2021 Update on Pediatric Neoplasms
(Pediatric, Adolescent and Young Adults)

FCDS EDUCATIONAL WEBCAST SERIES
JANUARY 21, 2021
STEVEN PEACE

1 in 285 children

15,780

CDC & Florida DOH Attribution

"Funding for this conference was made possible (in part) by the Centers for Disease Control and Prevention. The views expressed in written conference materials or publications and by speakers and moderators do not necessarily reflect the official policies of the Department of Health and Human Services, nor does the mention of trade names, commercial practices, or organizations imply endorsement by the US Government."

FCDS would also like to acknowledge the Florida Department of Health for its support of the Florida Cancer Data System, including the development, printing and distribution of materials for the 2020 FCDS Annual Conference and the 2020-2021 FCDS Webcast Series under state contract CODJU. The findings and conclusions in this series are those of the author(s) and do not necessarily represent the official position of the Florida Department of Health.
FLccSC LMS – CEU Quiz – FCDS IDEA

- Attendees must take and pass a 3-5 question CEU Quiz to get CEUs
- CEU Awards are Restricted to Attendees with a FLccSC LMS Account
- The CEU Quiz will be posted to FLccSC 1-2 hours after the webcast ends
- Only registered FLccSC Users will be given access to the CEU Quiz
- Florida attendees must have a Florida FLccSC Account to take the Quiz
- South Carolina attendees must have a South Carolina FLccSC Account
- New FLccSC States will follow similar instructions for the CEU Quiz

- Attendees can attend any of the live webcasts without receiving CEUs
- Recorded Sessions are also available for non-FLccSC Users – No CEUs

Presentation Outline

- Introduction – Facts & Figures
- Pediatric/Adolescent/Young Adults
- SEER & NPCR Pediatric & AYA Initiatives
- ICCC Classification of Childhood Cancers
- Types of Neoplasms by Age Group
- Pediatric & AYA Brain and CNS Tumors
- Pediatric & AYA Sarcoma (bone/soft tissue)
- Pediatric & AYA Leukemia
- Pediatric & AYA Lymphoma
- Pediatric & AYA Neuroblastoma
- Pediatric & AYA Germ Cell Neoplasms
- Pediatric & AYA Kidney & Liver Neoplasms
- Rare Pediatric & AYA Cancers
- Childhood Cancer Genomics
- Site & Histology Coding Tips – Brain, Neuroblastoma, Leukemia
- NCI-COG Pediatric MATCH Trial
- Staging Resources for Pediatric Neoplasms
- Other Clinical Trials and Treatment Options
- Documentation for Pediatric & AYA Cancers
- Visual Editing & FAPTP Audit of Pediatric & AYA Cancers
- Q&A
Introduction – Facts & Figures

Trends in Cancer Incidence\(^*\) and Death Rates in Children and Adolescents (0-19 Years), 1975-2018

<table>
<thead>
<tr>
<th>Year of Diagnosis</th>
<th>Incidence</th>
<th>Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>1975</td>
<td>10.0</td>
<td>3.0</td>
</tr>
<tr>
<td>1980</td>
<td>11.0</td>
<td>3.1</td>
</tr>
<tr>
<td>1985</td>
<td>12.0</td>
<td>3.2</td>
</tr>
<tr>
<td>1990</td>
<td>13.0</td>
<td>3.3</td>
</tr>
<tr>
<td>1995</td>
<td>14.0</td>
<td>3.4</td>
</tr>
<tr>
<td>2000</td>
<td>15.0</td>
<td>3.5</td>
</tr>
<tr>
<td>2005</td>
<td>16.0</td>
<td>3.6</td>
</tr>
<tr>
<td>2010</td>
<td>17.0</td>
<td>3.7</td>
</tr>
<tr>
<td>2015</td>
<td>18.0</td>
<td>3.8</td>
</tr>
</tbody>
</table>


Table 13: Case Distribution (2010-2017) and 5-Year Relative Survival (2010-2014) by Age and ICC Type, Ages 0-19 Years, United States

<table>
<thead>
<tr>
<th>ICC Type</th>
<th>5-Year Relative Survival (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bone cancer</td>
<td>90.0</td>
</tr>
<tr>
<td>Brain cancer</td>
<td>70.0</td>
</tr>
<tr>
<td>Breast cancer</td>
<td>92.0</td>
</tr>
<tr>
<td>Cervix cancer</td>
<td>80.0</td>
</tr>
<tr>
<td>Colon cancer</td>
<td>85.0</td>
</tr>
<tr>
<td>Esophageal cancer</td>
<td>10.0</td>
</tr>
<tr>
<td>Gallbladder cancer</td>
<td>50.0</td>
</tr>
<tr>
<td>Genitourinary cancer</td>
<td>80.0</td>
</tr>
<tr>
<td>Leukemia</td>
<td>80.0</td>
</tr>
<tr>
<td>Liver cancer</td>
<td>5.0</td>
</tr>
<tr>
<td>Lung cancer</td>
<td>15.0</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>85.0</td>
</tr>
<tr>
<td>Melanoma</td>
<td>90.0</td>
</tr>
<tr>
<td>Multiple myeloma</td>
<td>20.0</td>
</tr>
<tr>
<td>Myelodysplastic syndromes</td>
<td>15.0</td>
</tr>
<tr>
<td>Non-Hodgkin lymphoma (NHL)</td>
<td>60.0</td>
</tr>
<tr>
<td>Neuroblastoma</td>
<td>50.0</td>
</tr>
<tr>
<td>Nerve sheath tumors</td>
<td>60.0</td>
</tr>
<tr>
<td>Oral cavity cancer</td>
<td>75.0</td>
</tr>
<tr>
<td>Pancreas cancer</td>
<td>5.0</td>
</tr>
<tr>
<td>Paraganglioma</td>
<td>60.0</td>
</tr>
<tr>
<td>Pharynx cancer</td>
<td>70.0</td>
</tr>
<tr>
<td>Pigmented lesions</td>
<td>90.0</td>
</tr>
<tr>
<td>Prostate cancer</td>
<td>30.0</td>
</tr>
<tr>
<td>Retinoblastoma</td>
<td>90.0</td>
</tr>
<tr>
<td>Soft tissue cancer</td>
<td>80.0</td>
</tr>
<tr>
<td>Spinal cord cancers</td>
<td>30.0</td>
</tr>
<tr>
<td>Stomach cancer</td>
<td>50.0</td>
</tr>
<tr>
<td>Thyroid cancer</td>
<td>90.0</td>
</tr>
</tbody>
</table>

Introduction – Facts & Figures

CA Cancer J Clin 2021;71:7-33. © 2021 American Cancer Society
Introduction – Facts & Figures

Building on 50 Years of Cooperative Research

<table>
<thead>
<tr>
<th>PEDIATRIC CLINICAL TRIAL ENROLLMENT</th>
</tr>
</thead>
<tbody>
<tr>
<td>5 and younger</td>
</tr>
<tr>
<td>10 and younger</td>
</tr>
<tr>
<td>10 to 15</td>
</tr>
<tr>
<td>Adolescents aged 15 to 19</td>
</tr>
</tbody>
</table>

Source: Progress in Childhood Cancer: 50 Years of Research Collaboration, A Report from the Children’s Oncology Group, Semin Oncol
Introduction – Facts & Figures

Building on 50 Years of Cooperative Research

1940s

Remission achieved in pediatric leukemia patients using an antifolate drug, aminopterin

Source: Progress in Childhood Cancer: 50 Years of Research Collaboration, A Report from the Children’s Oncology Group, Semin Oncology

1950s

- 6-mercaptopurine treats pediatric acute lymphoblastic leukemia
- Combination chemotherapy introduced by NCI researchers
- NCI begins funding pediatric cooperative clinical trials

