Giving Children with Cancer the Right Treatment at the Right Time

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Seattle Children's Hospital, University of Washington

CHILDREN'S ONCOLOGY GROUP

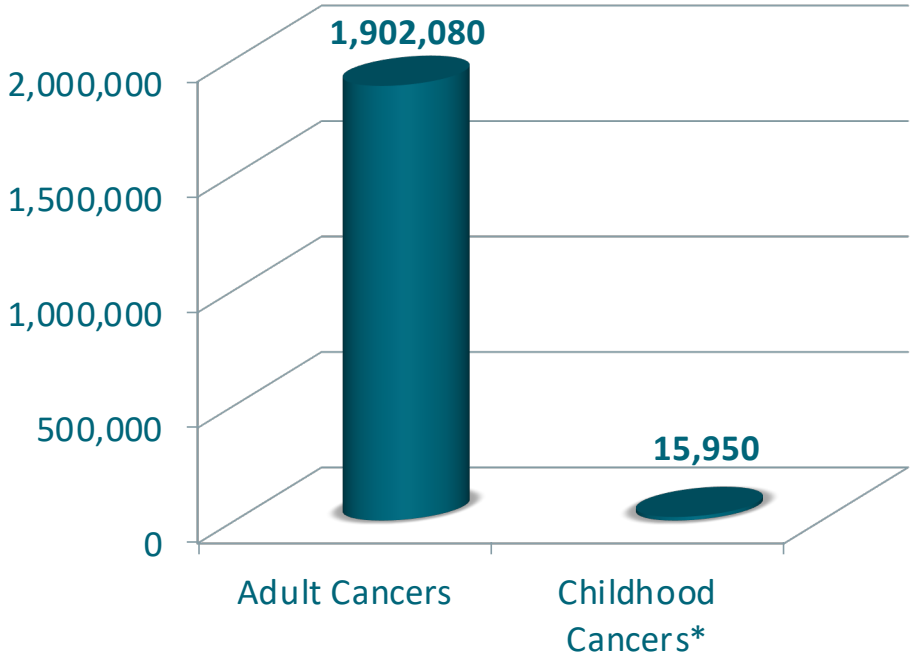
Coalition Against Childhood Cancer Annual Summit

June 23, 2022

Topics for today

- Role of clinical trials to define standards of care
  - Power of randomized studies
  - How information is shared
  - FDA approval of pediatric indications
- Increased importance of molecular testing
- Access to investigational agents
- Increasing equity in treatment outcome

Childhood Cancer Facts



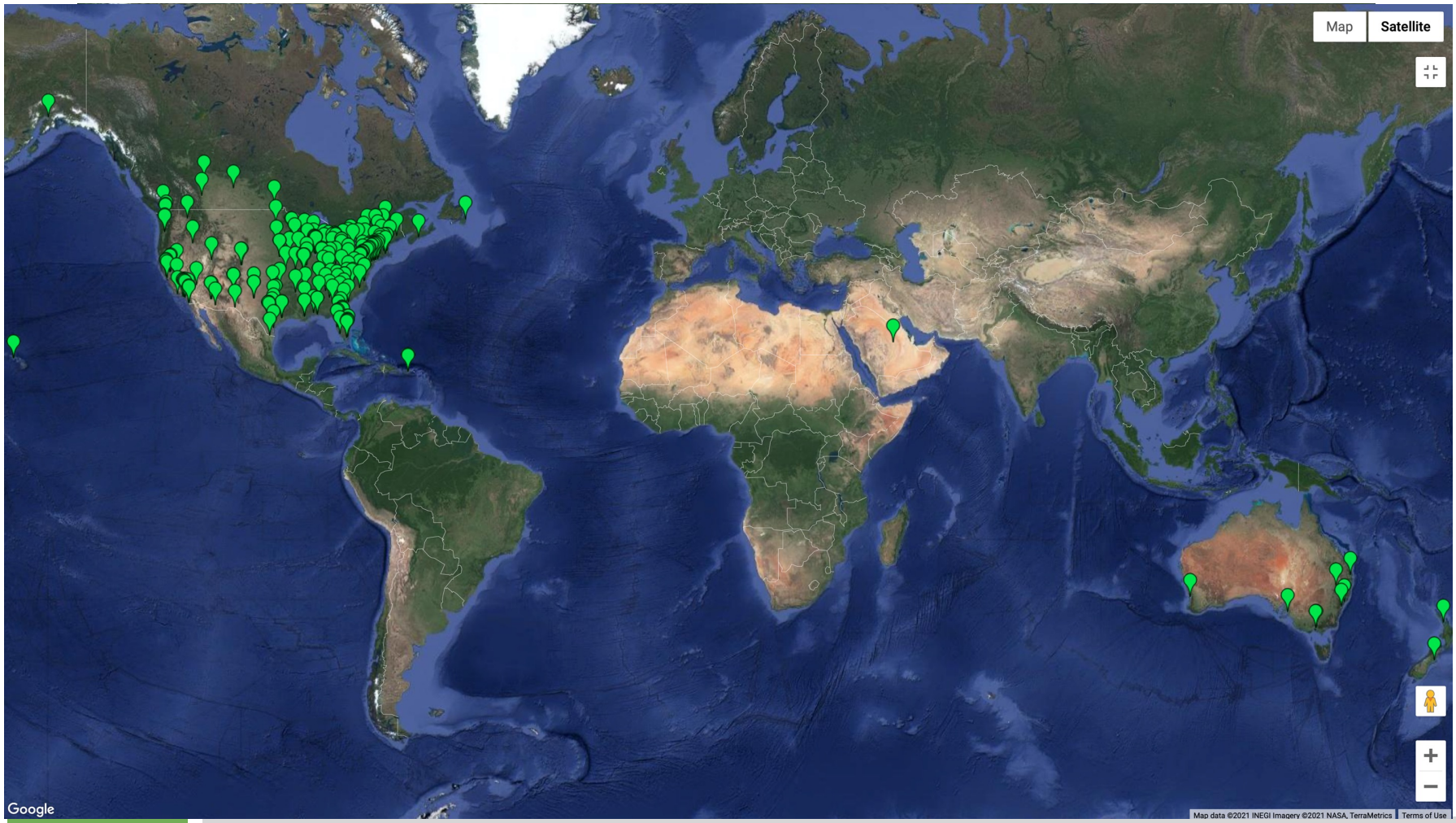
* 0-19 years old

- Cancer is the leading cause of death from disease in children
- Progress requires multi-institutional collaboration given rarity of pediatric cancer

CA Cancer J Clin 2022;72:7-33

Children's Oncology Group (COG)

- Formed in 2000 by merger of four legacy pediatric oncology cooperative groups
- NCI-funded National Clinical Trial Network (NCTN) member; four other US adult cooperative groups
- Fast facts:
  - > 220 institutions in US (~200), Canada, Australia, New Zealand
  - > 8000 members
  - ~80-90% of children with cancer in US are treated at COG institutions



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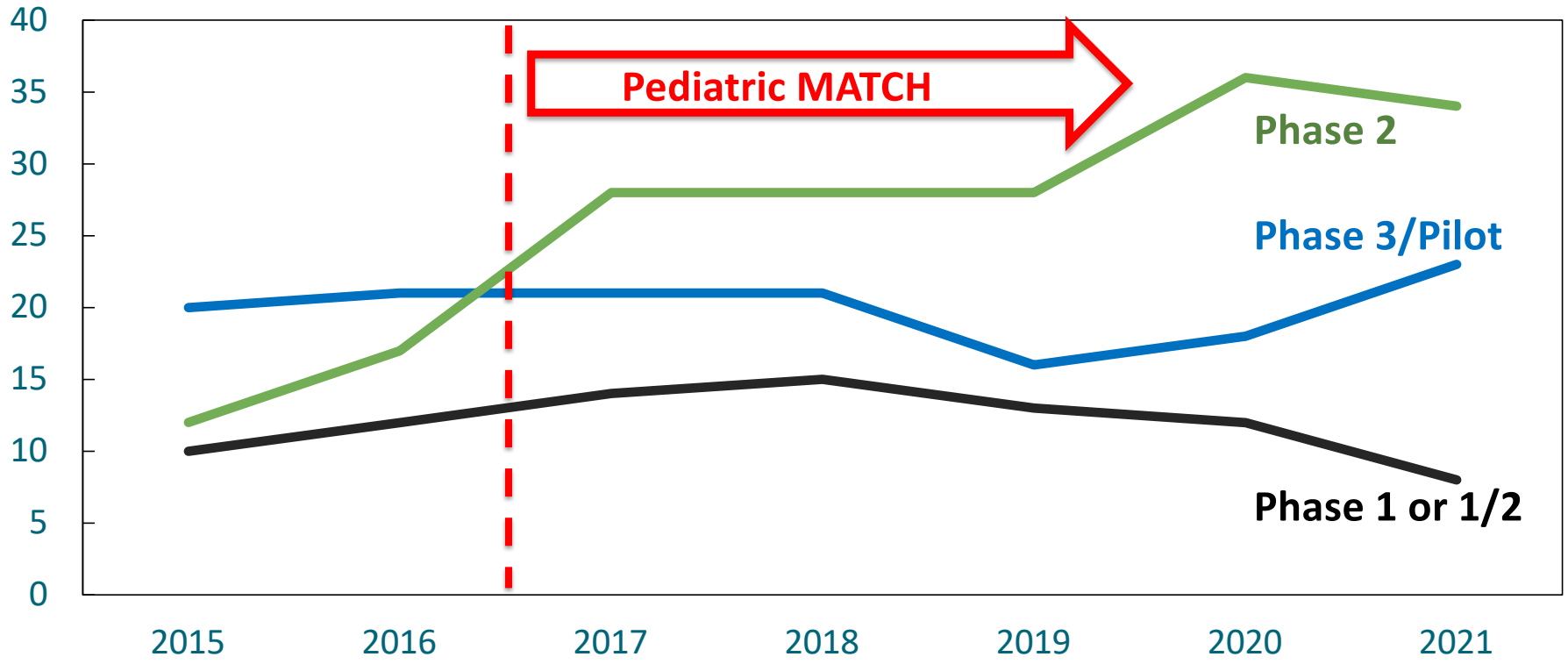
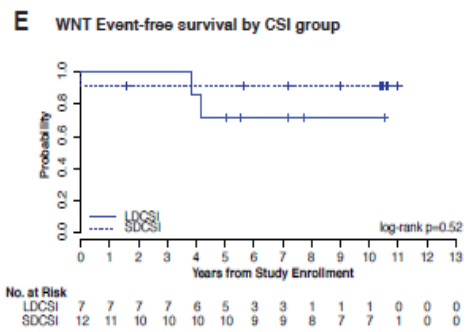
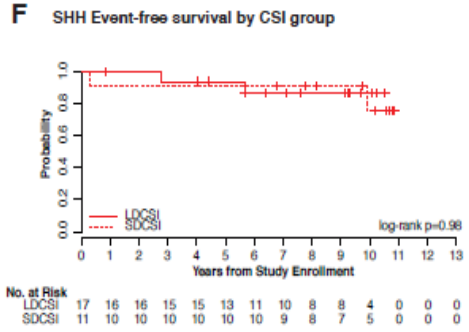
Active COG Studies: 2015-2021

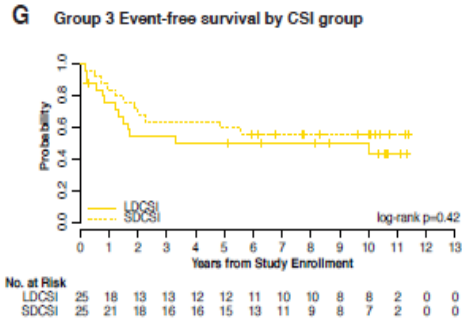


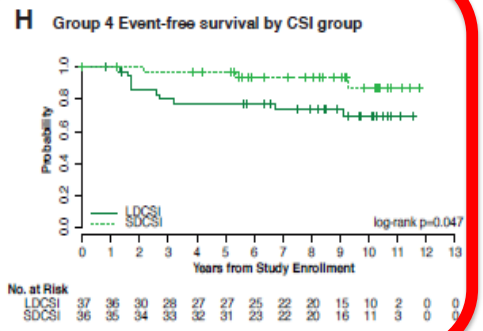
COG Average Risk Medulloblastoma Trial

- 2004-2014
- 549 enrolled patients
- Two randomizations:
  - Whole PF vs involved field RT
  - 3-7 years: 18 vs 23.4 Gy CS RT
- Impact of CS RT intervention differed by molecular subgroup









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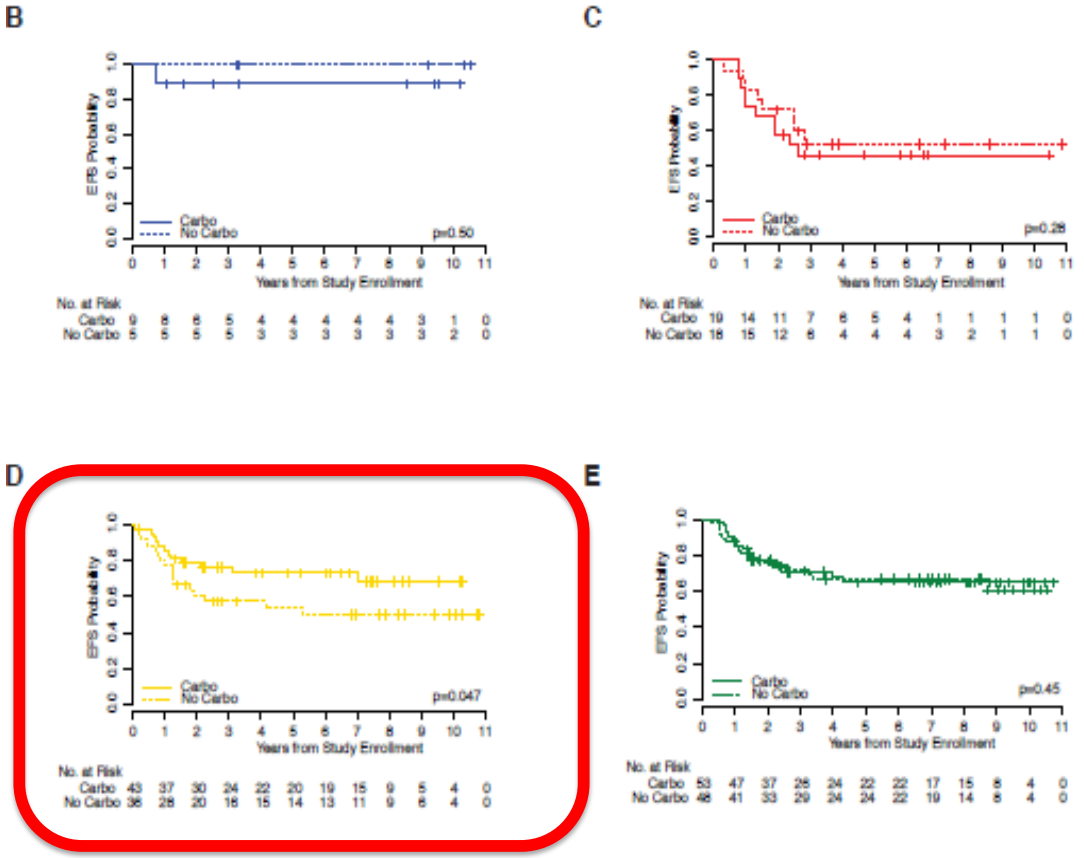
Michalski JM, J Clin Oncol 2021; 39:2685-2697

