow aspiration was carried out, no obvious abnormality was found by routine MRI examination.

https://dx.doi.org/10.21037/qims-21-748