CHILDHOOD CANCER SURVIVORS:
OUTWIT, OUTPLAY, OUTLAST

Robert Raphael, MD
Director, Survivors of Childhood Cancer Program
Surviving Childhood Cancer: Success

- >80% survival rate for childhood cancer
- >375,000 childhood cancer survivors in U.S.
- One in 640 adults up to age 40

5-Year Relative Survival Rates (%) for Children Under 15 Years (1975-2003)

Source: Surveillance, Epidemiology, and End Results (SEER) Program (www.seer.cancer.gov)
SEER 9 area. Based on follow-up of patients into 2012

Surviving Childhood Cancer: the Cost

- 2/3 of survivors have chronic late effects of treatment\(^1\)
- 1/3 of late effects are severe or life-threatening\(^1\)
- 1/4 of survivors have significant psychosocial problems\(^2\)
- 10% report persistent cancer-related pain\(^1\)
- Risk of death 30 years after diagnosis 8 x higher than general population\(^3\)
- Cumulative prevalence of chronic medical condition 95% by age 45 (80% disabling/life-threatening)\(^4\)
- Survivors 2-5 times more likely to experience\(^5\):
  - Poor health
  - Mental health concerns
  - Functional impairment
  - Activity limitations

\(^1\) Oeffinger K et al. NEJM 2006; 355:1572-82
\(^3\) Mertens AC et al. J. Natl Cancer Inst 2009; 100:1368-1379
\(^4\) Hudson M et al. JAMA 2013; 309:2371–2381
\(^5\) Hudson MM et al. JAMA 2003; 290:1583-1582
## Classifying Late Effects

### Medical
- Second malignancies
- Organ dysfunction
- Infertility
- Endocrine disorders
- Obesity and diabetes
- Musculoskeletal and physical defects
- Impaired growth
- Neurologic problems
- Chronic pain
- Early death

### Psychosocial
- Cognitive dysfunction
- Depression, anxiety, PTSD
- Low self esteem
- Academic problems
- Unemployment
- Time off work
- Substance abuse
- Interpersonal difficulties
- Lack of insurance
- Financial toxicity
Studying Late Effects

- Childhood Cancer Survivor Study (CCSS)
  - Largest and most studied cohort of childhood cancer survivors
  - 14,364 survivors age <21 years at diagnosis
  - Treated 1970-1986, survived at least 5 years from diagnosis
  - 26 participating centers across U.S. and Canada
  - Diagnoses: leukemia, lymphoma, neuroblastoma, soft tissue sarcoma, bone tumors, brain tumors, Wilms tumor
  - Database includes diagnosis and treatment details
  - Extensive health questionnaires completed at enrollment
  - Random sample of nearest-age living siblings included for comparisons
  - Follow up questionnaires, expanded cohort to 1999

- Children’s Oncology Group, St. Jude’s, others

Early Mortality

- 18% mortality rate 30 years from diagnosis
- Causes of death
  - Recurrence/progressive disease: 58%
  - Subsequent neoplasm: 18.5%
  - Cardiovascular: 6.9%
- Transition in cause of death over time
- Risk factors
  - SMN death: radiation therapy, alkylators, etoposide
  - Cardiovascular death: cardiac radiation, high-dose anthracycline

Early Mortality

- Reduction in 15 year mortality among expanded CCSS cohort from 1970s-1990s: from 12.4% to 6%
- Reduction in mortality from SMN, cardiac and pulmonary causes
- Improvement associated with reductions in radiation and anthracycline exposure over time

Armstrong G et al. NEJM 2016; 374: 833-42
Morbidity/Chronic Disease

- Survivors 2.5 x more likely than matched sibling controls to report adverse general health\(^1\)
  - 10.9% vs 4.9% at mean age 26.8 years
  - 3 x more likely to report activity limitations, 5 x for functional impairment
- 62.3% of survivors report ≥1 chronic condition (mean age 26.6 years)\(^2\)
  - 27.5% severe/life threatening
- 23.8% report ≥3 health conditions
- Relative risk for chronic disease 3.3 times sibling controls
  - 8.2 times higher for grade 3/4 conditions
- Cumulative incidence of chronic disease 73.4% at 30 years from diagnosis
  - 42.4% for grade 3/4

