High Risk Neuroblastoma in the New Decade: Incorporating Targeted Therapies To Maximize Impact in Current Children’s Oncology Group Trials

Presenters
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Denise Mills, RN(EC), MN, CPHON

COG Educational Track at APHON 2020
Disclosure

- Wendy Fitzgerald and Denise Mills have no industry relationships.
- Off label use of Eflornithine (DFMO) and Crizotinib will be discussed.
COG Disclosure

The information in this presentation is intended for educational purposes only and is solely for the use of the individual nurse learner. This information is not intended as the sole source of guidance in providing Children’s Oncology Group (COG) protocol-directed nursing care, and current COG protocols should always be consulted prior to making patient care decisions for any patient enrolled on a COG protocol. Learners should also be aware that COG protocols are research plans designed to investigate particular study questions, that recommendations for treatment and dosing are made within the context of specific research aims, and that these recommendations are intended only for use within a structured research setting. Although every attempt has been made to assure that the informational content contained herein is as accurate and complete as possible as of the date of presentation, no warranty or representation, express or implied, is made as to the accuracy, reliability, completeness, relevance, or timeliness of this content. This information may not be copied or redistributed in any form, or used for any purpose other than nursing education.
Learning Objectives

The learner will

- identify the current standard of care for high risk neuroblastoma as established through COG trials.
- understand the mechanism of action for the agents being introduced into upfront and relapse trials in contemporary COG: eflornithine, $^{131}$I-MIBG, crizotinib, busulfan in combination with melphalan for auto HCT and dinutuximab.
- appreciate nursing considerations surrounding administration of these agents, highlighting the unique toxicity profiles of dinutuximab and $^{131}$I-MIBG in relation to toxicities.
Neuroblastoma (NBL): Risk Stratification and Prognosis

![Graph showing risk stratification and prognosis of Neuroblastoma (NBL).](image)
Risk Groups in NBL

- New classification within COG:
  - Non high risk > 90% survival
  - High risk < 50% survival
- At diagnosis stratified into prognostic categories with varying outcomes
- Risk group assigned based on:
  - Age
  - Stage
  - Biologic factors

Irwin, Park, 2015
Neuroblastoma

- Tumor of neural crest cell precursors (primordial sympathetic nervous system)
- Most common solid tumor outside of CNS
- > 700 diagnosed/yr (US)
- Prevalence
  - 10% of pediatric cancer diagnoses
  - Median age of diagnosis 19 mos
  - Rare cases of familial inheritance
- Widely variable prognosis
  - African Americans and Native Americans more likely to have HR disease and fatal outcome

Wittle, 2017, Irwin, Park, 2015
COG Risk Stratification

- Historically very complex
- Current goal
  - Simplify
  - Use INRG classification system (goal of less surgical intervention)
- Risk stratification by INRG classification system
  - Combination of clinical, pathologic, and genetic markers to determine prognosis
    - Defines risk as
      - VLR, LR, IMR, HR
### INRG Classification

<table>
<thead>
<tr>
<th>INRG Stage</th>
<th>Age (months)</th>
<th>Histologic Category</th>
<th>Grade of Tumor Differentiation</th>
<th>MYCN</th>
<th>11q Aberration</th>
<th>Ploidy</th>
<th>Pretreatment Risk Group</th>
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<tbody>
<tr>
<td>L1/L2</td>
<td></td>
<td>GN maturing; GNB intermixed</td>
<td>NA</td>
<td>NA</td>
<td>Amp</td>
<td>A</td>
<td>Very low</td>
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<tr>
<td>L1</td>
<td></td>
<td>Any, except GN maturing or GNB intermixed</td>
<td>NA</td>
<td>Amp</td>
<td>K</td>
<td>B</td>
<td>Very low</td>
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<tr>
<td>L2</td>
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<td>Any, except GN maturing or GNB intermixed</td>
<td>NA</td>
<td>Amp</td>
<td>E</td>
<td>G</td>
<td>Intermediate</td>
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<td>L2</td>
<td>≤ 18</td>
<td>GNB nodular; neuroblastoma</td>
<td>NA</td>
<td>Yes</td>
<td>H</td>
<td>D</td>
<td>Low</td>
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<tr>
<td>L2</td>
<td>≥ 18</td>
<td>GNB nodular; neuroblastoma</td>
<td>NA</td>
<td>Yes</td>
<td>F</td>
<td>E</td>
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</tr>
<tr>
<td>M</td>
<td>≤ 18</td>
<td>Hyperdiploid</td>
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<td>&lt; 12</td>
<td>Diploid</td>
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<td>Yes</td>
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<td>Diploid</td>
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<td>MS</td>
<td>Q</td>
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</tr>
<tr>
<td>M</td>
<td>≥ 18</td>
<td>Diploid</td>
<td>NA</td>
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<td>R</td>
<td>Q</td>
<td>High</td>
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<tr>
<td>MS</td>
<td>&lt; 18</td>
<td>Diploid</td>
<td>NA</td>
<td>Yes</td>
<td>Amp</td>
<td>R</td>
<td>High</td>
</tr>
</tbody>
</table>
Neuroblastoma Staging is Complex!

