The Changing Landscape of Pediatric Cancer Drug Development
Implementing the Research to Accelerate Cures and Equity for Children Act (RACE)

Thank you for joining today’s webinar. For best audio quality, we suggest using your computer’s audio controls.

If you are listening through your computer, but would prefer to join by phone, click on “audio options” and “phone” and dial-in numbers will be displayed.

Today’s webinar is being recorded and will be available afterwards on www.childrenscause.org

All lines are muted, but you will have the ability to submit questions. If you are joining by computer or app, you can ask a question by typing it into the Questions section of the control panel on the right. You can also use the ‘raise my hand’ feature.

If you need technical assistance during the webinar, please dial 202-487-3270
The Changing Landscape of Pediatric Cancer Drug Development

Implementing the Research to Accelerate Cures and Equity for Children Act (RACE)

Gregory Reaman, M.D.
Associate Director for Pediatric Oncology
Oncology Center of Excellence,
Office of the Commissioner
U.S. Food & Drug Administration

Elizabeth Fox, M.D.
Senior Vice President
Clinical Trials Research
St. Jude Children’s Research Hospital

Mark W Kieran, MD, PhD
Pediatric Clinical Trial Lead,
Bristol-Myers Squibb
<table>
<thead>
<tr>
<th>Best Pharmaceuticals for Children Act (BPCA)</th>
<th>Pediatric Research Equity Act (PREA)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>2002</strong> – Authorized for five years.</td>
<td><strong>2003</strong> – Following court ruling</td>
</tr>
<tr>
<td>Both BPCA &amp; PREA Reauthorized in 2007 – Reauthorized Permanently 2012</td>
<td></td>
</tr>
</tbody>
</table>

- **“The Carrot”**
- Incentive: Six months of market exclusivity
- Studies may be requested for orphan designated products.
- Pediatric Studies Must Be Targeted Toward Labeling

- **“The Stick”**
- Requirement: Company “must” do pediatric studies.
- Except: Requirement for studies may be waived for certain indications.
- AND: Products with orphan designation are exempt.
- Pediatric Studies Must Be Targeted Toward Labeling
- No substantial impact.
Research to Accelerate Cures and Equity (RACE) for Children Act

- Signed into law as part of FDARA of 2017
- Purpose is to promote reach and development of new cancer treatments for children
- Pediatric investigation can be required based on molecular target
- Orphan designated drugs are no longer exempt.
- Other requirements, including public meeting, timing, target identifications, limitations, etc.

LAW GOES INTO EFFECT
August 18, 2020
RACE for Children Act, FDARA Sec 504: The Evolving Landscape for Pediatric Cancer Drug Development

Children’s Cancer Cause

Gregory Reaman, M.D.
Associate Director for Pediatric Oncology
Oncology Center of Excellence, Office of the Commissioner
Associate Director, Pediatrics, Office of Oncologic Diseases,
Office of New Drugs, Center for Drug Evaluation and Research
RACE for Children Act:

- Incorporated as Title V Sec. 504 of the **FDA Reauthorization Act (FDARA)**, enacted August 18, 2017
- Amends Pediatric Research Equity Act **PREA** (Sec. 505B of the FD&C Act)
- Requires evaluation of new molecularly targeted drugs and biologics “intended for the treatment of adult cancers and directed at a molecular target substantially relevant to the growth or progression of a pediatric cancer.”
- **Substantially relevant** based on evidence deemed adequate by the Secretary of HHS: no pre-clinical evidence **required**.
- **Molecularly targeted pediatric cancer investigation**: clinically meaningful study data, “using appropriate formulations, regarding dosing, safety and preliminary efficacy to inform potential pediatric labeling.” [FDARA Title V Sec 504 (a)(3)(A) or FD&C Act Sec. 505B (a)(3)(A)].
- Elimination of **orphan exemption for pediatric studies** for cancer drugs directed at relevant molecular targets.
Sponsor Requirements

• Sec 505B(e) of the FD&C Act requires sponsors have an Agreed initial Pediatric Study Plan (iPSP) prior to submission of a NDA/BLA.