COG High Risk Medulloblastoma/PNET Trial

- 2007-2018
- 294 enrolled patients
- Two randomizations:
  - +/- isotrentinoin
  - +/- carboplatin during RT
- Improved outcome with carboplatin during RT in Group 3 only



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Leary SES, JAMA Oncology 2021; 7:1313-1321

CHILDREN'S ONCOLOGY GROUP

AHOD1331

Activated: 03/16/2015
Closed: 08/02/2019

Version Date: 06/22/2020
Amendment #: 6

CHILDREN'S ONCOLOGY GROUP

AHOD1331

A Randomized Phase 3 Study of Brentuximab Vedotin (SGN-35, IND #117117) for Newly Diagnosed High-Risk Classical Hodgkin Lymphoma (cHL) in Children and Young Adults

- Phase 3 study of advanced Hodgkin lymphoma
- Randomized +/- brentuximab
- Activated: March 2015
- Last enrollment: April 2019
- Data & Safety Monitoring Committee released results: 1/18/22

Data & Safety Monitoring Committee

- Independent committee with experts in statistics, clinical trials, and patient advocacy
- Reviews unblinded side effect and outcome data
- Follows prospective rules defined in the protocol
- Has authority to stop studies early and release data when statistical goals are met or safety boundary is crossed

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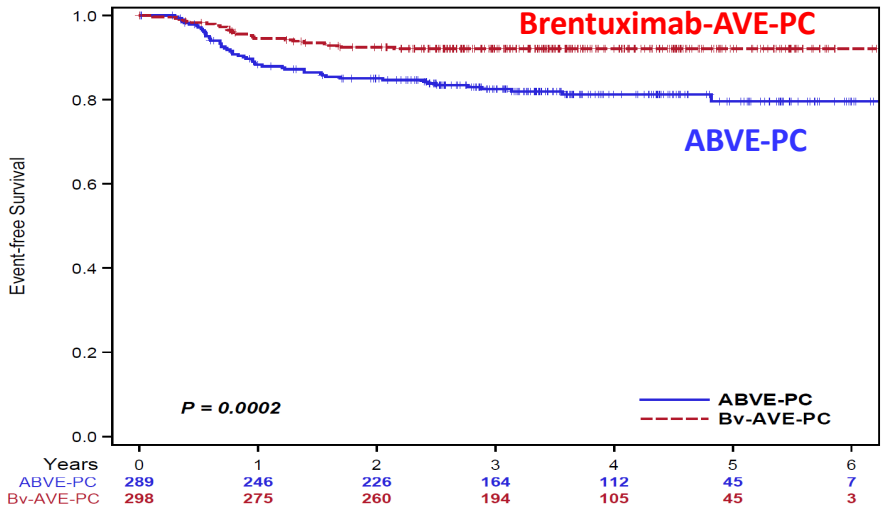


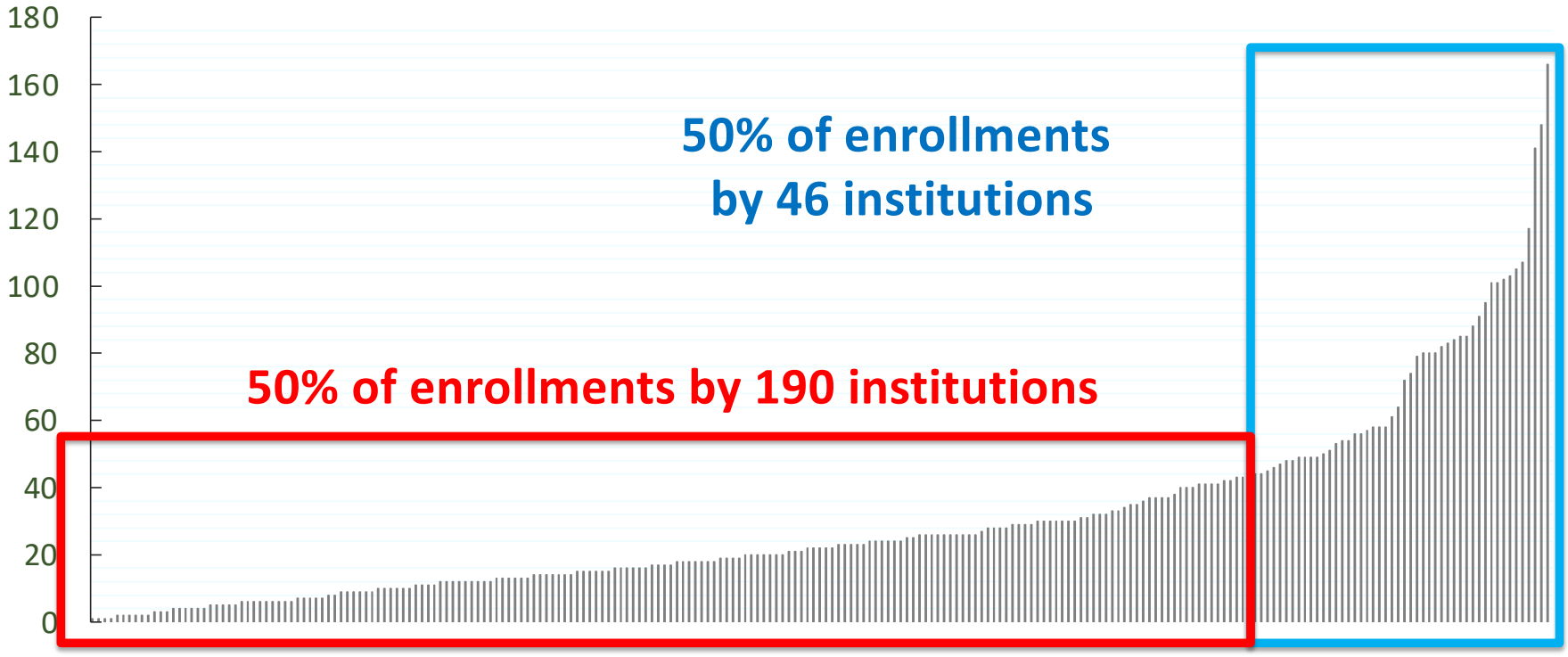
- Phase 3 study of advanced Hodgkin lymphoma
- Randomized +/- brentuximab
- Activated: March 2015
- Last enrollment: April 2019
- Data & Safety Monitoring Committee released results: 1/18/22
- COG website posting: 1/31/22
- Manuscript submitted: 5/19/22
- Presentation at ASCO: 6/3/22

What COG does and does not do

- COG does:
  - Conduct large clinical trials, especially randomized studies
  - Include small, medium, and large institutions
  - Facilitate the collection of biospecimens for research

- COG does not:
  - Determine standard of care
  - Provide medical care
  - Provide second-opinion consultation

COG Institutional Enrollment on Phase 3/Pilot Studies 2019-2021



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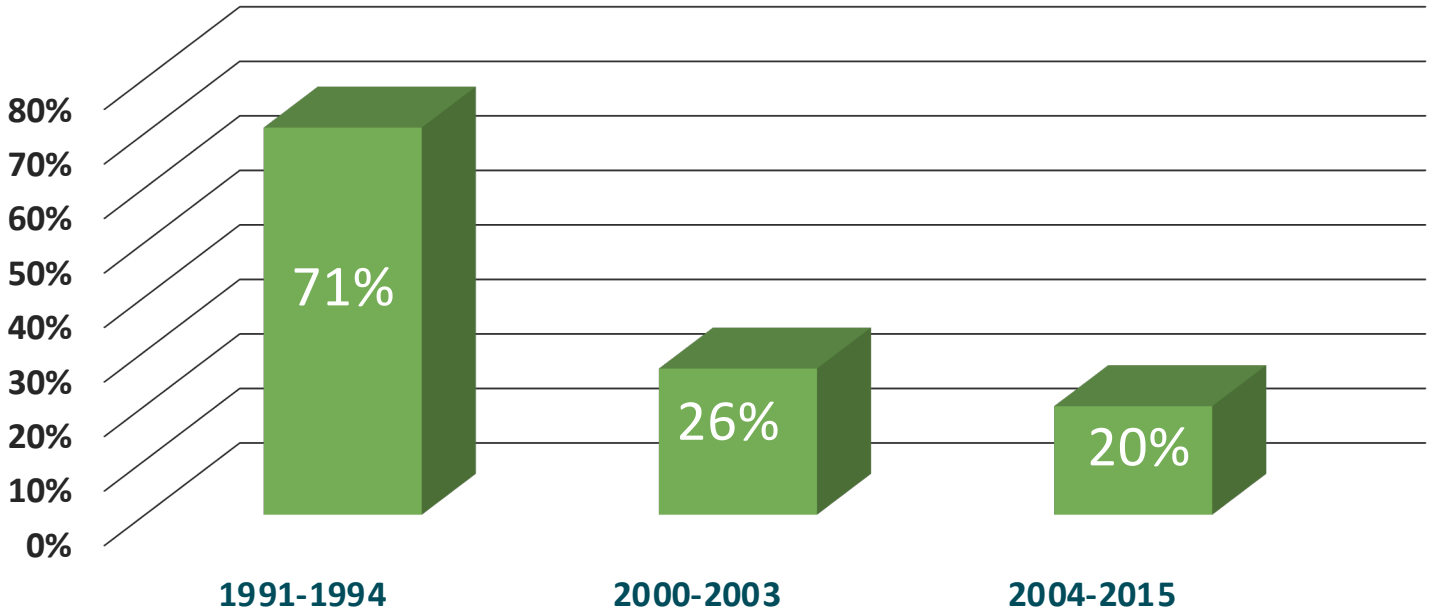
Cooperative Group Clinical Trial Enrollment



*Age 0-19 years only; compared to estimated number of cases based upon SEER data

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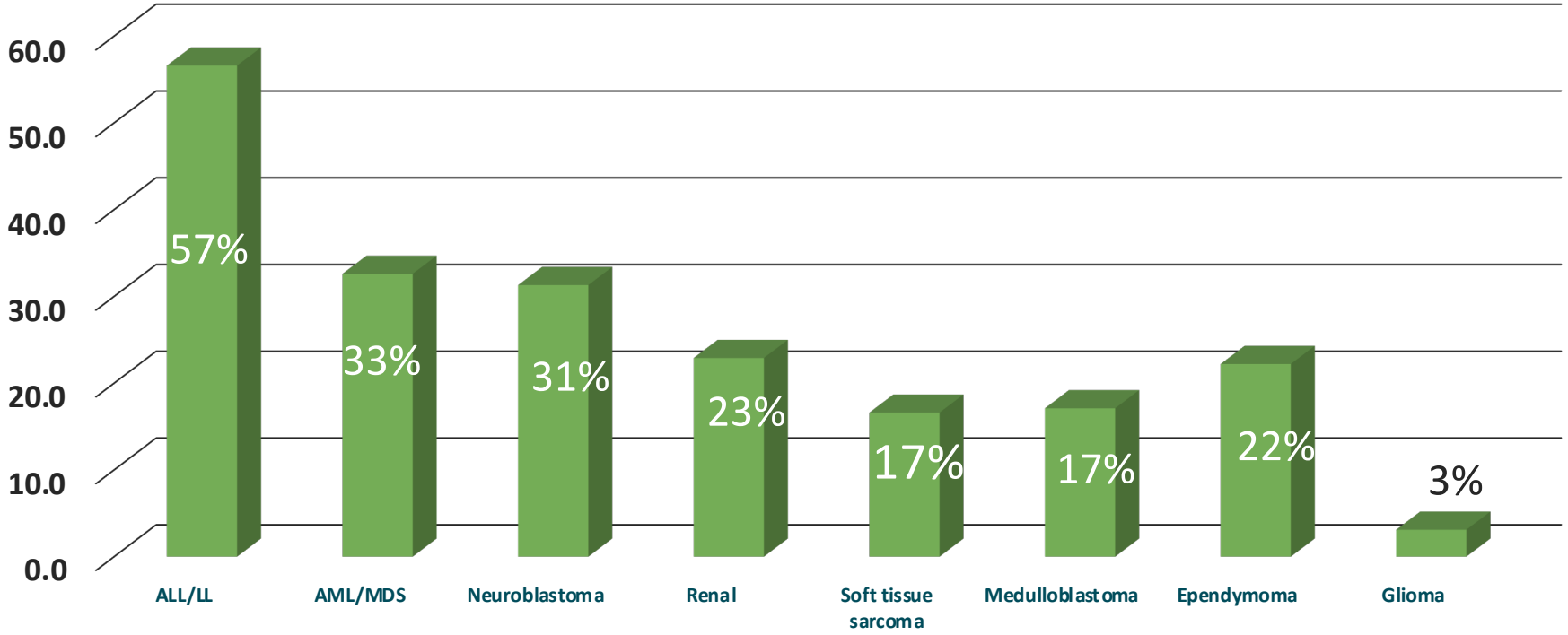
JNCI 1996; 88: 812-816; Cancer 2009; 115:3808-3816;
PLOS ONE 2020; 15:e0230824

COG Enrollment vs Expected by Histology



*Age 0-9 years only; compared to estimated number of cases based upon SEER data, 2004-2015

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PLOS ONE 2020; 15:e0230824

How COG facilitates care outside of studies

- Publish study results quickly (we try)
- COG studies used by institutions to set standards of care
- Completed study protocols on COG website
- COG members are on National Comprehensive Cancer Network (NCCN) committees for treatment standards:
  - Pediatric Hodgkin lymphoma
  - Pediatric mature B cell lymphoma
  - Pediatric ALL
  - Wilms tumor
- ***We all talk with each other***

