Childhood Cancer Data Initiative Virtual Symposium Series

Warren Kibbe, Jack Shern, Malcolm Smith, Erin Rudzinski, Diana Thomas, and Sarah Leary

NIH NATIONAL CANCER INSTITUTE

March 12, 2026

Welcome & Opening Remarks

Warren Kibbe, Ph.D.
and Jack Shern, M.D.

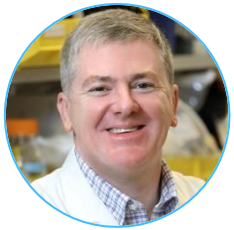
Today's Speakers

WARREN KIBBE, PH.D.

Deputy Director for Data Science and Strategy

National Cancer Institute

JACK SHERN, M.D.



CCDI Scientific Director & Head of the Tumor Evolution and Genomics Section, Pediatric Oncology Branch

National Cancer Institute

MALCOLM SMITH, M.D., PH.D.

Associate Branch Chief for Pediatric Oncology, Cancer Therapy Evaluation Program

National Cancer Institute

ERIN RUDZINSKI, M.D.

Director of Pediatric Pathology & Professor of Laboratory Medicine and Pathology

Indiana University

DIANA THOMAS, M.D., PH.D.

Neuropathologist

Nationwide Children's Hospital

SARAH LEARY, M.D., M.S.

Pediatric Oncologist

Seattle Children's Hospital

Childhood Cancer Data Initiative Virtual Symposium Series

History of CCDI: From Ad Hoc Working Group to 2026

Warren Kibbe, Ph.D. and Jack Shern, M.D.

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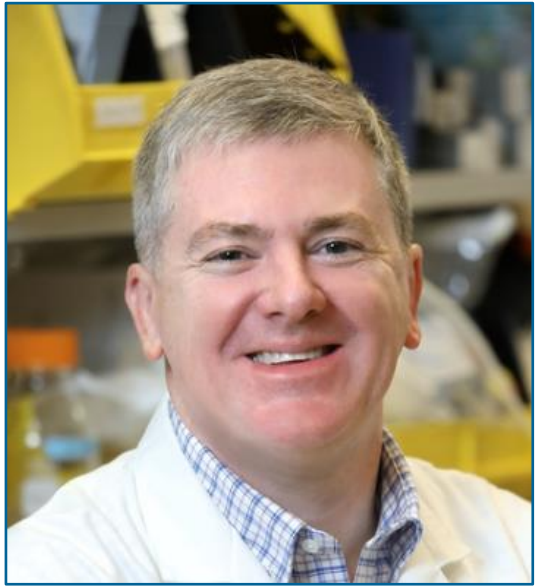
Agenda

1. *CCDI Leadership Update*
2. *CCDI History and Progress*
3. *CCDI Resources and Programs*
4. *User Metrics*
5. *Looking Ahead*

CCDI Leadership Update

NCI has appointed a new CCDI Scientific Director

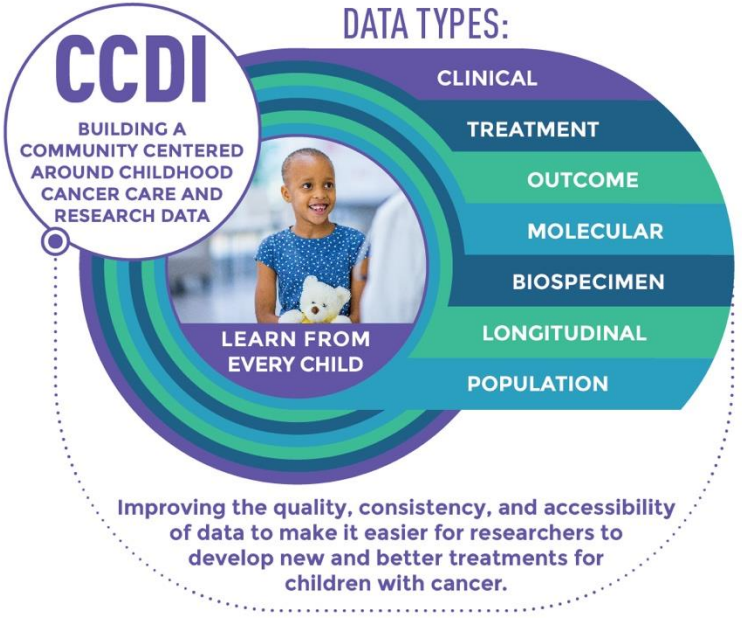
Thank you for your leadership and dedication, Dr. Gregory Reaman!



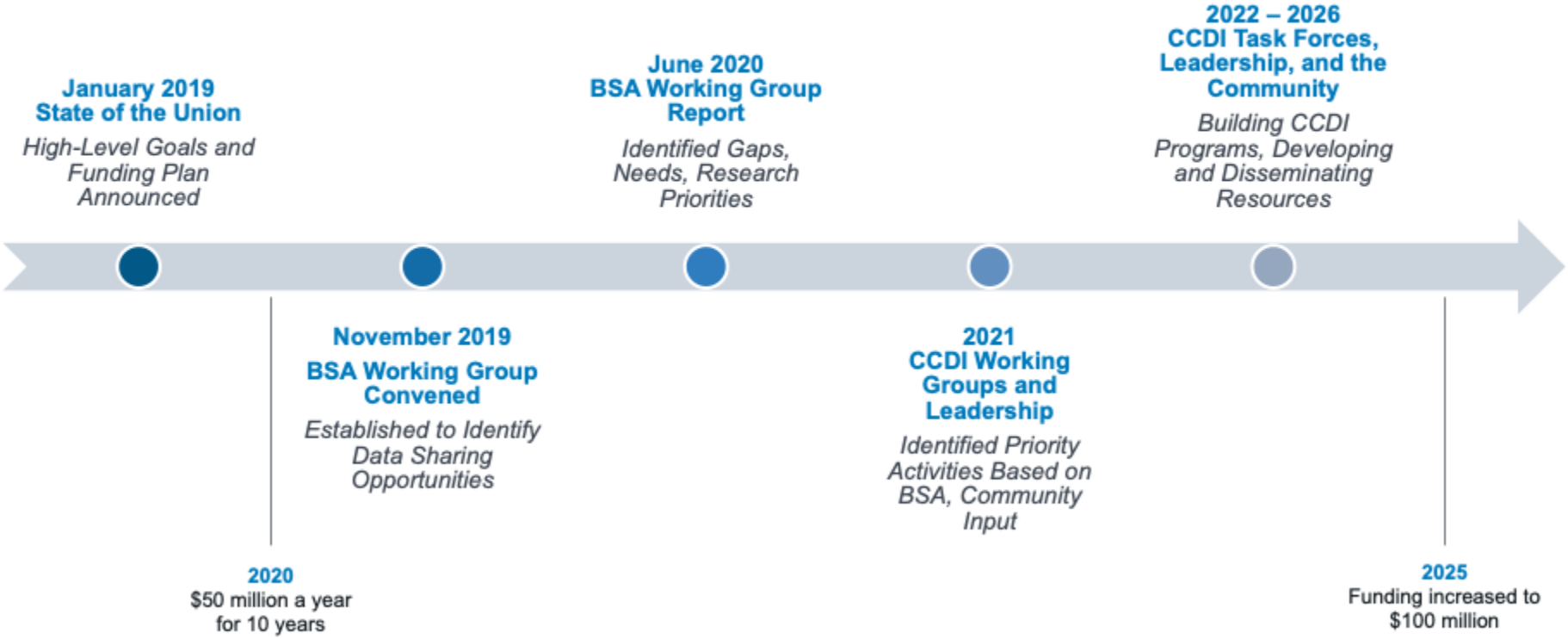
Welcome to the role of CCDI Scientific Director, Dr. Jack Shern!

CCDI Goals

- Gather and integrate **data from every child, adolescent, and young adult** diagnosed with a childhood cancer
- **Create a national strategy** of molecular characterization to inform diagnosis and treatment
- **Develop a platform and tools** to bring together clinical and research data that will inform new insights in biology/etiology to improve preventive measures, treatment, quality of life, and survivorship for childhood cancers



Brief History of CCDI



CCDI Data Ecosystem: A Connected Network of Resources

GDC & cBioPortal:
Visualization Tools

Federation & CPI APIs:
Data Discovery & Integration

Cancer Genomics Cloud:
Data Integration &
Analysis

C3DC & NCCR:
Clinical & Real World Data

Hub Explore: Build Cohorts

Hub: Entry Point

Catalog, MTP, & CIViC:
Knowledgebases

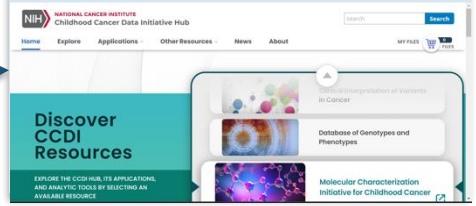
Pediatric/AYA Data From Multiple Sources

SEER
PPCR Pediatric Proton/Photon Consortium Registry
PBTC Pediatric Brain Tumor Consortium
cancer immunotherapy trials network
NCI MyPART My Pediatric and Adult Rare Tumor Network
St. Jude Cloud
CHILDHOOD CANCER DATA LAB Powered by Alex's Lemonade Stand Foundation
NPCR NATIONAL PROGRAM of CANCER REGISTRIES
NCI - COG
Pediatric MATCH
HCMI
Gabriella Miller Kids First PEDIATRIC RESEARCH PROGRAM
CCSS CHILDHOOD CANCER SURVIVOR STUDY
CHILDREN'S ONCOLOGY GROUP
NIH NATIONAL CANCER INSTITUTE Childhood Cancer Data Initiative cBioPortal Cancer Data Explorer
FusOnc2
Treehouse CHILDHOOD CANCER INITIATIVE
Childhood Cancer STAR ACT
Pediatric Cancer Programs of Comprehensive Cancer Centers
PROJECT:EVERYCHILD
PedcBioPortal for Integrated Childhood Cancer Genomics
OncoGenomics National Cancer Institute
NCI PPTC Pediatric Preclinical Testing Consortium
Children's Brain Tumor Network Until every child is cured
PIVOT Pediatric Preclinical In Vivo Testing
FOUNDATION MEDICINE
TARGET
PIN Pediatric Immunotherapy Network

Aggregate and generate data; enable access and analysis

CCDI

CCDI Hub



Understand biology of treatment response and resistance → Generate improved strategies for intervention ← Develop new research and analytical tools

CCDI Studies Available to the Research Community

CCDI provides access to a growing collection of pediatric and AYA cancer studies, with **40 multimodal studies currently available**.

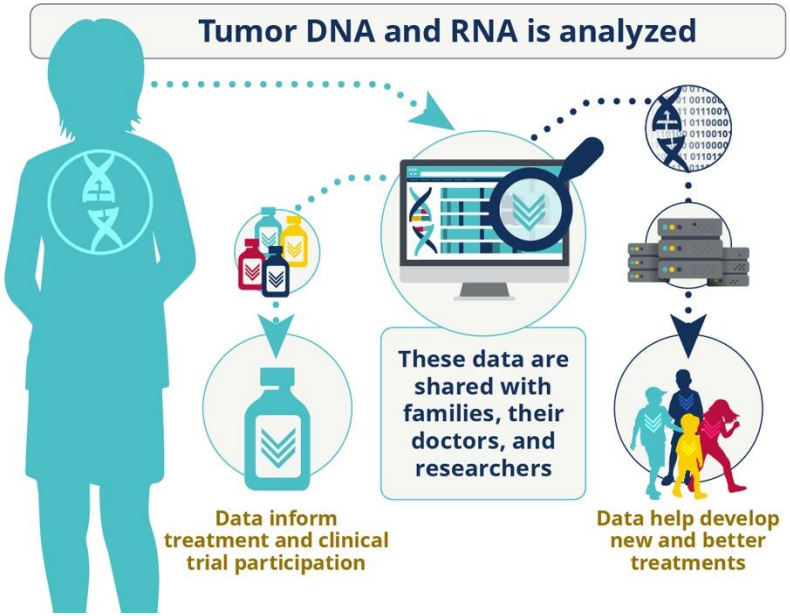
Sample List of Studies:

- Pediatric MATCH Precision Medicine Clinical Trial
- Childhood Cancer Survivor Study
- Longitudinal Clinical, Sociodemographic, and Genomic Data
- Michigan Oncology Sequencing Center
- OncoKids Gene Panel at Children's Hospital Los Angeles
- Children's Brain Tumor Network
- Admixture Analysis of Acute Lymphoblastic Leukemia in African American Children
- Pediatric Preclinical In Vivo Testing Consortium

Additional studies are available on the CCDI Hub at **ccdi.cancer.gov/studies**.