Are you ready to learn more?
COG Nursing Resources on VIMEO

www.vimeo.com/cognursing

The Landscape of Neuroblastoma in COG: Yesterday’s, Today’s & Tomorrow’s Therapies

Joy Bartholomew, APRN
Wendy Fitzgerald RN MSN CPON® PPCNP-BC
Current standard of care for High Risk Neuroblastoma: How did we get here?
High Risk Standard of Care (SOC) Treatment

**INDUCTION**
- Chemotherapy
  - Cytoxan
  - Topotecan
  - Cisplatin
  - Doxorubicin
  - Vincristine
  - Etoposide
  - +/- Surgery

**CONSOLIDATION**
- Tandem Transplants
- Radiation Therapy

**MAINTENANCE**
- Anti-GD2 immunotherapy
- GM-CSF
- Isotretinoin
ANBL0532 Consolidation Therapy Outcomes – Tandem Transplant

Tandem transplant 3 year EFS 74% compared to single transplant 55%

ANBL0032 Maintenance Therapy Outcomes

COURSE 1
- Dinutuximab
- GM-CSF
- ISOT

COURSE 2
- Dinutuximab
- IL-2
- ISOT

COURSE 3
- Dinutuximab
- GM-CSF
- ISOT

COURSE 4
- Dinutuximab
- IL-2
- ISOT

COURSE 5
- Dinutuximab
- GM-CSF
- ISOT

COURSE 6
- ISOT

http://doi.org/10.1056/NEJMoa0911123

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Balancing the Toxicity

- How toxic is this therapy?
  - How can we still try to improve outcomes by adding more therapy but balancing toxicity?
- If we add more therapy, can anything be taken away to make it tolerable/feasible?
- What is showing promise in early phase trials that is being studied now in current open trials?
Improving Outcomes: What can we take away?
### Interleukin-2 in Maintenance (Post-Consolidation)

<table>
<thead>
<tr>
<th>Study</th>
<th>Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>SIOPEN</strong></td>
<td>(randomized trial of dinutuximab beta vs. dinutuximab beta + IL-2)</td>
</tr>
<tr>
<td></td>
<td>• No difference in EFS or 5-yr OS</td>
</tr>
<tr>
<td></td>
<td>• IL-2 had higher rates of:</td>
</tr>
<tr>
<td></td>
<td>- Pain, fever, allergic reaction, CLS</td>
</tr>
<tr>
<td></td>
<td>- Hematologic, neurologic, GI toxicity</td>
</tr>
<tr>
<td></td>
<td>- Inability to complete therapy due to toxicity</td>
</tr>
<tr>
<td><strong>SIOPEN F/U Study</strong></td>
<td>(randomized dinutuximab beta +/- reduced dose IL-2)</td>
</tr>
<tr>
<td></td>
<td>• IL-2 pts again with more pain and fever</td>
</tr>
<tr>
<td></td>
<td>• No significant difference between arms</td>
</tr>
<tr>
<td><strong>SIOPEN Phase 2 Trial</strong></td>
<td>(relapsed/refractory neuroblastoma)</td>
</tr>
<tr>
<td></td>
<td>• Showed similar EFS and OS for pts receiving dinutuximab <strong>with or without</strong> IL-2</td>
</tr>
</tbody>
</table>

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Ladenstein, 2018, Ladenstein, ASCO 2019
COG Memo – August 2019

- Post-Consolidation cycles in ANBL1531 and ANBL17P1
  - Removes IL-2 from therapy (Cycles 2 and 4)
  - GM-CSF will be given during all 5 cycles
Improving outcomes: What else can we add?
What about Metaiodobenzylguanidine ($^{131}$I-MIBG)?

