

Supplementary Table I. Treatment course in patients with high-risk neuroblastoma with multimodal treatment.

Treatment course	No. of patients
Induction chemotherapy/Surgery/SCT/RT/Maintenance	32 (86.5%)
Induction chemotherapy/Surgery/RT/Maintenance	3 (8.1%)
Induction chemotherapy/Surgery/SCT/RT	1 (2.7%)
Induction chemotherapy/Surgery/RT	1 (2.7%)

SCT, Stem cell transplantation; RT, Radiation therapy.

Supplementary Table II. Consolidative radiation therapy studies assessing patients with high-risk neuroblastoma.

	Year of publication, first author of the thesis				
	2009, Gatcombe	2016, Casey	2019, Chen	2020, Hosaka	Our study
Number of patients	34	246	24	18	37
FU period, months (range)	33.6 (0.5–70.5)	55.2 (8.4–187.2)	43.5 (25–100)	43 (10–110)	69.0 (12.0–237.6)
Median RT dose, Gy (range)	22.0 (18.0–30.6)	21.0 (all)	21.6 (21.6 – 35)	19.8, 30.6**	21 (14–36)
LRF, Crude rate, %	5.8	8.9	20.8	0.0	10.8
3-year FFLRF rate, %	94.0	90.2 (5-year)	78.9	100	88.7 (3-year), 88.7 (5-year)
3-year DFS rate, %	66.0	40.0 (5-year)	45.8	44	70.3 (3-year), 59.1 (5-year)
3-year OS rate, %	86.0	64.6 (5-year)	62.9	71	83.6 (3-year), 83.6 (5-year)

DFS, Disease-free survival; FFLRF, Free-from locoregional failure; FU, Follow-up; LRF, Locoregional failure; OS, Overall survival; RT, Radiation therapy.

* 19.8 Gy was administered to patients with gross total resection and 30.6 Gy to patients with subtotal resection.

† The unit of the dose is Gy (RBE, Relative biologic equivalent) for proton beam therapy and is defined as the physical dose (Gy) ×1.1.

Supplementary Table III. Treatment sites and dose for patients receiving radiation therapy to metastatic sites.

Case number	Metastatic sites with RT	Total RT dose	36 (12-49) *	0.426
#1	Whole brain	20 Gy	1.42	0.572
	Bone (Maxilla)	20 Gy	2.4	0.466
#2	Supraclavicular lymph node	24 Gy	10 (7-20) *	0.039
#3	Brain, Spinal cord	20 Gy		
#4	Bone (Thoracic spine)	22.5 Gy		
	Ortbit	24.2 Gy		
#5	Bone (Tibia)	24 Gy		
#6	Skull base	20 Gy		

RT, Radiation therapy.

Supplementary Table IV. Factors influencing freedom-from locoregional failure, disease-free survival, and overall survival after consolidative radiation therapy.

Variable	3-year rate (%)					
	FFLRF	<i>P</i> -value	DFS rate	<i>P</i> -value	OS rate	<i>P</i> -value
Sex						
Male	81.6	0.226	64.7	0.595	88.2	0.963
Female	95.0		75.0		80.0	
Age at diagnosis						
<18 months	83.3	0.663	57.1	0.775	85.7	0.552
≥18 months	89.6		73.3		83.3	
Primary site						
Abdominal	87.4	0.482	69.7	0.494	84.7	0.982
Non-abdominal	100.0		75.0		75.0	
BM involvement at diagnosis						
Yes	94.7	0.112	65.2	0.248	86.5	0.893
No	78.6		78.6		78.6	
Skeletal metastasis						
Yes	90.2	0.673	68.2	0.416	81.8	0.528
No	85.7		73.3		86.7	
MYCN amplification						
Yes	81.4	0.070	61.1	0.324	77.4	0.228
No	100.0		82.4		94.1	
1p deletion						
Yes	80.0	0.598	50.0	0.279	100.0	0.286
No	90.3		74.2		80.6	
11q deletion						
Yes	86.2	0.332	42.9	0.021	71.4	0.051
No	100.0		76.7		86.7	
Trisomy 17q						
Yes	100.0	0.642	50.0	0.137	50.0	0.011
No	88.1		71.4		85.6	
Shimada histopathology						
Favorable histology	81.8	0.686	50.0	0.303	64.8	0.359
Unfavorable histology	94.7		78.9		89.5	
Unknown histology	83.3		83.3		100.0	
LDH at diagnosis						
≥1500 IU/L	82.5	0.566	58.3	0.166	83.3	0.177
<1500 IU/L	90.9		77.3		81.8	
NSE at diagnosis						
≥100 ng/mL	81.1	0.135	52.2	0.036	73.4	0.048
<100 ng/mL	100.0		100.0		100.0	