Source: Progress in Childhood Cancer: 50 Years of Research Collaboration, A Report from the Children’s Oncology Group, Semin Oncology
Introduction – Facts & Figures

1960s

- Dactinomycin first used to treat Wilms tumor
- National Wilms Tumor Study Group formed and multi-modality therapy first used in pediatric patients (surgery, radiation, chemo)
- Prophylaxis of occult central nervous system leukemia markedly improves outcome for children with ALL
- Laminar airflow technology creates "sterile rooms" for chemotherapy patients

Source: Progress in Childhood Cancer: 50 Years of Research Collaboration, A Report from the Children's Oncology Group, Semin Oncol

1970s

- Intergroup Rhabdomyosarcoma Study Group Committee pioneers repetitive-course, multi-agent chemotherapy for advanced rhabdomyosarcoma
- First successful bone marrow transplant (BMT) for leukemia
- Knudson describes the 2-hit hypothesis for retinoblastoma to describe genetics and heredity of cancer

Source: Progress in Childhood Cancer: 50 Years of Research Collaboration, A Report from the Children's Oncology Group, Semin Oncol
1980s

- First tumor-suppressor gene, in retinoblastoma, is cloned
- MYCN identified as a target of genomic amplification in neuroblastoma
- Adjuvant chemotherapy improves relapse-free survival for pediatric osteosarcoma
- Different treatment for lymphoblastic lymphoma vs other lymphomas are realized
- Platinum-based chemo improves response rates in pediatric germ cell tumors
- National Marrow Donor Program begins

Source: Progress in Childhood Cancer: 50 Years of Research Collaboration, A Report from the Children’s Oncology Group, Semin Oncology

1990s

- Autologous BMT and 13-cis-retinoic acid improve survival for neuroblastoma
- Characteristic fusion genes identified for pediatric solid tumors
- Combined ifosfamide and etoposide improve outcomes for Ewing sarcoma
- Long-term survival rates of 80-90% achieved for advanced Burkitt lymphoma
- Genetic test for thyroid cancer enables prophylactic thyroidectomy before age 2
- NCI-funded Childhood Cancer Survivors Study begins

Source: Progress in Childhood Cancer: 50 Years of Research Collaboration, A Report from the Children’s Oncology Group, Semin Oncology
Introduction – Facts & Figures

2000s

- Four legacy research groups merge as the Children’s Oncology Group (COG)
- COG publishes long-term follow-up guidelines for pediatric cancer survivors
- Imatinib added to intensive chemotherapy improves early outcomes for Ph+ ALL
- 5-year survival rates for children with cancer (age 0-14 years) approach 80%

Source: Progress in Childhood Cancer: 50 Years of Research Collaboration, A Report from the Children’s Oncology Group, Semin Oncology

Pediatric/Adolescent/Young Adults

- US. Cancer incidence and mortality trends:
  - Reported at # cases per 1,000,000 population
  - Adults are reported at # cases per 100,000 population
    - Children (ages 0 to 14 years)
    - Adolescents (ages 15 to 19 years)
    - Young Adults (ages 20 – 39).
  - Since 1975, cancer incidence rates among children and adolescent combined have been increasing slightly by 0.7% per year, while cancer death rates have decreased by more than half.
Pediatric/Adolescent/Young Adults

Number of Childhood Cancer Diagnoses Per Year
Total = 16,615, Age 0–19

- Leukemia: 24%
- Brain and Central Nervous System: 25%
- Neuroblastoma and other peripheral nerve cell tumor: 4%
- Lymphoma and Reticuloendothelial Neoplasms: 13%
- Kidney Tumors (including Wilms Tumor): 3%
- Liver Tumors (including Hepatoblastoma): 1%
- Bone Tumors: 5%
- Rhabdomyosarcoma: 2%
- Retinoblastoma: 2%
- Thyroid Carcinoma: 5%
- Germ Cell Tumors: 6%
- Melanoma: 2%
- Other: 8%

Source: Surveillance, Epidemiology, and End Results (SEER) Program (seer.cancer.gov)

Pediatric/Adolescent/Young Adults

Age-Adjusted and Age-Specific Cancer Incidence Rates for Patients 0-19 Years of Age (SEER 2005-2009)

http://cancer.gov/
Since 1975, cancer incidence rates among children and adolescents combined have been increasing slightly by 0.7% per year, while cancer death rates have decreased by more than half.

### Cancer Incidence Rates* Among Children (0-14 years) and Adolescents (15-19 years), 2013-2017

<table>
<thead>
<tr>
<th>Cancer Type</th>
<th>Rate 0-14 years</th>
<th>Rate 15-19 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>All sites (including benign brain)</td>
<td>18.8</td>
<td>26.9</td>
</tr>
<tr>
<td>Leukemia</td>
<td>5.3</td>
<td>3.5</td>
</tr>
<tr>
<td>Brain &amp; CNS</td>
<td>5.7</td>
<td>6.0</td>
</tr>
<tr>
<td>Hodgkin lymphoma</td>
<td>0.6</td>
<td>0.3</td>
</tr>
<tr>
<td>Rhabdomyosarcoma</td>
<td>0.4</td>
<td>0.5</td>
</tr>
<tr>
<td>Bone tumors</td>
<td>0.8</td>
<td>1.4</td>
</tr>
<tr>
<td>Non-Hodgkin Lymphoma</td>
<td>0.1</td>
<td>1.9</td>
</tr>
<tr>
<td>Neuroblastoma</td>
<td>0.1</td>
<td>0.2</td>
</tr>
<tr>
<td>Gonadal germ cell tumors</td>
<td>0.8</td>
<td>2.2</td>
</tr>
<tr>
<td>Wilms tumor (neuroblastoma)</td>
<td>&lt;0.1</td>
<td>0.8</td>
</tr>
</tbody>
</table>

*Rate per 100,000 Population

CNS = central nervous system

*Rates are age-adjusted to the 2000 US standard population. Includes benign brain and CNS tumors. Includes other peripheral nervous system tumors.


### Top Three Causes of Cancer Death in Children and Adolescents, 2014-2018

#### Children (0-14 years)

<table>
<thead>
<tr>
<th>Site</th>
<th>Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>All sites</td>
<td>2.1</td>
</tr>
<tr>
<td>Brain/ONS</td>
<td>0.7</td>
</tr>
<tr>
<td>Leukemia</td>
<td>0.5</td>
</tr>
<tr>
<td>Soft tissue (including heart)</td>
<td>0.2</td>
</tr>
</tbody>
</table>

#### Adolescents (15-19 years)

<table>
<thead>
<tr>
<th>All sites</th>
<th>Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leukemia</td>
<td>0.7</td>
</tr>
<tr>
<td>Brain/ONS</td>
<td>0.5</td>
</tr>
<tr>
<td>Bone &amp; joints</td>
<td>0.5</td>
</tr>
</tbody>
</table>

CNS = central nervous system.

Per 100,000, age-adjusted to the 2000 US standard population. Brain/ONS excludes benign brain tumors.

