POGO
PEDIATRIC ONCOLOGY GROUP OF ONTARIO
FOR KIDS WITH CANCER
FOR NOW, FOR LIFE.

ANBL 1531

Satellite Educational Training Module

DECEMBER 2022

Presented to: Satellite Clinic Healthcare Providers
Presented by: Dr. Paul Gibson and Christina McCauley

ANBL 1531

The current Phase III trial seeks to improve the event-free survival (EFS) for children with high-risk neuroblastoma through early integration of promising novel targeted therapies: Targeted radiopharmaceutical therapy with ^{131}|-MIBG or the ALK inhibitor, crizotinib.

June 22, 2018

Study Chair: Rochelle Bagatell, MD

Background

Despite recent improvements in outcome for children with newly diagnosed high-risk neuroblastoma (NBL), cure rates remain unsatisfactory.

A substantial number of children with high-risk NBL still progress during induction therapy, show evidence of persistent metastatic disease, or relapse after completion of treatment.

Background

Current therapy treatments:

- Tandem autologous stem cell transplant during consolidation
- Immunotherapy (dinutuximab) during post-consolidation
- ^{131}|-MIBG for the treatment of patients with relapsed and refractory NBL

ANBL1531: Primary Aim

- Determine whether ^{131}|-MIBG improves EFS with acceptable long-term toxicity in patients with MIBG-avid tumours.
- Assess whether the addition of crizotinib to standard multi-modality therapy improves outcomes for newly diagnosed patients with tumours harbouring ALK aberrations.
- Estimate EFS and describe toxicities associated with ^{131}|-MIBG/BuMel transplant.
- Define the outcomes for patients with MIBG non-avid tumours.

^{131}I-MIBG Therapy

The integration of ^{131}I-MIBG earlier in therapy for the high-risk NBL population hopes to address the issue of early disease progression during induction therapy.