CCDI Molecular Characterization Initiative (MCI)

- A partnership between NCI and the Children's Oncology Group (COG) Project:EveryChild
- Provides **state-of-the-art molecular characterization at diagnosis** (WES, fusions, methylation) to inform best treatment at no cost to participants
- **Results returned** to participants and treating physicians **within 21 days**
- **~9,000 children and adolescent, and young adults (AYAs) have enrolled** in the program
- Remaining samples will be stored in a biobank for **future research**
  - Research characterization (WGS, RNA Seq, single cell, and proteomics/metabolomics assays) performed to deepen our understanding of cancer biology
- **Longitudinal follow-up** of patients with germline abnormalities and cascade testing in unaffected immediate family members



cancer.gov/CCDI-molecular

CCDI Pediatric and AYA Rare Cancer Study

- **Launching soon**!
- A **collaboration** between CCDI and organizations and initiatives in the U.S. and abroad, including COG
- A **longitudinal, observational study** that will follow children and AYAs with **very rare cancers** over time
- Primary goals:
  - To **develop a registry** containing a core data set on all rare cancer participants
  - Include real-world data that can **inform the design of rare childhood cancer clinical trials**

cancer.gov/ccdi-rare-cancer

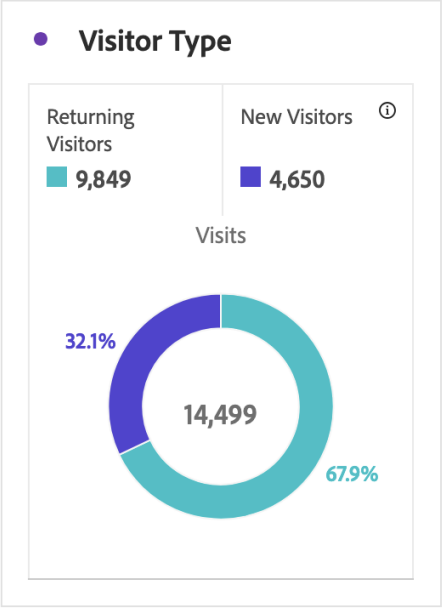
Research Opportunities to Leverage Artificial Intelligence (AI)

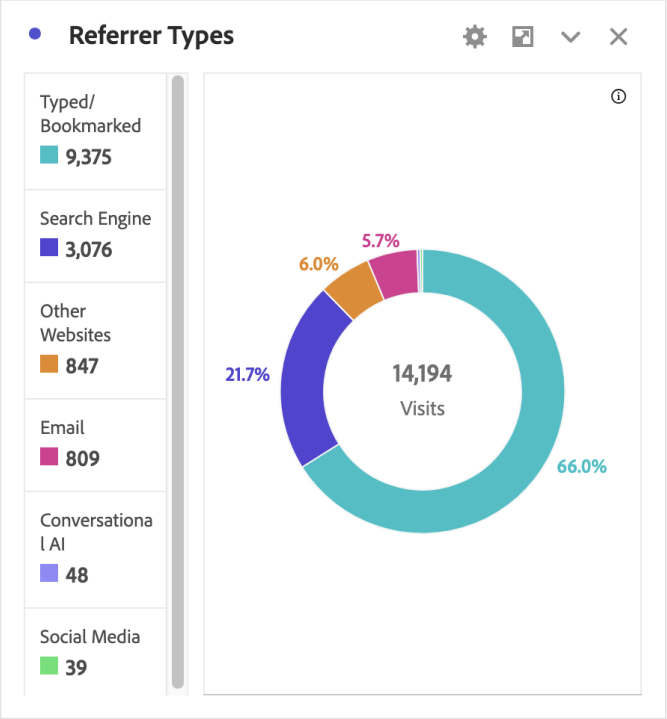
Topics of interest are not limited to those listed here:

- AI-enabled extraction and structuring of clinical and research data to enhance CCDI data assets
- AI/machine learning approaches to harmonize and leverage heterogenous pediatric data sets into interoperable, AI-ready formats
- Tools for multimodal data integration and validation
- Privacy-preserving and distributed AI approaches

CCDI Hub User Metrics

- In the last 12 months, there were nearly **5,000 new visitors** to the CCDI Hub.
- During the same timeframe, the Hub had about **47,000 page views** and nearly **14,500 visits.**





MCI Is the Second Most Downloaded Data Set from the Genomic Data Commons

January 2026

Project Name (ID)	File Size Downloaded (TB)
Breast Invasive Carcinoma (TCGA-BRCA)	755.95
CCDI-MCI	592.57
CPTAC-Brain, Head and Neck, Kidney, Lung, Pancreas, Uterus (CPTAC-3)	338.23
Head and Neck Squamous Cell Carcinoma (TCGA-HNSC)	332.81
Colon Adenocarcinoma (TCGA-COAD)	220.60
Glioblastoma Multiforme (TCGA-GBM)	198.71
Lung Adenocarcinoma (TCGA-LUAD)	134.32
Cervical Squamous Cell Carcinoma and Endocervical Adenocarcinoma (TCGA-CESC)	128.47
Kidney Renal Clear Cell Carcinoma (TCGA-KIRC)	105.34
Skin Cutaneous Melanoma (TCGA-SKCM)	93.25
Sarcoma (TCGA-SARC)	91.52

How You Can Engage with CCDI

Learn about CCDI and subscribe to our monthly newsletter:
cancer.gov/CCDI

Access CCDI data and resources:
ccdi.cancer.gov

Questions? Email us at:
NCIChildhoodCancerDataInitiative@mail.nih.gov

Childhood Cancer Data Initiative Virtual Symposium Series

Molecular Characterization Initiative: Identification and Implementation of a Standardized Genomic Characterization of Childhood Cancers

Malcolm Smith, M.D., Ph.D.,
Erin Rudzinski, M.D., and Jack Shern, M.D.

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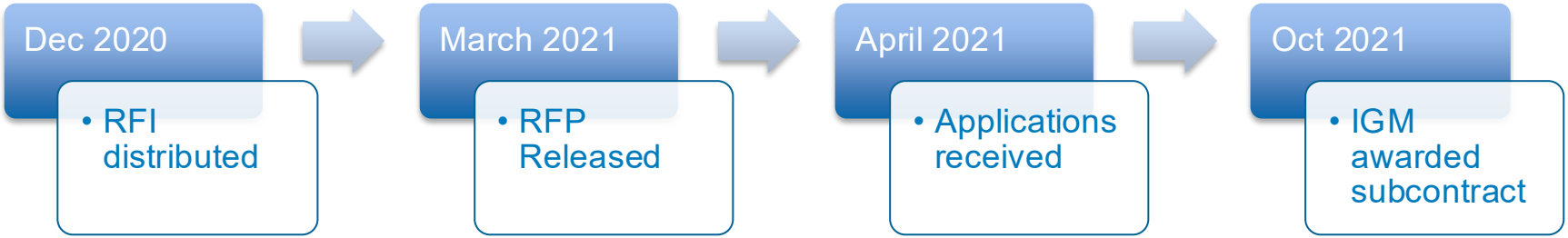
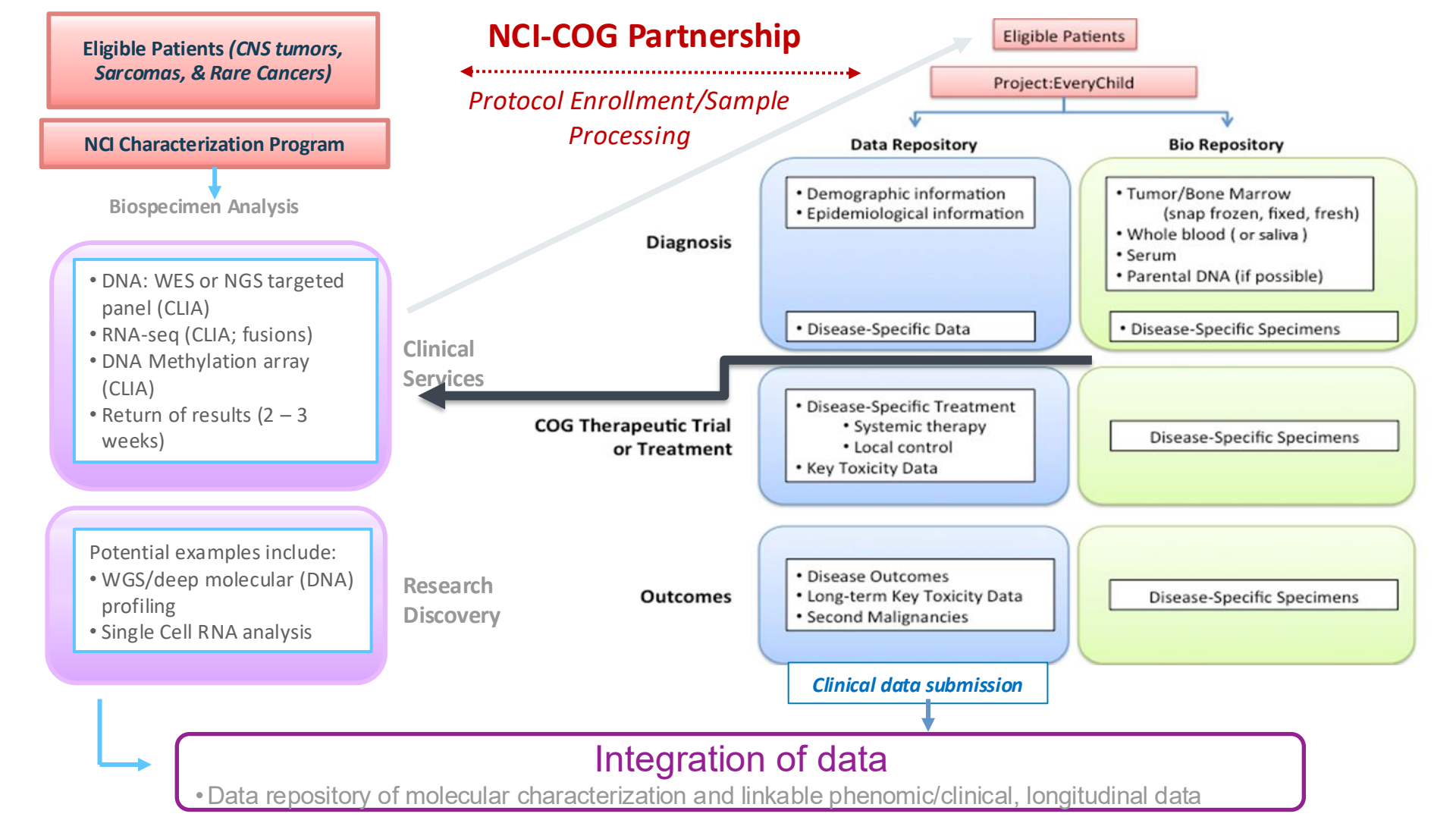
Malcolm Smith, M.D., Ph.D.

Creating the Molecular Characterization Initiative

Vision: Expand access to comprehensive molecular sequencing, with goal of reaching all children with pediatric cancer

Pathway: Building upon Project:EveryChild (APEC14B1) to offer genomic characterization at diagnosis across all COG institutions




Eligible Patients (CNS tumors, Sarcomas, & Rare Cancers)
NCI Characterization Program
Biospecimen Analysis
• DNA: WES or NGS targeted panel (CLIA)
• RNA-seq (CLIA; fusions)
• DNA Methylation array (CLIA)
• Return of results (2 – 3 weeks)
Potential examples include:
• WGS/deep molecular (DNA) profiling
• Single Cell RNA analysis
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
Research Discovery
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

MCI Begins!!!

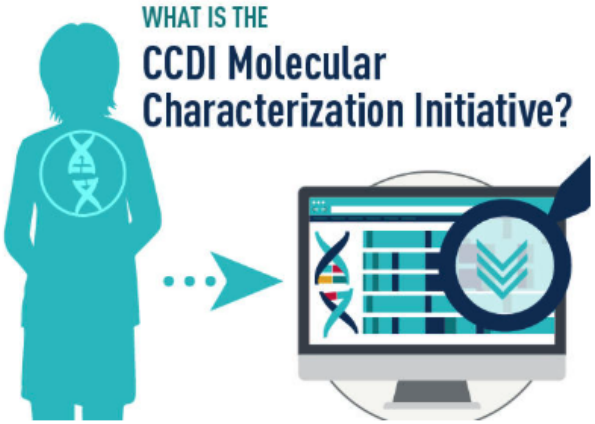
NCI launches program to offer molecular characterization of childhood cancers

Posted: March 21, 2022

Contact: NCI Press Office
240-760-6600

In support of President Biden's Cancer Moonshot℠ goal of fostering data sharing in cancer research, the National Cancer Institute, part of the National Institutes of Health, has launched the Molecular Characterization Initiative for pediatric tumors. This program offers tumor molecular characterization, also called biomarker testing, to children, adolescents, and young adults with newly diagnosed central nervous system tumors who are being treated at hospitals that are affiliated with the Children's Oncology Group (COG), an NCI-supported clinical trials group that includes more than 200 hospitals and institutions that treat most children diagnosed with cancer in the United States.

