Disclosure Information:

a) Moderators/panelists/presenters: Dr. Sophia Bornstein has nothing to disclose.

b) Planning Committee: Drs. Linda Stork, Suman Malempati and Michael Recht have nothing to disclose.

Learning Objectives:
1. Pathophysiology and workup
2. Studies
3. Radiation oncology techniques
Patient History

History of Present Illness:
- 2 year old female
- R hip pain
- R eye swelling and bruising
- Flu like symptoms—fever, vomiting, anorexia, lethargy
- Abdominal pain
- Seen at Providence and found to be anemic (Hgb 6.5) with abnormal CT findings
- Admitted to OHSU

PMH: none
PSH: none
Immunizations: up to date
Medications: none
Allergies: NKDA
FHx: none
Social History: from Hood River, parents divorced and have joint custody
ROS: negative other than HPI
Patient LS
Physical Exam

Ht 86cm (41%), Wt 10.5kg (7%), BP 89/65, HR 147, T 37.3 °C, RR 40, SpO2 100%

- General: Sleeping, NAD
- HEENT: Eyes PERRL, significant bruising around right eye. Unable to palpate head due to positioning and irritability. Nose: normal. Mouth: Normal pharynx, mucosa and teeth.
- Neck: Supple
- Lungs: chest clear to auscultation bilaterally, respirations even and unlabored.
- Heart: regular rate and rhythm, no extra sounds.
- Abdomen: L abdominal fullness. BS normal. Pt guards abdomen and is fussy during exam, unable to palpate mass, very limited exam.
- Musculoskeletal: well developed, good perfusion.
- Skin: + bruising to face, as above. No petechiae.
Labs

• CMP: normal other than AST of 111 24-47 U/L

• CBC with Differential
  – White Cell Count 8.8 5.0 - 13.2 k/cu mm
  – Hemoglobin 6.5 11.5 - 13.5 g/dl
  – Hematocrit 19.2 34.0 - 40.0 %
  – Platelet Count 115 150 - 420 k/cu mm

• Urine HVA (MG/GCR) 466 (H) < 43 mg/g

• Urine VMA (MG/GCR) 171 (H) < 28 mg/g
Aspirate smear
Paraffin embedded clot section
Paraffin embedded bone marrow bx
Work-up

• Neuroblastoma, r/o other SRBCT of childhood (Ewings)
• Synaptophysin, chromogranin (CD56, NSE): positive in neuroblastoma, can also be positive in Ewings/PNET and some rhabdomyosarcomas may pick up synapto
• Neuroblastoma is CD99 negative
• Consider: CK, desmin, myogenin, WT-1, CD45, ect
Cytogenetics

• Patient: 11/20 metaphase cells examined comprised a single abnormal clone, most with an isochromosome 1q, and additional material of unknown origin on chromosomes 2p and 13q; all cells had tens of double minute chromosomes, which stained positive for N-MYC by FISH (below). Nine cells appeared normal female.

• FISH was performed with the N-MYC probe set, as listed below. 89% of cells had >10 signals for N-MYC and two for the CEP2, consistent with N-MYC amplification, which was observed on available metaphases as hybridizing to double minute chromosomes.

• Poor prognosis: N-myc amplification, -1p, +17q
• Good prognosis: age <1 year, hyperdiploidy
Imaging

- CT Head 9/7/12
- CT Chest Abdomen Pelvis 9/8/12
- MIBG Scan 9/13/12
Neuroblastoma: Head CT 9/7/12
CAP CT 9/8/12
MIBG scan 9/13/12
Treatment plan per A3973

- Induction
- Cycle 1-6: 9/12/12 - 1/15/13

### Induction

- Topotecan 0.75 mg/m² + Cyclophosphamide 250 mg/m² Day 0-4
- Local XRT
- 13-cis-retinoic acid

### Maintenance Therapy

- Eligible for Myeloablative Therapy
- Consolidation Myeloablative therapy with stem cell support