Topics for today

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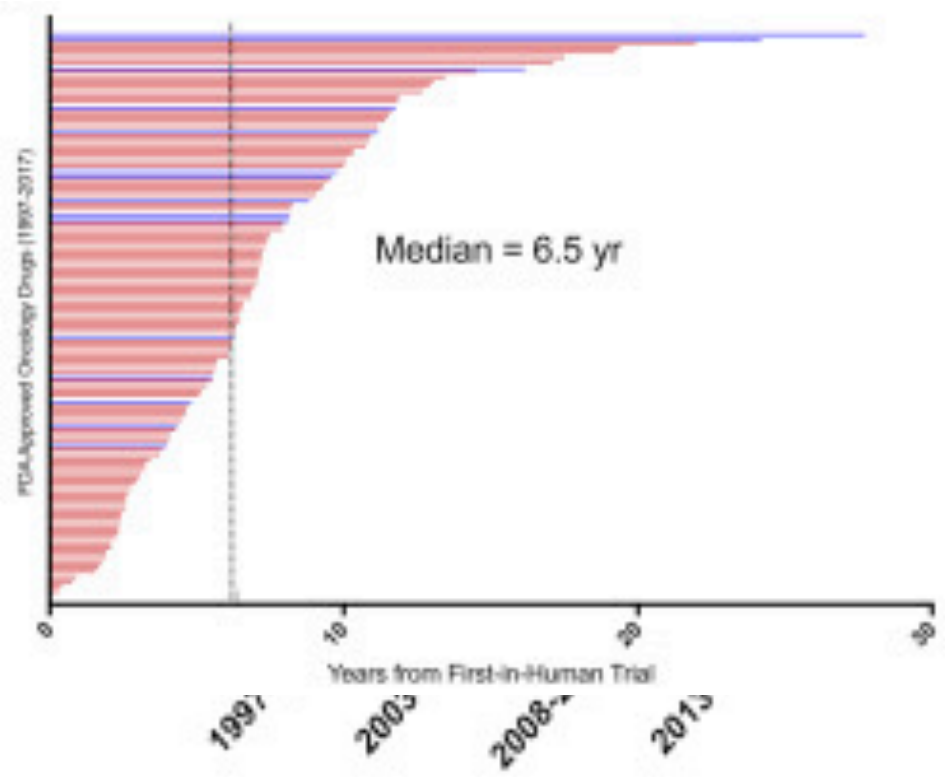
- Access to investigational agents
- Increasing equity in treatment outcome

Cancer drug development is slow in children

- In 1997-2017, 117 non-hormonal chemotherapy agents approved by FDA
- Only 6 (5.1%) included children in the initial approval
- Median delay between first-in-human and first-in-child studies: 6.5 years



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Neel DV, Eur J Cancer 2019; 112:49-56

COG studies used for pediatric labeling by FDA

Pediatric labeling	Agent	Indication	COG study
2005	Nelarabine	T-cell leukemia/lymphoma	P9673
2006	PEG asparaginase	Acute lymphoblastic leukemia	1962
2011	Erwinia asparaginase	Acute lymphoblastic leukemia	AALL07P2
2011 2013	Imatinib	Ph+ chronic myelogenous leukemia Ph+ acute lymphoblastic leukemia	AAML0123 AALL0031
2015	Dinutuximab	Neuroblastoma	ANBL0032
2017	*Pembrolizumab*	*Hodgkin lymphoma, MSI-H, TMB-H*	*ADVL1621*
2018	SC-PEG asparaginase	Acute lymphoblastic leukemia	AALL07P4
2018	*Blinatumomab*	*Acute lymphoblastic leukemia*	*AALL1121*
2019	*Dasatinib*	*Ph+ acute lymphoblastic leukemia*	*AALL1122*
2020	Gemtuzumab Ozogamicin	Acute myelogenous leukemia	AAML0531
2021	Crizotinib	Anaplastic large cell lymphoma	ADVL0912
2021	Liposomal daunorubicin/cytarabine	Acute myelogenous leukemia	AAML1421
2021	*Recombinant Erwinia asparaginase*	*Acute lymphoblastic leukemia*	*AALL1931*
2021	Rituximab	CD20+ non-Hodgkin lymphoma	ANHL1131

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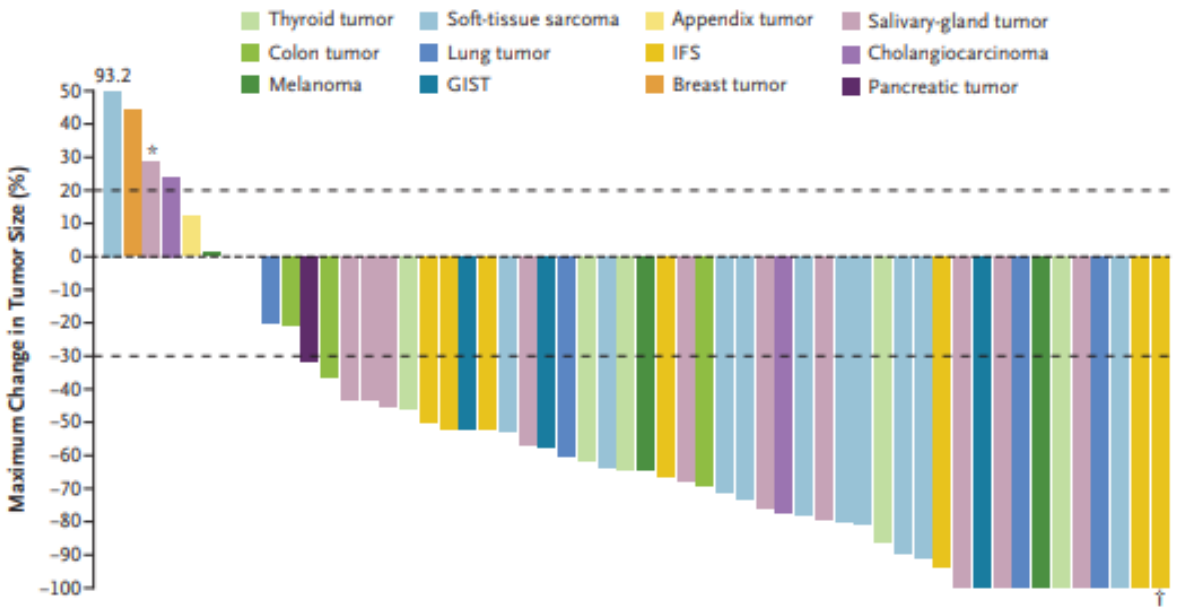
Larotrectinib for NTRK-fused solid tumors

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Efficacy of Larotrectinib in *TRK* Fusion–Positive Cancers in Adults and Children

A. Drilon, T.W. Laetsch, S. Kummar, S.G. DuBois, U.N. Lassen, G.D. Demetri, M. Nathenson, R.C. Doebele, A.F. Farago, A.S. Pappo, B. Turpin, A. Dowlati, M.S. Brose, L. Mascarenhas, N. Federman, J. Berlin, W.S. El-Deiry, C. Baik, J. Deeken, V. Boni, R. Nagasubramanian, M. Taylor, E.R. Rudzinski, F. Meric-Bernstam, D.P.S. Sohal, P.C. Ma, L.E. Raez, J.F. Hechtman, R. Benayed, M. Ladanyi, B.B. Tuch, K. Ebata, S. Cruickshank, N.C. Ku, M.C. Cox, D.S. Hawkins, D.S. Hong, and D.M. Hyman



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Drison A, N Engl J Med 2018; 378:731-739

	Institution	N	Tumor Types	Potentially Actionable Findings	Matched Targeted Therapy	Germline Findings	Reference
PEDS-MIONCOSEQ	U Michigan	102	High Risk (HR) Solid, CNS, Heme	46%	14 (33%)	10%	Mody et al. JAMA, 2015
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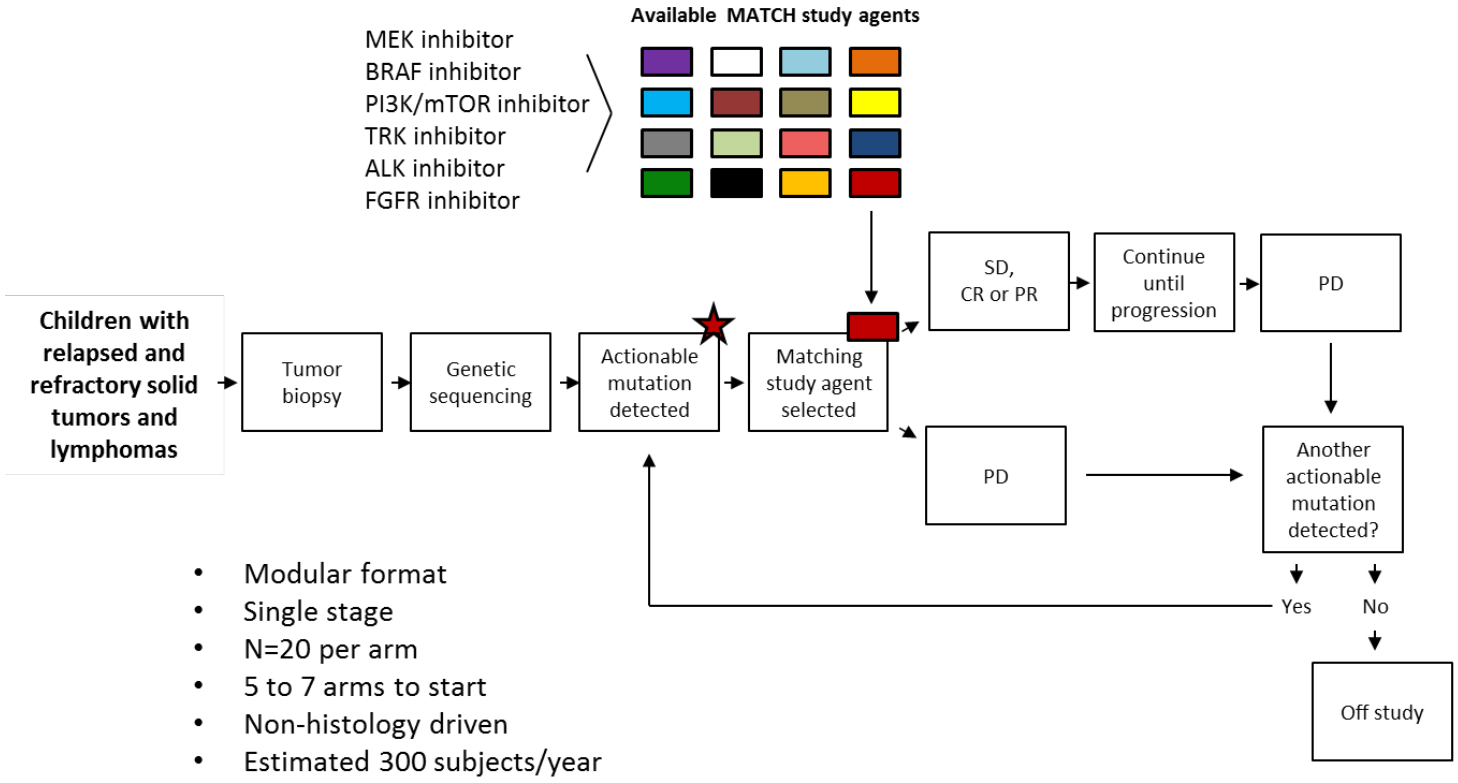
Courtesy of Julia Glade Bender, MD

Genomic sequencing for patient care

- Historically, genomic testing limited to institutions with internal support or grant funding
- Insurance coverage for genomic testing inconsistent
- Turn-around time for genomic testing may be too long to impact treatment

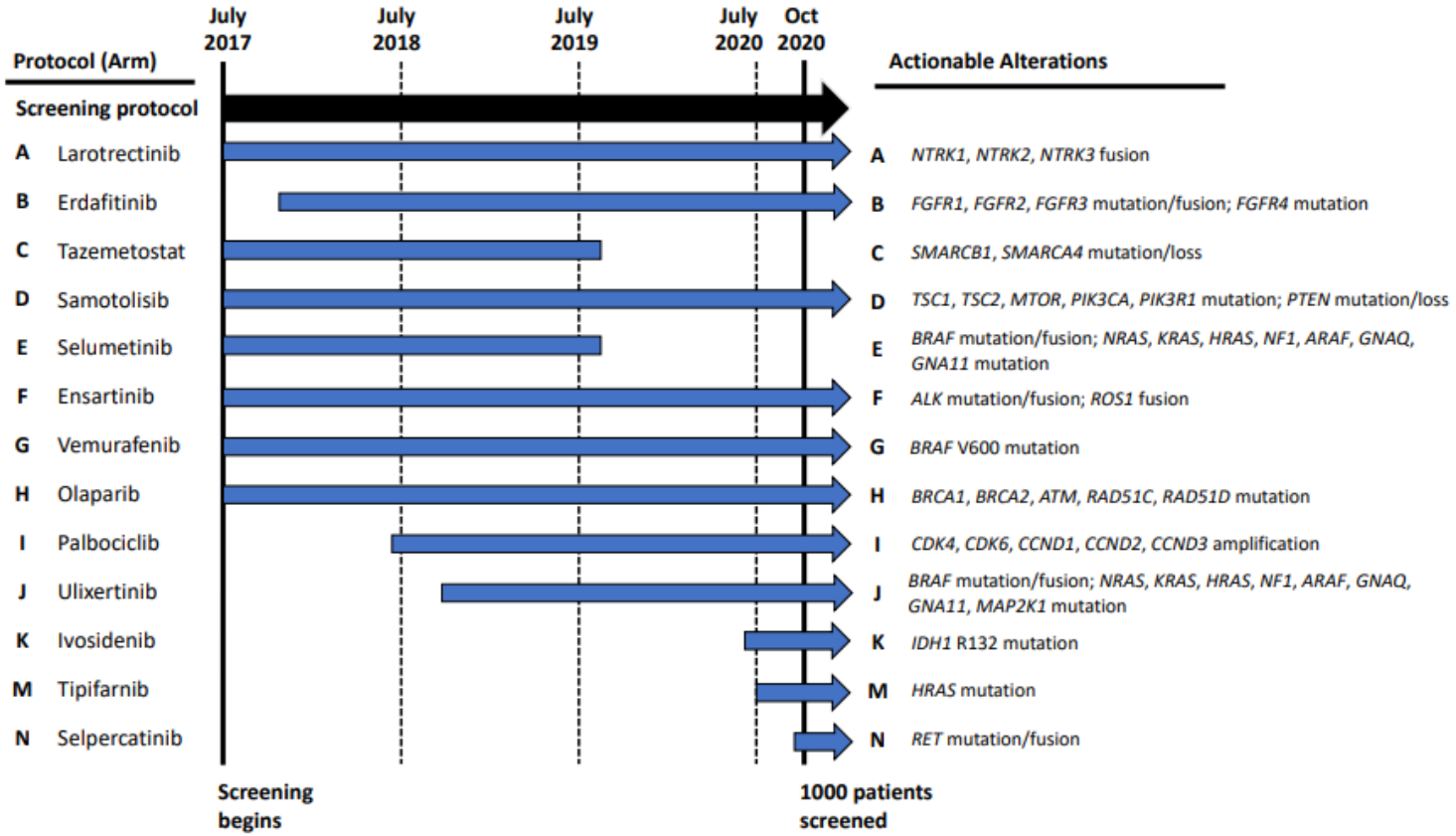
Identifying a potential target does not provide access to investigational agent