\(^1\)Hudson M et al. *JAMA* 2003; 290:1583-1592
\(^2\)Oeffinger K et al. *NEJM* 2006; 355:1572-82
### Morbidity/Chronic Disease

**Table 3. Relative Risk of Selected Severe (Grade 3) or Life-Threatening or Disabling (Grade 4) Health Conditions among Cancer Survivors, as Compared with Siblings.**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Survivors (N = 10,397)</th>
<th>Siblings (N = 3034)</th>
<th>Relative Risk (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Major joint replacement*</td>
<td>1.61</td>
<td>0.03</td>
<td>54.0 (7.6–386.3)</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>1.24</td>
<td>0.10</td>
<td>15.1 (4.8–47.9)</td>
</tr>
<tr>
<td>Second malignant neoplasm†</td>
<td>2.38</td>
<td>0.33</td>
<td>14.8 (7.2–30.4)</td>
</tr>
<tr>
<td>Cognitive dysfunction, severe</td>
<td>0.65</td>
<td>0.10</td>
<td>10.5 (2.6–43.0)</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>1.11</td>
<td>0.20</td>
<td>10.4 (4.1–25.9)</td>
</tr>
<tr>
<td>Cerebrovascular accident</td>
<td>1.56</td>
<td>0.20</td>
<td>9.3 (4.1–21.2)</td>
</tr>
<tr>
<td>Renal failure or dialysis</td>
<td>0.52</td>
<td>0.07</td>
<td>8.9 (2.2–36.6)</td>
</tr>
<tr>
<td>Hearing loss not corrected by aid</td>
<td>1.96</td>
<td>0.36</td>
<td>6.3 (3.3–11.8)</td>
</tr>
<tr>
<td>Legally blind or loss of an eye</td>
<td>2.92</td>
<td>0.69</td>
<td>5.8 (3.5–9.5)</td>
</tr>
<tr>
<td>Ovarian failure‡</td>
<td>2.79</td>
<td>0.99</td>
<td>3.5 (2.7–5.2)</td>
</tr>
</tbody>
</table>

Oeffinger K et al. *NEJM* 2006; 355:1572-82
Morbidity and Chronic Disease

Cumulative incidence of chronic health conditions in CCSS cohort, by cancer diagnosis and severity

Oeffinger K et al. *NEJM* 2006; 355:1572-82
Morbidity and Chronic Disease

20-year incidence of grade 3-5 chronic condition lower for more recently treated patients
- 1970-79: 33.2%
- 1980-89: 29.3%
- 1990-99: 27.5%
- Siblings: 4.6%

Decreased incidence of
- Endocrinopathy
- SMN
- Musculoskeletal
- Gastrointestinal

Higher incidence for some diagnoses treated 1990-99 as treatment intensity has increased
- Medulloblastoma
- Neuroblastoma

Second Neoplasms

- Incidence 20-30 years from diagnosis: 3.2%-7.9% (6 x general population)\(^1\)
- 43-fold increased risk of breast cancer after lung radiation
- 4-fold higher risk of breast cancer after chemotherapy\(^2\)
- 3.5-fold higher risk of sarcoma after anthracycline
- SN incidence at age 40-55: 16.3\(^3\)
  - 2.2 x higher risk than general population
  - Non-melanoma skin cancer: 19.6\%

\(^{1}\)Friedman DL et al. *J Natl Cancer Inst* 2010; 102: 1083-1095
\(^{2}\)Henderson TO et al. *J Clin Oncol* 2016; 34: 910-918
\(^{3}\)Turcotte LM et al. *J Clin Oncology* 2015; 33: 3568-3575
Cardiovascular Disease

