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ANBL2131

A Phase 3 Study of Dinutuximab Added to Intensive Multimodal Therapy for Children with Newly

Diagnosed High-Risk Neuroblastoma A COG Phase 3 Study

NCI Supplied Agent: Dinutuximab (NSC# 764038, IND# 168387)

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- This randomized study is evaluating whether chemo-immunoinduction (Arm B) is superior to ANBL0532 induction (Arm A).
- Those with a poor end of induction response will receive extended induction therapy with Irin/TMZ/Din/GMCSF in an effort to convert a greater proportion of patients to a good end of induction response and thus increase the proportion of patients going to tandem transplant.
- Recent data suggests that subsets of HRNBL patients have equivalent local control with deescalated local radiotherapy¹, as a result we will test a dose painting strategy in this multiinstitutional phase 3 study.
- Finally, because MIBG persistence has been shown to be a marker of increased risk for metastatic site failure², varied response timing for selection of metastatic site radiotherapy will be evaluated in Arm A patients who convert from a PEIR to GEIR with extended induction.

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¹PMID: 30763661, PMID: 30496881 ²PMID: 35345864

Trial Schema

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- Patient randomization occurs after cycle 1.
- Surgery is recommended after cycle 4.
- A total of 5 cycles of induction will be given in Arm B, while Arm A patients with a PEIR may receive up to 11 cycles prior to transplant.
- TC/CEM conditioning with Tandem transplant is recommended for all GEIR patients.
- Radiotherapy will be delivered either at diagnosis for patients with threatened function (i.e., vision, paralysis) and/or following transplant.
- Additional post-consolidation immunotherapy and differentiation therapy is required for all patients following radiotherapy.



Trial Response Evaluations

- Patients will undergo response assessment at multiple timepoints:
 - Post Cycle 5
 - +/- Post-transplant (for patients with >5 metastatic sites) pre-ASCT)
 - After each 2-cycle block during extending induction in Arm A if a PEIR is obtained
- Response is split into:
 - Primary site
 - Soft Tissue & Bone Metastatic site
 - Bone marrow
- Various combinations of the above define the Overall Response category which defines status assignments on study (Good End of Induction Response or Poor End of Induction Response) (See adjacent from Appendix VI).

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ALLENDIA	VI. OVERALL RESPONSE A	CKITEKIA		
Primary Tumor	Soft Tissue and Bone Metastatic Disease (MIBG or ¹⁸ F-FDG-PET/CT or PET/MP)	Bone Marrow Metastatic Disease	Overall Response	End of Induction GEIR or PEIR
CR	CR	CR	CR	GEIR
CR for one	response component with either CR or NI for	other components	CR	GEIR
CR	CR	MD	PR	GEIR
CR	PR	CR	PR	GEIR
CR	PR	MD	PR	GEIR
CR	PR	NI	PR	GEIR
CR	NI	MD	PR	GEIR
PR	CR	CR	PR	GEIR
PR	CR	NI	PR	GEIR
PR	CR	MD	PR	GEIR
PR	PR	CR	PR	GEIR
PR	PR	NI	PR	GEIR
PR	PK	MD	PR	GEIR
PK	NI	CR	PK	GEIR
PK	NI	MD	PK	GEIR
FK NI	CP	MD	DD	GEIR
NI	DD	CR	PD	GEIR
NI	PP	MD	PP	GEIR
NI	PR	PR	PR	GEIR
NI	PR	NI	PR	GEIR
CR	CR	SD	MR	PEIR
CR	PR	SD	MR	PEIR
CR	SD	CR	MR	PEIR
CR	SD	MD	MR	PEIR
CR	SD	SD	MR	PEIR
CR	SD	NI	MR	PEIR
CR	NI	SD	MR	PEIR
PR	CR	SD	MR	PEIR
PR	PR	SD	MR	PEIR
PR	SD	CR	MR	PEIR
PR	SD	MD	MR	PEIR
PK	SD	SD	MR	PEIR
PK	SD	NI SD	MK	PEIR
SD	CR	CR	MR	CEIR
SD	CR	MD	MR	GEIR
SD	CR	SD	MR	PEIR
SD	CR	NI	MR	GEIR
SD	PR	CR	MR	GEIR
SD	PR	MD	MR	GEIR
SD	PR	SD	MR	PEIR
SD	PR	NI	MR	GEIR
SD	SD	CR	MR	PEIR
SD	NI	CR	MR	GEIR
NI	CR	SD	MR	PEIR
NI	PR	SD	MR	PEIR
NI	SD	CR	MR	PEIR
SD	SD	MD	SD	PEIR
NI	SD NI	MD	50	PEIK
SD	NI	MD	SD	GEIR
SD	SD	SD	SD	PEIR
SD	NI	SD SD	SD SD	PEIK
SD	SD	NI	SD	PEIR
SD	NI	NI	SD	GEIR
NI	SD	SD	SD	PEIR
NI	SD	NI	SD	PEIR
NI	NI	SD	SD	PEIR
	Response of PD in any one of the 3 comport	ents	PD	PEIR
	Response of NR for any one of the 3 comport	*	ND	
Parmonea of NID in any one of the 2 component-			NID	ND