## Signs and Symptoms

- **Continued, unexplained weight loss**
- **Headaches, often with early morning vomiting**
- **Increased swelling or persistent pain in bones, joints, back, or legs**
- **Lump or mass, especially in the abdomen, neck, chest, pelvis, or armpits**
- **Development of excessive bruising, bleeding, or rash**
- **Constant infections**
- **Whitish color behind the pupil**
- **Nausea which persists or vomiting without nausea**
- **Constant tiredness or noticeable paleness**
- **Eye or vision changes which occur suddenly and persist**
- **Recurrent or persistent fevers of unknown origin**

http://www.ped-onc.org/diseases/SOCC.html
Causes and Risk Factors

- Genetic Abnormalities
- Ionizing Radiation Exposure
- History of Chemotherapy and/or Radiation Therapy
- Infectious Agents Including Prenatal Infection
  - HIV
- Environmental Including Parental Exposure
  - Toxins
  - Solvents
  - Pesticides
  - Magnetic Fields
- Cancer Predisposition Syndromes
  - Down Syndrome
  - Li-Fraumeni Syndrome
  - Neurofibromatosis
  - Gorlin Syndrome

http://cancer.gov/

Children’s Oncology Group

The world's childhood cancer experts

http://cancer.gov/
SEER & NPCR Pediatric & AYA Initiatives

- CDC STAR Project - Childhood Cancer Survivorship, Treatment, Access, and Research (STAR) Act – 2019
  - Goal: expand capacity within CDC NPCR Registries to collect and make the data on pediatric cancer cases available within weeks of diagnosis

- NCI’s Childhood Cancer Data Initiative (CCDI) – 2019

- NIH/NCI Childhood Cancer Data Initiative (CCDI)
  - comprehensive review of existing childhood and AYA cancer data, data repositories, and analytic tools that can be connected under the CCDI
  - Developing the National Childhood Cancer Registry (NCCR)
  - Supporting ongoing research to develop a preclinical data common
  - Building the technical infrastructure of the data ecosystem
  - Expanding comprehensive data collection to include more institutions engaged in childhood and AYA cancer and survivorship research
  - enhance data sharing and publication policies to promote open access to data and journal articles without paywalls

Types of Pediatric Neoplasms
Major Types of Pediatric Neoplasms

Childhood Cancer Incidence Rates (SEER) by ICCC Group 2001-2004 – All Sex, All Race

<table>
<thead>
<tr>
<th>Type</th>
<th>Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leukemia</td>
<td>44.2</td>
</tr>
<tr>
<td>Brain/CNS</td>
<td>27.4</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>23.2</td>
</tr>
<tr>
<td>Soft Tissue</td>
<td>12.0</td>
</tr>
<tr>
<td>Germ Cell</td>
<td>11.8</td>
</tr>
<tr>
<td>Bone</td>
<td>8.9</td>
</tr>
<tr>
<td>Neuroblastoma</td>
<td>7.6</td>
</tr>
<tr>
<td>Renal</td>
<td>6.0</td>
</tr>
<tr>
<td>Retinoblastoma</td>
<td>3.0</td>
</tr>
</tbody>
</table>

Note: Rates are per 1,000,000 population

http://cancer.gov/

Pediatric Cancers Not Like Adult Cancers

TARGET Study Finds Major Differences between Childhood and Adult AML

Subscribe

January 20, 2018, by NCI Staff

UPDATE: Content about a related study published February 28 in Nature, has been added to this post. See the blue box at the bottom of the page.

An NCI-funded study has found that, at the genetic level, acute myeloid leukemia (AML) differs greatly between younger and older patients.

"AML in younger patients and AML in older patients are entirely distinct diseases," said the study's senior investigator, Soheil Meshinchi, M.D., Ph.D., of the Hutchinson Cancer Research Center. "It's almost like comparing breast cancer to colon cancer."

The findings, published in the January 2018 issue of Nature Medicine, came from a genomic analysis of nearly 1,000 children and young adults with AML. The study is part of the Therapeutically Applicable Research to Generate Effective Treatments (TARGET) initiative, a collaborative effort between NCI and the Children's Oncology Group (COG) to better understand the biology of several high-risk or hard-to-treat pediatric cancers.
Types of Neoplasms by Age Group

ICCC Classification of Childhood Cancers

- Current Version of the ICCC is made up of 12 categories
  1) Leukemias, myeloproliferative diseases, and myelodysplastic diseases
  2) Lymphomas and reticuloendothelial neoplasms
  3) CNS and miscellaneous intracranial and intraspinal neoplasms
  4) Neuroblastoma and other peripheral nervous cell tumors
  5) Retinoblastoma
  6) Renal tumors
  7) Hepatic tumors
  8) Malignant bone tumors
  9) Soft tissue and other extraosseous sarcomas
  10) Germ cell tumors, trophoblastic tumors, and neoplasms of gonads
  11) Other malignant epithelial neoplasms and malignant melanomas
  12) Other and unspecified malignant neoplasms
# ICCC Classification of Childhood Cancers

### Pediatric and AYA Leukemia

## Acute Lymphoblastic Leukemia

### GENETIC RISK GROUPS FOR B-ALL

<table>
<thead>
<tr>
<th>Risk Groups</th>
<th>Genotypes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Favorable risk features</td>
<td>High hyperdiploidy (51-67 chromosomes)</td>
</tr>
<tr>
<td>Unfavorable risk features</td>
<td>Hyperdiploidy (44 chromosomes)</td>
</tr>
</tbody>
</table>

### Risk Factors
- Patient age
- WBC Count
- Immunophenotype
- Cytogenetics
- Genetic Subtype
- CNS Disease Presence/Absence
- Response to Therapy
Pediatric and AYA Leukemia
Acute Lymphoblastic Leukemia

**RISK STRATIFICATION DEFINITIONS**

<table>
<thead>
<tr>
<th>Low Risk</th>
<th>Standard Risk</th>
<th>High Risk</th>
<th>Very High Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Children's Oncology Group (COG) (B-ALL only)</td>
<td>N/A</td>
<td>Age 1 to &lt;10 y and WBC &lt;50,000/mm³</td>
<td>Age &gt;10 y and/or WBC ≥50,000/mm³</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>CNS-3 extracranial disease¹²</td>
</tr>
<tr>
<td>St. Jude Consortium</td>
<td>B-ALL with DNA index ≤1.16, ETV6-RUNX1 fusion OR B-ALL with age 1-4.9 y and presenting WBC count &lt;50,000/mm³ OR Absence of standard risk features</td>
<td>B-ALL with age ≥50 years or presenting WBC count ≥350,000/mm³ (not DNA index ≥1.16 or ETV6-RUNX1 fusion) OR B-ALL with the following features: CNS-3 status¹² OR Overt testicular leukemia OR Adverse genetic features¹² OR T-ALL</td>
<td>N/A</td>
</tr>
<tr>
<td>Dana-Farber Cancer Institute (DFCI) ALL Consortium</td>
<td>N/A</td>
<td>B-ALL</td>
<td>T-ALL</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>T-ALL</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>T-ALL</td>
</tr>
</tbody>
</table>

**Cyogenetic number and structural abnormalities in pediatric ALL**

(Patients of the children hospital of Morocco)
Pediatric and AYA Leukemia
Acute Lymphoblastic Leukemia

### Favorable Risk Features
- Hyperdiploidy (>50 chromosomes)
- ETV6-RUNX1 subtype
- Translocation t(12;21)

### Unfavorable Risk Features
Several chromosomal abnormalities are well-recognized prognostic biomarkers of high-risk disease at all ages, including:
- Hyperdiploidy (30–39 chromosomes), near haploidy (<20 chromosomes), and hyperploidy (>50 chromosomes)
- **KMT2A** rearrangements and **TP53** alterations
- **TCF3-** **HLF** Fusion ALL
- **BCR-** **ABL1** with iAMP21 ALL
- **BCR-** **ABL1** ALL
- **B-ALL (IKZF1)** ALL
- **BCR-** **ABL1-like or Ph-like ALL**