NCI-COG Pediatric MATCH Study



- Modular format
- Single stage
- N=20 per arm
- 5 to 7 arms to start
- Non-histology driven
- Estimated 300 subjects/year

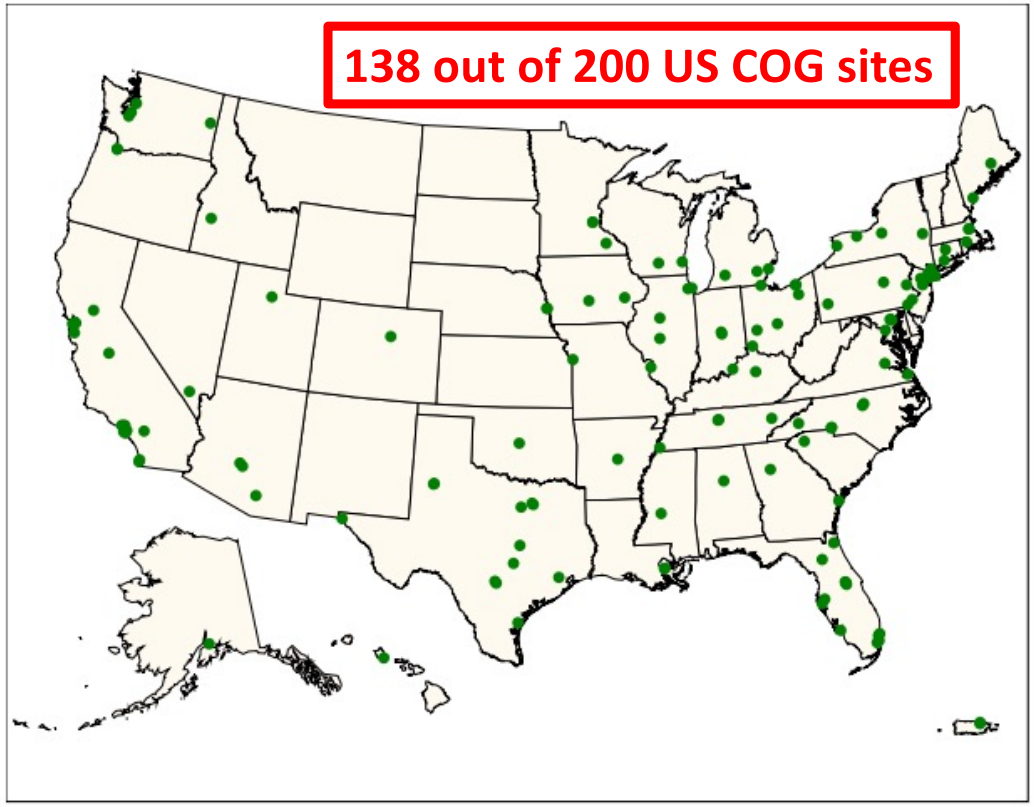
NCI-COG Pediatric MATCH Study

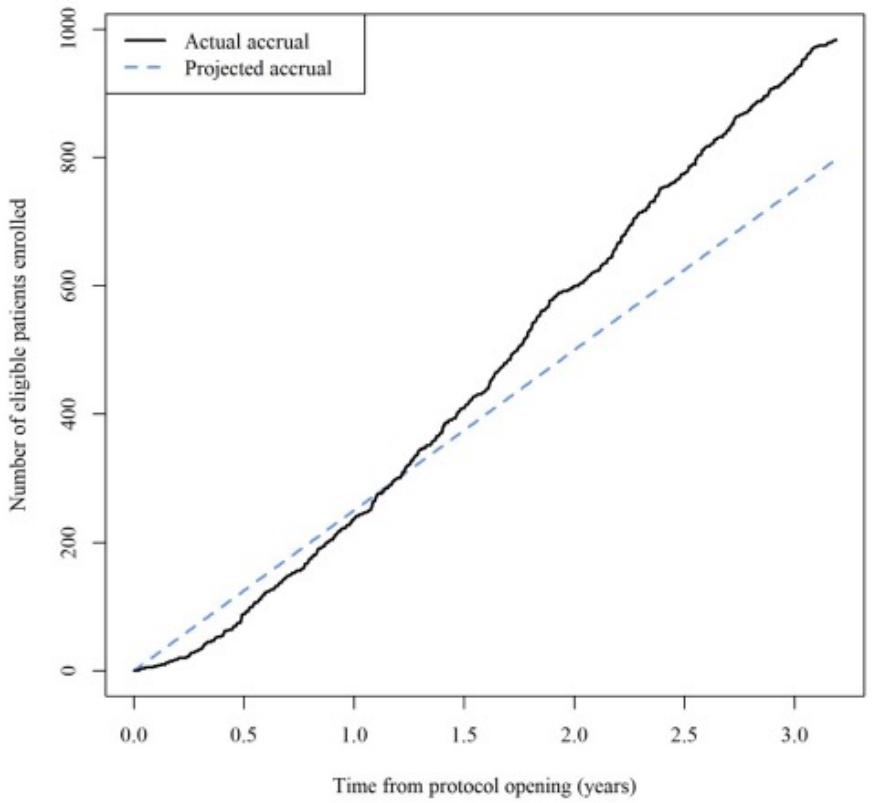


CHILDREN'S ONCOLOGY GROUP

Parsons DW, J Clin Oncol, in press

NCI-COG Pediatric MATCH

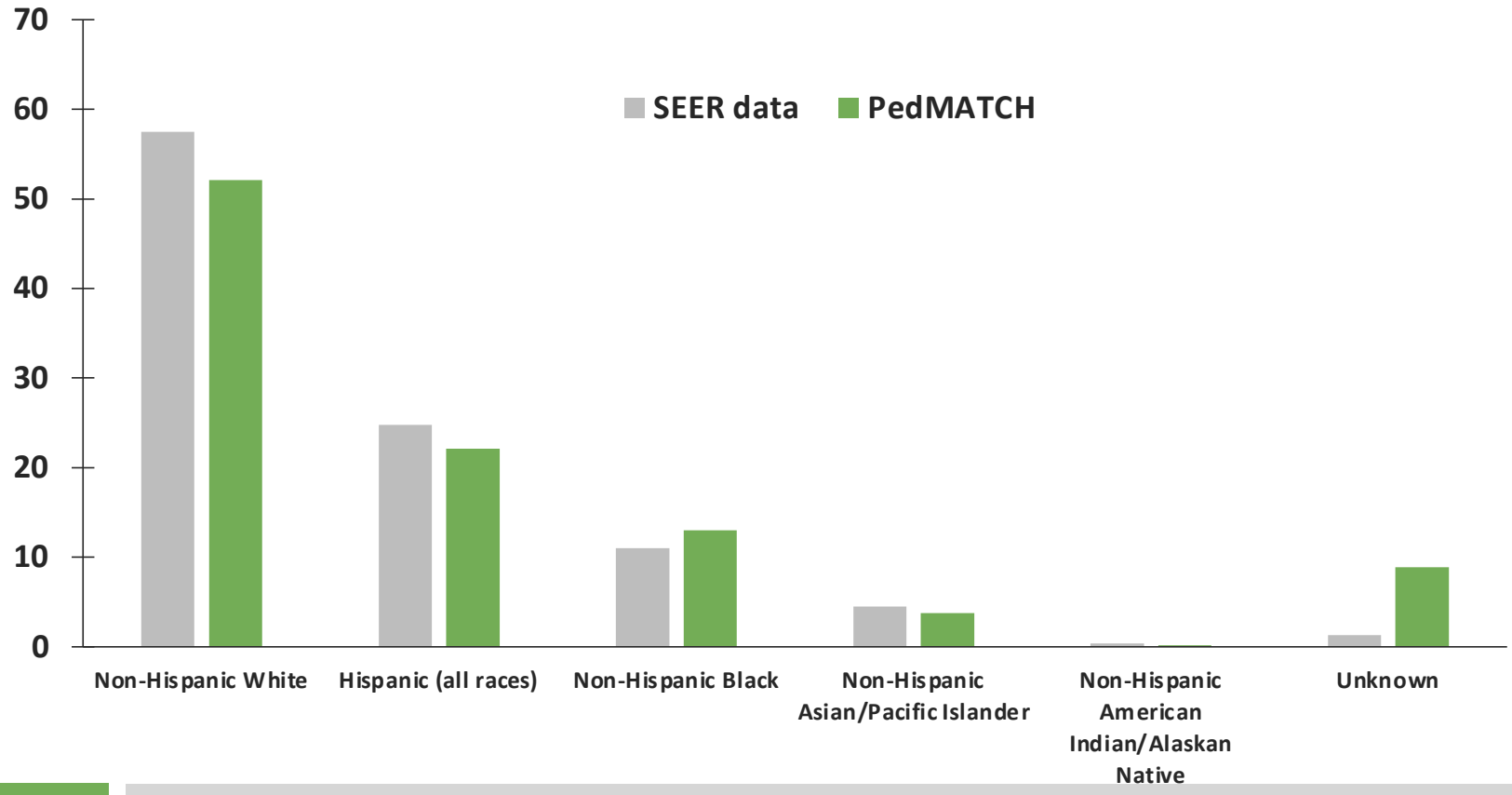




CHILDREN'S ONCOLOGY GROUP

Parsons DW, J Clin Oncol, in press

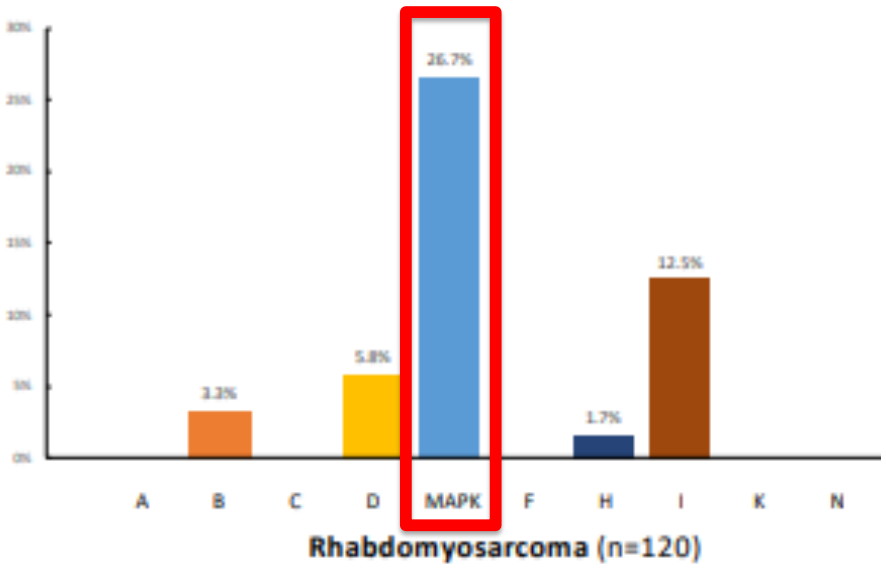
NCI-COG Pediatric MATCH: Race, Ethnicity

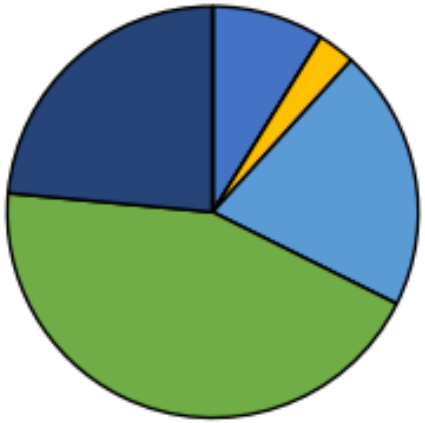


CHILDREN'S ONCOLOGY GROUP

Parsons DW, J Clin Oncol, in press

NCI-COG Pediatric MATCH Study





RMS
(n=34)

- *NF1* mutation
- *BRAF* V600E
- *BRAF* fusion
- *BRAF* non-V600
- *KRAS* mutation
- *NRAS* mutation
- *HRAS* mutation
- *GNAQ* mutation
- *MAPK1* mutation

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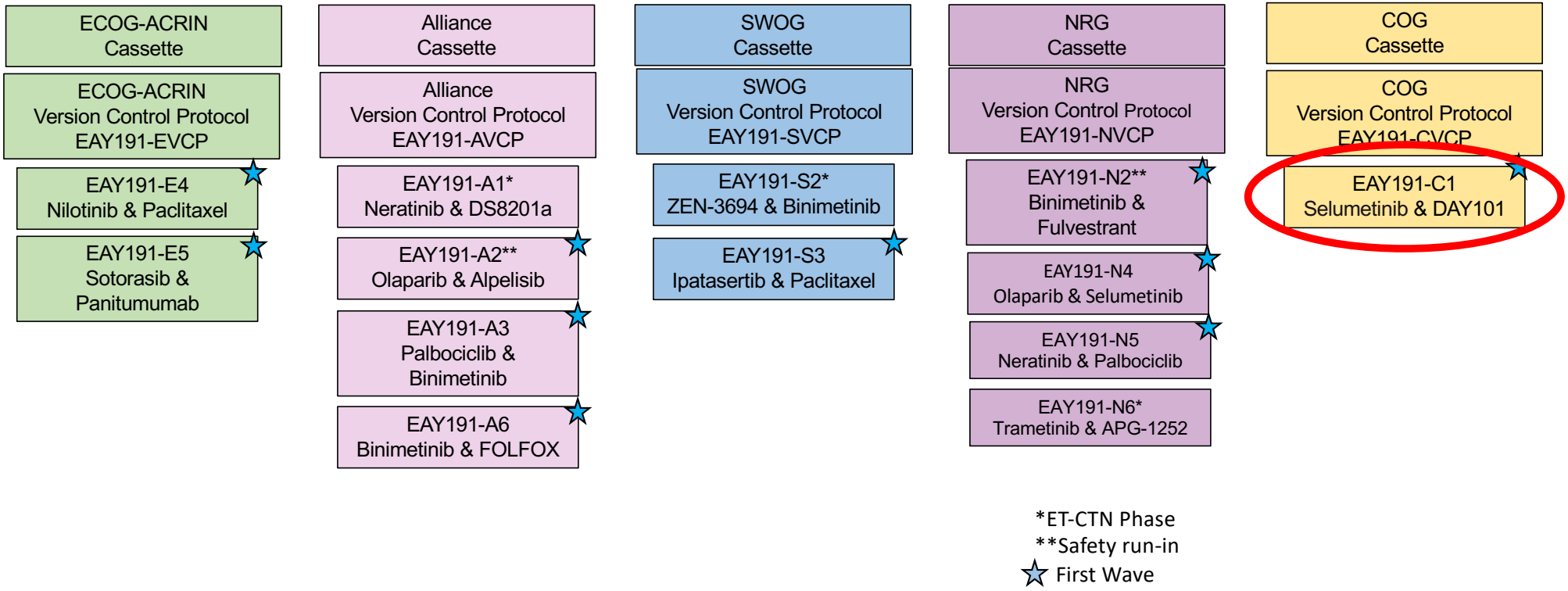
Parsons DW, J Clin Oncol, in press