Improve early response = Improve overall outcomes

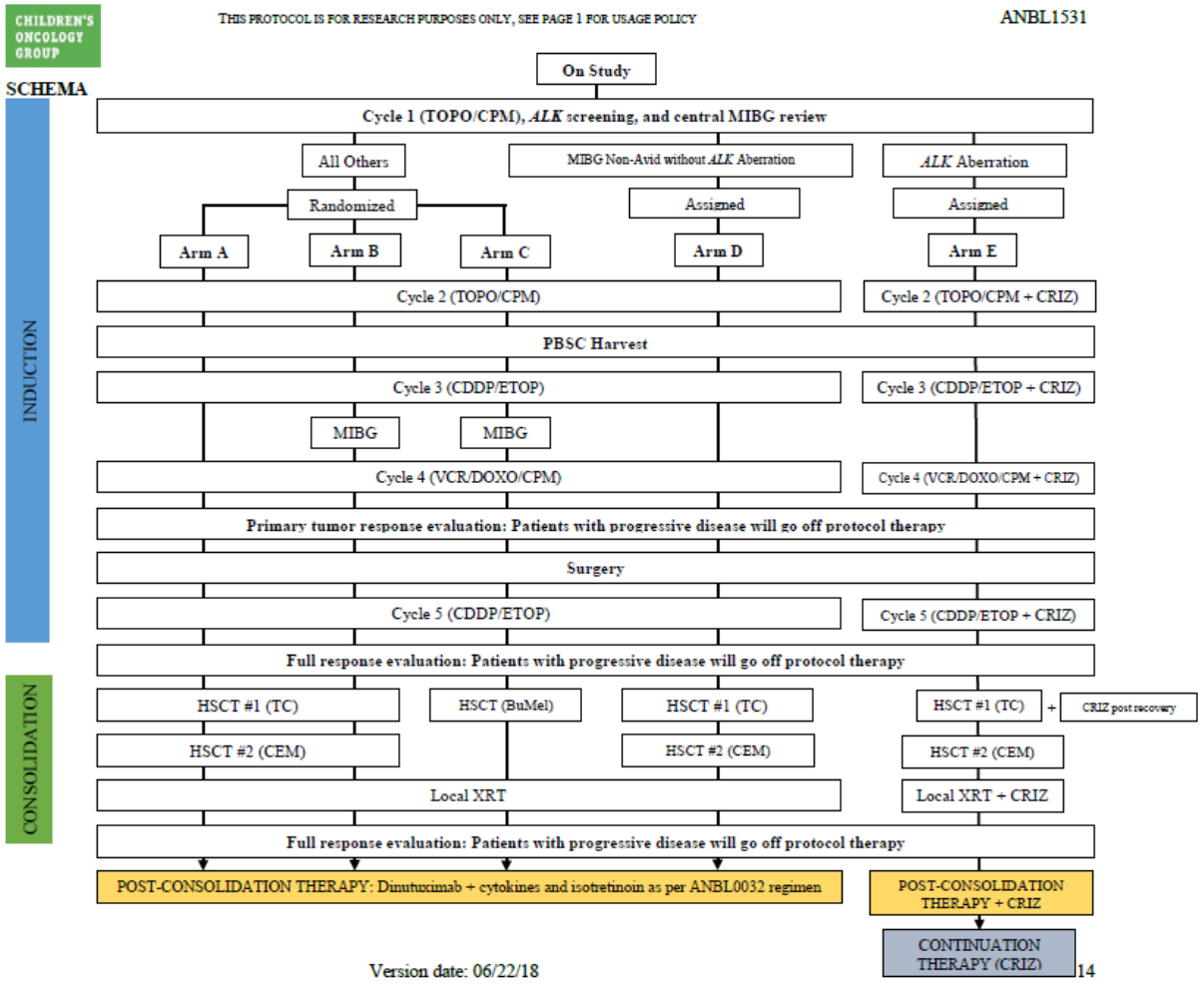
ASCT – Tandem vs. Single

Tandem ASCT is the current COG-recommended consolidation regimen for patients with high-risk neuroblastoma.

Which one's better?

In this study, both the toxicity and EFS associated with single ASCT – Bu/Mel vs. Tandem ASCT – TC/CEM during consolidation will be evaluated.

Study Schema



Induction Therapy:

- 5 cycles of induction chemotherapy
- Surgery
- 131|-MIBG Therapy (Arms B & C only)

Consolidation Therapy:

- 2 transplants + Local radiation
- 1 transplant (Arm C only)

Post-Consolidation Therapy:

- Dinutuximab + cytokines and Isotretinoin

Continuation Therapy:

- Crizotinib (Arm E only)