### Risk Stratification Definitions
**Post-induction Therapy Risk Group Stratification**

### Principles of Systemic Therapy

---

---
Pediatric and AYA Leukemia
Acute Lymphoblastic Leukemia

RESPONSE ASSESSMENT

Response Criteria for Blood and Bone Marrow:
- CR: No circulating blasts or extramedullary disease
  - No lymphadenopathy, splenomegaly, skin/gum infiltration/lesserular mass/CNS involvement
  - Marrow with trilinse hematopoiesis (TALH) and <5% (M1) or <1% by flow or molecular testing
  - With blood count recovery = absolute neutrophil count (ANC) >1000/μL and platelets >100,000/μL
  - No recurrence for 4 weeks
  - CR with incomplete blood count recovery (CRI)
  - Meets all criteria for CR except platelet count and/or ANC
  - Overall response rate (ORR = CR + CRI)
  - Refractory disease
  - Failure to achieve CR at the end of induction

Progressive disease (PD)
- Increase of at least 25% in the absolute number of circulating or bone marrow blasts or development of extramedullary disease

Relapsed disease
- Reappearance of blasts in the blood or bone marrow >5% (M2 or greater) or >1% with previous/supportive molecular findings or in any extramedullary site after a CR

Response Criteria for CNS Disease:
- CNS remission: Achievement of CNS-1 status (see PEDALL-C) in a patient with CNS-2 or CNS-3 status at diagnosis.
- CNS relapse: New development of CNS-2 status or clinical signs of CNS leukemia such as facial nerve palsy, cranial nerve involvement, or hypothalamic syndrome without another explanation. New development of CNS-2 status on 2 consecutive lumbar punctures (between 2-4 weeks apart) with confirmation by immunophenotyping or other molecular testing methods.

Pediatric and AYA Leukemia
Acute Lymphoblastic Leukemia

Initial diagnosis of ALL

Induction phase
- Induce remission immediately
  - Vincristine, steroid (dexamethasone or prednisone)
  - Probability anthracyclines (typically doxorubicin)
  - 4–6 weeks long

Consolidation phase
- Eliminate residual sub-microscopic cancer cells
  - Multiple treatment regimens chosen based on patient’s risk factors
  - Cyclophosphamide, cytarabine, 6-MP or other thiopturic
  - Probably with interim maintenance phase and/or reinstation
  - 6–9 months long

Maintenance phase
- Decrease relapse risk post-treatment
  - 6-MP and methotrexate
  - Probably occasional pulses of corticosteroids and vincristine
  - 2–3 years long

Induction failure
- Allogeneic BMT to induce remission
Pediatric & AYA Leukemia
Myeloproliferative and Myelodysplasia

- Myelodysplastic and myeloproliferative disorders are rare in children and have different morphologic features, cytogenetic findings, prognostic factors, and therapeutic aims than in adults.
- To recognize the challenges in making a diagnosis of MDS in children
- To know the different therapeutic strategies in low-grade and advanced MDS
- To understand the genetics of JMML and how it may be used for treatment stratification

<table>
<thead>
<tr>
<th>Characteristics of MDS in children and adults</th>
</tr>
</thead>
<tbody>
<tr>
<td>Characteristic</td>
</tr>
<tr>
<td>---------------------------------</td>
</tr>
<tr>
<td>Annual incidence per million</td>
</tr>
<tr>
<td>Associated abnormalities</td>
</tr>
<tr>
<td><strong>Morphologic groups</strong></td>
</tr>
<tr>
<td>Refractory anemia with ringed sideroblasts</td>
</tr>
<tr>
<td>Hypoplastic MDS</td>
</tr>
<tr>
<td>Abnormal cytogenetics</td>
</tr>
<tr>
<td>−7/del(7q)</td>
</tr>
<tr>
<td>−5/del(5q)</td>
</tr>
<tr>
<td><strong>Hypermethylation</strong></td>
</tr>
<tr>
<td>Spliceosomal gene aberration</td>
</tr>
<tr>
<td>Aim of treatment</td>
</tr>
</tbody>
</table>

Blast count and relative distribution of AML and MDS illustrates that AML can be diagnosed at any blast level.

Adapted from Hasle and Niemeyer.
Benign, Borderline, Low Grade Malignant, High Grade Malignant

Brain, Intracranial, Intracranial Glands, Spinal Cord, Meninges, Cranial Nerves and Any Other Site within the Cranium/Spinal Cord

Source: The Simpsons – Homer Brain X-Ray

**Gliomas** Gliomas are not a specific type of tumor. Glioma is a general term for a group of tumors (50%)
- Sometimes Gliomas are described by their WHO Grade
- Sometimes Gliomas are described by their Anatomic Location
- Sometimes Gliomas are described by Type of Glial Cell Involved
  - Astrocytomas (which include glioblastomas)
    - Fibrillary, Pilocytic or Anaplastic
  - Oligodendroglioma
  - Pleomorphic Xanthoastrocytoma (PXA)
  - Brain stem glioma
  - Optic Nerve Glioma/glioAstrocytomas
  - Galglioglioma
  - Thalamic and Hypothalamic Astrocytoma
  - Diffuse Intrinsic Ponting Glioma (DIPG)
  - Tectal Glioma (a brainstem glioma)
  - Dysembryonic Neuroepithelial Tumor (DNET or DNT)
  - Gliomas are grouped by WHO Grade of Tumor
Astrocytomas are tumors that start in astrocytes, a kind of glial cell – so, these neoplasms appear very similar:

- Some astrocytomas can spread widely throughout the brain and blend with the normal brain tissue, which can make them hard to remove by surgery.
- Sometimes they spread along the cerebrospinal (CSV) pathways.
- It is very rare for them to spread outside the brain.
- Astrocytomas are grouped by WHO Grade of Tumor.
Pediatric & AYA Brain and CNS Tumors

- **Low-grade (Grade I or II) Astrocytoma** – grow slowly and most common in children – do not infiltrate tissues
  - Pilocytic astrocytoma
  - Subependymal giant cell astrocytoma (SEGA)
  - Diffuse Astrocytoma
  - Pleomorphic xanthoastrocytomas (XSAs)
  - Optic Glioma

- **High-grade (Grade III or IV) Astrocytoma** – grow quickly and invade surrounding normal brain tissue
  - Glioblastoma Multiforme - Grade IV
  - Anaplastic Astrocytoma - Grade III

Source: Childhood Astrocytoma Treatment (PDQ)
Pediatric & AYA Brain and CNS Tumors

CBTTC PEDIATRIC BRAIN TUMOR ATLAS

1ST RELEASE – LARGEST COLLECTION OF PEDIATRIC BRAIN TUMOR DATA

- 30 brain tumor types
- Data from over 1,000 patients
- Releasing data in REAL-TIME
- More than 16 partner institutions
- Over 50 foundation sponsors
- Includes WGS, RNAseq, Proteomics, Clinical, Imaging & Histology Data

Children’s Brain Tumor Network
Until every child is cured

http://cbtn.org/

Pediatric & AYA Brain and CNS Tumors

- Oligodendroglioma
- Ependymoma
- Brain Stem Glioma
- Medulloblastoma
- Pinioblastoma
- Atypical Teratoid Rhabdoid Tumor (ATRT)
- Primitive Neuroectocermal Tumors (PNET)
Pediatric & AYA Brain and CNS Tumors

Embryonal Cell Tumors
- Medulloblastoma
- Atypical Teratoid/Rhabdoid Tumor (ATRT)
- Embryonal Tumor with Multilayered Rosettes

Pituitary Tumors

Pineal Tumors
- Pineoblastoma
- Craniopharyngeoma – just above the pituitary gland

Mixed Glial and Neural Tumors
- Chorioid Plexus Tumors
  - Schwannoma (neurilemmoma – Acoustic Schwannoma)
- Meningioma
- Chordoma

Source: http://www.vivo.colostate.edu/hbooks/pathphys/endocrine/hypopit/anatomy.html
Molecular Genetic Mutations - Ependymoma

Other Brain and CNS Sources

Neuro-Oncology

CBTRUS Statistical Report: Primary Brain and Other Central Nervous System Tumors Diagnosed in the United States in 2013–2017
Pediatric & AYA Lymphoma

2015

Pediatric & AYA Neuroblastoma

International Neuroblastoma Staging System Committee (INSS) system

The following is a brief summary of each INSS stage:

**Stage 1**: The tumor can be removed completely during surgery. Lymph nodes attached to the tumor removed during surgery may or may not contain cancer, but other lymph nodes near the tumor do not.