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CR: Complete Response; MD: Minimal Disease; PR: Partial Response; MR: Minor Response; SD: Stable Disease; PD: Progressive disease; not involved; site not involved at study entry and remains not involved; GEIR: Good End Induction Response; PEIR: Poor End Induction Response;

Trial Response Criteria

• Adapted from INRC Criteria in Park et al. JCO 2017

Primary (soft tissue) Tumor Response*		Bone Marrow Response		
Resp	Anatomic + MIBG/FDG-PET	Resp	Anatomic + MIBG/FDG-PET	
CR	<10 mm residual soft tissue at 1° site AND	CR	Bone marrow with no tumor infiltration on reassessment, independent of baseline tumor involvement	
	Complete resolution of MIBG/FDG-PET [†]		Any of the following:	
	 ≥ 30% decrease in longest diameter of 1° 	PR	Bone marrow without tumor infiltration that becomes > 5% tumor infiltration on reassessment OR	
PR	site AND		Bone marrow with tumor infiltration that increases by >	
	MIBG/FDG-PET ⁺ uptake at 1° site stable, improved, or resolved		two-fold and has > 20% tumor infiltration on reassessment	
PD	> 20% increase in longest diameter (ref = smallest sum on study) AND	MD	Any of the following: Bone marrow with $\leq 5\%$ tumor infiltration and remains > 0 to $\leq 5\%$ tumor infiltration on reassessment OR	
	Minimum absolute increase of 5 mm in longest dimension‡		Bone marrow with no tumor infiltration that has ≤ 5% tumor infiltration on reassessment OR	
SD	Neither sufficient shrinkage for PR nor sufficient increase for PD at the 1° site		Bone marrow with > 20% tumor infiltration that has > 0 to ≤5% tumor infiltration on reassessment	
[†] Used for MIBG-non-avid tumors. ‡Mass that does not meet PD measurement criteria but has fluctuating MIBG avidity will not be considered PD.		SD	Bone marrow with tumor infiltration that remains positive with >5% tumor infiltration on reassessment but does not meet CR, MD, or PD criteria	