• After Aug. 18, 2020, the PREA requirements for applications of NEW active ingredients will no longer be based on indication, rather the molecular MOA of an investigational product (including orphan-designated); impact on automatic waivers

• The iPSP must include details of the “molecularly targeted pediatric cancer investigation”: non-hypothesis testing, dose finding, signal of activity-seeking study or justification for waiver or deferral plan

• Early communication between Industry and Investigator community encouraged

• Statute provides for early advice meetings with FDA to discuss development of iPSP (Sec. 503 FDARA)
Statutory Requirements for FDA

• Establish with NCI, update regularly, and post on FDA website a list of “relevant” targets (1 year)
• Establish and post a list of targets (non-relevant) leading to waivers of pediatric studies (1 year)
• Work with NCI, Pediatric Subcommittee of ODAC, PeRC, investigators, sponsors, experts, and advocates on implementation and required studies
• Convene an open public meeting (1 year)
• Issue guidance on implementation (2 years)

https://www.fda.gov/drugs/guidance-compliance-regulatory-information/guidances-drugs

• Focus on accelerating appropriate initial pediatric evaluations early in development timeline not increasing number of pediatric phase 1 studies
Target Lists

• Statutory requirement to purportedly address regulatory uncertainty for Industry and **guide (not dictate)** decision-making re. early evaluation plans and iPSP submission for a specific agent in accordance with the amended PREA requirement

• Lists subject to change due to emerging science

• **Designation as relevant neither an absolute nor exclusive requirement for decisions related to pediatric evaluation:** studies of new products may be required if directed at a target **not** on the list and waivers may be justified for products directed at targets considered relevant

• **Not envisioned to restrict authority or flexibility**

• **Candidate** Target List constructed by OCE with NCI and input from international content experts in open public meetings

• Association of a target with one or more pediatric cancers as reported in published, peer-reviewed literature, abstracts, and multiple public databases

• Efforts to strengthen the base of evidence- a continuing process
Relevant Target Lists

• Targets associated with specific gene abnormalities
• Targets associated with cell lineage determinants
• Targets on normal immune cells and cells within the Tumor Microenvironment
• Other Targets: Pathways and Functional Mechanisms
• Plans to regularly review and update lists: open Federal Register docket for recommendations for additions or deletions

• Lists posted on FDA’s OCE website Pediatric Oncology Program (https://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/OCE/default.htm)
Deferral Considerations for Agents Directed at Relevant Molecular Targets

- Pending sufficient evidence of pre-clinical/clinical activity observed in response to target inhibition
- Uncertainty regarding the single agent activity of a drug until such time that one or more biologically rational combinations demonstrate an effect (pre-clinical or clinical)
- Absence of an appropriate formulation for investigational purposes provided there has been due diligence in development and establishing bioequivalence
Waiver Considerations for Agents Directed at Relevant Targets

- Serious known or expected developmental toxicity - consideration for **full or age dependent partial waiver**
- Multiple “in class” product (single agent) without compelling evidence of substantial differences in efficacy, safety, PK profiles, or formulation to warrant additional pediatric studies
- Feasibility and practicability due to small study populations potentially addressed by limited study requirements and innovative study design and conduct: embedded pediatric trials, expansion cohorts, histology-agnostic development
- Age-dependent waivers based on available formulations for specific age groups
Considerations for Target and Product Prioritization

• Likely variable by target class and disease
• Prevalence of target expression in a single disease or across histologies
• Level of evidence that target inhibition modulates specific tumor growth: Non-clinical, Adult clinical or Pediatric pre-clinical data
• Extent of unmet clinical need (disease-specific) and potential public health impact
• Availability of and access to agent; formulation
• Availability of predictive or response biomarkers
• Collaboration between Industry and clinical investigator community: External multi-stakeholder input to inform FDA decision-making
Sec. 503 Early Advice Meetings

• Focus on clarifying iPSP requirements for original NDA/BLAs to be submitted on/after Aug. 18, 2020 resulting from PREA amendments
• Scheduled and held within 30 days of request
• Briefing Document and Questions required
• Meeting request to Review Division; scheduled with and by OCE Pediatric Oncology Program at OCEperc@fda.hhs.gov
• Internal meeting scheduled
• Written responses to questions prior to meeting
• Meeting management and minutes responsibility of OCE Pediatric Oncology Program
Closing