**Stage 2A**: The tumor is located only in the area it started and cannot be completely removed during surgery. Nearby lymph nodes do not contain cancer.

**Stage 2B**: The tumor is located only in the area where it started and may or may not be completely removed during surgery, but nearby lymph nodes do contain cancer.

**Stage 3**: The tumor cannot be removed with surgery. It has spread to regional lymph nodes (lymph nodes near the tumor) or other areas near the tumor, but not to other parts of the body.

**Stage 4**: The original tumor has spread to distant lymph nodes (lymph nodes in other parts of the body), bones, bone marrow, liver, skin, and/or other organs, except for those listed in stage 4S, below.

**Stage 4S**: The original tumor is located only where it started (as in stage 1, 2A, or 2B), and it has spread only to the skin, liver, and/or bone marrow, in infants younger than one. The spread to the bone marrow is minimal, usually less than 10% of cells examined show cancer.
Pediatric & AYA Neuroblastoma

**Statistics, Risk Factors, Incidence**
- Approximately 500-1000 cases/year in the US.
- 8% of all cancers, but responsible for over 15% of deaths.
- Median age at diagnosis is 2 years old.
- In 70% of the cases the disease has spread to other parts of the body at diagnosis.
- The prognosis for high-risk neuroblastoma was 20% until recently.

**Symptoms can include:**
- lump or mass in the abdomen, neck, chest, or pelvis
- loss of appetite, nausea, weight loss, stomach pain, constipation, diarrhea, difficulty urinating
- changes in the eyes: black eyes, a droopy eyelid, a pupil that doesn’t constrict, vision problems
- pain in the chest, difficulty breathing, persistent cough
- in infants, painless, bluish lumps under the skin
- bone pain, fever, irritability, listlessness
- backaches
- pain or numbness in the lower extremities, limping, inability to stand, stumbling

---

The International Neuroblastoma Risk Group Staging System (INRGSS)

The INRGSS was designed specifically for the International Neuroblastoma Risk Group (INRG) pre-treatment classification system (see Risk groups, below). Unlike the INSS explained above, the INRGSS uses only the results of imaging tests taken before surgery. It does not include surgical results or spread to lymph nodes to determine the stage. Knowledge regarding the presence or absence of image defined risk factors (IDRF) are required for this staging system.

**Stage L1:** The tumor is located only in the area where it started; no IDRFs are found on imaging scans, such as CT or MRI.

**Stage L2:** The tumor has not spread beyond the area where it started and the nearby tissue; IDRFs are found on imaging scans, such as CT or MRI.

**Stage M1:** The tumor has spread to other parts of the body (except stage M5, see below)

**Stage M5:** The tumor has spread to only the skin, liver, and/or bone marrow (less than 10% bone marrow involvement) in patients younger than 18 months.
Pediatric & AYA Sarcoma (bone/soft tissue)

- **Bone Cancers start in bone (primary bone cancer)**
  - Occur most often in older children and teens
  - Can develop at any age.
  - Can develop in bone (medullary) or outside bone (extra-medullary)
  - Account for about 3% of childhood cancers.

- **Two Main Types**
  - Osteosarcoma – most common in teens and usually develops in areas where the bone is growing quickly, such as near the ends of the leg or arm bones and at the knees and shoulders.
  - Ewing Sarcoma - a less common type of bone cancer. It is most often found in young teens. The most common places for it to start are the pelvic (hip) bones, the chest wall (such as the ribs or shoulder blades), or in the middle of the leg bones.
### Pediatric & AYA Sarcoma (bone/soft tissue)

- Soft Tissue Sarcoma start in a variety of supportive connective tissue that includes muscle, fat, tendons, peripheral nerves, fibrous tissue, walls of organs and blood vessels, etc.

- Rhabdomyosarcoma accounts for 5-8% of childhood cancers.

- Rhabdomyosarcoma accounts for about half of the cases of pediatric soft tissue sarcomas.

- 50% of the children with rhabdomyosarcoma survive 5 years.

- Less frequent pediatric soft tissue sarcomas include fibrosarcoma, mesenchymoma, synovial sarcoma, and liposarcoma.

### Pediatric & AYA – Ewing’s Tumor

- Ewing Tumors account for 1% of all childhood cancers
- 200 children/teens are diagnosed with Ewing tumors in the U.S. each year

- Ewing Sarcoma Histology Coded for Years as 9260/3
  - Code 9260/0 still exists – Aneurysmal bone cyst – only.
- 2021 Start Coding Ewing Tumors to 9364/3
- What else is under code 9364/3?
  - Ewing sarcoma
  - Peripheral neuroectodermal tumor (PNET)
  - Neuroectodermal tumor, NOS
  - Peripheral primitive neuroectodermal tumor (PPNET)

- Tumor Locations
  - Pelvis (hip bones)
  - Chest Wall (ribs/shoulder blades)
  - Legs (middle of long bones)

- NOTE: Osteosarcoma usually occurs at the ends of the long bones around the knees – not in the middle of the bone.
Pediatric & AYA Germ Cell Neoplasms

- Germ cell tumors (GCTs) are rare in childhood, representing only 3.5% of childhood cancers
- GCTs are a common malignancy in adolescents and young adults (AYAs), accounting for 13.9% of neoplasms in adolescents age 15 and 19 years.
- The overall outcomes for GCTs are excellent.
Pediatric & AYA Germ Cell Neoplasms

MEMBERS BY SUB-SPECIALTY

Thyroid Cancers

Thyroid Cancers To Be Discussed Another Time
Pediatric, Adolescent, Young Adult and Older Adult
Rare Pediatric & AYA Cancers


- **Retinoblastoma** – Cancer of the retina of the eye. Makes Up about 2% of childhood cancers. It usually occurs around age 2 and rare if found under age of 6.

- Changes in how the child’s eye looks (inside or out, movement, vision).

- Normally when you shine a light in a child’s eye (or take a flash picture), the pupil (the dark spot in the center of the eye) looks red because of the blood in the vessels in back of the eye – the pupil will look white or pink.

- **Ependymoma** - tumors that grow in your brain or any part of the spine, including your neck and upper and lower back. They form at first in your ependymal cells in the middle of your spinal cord and in the fluid-filled spaces in your brain known as ventricles.

---

Rare Pediatric & AYA Cancers

- Pheochromocytoma and Paraganglioma
- Multiple Endocrine Neoplasia Syndromes (MEN)
- Nasopharyngeal Cancer
- Esthesioneuroblastoma
- Thyroid Cancer
- Oral Cavity and Salivary Gland Tumors
- Laryngeal Cancers and Papillomatosis
- NUT Midline Carcinoma
- Breast Cancer
- Lung Cancer
- Thymoma
- Mesothelioma
- Adrenocortical Carcinoma
- Cervical and Vaginal Cancer
- Ovarian Cancer
- Skin Cancers
- Intraocular (Uveal) Melanoma
- Chordoma
- Unknown Primary Carcinoma
Childhood Cancer Genomics

- **Genenomic Lesions with Immediate Therapeutic Direction Found**
  - NPM-ALK fusion genes associated with anaplastic large cell lymphoma cases.
  - ALK point mutations associated with a subset of neuroblastoma cases.
  - BRAF and other kinase genomic alterations associated with subsets of pediatric glioma cases.
  - Hedgehog pathway mutations associated with a subset of medulloblastoma cases.
  - ABL family genes activated by translocation in a subset of acute lymphoblastic leukemia (ALL) cases.