Pediatric MATCH Successes/Failures

- Successes:
  - > 1300 patients enrolled at 138 US COG institutions
  - Central molecular testing completed in 95% of cases
  - Paired diagnostic specimens
  - aMOI for 31% of patients; 13% enrolled on treatment
- Failures:
  - Limited responses:
    - Selumetinib (0/20), Tazemetostat (1/20), Ulixertinib (0/20)
  - All arms are single agent

Parsons DW, J Clin Oncol, in press; Eckstein OS, J Clin Oncol, in press
Chi SN, ASCO 2022; Vo KT, ASCO 2022

NCI-ComboMATCH Patient Registration Protocol - EAY191



*ET-CTN Phase
**Safety run-in
☆ First Wave

Pediatric MATCH Stage 2

- Pediatric MATCH re-opened to enrollment March 7, 2022
- ***Centralized molecular testing replaced by commercial or academic testing***
- Reduced number of arms, no new arms
- Open to Canadian, Australian, and New Zealand sites

NCI-COG Pediatric MATCH Study

Protocol ID	Agent Class	Agent	Status
APEC1621-A	TRK Inhibitor	Larotrectinib	Open
APEC 1621-B	FGFR Inhibitor	Erdafitinib	*Temporarily suspended*
APEC 1621-C	EZH2 Inhibitor	Tazemetostat	*Completed*
APEC 1621-D	PI3K/mTOR Inhibitor	LY3023414	Open
APEC 1621-E	MEK Inhibitor	Selumetinib	*Completed*
APEC 1621-F	ALK Inhibitor	Ensartinib	Open
APEC 1621-G	BRAF Inhibitor	Vemurafenib	*Closed for low accrual*
APEC 1621-H	PARP Inhibitor	Olaparib	*Closed for low accrual*
APEC 1621-I	CDK 4/6 inhibitor	Palbociclib	*Temporarily suspended*
APEC 1621-J	MAPK pathway inhibitor	Ulixertinib	*Completed*
APEC 1621-K	IDH1 inhibitor	Ivosidenib	Open
APEC 1621-M	H-RAS inhibitor	Tipifarnib	Open
APEC 1621-N	RET inhibitor	Selpercatinib	Open

Genomic sequencing for patient care

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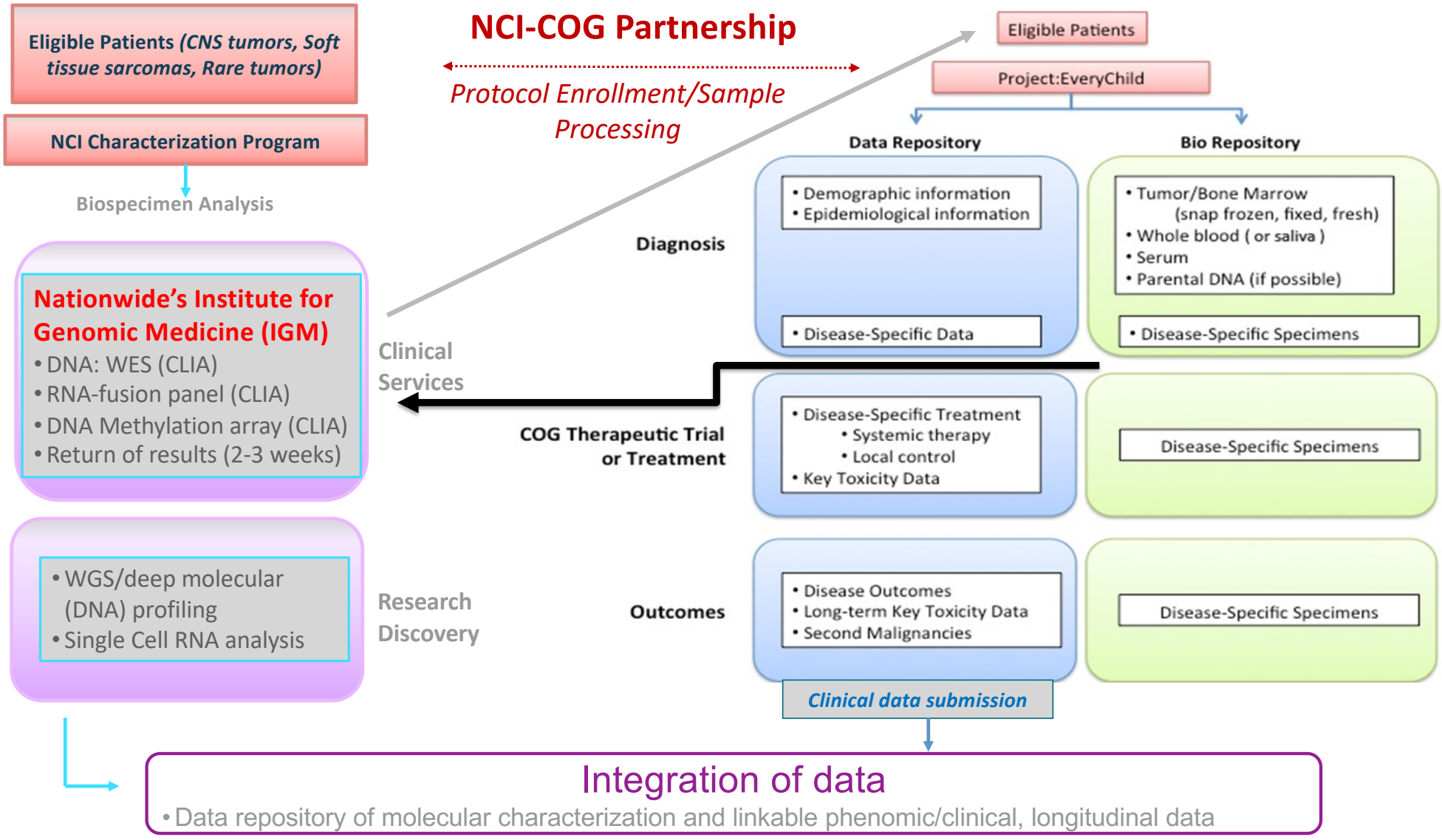
- Insurance coverage for genomic testing inconsistent
- Turn-around time for genomic testing may be too long to impact treatment

What about genomic sequencing at initial diagnosis?

Molecular Characterization Initiative

- Patients enter by enrolling on APEC14B1 registry/biobanking study, Project:EveryChild
- Will roll out in stages:
  - ***CNS tumors started March 21, 2022***
  - Soft Tissue Sarcomas
  - Rare Tumors
- Estimating 3000 patients annually


Eligible Patients (CNS tumors, Soft tissue sarcomas, Rare tumors)
NCI Characterization Program
Biospecimen Analysis
Nationwide's Institute for Genomic Medicine (IGM)
• DNA: WES (CLIA)
• RNA-fusion panel (CLIA)
• DNA Methylation array (CLIA)
• Return of results (2-3 weeks)
• WGS/deep molecular (DNA) profiling
• Single Cell RNA analysis
Research Discovery
NCI-COG Partnership
Protocol Enrollment/Sample Processing
Eligible Patients
Project:EveryChild
Data Repository
Bio Repository
Diagnosis
• Demographic information
• Epidemiological information
• Tumor/Bone Marrow (snap frozen, fixed, fresh)
• Whole blood (or saliva)
• Serum
• Parental DNA (if possible)
• Disease-Specific Data
• Disease-Specific Specimens
Clinical Services
COG Therapeutic Trial or Treatment
• Disease-Specific Treatment
• Systemic therapy
• Local control
• Key Toxicity Data
Disease-Specific Specimens
Outcomes
• Disease Outcomes
• Long-term Key Toxicity Data
• Second Malignancies
Disease-Specific Specimens
Clinical data submission
Integration of data
• Data repository of molecular characterization and linkable phenomic/clinical, longitudinal data

Molecular Characterization Initiative

- Enhanced whole exome sequencing (WES), tumor and blood
- RNA Archer Fusion-Plex assay, tumor
- Illumina 850K Epic DNA methylation array, tumor and blood

Molecular Characterization Initiative

- Open to children with selected diagnoses through COG Project:EveryChild
- Comprehensive molecular testing at diagnosis, including germline
- Return of results to patients and treating physicians with 21 days of receipt of material

Results may refine diagnosis and suggest alternative treatments

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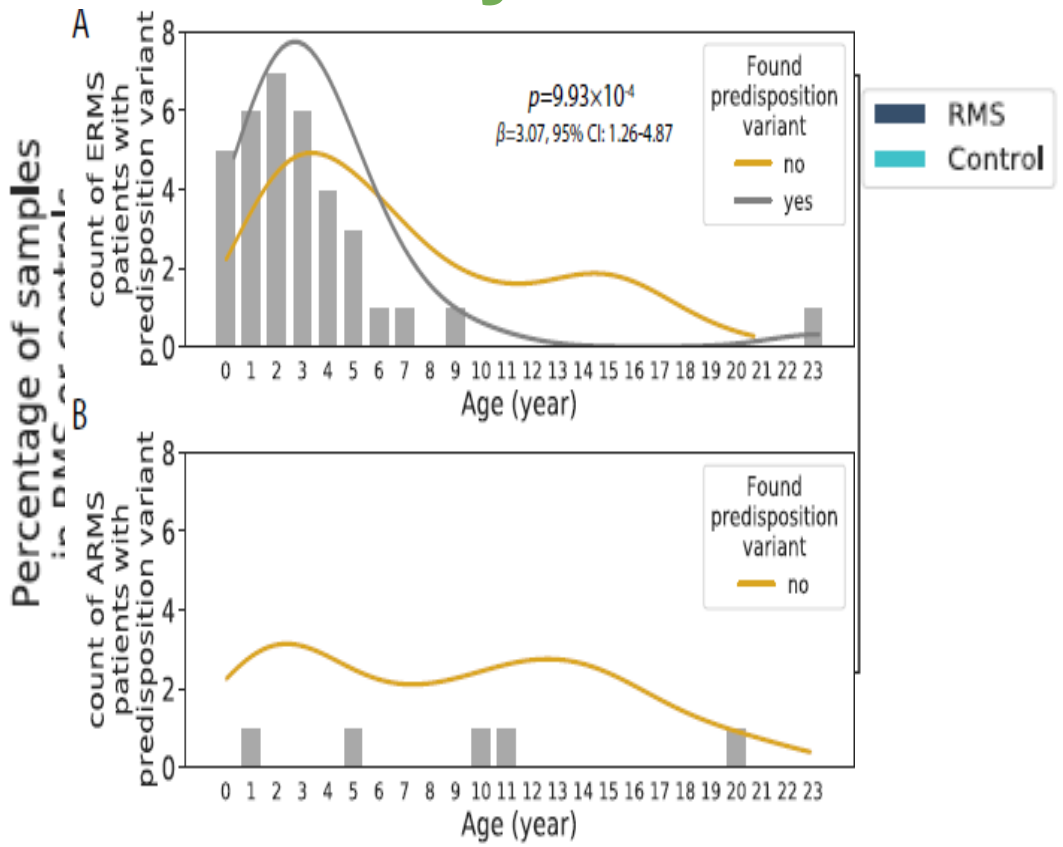
Courtesy of Julia Glade Bender, MD

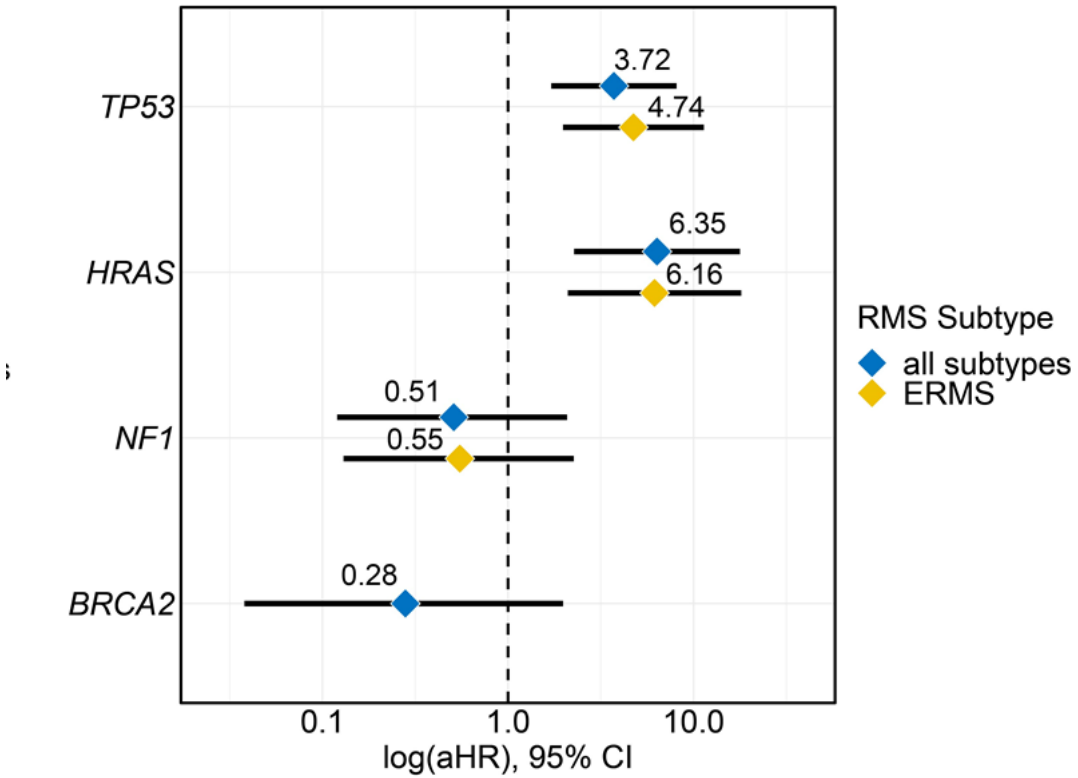
COG germline study of rhabdomyosarcoma

- 627 children with rhabdomyosarcoma
- Clinical annotation available
- 7.8% pathogenic/ likely pathogenic variant
- Additional genes identified