- $^{131}$I-MIBG
  - Concentrates selectively in sympathetic nervous tissue
  - Is taken up in 90% of neuroblastomas
  - Used for diagnostic scans in low dose
  - When conjugated with $^{131}$I becomes targeted therapy

- Available since the 1980s
- Studied in relapse setting

Matthay et al, JCO, 2007
Indications for $^{131}$I-MIBG Therapy

- $^{131}$I-MIBG for the treatment of relapsed or refractory disease has been studied since the late 1980's
- Numerous clinical trials examining $^{131}$I-MIBG as monotherapy or in combination with other agents have been conducted
- Large phase 2 multi-institution study demonstrated overall complete plus partial response rate of 36%
- $^{131}$I-MIBG has been proven to be an effective treatment modality for relapsed or refractory neuroblastoma with minimal toxicities

"Phase II Study on the Effect of Disease Sites, Age, and Prior Therapy on Response to Iodine-131-Metaiodobenzylguanidine Therapy in Refractory Neuroblastoma"

ANBL09P1

Induction: Cycles 1&2
- TOPO
- CPM

Induction: Cycles 3, 4
- CDDP
- ETOP

Induction: Cycle 5
- CPM
- VCR
- DOXO

Induction: MIBG
- CDDP
- ETOP
- 131MIBG + ASCR

PBSC Harvest

Surgery

Induction: Cycles 1&2

Maintenance
- Per ANBL0032

XRT

Consolidation
- Bu/Mel + ASCR

Disease Response
- CR
- VGPR
- PR
- MR
- SD

End of Therapy

Yes

No
ANBL09P1 – findings

- Adding MIBG to front-line induction chemotherapy is financially/clinically feasible
- 3 patients developed SOS with BuMel auto HCT

Weiss, ANR Abstract, 2018
**ALK Inhibitors in High Risk Neuroblastoma**

- **ALK** = Anaplastic Lymphoma Kinase – expressed in embryonal and neonatal brain
- Mutations or amplifications of ALK are “activating” and serve as oncogenes responsible for development and maintenance of tumors.
  - Seen in HR-NBL, NSCLC, ALCL
- 14% HR-NBL tumors with ALK mutation or amplification
- The presence of an ALK Aberration is associated with inferior EFS

Refractory Neuroblastoma
Crizotinib

- In vitro studies show synergistic activity when combined with CPM/Topo
- Early studies in children
  - ADVL0912 – established tolerability and safety with ALCL
  - ANBL12P1:
    - Determination of ALK status in real time
- Studies in conjunction with chemotherapy in patients:
  - ANHL12P1 – added to cytotoxic chemotherapy – risk for thromboembolic events
    - Amended to require prophylactic anticoagulation
    - Continued cases ➔ stopping rules met – arm suspended
  - ADVL1212 – Added to CPM/Topo or VCR/DOXO/DRZ for relapsed solid tumors and ALCL
## Single transplant with Busulfan and Melphalan

<table>
<thead>
<tr>
<th>Study</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>SIOPEN HR-NBL-1</strong></td>
<td>Compared single CEM HCT with BuMel HCT</td>
</tr>
<tr>
<td></td>
<td>Bu/Mel had improved survival</td>
</tr>
<tr>
<td></td>
<td>50% vs. 38% 3-yr EFS</td>
</tr>
<tr>
<td></td>
<td>54% vs. 41% OS</td>
</tr>
<tr>
<td></td>
<td>↓ toxicity <strong>EXCEPT</strong> for ↑ SOS</td>
</tr>
<tr>
<td><strong>ANBL12p1</strong></td>
<td>Pilot Study Using Myeloablative BuMel Consolidation Following Induction Chemo For Pts. With Newly Diagnosed HR-NBL</td>
</tr>
</tbody>
</table>