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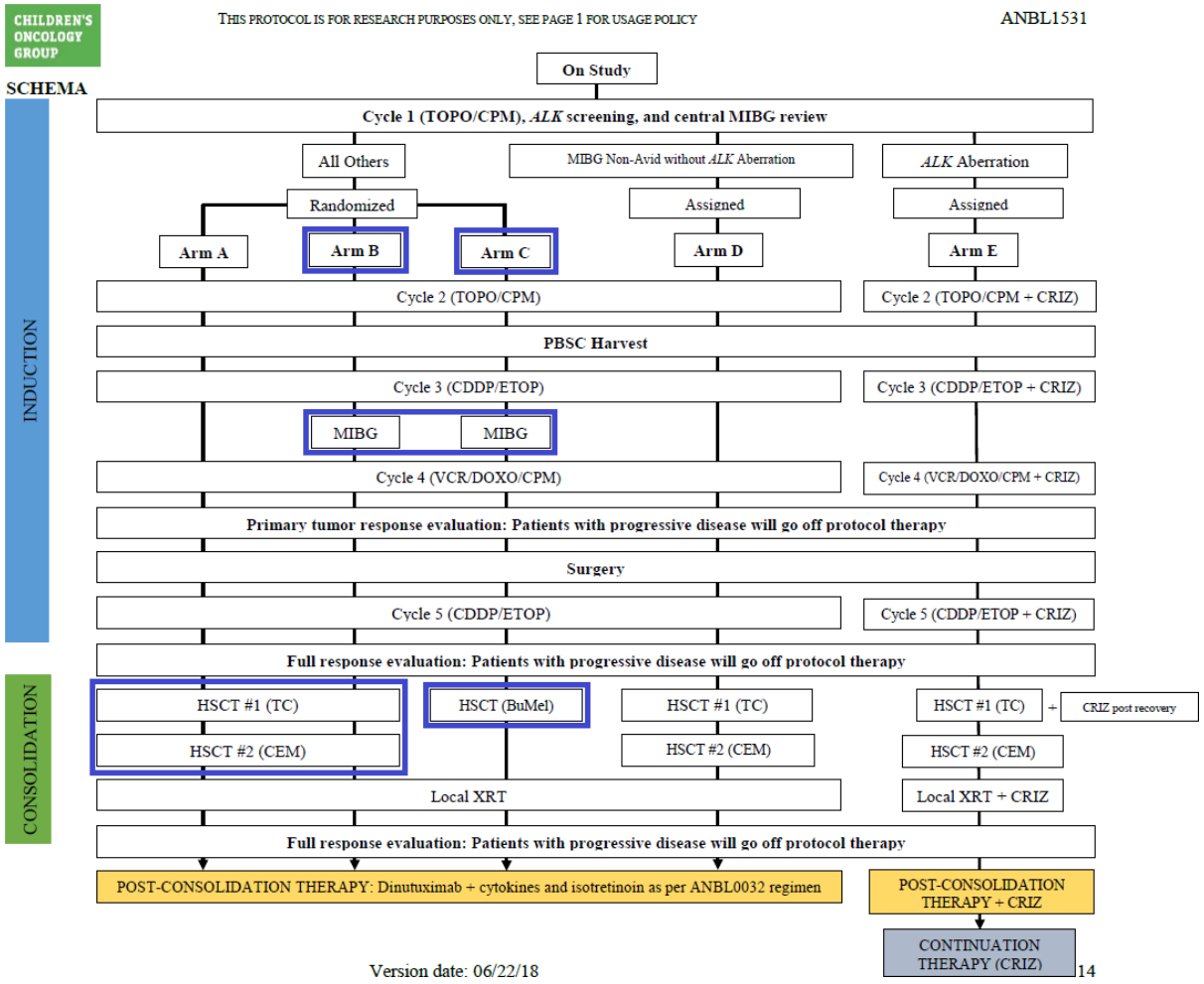
Arm B vs. Arm C



- Both Arms receive ^{131}|-MIBG after the 3rd cycle of Induction.
- Arm B receives tandem ASCT (TC + CEM)
- Arm C receives single ASCT (BuMel)
- – ASCT and ^{131}|-MIBG will be done in the tertiary centres
- DECEMBER 17, 2020: CLOSED “highly unlikely to be shown non-inferior”

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^{131}|-MIBG Induction Therapy

Ht_____cm Wt_____kg BSA_____m^2

Date Due	Date Given	Day	^{131}I-MIBG _____mCi	KI LD ___mg MD ___mg	Myeloid growth factor used: _____ Calc. dose ___		Studies
			Enter calculated dose above and actual dose administered below		Start Date	Stop Date	
		1	____mCi	LD ___mg MD ___mg ___mg ___mg ___mg ___mg			a-h
		2		MD ___mg ___mg ___mg ___mg ___mg ___mg			
		3		MD ___mg ___mg ___mg ___mg ___mg ___mg			
		4		MD ___mg ___mg ___mg ___mg ___mg ___mg			g, h, i
		5		MD ___mg ___mg ___mg ___mg ___mg ___mg			
		6		MD ___mg ___mg ___mg ___mg ___mg ___mg			
		7		MD ___mg ___mg ___mg ___mg ___mg ___mg			
		8		MD _____mg Daily			b-d
		13	PBSCs to be given on Day 13 ± 3 days. See Section 4.15.3.2				b-d
		15					b-d
		22					b-d
		29					b-d
		35	Start Cycle 4 once criteria in Section 4.15.4 are met; continue KI through Day 45				a-d
		45					

- ^{131}|-MIBG will be delivered at an approved centre after the 3rd cycle of induction.
- Weekly CBC/Lytes post-MIBG and PBSC can be done at the Satellite Clinic.

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Things to Consider

A patient is radioactive once ^{131}|-MIBG Therapy has been administered.