### Induction

- Cycles 1, 2, 4, 6
  - Cyclophosphamide: 2.1 g/m² IV with MESNA over 6 hours Day 0, 1 (total dose 4.2 g/m²)
  - Doxorubicin: 25 mg/m² IV over 24 hours Day 0-2 (total dose 75 mg/m²)
  - Vincristine: 0.67 mg/m² IV over 24 hours Day 0-2 (total dose 2 mg/m²)
- Cycles 3, 5
  - Cisplatin: 50 mg/m² IV over 1 hour Day 0-3 (total dose 200 mg/m²)
  - Etoposide: 200 mg/m² IV over 2 hours Day 0-2 (total dose 600 mg/m²)

### Induction

- Harvest
- Surgery

If Patient has CR, VGPR, PR*
Treatment plan per A3973

• Restaging: CT Chest Abdomen Pelvis 1/31/13 (pre-op)
• MIBG scan 2/21/13 (pre-BMT)
MIBG scan 2/21/13
Treatment plan per A3973

  – Per the op note, estimated 60% resected
  – Surgical Pathology 2/11/13
Marrow

- **Final Pathologic Diagnosis:**
  - Peripheral blood:
    - Normocytic anemia
  - Right and left bone marrow aspirate, clots, and core biopsies:
    - Mildly hypocellular bone marrow (80 - 85%) with trilineage hematopoiesis
    - Focal involvement by neuroblastoma (see note)

- Note: There are rare single cells and small groups of 2 or 3 cells that stain with synaptophysin and chromogranin consistent with focal residual involvement by neuroblastoma. Overall, these cells comprise much less than 1% of the overall cellularity.

- All twenty metaphase cells examined appeared normal female.

- FISH was performed with the N-MYC probe set, as listed below. All results were within the normal limits established by our laboratory.
Treatment plan per A3973

- Seen in Radiation Oncology Day 26 after transplant.
- Was doing will since DC: eating, talking. Still requiring RBC and platelet transfusions.
- Radiation Treatment: 4/8-4/24/13 (to be discussed later)
Epidemiology

• Third most common childhood cancer (8-10%), after leukemia/lymphoma and brain tumors
  – Most common extracranial solid malignancy of childhood
  – Most common malignancy of infants (1/2 of all cases)

• Incidence 9/1,000,000 -> ~650 children per year in U.S.
  – Boys>Girls (slightly)
  – Responsible for 15% childhood cancer mortality

• Median age at diagnosis 17-22 months
  – 75% <2 years
  – 90% <5 years

• Majority is sporadic
  – 1-2% autosomal dominant, present earlier
  – Hirschsprung Dz, congenital central hypoventilation syndrome, NF
  – Exposures: fetal hydantoin syndrome (from maternal AEDs); no great data
A spectrum of tumors arising from primitive sympathetic ganglion cells

**Neural crest:**
Multipotent migratory cell population that gives rise to melanocytes, craniofacial cartilage, bone, smooth muscle, peripheral and enteric neurons, glia
Neuroblastoma Sites

- Adrenal gland 40%
- Abdominal ganglia 25%
- Thoracic ganglia 15% (infants)
- Cervical ganglia 5%
- Pelvic ganglia 5%

Abdomen primary in 50-80%

Paraspinal ganglia in the low thoracic, abdominal 30% [26%, 32%], or pelvic chains 2% [3%, 2.5%]

Other 12% [13%, 9%]

Cervical sympathetic ganglion 1% [4%, 0.5%]

Posterior mediastinum 19% [29%, 14%]

Adrenal gland 35% [25%, 40%]

Metastases: Bone, Bone marrow, Liver, Lymph nodes, Skin

Halperin
Presentation

- Broad spectrum of clinical presentations and paraneoplastic syndromes
- "Quirky natural history" from benign localized lesions to spontaneous remission of metastatic disease to aggressive widely disseminated tumors
- Signs: abdominal mass, swelling or pain, diarrhea, constipation, unilateral neck mass with Horner's, FTT (constitutional sx)
- Skin mets: blueberry muffin sign (reddish-purple raised lesions)
- Bone mets: skull and orbit (bone pain, periorbital swelling/ecchymosis (raccoon eyes)
Presentation