**Figure 1. EFS and OS for ANBL12P1 (n=146).**

*Journal of Clinical Oncology*

Current Phase 3 ANBL1531 Upfront COG study for HR-NBL: Incorporating what we have learned!
ANBL1531: 5 arm study

New Diagnosis HR-NBL

Cycle 1 Induction while waiting for MIBG scan and ALK mutation testing

- MIBG Positive
  - Randomize
  - Arm A SOC

- MIBG/ALK negative
  - Arm D SOC

- ALK Mutation Positive
  - Arm E SOC + Crizotinib

- Induction MIBG
  - Arm B Induction MIBG

- Single Transplant with BuMel
  - Arm C Induction MIBG Single Transplant with BuMel
**ANBL1531 Overview**

**Study Goal:** to improve outcomes by integrating targeted therapy ($^{131}$I-MIBG, ALK inhibition) early on in the treatment of children with HR-NBL. This protocol builds on the goals of past protocols to:

- Determine whether $^{131}$I-MIBG improves EFS with acceptable long-term toxicity in patients with MIBG-avid tumors.
- Assess whether the addition of crizotinib to standard multi-modality therapy improves outcomes for newly diagnosed patients with tumors harboring ALK aberrations.
- Estimate EFS and describe toxicities with $^{131}$I-MIBG/ BuMel transplant.
- Define the outcomes for patients with MIBG non-avid tumors.
Arms A (Randomized) and D (MIBG negative): Standard of Care

**INDUCTION**
Chemotherapy
Cycles 1 and 2: TOPO/CPM
Peripheral Blood Stem Cell Harvest
Cycle 3: CDDP/ETOP
Cycle 4: VCR/DOXO/CPM

**Consolidation**
Tandem Consolidation Chemotherapy with ASCR XRT

**Post-Consolidation**
5 Cycles of Anti-GD-2 immunotherapy + GM-CSF +Isotretinoin
6th Cycle Isotretinoin

**Surgical Resection**

**Cycle 5: CDDP/ETOP**
Arm B: Induction MIBG

INDUCTION Chemotherapy

Cycles 1 and 2: TOPO/CPM

Peripheral Blood Stem Cell Harvest

Cycle 3: CDDP/ETOP

MIBG

CONSOLIDATION

Tandem Consolidation Chemotherapy with ASCR XRT

POST-CONSOLIDATION

5 Cycles of Anti-GD-2 immunotherapy + GM-CSF + Isotretinoin 6th Cycle Isotretinoin

Cycle 5: CDDP/ETOP

Surgical Resection

CYCLE 4: VCR/DOXO/CPM

C226 _ High Risk Neuroblastoma
**1^{31}I-MIBG Therapy**

- **MIBG IV**
  - Limited to certain hospitals
- **Whole body dosimetry**
- **Side effects based upon radiation effect to bone marrow – ASCR and growth factor**
- **Uptake by thyroid - SSKI**
17 Approved MIBG Therapy Centers: USA and Canada
Planning for MIBG Therapy in ANBL1531?

- Once a patient is enrolled on ANBL1531, non-MIBG sites should identify two preferred MIBG centers for the patient
  - MIBG therapy can only be given at COG approved MIBG centers
  - Enrolling centers that are not transplant centers can send patient to any COG-approved transplant center as long as that center has ANBL1531 open

- To avoid delays in care, the insurance process for MIBG therapy should be started during Cycle 1 for all patients with MIBG-avid disease
ANBL1531 – MIBG Planning Continued

- MIBG coordinator on the study to assist with communication between sites and determine which site is feasible for treatment
- Template insurance letter on protocol website
- Optional Household Material Hardship (HMH) study to be administered by primary site before cycle 2 induction
ANBL1531 – MIBG Guide for Caregivers

Children's Oncology Group

ANBL1531:

\(^{131}\text{I}-\text{MIBG TREATMENT FOR HIGH-RISK NEUROBLASTOMA}\)

A Guide for Parents & Caregivers

Version 1
I-MIBG Side Effects

- GI
  - N&V: usually within the first 24-48 hrs post the infusion
  - Temporary loss of appetite
  - Parotid pain and/or dry mouth
- GU
  - Discomfort from the urinary catheter
- Hematopoietic
  - Low blood counts requiring stem cell support