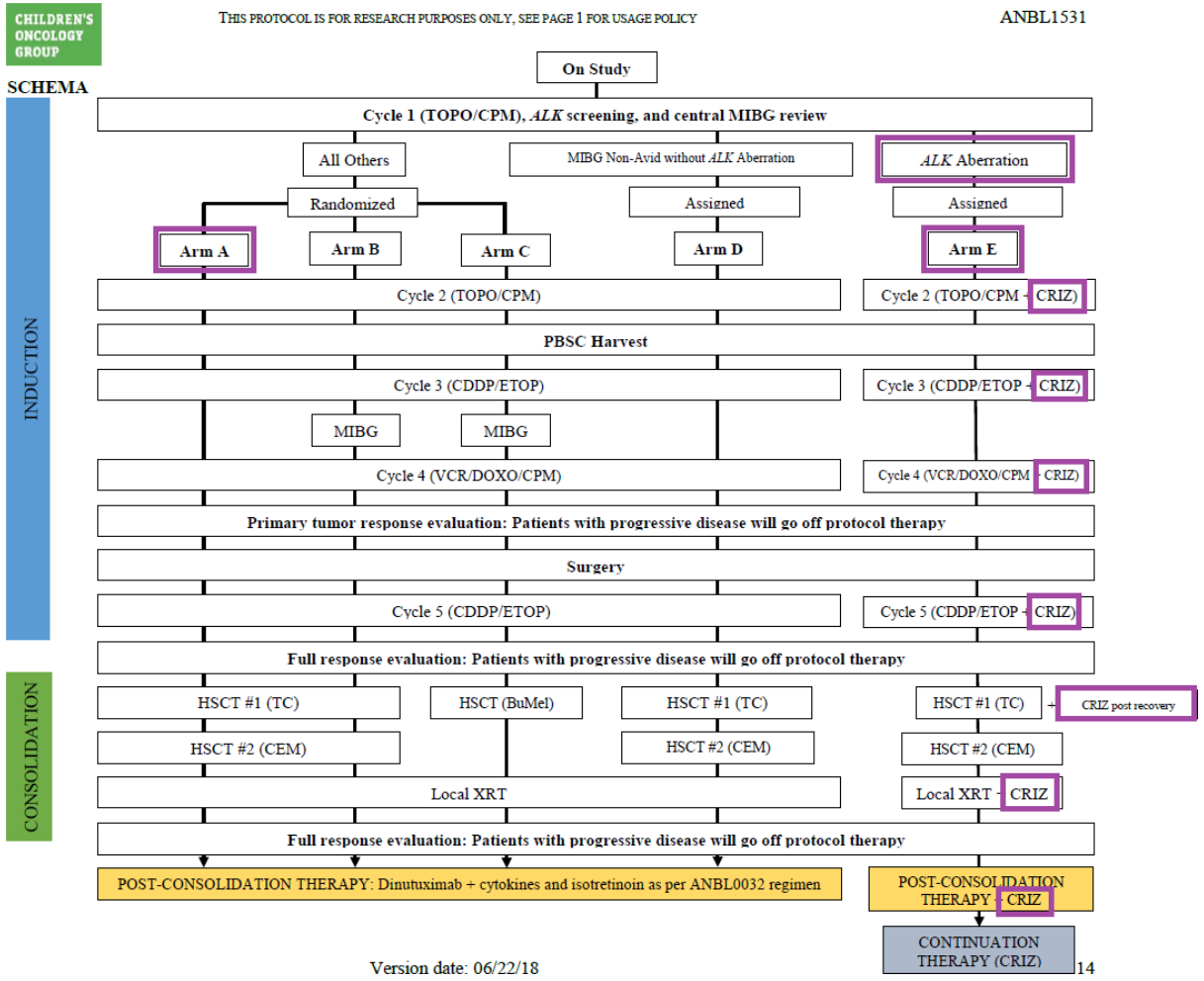
Upon discharge from the tertiary hospital, most of the radioactivity is eliminated; however, small amounts will continue to be eliminated in the urine and feces.

Basic principles for radiation safety should be followed for approximately 14 days post-discharge.