The Molecular Characterization Initiative is offered through NCI's Childhood Cancer Data Initiative, which was launched in 2019 to promote data sharing and collection of new data among researchers who study childhood cancers.



Credit: National Cancer Institute

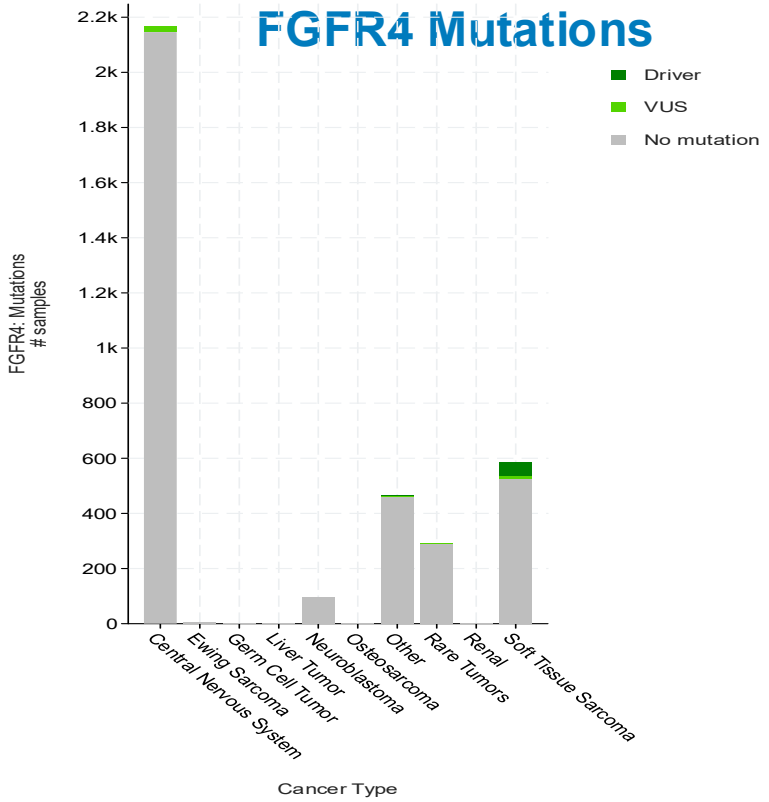
CCDI cBioPortal Cancer Data Explorer

cBioPortal Cancer Data Explorer

User-friendly instance that allows users to search by gene, mutation, cancer type, and quickly visualize relationships, patterns, and trends in the data

cbioportal.ccdi.cancer.gov

Example Use Case: A research can create cohorts of rhabdomyosarcoma patients with a PAX3-FOXO1 fusion or with FGFR4 driver mutations, etc.

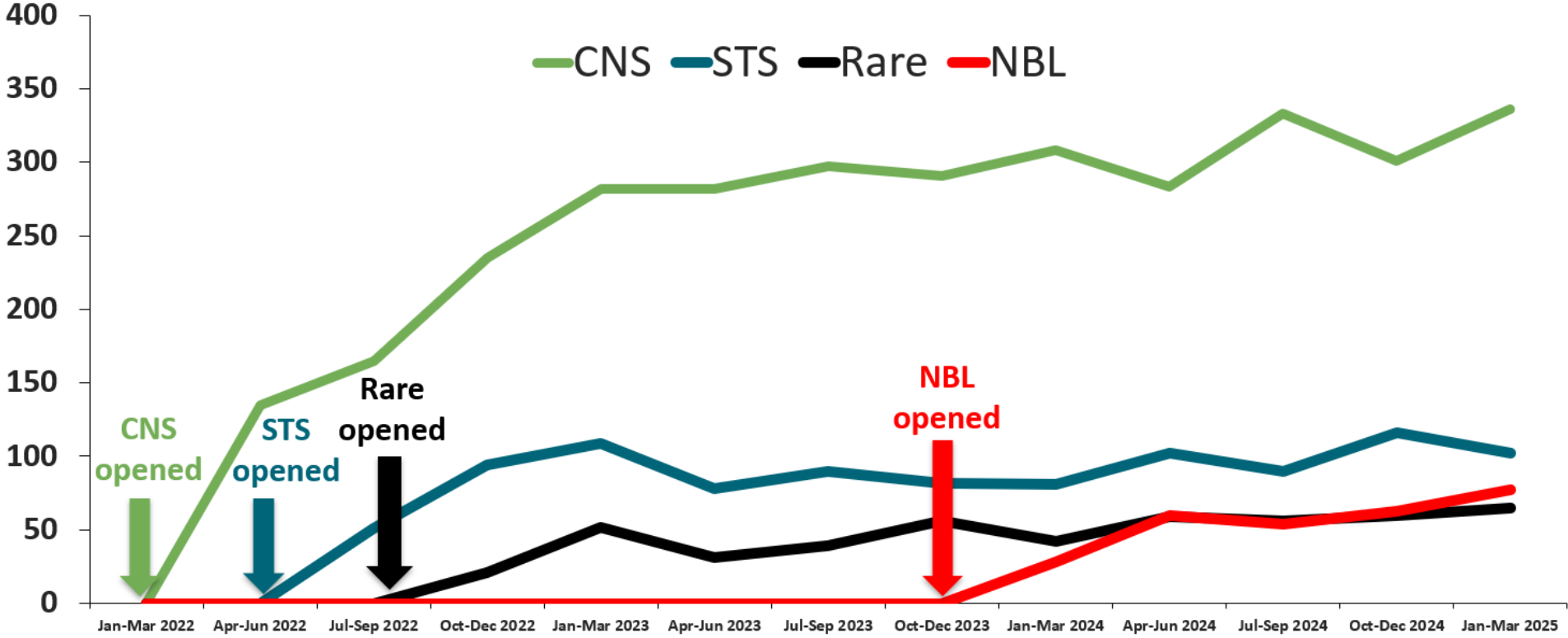


Erin Rudzinski, M.D.

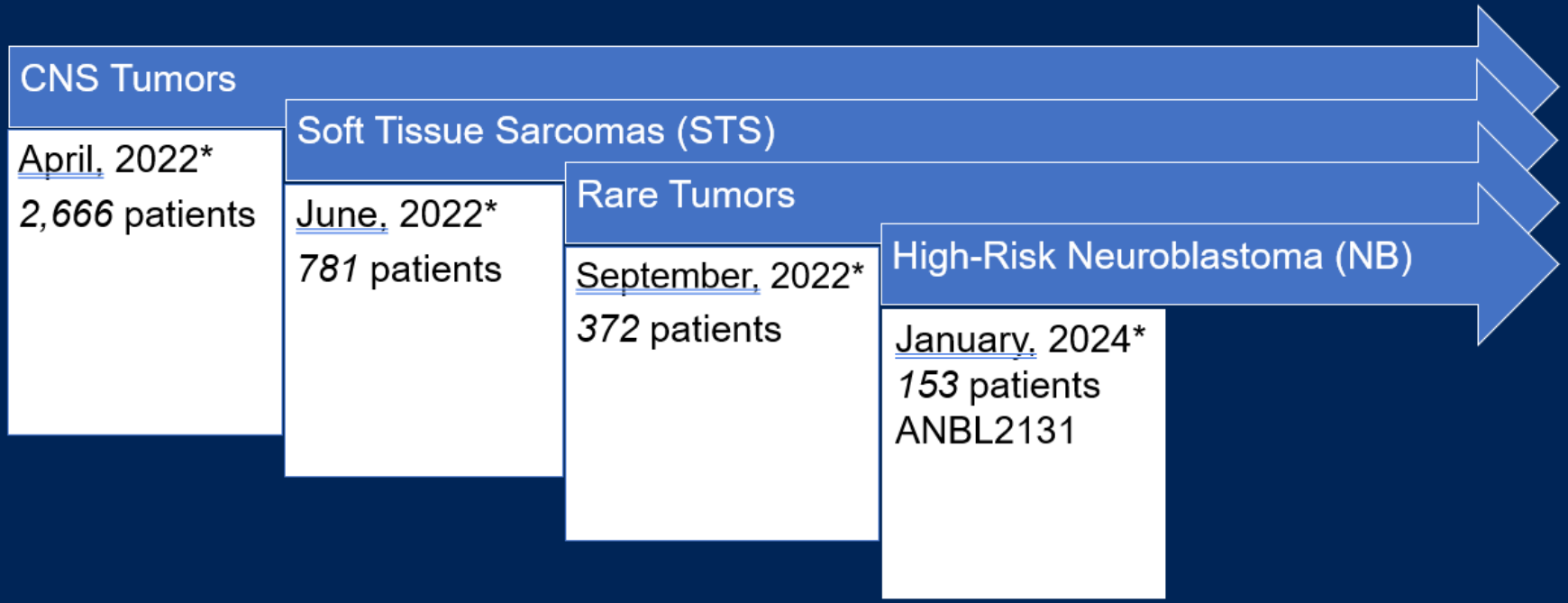
Children's Oncology Group and Project:EveryChild

- Project:EveryChild (APEC14B1) – Tumor registry and tissue banking study open to all pediatric patients with cancer
  - Patients 25 years of age or younger
- APEC14B1 – MCI
  - Rolling open to specific eligible diagnoses

Specimens for Sequencing (By Quarter)

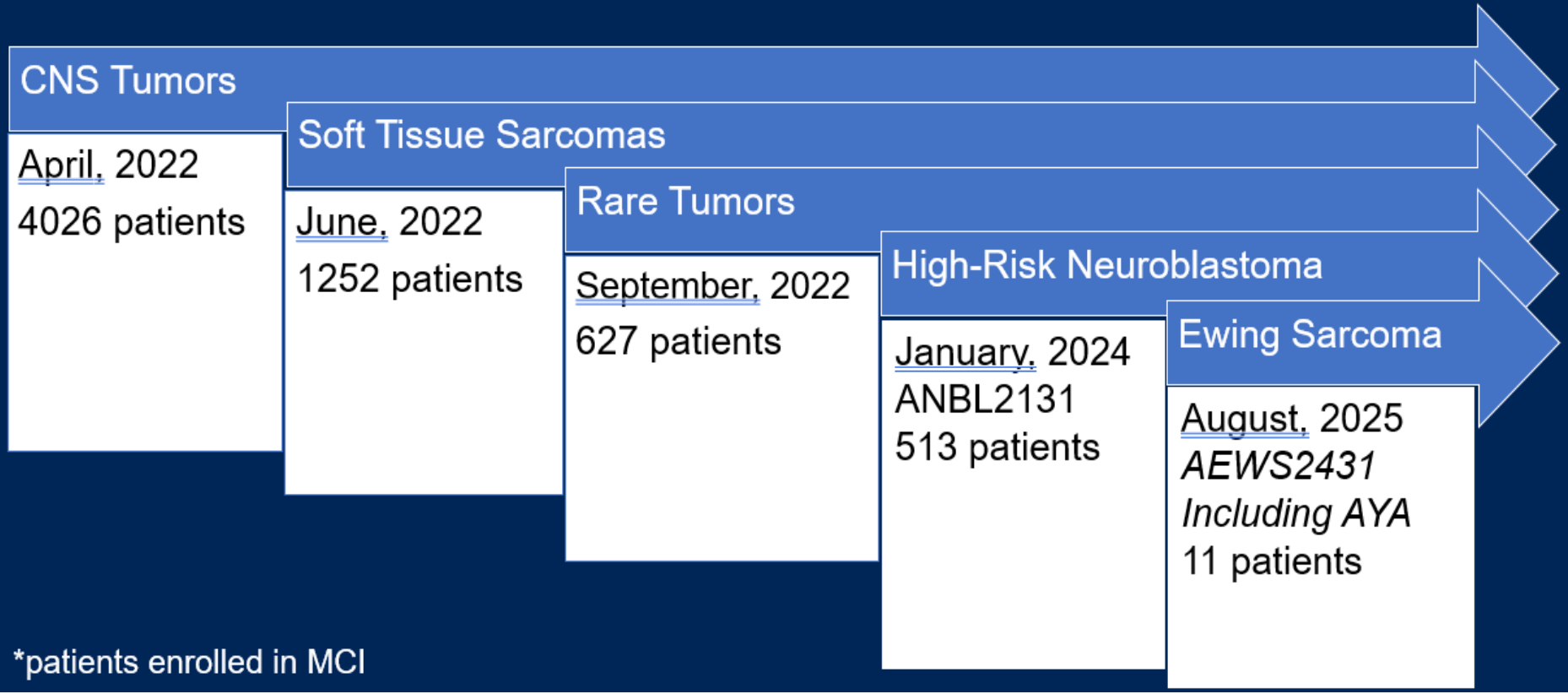


MCI Timeline (March 31, 2022 - November 1, 2024)