BOREDOM from having to stay in bed!
The common length of admission is 5 days but may be longer depending on travel.
Arm C: Induction MIBG

**INDUCTION Chemotherapy**
- Cycles 1 and 2: TOPO/CPM
  - Peripheral Blood Stem Cell Harvest
- Cycle 3: CDDP/ETOP

**CYCLE 4: VCR/DOXO/CPM**

**Cycle 5: CDDP/ETOP**

**Surgical Resection**

**CONSOLIDATION**
- Single Consolidation Chemotherapy with BuMel + ASCR XRT

**POST-CONSOLIDATION**
- 5 Cycles of Anti-GD-2 immunotherapy + GM-CSF + Isotretinoin
- 6th Cycle Isotretinoin
BuMel Transplant – Nursing Considerations

- Anti-seizure prophylaxis mandatory
- Observe for signs/symptoms of SOS
  - Anti-SOS prophylaxis with ursodiol recommended
- Busulfan PK studies **REQUIRED** for pts on ARM C
  - Often sent to Seattle Cancer Care Alliance Pharmacokinetics Laboratory
    - Requisition form to accompany samples
Sinusoidal Obstruction Syndrome (SOS)

- **Baltimore Criteria:**
  - Serum total bilirubin > 2mg/dL within 21 days of HCT
  - 2 of the following:
    - Hepatomegaly
    - > 5% weight gain
    - Ascites

- **Modified Seattle Criteria:**
  - Serum total bilirubin > 2mg/dL within 20 days of HSCT
  - Hepatomegaly with RUQ pain
  - > 2% weight gain from baseline

- **European Society for Blood and Marrow Transplantation (EBMT)**
  - Adds unexplained transfusion refractory thrombocytopenia
SOS Management

- Significant mortality with SOS + multi-organ system failure
  - Diuretics
  - Defibrotide
    - Side effect – bleeding
    - Thrombocytopenia – transfuse to maintain platelets > 50,000/microliter
**Arm E: ALK Inhibition - Crizotinib**

**INDUCTION**
- Chemotherapy
  - Cycles 1 and 2: TOPO/CPM + CRIZ
  - Peripheral Blood Stem Cell Harvest
  - Cycle 3: CDDP/ETOP + CRIZ
  - Cycle 4: VCR/DOXO/CPM + CRIZ

**CONSOLIDATION**
- Tandem Consolidation
  - Chemotherapy with ASCR XRT

**POST-CONSOLIDATION**
- 5 Cycles of Anti-GD-2 immunotherapy + GM-CSF + Isotretinoin + CRIZ
  - 6th Cycle Isotretinoin + CRIZ
- Continuation Therapy CRIZ

**Surgical Resection**
Crizotinib – Nursing Considerations

- Investigational product supplied by manufacturer
- Available as liquid or capsule formulation
- Appendix XII of protocol – liquid dosing education for parents:
  - Keep drug in refrigerator
  - OK to use in feeding tube
    - Flushing with water per Appendix XII based on size
  - Do not repeat dose if vomited
- Testing to Factor V Leiden and prothrombin gene mutations recommended for patients with a first degree relative with h/o TE event prior to age 40 yrs
  - Recommend Anticoagulation ppx if mutation associated with significant risk identified
- Discourage dexamethasone as antiemetic for less emetogenic cycles
- QTc prolonging agents and CYP3A active discouraged
Crizotinib (Arm E) – Nursing Considerations

- Crizotinib should start by cycle 2 or 3 at the latest
- Crizotinib timing:
  - Hold 48 hours prior to PBSC collection. Continue to hold during the collection
  - Hold on admission for HCT #1 and HCT#2
    - Restart post-HCT once ANC >750, PLT >50K and stable organ function
  - Continue Crizotinib during XRT and during Immunotherapy for 18 month course post HCT #2.
- Patient Safety: Wallet Card

![Crizotinib Wallet Card](image)
Crizotinib Side Effects

- **GI**
  - Increase in transaminases
  - N&V/diarrhea/constipation
  - Decreased appetite/taste disturbance

