

Low and Intermediate Risk Neuroblastoma* Pediatric Surveillance & Follow-up Guidelines

	Months from end of therapy	Date	Location	H&P	CBC	Chem	HVA & VMA @	Tumour Imaging CXR/US	MIBG /CT **	Urine tests	ECHO#	Audiol	TSH, T4	LH, FSH, Test or Est	Additn'l Screen	Other		
Early Follow-up Clinic	0				End of treatment evaluations (per protocol)													
	1			+													Summary for LTFU clinic	
	2			+														
	3			+	+	+	+	+	+	+			+					
	4			+														
	5			+														
	6			+	+	+	+	+	+									Attenuated vaccine re-immunization
	7			+														
	8			+														
	9			+	+	+	+	+	+									
	10			+														
	11			+														
	12			+	+	+	+	+	+	+	+	+	+	+				Live vaccine immunization
	15			+	+													
18			+	+			+	+										
21			+	+														
24			+	+	+	+	+	+					+					
LTFU Clinic	30			+	+													
	36			+	+	+	+	+	+									
	48			+	+		+	+										
	60			+	+	+	+	+		+								Refer to Late Effects clinic
	Notes					Lytes, Ca, Mg, PO4, Cr, urea, +/-LFTs	Spot test @ Only if positive at Dx.		** see note	U/A, urine Prot:Cr & Alb:Cr ratio	#Insert added freq based on cardiac guidelines (see over). ECG if clinical concerns	Rpt if abN		Baseline age 12 y if CED ≥4 or clinical concerns. Rpt Q1y	Based on site of disease, surgery or RT (ie ophtho; spine xray)			

* Excludes high risk patients

**Only for patients with stage 4 MIBG-positive disease at Dx and patients with localized or 4S disease that remains MIBG-positive at end of therapy

^CED: Cyclophosphamide Equivalence Dose (see over)

Further Surveillance	
Semen Analysis	From age 18y in males
Anti-Mullerian Hormone	From age 16y in females if CED ≥ 6 g/m ² or pelvic RT; or earlier if clinical concerns
Breast MRI and Mammogram	From later of age 25y or 8y after exposure if chest RT
Colonoscopy	From later of age 30y or 5y after exposure to abdominal RT

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. Wynn 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