4. TREATMENT GUIDANCE FOR STANDARD AND HIGH RISK iMB:

Patients with standard and high risk infant medulloblastoma will receive **5 cycles of intensive induction chemotherapy** in accordance with Head Start II Regimen A2 (Chi JCO 2004). Chemotherapy should aim to start within 28 days after surgery. The cycles should be given every 21-28 days.

The induction chemotherapy doses (esp. cyclophosphamide and methotrexate) are based on the original Head Start Regimen A2 regimen and not the modified Head Start approach which was adopted in the UK. The toxicity of the Regimen A2 did not appear more severe than the modified Head Start 3 Regimen D (personal communication Prof J Finlay).

Stem cell collection should be undertaken as per local policy. There is no particular guidance for stem cell collection off the back of induction chemotherapy. Cold harvest with GCSF prior to commencing induction chemotherapy or after 5th cycle of induction chemotherapy is acceptable. Child considered ineligible for stem cell collection should be discussed with the Embryonal Tumour Group.

Second look surgery should be considered if clinical remission has not been achieved after induction chemotherapy and the tumour is amenable to further surgery.

Consolidation with high dose chemotherapy (Carboplatin, Etoposide and Thiotepa) and autologous stem cell rescue will take place in patients who have not progressed during the induction phase of therapy.

4.1. Induction chemotherapy for High and Standard Risk Medulloblastoma

The cycles should be given every 21-28 days.

Drug	Dose	Route	1	2	3	4	5	6	7	8	15
Vincristine *	0.05 mg/kg (max 2mg)	IV	●							●	●
Cisplatin	3.5 mg/kg	IVI 6hr	●								
Cyclophosphamide	65 mg/kg	IVI 1hr		●	●						
Etoposide	4 mg/kg	IVI 2hr		●	●						
Methotrexate	400mg/kg (max 20g)	IVI 4hr				●					

***Cycles 1-3: vincristine in cycles 1,2 and 3 (total of 9 doses of vincristine). Cycle 4 and 5: no vincristine**

Expected Methotrexate concentrations (NB: this is different to the Low Risk iMB schedule)

Please note: these methotrexate concentration levels are not the usual CCLG levels. The lower levels of methotrexate (MTX) concentration are taken from the Head Start programme with the goal of reducing methotrexate-induced white matter changes.

If the serum MTX concentration is lower than target levels, as expected, folinic acid rescue should continue as below until MTX-serum concentration is ≤0.1µmol/l.

Hour	MTX-serum concentration in µmol/l	Folinic acid-rescue
24	< 10	15mg/m^2 IV q6 hourly
48	< 1	15mg/m^2 IV q6 hourly
72	≤ 0.1	Stop rescue and hydration

If the serum MTX concentration is not below the target levels as expected, folinic acid rescue should follow guidance as per Appendix D.

Start Granulocyte colony stimulating factor (GCSF) 5 micrograms/kg/day IV/SC from day 5 until count recovery.