• Metastatic 60-75% at presentation
  – 50% bone, 35% LN; lung mets are rare
  – "Favorable" typically to liver, skin
  – "Unfavorable" typically to bone marrow, bones (orbits, skull)

• Paraneoplastic syndromes (rare)
  – Vasoactive intestinal polypeptide secretion: intractable diarrhea
  – Opsoclonus-myoclonus-ataxia syndrome (1-3%): dancing eye, rhythmic jerking, ataxia

• Spinal cord compression (7-15%)

• catecholamines VMA or HVA are present in urine 90% of patients
  – Normal sympathetic tissues secrete VMA/HVA
  – VMA or HVA have screening no value (screening studies in Japan, Germany and Canada show increased detection of clinically irrelevant NB that would’ve regressed)
Workup

- **History:** diarrhea/constipation, ataxia
- **Physical exam:** HEENT, Neuro, Abdomen, Skin
- **Labs:** urine catecholamines (epinephrine, norepinephrine, VMA and HVA)
- **Imaging:**
  - **Primary:** abdominal ultrasound, CT/MRI to define extent
  - **Calcifications, hemorrhage**
Workup

Mets:

- Bone scan
  - MIBG scan (meta-iodobenzylguanidine, chemical analog of norepinephrine)
  - Technetium if tumor doesn’t take up MIBG (10%)
  - PET: emerging role

- Bone marrow biopsy
  - BM+ in 70-90% with metastatic disease
  - bilateral BMBx with 4 adequate cores needed to exclude involvement
Pathology

- **Primitive sympathetic ganglion cells (least to most differentiated)**
  - Neuroblastoma (~85%)
    - Small round blue cells
    - (DDx: NHL, Ewings, Rhabdo, PNET)
    - Homer-Wright pseudorosettes (neuroblasts with eosinophilic centers) 15-50%
  
  - Ganglioneuroblastoma (~10%)
  
- Ganglieneuroma (~1%) - considered a benign tumor
Pathology

- **Markers:**
  - IHC: neuron-specific enolase, synaptophysin, chromogranin A, neuronal filaments, S100, NB84
  - Molecular: More aggressive
    - MYCN (N-Myc) gene amplification (5-400x) in ~30%
      - Infants 4S with MYCN 3-year OS <50% vs. without MYCN >90%
    - Chromosomal deletions 1p and 11q
    - Chromosomal gains 17q
    - Increased telomerase
  - Molecular: Less aggressive:
    - Better prognosis/chemo response if hyperploidy. 3-year OS 94% for hyperploid vs 55% diploid
    - Can counteract MYCN amplification in low-stage tumors
Staging

(first consensus system, relies on surgical staging)

International Neuroblastoma Staging System (INSS)

• **Stage 1** - Localized tumor with GTR (can have microscopic+ margins)
  – Representative ipsilateral lymph nodes negative microscopically (nodes attached and removed with the primary tumor may be positive)

• **Stage 2A** - Localized tumor with STR
  – Representative ipsilateral nonadherent lymph nodes negative microscopically

• **Stage 2B** - Localized tumor GTR or STR
  – Positive nonadherent ipsilateral lymph nodes.
  – Enlarged contralateral lymph nodes negative microscopically

• **Stage 3** - Unresectable tumor
  – Infiltrating across the midline with or without regional lymph node involvement.
  – Unilateral tumor with contralateral regional lymph node involvement. Midline tumor with bilateral extension by infiltration (unresectable) or by regional lymph node involvement

• **Stage 4S** - Localized primary tumor (Primary fits Stage 1, 2A or 2B)
  – Dissemination limited to liver, skin and/or bone marrow (*in infants <1 year of age*)

• **Stage 4** - Dissemination of tumor to distant lymph nodes, bone, bone marrow, liver, and/or other organs (but not stage 4S)
## Risk Grouping