• Amendments to PREA by the RACE for Children Act finally bring equity to children with cancer globally.
• FDARA Sec. 504 will dramatically alter the landscape for pediatric cancer drug development.
• Earlier consideration of pre-clinical assessment of new assets using pediatric-specific models will be critical.
• Innovation in study design and coordination/conduct on a global scale is essential.
• Multi-stakeholder input to rational decision-making is required.
• RACE for Children Act will not solve all the obstacles to pediatric cancer drug development.
• Improvement in cancer outcomes for children through timely assessment of appropriate novel drugs requires successful implementation.
• Regulatory agency coordination/collaboration is essential.
RACE for Children Act: Academic Perspective

Elizabeth Fox, MD
March 25, 2020  3 PM Eastern/2 PM Central
Aims:

• Discuss prioritization of new agents in clinical trials for children with cancer

• Discuss potential impact of RACE for Children Act on development of clinical trials for children with cancer

• Review the importance of the partnership between academics and industry during implementation of the RACE for Children Act

Disclosures: None
US Childhood Cancer Statistics

Ward et al CA-Cancer J Clin 2014: 64 83-107

Incidence

Mortality
Evolution of Anticancer Drugs

Cytotoxic chemotherapy
- Mechlorethamine (1949)

Hormonal therapy
- Tamoxifen (1977)
  - Allogeneic BMT (1968)

Cell therapy
- Aldesleukin (1992)

Immunotherapy
- Rituximab (1997)

Targeted therapy
- Imatinib (2001)
Oncology Drug Approvals in the US

Courtesy of Frank Balis, MD
New Anti-Cancer Drugs

New FDA Approved Oncology Drugs

- **-tinib**: Tyrosine kinase inhibitor
- **-anib**: Angiogenesis inhibitor
- **-ciclib**: Cyclin-dependent kinase inhibitor
- **-zomib**: Proteosome inhibitor
- **-lisib**: PI3 kinase inhibitor
- **-parib**: PARP inhibitor
- **-stat**: Enzyme inhibitors
- **-ase**: Enzyme
- **-kin**: Interleukin (-leukin is IL-2)
- **-mab**: Monoclonal antibody
- **-leucel**: Cell therapy
- **-stim**: Colony stimulating factors
- **-tide**: Peptide
Globally, each year 300,000 children are diagnosed with cancer

1997-2017, the FDA approved 126 new drugs for cancer (Neel et al. EJC 2019)
- 5% had initial approval that included children
- 6.5 years elapsed between the first in human study to first in pediatric study

In 2018, the FDA approved 36 new drugs for adults with cancer
- 19% had individuals < 18 yo included in the approval
- 64% had clinical trials in children by 2020
- 100% of the targets had clinical trial in children (excluding hormonal antagonists)

Considerations
- Timeline for approval – FDA approval increases likelihood of a pediatric trial
- First in Class, Best in Class, or Best in class for children
- Drugs that are not approved but are of interest in pediatrics
Prioritization of New Agent Clinical Trials in Childhood Cancer

Childhood cancer is a rare disease, clinical trials with biomarker selection will further limit the population of eligible patients

- Evidence of drug-target-response relationship
- Toxicity profile, developmental considerations and reversibility
- Formulation
NTRK Inhibitors: Larotrectinib in Adults in and Children

Efficacy regardless of tumor type

FDA approved for adult and pediatric patients with solid tumors that have NTRK gene fusion without a known acquired resistance mutation, that are either metastatic or where surgical resection is likely to result in severe morbidity, and who have no satisfactory alternative treatments or whose cancer has progressed following treatment.

Laetsch et al Lancet Oncology 2018
NTRK, ROS, ALK inhibitor: Entrectinib in Brain Tumors

