Online Resource 1 Treatment and radiotherapy strategies of the HIT2000 trial

Surgery	Re-surgery	Radiotherapy	8 x Maintenance
HIT 2000-AB4		*CMB, DMB/MBEN:* Brain/spinal canal: 23.4 Gy Posterior fossa and primary tumor region 30.6 Gy *LCAMB:* Brain/spinal canal: 35.2 Gy Posterior fossa and primary tumor region 19.8 Gy	Cisplatin (70mg/m²) Lomustine (75mg/m²) VCR (1.5mg/m²)

Surgery	Re-surgery	Radiotherapy	8 x Maintenance
MET-HIT 2000-AB4-M1		Brain/spinal canal: 35.2 Gy Metastases: 14.4 Gy	Cisplatin (70mg/m²) Lomustine (75mg/m²) VCR (1.5mg/m²)

Surgery	Re-surgery	3 x SKK (CMB, LCAMB) 5 x SKK (DMB/MBEN)	Radiotherapy
HIT 2000-BIS4		*E IIS:* Cyclophosphamide (2.4 g/m²) Vincristine (1.5 mg/m²) i. vtr. Methotrexate (2mg) *E IIS (1):* Methotrexate i. v. (5g/m²) Vincristine(1.5 mg/m²) i. vtr. Methotrexate (2mg) *E IIS (2):* Methotrexate i. v. (5g/m²) Vincristine (1.5 mg/m²) i. vtr. Methotrexate (2mg) *E IVS:* Carboplatin (200 mg/m²) Etoposide (150 mg/m²) i. vtr. Methotrexate (2mg)	Extended tumor region: 54 Gy Only CMB, LCAMB and DMB/MBEN in case of detectable residual tumor after the 3rd SKK cycle.

Surgery	2 x SKK	Re-surgery	Radiotherapy		4 x Maintenance
MET-HIT 2000-AB4-M2-M4	*E IIS:* Cyclophosphamide (2.4 g/m²) Vincristine (1.5 mg/m²) i. vtr. Methotrexate (2mg) *E IIS (1):* Methotrexate i. v. (5g/m²) Vincristine(1.5 mg/m²) i. vtr. Methotrexate (2mg) *E IIS (2):* Methotrexate i. v. (5g/m²) Vincristine (1.5 mg/m²) i. vtr. Methotrexate (2mg) *E IVS:* Carboplatin (200 mg/m²) Etoposide (150 mg/m²) i. vtr. Methotrexate (2mg)		Brain/spinal canal Posterior fossa Primary tumor region Metastases (spinal) Metastases (supratent.)	40 Gy 20 Gy 8 Gy 10 Gy 28 Gy	Cisplatin (70mg/m²) Lomustine (75mg/m²) VCR (1.5mg/m²)

Surgery	Re-surgery	3 x Modified induction chemotherapy	2 x High-dose chemotherapy	Autologous stem cell therapy
MET-HIT 2000-BIS4		Cisplatin 3.5 mg/kg day 1 VP-16 4 mg/kg/d day 2,3 Cyclophosphamide 65 mg/kg/d day 2,3 Methotrexate 5 g/m² day 15 VCR 0.05 mg/kg (max 2mg) day 1,15 MTX i.v. 2 mg	Thiotepa 150 mg/m²/d 4 days Carboplatin 500mg/m²/d 96h VP-16 250 mg/m²/d 96h MTX i.v. 2 mg	

Surgery	Re-surgery	Radiotherapy	5x each alternating element EIIS and EIVS of SKK chemotherapy (EP III only)
E-HIT2000-AB4		Extended tumor region: 68 Gy	*E IIS (2):* Methotrexate i. v. (5g/m²) Vincristine (1.5 mg/m²) i. vtr. Methotrexate (2mg) *E IVS:* Carboplatin (200 mg/m²) Etoposide (150 mg/m²) i. vtr. Methotrexate (2mg)

Surgery	Re-surgery	5 x modified SKK	Radiotherapy
E-HIT2000- BIS4		*E IIS:* Cyclophosphamide (2.4 g/m²) Vincristine (1.5 mg/m²) *E IIS (1):* Methotrexate i. v. (5g/m²) Vincristine(1.5 mg/m²) *E IIS (2):* Methotrexate i. v. (5g/m²) Vincristine (1.5 mg/m²) *E IVS:* Carboplatin (200 mg/m²) Etoposide (150 mg/m²)	Extended tumor region: 55 Gy

Irradiation fields in different histological subtypes according to the HIT2000 study.

CMB, DMB/MBEN				**LCAMB**			
≥ 4 years		≥ 18 months and < 4 years		≥ 4 years		≥ 18 months and < 4 years	
M0		**M0**		**M0**		**M0**	
Brain/spinal canal	23.4 Gy	Extended tumor region**	54 Gy	Brain/spinal canal	35.2 Gy	Extended tumor region**	54 Gy
Posterior fossa* and primary tumor region	30.6 Gy			Posterior fossa* and primary tumor region	19.8 Gy		
M1		**M1-4**		**M1**		**M1-4**	
Brain/spinal canal	35.2 Gy	Brain/spinal canal	24 Gy	Brain/spinal canal	35.2 Gy	Brain/spinal canal	24 Gy
Metastases	14.4 Gy	Posterior fossa*	30.6 Gy	Metastases	14.4 Gy	Posterior fossa*	30.6 Gy
		Metastases	25.2 Gy			Metastases	25.2 Gy
M2-M4				**M2-M4**			
Brain/spinal canal	40 Gy			Brain/spinal canal	40 Gy		
Posterior fossa*	20 Gy			Posterior fossa*	20 Gy		
Primary tumor region	8 Gy			Primary tumor region	8 Gy		
Metastases (spinal)	10 Gy			Metastases (spinal)	10 Gy		
Metastases (supratent.)	28 Gy			Metastases (supratent.)	28 Gy		

*The safety margin is 1 cm.
**The planning target volume includes the postoperative tumor bed and regions of initial tumor contact with a safety margin of 2 cm .

Grade 2 +3 ependymoma			
≥ 4 years		< 4 years	
M0/R0		**M0/R0**	
Extended tumor region	68 Gy	Extended tumor region	55 Gy
M0/R+		**M0/R+**	
Extended tumor region	72 Gy	Extented tumor region	54 Gy
M+		**M+**	
Extented tumor region	68 Gy	Extented tumor region	55 Gy
Residual tumor	72 Gy	Metastases	49.6 Gy
Metastases	50 Gy		

In patients with ependymoma, radiation is limited to the extended tumor region (not to the entire posterior fossa). The safety margin is 2 cm.