### Table 6.5 A: Children’s Oncology Group Neuroblastoma Risk Groups for Treatment

<table>
<thead>
<tr>
<th>International neuroblastoma staging system</th>
<th>Age (Days)</th>
<th>MYCN</th>
<th>Histology</th>
<th>Ploidy</th>
<th>Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Any</td>
<td>Any</td>
<td>Any</td>
<td>Any</td>
<td>Low</td>
</tr>
<tr>
<td>2/2B</td>
<td>Any</td>
<td>Nonamplified</td>
<td>Any</td>
<td>Any</td>
<td>Low</td>
</tr>
<tr>
<td></td>
<td>Any</td>
<td>Amplified</td>
<td>Any</td>
<td>Any</td>
<td>High</td>
</tr>
<tr>
<td>3</td>
<td>&lt;547</td>
<td>Nonamplified</td>
<td>Any</td>
<td>Any</td>
<td>Intermediate</td>
</tr>
<tr>
<td></td>
<td>≥547</td>
<td>Amplified</td>
<td>Favorable</td>
<td>Any</td>
<td>High</td>
</tr>
<tr>
<td></td>
<td>&gt;365 &lt; 547</td>
<td>Nonamplified</td>
<td>Unfavorable</td>
<td>Any</td>
<td>Intermediate</td>
</tr>
<tr>
<td>4</td>
<td>&lt;547</td>
<td>Nonamplified</td>
<td>Any</td>
<td>Any</td>
<td>Intermediate</td>
</tr>
<tr>
<td></td>
<td>Any</td>
<td>Amplified</td>
<td>Any</td>
<td>Any</td>
<td>Intermediate</td>
</tr>
<tr>
<td>4S</td>
<td>&lt;365</td>
<td>Nonamplified</td>
<td>Favorable</td>
<td>DI &gt; 1</td>
<td>Low</td>
</tr>
<tr>
<td></td>
<td>&lt;365</td>
<td>Nonamplified</td>
<td>Favorable</td>
<td>DI = 1</td>
<td>Intermediate</td>
</tr>
<tr>
<td></td>
<td>&lt;365</td>
<td>Nonamplified</td>
<td>Unfavorable</td>
<td>Any</td>
<td>Intermediate</td>
</tr>
<tr>
<td></td>
<td>&lt;365</td>
<td>Amplified</td>
<td>Any</td>
<td>Any</td>
<td>High</td>
</tr>
</tbody>
</table>

Aberrations of 1p and 11q may be additionally used to adjust therapy intensity, but do not change intermediate-risk patients to high-risk group for outcome.

DI, DNA index.

**Histology (Shimada classification: favorable or unfavorable):** Favorable: stroma-rich, young age, well differentiation, low mitotic/karyorrhectic (fragmentation of cellular nuclei that usually symbolizes cell death) index, non nodular

**SANDS:** Stage, Age, N-Myc, DNA ploidy, Shimada classification
55% of pts are high risk at diagnosis vs 30% low risk

3 yr OS
Low: 95-100%
Int: 75-98%
High: <30%
Treatment Overview

• **Low-risk:**
  – Surgery alone; GTR not required but is curative. No post-op RT or chemo.
  – Chemotherapy for persistence or recurrence (carbo/etoposide or carbo/cyclophosphamide/doxorubicin)
  – RT minor role (emergencies, unresectable, refractory/recurrent)

• **Low-risk 4S:**
  – These patients do very well (>90% 5 yr OS); spontaneous regression
  – Resection doesn’t influence survival here
  – Supportive care, chemo+-/RT for symptoms or emergencies

• **Intermediate-risk:**
  – Surgery → chemotherapy +/- more surgery if needed (GTR better)
  – Chemotherapy: Short course of chemotherapy (4 courses) if favorable histology. Longer course (8 courses) if unfavorable histology.
  – RT minor role

RT 911: SVC, cord compression, abd compartment syndrome, respiratory distress from hepatomegaly
Treatment Overview