- Leading cause of non-cancer morbidity and mortality
- Risk 8 x higher than age-matched siblings
- Risk factors:
  - anthracyclines
  - radiation
- Over 50% have signs of damage within 5-10 years

Mulrooney D et al. *BMJ* 2014; 239: b4606
Infertility

- Survivors less likely than siblings to have been pregnant/sired a pregnancy (38% vs. 62%)\(^1\)
- Risk factors: radiation, cyclophosphamide
- Male fertility more sensitive to chemotherapy than female
  - 46% infertility among male survivors vs 17.5% for their brothers\(^2\)
    - 37% fathered a child (vs. 69% of siblings)
  - Female survivors 1.5 x more likely to have infertility than siblings\(^3\)
    - 2/3 did achieve pregnancy, but longer time to become pregnant
- Premature ovarian failure prevalence 10.9%
  - median age 31.7 at 24 years from diagnosis\(^4\)

\(^1\)Barton SE et al. Lancet Oncol 2013; 14(9)  
\(^2\)Wasilewski-Masker K et al. J Cancer Surviv 2014; 8: 437-447  
\(^3\)Green DM et al. J Clin Oncology 2009; 2677-2685  
\(^4\)Chemaitilly W et al. J Clin Endo Metabol 2017 [epub]
Other Late Effects

A Systematic Review of Selected Musculoskeletal Late Effects in Survivors of Childhood Cancer

Physical Performance Limitations in the Childhood Cancer Survivor Study Cohort

Pain in Long-Term Adult Survivors of Childhood Cancers and Their Siblings: A Report from the Childhood Cancer Survivor Study

Endocrine Abnormalities in Aging Survivors of Childhood Cancer: A Report From the Childhood Cancer Survivor Study

Obesity and Metabolic Syndrome Among Adult Survivors of Childhood Leukemia
Other Late Effects

Central Nervous System Complications in Children Receiving Chemotherapy or Hematopoietic Stem Cell Transplantation

Chemotherapy-Induced Peripheral Neuropathy in Long-term Survivors of Childhood Cancer

Ocular Late Effects in Childhood and Adolescent Cancer Survivors: A Report from the Childhood Cancer Survivor Study

Evaluation and Management of Hearing Loss in Survivors of Childhood and Adolescent Cancers: a Report from the Children’s Oncology Group

A Systematic Review of Dental Late Effects in Survivors of Childhood Cancer
Other Late Effects

Long-Term Pulmonary Function in Survivors of Childhood Cancer

Hepato-Biliary Late Effects in Survivors of Childhood and Adolescent Cancer: A Report from the Children’s Oncology Group

Late renal toxicity of treatment for childhood malignancy: risk factors, long-term outcomes, and surveillance

Late Effects on the Urinary Bladder in Patients Treated for Cancer in Childhood: A Report from the Children’s Oncology Group
Psychosocial Problems

- Most survivors psychosocially well-adjusted, but…
- Twice as likely as siblings to report adverse mental health
- Increased risk for depression, anxiety, PTSD, suicidal ideation
- Risk for delayed psychosexual development
- Lower rate of marriage/cohabitation, college graduation, full-time employment
- Similar or slightly lower rate of risky behaviors
- Risk factors for poor psychosocial outcomes:
  - Cranial radiation
  - CNS tumor
  - Physical/medical late effects of treatment
- ALL survivors treated without radiation at risk for ADHD, problems with learning, executive functioning, processing speed, memory, IQ

Hudson M et al. *JAMA* 2003; 290: 1583-1592
Risk Factors for Late Effects

- Type of cancer
- Treatment exposures
  - Chemotherapy
  - Radiation therapy
  - Bone marrow transplantation
  - Surgery
- Age
  - At diagnosis
  - At follow up
- Sex
- Genetics
Why Long-Term Follow Up Matters

• Medical and psychosocial late effects are significant
  • Opportunity to identify problems early
  • Opportunity to intervene

• Patients need to understand the risks
  • May have no problems or symptoms for years
  • Need to avoid additional risks
  • Need to know when something is wrong