Li H, J Natl Cancer Inst 2021; 113:875-883

COG germline study of rhabdomyosarcoma



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Martin-Giacalone B, manuscript under preparation

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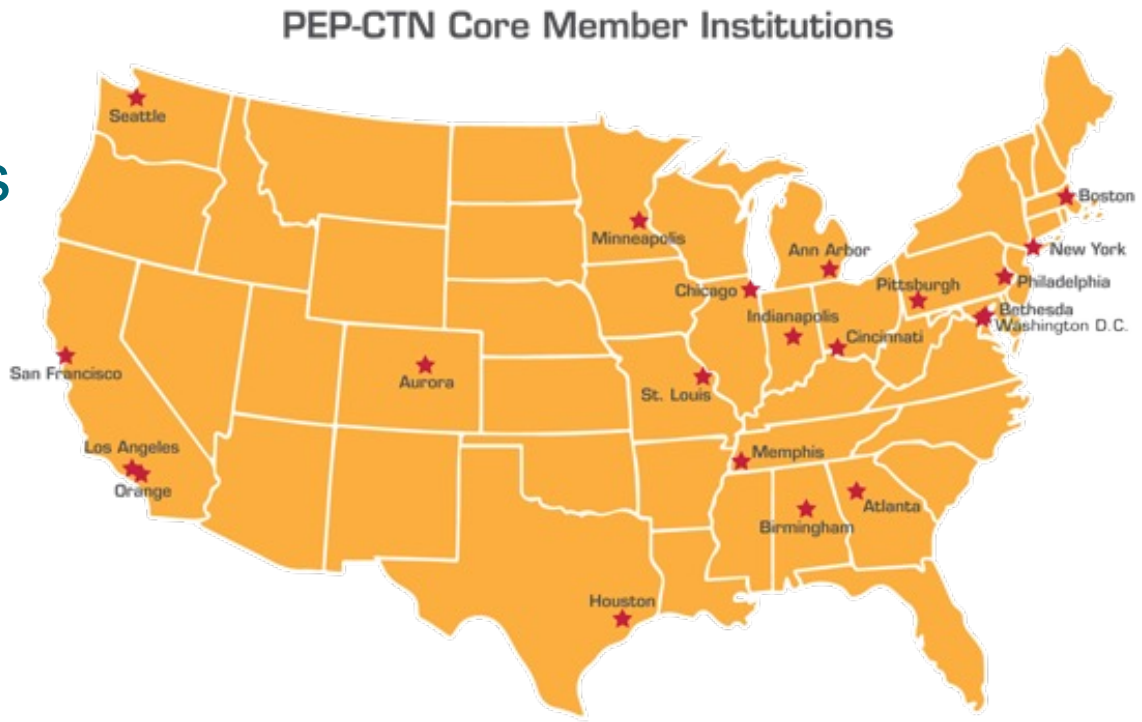
COG Developmental Therapeutics

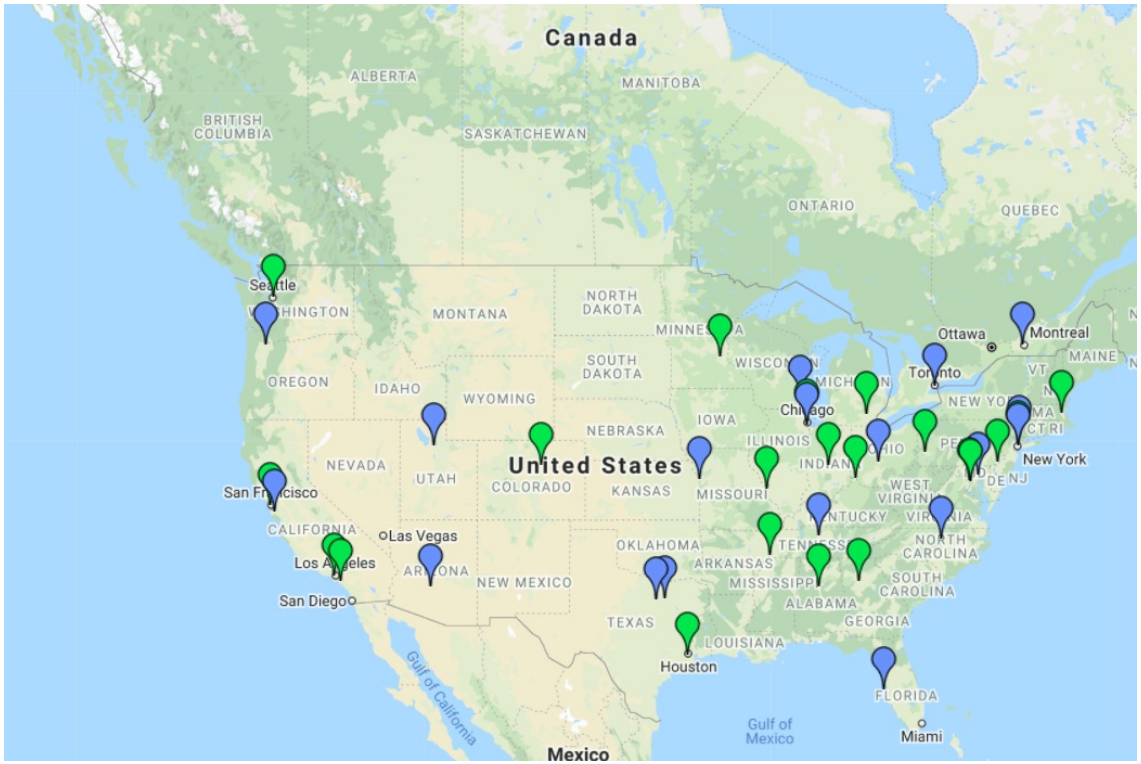
- Organizational structure driven by terms of NCI grant
- Overlying principles:
  - Limited network of institutions
  - Phase 1 vs phase 2 sites
- Linkage to disease committee strategies

COG PEP-CTN

- Core member sites limited to 21 institutions
- In 2021, added 21 additional non-core members sites
- Phase 1 restricted to core-member sites



COG PEP-CTN



- Core Member Institutions
- Non-Core Member Institutions

Investigational trial options

- Industry-sponsored
  - Limited number of institutions participating
  - Designed to meet regulatory requirements
- Single institution studies
- Multi-institutional consortia:
  - SJCRH: medulloblastoma, ALL, AML, Hodgkin lymphoma
  - DFCI: ALL

Multiple non-COG consortia

PACIFIC PEDIATRIC
NEURO-ONCOLOGY
CONSORTIUM

NATIONAL
PEDIATRIC CANCER
FOUNDATION
RISE UP FOR A FASTER CURE

Beat
Childhood
Cancer

Relapsed patients struggle to find therapies

Child with relapsed AML

Traditional therapy

Additional testing

Weeks/months

Phase I/II/III clinical trial

Relapsed patients struggle to find therapies

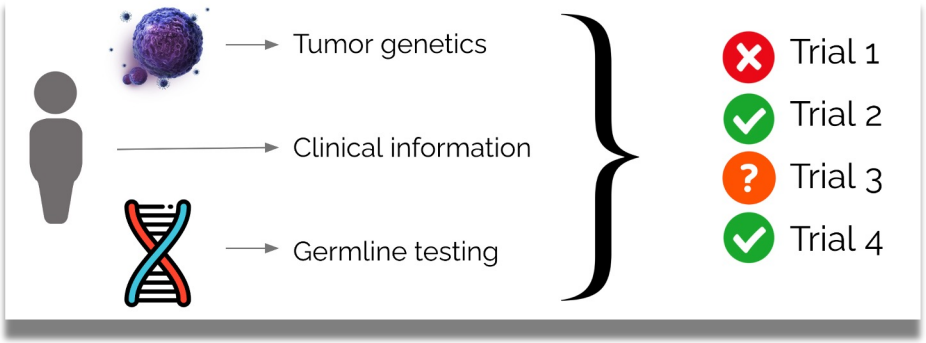
Child with relapsed AML

Traditional therapy

Additional testing

Weeks/months

Phase I/II/III clinical trial



ClinicalTrials.gov is difficult to use

Inclusion Criteria:

- Patient must be enrolled on APAL2020SC (NCT04726241)
- Patients must be < 18 years of age at the time of study enrollment
- Patients, with or without Down syndrome (DS), and with de novo acute myeloid leukemia, therapy-related acute myeloid leukemia, myelodysplastic syndrome or mixed phenotype acute leukemia that expresses E-selectin ligand on the cell membrane according to APAL2020SC screening results and meet one of the following:
  - Second or greater relapse or refractory AML as defined below, including isolated extramedullary disease (EMD), but excluding isolated central nervous system (CNS) or isolated testicular disease
  - Second or greater relapse or refractory myelodysplastic syndrome (MDS)
  - Second or greater relapse or refractory mixed phenotype acute leukemia (MPAL)
- Bone marrow relapse: (patients must meet one of the following criteria to be defined as having relapse disease)
  - A single bone marrow sample showing >= 5% leukemic blasts by flow cytometry performed at the central laboratory, fluorescence in situ hybridization (FISH) testing or other molecular method
  - A single bone marrow with at least two tests showing >= 1% leukemic blasts; examples of tests include:
    - Flow cytometry showing leukemia >= 1% by multidimensional flow cytometry (MDF) performed at the central laboratory (performed at hematologics through the screening study APAL2020SC)
    - Karyotypic abnormality with at least one metaphase similar or identical to diagnosis
    - FISH abnormality identical to one present at diagnosis
    - Polymerase chain reaction (PCR) or next generation sequencing (NGS)-based demonstration of leukemogenic lesion identical to diagnosis and >= 1%
  - In cases where a bone marrow aspirate cannot be obtained because of extensive fibrosis, blast count can be obtained from touch imprints or estimated from an adequate bone marrow core biopsy. A complete blood count documenting the presence of at least 1,000/ uL (i.e., a white blood count [WBC] count >= 10,000/uL with >= 10% blasts or a WBC count of >= 5,000/uL with >= 20% blasts) circulating leukemic cells (blasts) can also be used if a bone marrow aspirate or biopsy cannot be performed
- Extramedullary relapse: Biopsy proven extramedullary disease after documented complete remission
- Refractory disease: Following a re-induction cycle after a second relapse, presence of ≥1% leukemic blasts by flow cytometry performed at the central laboratory (performed only at Hematologics through the screening study APAL2020SC), OR there is persistent extramedullary disease
- Patient's current disease state must be one for which there is no known curative therapy or therapy proven to prolong survival with an acceptable quality of life
- Karnofsky >= 50 for patients > 16 years of age and Lansky >= 50 for patients =< 16 years of age. Patients must have a performance status corresponding to Eastern Cooperative Oncology Group (ECOG) scores of 0, 1 or 2. Use Karnofsky for patients > 16 years of age and Lansky for patients =< 16 years of age
- Patients must have fully recovered from the acute toxic effects of all prior anti-cancer therapy and must meet the following minimum duration from prior anti-cancer directed therapy prior to enrollment. If after the required timeframe, the numerical eligibility criteria are met, eg, blood count criteria, the patient is considered to have recovered adequately
  - Cytotoxic chemotherapy or other anti-cancer agents known to be myelosuppressive:
    - >= 14 days must have elapsed after the completion of other cytotoxic therapy, with the exception of hydroxyurea
    - NOTE: Cytoreduction with hydroxyurea must be discontinued >= 24 hours prior to the start of protocol therapy
  - Anti-cancer agents not known to be myelosuppressive (eg, not associated with reduced platelet or absolute neutrophil count [ANC] counts): >= 7 days after the last dose of agent
  - Antibodies: >= 21 days must have elapsed from infusion of last dose of antibody, and toxicity related to prior antibody therapy must be recovered to grade =< 1
  - Corticosteroids: If used to modify immune adverse events related to prior therapy, >= 14 days must have elapsed since last dose of corticosteroid
  - Hematopoietic growth factors: >= 14 days after the last dose of a long-acting growth factor (eg. pegfilgrastim) or 7 days for short acting growth factor. For agents that have known adverse events occurring beyond 7 days after administration, this period must be extended beyond the time during which adverse events are known to occur

Partial inclusion criteria for PEPN2113

"Highest Dose of Uproleselan in Combination With Fludarabine and Cytarabine for Patients With Acute Myeloid Leukemia, Myelodysplastic Syndrome, or Mixed Phenotype Acute Leukemia Relapsed or Refractory and That Expresses E-selectin Ligand on the Cell Membrane"