See PMID: 28471719 for further details

umor Re	mor Response at Metastatic Soft Tissue and Bone Sites				
esp	Anatomic + MIBG/FDG-PET				
R	Resolution of all sites of disease, defined as: Non-1º target & nontarget lesions measure , <10 mm AND				
	Lymph nodes identified as target lesions decrease to a short axis , <10 mm AND				
	MIBG uptake or FDG-PET uptake (for MIBG-non-avid tumors) of non-1° lesions resolves completely				
	≥30% decrease in sum of diameters† of non-1° target lesions compared with baseline AND all of the following:				
-	Nontarget lesions may be stable or smaller in size AND				
n	No new lesions AND				
	\geq 50% reduction in MIBG absolute bone score (relative MIBG bone score \geq 0.1 to \leq 0.5) or \geq 50% reduction in number of FDG-PET-avid bone lesions‡§				
	Any of the following: Any new soft tissue lesion detected by CT/MRI that is also MIBG or FDG-PET avid				
	Any new soft tissue lesion seen on anatomic imaging that is biopsied & confirmed to be neuroblastoma or Ganglioneuroblastoma				
	Any new bone site that is MIBG avid				
D	A new bone site that is FDG-PET avid (for MIBG-non-avid tumors) AND has CT/MRI findings consistent with tumor OR has been confirmed histologically to be neuroblastoma or Ganglioneuroblastoma				
	>20% increase in longest diameter taking as reference the smallest sum on study (this includes the baseline sum if that is the smallest on study) AND minimum absolute increase of 5 mm in sum of diameters of target soft tissue lesions				
	Relative MIBG score ≥ 1.2§				
	Neither sufficient shrinkage for PR nor sufficient increase for PD of				

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SD

С

P

Ρ

See PMID: 28471719 for further details

non-1° lesions

Indications for Radiotherapy

- A small subset of patients may present with functional compromise (respiratory, visual, neurologic) at diagnosis which may warrant emergent radiotherapy prior to initiation of protocol therapy.
- All patients receive primary site radiotherapy
- Consolidative metastatic site radiotherapy to incompletely responding metastases should occur at the site time as the treatment of the primary site.

Changes in the Radiotherapy paradigm in ANBL2131

- Reduced dose (18 Gy) to the CTV when treating the primary site target volume is allowed in a subset of patients:
 - Good end of induction response (GEIR)
 - Primary Site CR (<10mm residual at the primary site following resection)
- Selection of metastatic sites for radiotherapy:
 - Those treated on Arm A will have metastatic sites chose based on the postcycle 5 response evaluation.
 - Those treated on Arm B with a poor end of induction response will be selected based on extended induction response evaluations.

1° Site Dose Reduction

Dose Reduced Patients

- -Dose reduction has been successful in single institution studies¹.
- -This has the potential to limit renal, pancreatic, spleen and liver acute and late complications.





Altered Metastatic Site Selection in Arm A Patients

- -Persistent MIBG avidity is associated with an increased risk of metastatic site relapse¹.
- -PEIR patients in Arm A are reevaluated every 2 cycles for up to 6 cycles.
- -If a GEIR is obtained after extended induction, then the patient goes to ASCT.
- -The immediate pre-ASCT response evaluation study will define the sites to be consolidated with RT.
- -Arm B cases will be treated based on the post-cycle 5 response evaluation.



*Patients who have achieved GTR, and had a GEIR are eligible for dose reduction to 18 Gy - See section 17.9.2.4 Treatment Sites and Doses for details. EOI=End of Induction; GEIR=Good End of Induction Response; PEIR=Poor End of Induction Response; RT=Radiation Therapy; d=days; ASCT=Autologous stem cell transplant. ¹See section 10.3 for definitions of GEIR and PEIR, ²See section 17.4 for further details, ³PET scans will be used for patients with MIBG non-avid tumors.

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¹PMID: 35345864

Radiotherapy Timing & Delay Criteria

- Radiation will be given after recovery from the ASCT.
- It is recommended that radiation therapy begin no sooner than Day +42 and no later than Day +80 following the second ASCT.
- Organ toxicity within the radiation field should have resolved.