• Patients need to know their history
  • Details of cancer treatment are complex, but they matter
  • Risk of late effects depends on treatment history
  • Difficult to keep track of medical records
Why Long-Term Follow Up Matters

• Health care providers need information
  • Diagnosis and treatment history
  • Current and potential late effects
  • Communication between:
    • Pediatric oncologist
    • Primary care provider
    • Other specialists

• We all need more research
  • Cancer treatment is constantly evolving
  • Recommendations change to reflect new knowledge

• Children grow up
  • Transition to adult health care setting
  • Responsibility for personal health
2003 Institute of Medicine Report

• Recommendations to improve care and quality of life for childhood cancer survivors:
  • Develop evidence-based clinical practice guidelines
  • Define minimum standards, establish programs in all pediatric oncology centers and evaluate models of care
  • Improve awareness of late effects among survivors and their families
  • Improve education and training for specialists and PCPs
  • Dedicate government and private resources to ensure access to care for survivors
  • Increase research to prevent and ameliorate late effects
  • “Call to arms” for creation of survivorship clinics

Goals of Long-Term Follow Up

- Education
  - Patient and family
  - Health care providers
- Surveillance
  - Screening tests
  - Comprehensive history and physical
- Coordination
  - Communication with other providers
  - Documentation
  - Transition of care
- Support
  - Psychosocial services
  - Financial/insurance issues
- Research

- Cancer Treatment Summary
- Survivor Care Plan
Barriers to Long-Term Follow Up

- Less than 50% of adult survivors report having cancer-related follow up in the last 2 years
- Less than 20% report being counseled on risk reduction and screening tests
- Risk factors: age, time from diagnosis, race, lack of insurance, distance, SES

Models of Survivorship Care

- Cancer center programs
  - Primary oncology care (pediatric-adult)
  - Dedicated LTFU program

- Community-based programs
  - Primary care (complete transition)
  - Hybrid program (collaboration between PCP and oncologist)

- Risk-based programs
  - Primary care for low-risk
  - LTFU clinic for high-risk

- AYA transition models
  - Continued care with pediatric oncology
  - Joint pediatric-adult programs/partnerships
  - Graduation to adult oncology or primary care
Key Aspects of LTFU Programs

• Multidisciplinary
  • Psychology
  • Social work
  • Research and nursing staff
  • Others: nutrition, genetics, endocrinology

• Goals:
  • Late effects surveillance/management
  • Education for patients/caregivers and physicians
  • Psychosocial support and assistance
  • Contribute to survivorship research

• All patients receive:
  • Comprehensive treatment summary
  • Survivorship care plan
Children’s Oncology Group Guidelines

- Developed by COG late effects/nursing taskforce in response to IOM report
- First guidelines released September 2003
- Evidence-based, graded recommendations grouped by treatment exposure and organ system
- For surveillance of late effects in survivors >2 years from end of treatment
- Most recent revision: Version 5.0, November 2018
- Include “Health Links” for patient/family education
- Public website: http://www.survivorshipguidelines.org
**CHEMOTHERAPY**

<table>
<thead>
<tr>
<th>Sec #</th>
<th>Therapeutic Exposure</th>
<th>Potential Late Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>33</td>
<td>Anthracycline Antibiotics</td>
<td>Cardiac toxicity</td>
</tr>
<tr>
<td></td>
<td>Daunorubicin</td>
<td>Cardiomyopathy</td>
</tr>
<tr>
<td></td>
<td>Doxorubicin</td>
<td>Subclinical left ventricular dysfunction</td>
</tr>
<tr>
<td></td>
<td>Epirubicin</td>
<td>Congestive heart failure</td>
</tr>
<tr>
<td></td>
<td>Idarubicin</td>
<td>Arrhythmia</td>
</tr>
</tbody>
</table>

**Dose Conversion**

To gauge the frequency of screening, use the following formulas to convert to doxorubicin isotoxic equivalents prior to calculating total cumulative anthracycline dose. Clinical judgment should ultimately be used to determine indicated screening for individual patients.