Relapsed patients struggle to find therapies

Child with relapsed AML

Traditional therapy

Additional testing

Weeks/months

GEARBOx

48-72 hours

Phase I/II/III clinical trial

Genomic Eligibility Algorithm at Relapse for Better Outcomes

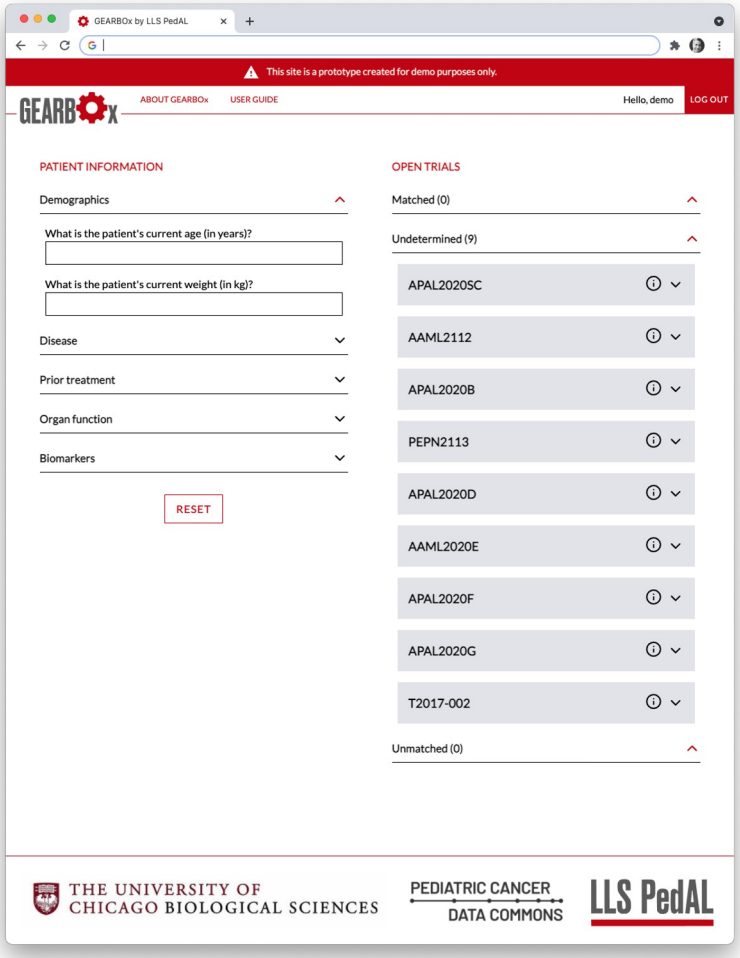
LEUKEMIA & LYMPHOMA SOCIETY®

Patient characteristics

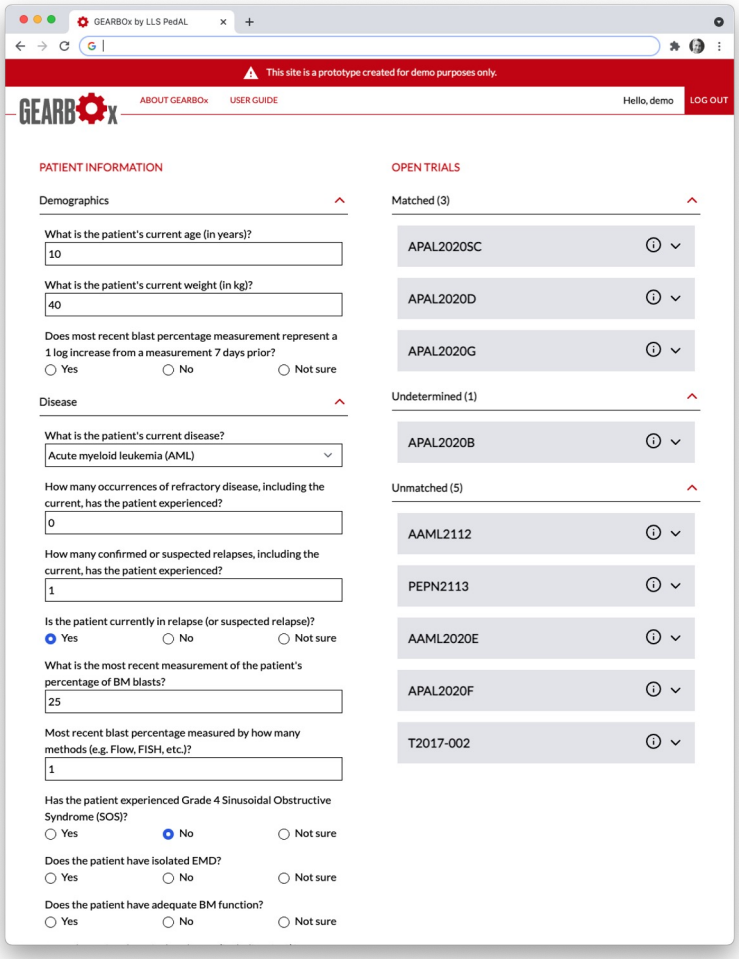
Disease characteristics

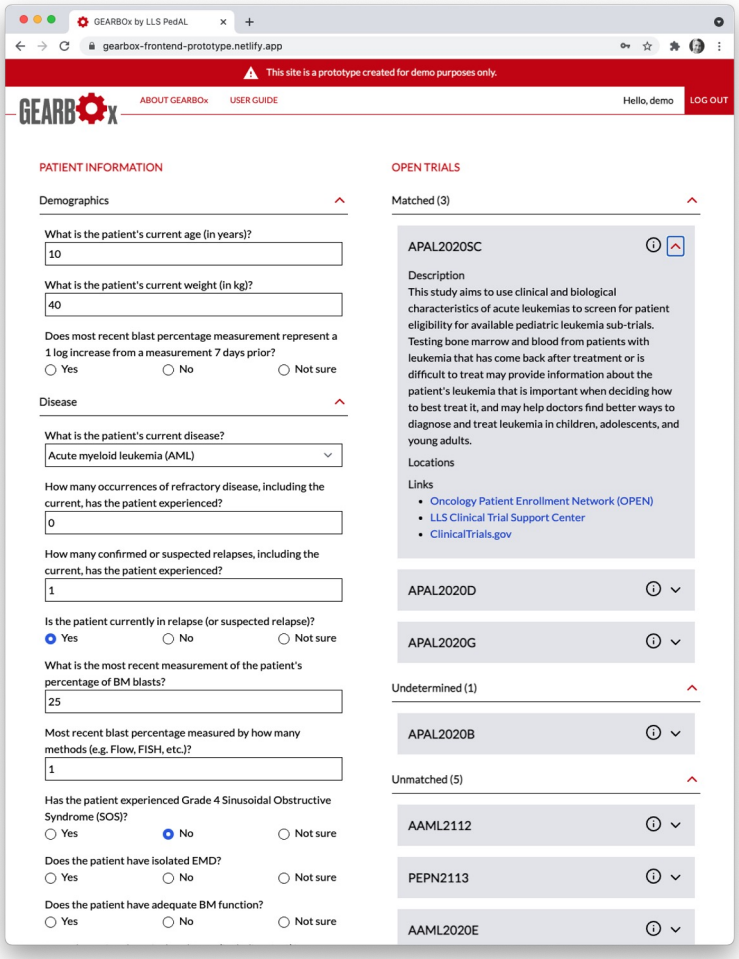
Lab tests

Genomic testing



Clinical trials
Information about enrollment
Study locations


GEARBOx by LLS PedAL
This site is a prototype created for demo purposes only.
GEARBOx
ABOUT GEARBOx
USER GUIDE
Hello, demo
LOG OUT
PATIENT INFORMATION
Demographics
What is the patient's current age (in years)?
10
What is the patient's current weight (in kg)?
40
Does most recent blast percentage measurement represent a 1 log increase from a measurement 7 days prior?
Yes
No
Not sure
Disease
What is the patient's current disease?
Acute myeloid leukemia (AML)
How many occurrences of refractory disease, including the current, has the patient experienced?
0
How many confirmed or suspected relapses, including the current, has the patient experienced?
1
Is the patient currently in relapse (or suspected relapse)?
Yes
No
Not sure
What is the most recent measurement of the patient's percentage of BM blasts?
25
Most recent blast percentage measured by how many methods (e.g. Flow, FISH, etc.)?
1
Has the patient experienced Grade 4 Sinusoidal Obstructive Syndrome (SOS)?
Yes
No
Not sure
Does the patient have isolated EMD?
Yes
No
Not sure
Does the patient have adequate BM function?
Yes
No
Not sure
OPEN TRIALS
Matched (3)
APAL2020SC
APAL2020D
APAL2020G
Undetermined (1)
APAL2020B
Unmatched (5)
AAML2112
PEPN2113
AAML2020E
APAL2020F
T2017-002


GEARBOx by LLS PedAL
gearbox-frontend-prototype.netlify.app
This site is a prototype created for demo purposes only.
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1
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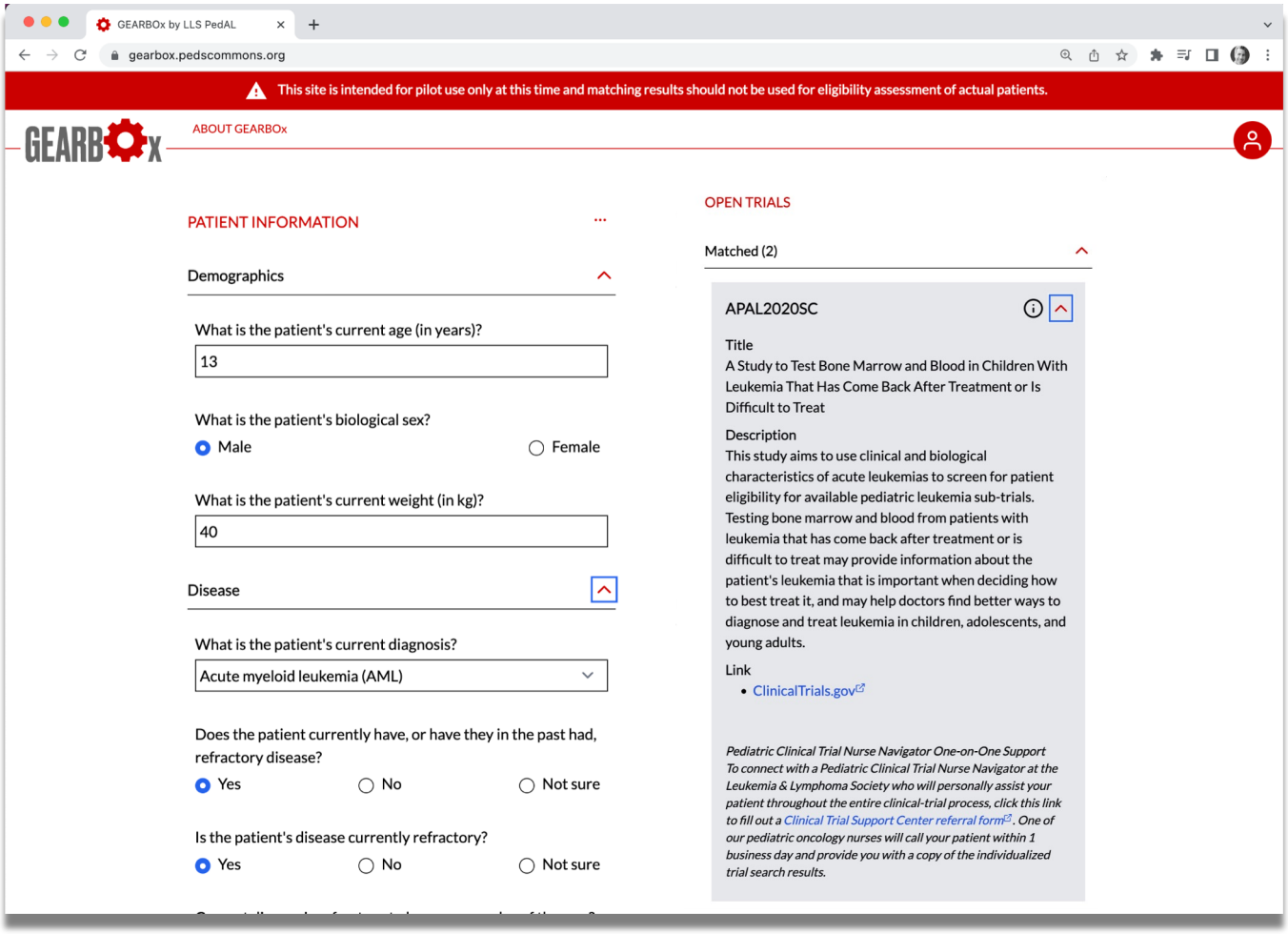
No
Not sure
Does the patient have isolated EMD?
Yes
No
Not sure
Does the patient have adequate BM function?
Yes
No
Not sure
OPEN TRIALS
Matched (3)
APAL2020SC
Description
This study aims to use clinical and biological characteristics of acute leukemias to screen for patient eligibility for available pediatric leukemia sub-trials. Testing bone marrow and blood from patients with leukemia that has come back after treatment or is difficult to treat may provide information about the patient's leukemia that is important when deciding how to best treat it, and may help doctors find better ways to diagnose and treat leukemia in children, adolescents, and young adults.
Locations
Links
Oncology Patient Enrollment Network (OPEN)
LLS Clinical Trial Support Center
ClinicalTrials.gov
APAL2020D
APAL2020G
Undetermined (1)
APAL2020B
Unmatched (5)
AAML2112
PEPN2113
AAML2020E


GEARBOx by LLS PedAL
gearbox.pedscommons.org
This site is intended for pilot use only at this time and matching results should not be used for eligibility assessment of actual patients.
GEARBOx
ABOUT GEARBOx
PATIENT INFORMATION
Demographics
What is the patient's current age (in years)?
13
What is the patient's biological sex?
Male
Female
What is the patient's current weight (in kg)?
40
Disease
What is the patient's current diagnosis?
Acute myeloid leukemia (AML)
Does the patient currently have, or have they in the past had, refractory disease?
Yes
No
Not sure
Is the patient's disease currently refractory?
Yes
No
Not sure
OPEN TRIALS
Matched (2)
APAL2020SC
Title
A Study to Test Bone Marrow and Blood in Children With Leukemia That Has Come Back After Treatment or Is Difficult to Treat
Description
This study aims to use clinical and biological characteristics of acute leukemias to screen for patient eligibility for available pediatric leukemia sub-trials. Testing bone marrow and blood from patients with leukemia that has come back after treatment or is difficult to treat may provide information about the patient's leukemia that is important when deciding how to best treat it, and may help doctors find better ways to diagnose and treat leukemia in children, adolescents, and young adults.
Link
ClinicalTrials.gov
Pediatric Clinical Trial Nurse Navigator One-on-One Support
To connect with a Pediatric Clinical Trial Nurse Navigator at the Leukemia & Lymphoma Society who will personally assist your patient throughout the entire clinical-trial process, click this link to fill out a Clinical Trial Support Center referral form. One of our pediatric oncology nurses will call your patient within 1 business day and provide you with a copy of the individualized trial search results.