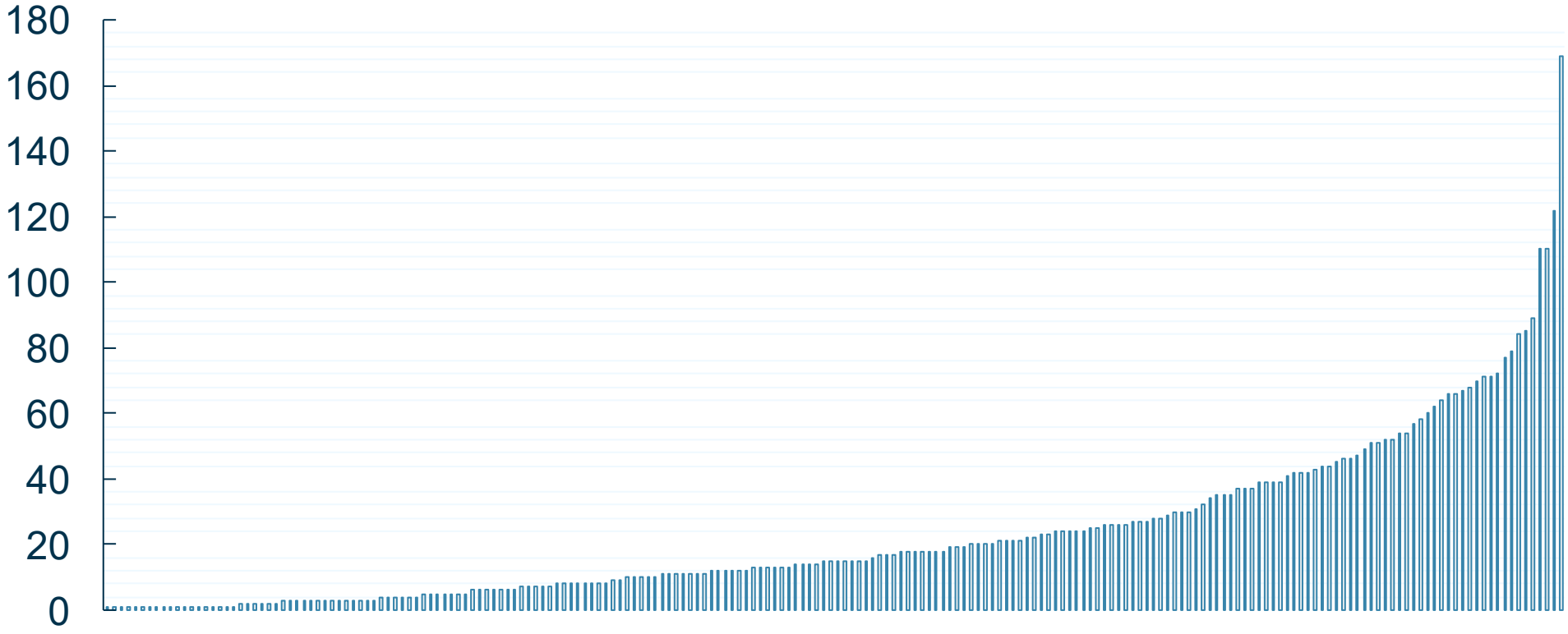
*patients sequenced at Institute for Genomic Medicine

MCI Timeline (March 31, 2022 – September 8, 2025)

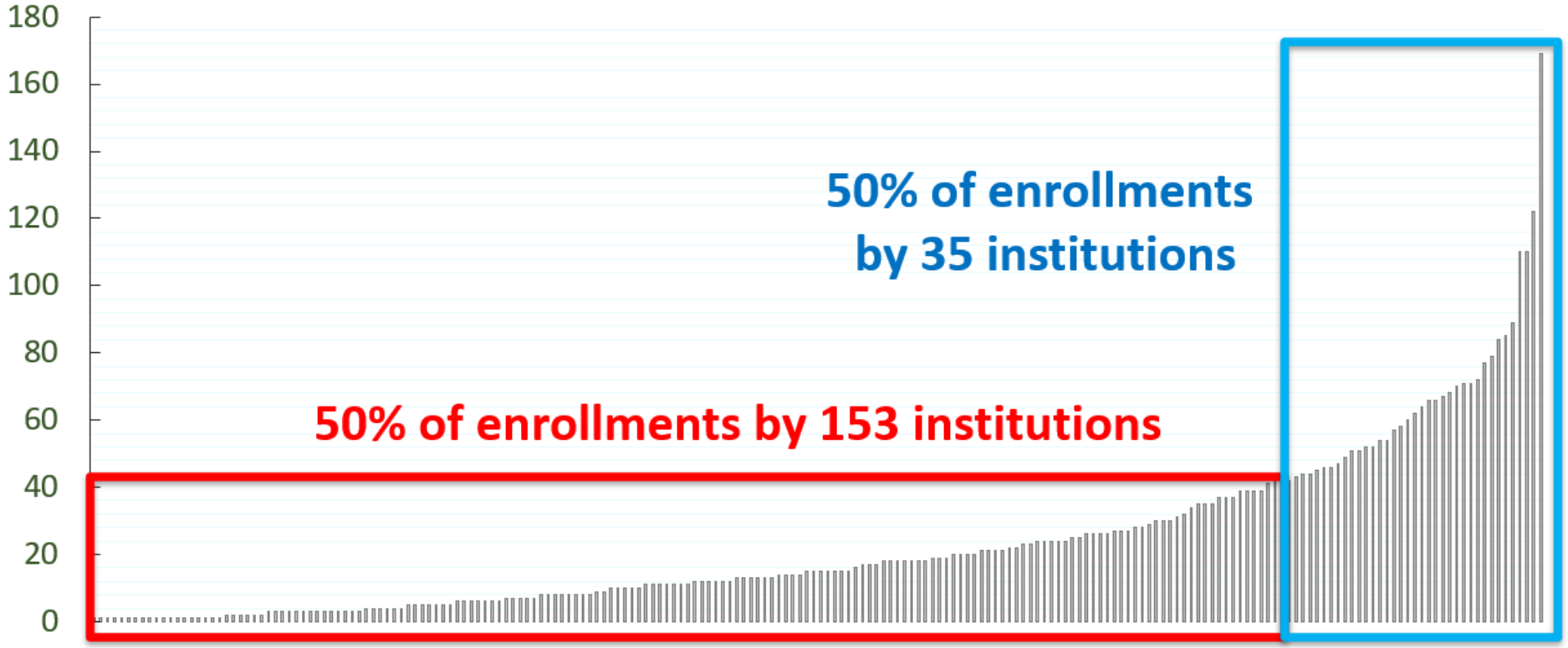


*patients enrolled in MCI

Institutional Enrollment on MCI



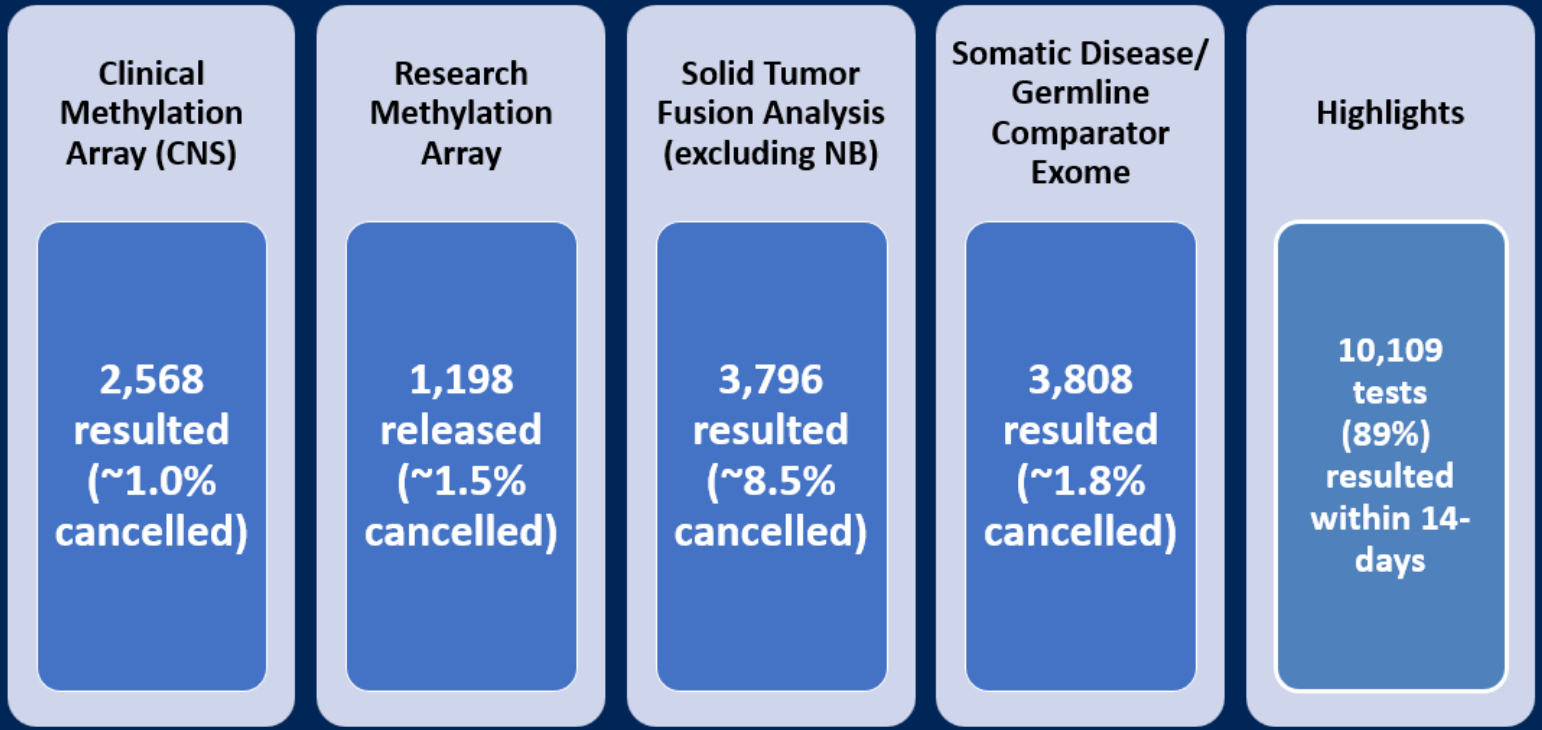
COG Institutional Enrollment on MCI



MCI: What Do the Data Show Across Disease Groups?

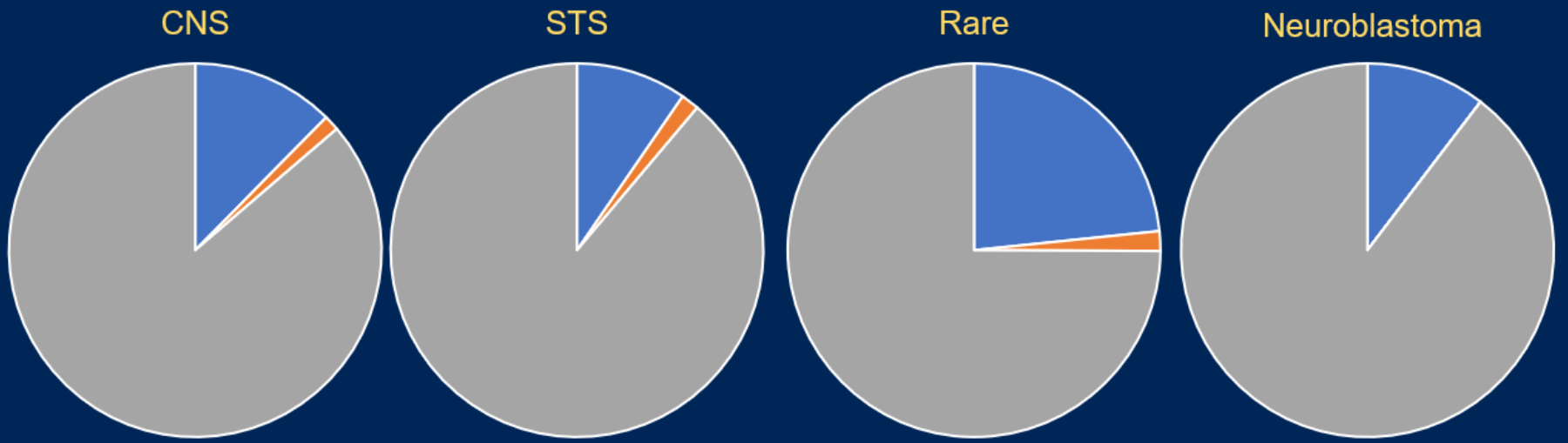
- Early analyses of the first 31 months of data
  - Data courtesy of Institute for Genomic Medicine

CCDI-COG MCI test volumes



Slide provided by Kareesma Parbhoo

Germline alterations



14.1% of patients had a reportable SNV or CNV germline finding

Germline alterations

- Single nucleotide variants (SNV) identified in
  - *TP53* in 1.4% of patients
  - *CHEK2* in 1.3% of patients
  - *DICER1* in 0.9% of patients
  - *NF1* in 0.8% of patients
  - *ATM* in 0.6% of patients
- Recurrent copy number variants (CNV) include
  - 17q11.2 loss (*NF1/SUZ12*)
  - 22q11.21 loss (*SMARCB1*)
  - 9p21.3 loss (*CDKN2A/B*)
  - *Rb* loss
  - Ch1p involving *SDHB*