- **Genomics Identify Constellations moving to Disease Categories**
  - The presence of H3.3 and H3.1 K27M mutations almost exclusively among pediatric midline high-grade gliomas.
  - The loss of SMARCB1 in rhabdoid tumors.
  - The presence of RELA translocations in supratentorial ependymomas.
  - The presence of specific fusion proteins in different pediatric sarcomas.


Childhood Cancer Genomics

Source: PDO NCI – Childhood Cancer Genomics - Figure 1. Subclassification of childhood ALL. Blue wedges refer to B-progenitor ALL, yellow to recently identified subtypes of B-ALL, and red wedges to T-lineage ALL. Reprinted from *Seminars in Hematology*, Exit Disclaimer, Volume 50, Charles G. Mullighan, Genomic Characterization of Childhood Acute Lymphoblastic Leukemia, Pages 314–324, Copyright (2013), with permission from Elsevier.

Childhood Cancer Genomics

- High hyperdiploidy (51–65 chromosomes).
- Hypodiploidy (<44 chromosomes)
- t(12;21)(p13.2;q22.1); ETV6-RUNX1 (formerly known as TEL-AML1)
- t(9;22)(q34.1;q11.2); BCR-ABL1 (Ph+)
- t(v;11q23.3); KMT2A-rearranged
- t(1;19)(q23;p13.3); TCF3-PBX1 and t(17;19)(q22;p13); TCF3-HLF
- DUX4-rearranged ALL with frequent ERG deletions
- Intrachromosomal amplification of Chromosome 21 (iAMP21)
- PAX5 Alterations
- PAX5 with p.PRO80Arg Mutation
- MEF2D-rearranged ALL
- ZNF384-rearranged ALL
- t(5;14)(q31.1;q32.3); IL3-IGH
- Ph-like (BR-ABL1-like)
- IKZF1 Deletions
- Chromosomal Translocations
- Gene Fusions
- Notch Pathway Signaling

Childhood Cancer Genomics

- Multiple Types of Specific Brain Tumors
  - BRAF V600E mutations
  - IDH1 mutation
  - K27 mutations: H3.3 (H3F3A) and H3.1 (HIST1H3B and, rarely, HIST1H3C) mutations at K27
  - High-grade gliomas in infants
  - Diffuse leptomeningeal glioneuronal tumor (DLGNT)
  - Rosette-forming glioneuronal tumor (RGNT)
  - Desmoplastic infantile astrocytomas (DIA) and desmoplastic infantile gangliogliomas (DIG)
  - Dysembryoplastic neuroepithelial tumor (DNET)

- Multiple Types of Specific CNS Tumors
  - Adult Teratoid/Rhaboid Tumors - SMARCB1 gene
  - Medulloblastoma, WNT-activated
  - CNS NS high-grade neuroepithelial tumor with MN1 alteration (CNS HGNET-MN1)
  - And, many Non-Brain/CNS Pediatric & Young Adult Neoplasms with specific genetic characteristics...including solid tumors like Ewing Sarcoma and Neuroblastoma and Retinoblastoma and Wilms Tumor are also defined by molecular genetics with targets for treatment that are clearly identified without multiple genetic mutations.


---

NCI-COG Pediatric MATCH Trial
Pediatric MATCH is enrolling children, adolescents, and young adults 1–21 years old with advanced solid tumors whose cancer has gotten worse while on treatment or has come back, or relapsed, after treatment.

The trial’s initial screening step uses a single test that looks for changes in more than 160 genes associated with cancer that can be targeted by one of the drugs being tested in the study. Researchers plan to screen at least 1,000 to 1,500 pediatric patients for the trial, Dr. Seibel said.

Those patients whose tumors have a genetic change that can be targeted by a drug included in the study may then go on to the second step of the trial, which is to enroll in the treatment group, or arm, for that drug. Ten drugs are being tested now and more will be added as the study continues.

<table>
<thead>
<tr>
<th>Arm</th>
<th>Target</th>
<th>Drug</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>pan-TRK</td>
<td>larotrectinib</td>
</tr>
<tr>
<td>B</td>
<td>FGFR</td>
<td>erdafitinib</td>
</tr>
<tr>
<td>C</td>
<td>EZH2</td>
<td>tazemetostat</td>
</tr>
<tr>
<td>D</td>
<td>P13K/mTOR</td>
<td>LY3023414</td>
</tr>
<tr>
<td>F</td>
<td>ALK</td>
<td>ensartinib</td>
</tr>
<tr>
<td>G</td>
<td>BRAF</td>
<td>vemurafenib</td>
</tr>
<tr>
<td>H</td>
<td>PARP</td>
<td>olaparib</td>
</tr>
<tr>
<td>I</td>
<td>CDK4/6</td>
<td>palbociclib</td>
</tr>
<tr>
<td>K</td>
<td>IDH 1 inhibitor</td>
<td>ivosidenib</td>
</tr>
<tr>
<td>M</td>
<td>HRAS inhibitor</td>
<td>tipifarnib</td>
</tr>
<tr>
<td>N</td>
<td>RET</td>
<td>selpercatinib (LOXO-292)</td>
</tr>
</tbody>
</table>
Staging Pediatric Tumors

Staging Resources Pediatric Tumors

- Wilms Tumor Study Group Staging
- International Neuroblastoma Staging System
- Children’s Oncology Group Neuroblastoma Risk Grouping
- Intergroup Rhabdomyosarcoma Study Staging System
- Soft Tissue Sarcoma Tumor Pathological Grading System
- FNCLCC Grading System
- TNM Staging System
- SEER Summary Stage 2018
- Collaborative Stage Data Collection
- Childhood Cancer Staging for Population Registries
- Toronto Childhood Cancer Staging Guidelines

http://cancer.gov/
Solid Tumor Staging - Example

- Wilms Tumor
- Stage I – 43%
  - Tumor is limited to the kidney
  - Tumor is completely resected.
  - The renal capsule is intact.
  - Tumor is not ruptured or biopsied prior to removal.
  - No involvement of renal sinus vessels.
- Stage II – 20%
  - Tumor is completely resected,
  - The tumor extends beyond the kidney as evidenced by any one of the following:
    - There is regional extension of the tumor (i.e., penetration of the renal sinus capsule).
    - Blood vessels in the nephrectomy specimen outside the renal parenchyma with tumor
- Stage III – 21%
  - Residual non-hematogenous tumor present following surgery confined to the abdomen
- Stage IV – 11%
  - Hematogenous metastases (lung, liver, bone, brain).
  - Lymph node metastases outside the abdomino-pelvic region are present
- Stage V – 5%
  - Bilateral involvement by tumor is present at diagnosis

Staging Resources for Pediatric Neoplasms

https://cancerqld.blob.core.windows.net/content/docs/childhood-cancer-staging-for-population-registries.pdf
Staging Resources for Pediatric Neoplasms

Paediatric cancer stage in population-based cancer registries: the Toronto consensus principles and guidelines


Population-based cancer registries generate estimates of incidence and survival that are essential for cancer surveillance, research, and control strategies. Although data on cancer stage allow meaningful assessments of changes in cancer incidence and outcomes, stage is not recorded by most population-based cancer registries. The main method of staging adult cancers is the TNM classification. The criteria for staging pediatric cancers, however, vary by diagnostic entity and over time, and sometimes vary by cooperative trial group. Consistency in the collection of staging data has therefore been challenging for population-based cancer registries. We assembled key experts and stakeholders (oncologists, cancer registrars, epidemiologists) and used a modified Delphi approach to establish principles for pediatric cancer stage collection. In this Review, we make recommendations on which staging systems should be adopted by population-based cancer registries for the major childhood cancers, including adaptations for low-income countries. Wide adoption of these guidelines in registries will ease international comparative incidence and outcome studies.