Radiation Safety Principles

- **Distance** – The greater the distance from others, the less radiation they will receive. Therefore, maximize your distance from the patient whenever possible.
- **Time** – Radiation exposure to others depends on how long you remain close to them. Try to minimize the time spent in close contact with the patient.
- **Hygiene** – Good hygiene reduces the possibility that other people will be contaminated with the radioactivity as it leaves the body, particularly good toilet hygiene (i.e. flush toilet twice after each use).

Study Schema

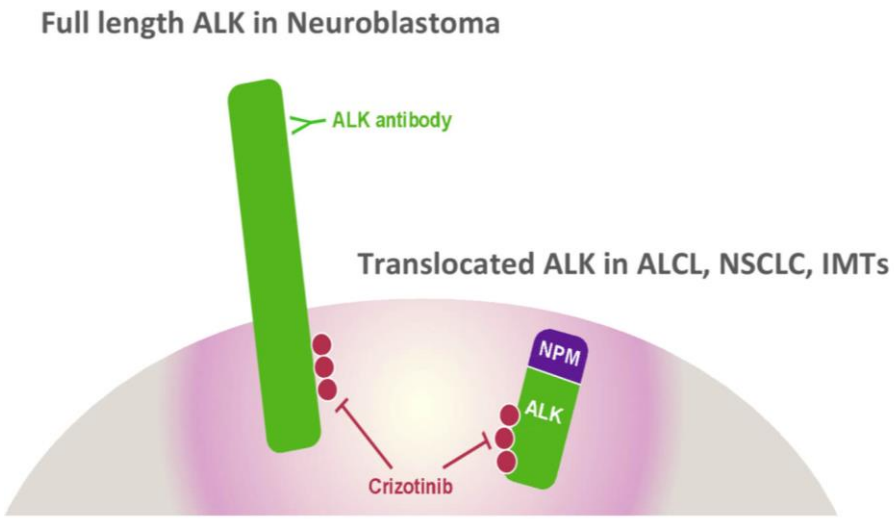


Arm A vs. Arm E: Compares the current COG-recommended regimen with the addition of Crizotinib.

AMMENDMENT 8D: Lorlatinib replaced crizotinib

Lorlatinib

- Lorlatinib is a third-generation oral small molecule inhibitor that targets and binds to the ALK tyrosine kinase, inhibiting its tumorgenesis activity
- Improved binding and CNS penetration vs. crizotinib and compelling pre-clinical data led to the change mid-study



Source: Mano H. Proc Jpn Acad Ser B Phys Biol Sci. May 2015

Lorlatinib Toxicities

Common (>20% of Patients)	Occasional (4-20% of Patients)	Rare
• Edema • Disordered lipids (Triglycerides and cholesterol)	• Anemia • Diarrhea • Fatigue • ALT increase • Lipase increase • Weight Gain • Arthralgia • Cognitive disturbance/memory impairment • Parestesia/neuropathy • Psychiatric Disorders	• A-V Block • Pancreatitis • Hyperglycemia • Hyperlipidemia • CNS Necrosis • Seizure • Hallucination • Suicidal ideation • Pneumonitis • Hypertension

Lorlatinib: When to Administer

- Lorlatinib will be administered Days 1-21 during induction cycles (families should have their study supply with them)
- It should NOT be held for route F&N admissions
- If cycles are delayed beyond 35 days, dose MAY Be modified as per Tertiary Centre
- When it doubt, contact the tertiary!

Summary

After enrollment, patients will receive one cycle of Induction chemotherapy. Subsequent therapy will be based upon MIBG avidity and ALK status.

The majority of treatment in this study will be provided in the Tertiary Centres - ^{131}MIBG Therapy, Induction cycles 3-5, HSCT and radiation.

Satellite Clinic involvement will primarily be to provide supportive care, collect bloodwork and administer chemotherapy in Induction cycles 1 & 2.

All adverse events should be documented and reported to the Tertiary Centre.

Training Complete

Click here for your Certificate of Completion for ANBL 1531.

1. Download your certificate.
2. Enter your name, POGO Satellite Clinic, and the date.
3. Save your Certificate of Completion for your records.
4. Email a copy to Usama Memon (umemon@pogo.ca).

Upon receiving your Certificate of Completion, POGO notifies your affiliated tertiary hospital(s) that your training for ANBL 1531 is complete.

Please consider the environment before printing your Certificate of Completion.

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