Somatic DNA alterations

- 85% of patient samples had a reported somatic Tier 1 or Tier 2 SNV or CNV

	Total Cases	Somatic SNV	Somatic CNV
CNS	2539	1125 (44.3%)	1944 (76.6%)
STS	696	326 (46.8%)	579 (83.2%)
RARE	351	162 (46.2%)	182 (51.9%)
NB	154	45 (29.2%)	144 (93.5%)

Somatic DNA alterations

- Single nucleotide variants were most commonly identified in:
  - *TP53* in 8.3%
  - *BRAF* in 6.9%
  - *CTNNB1* in 4.4%

  - *ALK* (11% of neuroblastomas)

Targeted RNA sequencing

- Gene fusions identified in 30% of patient samples

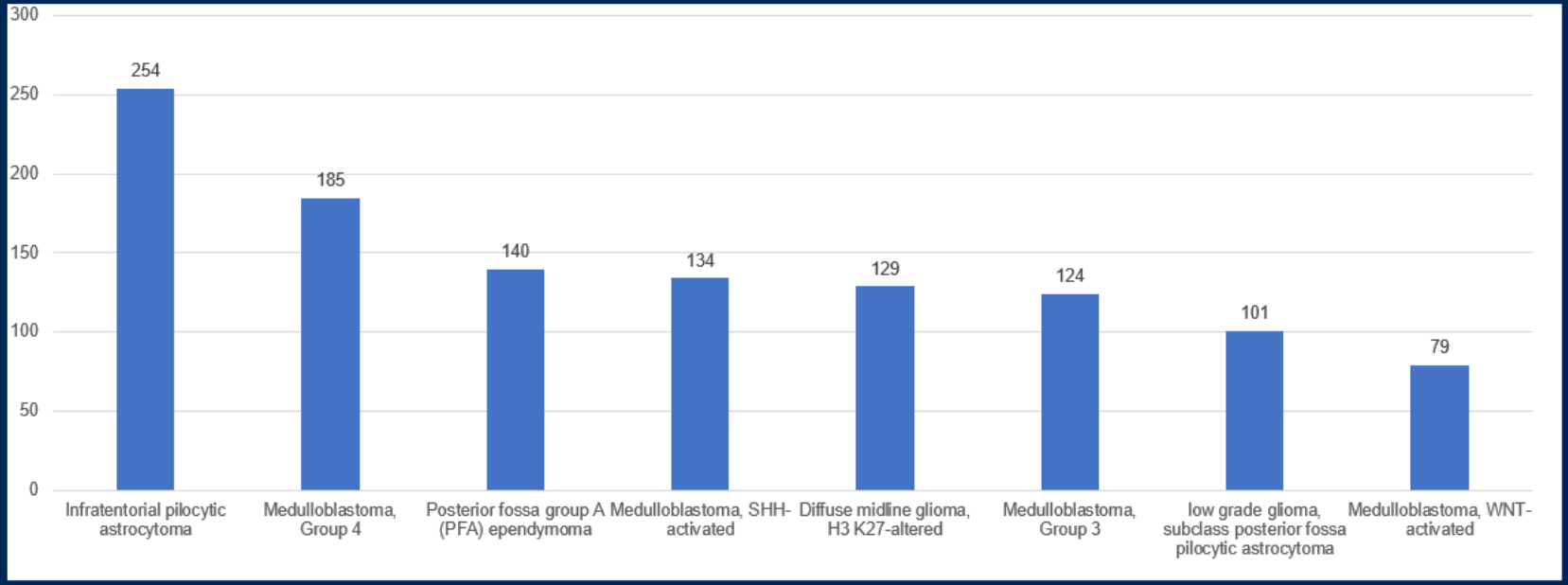
Disease Group	Total Cases Resulted	Positive Results
CNS	2453	668 (27.2%)
STS	719	289 (40.2%)
RAR	302	69 (22.8%)

Targeted RNA sequencing

- Most common fusions identified include
  - *KIAA15::BRAF*
  - *PAX3::FOXO1*
  - *SS18::SSX1/2*
  - *EWSR1::FLI1*
  - *CIC::DUX4*
  - *COL1A1::PDGFB*
  - *CCDC6::RET*

Methylation Array – Tumor Classification

- Clinical methylation classification was returned in 90% of all CNS samples



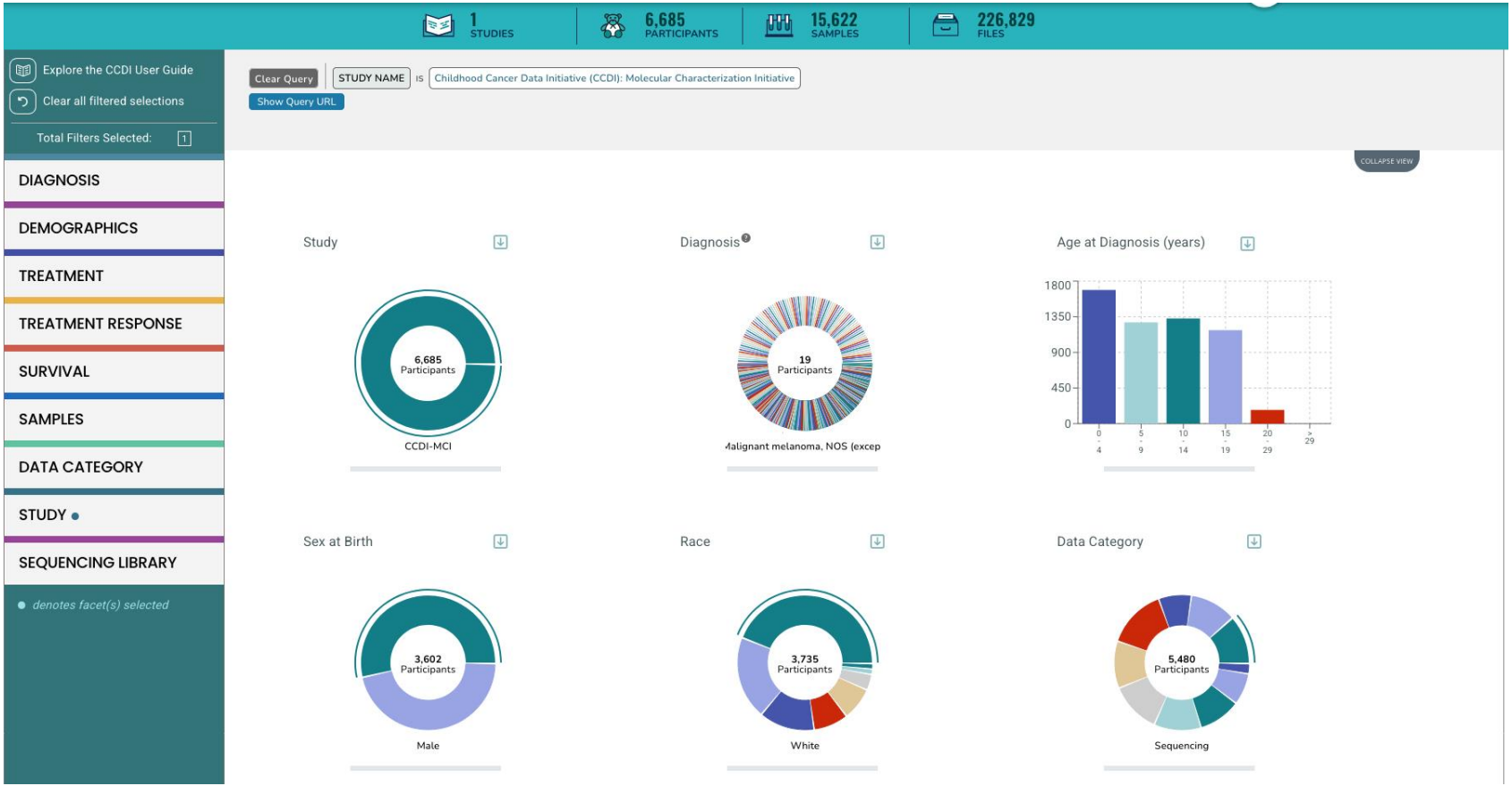
Evaluating the Utility of MCI Testing

- Did the patient enroll on a clinical trial?
  - 86/749 patients (11.5%) enrolled on a clinical trial based on MCI results
- Did the patient receive a targeted therapy?
  - 80/749 patients (10.7%) received a targeted therapy based on the MCI results
- Did the MCI results help refine the pathologic diagnosis?
  - 223/749 patients (29.5%) used the MCI results to help refine the final integrated pathologic diagnosis

Updates and Advances in MCI Testing

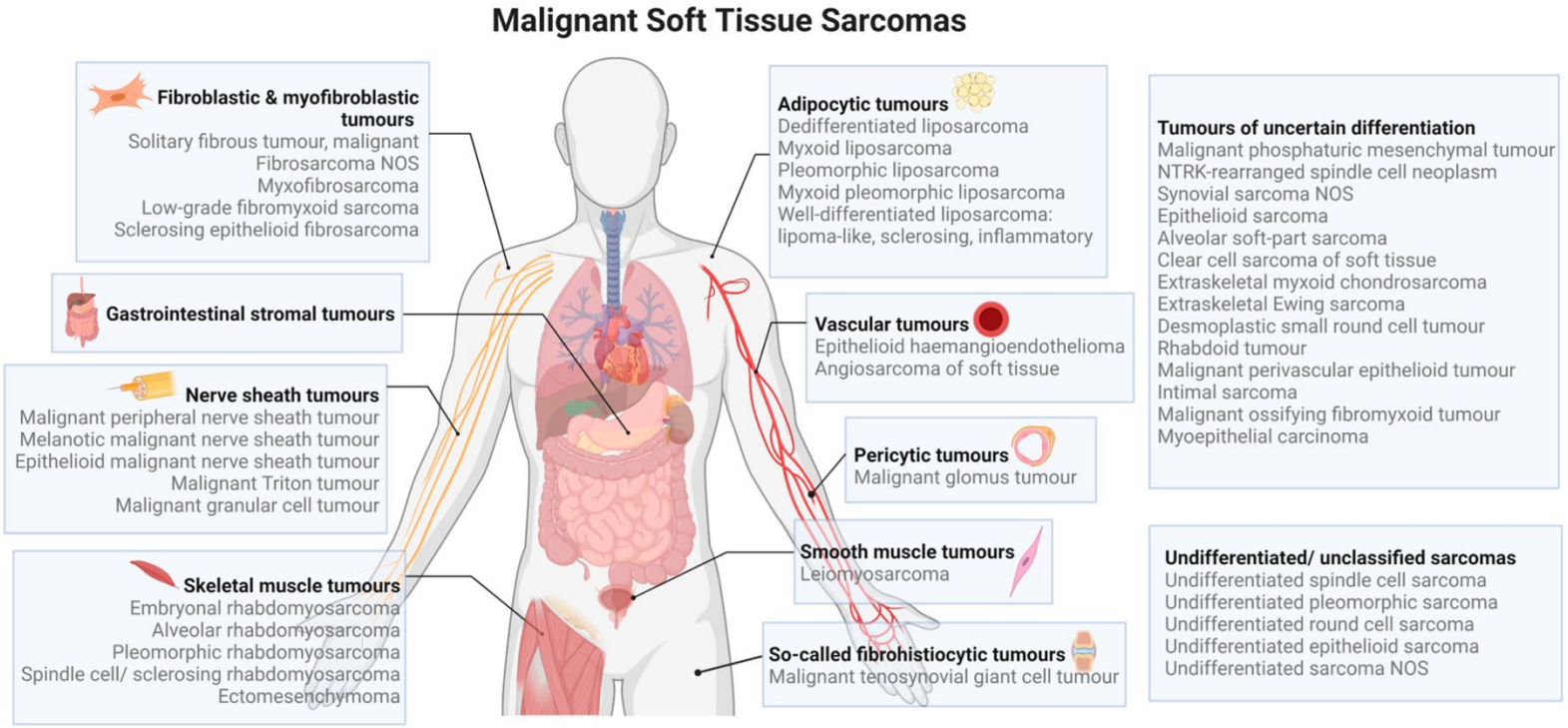
- Expansion to the young adult population (Project AYA)
  - Enroll on AEWS2431 at a non-COG institution
- IGM updates include validation of new library prep requiring lower volume of DNA for Exome sequencing, reporting tumor mutational burden, acceptance of Formical (soft acid) decalcified specimens
  - August/September 2025
- Validation of RNA sequencing with exome capture
  - Early 2026
- Expand to relapsed/recurrent patients already enrolled in MCI

Accessing the MCI Data



Jack Shern, M.D.