- **CNS**
  - Visual changes (shadows, streaking)
  - Dizziness
  - Neuropathy

- **Neutropenia**

- Rare – Thromboembolic event

- Dose modifications outlined in protocol

Illustration by Aimee Ermel, 2013
ANBL1531 Clinical Trial Summary for Families

ANBL1531: A Phase 3 Study of 131I-Metaiodobenzylguanidine (131I-MIBG) or Crizotinib Added to Standard Therapy for Children with Newly Diagnosed High-Risk Neuroblastoma

Introduction

This clinical trial summary is about the Children’s Oncology Group study ANBL1531. It tells who is eligible and gives basic information about the study. More details about the study are in the consent form. You can get this from your oncologist.

ANBL1531 is a Phase 3 clinical trial. A trial is another word for a study. This study (clinical trial) is a therapeutic clinical trial. The purpose of a Phase III trial is to learn if a drug or therapy known to work in treating a certain type of cancer is better than the standard treatment. For example: better cure rates, longer control of disease, fewer or less serious side effects, or fewer days in the hospital.
COG Nursing Resources on VIMEO

www.vimeo.com/cognursing

The Landscape of Neuroblastoma in COG: Yesterday’s, Today’s & Tomorrow’s Therapies

Joy Bartholomew, APRN
Wendy Fitzgerald RN MSN CPON® PPCNP-BC
Improving Outcomes: A Glimpse at the Future
Eflornithine (DFMO)

- Inhibitor of ODC1 protein which is a transcriptional target gene of MYCN
- Patients without MYCN amplification have hyperactive MYC signaling.
- FDA approved for Typanosomiasis “sleeping sickness” encephalitis in Africa
- Well tolerated in pediatric trials
  - Phase 1 trial as a single agent
  - NANT 1201 with celecoxib, CPM and Topo
  - Multi-institution study adding as maintenance
- Oral medication
  - Few adverse events
  - Mild transaminitis
- Monitor for ototoxicity

Hogarty, M, ANR abstract 2018; Saulnier Sholler, PLoS, 2015; Saulnier Sholler, Scientific Reports, 2018
ANBL1821 Goal

To determine if adding difluoromehylornithine (DFMO), Eflornithine) to a chemo-immunotherapy backbone (dinutuximab, irinotecan and temozolomide) has improved response rate compared to dinutuximab, irinotecan and temozolomide in patients with relapsed or refractory neuroblastoma and therefore is a therapeutic regimen worthy of further testing in patients with newly diagnosed high-risk neuroblastoma.
ANBL1821

On Study Randomization

Regimen A
Irinotecan/Temozolomide/
Dinutuximab/GM-CSF

2 cycles of therapy

Disease Evaluation

No PD

2 cycles of therapy

PD

2 cycles of therapy

No PD

2 cycles of therapy

CR, PR, MR

Continue therapy for 11 additional cycles
(17 total)

Regimen B
Irinotecan/Temozolomide/
Dinutuximab/GM-CSF/DFMO

2 cycles of therapy

Disease Evaluation

No PD

2 cycles of therapy

PD

2 cycles of therapy

No PD

2 cycles of therapy

CR, PR, MR

Continue therapy for 11 additional cycles
(17 total)

PD

No PD

2 cycles of therapy

SD or PD

Off protocol therapy

The world's childhood cancer experts
Eflornine (DFMO) – Nursing Implications

- Supplied as powdered drug
- Parents to dissolve in sterile water based in drug dose (see table in Appendix XII)
  - Use gloves
  - Pregnant women should not prepare
  - Must be administered within 30 minutes of being dissolved
- May add juice for flavor.
  - Avoid grapefruit, orange and tomato juice
  - Prefer lemonade, apple, cranberry and grape juice
ANBL1821 – Nursing Implications

- Concomitant Therapy
  - The use of dexamethasone as an antiemetic therapy is **not** permitted
- Patients **must** receive pneumocystis prophylaxis during study therapy
- Cefixime should be started 2 days prior to the first dose of irinotecan and continued for a total of 10 days in each cycle

![Dexamethasone](image)
Dinutuximab in combination with chemotherapy

- **ANBL1221**
  - Relapse patients randomized to 1 of 2 arms:
    - Irinotecan-temozolomide-temsirolimus or
    - Irinotecan-temozolomide-dinutuximab
Dinutuximab Arm Superior

