

S3 Table. Summary of clinical trials in high-risk medulloblastoma

Study	No.	Cohort definition	Radiotherapy		Chemotherapy	Total dose	Duration (wk)	Toxic death	Progression on treatment	Event-free survival
			CSI (Gy)	Tumor bed (Gy)						
POG9031 [6]	224 (M0=116, M1=29, M2=36, M3=34, M4=9)	T3b/T4, M+ or R+	35.2-44.0	53.2-54.	Randomized 3 cycles of cisplatin and etoposide before and after radiotherapy; Maintenance with 7 cycles of cyclophosphamide and vincristine	Cyclophosphamide 16,000 mg/m ² , etoposide 900 mg/m ² , vincristine 16 mg/m ² , cisplatin 270 mg/m ²	44	None reported	12 in the CT 1st	5-yr EFS 66% CT 1st 70% RT 1st
SJMB96 ^a) [1]	48 (M0=6, M1=9, M2=6, M3=27)	R+ or M1-M3	36-39.6	50.4	4 Cycles of HDC (cisplatin, cyclophosphamide, and vincristine)	Cisplatin 300 mg/m ² , vincristine 12 mg/m ² , cyclophosphamide 16,000 mg/m ²	16	0	1	5-yr EFS 70%
COGA9970 1 [6]	161 (M1=18, M2=10, M3=49)	R+ or M+	36	55.8	Carboplatin and vincristine during radiotherapy as radiosensitizer; Maintenance with 6 cycles of cyclophosphamide and vincristine with or without cisplatin	Cyclophosphamide 12,000 mg/m ² , vincristine 9 mg/m ² , ±carboplatin 1,050 mg/m ² ±cisplatin 450 mg/m ²	24	0	4	5-yr EFS M1=77% M2=50% M3=67%
SIOP PNET-3 [7]	68 (M2=13, M3=55)	M2-3	35	55	4 Cycles of vincristine etoposide, carboplatin and vincristine etoposide cyclophosphamide, alternatively	Carboplatin 2,000 mg/m ² , etoposide 2,400 mg/m ² , cyclophosphamide 3,000 mg/m ² , Vincristine 15	12	2	None reported	5-yr EFS 34.7%

GPOH HIT91 [8]	137 (M1=21, M2=19, M3=26)	R+ or M2-3	35.2	55.2	2 Cycles of pre-RT (ifosfamide, etoposide, methotrexate, cisplatin, cytarabine) with 8 cycles of maintenance chemotherapy after RT (vincristine, CCNU, cisplatin)	mg/m ² Ifosfamide 30 g/m ² , etoposide 900 mg/m ² , MTX 10 g/m ² , cisplatin 240 mg/m ² , cytarabine 3,600 mg/m ² +cisplatin 560mg/m ² , vincristine 12 mg/m ² +CCNU 600 mg/m ²	64	2	None reporte d	3-yr EFS 67%
HIT2000 [4]	123 (M1=36, M2/3=87)	M+	HFRT 40	HFRT 60- 72	2 Cycles of pre-RT (cyclophosphamide, etoposide, methotrexate, carboplatin and intraventricular methotrexate) with 4 cycles of maintenance chemotherapy after RT (vincristine, CCNU, cisplatin)	Cyclophosphamide 4,800 mg/m ² , methotrexate 20 g/m ² , carboplatin 1,200 mg, etoposide 900 mg/m ² , vincristine 9 g/m ² +cisplatin 280 mg/m ² , vincristine 18 mg, CCNU 300 mg/m ²	40	0	14 (pre- RT) 1 (post- RT), 31 (during mainte nance)	5-yr EFS 62% 5-yr OS 74%
ACNS 0332 [9]	294 (M1=33, M2=41, M3=115)	R+ or M+ or anaplast ic	36	55.8	Carboplatin and vincristine during radiotherapy as radiosensitizer; Maintenance with 6 cycles of cyclophosphamide, vincristine, cisplatin with or without isotretinoin	Cisplatin 450 mg/m ² , cyclophosphamide 6,000 mg/m ² , vincristine 18 mg/m ² ±carboplatin 210 mg/m ² ±isotinoi	30	0	None reporte d	5-yr EFS 62.9% 5-yr OS 73.4%
SJMB03 ^{a)} [3]	103 (M1=17, M2=28, M3=56)	R+ or M+	36-39.6	55.8- 59.4	4 Cycles of HDC (cisplatin, cyclophosphamide, and vincrisinte)	Cisplatin 300 mg/m ² , vincristine 8 mg/m ² , Cyclophosphamide	16	17/330	None reporte d	5-yr EFS 58.7%

Milan ^{a)} [10]	33 (M1=9, M2=6, M3=17, M4=1)	M+	HFRT 31.2-39	60	10 weeks of pre-RT chemotherapy (methotrexate, etoposide, cyclophosphamide, carboplatin), if CR pre- RT, maintenance (vincristine, CCNU), if not CR pre-RT, high-dose chemotherapy performed 2 Cycles of high-dose thiotepa	16,000 mg/m ² Methotrexate 8 g/m ² Etoposide 2.4 g/m ² Cyclophosphamide 4 g/m ² Vincristine 5.6 mg Carboplatin 800 mg/m ² Thiotepa 1,800 mg/m ² or CCNU 480mg+vincristine 25.2mg/m ²	22 or 64	None report ed	7	5-yr EFS 72%
PNET HR+5 ^{a)} [11]	51 (M0=14, M1=3, M2/3=34)	R+, M+, Myc amplifi cation	36	54	2 cycles of carboplatin, etoposide, 2 cycles of HD thiotepa, and maintenance of temozolomide 2 cycles of high-dose thiotepa	Carboplatin 1,600mg/m ² , etoposide 1,000mg/m ² , thiotepa 1,200mg, temozolomide 4,500mg/m ²	36	0	0	5-yr PFS 76% 5-yr OS 76%
KSPNO S081 ^{a)}	35 (M1=5, M2=4, M3=20)	R+ or M+	30.6	54	Alternative 6 cycles of cisplatin, etoposide, cyclophosphamide, vincristine and carboplatin, etoposide, ifosfamide, vincristine 2 Cycles of carboplatin thiotepa, etoposide and cyclophosphamide, melphalan	Cisplatin 225 mg/m ² , etoposide 2,250 mg/m ² , cyclophosphamide 13,500 mg/m ² , vincristine 18 mg/m ² , carboplatin 3,000 mg/m ² , ifosfamide 18,750 mg/m ² , thiotepa 900 mg/m ² , melphalan 180 mg/m ²	48	3	2	5-yr EFS 66.4% 5-yr OS 68.3%

CCNU, 1-(2-chloroethyl)-3-cyclohexyl-1-nitrosourea; CSI, craniospinal irradiation; CT, computed tomography; EFS, event-free survival; HD, high-dose; HDC, high-dose chemotherapy; OS, overall survival; RT, radiotherapy. ^{a)}High-dose chemotherapy was attempted in this study.

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