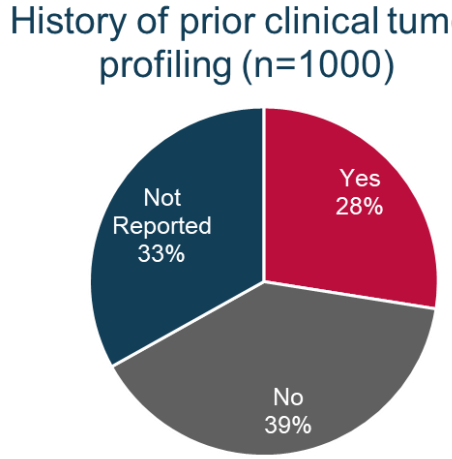
Soft Tissue Sarcomas Based on 2020 WHO Classification



Teo et al 2023

Many Patients Do Not Get the Opportunity to Benefit From Molecular Testing

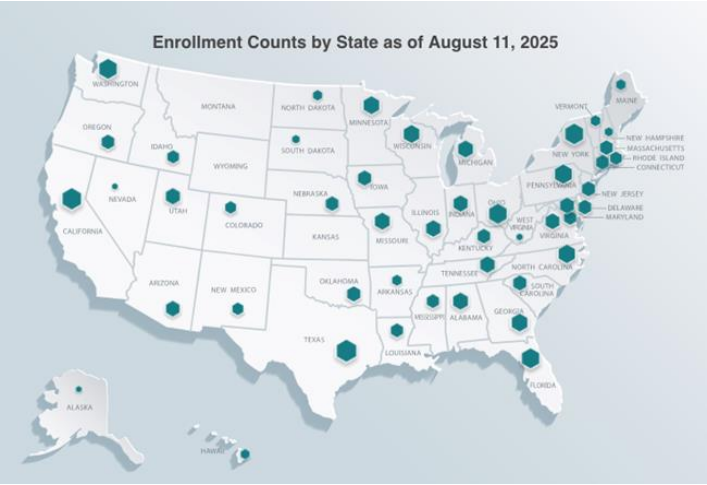
- No national coverage determinations or practice guidelines regarding molecular profiling for STS tumors
- 28% participants had evidence of molecular profiling
- 39% had definitive evidence of **not** having had molecular profiling
- Private partners have little incentive to "help" the cause



NCI-COG Pediatric Molecular Analysis for Therapy Choice (MATCH)

Parsons 2022, JCO

Molecular Characterization Initiative (MCI) Provides a National Framework



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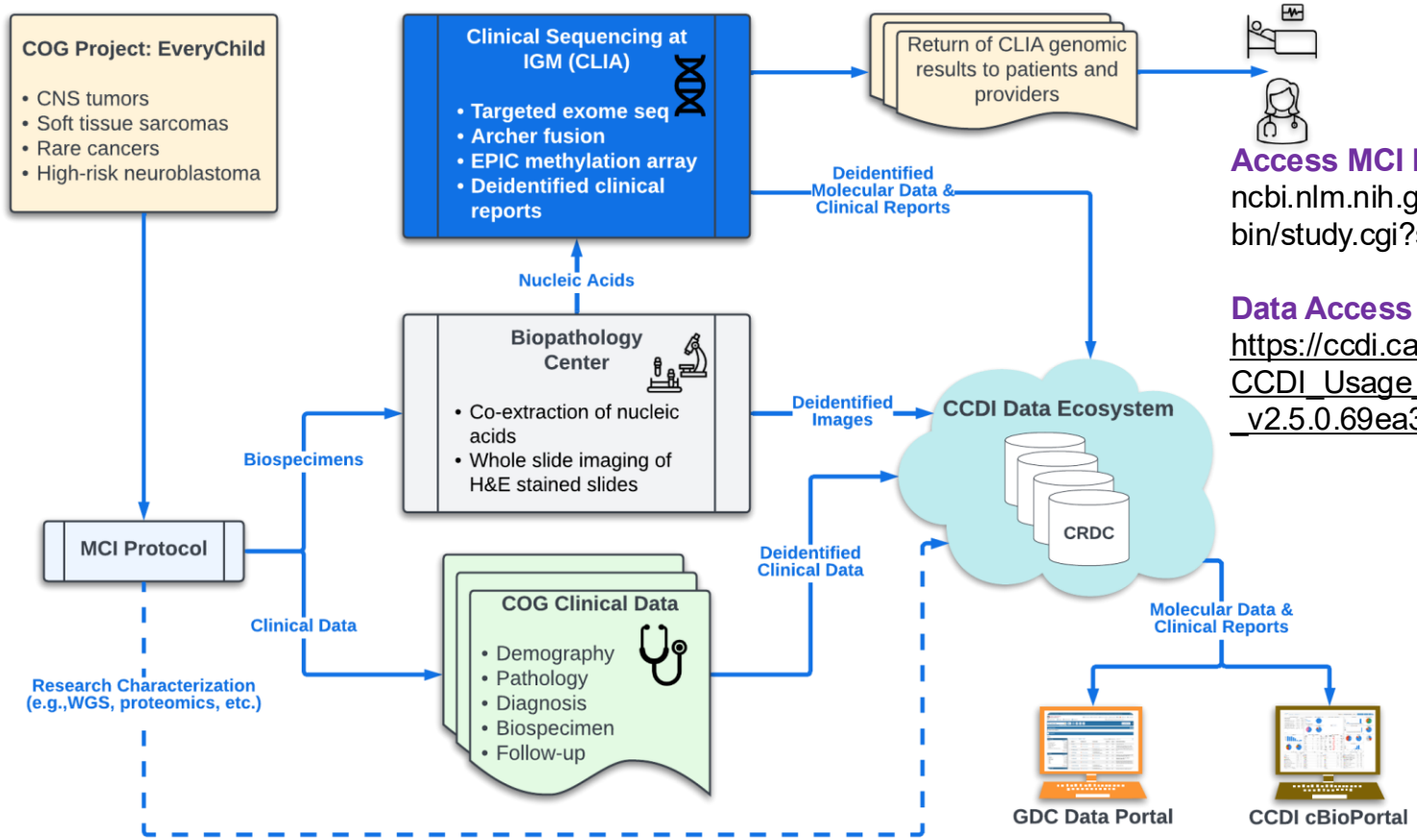
CHILDREN'S ONCOLOGY GROUP

- Currently open to any newly diagnosed CNS, STS, Rare, High-risk Neuroblastoma and Ewing sarcoma
- Consent and enrollment via Project: EveryChild (APEC-14B1 MCI)
- Enrolled 8000+ participants from all 50 states
- CLIA certified results in a 21-day window
- Molecular and clinical data become available to the research community (dbGaP phs002790)
- Remaining sample is banked for future research
- Research characterization (WGS, RNA Seq, single cell, and proteomics/metabolomics assays) is being used to deepen our understanding of cancer biology

MCI Data Flow

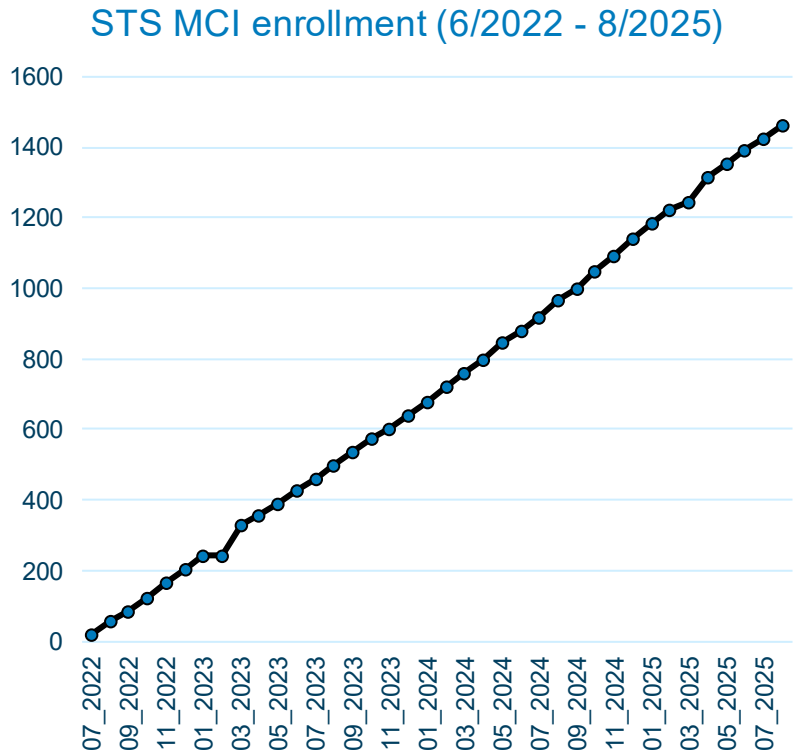


Access MCI Data:
ncbi.nlm.nih.gov/projects/ga p/cgi-bin/study.cgi?study_id=phs002790

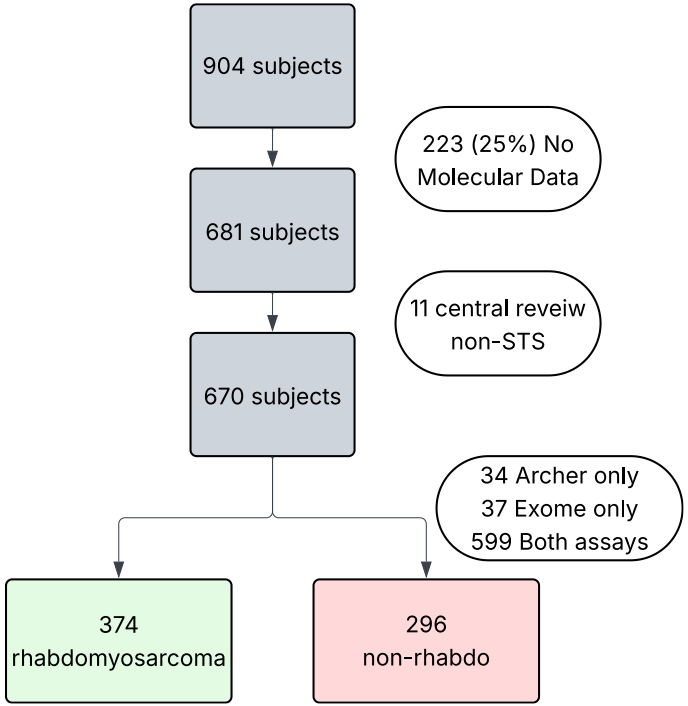
Data Access Guide:
https://ccdi.cancer.gov/static/media/CCDI_Usage_Instructions_Nov2024_v2.5.0.69ea3cd5.pdf

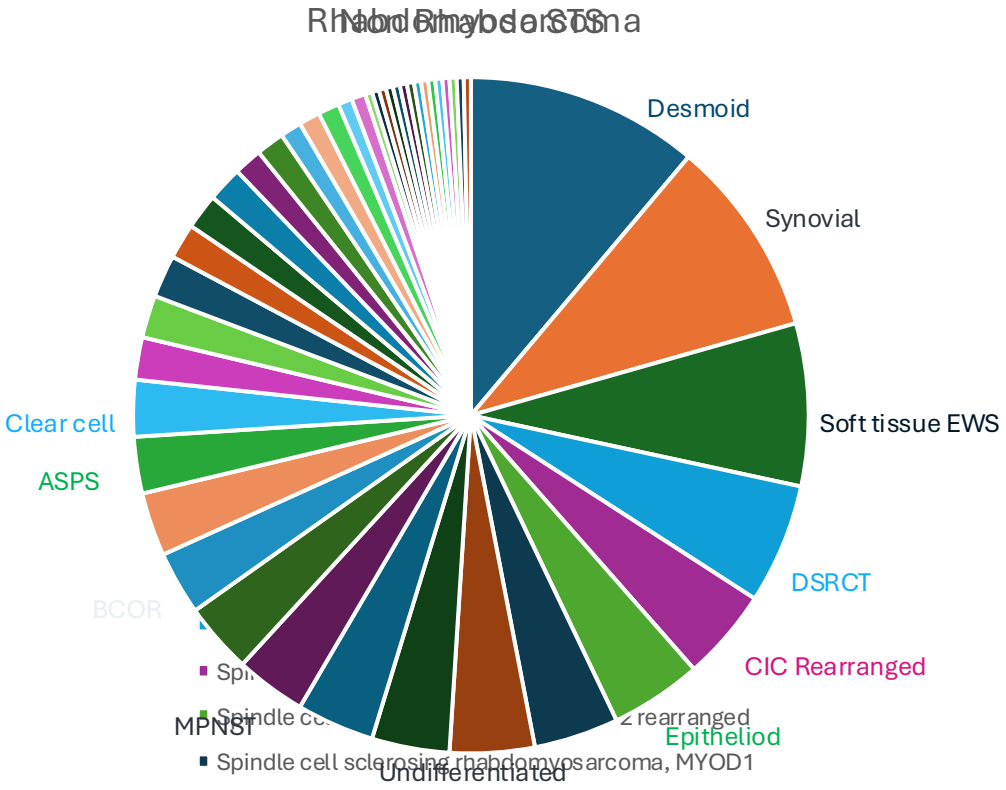
APEC14B1-MCI STS Enrollment

- 1484 enrolled STS patients
- 1112 (75%) of enrollees have a submitted paired blood/tumor specimen
- Over 3000 completed assays