BM, Bone marrow; DFS, Disease-free survival; FFLRF, Freedom-from locoregional failure; GTR; Gross total resection; LDH, Lactate dehydrogenase, MR, Mixed response; NR, No response; NSE, Neuron-specific enolase; OS, Overall survival; PR, Partial response; STR, Subtotal resection; VGPR, Very good partial response.

Supplementary Table IV. Continued.

Variable	3-year rate (%)					
	FFLRF	<i>P</i> -value	DFS rate	<i>P</i> -value	OS rate	<i>P</i> -value
Ferritin at diagnosis						
≥142 ng/mL	87.4	0.968	61.5	0.192	80.4	0.585
<142 ng/mL	88.9		88.9		88.9	
Response to induction chemotherapy						
VGPR/PR	83.7	0.173	61.5	0.059	80.6	0.107
MR/NR	100.0		90.9		90.9	
Resection extent						
GTR	86.7	0.689	66.7	0.767	87.3	0.258
STR	92.3		76.9		76.9	
Disease status before irradiation						
No residual disease	89.5	0.807	75.0	0.496	95.0	0.029
Residual disease	88.2		64.7		70.6	
Total radiation dose						
≤2100 cGy	87.9	0.846	73.1	0.813	80.8	0.323
>2100 cGy	90.0		63.6		90.9	

BM, Bone marrow; DFS, Disease-free survival; FFLRF, Freedom-from locoregional failure; GTR; Gross total resection; LDH, Lactate dehydrogenase, MR, Mixed response; NR, No response; NSE, Neuron-specific enolase; OS, Overall survival; PR, Partial response; STR, Subtotal resection; VGPR, Very good partial response.

Supplementary Table V. Univariate comparison between patients with and without late toxicity ≥grade 3.

Variables	No. of patients		<i>p</i> -value
	Grade 0–2 (n = 33)	Grade 3–5 (n = 4)	
Sex, Male	15 (45.5%)	2 (50.0%)	1.000
Age, <18months	7 (21.2%)	0 (0.0%)	0.570
Primary site, Abdomen	29 (87.9%)	4 (100.0%)	1.000
INRG, Stage M or MS	27 (81.8%)	4 (100.0%)	1.000
MYCN amplification, Yes	17 (54.8%)	1 (25.0%)	0.338
Extent of surgery, GTR	20 (60.6%)	4 (100.0%)	0.276
TBI, Yes	3 (9.1%)	0 (0.0%)	1.000
SCT, Yes	29 (87.9%)	4 (100.0%)	1.000
Maintenance therapy, Yes	30 (90.9%)	4 (100.0%)	1.000
Status before RT, residual	16 (48.5%)	1 (25.0%)	0.609
RT technique, 2D	8 (24.2%)	0 (0.0%)	0.557
Total radiation dose, >21Gy	10 (30.3%)	1 (25.0%)	1.000

GTR, Gross total resection; INRG, International Neuroblastoma Risk Group; RT, Radiation therapy; SCT, Stem cell transplantation; TBI, Total body irradiation.