Organ in Radiation Field	Considerations for Delay of Radiation Therapy			
Popo MorrowA	Persistent cytopenias, including absolute neutrophil count (ANC) \leq 500/µL (off G-CSF for \geq 48 hours), and/or transfusion-refractory			
Bolle Mallow	thrombocytopenia with platelet count < 40,000/ μL.			
Liver	Active sinusoidal obstruction syndrome without signs of resolution*			
Trachea	Grade 2 or higher airway edema that requires respiratory support			
Abdomen	Refractory diarrhea, greater than CTCAE Grade 2			
Kidpovo**	Persistently elevated serum creatinine for age/sex (see Section 3.3.4) or 2 x the creatinine value obtained at the start of Consolidation			
Ridneys	therapy			
Bladder	Persistent hematuria			
^Volume of potential marrow radiation exceeding 10% of total marrow (see Table 3)				
*Radiation involving the liver should be delayed for active sinusoidal obstruction syndrome (SOS) of any grade. Hepatomegaly and fluid accumulation may persist after SOS				
has begun to resolve, and radiation may be initiated provided that physiologic portal flow has returned, hyperbilirubinemia and pain are improving, and the patient has been				
stable on room air for five days. Consultation with anesthesiology should be pursued prior to initiation of sedated radiotherapy treatment.				
*Please refer to Table 11 for discussion of renal scintigraphy if recommended kidney dose constraints are exceeded.				

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Radiotherapy Prescriptions

GEIR AND Primary Site CR (<10mm residual)					
Site	Target	Dose	Dose/ Fraction	Fractions	
Drimony tymor aita initially involved lymph pedag, aurgical bod	CTV	18 Gy/GyRBE	1.5 Gy/GyRBE	12	
Finnary turnor site, initially involved tyripin houes, surgical bed	GTV	21.6 Gy/GyRBE	1.8 Gy/GyRBE	12	
Approximating Vertebral Bodies	OTV_VB	18 Gy/GyRBE	1.5 Gy/GyRBE	12	

Primary Site: GEIR and < Primary Site CR (≥ 10mm residual)					
Site/Target	Target	Dose	Dose/ Fraction	Fractions	
Primary tumor site, initially involved lymph nodes, surgical bed	CTV	21.6 Gy/GyRBE	1.8 Gy/GyRBE	12	
Approximating Vertebral Bodies	OTV_VB	18 Gy/GyRBE	1.5 Gy/GyRBE	12	

Metastatic Site Consolidation					
Site/Target	Target*	Dose	Dose/Fraction	Fractions	
Metastatic disease after Induction or Extended Induction	mCTVx/ ITVx/ PTVx*	21.6 Gy/GyRBE	1.8 Gy/GyRBE	12	
Hepatomegaly leading to respiratory distress	Partial Liver^	4.5 Gy	1.5 Gy	3	
Visual Compromise at Diagnosis	Base of Skull^	5.4 Gy	1.8 Gy	3	
Craniospinal Radiotherapy Dose**		21.6 Gy/GyRBE	1.8 Gy/GyRBE	12	

*When proton therapy is used, the prescription target will be the CTV or ITV depending on whether target motion is present at the primary or metastatic site. When photon radiotherapy is used, the prescription target for coverage will be the PTV.

**If leptomeningeal disease is discovered during therapy, the study team should be contacted regarding optimal management as craniospinal radiotherapy may be required. ^Contoured Target Volumes are not required for emergency cases.

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Organs at Risk

- OARs are categorized into 3 groups:
 - Required, Conditional, or Suggested
- Definitions:
 - Required: these should be delineated for all cases where that treatment site is treated with radiotherapy.
 - Conditional: these organs may or may not be present based on the patient's gender i.e., Vagina/Uterus are only contoured for girls.
 - Suggested: these organs are variably be at risk for subsequent treatment related injury depending on the specific site i.e., the lacrimal gland would only be relevant for disease volumes which approximate the orbit, parotid/submandibular gland volumes would only be appropriate for persistent soft tissue adenopathy in the high neck which might compromise late salivary function.

