

High Risk Neuroblastoma* Pediatric Surveillance & Follow-up Guidelines

	Months from end of therapy	Date	Location	H&P	CBC	Chem	HVA & VMA @	MIBG /CT	CXR & Abdo US	Tumour Imaging	Urine tests	ECHO [#]	Audiol	TSH, T4	Neuropsych	LH, FSH, Test or Est	Additn'l Screen	Other		
Early Follow-Up Clinic	0				End of treatment evaluations (per protocol)														Summary for LTFU clinic	
	3			+	+	+		+		+				+					Ferritin	
	6			+	+	+	+	+		+	+								Attenuated vaccine re-immunization	
	9			+	+															
	12			+	+	+	+	+		+	+	+	+	+					Live vaccine immunization	
	15			+	+															
	18			+	+		+	+		+										
	21			+	+															
24			+	+	+	+	+		+	+										
LTFU Clinic	30			+	+			+												
	36			+	+	+	+	+		+		+	+							
	42			+	+				+											
	48			+	+	+	+		+											
	54			+	+				+											
	60			+	+		+		+		+			+						
Notes					Lytes, Ca, Mg, PO4, Cr, urea, LFTs	[@] Only if positive at Dx	Only if positive at Dx.		Special Sites, ie. MRI spine	U/A, urine Prot:Cr & Alb:Cr ratio	[#] Insert added freq based on cardiac guideline (see over). ECG if clinical concerns	Rpt if abN		If clinical concerns, first assessment prior to school entry & repeat at school transitions	Baseline age 12 y if CED ≥4 or clinical concerns. Rpt Q1y	Based on site of disease, surgery or RT (ie ophtho; spine xray)				

*Defined based on clinical designation or treatment with High Risk Protocol (autologous SCT +/- immunotherapy)

End of therapy begins after completion of cis-retinoic acid (if applicable)

[^]CED: Cyclophosphamide Equivalence Dose (see over)

<p>Further Surveillance Semen Analysis Anti-Mullerian Hormone Breast MRI and Mammogram Colonoscopy</p>	<p>From age 18y in males From age 16y in females if CED ≥ 6 g/m² or pelvic RT; or earlier if clinical concerns From later of age 25y or 8y after exposure if chest RT From later of age 30y or 5y after exposure to abdominal RT</p>
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Cardiac Surveillance Guidelines (BC)

Anthracycline Dose*	Radiation Dose**	Recommended Frequency of Echo
None	< 15 Gy or none	No Screening
	15 - < 35 Gy	Every 5 years
	35 Gy	Every 2 years
< 250 mg/m ²	< 15 Gy or none	Every 5 years
	15 Gy	Every 2 years
250 mg/m ²	Any or none	Every 2 years

*Based on total doses of doxorubicin or the equivalent doses of other anthracyclines

**Based on radiation dose with potential impact to heart (radiation to chest, abdomen, spine [thoracic, whole], total body [TBI])

COG LTFU Guidelines version 5.0 (Oct 2018)

Anthracycline Equivalent Dose

Agent	Correction factor
Doxorubicin	1.0
Daunorubicin	0.5
Epirubicin	0.67
Mitoxantrone	4.0
Idarubicin	5.0

Chow J Clin Oncol 2015;33(5):394-402

Risk of Prolonged Oligospermia or Azoospermia

Agent	Possible Risk	High Risk
Cyclophosphamide	> 4g/m ²	> 7.5 g/m ²
Busulphan		> 600 mg/m ²
Melphalan		> 140 mg/m ²
Ifosfamide	> 42 g/m ²	> 60 g/m ²
Procarbazine	> 3 g/m ²	> 4 g/m ²
Chlorambucil		> 1.4 g/m ²
BCNU	> 300 mg/m ²	> 1 g/m ²
CCNU		> 500 mg/m ²
Cisplatin	> 300 mg/m ²	> 600 mg/m ²
Testicular RT dose	> 200 cGy	> 1200 cGy

*Lower doses are still possible risk

1. Green J Clin Oncol 2010;28:332-9
2. Meistrich Pediatr Blood Cancer 2009;53:261-6
3. Wyns Human Reprod Update 2010;16(3):312-328

Risk of Premature Ovarian Insufficiency or Infertility

Agent	Possible Risk	High Risk	Ref
CED	> 4 g/m ²	> 8 g/m ²	1
Procarbazine	> 2 g/m ²	> 4 g/m ²	2
Cisplatin	> 300 mg/m ²		3
Dactinomycin	>12.2 mg/m ²		4
Ovarian RT dose*	> 100 cGy	> 1000 cGy	5

*Age dependent (see nomogram⁵)

[^]Bevacizumab can cause ovarian failure; possibly acute and transient only⁶

1. Green Pediatr Blood Cancer 2014;61(1):53-67
2. Van der Kaaij J Clin Oncol 2012;30(3):291-299
3. Solheim Gyne Oncol 2015;136(2):224-229
4. Van Den Berg Hum Reprod 2018; 33(8):1474-1488
5. Wallace Int J Radiat Oncol;62(3):738-744
6. Imai Molec Clin Oncol 2017;6:807-810

Cyclophosphamide Equivalent Dose (CED)

Agent	Correction factor
Cyclophosphamide	1.0
Ifosfamide	0.244
Procarbazine	0.857
Chlorambucil	14.286
BCNU	15
CCNU	16
Melphalan	40
Thiotepa	50
Nitrogen Mustard	100
Busulphan	8.823

Green Pediatr Blood Ca 2014;61:53-67