- Doxorubicin: Multiply total dose x 1
- Daunorubicin: Multiply total dose x 0.5
- Epirubicin: Multiply total dose x 0.67
- Idarubicin: Multiply total dose x 5
- Mitoxantrone: Multiply total dose x 4

**Potential Late Effects**

- **Cardiac toxicity**
- **Cardiomyopathy**
- **Subclinical left ventricular dysfunction**
- **Congestive heart failure**
- **Arrhythmia**

**Periodic Evaluation**

- **HISTORY**
  - Shortness of breath
  - Dyspnea on exertion
  - Orthopnea
  - Chest pain
  - Palpitations
  - If under 25 yrs: abdominal symptoms (nausea, vomiting)

- **Yearly**
  - Blood pressure
  - Cardiac exam

**SCREENING**

- **ECHO (or comparable imaging to evaluate cardiac function)**

  **Recommended Frequency of Echocardiogram**

- **Anthracycline Dose**
- **Radiation Dose**
- **Recommended Frequency**

<table>
<thead>
<tr>
<th>Anthracycline Dose*</th>
<th>Radiation Dose**</th>
<th>Recommended Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>&lt;15 Gy/m²</td>
<td>No screening</td>
</tr>
<tr>
<td>&gt;15 Gy/m² - &lt;35 Gy</td>
<td>&lt;15 Gy/m²</td>
<td>Every 5 years</td>
</tr>
<tr>
<td>&gt;35 Gy/m²</td>
<td>&lt;35 Gy/m²</td>
<td>Every 2 years</td>
</tr>
<tr>
<td>&gt;35 Gy/m² - &lt;150 Gy/m²</td>
<td>&lt;15 Gy/m²</td>
<td>Every 5 years</td>
</tr>
<tr>
<td>&gt;150 Gy/m²</td>
<td>&lt;15 Gy/m²</td>
<td>Every 2 years</td>
</tr>
<tr>
<td>&gt;150 Gy/m²</td>
<td>&gt;15 Gy/m²</td>
<td>Every 5 years</td>
</tr>
<tr>
<td>&gt;250 Gy/m²</td>
<td>Any GY/m²</td>
<td>Every 2 years</td>
</tr>
</tbody>
</table>

  *Based on doxorubicin isotoxic equivalent dose. See dose conversion instructions in section 10.
  **Based on radiation dose with potential impact to heart (radiation to chest, spine, brain, etc.). See section 10.

- **EKG (include evaluation of QTc interval)**
  - Baseline at entry into long-term follow-up, repeat as clinically indicated

**ANTHRACYCLINE ANTIBIOTICS (CONT)**

**Health Counseling/Further Considerations**

- **HEALTH HINTS**
  - **Heart Health**
  - **Cardiovascular Risk Factors**
  - **Diet and Physical Activity**

- **COUNSELING**
  - Maintain appropriate weight, blood pressure and heart-healthy diet.
  - Regarding exercise:
    - Regular exercise is generally safe and should be encouraged for patients who have normal LV systolic function.
    - Survivors with asymptomatic cardiomyopathy should consult cardiology to define limits and precautions for physical activity.
    - Cardiology consultation may be reasonable to define limits and precautions for physical activity for high risk survivors (i.e., those requiring an ECHO every 2 years) who plan to participate in intensive exercise.
    - If QTc interval is prolonged: Caution regarding use of medications that may further prolong the QTc interval e.g., tricyclic antidepressants, antihistamines, macrolide antibiotics, metronidazole.