• **High-risk:** *where radiation is used most often*
  
  – Three phases
    
    1. **Intensive induction chemo** to debulk and treat bone marrow disease
    2. LC of bulk with *delayed surgery and local RT* (either before or after myeloablation; more often after now)
    3. High dose **marrow ablative therapy** -> **HCT** (now usually without TBI) to control resistant clones
  
  – Still 40% relapse rate
Radiation

- To consolidate local control in addition to surgery

<table>
<thead>
<tr>
<th>Reference</th>
<th>Stage/C</th>
<th>Local Relapse Rate</th>
<th>Local Radiation</th>
<th>Total Body</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>With Local EBRT (%)</td>
<td>Without Local EBRT (%)</td>
<td>Dosage Median (Range), in Gy</td>
</tr>
<tr>
<td>161</td>
<td>C</td>
<td>32</td>
<td>81</td>
<td>12–37.5</td>
</tr>
<tr>
<td>162</td>
<td></td>
<td>24</td>
<td>54</td>
<td>24–30</td>
</tr>
<tr>
<td>98</td>
<td></td>
<td>26&lt;sup&gt;a&lt;/sup&gt;</td>
<td>31</td>
<td>Intra-abdominal: 10</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Other sites: 20</td>
</tr>
<tr>
<td>163</td>
<td>C</td>
<td>15</td>
<td>NA&lt;sup&gt;b&lt;/sup&gt;</td>
<td>21 (1.5 b.i.d.)</td>
</tr>
<tr>
<td>164</td>
<td></td>
<td>10</td>
<td>21</td>
<td>10 (8–24)</td>
</tr>
<tr>
<td>165</td>
<td></td>
<td>10</td>
<td>NA&lt;sup&gt;b&lt;/sup&gt;</td>
<td>21 (1.5 b.i.d.)</td>
</tr>
<tr>
<td>150</td>
<td>ABMT</td>
<td>22&lt;sup&gt;a&lt;/sup&gt;</td>
<td>35</td>
<td>Intra-abdominal: 10</td>
</tr>
<tr>
<td></td>
<td>CC</td>
<td>52&lt;sup&gt;a&lt;/sup&gt;</td>
<td>50</td>
<td>Other sites: 20</td>
</tr>
</tbody>
</table>
Intermediate Risk
(Stage 3-4 infant or stage 3 non-infant favorable; MYCN NA, 4S with 1 risk factor)

- Evolving area particularly with staging evolution. RT not *routinely* used here.
- Post-op RT benefit shown but limited data.
  - One randomized RT study from the POG:
  - 62 pts post-op chemo alone or chemo -RT to 24-30Gy in 16-20 fx
  - Chemo alone 45% CR, 31% DFS
  - *vs* chemo-RT 67% CR, 58% DFS at median follow up of 23mo
Intermediate Risk:
(Stage 3-4 infant or stage 3 non-infant favorable; MYCN NA, 4S with 1 risk factor)

**A3961 (1997-2005)**

- Prospective phase III nonrandomized trial, 479 enrolled
- Surgery for prognosis → chemo with cyclophosphamide, doxorubicin, carbo, etop → max safe resection
- RT:
  - Only 12 of 479 patients (2.5%) received local radiotherapy (21 Gy)
  - Clinical deterioration despite chemo and surgery (symptom palliation)
  - Residual macroscopic disease and unfavorable biology
  - Relapse
- >90% survival
High Risk:
(Stage 3-4/4S Non-infant and/or MYCN A; need both for stage 2)

• **CCG 3891** (1991-96)
  - Randomized. 539 pts. High-risk, Evans Stage IV, or Stage III with MYCN amplification, elevated ferritin, or unfavorable histology.
    • *Initial chemotherapy*: 5 cycles of cisplatin, doxorubicin, etoposide, and cyclophosphamide. *Surgery and RT: 10Gy given between cycles 4 and 5 for gross residual disease.*
    • Randomized to: 1) Myeloablative therapy and *autoBMT with 10Gy TBI* vs. 2) *intensive nonmyeloablative consolidation chemo* (cisplatin, etoposide, doxorubicin, ifosfamide x 3 cycles)
    • *2nd randomization: +/- 6 cycles of 13-cis-retinoic acid (isotretinoin)*
High Risk
CCG 3891 (1991-96)

