Survival and Challenges with Multimodal Treatment in Children with Rhabdomyosarcoma - Real Scenario from A Resource-limited Center of Bangladesh

Supplementary files

Assigning a stage (Table A) by primary site, tumor size, and presence or absence of regional lymph node and/or distant metastases [13,14].

Table A. Pretreatment staging

Stage	Sites	Size	Nodes	Metastases
1	Orbit, Head & Neck (NPM), GU (non-B/P), Biliary tract	a/b	N0/N1/Nx	M0
2	Head & Neck (PM), GU(B/P), Extremity, Others (includes trunk, retroperitoneum, etc.)	a	N0/Nx	M0
3	Head & Neck (PM), GU(B/P), Extremity, Others (includes trunk, retroperitoneum, etc.)	a b	N1 N0/N1/Nx	M0
4	Any	a or b	N0/N1/Nx	M1
GU Genito-urinary, NPM Non-para-meningeal, PM Para-Meningeal, B/P Bladder/ Prostate.		a ≤5 cm b>5cm	Nx Un-known	

Assigning an IRS Clinical Group (Table B) by postsurgical resection status /biopsy, with pathologic assessment of the tumor margin and lymph node disease [7,15].

Table B. IRS Clinical Group Classification (CG)

Clinical Group (CG)	Definition
Group I	Localized disease, completely resected
Group II A B C	Total gross resection with evidence of regional spread like----- Grossly resected with microscopic residue/ Resected involved lymph node without microscopic residue/ or With microscopic residue
Group III	Biopsy only or incomplete resection with gross residue

Group IV	Distant metastatic disease

Determining Risk Group (Table C) by stage, clinical group, and histology **[6,11]. Risk-stratified** COG treatment was applied for each risk group.

Table C. COG-STS risk group stratification of Patient (TNM stage, histology & CG)

Risk-Group	Histology	TNM-Stage	IRS-Clinical Group
Low-risk	Embryonal Embryonal	1 2,3	I, II, III (orbit) I, II
Intermediate-risk	Embryonal or Alveolar	2,3 1,2,3	III I, II, III
High-risk	Embryonal or Alveolar	4	IV

Table D. Radiation Therapy (RT) Dose According to Rhabdomyosarcoma Group, Histology, and Site of Disease (COG) [9].

Group	Doses of RT
Group I Embryonal RMS Alveolar RMS	• No RT • 36 Gy to pre-chemotherapy site
Group II N0 N1	• 36 Gy to pre-chemotherapy site • 36 Gy to the pre-chemotherapy site and 41.4 Gy to the nodes
Group III	
Orbital Non-orbital	• 45 Gy for orbital tumors if complete response to chemotherapy, but 50.4 Gy if partial remission. • 50.4 Gy for invasive tumors • 59.4 Gy boost to residual disease for tumors >5 cm at diagnosis
N1 with gross residual disease after surgery or chemotherapy	• 50.4 Gy.
Group IV	• As other Groups, with the inclusion of all metastatic sites, if feasible. Exception: pulmonary metastases treated with 12 Gy to 15 Gy.

Table E. Chemotherapy protocol

Table E.1 Regimen for the low-risk group [18]

Week	1	4	7	10	13	16	19	22	25	28	31	34	37	40	43	46
Drug	V A C	V A C	V A C	V A C	V A* C	V A* C	V A* C	V A	V A	V A	V A	V A	V A	V A	V A	V A
					-------RT------			V- Vincristine-day1; A -actinomycin-D- day1 C- Cyclophosphamide -day 1; A*-omitted								

Table E.2 Regimen for the intermediate-risk group

Week	1	4	7	10	13	16	19	22	25	28	31	34	37	40
Drug	V A C	V A* C	V A* C	V A* C	V A C	V A C	V A C	V A C	V A C	V A C	V A C	V A C	V A C	V A C
		-----RT--------			V- Vincristine -day1; A -actinomycin-D-day 1; C- Cyclophosphamide-day1; A*-omitted									

Table E.3 Protocol for high-risk group [22]

Week	1	4	7	9	11	13	15	17	20	23	26	28	30	32	35	38	41	44	47	50
Drug	V Ir	V Ir	V D C	I E	V D C	I E	V D C	I E	V Ir	V Ir	I E	V D C	I E	V D C	V A C	V A C	V A C	V A C	V Ir	V Ir
									------RT------											
V- Vincristine-day1; Ir -Irinotecan-day1-5; A -actinomycin-D-day1; C- Cyclophosphamide -day1; D-Doxorubicin -day1-2; I-Ifosfamide-day1-5; E-etoposide-day1-5; A*-omitted																				

Table F. Doses of chemotherapy [18, 20, 22]

Age	Inj.Vincristine	Inj.Actino-mycin -D	Inj.Cyclophos phamide	Inj.Irino-tecan	Inj.Doxo-rubicin	Inj.Ifos-phamide	Inj.Eto poside

< 1 year	0.025mg/kg/d	0.025mg/kg	40mg/kg/ d	50mg/$m^{2/}$d	50% dose	50%	50%
≥1 to 3 years	0.05mg/kg/d	0.045mg/kg	1.2gm/m^2 /d	50mg/$m^{2/}$d	37.5mg/m^2/d	1800mg/m^2 /d	100mg/ m^2 / d
>3 year	1.5 m/m^2 /d	0.045mg/m^2	1.2gm/m^2 /d	50mg/m^2/d	37.5mg/m^2/d	1800mg/m^2 / d	100mg/ m^2 /d