**EEF1G-ROS1**
- Baseline
- After 2 courses
- After 9 courses

**GOPC-ROS1**
- Baseline
- After 2 courses
- After 6 courses

**TPR-NTRK1**
- Baseline
- After 2 courses
- After 10 courses

**EML-NTRK2**
- Baseline
- After 2 courses
- After 6 courses

**ETV6-NTRK3**
- Baseline
- After 2 courses
- After 8 courses

Robinson ASCO 2019
# Same in Class Comparison

<table>
<thead>
<tr>
<th></th>
<th>Larotrectinib</th>
<th>Entrectinib</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Reference</strong></td>
<td>Laetsch et al  Lancet Oncology 2018</td>
<td>Desai et al ASCO 2018</td>
</tr>
<tr>
<td><strong>Population</strong></td>
<td>Biomarker enriched/selected</td>
<td>Solid tumor Dose Escalation; biomarker expansion</td>
</tr>
<tr>
<td><strong>N</strong></td>
<td>24 (17 fusion positive)</td>
<td>16 (3 fusion positive)</td>
</tr>
<tr>
<td><strong>Median Age (years)</strong></td>
<td>4.5</td>
<td>10</td>
</tr>
<tr>
<td><strong>DLTs</strong></td>
<td>increased ALT</td>
<td>pulmonary edema, fatigue, dysguesia, elevated creatinine</td>
</tr>
<tr>
<td><strong>MTD</strong></td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>Pediatric RP2D</strong></td>
<td>100 mg/m² BID (max 100 mg/dose)</td>
<td>550 mg/m²  Daily</td>
</tr>
<tr>
<td><strong>Adult RP2D</strong></td>
<td>100 mg BID</td>
<td>600 mg/day (-350 mg/m²)</td>
</tr>
<tr>
<td><strong>Objective Response</strong></td>
<td>14/15 patients with fusion positive tumors</td>
<td>3/3 patients with fusion positive tumors</td>
</tr>
<tr>
<td><strong>Formulations</strong></td>
<td>25 or 100 mg capsules; 20 mg/mL oral solution</td>
<td>100 and 200 mg capsules</td>
</tr>
</tbody>
</table>
# Toxicity Profile of Targeted Therapy

<table>
<thead>
<tr>
<th>Toxicity</th>
<th>Drugs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skin rash</td>
<td>EGFR, MEK, PI3K/mTOR inhibitors</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>EGFR, VEGFR, MEK, PI3K inhibitors</td>
</tr>
<tr>
<td>Hypertension</td>
<td>VEGFR inhibitors</td>
</tr>
<tr>
<td>Hypothyroidism</td>
<td>VEGFR inhibitors</td>
</tr>
<tr>
<td>Proteinuria</td>
<td>VEGFR inhibitors</td>
</tr>
<tr>
<td>Growth Plate Widening</td>
<td>VEGFR inhibitors/ multitargeted TKI</td>
</tr>
<tr>
<td>Hemorrhage/Thromboembolism (clots)</td>
<td>VEGFR inhibitors</td>
</tr>
<tr>
<td>Skin/hair depigmentation</td>
<td>PDGFR, RET inhibitors</td>
</tr>
<tr>
<td>Hepatic</td>
<td>Common to many</td>
</tr>
<tr>
<td>Hyperglycemia</td>
<td>PI3K/mTOR inhibitors</td>
</tr>
<tr>
<td>Autoimmune</td>
<td>Checkpoint (PD-1/PDL-1) inhibition</td>
</tr>
<tr>
<td>Weight Gain, Bone Fractures</td>
<td>NTRK inhibition</td>
</tr>
<tr>
<td>Cognitive Disfunction</td>
<td>NTRK inhibition</td>
</tr>
<tr>
<td>Increased Creatinine</td>
<td>ALK inhibition</td>
</tr>
</tbody>
</table>
Unique Toxicities: Growth Plate Abnormalities

**Pazopanib**
Voss et al Ped Blood Cancer, 2015

**Vismodegib**
Robinson et al Oncotarget, 2017

- Serial Evaluations
- Pediatric Specific Grading Criteria
  - Hypertension
  - Neuropathy
Formulation

- Bioavailability
- Taste
- Palatability
- Concentration
- Stability
- Preparation
- Administration

Balis et al Cancer Chemoth Pharmacol 2017
Formulation, Deliverable Dose and Pharmacokinetics

AUC_{0-24h} (µg·h/mL)

Dose Level (mg/m^2):
- 30
- 40
- 55

Ave. Daily Dose (mg/m^2/d):
- 30: (30.8 ± 3.6)
- 40: (31.5 ± 10.3)
- 55: (46 ± 11.1)

Chuk et al PBC 2018
NCI COG MATCH Study Design

Projected match rate: 10%

Parsons et al  ASCO 2019
Pre-Clinical Approaches

- **CRISPR-Cas9** is a form of gene editing in which complexes formed by small pieces of RNA target a specific region or gene in DNA (CRISPR) and enzyme that cuts DNA (Cas9) and replaces the section of DNA.