• **CCG 3891 (1991-96)**
  – 85% INSS stage 4
  – 379 pts: 189 autoBMT, 190 consolidation, 118 consolidation because of parent/investigator refusal
  – Toxicity and hospital stays equivalent
  – **AutoBMT vs Consolidation @ 5 years**
    • EFS 30% vs 19% (SS)
    • Locoregional Recurrence 33% autoBMT vs 51% consolidation
      – For MYCNamp 25% vs 70%
    • 5 yr OS 39% vs 30% (not SS)
    • Suggested benefit to addition of cis-retinoic acid to autoBMT 59% vs 41% (vs ~37% with consolidation+/−cis-RA)

JCO 2009 Matthay et al
High Risk
CCG 3891 (1991-96)

– Conclusion:
  • Event free survival and suggestion of OS benefit for autoBMT and 13-cis-retinoic acid in high risk pts
  • Local recurrence benefit with RT

– High-risk now receive RT to primary site and MIBG-avid metastatic sites on pre-transplant scans regardless of extent of surgical resection

– Newer auto-BMT regimens are moving away from TBI-based regimens (late toxicity, limits chemo)
RT Techniques

• AP/PA
• 3D conformal
• IMRT (particularly to shield kidneys)
• Intra-op RT (UCSF experience: excellent LC)

• Balance between
  – Achieving Rx dose
  – Meeting dose constraints
  – Given no clear role in OS, focus on 1\textsuperscript{st} doing no harm
  – At times, boosts/metastatic RT are easy to safely achieve, other times not
  – Boosts/metastatic lesions driven often by COG protocol guidelines
  – No elective lymph node coverage 2/2 toxicity
RT Targets: Primary

- Gross Tumor Volume (GTV, what you can see on imaging)
  - Initial volume (GTV1): post chemo, pre surgery volume (use CT/MRI, MIBG)
  - Boost volume (GTV2): gross disease at time of simulation (post chemo, post surgery residual measuring >1cm3)
RT Dose: Primary

- Clinical Target Volume (CTV, microscopic disease)
  - CTV1: Expansion on GTV1 of 1.5cm, CTV2: 1cm
- Planning Target Volume (PTV, motion/set up error)
  - Expansion on CTV of 0.5-1cm

CTV1: red
CTV2: blue
36Gy isodose: green
RT Prescription

- PTV1: 21.6 Gy over 12 fractions of 1.8 Gy
- PTV2: boost of 14.4 Gy over 8 fractions of 1.8 Gy to total dose 36 Gy @ 180 cGy
- Minimum of 21 Gy to initial volume based on superior control 20 Gy vs 10 Gy older protocols; 36 Gy from German study for control of incompletely resected primaries
RT Technique

• Metastatic Sites
  – Those present prior to myeloablation or on Day 28; <5 MIBG sites, caution with amount of bone marrow included.
  – Treat at same time as primary with a 2cm margin to 2160 cGy in 12 fx of 180cGy
    • No great dose response data

• Palliation at relapse (usually bone mets)
  – Generally small fields 16-20Gy/4-5fx and larger fields 20-30Gy/10fx
    • If short life expectancy can do 6-8Gy x 1-2fx
Organs at Risk

Body Constraints

• Contralateral Kidney ≤20%   12Gy
• Liver ≤50%   9Gy
• Lung ≤33%   15Gy
• Epiphyses (closure)   20 Gy
Side Effects

**Acute**
- Usually still recovering from transplant with feeding tubes in place
  - Nausea, vomiting, diarrhea
  - Anorexia
  - Reduced blood counts