A. PFS by Regimen

Number at risk (Censored)

ITT-GN
17 (0)
14 (0)
13 (0)
10 (0)
0 (0)

ITT-TEM
18 (0)
6 (1)
3 (2)
0 (3)
0 (3)
0 (3)

p = 0.0003

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Mody, R, 2020
ANBL17P1 – Now Complete

**INDUCTION**
Chemotherapy

- Cycles 1 and 2: TOPO/CPM
- Peripheral Blood Stem Cell Harvest
- Cycle 3: CDDP/ETOP + Dinutuximab/GM-CSF
- Cycle 4: VCR/DOXO/CPM + Dinutuximab/GM-CSF

**CONSOLIDATION**

- Cycle 5: CDDP/ETOP + Dinutuximab/GM-CSF
- Tandem Consolidation Chemotherapy with ASCR XRT

**POST-CONSOLIDATION**

- Surgical Resection
- 5 Cycles of Anti-GD-2 immunotherapy + GM-CSF + Isotretinoin
- 6th Cycle Isotretinoin
ANBL17P1 – Nursing Implications

- What is the challenge of administering dinutuximab in conjunction with supportive hydration for chemotherapy?
- Furosemide discouraged except for respiratory compromise
- Monitor fluid status very carefully (BID weights)
- Close observations and physical exams
- Daily serum electrolytes
- Strict I&O
Summary

- High risk neuroblastoma continues to be a challenge to cure
- State of the art therapy for high risk neuroblastoma is lengthy and toxic
- New therapies entering up-front neuroblastoma trials include targeted agents including ALK inhibitors, anti-GD2 antibodies and $^{131}$I-MIBG.
- Future considerations for therapy include DFMO
## Abbreviations

<table>
<thead>
<tr>
<th>FULL TERM</th>
<th>ABBREVIATION</th>
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<tbody>
<tr>
<td>131Iodine</td>
<td>131I</td>
</tr>
<tr>
<td>Anaplastic large cell lymphoma</td>
<td>ALCL</td>
</tr>
<tr>
<td>Anaplastic lymphoma kinase</td>
<td>ALK</td>
</tr>
<tr>
<td>Association Pediatric Hematology Oncology Nurses</td>
<td>APHON</td>
</tr>
<tr>
<td>Autologous</td>
<td>auto</td>
</tr>
<tr>
<td>Autologous Stem Cell Rescue</td>
<td>ASCR</td>
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<tr>
<td>Busulfan</td>
<td>BU</td>
</tr>
<tr>
<td>Busulfan/Melphalan</td>
<td>Bu/Mel</td>
</tr>
<tr>
<td>Capillary Leak Syndrome</td>
<td>CLS</td>
</tr>
<tr>
<td>Central nervous system</td>
<td>CNS</td>
</tr>
<tr>
<td>Children's Oncology Group</td>
<td>COG</td>
</tr>
<tr>
<td>Cisplatin</td>
<td>CDDP</td>
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</table>

The world's childhood cancer experts
## Abbreviations

<table>
<thead>
<tr>
<th>FULL TERM</th>
<th>ABBREVIATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete remission</td>
<td>CR</td>
</tr>
<tr>
<td>Crizotinib</td>
<td>Criz</td>
</tr>
<tr>
<td>Cyclophosphamide</td>
<td>CPM</td>
</tr>
<tr>
<td>Cyclophosphamide/Etoposide/Melphalan</td>
<td>CEM</td>
</tr>
<tr>
<td>Dexrazoxane</td>
<td>DRZ</td>
</tr>
<tr>
<td>Difluoromethylornithine</td>
<td>DFMO</td>
</tr>
<tr>
<td>Disialoganglioside</td>
<td>GD2</td>
</tr>
<tr>
<td>Doxorubicin</td>
<td>DOXO</td>
</tr>
<tr>
<td>Etoposide</td>
<td>ETOP or VP</td>
</tr>
<tr>
<td>European Bone Marrow Transplant</td>
<td>EBMT</td>
</tr>
<tr>
<td>Event free survival</td>
<td>EFS</td>
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</table>
## Abbreviations