Table 11. Required Organs at Risk According to Treatment Site Site TG263 Name Required DVH Status Constraint Brain Brain R NA Cochlea Left Cochlea R Dmean < 30 Gy Cochlea R Right Cochlea R Glnd Lacrimal L Left Lacrimal Gland S Glnd Lacrimal R Right Lacrimal Gland S Dmean < 26 Gy S Glnd Submand L Left Submandibular Gland Glnd Submand R Right Submandibular Gland S Lens L Left Lens R ALARA R ALARA Lens R Right Lens Cranium/ OpticNrv L Left Optic Nerve R NA^o Head & OpticNrv R Right Optic Nerve R D50% < 5400 cGv Neck OpticChiasm Optic Chiasm R D0.1cc < 5600 cGy Orbit I Left Orbit R NA^o Orbit R Right Orbit R NA^D Parotid L Left Parotid S Dmean < 26 Gy S **Right Parotid** Parotid R R SpinalCord Spinal Cord NA^o Retina I Left Retina R Dmean < 30 Gy173 Retina R Right Retina R Thyroid Thyroid R Dmax <10 Gy174 A LAD Left Anterior Descending a. S Dmcan < 5 Gv* 17: Heart Heart* R Dmean < 26 Gy Ventricle I Dmcan < 5 Gy*17 Left Ventricle S Bladder Bladder R NA Esophagus Esophagus R NA^D Contralateral⁶ Kidney_L D25% < 18 Gy Left Kidney R Ipsilateral® D75% < 18 Gv D100% < 14.4 Gy R Kidney R Right Kidney Abdomen Dmean ≤ 18 Gy D50% < 24Gy Pelvis Kidnevs Kidnevs R Liver Liver R Dmean < 15 Gv⁴ Left Ovary (Females Only) Ovary L С Right Ovary (Females ALARA С Ovary R Only) Pancreas Pancreas R **ALARA**Ω SpinalCord Spinal Cord R NAⁿ Testis I Left Testis (Males Only) C С Testis R Right Testis (Males Only) ALARA С Uterus Uterus (Females Only) С Vagina Vagina (Females Only) A LAD Dmean < 5 Gy* 175 Left Anterior Descending a. S Chest/ Breast L Left Breast (Females Only) C ALARA Paraspinal Breast R Right Breast (Females ALARA С Only) Esophagus Esophagus NA^D R Heart Heart* R Dmean < 26 Gy Ipsilateral Lung L Left Lung R V20 < 30% Contralateral Lung R Right Lung R V20 <10% Lungs Lungs R V20 < 30%SpinalCord Spinal Cord R NAⁿ Thyroid Thyroid Dmax <10 Gy^ 174 Ventricle I Left Ventricle Dmean < 5 Gy* 17: S Required = R, Conditional = C, Suggested = S, ALARA = As Low As Reasonably Achievable, NA^{n} = Dose constraints are not expected to be exceeded for this organ but reporting of the DVH may be relevant for late effects surveillance and as such has been included, [©] = If kidney dose exceeds the constraints outlined, renal scintigraphy is recommended to ensure that both kidneys are functioning prior to beginning radiotherapy. *= If liver constraints are exceeded due to need to radiate a liver lesion, extra concern should be exercised for patients who are recovering from SOS. Ω = The pancreas frequently approximates the primary site target and as

such, limited potential exists for sparing; however, this remains a source of late morbidity (Glucose Intolerance/Diabetes Mellitus) in childhood cancer patients ⁹¹. As such, attempts

Risk of Coronary Artery Disease. ^ = Risk of Hypothyroidism, a. = artery

should be made to limit dose to the pancreatic tail when possible⁹⁰. " = Risk of Pericarditis. * =

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Contouring Process

The following steps are suggested for primary site volume delineation.

- 1) Delineate all required OARs, & patient and site specific conditional and suggested OARs.
- 2) Co-register the post-induction Cycle 4, pre-surgery scans with the simulation CT scan.