**Late**
- Spinal deformities, (kyphosis, scoliosis)-2/2 to assym Tx
- 20Gy can produce bone shortening if epiphyses get dose
- Infant kidney is more sensitive than adult
- Infertility, neuropych, endocrine, cardiac, pulm, fibrosis, bladder dysfunction, cataracts, dental, 2nd malignancy
Treatment Plan

• Primary
  – GTV1 (pre-op CT LN and primary)
  – CTV1 = GTV1 + 1.5cm + trimmed
  – PTV1 = 0.3cm
  – PTV Rx = 1.8 Gy x 12 fractions to 21.6 Gy

• No boost given no clear post-op disease visualized on CT simulation

• No metastatic sites (no discrete lesions on pre-transplant MIBG)
Treatment Plan
Rapid Arc IMRT

Treatment Plan
Treatment Plan Review

Cumulative Dose Volume Histogram

- Relative dose [%]
  - 23.148
  - 46.296
  - 69.444
  - 92.592

- Ratio of Total Structure Volume [%]
  - 100
  - 90
  - 80
  - 70
  - 60
  - 50
  - 40
  - 30
  - 20
  - 10
  - 0

- Dose [cGy]
  - 0
  - 500
  - 1000
  - 1500
  - 2000

- Structure Status
- Coverage [%/%]
- Volume [cm³]
- Min Dose [cGy]
- Max Dose [cGy]
- Mean Dose [cGy]
- Modal Dose [cGy]
- Median Dose [cGy]
- Std Dev [cGy]

- Kidney LT: Approved, 100.0/100.0, 46.8 cm³, 550.4 cGy, 2329.2 cGy, 1491.9 cGy, 2243.0 cGy, 1364.1 cGy, 582.5 cGy
- Kidney Rt: Approved, 100.0/100.0, 57.9 cm³, 264.5 cGy, 2319.9 cGy, 604.3 cGy, 459.2 cGy, 535.1 cGy, 248.9 cGy
- Liver: Approved, 100.0/100.0, 414.7 cm³, 284.5 cGy, 2276.9 cGy, 676.7 cGy, 237.4 cGy, 598.6 cGy, 427.4 cGy
- PTV: Approved, 100.0/100.0, 268.8 cm³, 2276.9 cGy, 2286.8 cGy, 2224.3 cGy, 2220.7 cGy, 2226.6 cGy, 37.7 cGy
- CTV: Approved, 100.0/100.0, 192.2 cm³, 2276.9 cGy, 2230.8 cGy, 2220.7 cGy, 2231.0 cGy, 30.2 cGy
- Preop LN: Approved, 100.0/100.0, 25.8 cm³, 2276.9 cGy, 2230.8 cGy, 2230.7 cGy, 2230.7 cGy, 2230.7 cGy, 25.7 cGy
- Partial LUNG: Approved, 100.0/99.7, 270.9 cm³, 18.5 cGy, 2281.7 cGy, 149.9 cGy, 35.4 cGy, 61.6 cGy, 284.6 cGy

Prescription Dose

R kidney constraint
Treatment Course

- Currently on cycle 4 of ANBL0032 and doing well
  - Phase III randomized study of chimeric antibody 14.18 (Ch14.18) in high risk neuroblastoma following myeloablative therapy and autologous stem cell rescue
  - Uses a human-mouse chimeric mab, ch14.18 against GD2

**FOOTNOTE**

NBL – Neuroblastoma  
ASCT – Autologous stem cell transplant  
XRT – Radiation therapy  
MRD – Minimal residual disease  
IC - Informed consent

*Optional MRD assessment:* Bone marrow for RT-PCR to Seeger’s lab.

**Study therapy: Regimen B**

Courses#1,3,5: ch14.18+ GM-CSF+ isotretinoin 
Courses # 2,4 : ch14.18 + IL-2 + isotretinoin 
Course # 6: Isotretinoin ONLY 

Optional *MRD#2 – End of 6th course of isotretinoin.
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  – Linda Stork, Suman Malempati and Michael Recht
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