- **Pediatric Cancer Dependency Map** created from genome-scale CRISPR-Cas9 screening and computational analysis of pediatric cell lines. (Dharia et al AACR 2018)

- **Discover novel biology and new therapeutic opportunities**
  
  - Tyrosine Kinase and SHP2 Dependencies in Rhaboid tumors (Oberlick et Cell Reports 2019)
  
  - MDM2, MDM4, USP7, PPM1D in EWS (Stolte et al JEM 2018)
Impact of RACE for Children Act

- Opportunity for earlier access to targeted agents for children
- Expectation for increase in preclinical evaluations
- Consideration for master trials or “basket trials”
- Concern for maintaining drug development plans rather than single trial
- Continued need for agents to target pediatric cancer specific targets
- Desire to maintain industry-academic partnerships
Thank You!
Impact of the RACE for Children Act on the Pharmaceutical Approach to Pediatric Clinical Trials

Children’s Cancer Cause Webinar
Wednesday March 25th, 2020

Mark W Kieran, MD, PhD
Pediatric Clinical Trial Lead, BMS
Conflict of Interests

- I am an employee of and hold stock in Bristol-Myers Squibb (BMS)

- I am on the medical staff of Children’s Hospital of Philadelphia (CHOP)

- This presentation may contain copyrighted images and material and is intended solely for use in a live classroom education setting. Further distribution or reproduction is prohibited.
Objectives

- Goals and role of the pharma industry in pediatric oncology
- Critical factors for academic, regulatory agency collaboration with industry
- How new FDA regulations are changing the clinical trial landscape
What are the Goals of Academia, Regulators and Industry

- Academia; Be the world leader in the advancement of healthcare for children by integrating excellent patient care, innovative research and quality professional education into all of its programs[^1]

- Food and Drug Administration (FDA): Protect the public health by ensuring the safety, efficacy, and security of human and veterinary drugs, biological products, and medical devices; and ensure the safety of our nation's food supply, cosmetics, and products that emit radiation.[^2]

- European Medicines Agency (EMA): To foster scientific excellence in the evaluation and supervision of medicines, for the benefit of public and animal health in the European Union[^3]

- Children’s Cancer Cause: The leading national advocacy organization working to achieve access to less toxic and more effective pediatric cancer therapies[^4]

- Pharma: To discover, develop and deliver innovative medicines that help patients prevail over serious diseases[^5]

Mission Statements: ^1CHOP; ^2www.fda.gov; ^3www.ema.europa.eu; ^4www.childrenscancercause; ^5BMS
Progress is Being Made

More Progress is Needed


Source: www.seer.cancer.gov
Much More Progress is Needed

Striking disparity in average years of life lost

Approximately 80% of all children with cancer are now cured of their disease
- Unacceptable for the other 20%
- Significant long-term toxicity in most

Source: www.seer.cancer.gov
Chronic Leukemia: Increased Survival Rates

When the first-in-class drug imatinib was approved in 2001 to treat chronic myeloid leukemia (CML), the transformative impact of this new class of medicines had not been completely realized.23

- After initial approval, continued research revealed that imatinib had a greater impact when initiated earlier in the progression of the disease.
- Further research also revealed that imatinib was effective in combating other types of cancer.
- Additional drugs in this class have since been approved that target mutated forms of CML in patients who have become resistant or intolerant to imatinib.24
- Today, survival rates have improved dramatically, and CML patients are living close to normal life spans.25

5-Year Survival Rates for CML Patients26,27

Before Introduction of Imatinib

After Introduction of Imatinib

31%

89%

Sources: Boston Healthcare Associates23; PhRMA24; Gambacorti-Passerini C et al.21; ACS26; Druker BJ et al.27

Taking from www.PhRMA.org
The R&D Process for New Drugs
Is Lengthy and Costly, With High Risk of Failure

From drug discovery through FDA approval, developing a new medicine on average takes 10 to 15 years and costs $2.6 billion.* Less than 12% of the candidate medicines that make it into phase I clinical trials are approved by the FDA.