- **Potential Considerations for Further Testing and Intervention**
  - Cardiac MRI as an adjunct imaging modality when echocardiographic images are suboptimal.
  - Cardiology consultation in patients with subclinical abnormalities on screening evaluations, left ventricular dysfunction, dysrhythmia, or prolonged QTc interval.
  - Female patients only: For patients who are pregnant or planning to become pregnant, additional cardiology evaluation is indicated in patients who received:
    - >250 mg/m² anthracyclines
    - >35 GY chest radiation, or
    - Anthracycline (any dose) combined with chest radiation (>15 GY)
  - Evaluation should include a baseline echocardiogram (pre- or early-pregnancy). For those without prior abnormalities and with normal pre- or early-pregnancy baseline echocardiograms, follow-up echocardiograms may be obtained at the provider's discretion.
  - Those with a history of systolic dysfunction or with pre- or early-pregnancy systolic dysfunction are at highest risk for pregnancy-associated cardiomyopathy. Such individuals should be monitored periodically during pregnancy and during labor and delivery due to increased risk for cardiac failure.

**SYSTEM = Cardiovascular**

**SCORE = 1**

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**Additional Information**

Although Mitoxantrone technically belongs to the anthracycline class of anti-tumor antibiotics, it is related to the anthracycline family and is included in this section because of its cardiotoxic potential.
Passport for Care

Cancer. You survived. And now you've got a lot of life to live. Take care of yourself.

Passport for Care.

Long-term follow-up care recommendations for survivors of childhood cancer.

What is Passport for Care?

Passport for Care is a summary of your cancer treatment history, individualized follow-up recommendations for screening potential late effects, educational materials, and a notebook to create and store information.

Would you like to use the PFC?

If so, your cancer treatment information has to be entered and you need an access code. Please contact svp-helpdesk@bcm.edu for assistance.

Treatment Summary

Your treatment summary is your cancer treatment history. This summary is used to generate your long-term follow-up care plan.

Follow-Up Care Plan

Recommendations for screening of late effects that may potentially arise as a result of the cancer treatment that you received as a child.

Your Notes

Create notes to remember details related to your treatment history or to remind you of things you'd like to bring up with your doctor.
Survivors of Childhood Cancer Program
at UCSF Benioff Children’s Hospital Oakland

What we do:

- Comprehensive H&P
- Multidisciplinary team: oncologist, social worker, psychologist, nutritionist, endocrinologist
- Education and documentation:
  - Cancer Treatment Summary & Survivor Care Plan
- Order/review screening tests
- Coordination: specialist referrals, follow up
- Research
  - Focus on AYA patients ready to transition
  - Most patients “graduate” from pediatric oncology, to follow up with primary care provider
Primary Care

- Essential to proper LTFU of survivors
- Patients may need to transition from pediatrics to adult-oriented care
- Annual health care maintenance visit
- H&P adequate screening for most potential late effects
  - Targeted history based on exposures and risks
  - As per survivor care plan
- Other screening studies based on exposure
  - Echocardiogram q 2-5 years (anthracycline/chest radiation)
  - Thyroid function annually (neck/cranial radiation)
  - Breast/colon cancer screening (chest/abdominal radiation)
- Coordination of care
CASE STUDIES
J.M.

- 15 yo female with high risk B-ALL diagnosed at 21 months
- Treated per CCG 1961 protocol
- Chemotherapy:
  - Asparaginase
  - Cyclophosphamide 4000 mg/m2
  - Cytarabine (IV/IT)
  - Daunorubicin 100 mg/m2
  - Dexamethasone
  - Doxorubicin 150 mg/m2
  - Mercaptopurine
  - Methotrexate (IV/IT/PO)
  - Prednisone
  - Thioguanine
  - Vincristine
- Radiation: 1200 cGy prophylactic cranial XRT
- In first remission, completed therapy 11 years ago
J.M.

• Active late effects:
  • Clinical leukoencephalopathy with epilepsy
  • Cognitive deficits: attention, memory, executive function

• Potential late effects:
  • Bladder: hemorrhagic cystitis, dysfunctional voiding, carcinoma
  • Cardiac: myocardial dysfunction, heart failure
  • Dental: carries, abnormal development
  • Endocrine: obesity, growth hormone deficiency, thyroid
  • Hepatic: fibrosis, cirrhosis
  • Musculoskeletal: osteoporosis, osteonecrosis
  • Ocular: cataracts
  • Peripheral neurovascular: neuropathy, Raynaud’s
  • Reproductive: infertility, ovarian dysfunction
  • Second malignancy: myeloid, brain, bone, skin, soft tissue, bladder
J.M.