(See Aligned PreOp scans for ANBL2131 Case 1)

- 3) Delineate the GTV_Preop (see green volume)
- 4) Copy the GTV_Preop and adjust for inclusion of clips, operative boundaries, pathologic findings & exclusion of pushing/non-infiltrated boundaries.
- 5) Rename the adjusted contour GTV (blue volume)

Post-C4 Induction, Preoperative Scans



Planning Scans



Contouring Process

- 6) Expand the GTV by 1cm to derive the CTV
- 7) Adjust the CTV such that uninvolved/non-infiltrated tissues only have a rim of 3-5mm extending into the adjacent organ, while ensuring that proximal infiltrated organs/tissues and the entirety of the operative bed are within the CTV.
- 8) Use accompanying scans to estimate organ motion (i.e., 4DCT or derived series [MIP])
- 9) Expand the CTV to ITV to reflect motion in all 3 planes.
- 10) Expand the ITV to PTV using an immobilization & image-guidance appropriate amount

Primary Site	Non-CBCT	CBCT
Head and Neck	5 mm	3 mm
Upper Paraspinal	5 mm	3-5 mm
Intra-thoracic	5 mm	5 mm
Abdomen	5-8 mm	3-5 mm
Lower Paraspinal/Pelvic	5 mm	3-5 mm

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Planning Scans – CTV delineation



4D Evaluation scans – Min IP & MaxIP



Planning Scans – ITV delineation



Metastatic Site Naming

- If metastatic sites are consolidated, they should be named according to the Curie Scoring system region. • i.e., A left sided extremity metastasis would be named mGTV7_L.
- Additional site-specific modifications to the metastatic target CTV are discussed in Section 17, Table 9. •

Region	Site	Curie score
1	Head / Neck	
2	Cervico-Thoracic spine	
3	Ribs / Sternum / Clavicles/ Chest	
4	Lumbar / Sacral spine	
5	Abdomen/Pelvis	
6	Upper Extremity (Proximal)	
7	Upper Extremity (Distal)	
8	Lower Extremity (Proximal)	
9	Lower Extremity (Distal)	
10	Soft Tissue	
TOTAL	Total scores from Regions 1 - 10	



Treatment	nons for metastatic site of v modifications
Site(s)	Methods to anatomically confine CTV
Calvarium	Adjust CTV to avoid extension into the cerebral cortex unless the lesion extends through the skull with suspected dural involvement. In cases where the entire calvarium needs to be treated, a brain sparing approach such as that used by Wolden et al ¹⁶³ should be used.
Base of Skull	Adjust CTV to avoid extension beyond bony structures unless there is radiographic evidence of extension into brain tissue. T2-weighted imaging can be useful in delineating the target.
Limb	Adjust CTV to avoid circumferential limb treatment, growth plates & joint spaces (unless involved). ^{62, 164-166}
Spine	Adjust CTV to facilitate uniform dose to the entire vertebrae including the transverse and spinous process, vertebral body, and pedicles (regardless of if non-uniformly involved by disease) to minimize the risk of scoliosis. ¹⁶⁷⁻¹⁶⁹ The entire vertebral body should receive >18 Gy if treatment is required.
Rib	The CTV should be adjusted such that CTV does not extend into the lung parenchyma unless there is strong evidence of parietal pleura involvement. Pleural space involvement is rare in neuroblastoma.
Lung/ Pleural Space	Lung involvement at diagnosis is rare, but when encountered is considered a risk factor for distant metastatic site failure and an overall adverse prognostic factor. ^{170,} ¹⁷¹ Only focal consolidative radiotherapy approaches will be employed on this protocol for incompletely responding lung disease.
Craniospinal	Leptomeningeal disease at diagnosis is rare in neuroblastoma, and craniospinal irradiation (CSI) should be avoided as it could potentially compromise the marrow reserve and limit the potential for Post-Consolidation therapy. ¹⁷²

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Treatment Planning

Planning Objectives

- 1.>95% IDL covers 100% PTV
- 2.>93% IDL covers 100% PTV
- 3. <10% PTV receives < 110% of the Rx dose
- 4. Meet renal dose constraints (if 1° abdomen case)
- 5. Meet required OAR constraints (Sec. 17, Table 11)
- 6. Coverage of OTV_VB with Dmean 18 Gy (if encroaches on adjacent spine).