Lancet Oncol 2016; 17: e163–72

---

Staging Resources for Pediatric Neoplasms

<table>
<thead>
<tr>
<th>Stage</th>
<th>Criteria for extent of disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>A single tumor (extranodal) or single anatomic area (nodal) with the exclusion of the mediastinum and abdomen</td>
</tr>
</tbody>
</table>
| II    | A single tumor (extranodal) with regional node involvement  
|       | Two or more nodal areas on the same side of the diaphragm  
|       | Two single (extranodal) tumors with or without regional node involvement on the same side of the diaphragm  
|       | A primary gastrointestinal tumor, usually in the ileocecal area, with or without involvement of associated mesenteric lymph nodes only, grossly completely resected |
| III   | Two single tumors (extranodal) on opposite sides of the diaphragm  
|       | Two or more nodal areas above and below the diaphragm  
|       | All the primary intrathoracic tumors (mediastinal, pleural, thymic)  
|       | All extensive primary intra-abdominal disease, unresectable  
|       | All paraspinous or epidural tumors, regardless of other tumor site(s) |
| IV    | Any of the above with initial CNS and/or bone marrow involvement |
Staging Resources for Pediatric Neoplasms

Table 1: Revised Pediatric NHL Staging System

Stage I
- Single tumor in lymph nodes
- No extranodal disease

Stage II
- Single tumor in lymph nodes with extranodal disease

Stage III
- Multiple tumors in lymph nodes
- Extranodal disease

Stage IV
- Multiple tumors in lymph nodes
- Diffuse disease

Note: One cohort: Distinction is made between separate, isolated, and coexisting lymphomas versus a single systemic disease. The absence of two isolated lymphomas or more than one extranodal disease. The absence of two isolated lymphomas or more than one extranodal disease.

Reference: SEER Summary Staging Manual 2020

Solid Tumor Staging

Source: SEER Summary Staging Manual 2020
Hematopoietic Staging Resources

Treatment
Treatment Options – Basic Concepts

- Pre-Induction Risk Assessment
- Induction Therapy
- Post-Induction Assessment
- Re-Induction Therapy
- Intensification/Consolidation Therapy
- Post-Consolidation Assessment
- BMT/Stem Cell Transplant
- Maintenance Therapy
- Maintenance Assessment

Initial diagnosis of ALL:

**Induction phase**
- Induce remission immediately
  - Vincristine, steroid (dexamethasone or prednisone)
  - Probably anthracyclines (typically doxorubicin)
  - 4-6 weeks long

**Consolidation phase**
- Eliminate residual sub-microscopic cancer cells
  - Multiple treatment regimens chosen based on patient's risk factors
  - Cytophosphamide, cytarabine, 6-MP or other therapeutics
  - Probably with interim maintenance phase and/or consolidation
  - 6-9 months long

**Maintenance phase**
- Decrease relapse risk post-treatment
  - 6-MP and methotrexate
  - Probably occasional pulses of corticosteroids and vincristine
  - 2-3 years long

Induction failure
- Allogeneic BMT to induce remission
Treatment Options – Basic Concepts

- Risk-Based Treatment – Pre-Induction Risk
  - Patient Characteristics
    - Age at Diagnosis
    - WBC Count at Diagnosis
    - CNS Involvement
    - Gender
  - Neoplasm Characteristics
    - Morphology
    - Immunophenotype
    - Cytogenetics
  - Genetic Characteristics of Neoplasm
    - Philadelphia Chromosome Translocation
    - MLL Translocations
    - CRLF2 and JAK Mutation

Source: [http://cancer.gov](http://cancer.gov) – Pediatric Lymphoid Neoplasm NCI PDQ for Health Professionals

---

Treatment Options – Basic Concepts

- Risk-Based Treatment – Induction Failure
  - Patients at highest risk of induction failure:
    - T-cell phenotype (especially without a mediastinal mass).
    - B-precursor ALL with very high presenting leukocyte counts.
    - 11q23 rearrangement.
    - Older age.
    - Philadelphia chromosome

- Risk-Based Treatment – Re-Induction/Consolidation
  - Re-Induction
  - Intensification
  - Consolidation

- Risk-Based Treatment – Sanctuary Sites

- Risk-Based Treatment – Maintenance Therapy

Source: [http://cancer.gov](http://cancer.gov) – Pediatric Lymphoid Neoplasm NCI PDQ for Health Professionals
Risk-Based Treatment Assessment

- Low Risk Disease – Stage I, II – no B symptoms, no bulky disease
- Intermediate Risk Disease – Stage I, II with B symptoms
- Intermediate Risk Disease – Stage I, II with bulky disease
- Intermediate Risk Disease – Stage IIIA, IVA
- High Risk Disease – Stage IIIB, IVB
- High Risk Disease – Poor response to initial chemotherapy

Source: [Pediatric Lymphoid Neoplasm NCI PDQ for Health Professionals](http://cancer.gov)
Treatment Options – Lymphoid Neoplasms

- Hodgkin Lymphoma
- Non-Hodgkin Lymphoma
- Chronic Lymphocytic Leukemia
- Acute Lymphocytic Leukemia
- Other Lymphoid Neoplasm


Treatment Options – Myeloid Neoplasms

- Myeloid Leukemia Associated with Down Syndrome
- Chronic Myeloid Leukemia
- Acute Myeloid Leukemia
- Other Myeloid Neoplasm
- MPD/MPS/MDS

Source: http://cancer.gov – Pediatric Myeloid Neoplasm NCI PDQ for Health Professionals
Late Effects of Treatment

- **Childhood Cancer Survivors Study**
  - Chance for long-term effects increase over time
  - > 70% at least 1 chronic illness related to treatment
  - > 25% have 3 or more chronic illnesses related to tx
  - Kidney Disease
  - Second Cancers
  - Cognitive Dysfunction
  - Cardiovascular Disease
  - Endocrine Abnormalities
  - Musculoskeletal Conditions

http://cancer.gov/

Survivorship and Long Term Follow-Up

It is also important to keep a record of the cancer treatment that a child received. This record should include:

- The type and stage of cancer
- Date of diagnosis and dates of any relapses
- Types and dates of imaging tests
- Contact information for the hospitals and doctors who provided treatment
- Names and total doses of all chemotherapy drugs used in treatment
- The parts of the body that were treated with radiation and the total doses of radiation that were given
- Types and dates of all surgeries
- Any other cancer treatments received
- Any serious complications that occurred during treatment and how those complications were treated
- The date that cancer treatment was completed

The record should be kept in a safe place, and copies of the record should be given to all doctors or other health care providers who are involved with the child’s follow-up care, even as the child grows into adulthood.
Social and Emotional Issues

- Dealing with physical changes (hair loss, weight gain, scars from surgery, etc.) that can result from the cancer or its treatment
- Worrying about the cancer returning or developing new health problems
- Resenting having cancer and having to go through treatment when others do not
- Having to become more reliant on parents at a time when a person is normally becoming more independent
- Having concerns about what to tell others or being treated differently or discriminated against (by friends, classmates, co-workers, employers, etc.)
- Having concerns about dating and someday marrying and having children
- Dealing with Mental Health Issues – anxiety, depression

Source: cancer.org

Other Clinical Trials and Treatment Options

[Diagrams showing different treatment options and processes]
# Documentation for Pediatric & AYA Cancers

- Always documenting Pediatric, Adolescent and young adult cancers turning every page to get out as much information as possible. Provide best chronology you can

- If a child is referred to you for any reason...get a complete a history as you can for their cancer – including why they are at your facility – code all first course treatment – not just what your facility did for the child – support, treatment, follow-up

- Even the smallest details could be important in the future of research for these cancers.