• Survivor Care Plan:
  • Surveillance:
    • Echocardiogram q 5 years
    • Annual TSH/Free T4
    • Baseline CBC, CMP, Vitamin D then as clinically indicated
    • Consider DEXA scan
  • Follow up:
    • Annual H&P with PMD
    • Annual follow up with pediatric oncology until ready to transition
    • Neurology
    • Regular dental and eye exams
E.B.

- 12 yo boy diagnosed with high-risk neuroblastoma at 18 months old
- Stage IV: left adrenal primary metastatic to bones, bone marrow
- Unfavorable histology, NMYC non-amplified
- Chemotherapy per MSKCC N7 protocol:
  - Cyclophosphamide: 22,800 mg/m2
  - Doxorubicin: 300 mg/m2
  - Cisplatin: 400 mg/m2
  - Etoposide: 1200 mg/m2
  - Topotecan: 18 mg/m2
  - Vincristine
- Surgery: left adrenalectomy
- Autologous stem cell transplant:
  - Busulfan/Melfalan prep, complicated by hepatic VOD
- Radiation: 2160 cGy to left adrenal, left proximal femur, left sphenoid and right proximal femur
- Maintenance: cis-retinoic acid x 6 months
E.B.

- Persistent disease left frontal skull after treatment
- Left frontal craniotomy, resection, reconstruction
- Chemotherapy: cyclophosphamide/topotecan x 2 cycles
- Radiation: 2000 cGy to left frontal skull
- Maintenance: cis-retinoic acid x 6 months
- Completed all therapy 7 years ago
- Remains in first remission
- Active late effects:
  - Cataract left eye (s/p extraction)
  - Hypodontia (needs extensive dental work)
  - High frequency hearing loss on left (no intervention needed)
  - Subclinical restrictive lung disease
Potential late effects:

- Bladder: hemorrhagic cystitis, dysfunctional voiding, carcinoma
- Cardiac: myocardial dysfunction, heart failure
- Endocrine: obesity, growth hormone deficiency, thyroid dysfunction
- Gastrointestinal: obstruction, gallstones, hepatotoxicity
- Musculoskeletal: osteopenia, altered growth:
- Neurologic: neurocognitive problems, leukoencephalopathy
- Peripheral neurovascular: neuropathy, Raynaud’s
- Renal: insufficiency, hypertension
- Reproductive: delayed puberty, infertility, testosterone deficiency
- Second malignancy: myeloid, skin, bone/soft tissue, thyroid, bladder, brain, colorectal cancer
E.B.

- Survivor Care Plan:
  - Surveillance:
    - Echocardiogram every 2 years
    - Annual TSH/Free T4
    - HbA1C every 2 years
    - Audiogram: yearly until stable, then as needed
    - Repeat PFTs, then as needed
    - Baseline CBC, CMP, ferritin, vitamin D, UA; then as clinically indicated
    - Baseline DEXA scan, bone age, PFTs; then as indicated
    - Colonoscopy q5 years (or stool DNA test q3 years) starting age 30
  - Follow up:
    - Annual H&P with PMD
    - Annual follow up with pediatric oncology until ready to transition
    - Regular dental and eye exams
Conclusions

• Cancer sucks…even after it’s gone
• “Survival is insufficient”
• Long term follow up is important

• Thank you!
Resources

- Children’s Oncology Group LTFU Guidelines
  - http://www.survivorshipguidelines.org
- National Children’s Cancer Society
  - https://www.thenccs.org/survivorship/
- Childhood Cancer Survivors Study
  - https://ccss.stjude.org/
- Passport for Care
  - https://cancersurvivor.passportforcare.org/
- National Cancer Institute