Motion Evaluation

 If significant motion is noted at the time of 4D/motion evaluation, consider beam angles with minimal change in amplitude (M⊥,AX).



- 2. Proton plans should have beam angles chosen which minimize the water equivalent thickness.
- 3. Photon cases are generally robust to motion, although accounting for motion during contouring and planning remains essential.

Protocol Deviation Criteria

- Protocol deviations are subclassified according to the following:
 - Dose, Uniformity, Volume Delineation, OAR Tolerances, and Timing.
 - Some variations are considered acceptable while others have the potential to either cause harm, compromise protocol objectives, and/or disease control.
- If a potential deviation is anticipated, its encouraged that the treating physician reach out for guidance regarding the case prior to initiation of radiotherapy.

	DEVIATION		
	Variation Acceptable	Deviation Unacceptable	
Prescription D	lose		
Primary or Metastasis	Difference in prescribed or computed dose is 6-10% of protocol specified dose	Difference in prescribed or computed dose is > 10% of protocol specified dose	
Dose Uniform	ity		
Primary or Metastasis	>10% PTV* received >110% of the prescription dose or <93% isodose covers 100% of PTV*	<90% isodose covers 100% of PTV*	
Target Volume			
Primary Site	CTV or PTV margins are less than the protocol specified margins in the absence of anatomic barriers to tumor invasion (CTV) or without written justification (PTV)	GTV does not encompass the dimensions defined by the GTV_Preop or Motion not accounted with the use of proton therapy	
Metastasis	mCTV or mPTV margins are less than the protocol specified margins in the absence of anatomic barriers to tumor invasion (CTV) or without written justification (PTV)	mGTV does not encompass the dimensions of the residual soft tissue metastatic disease or the dimensions of the area defined by persistent MIBG/PET avidity.	
Vertebral Body	Corpus only contoured in the setting of challenging renal constraints	Omission of OTV_VB when the treated region approximates the vertebral column.	
Organs at Risk	<u>,</u>		
Kidney	The OTV_VB may be reduced to corpus only to facilitate meeting renal dose constraints.	Exceeding renal dose constraints and corpus only OTV_VB.	
All Other OARs	OAR deviations will be assessed at the time of final review.	OAR deviations will be assessed at the time of final review.	
Radiotherapy Timing			
Timing	Radiation started more than 80 days after the 2 nd ASCT	Radiation started more than 120 days after the 2 nd ASCT or Radiation started during active SOS, ANC ≤ 500/µL, and/or platelet count < 40,000/ µL.	
* = While the target structure used for planning depending on treatment planning technique, motion management and modality, a PTV is generated for all patients and as such coverage, and uniformity will be			

iation will not be assigned based on PTV coverage, but instead based on CTV/ ITV coverage

Protocol Data Submission

- Please submit the following forms within 1 week following RT:
 - RT1/Proton Dosimetry Summary Form
 - RT-2 Radiotherapy Total Dose Record Form
 - Diagnostic imaging data CT, MRI, MIBG scans performed prior to surgery as well as operative and pathology reports.
 - Digital Radiotherapy Planning Data including:
 - DICOM Planning CT, RT structure, RT dose, and RT plan files.
 - Treatment planning system summary report that includes the monitor unit calculations, beam parameters, calculation algorithm, and volume of interest dose statistics.
 - Any written explanations for why there were deviations from the specified protocol therapy.
 - Smearing radius of compensator used for proton therapy (if applicable) as well as the setup and PTV margin used for each beam with an accompanying rationale.
 - Motion Management reporting form (if applicable)

ANBL2131 Case Downloads

 Example Cases are available for download at: <u>https://www.qarc.org/cog_protocol_resources.htm</u>