4,000 new drugs in development

1,200 in oncology
The Costs of Drug Development Have More Than Doubled Over the Past Decade

Many factors are driving increasing costs of biopharmaceutical R&D, including increased clinical trial complexity, larger clinical trial sizes, greater focus on targeting chronic and degenerative diseases, and higher failure rates for drugs tested in earlier-phase clinical studies.

AVERAGE COST TO DEVELOP ONE NEW APPROVED DRUG—INCLUDING THE COST OF FAILURES (in Constant 2013 Dollars)

- 1970s: $179M
- 1980s: $413M
- 1990s-Early 2000s: $1.0B
- 2000s-Early 2010s: $2.6B

Source: DiMasi JA et al.
Cancer Is Seen As An Adult Disease

From 2007 through 2016, the NCI expenditure for pediatric cancer research funding was 3.94%

National Cancer Institute, NCI/NIH Budget. Coalition Against Childhood Cancer (CAC2) Childhood Cancer Fact Library, June 8, 2018
Incidence of Pediatric Tumors

- Leukemia: 30%
- CNS: 25%
- Lymphoma: 10%
- Neuroblastoma: 7%
- Soft-Tissue Sarcoma: 7%
- Other: 7%
- Wilms: 5%
- Bone: 5%
- RB: 3%
- Liver: 1%
- Leukemia: 30%

- 1.6 million new cancer cases/year, 16,000 new cases in children
- Cancer is the most common cause of death by disease in children
A Systems Issue for Pediatric Versus Adult Patients

• Very high cost to discover and develop new therapies

• Industry focused on adult malignant incurable diseases
  – Already completed growth and development
  – Predominantly from carcinomas (breast, lung, colon, prostate)

• Pediatric comprises very large number of very rare tumors
  • Different biology
    – Mostly sarcomas and leukemia
    – Not the focus of drug development
    – Limited knowledge on developmental or long-term toxicity
Regulatory Agency Response to Pediatric Clinical Trial Needs

Paediatric Investigative Plans (PIPs) – EMA ➔ Briefly presented below
Pediatric Study Plans (PSPs) – FDA ➔ Covered by Greg Reaman
EMA Pediatric Investigative Plan (PIP)

- To be developed at the end of adult phase I
- Based on the proposed adult indication
- Requires:
  - Pediatric phase I (to determine the dose),
  - Pediatric phase II (demonstration of activity in the selected tumor types) and;
  - An outline of a randomized phase III trial if activity is observed
    - pediatric formulation not required
- All elements of the PIP are legally binding
- PIP approval is required **before** drug can be approved for adult commercial use
Critical Issues Going Forward in Pediatric Biology

• Research into pediatric cancer is increasingly complex
  – There are increasing numbers of pathways and mutations to understand (and required to study)
• Limited number of pediatric cancer models to test new drugs
  – Most are found in a single academic center
• Increasing numbers of novel agents to test
  – The combinatorial possibilities are huge
  – Many ‘Same-in-Class’ inhibitors from different companies compete for patients

Preclinical drug testing in pediatric models
• Academic collaborations
• Public-private partnerships: ITCC P4, FNIH PPP (PPTC)
Impact of the RACE for Children Act

• Pharma needs to commit to understanding biology of pediatric cancer
  – Much earlier than before
  – For all pediatric cancers where mechanism could be relevant
  – Including pharmacogenomics (PG), pharmacokinetics (PK) and pharmacodynamics (PD)

• Pharma needs international trials that fulfill all regulatory requirements
  – Novel trial designs to minimize # of patients exposed while maximizing signal detection
    • Adaptive, Bayesian, etc including basket (1 drug different cancers) and umbrella trials (many drugs, 1 cancer)
    • Extrapolation
    • Inclusion of AYA patients in adult phase I/II trials

• Pharma needs to consider oral drug formulation early in development
• Pharma needs improved biomarkers for better patient selection
• Need to learn from every patient
Summary

• Academia has the preclinical models and the patients
• Patients have control of their biology and decision to enroll on trials
• Regulators have set the requirements
• Pharma has the drugs and now need to adapt them to the new regulatory environment

Need to recognize the collaborative nature of these relationships and thus need for a team approach
Questions?

COVID-19 & Childhood Cancer

https://childrensoncologygroup.org/
http://www.survivorshipguidelines.org/