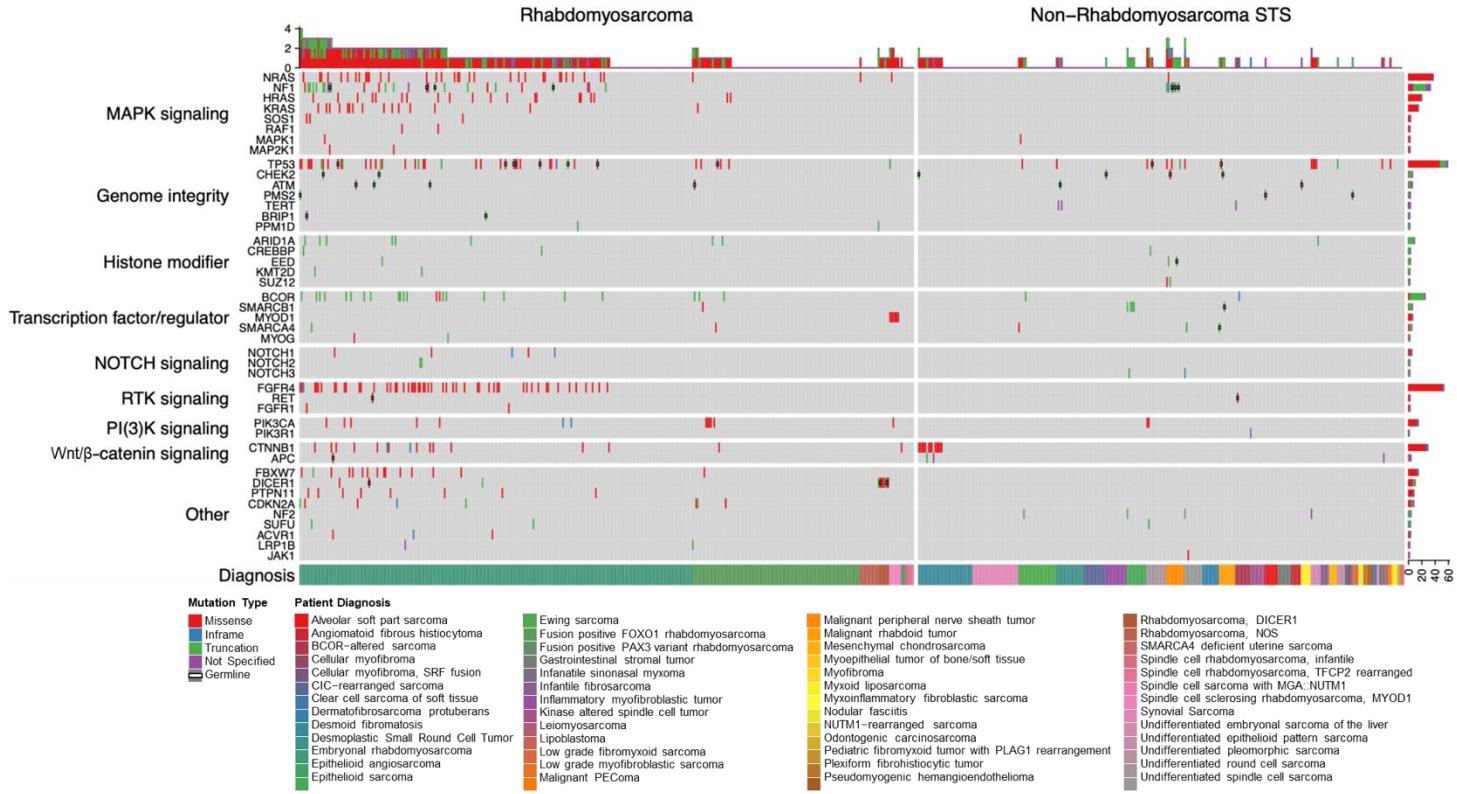


Data From the First Two Years of MCI-STS

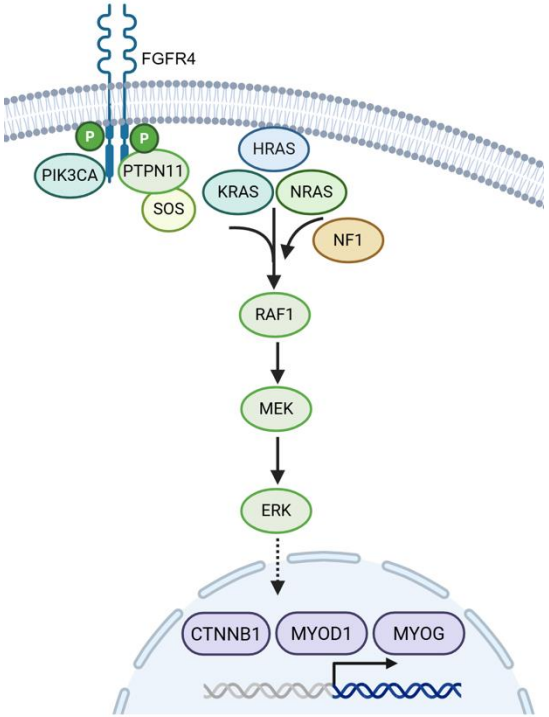


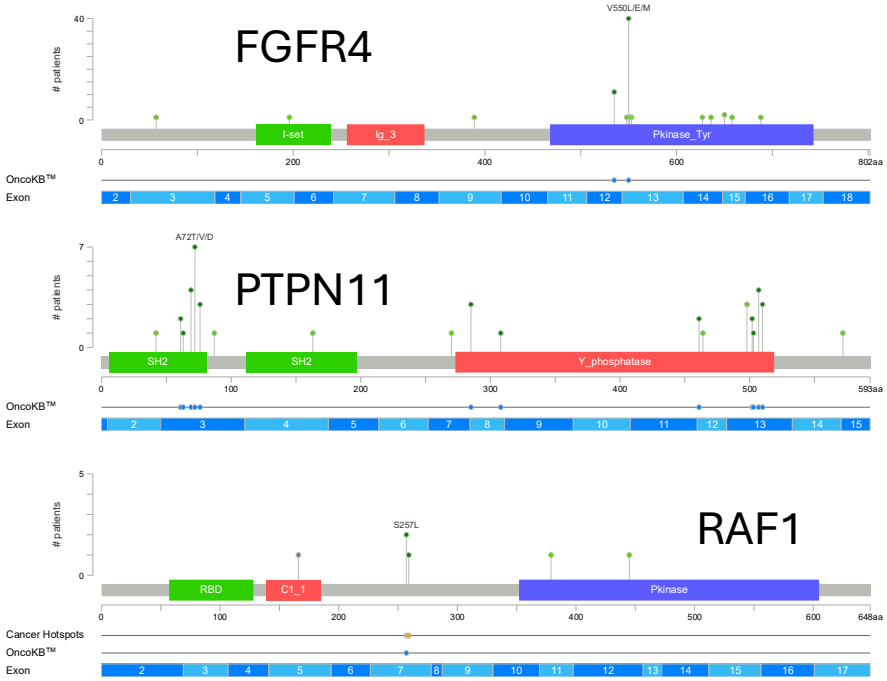


Mutational Summary

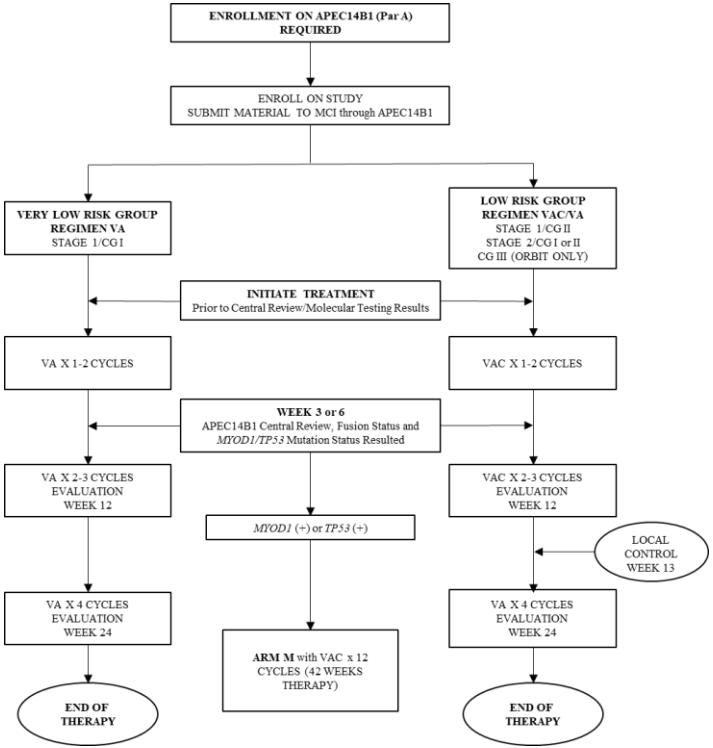


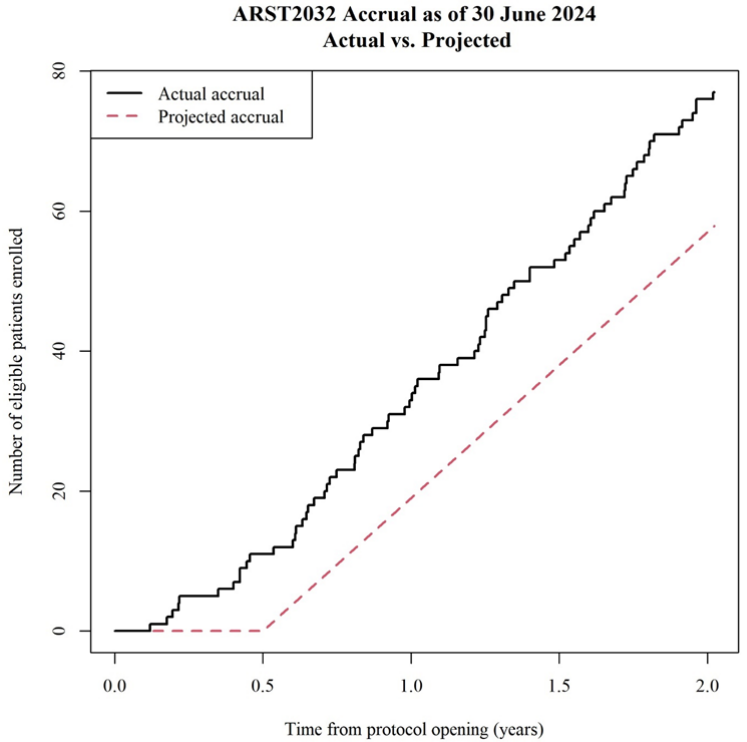
RAS Pathway Alterations in FN RMS



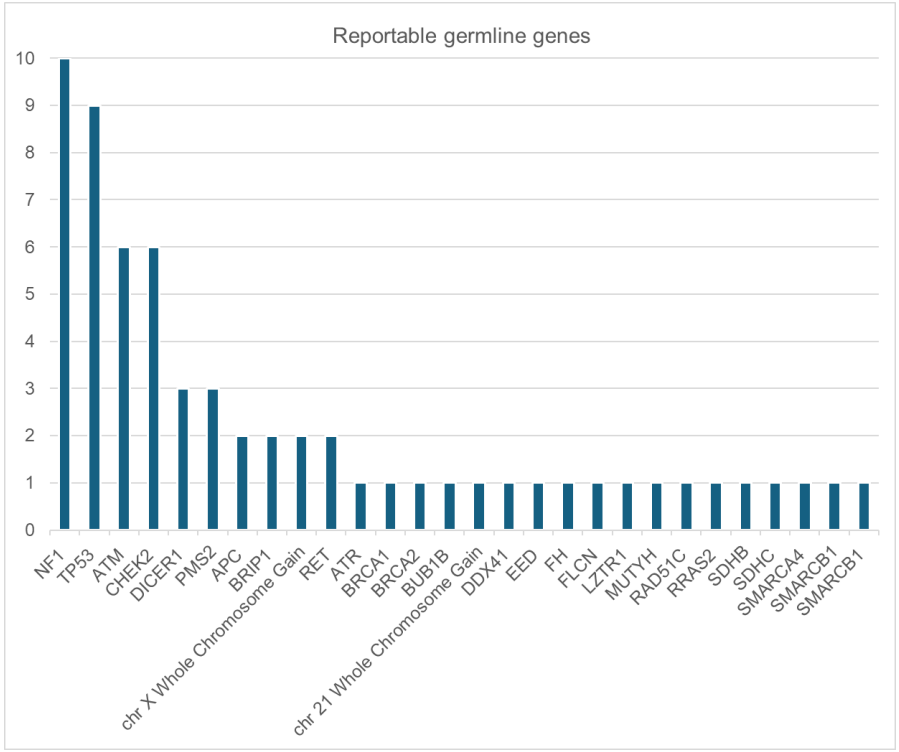


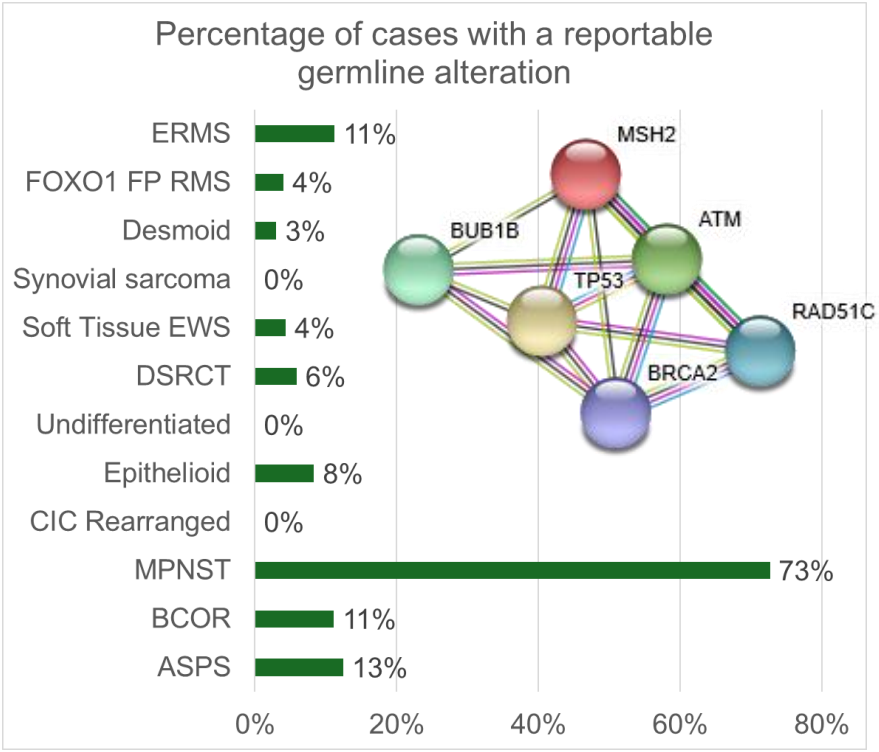
ARST2032 the First RMS Study to Incorporate Molecular Risk Stratification



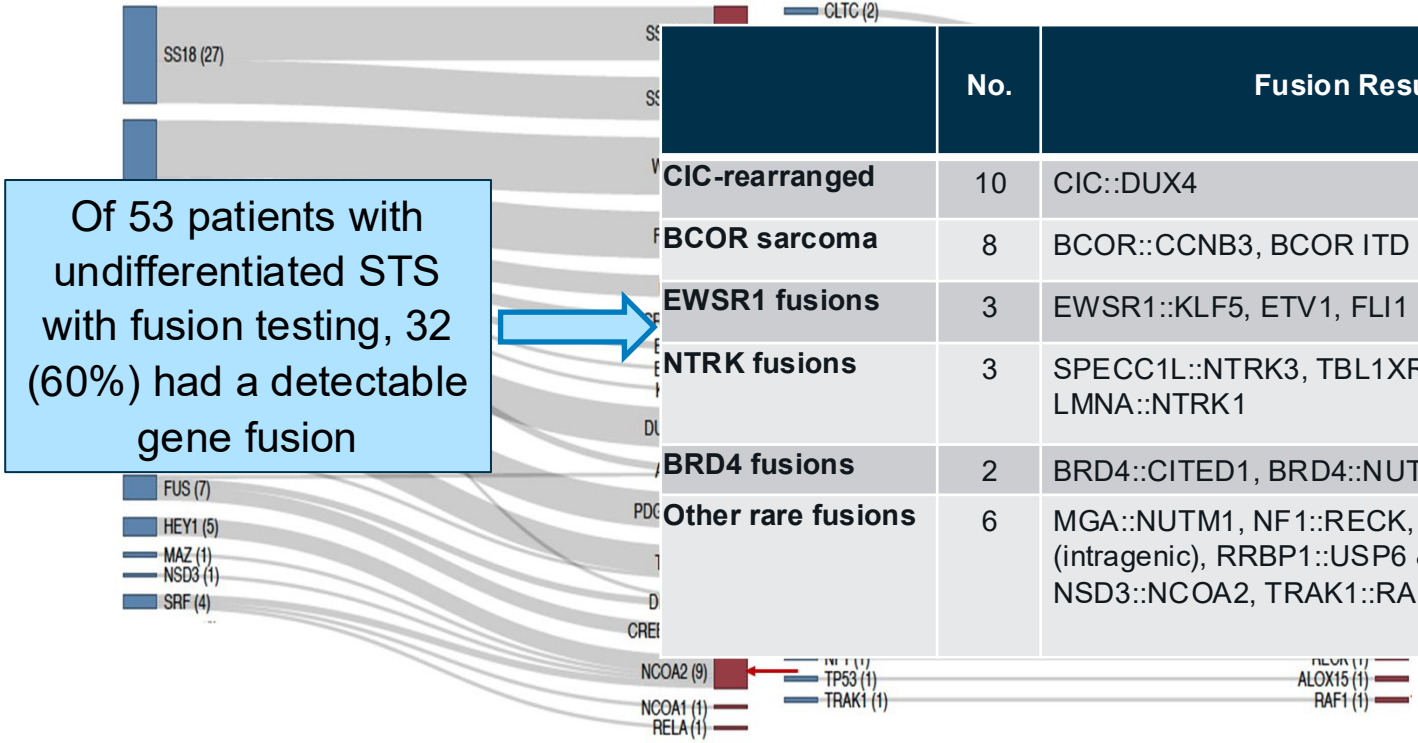


10% of Profiled STS Patients Have a Reportable Germline Finding





Fusion Detection Clarifies Diagnosis in NRSTS

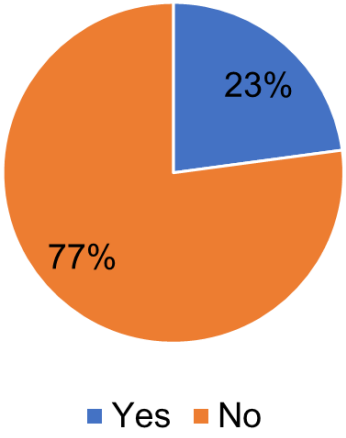


Of 53 patients with undifferentiated STS with fusion testing, 32 (60%) had a detectable gene fusion

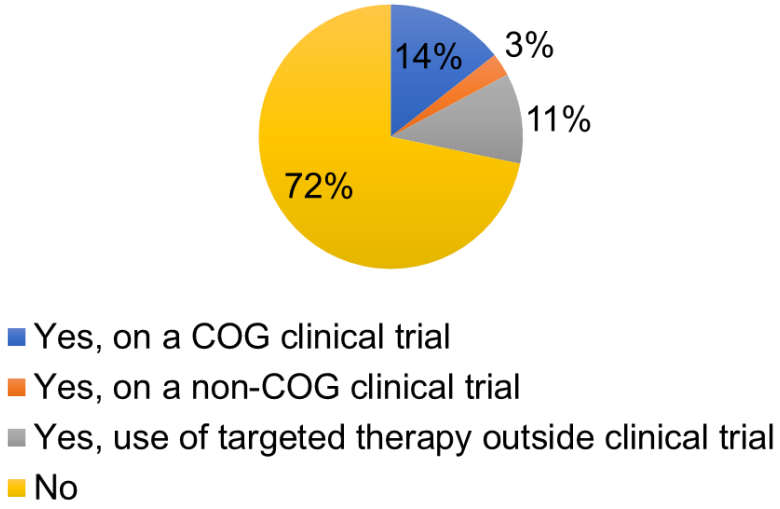
	No.	Fusion Results