- FCDS Visually Edits Every Single Pediatric Case We Get

- FCDS Conducts a Data Quality Annually Comparing FAPTP Data to FCDS Data and Programs Share Results

## Abbreviations

- ATRT atypical teratoid/rhabdoid tumor
- ATRX alpha thalassemia/mental retardation syndrome X-linked
- bMMRD biallelic mismatch repair deficiency
- CAR chimeric antigen receptor
- CNV copy number variation
- DIPG diffuse intrinsic pontine glioma ETANTR embryonal tumor with abundant neuropil and true rosettes
- ETMR embryonal tumor with multilayered rosettes
- FGFR1 fibroblast growth factor receptor 1
- GBM glioblastoma multiforme
- HGG high-grade glioma
- LGG low-grade glioma
- NF-1 neurofibromatosis type 1
- POS overall survival
- A pilocytic astrocytoma
- PF-EPN posterior fossa ependymoma
- PFS progression-free survival
- pHGG pediatric high-grade glioma
- pLGG pediatric low-grade glioma
- PMA pilomyxoid astrocytoma
- PNET primitive neuro-ectodermal tumor
- PR partial response
- PXA pleomorphic xanthoastrocytoma
- RTK receptor tyrosine kinase
- SEGA subependymal giant cell astrocytoma
- SNV somatic nucleotide variation
- SRBC small round blue cell tumor
- ST-RPN supratentorial ependymoma
## 2021 Changes

- Retire Flat File Format – will allow flat file submissions/data transmissions until 6/30/2021
- XML File Format – 7/1/2021 (tentative)/optional for submissions starting Jan 2021
- 2021 New Reportable Criteria – ALL GIST, ALL Thymoma, Evolving Melanoma –
- 2021 Not Reportable Criteria – Need to remove NIFTP, EFVPTC, EFVPTC and other histologies from thyroid and review non-invasive histologies for pancreas – need to clarify removals
- Schema ID – changes to criteria and one new schema added
- 2021 Solid Tumors – 2 newly revised chapters (Melanoma/Other) and changes to all 8 other chapters
- Expecting to see GYN Solid Tumor Rules before September 2021 according to ETC Training Schedules
- Please participate in any 2021 Updates Webinars sponsored by NAACCR, FCDS, SEER, CoC
- FCDS will be sponsoring some webinars – but, other experts may do a better job of explaining

### 2021 Changes

<table>
<thead>
<tr>
<th>2021 New Data Items Required</th>
<th>Grade Field Conversions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Name-Birth Surname – Replaces Maiden Name which will be Retired</td>
<td>Stage Conversions</td>
</tr>
<tr>
<td>Medicare Beneficiary ID</td>
<td>SSDI Conversions</td>
</tr>
<tr>
<td>Grade Post Therapy Clinical (yc)</td>
<td>2021 Retired Data Items – TNM 6 &amp; 7, Maiden Name</td>
</tr>
<tr>
<td>Gleason Pattern Clinical</td>
<td>2021 FCDS DAM Revision</td>
</tr>
<tr>
<td>Gleason Pattern Pathological</td>
<td>FCDSv21 EDITS Metafile</td>
</tr>
<tr>
<td>Gleason Score Clinical</td>
<td>FCDSv21 Updates to Abstractor Code</td>
</tr>
<tr>
<td>Gleason Score Pathological</td>
<td>Test &amp; Review of Existing Q&amp;A</td>
</tr>
<tr>
<td>Gleason Tertiary Pattern</td>
<td>2021 Grade Manual</td>
</tr>
<tr>
<td>Changed Data Items – LDH</td>
<td>2021 SSDI Manual</td>
</tr>
<tr>
<td>HER2 Overall Summary added to Esophagus and Stomach Schemas 00161, 00169, 00170</td>
<td>2021 Heme Updates</td>
</tr>
<tr>
<td>Radiation Modality New Codes</td>
<td>2021 Solid Tumors – 2 newly revised chapters (Melanoma/Other) and changes to all 8 other chapters</td>
</tr>
<tr>
<td>Changes to SSDIs</td>
<td>Expecting to see GYN Solid Tumor Rules before September 2021 according to ETC Training Schedules</td>
</tr>
<tr>
<td>FIGO Stage</td>
<td>2021 ICD-O-3 Updates</td>
</tr>
<tr>
<td>Grade – schema specific</td>
<td>2021 STORE Manual</td>
</tr>
</tbody>
</table>
### References and Resources

- **ASCO – Neuroblastoma – Childhood: Stages and Groups**
- **2021 Cancer Facts & Figures – American Cancer Society**
- **American Cancer Society Series on Pediatric Cancers**
  - Differences Between Adult and Childhood Cancers
  - Brain and Spinal Cord Tumors in Children
  - Types of Cancers that Develop in Children
  - Ewing Tumors
  - Osteosarcoma
  - Retinoblastoma
  - Wilms Tumor
  - Causes and Risk Factors in Childhood and Adolescent Cancers
  - Key Statistics in Childhood & Adolescent Cancers
  - Types of cancers that Develop in Adolescents
  - Treating Childhood and Adolescent Cancers
  - Long and Late Term Effects of Cancer Treatment in Adolescents
- **NIH/NCI – Cancer in Children and Adolescents**
- **Childhood Cancer Staging for Population Registries According to the Toronto Childhood Cancer Stage Guidelines – Cancer Council Queensland and Cancer Australia: Brisbane, Australia; 2017.** [https://cancerqld.blob.core.windows.net/content/docs/childhood-cancer-staging-for-population-registries.pdf](https://cancerqld.blob.core.windows.net/content/docs/childhood-cancer-staging-for-population-registries.pdf)

### References and Resources

- **National Cancer Institute Physician Data Query (PDQ) - Health Professionals**
  - Cancer in Children and Adolescents
  - Childhood Cancers Fact Sheet
  - Childhood Acute Lymphoblastic Leukemia
  - Childhood Acute Myeloid Leukemia
  - Childhood Brain and Spinal Cord Tumors Overview
  - Childhood Astrocytoma
  - Childhood CNS Embryonal Tumors
  - Childhood CNS Atypical Teratoid/Rhabdoid Tumors
  - Childhood Hodgkin Lymphoma
  - Childhood Non-Hodgkin Lymphoma
  - Ewing Sarcoma
  - Childhood Soft Tissue Sarcoma
  - Childhood Rhabdomyosarcoma
  - Neuroblastoma
  - Wilms Tumor
  - Rare Cancers of Childhood
References and Resources

- NCI Cancer Bulletin, Pediatric Oncology Partnerships are Models for Success, Volume 5/Number 6, March 18, 2008
- Advances in Neuroblastoma Risk Assessment and Treatment, Susan L Cohn, MD, University of Chicago Department of Pediatrics
- Florida Association of Pediatric Tumor Programs (FAPTP)
- Children’s Oncology Group (COG)
- NCI-COG Pediatric MATCH – National Cancer Institute – 2021

References and Resources

- Pediatric cancer stage in population-based cancer registries: Toronto consensus principles and guidelines; www.thelancet.com/oncology Vol 17 April 2016
- Advances in the molecular classification of pediatric brain tumors; a guide to the galaxy; J Pathol 2020; 251: 249–261., Published online 10 June 2020
- SEER Tables for ICCC, 3rd edition plus Age Adjusted Rates and Survival Analysis for Pediatric and AYA Cancers 1975-2017 by age group 0-14 and 0-19
- TARGET Study Finds Major Differences between Childhood and Adult AML, 2018
- Moonshot Update – Pediatric Moonshot Initiative – Fusion Oncoproteins in Childhood Cancers Consortium (FusOnC2), 2021
- Revised International Pediatric Non-Hodgkin Lymphoma Staging System; JCO, Vol 33 Num 18, June 20, 2015