<table>
<thead>
<tr>
<th>FULL TERM</th>
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<tbody>
<tr>
<td>Federal Drug Agency</td>
<td>FDA</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>GI</td>
</tr>
<tr>
<td>Genitourinary</td>
<td>GU</td>
</tr>
<tr>
<td>Granulocyte macrophage- colony stimulating factor</td>
<td>GMCSF or GM-CSF</td>
</tr>
<tr>
<td>Hematocrit</td>
<td>HCT</td>
</tr>
<tr>
<td>High risk</td>
<td>HR</td>
</tr>
<tr>
<td>High Risk-Neuroblastoma</td>
<td>HR-NBL</td>
</tr>
<tr>
<td>Hours</td>
<td>hrs</td>
</tr>
<tr>
<td>Household Material Hardship</td>
<td>HMH</td>
</tr>
<tr>
<td>Intake and output</td>
<td>I&amp;O</td>
</tr>
<tr>
<td>Interleukin-2</td>
<td>IL-2</td>
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<thead>
<tr>
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<tbody>
<tr>
<td>Intermediate risk</td>
<td>IMR</td>
</tr>
<tr>
<td>International Neuroblastoma Group</td>
<td>INRG</td>
</tr>
<tr>
<td>International Society of Paediatric Oncology European Neuroblastoma</td>
<td>SIOPEN</td>
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<tr>
<td>Intravenous</td>
<td>IV</td>
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<tr>
<td>Isotretinoin</td>
<td>ISOT</td>
</tr>
<tr>
<td>Low risk</td>
<td>LR</td>
</tr>
<tr>
<td>Medium Response</td>
<td>MR</td>
</tr>
<tr>
<td>Melphalan</td>
<td>Melph</td>
</tr>
<tr>
<td>Metaiodobenzylguanidine</td>
<td>131I-MIBG</td>
</tr>
<tr>
<td>Month(s)</td>
<td>mo(s)</td>
</tr>
<tr>
<td>Nausea and vomiting</td>
<td>N&amp;V or N/V</td>
</tr>
</tbody>
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<table>
<thead>
<tr>
<th>FULL TERM</th>
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<tbody>
<tr>
<td>Neuroblastoma</td>
<td>NBL</td>
</tr>
<tr>
<td>New Advances in Neuroblastoma Therapy</td>
<td>NANT</td>
</tr>
<tr>
<td>Overall survival</td>
<td>OS</td>
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<tr>
<td>Partial remission or response</td>
<td>PR</td>
</tr>
<tr>
<td>Peripheral blood stem cell</td>
<td>PBSCT</td>
</tr>
<tr>
<td>Pharmacokinetics</td>
<td>PK</td>
</tr>
<tr>
<td>Prophylaxis</td>
<td>ppx</td>
</tr>
<tr>
<td>Radiation therapy</td>
<td>XRT</td>
</tr>
<tr>
<td>Right upper quadrant</td>
<td>RUQ</td>
</tr>
<tr>
<td>Sinusoidal obstruction syndrome</td>
<td>SOS</td>
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<tr>
<td>Stable disease</td>
<td>SD</td>
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<thead>
<tr>
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<tbody>
<tr>
<td>Standard of care</td>
<td>SOC</td>
</tr>
<tr>
<td>Super Saturated Potassium Iodide</td>
<td>SSKI</td>
</tr>
<tr>
<td>Thromboembolycie</td>
<td>TE</td>
</tr>
<tr>
<td>Topotecan</td>
<td>TOPO</td>
</tr>
<tr>
<td>Two times/day</td>
<td>BID</td>
</tr>
<tr>
<td>United States of America</td>
<td>USA or US</td>
</tr>
<tr>
<td>Versus</td>
<td>vs.</td>
</tr>
<tr>
<td>Very good partial remission</td>
<td>VGPR</td>
</tr>
<tr>
<td>Very Low-Low Risk</td>
<td>VL-LR</td>
</tr>
<tr>
<td>Vincristine</td>
<td>VCR</td>
</tr>
<tr>
<td>Week(s)</td>
<td>wk(s)</td>
</tr>
<tr>
<td>Year(s)</td>
<td>yr(s)</td>
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