FDA's Expanded Access Program (EAP)

- Path to obtain investigational agent outside of trial
- 99% single patient use (SPU) requests approved
- High proportion of pediatric requests (34% overall)
- Four large institutions, 2014-2019:
  - Genomically targeted agents only
  - 45 SPUs for 44 patients
  - Most common reason: no clinical trial available (64.4%)
  - Median time for FDA approval: 3 days
  - Objective response rate: **39.5%**

Feit NZ, JAMA Oncol 2019; 5:570-572
Sabnis HS, J Clin Oncol 2021; 39:3822-3828

Topics for today

- Role of clinical trials to define standards of care
  - Power of randomized studies
  - How information is shared
  - FDA approval of pediatric indications
- Increased importance of molecular testing
- Access to investigational agents
- Increasing equity in treatment outcome

OXFORD

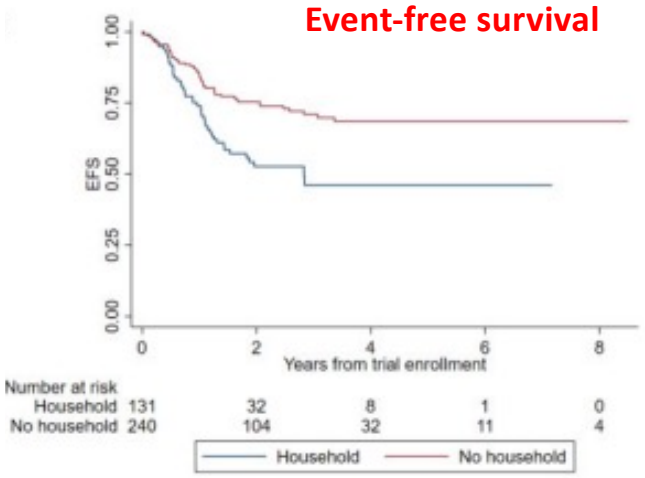
JNCI J Natl Cancer Inst (2021) 113(3): djaa107

doi: 10.1093/jnci/djaa107
First published online November 24, 2020
Article

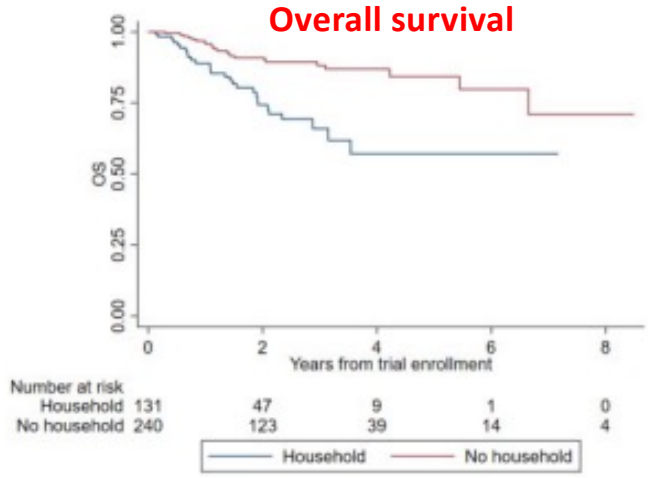
Poverty and Targeted Immunotherapy: Survival in Children's Oncology Group Clinical Trials for High-Risk Neuroblastoma

Kira Bona, MD, MPH,[1,*] Yimei Li, PhD,[2] Lena E. Winestone, MD,[3] Kelly D. Getz, MPH,[2,4] Yuan-Shung Huang, MS,[5] Brian T. Fisher, DO, MPH, MSCE,[4,6] Ami V. Desai, MD, MSCE,[7] Troy Richardson, PhD,[8] Matt Hall, PhD,[8] Arlene Naranjo, PhD,[9] Tara O. Henderson, MD, MPH,[7] Richard Aplenc, MD, PhD, MSCE,[4,10,11] Rochelle Bagatell, MD[11]

Event-free survival



Overall survival



- Enrolled on COG high-risk neuroblastoma immunotherapy studies
- Everyone had initial protocol treatment and anti-GD2 antibody
- ***Disparity of outcome by household poverty***

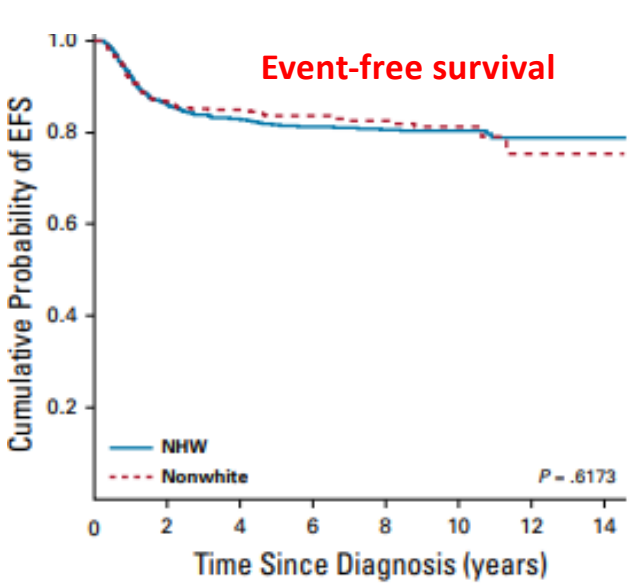
CHILDREN'S ONCOLOGY GROUP

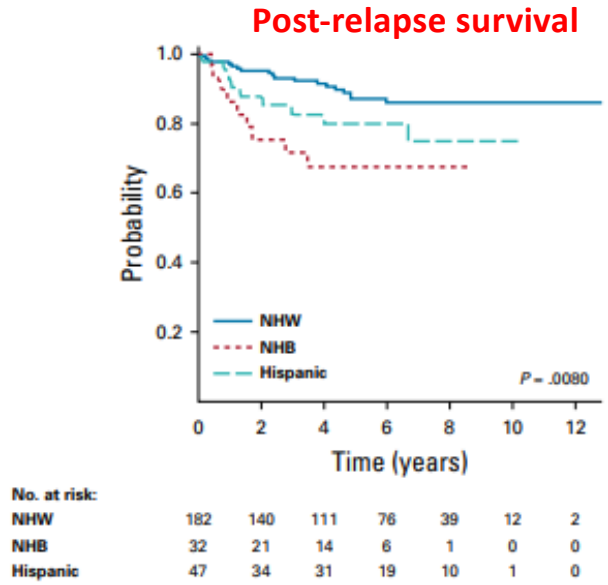
Bona K, J Natl Cancer Inst 2021; 113:282-291

original reports

Survival by Race and Ethnicity in Pediatric and Adolescent Patients With Hodgkin Lymphoma: A Children's Oncology Group Study

Justine M. Kahn, MD, MS[1]; Kara M. Kelly, MD[2]; Qinglin Pei, PhD[3]; Rizvan Bush, MS[4]; Debra L. Friedman, MD, MS[5]; Frank G. Keller, MD[6]; Smita Bhatia, MD, MPH[7]; Tara O. Henderson, MD, MPH[8]; Cindy L. Schwartz, MD[9]; and Sharon M. Castellino, MD, MSc[6]





No. at risk:							
NHW	182	140	111	76	39	12	2
NHB	32	21	14	6	1	0	0
Hispanic	47	34	31	19	10	1	0

- Enrolled on COG Hodgkin lymphoma studies
- No difference in EFS by race or ethnicity
- ***Disparity of post-relapse survival by race, ethnicity***

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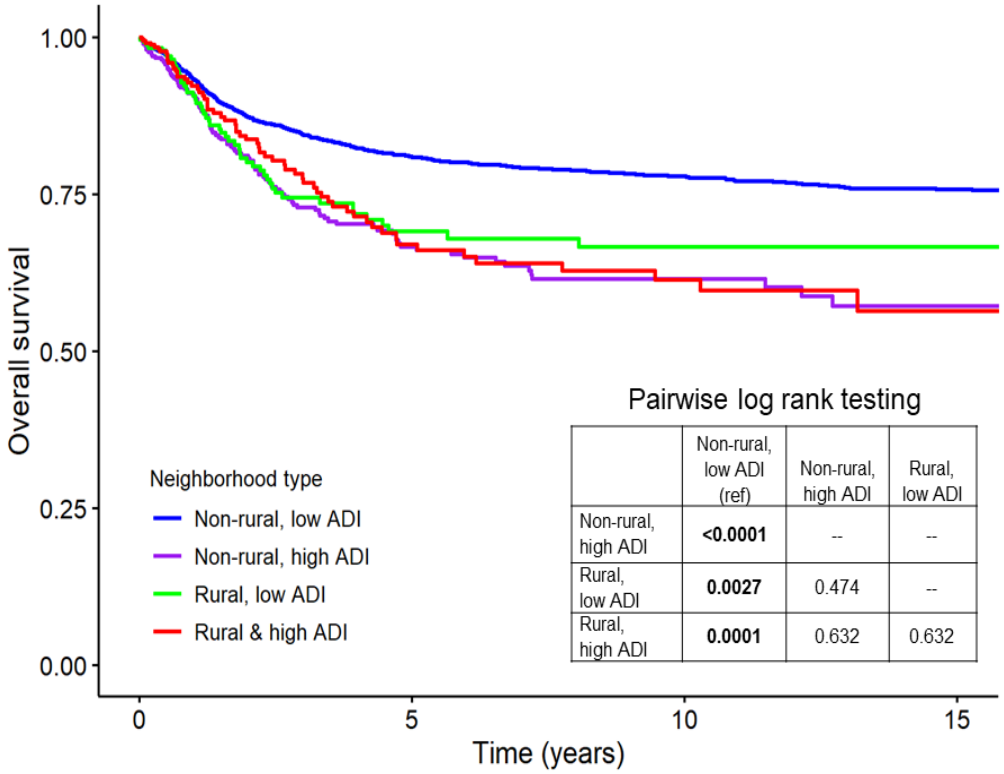
Kahn JM, J Clin Oncol 2019; 37:3009-3017

Pediatric cancer survival by neighborhood

- 4417 children with cancer diagnosed 1992-2013 in Washington
- Census data to define:
  - Rural residence
  - Neighborhood poverty (ADI)
- Lower survival for either rural residence or high ADI



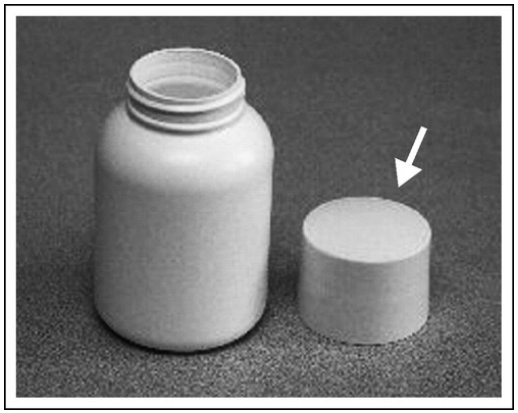
Pairwise log rank testing

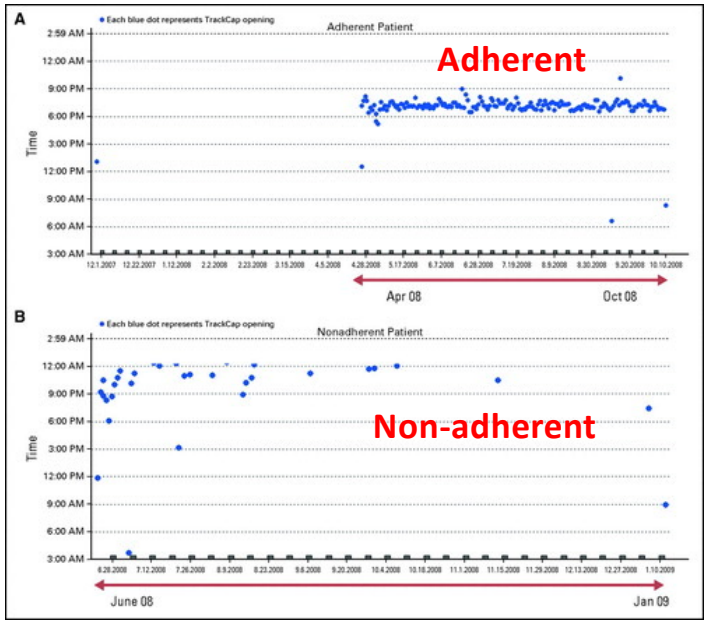
	Non-rural, low ADI (ref)	Non-rural, high ADI	Rural, low ADI
Non-rural, high ADI	**<0.0001**	--	--
Rural, low ADI	**0.0027**	0.474	--
Rural, high ADI	**0.0001**	0.632	0.632

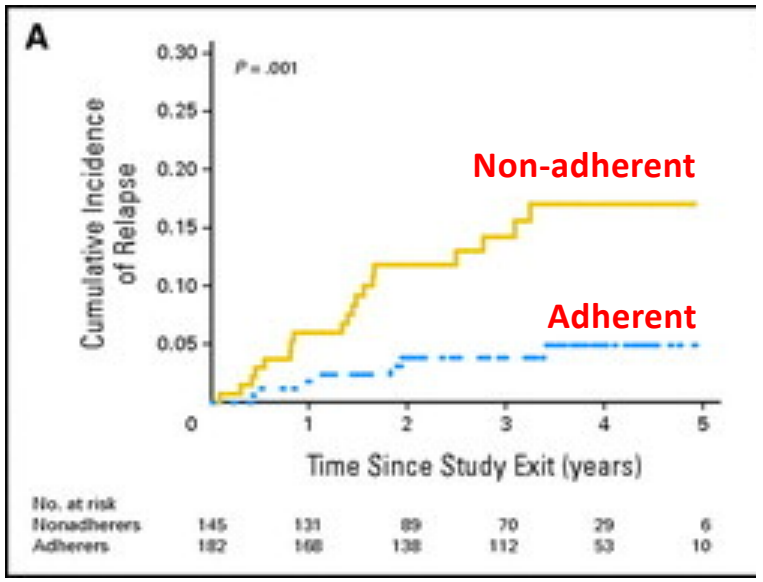
Nonadherence to Oral Mercaptopurine and Risk of Relapse in Hispanic and Non-Hispanic White Children With Acute Lymphoblastic Leukemia: A Report From the Children's Oncology Group

Smita Bhatia, Wendy Landier, Muyun Shangguan, Lindsey Hageman, Alexandra N. Schaible, Andrea R. Carter, Cara L. Hanby, Wendy Leisenring, Yutaka Yasui, Nancy M. Kornegay, Leo Mascarenhas, A. Kim Ritchey, Jacqueline N. Casillas, David S. Dickens, Jane Meza, William L. Carroll, Mary V. Relling, and F. Lennie Wong

- Oral chemotherapy is major part of treatment for ALL
- Does it matter if children take it?







CHILDREN'S ONCOLOGY GROUP

Bhatia S, J Clin Oncol 2012; 30:2094-2101

Conclusions

- Clinical trials are essential to define standard treatment, improve outcome, and support FDA pediatric labeling
- Molecular testing is often needed to guide therapy
- Many paths to access investigational agents; none are easy
- Reducing the inequities of access, opportunity, and delivery are central to improve pediatric cancer outcomes

Thanks to CAC2 for the invitation and your advocacy

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