CIC-rearranged	10	CIC::DUX4
BCOR sarcoma	8	BCOR::CCNB3, BCOR ITD
EWSR1 fusions	3	EWSR1::KLF5, ETV1, FLI1
NTRK fusions	3	SPECC1L::NTRK3, TBL1XR1::NTRK1, LMNA::NTRK1
BRD4 fusions	2	BRD4::CITED1, BRD4::NUTM1
Other rare fusions	6	MGA::NUTM1, NF1::RECK, EGFR (intragenic), RRBP1::USP6 & TP53::ALOX15, NSD3::NCOA2, TRAK1::RAF1

Implications of the Molecular Testing for Patients from Provider Perspective

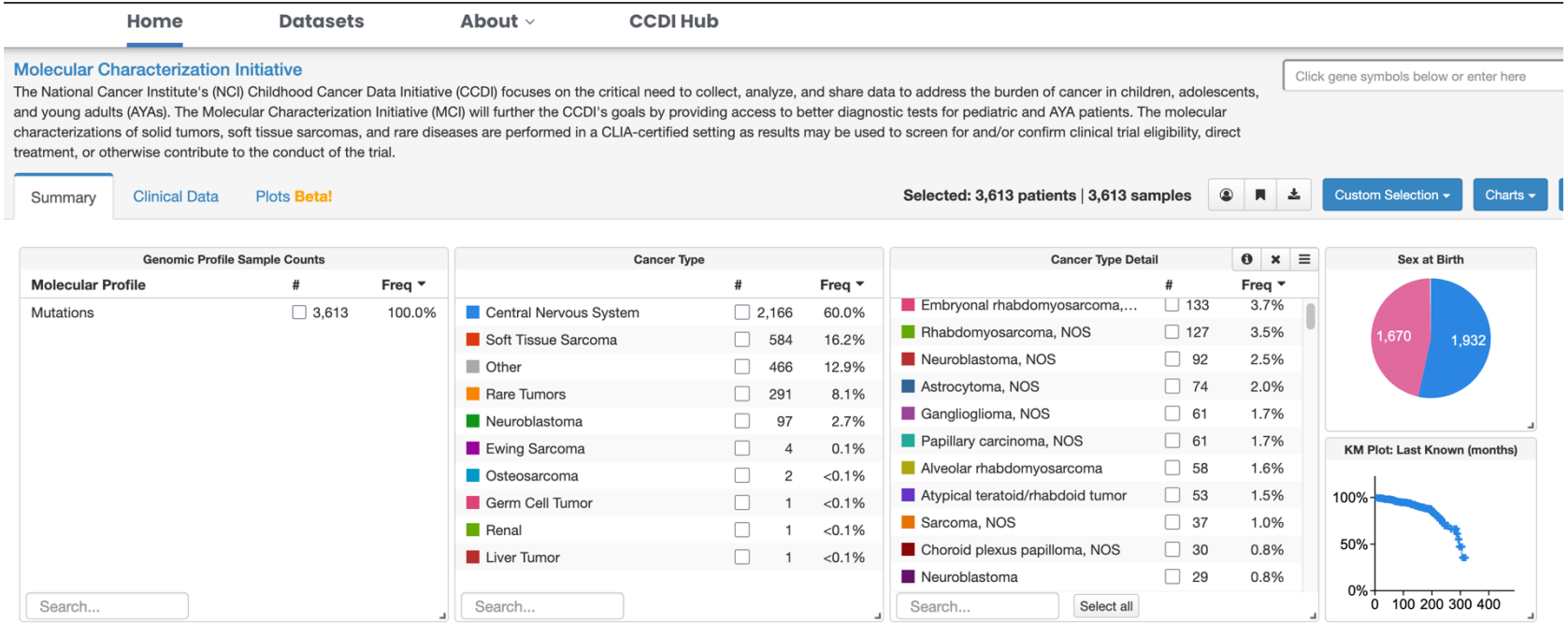
Refinement of final diagnosis based on molecular testing, (N=389)



Enrollment on a clinical trial/Use of targeted therapy outside clinical trial, (N=389)



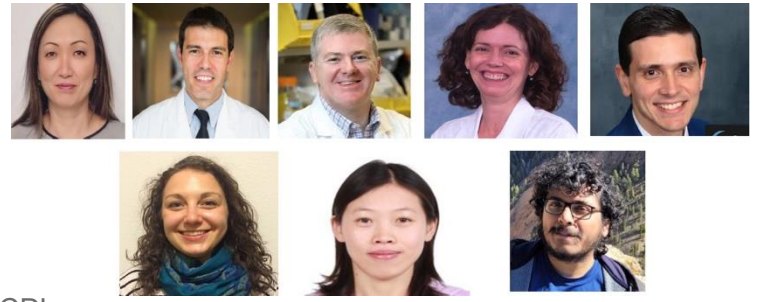
CCDI cBioPortal Cancer Data Explorer



https://cbioportal.ccdi.cancer.gov

Immune Characterization of Pediatric STS: A Case Study for the Use of the MCI Dataset

- Project developed by trainees for participation in the NCI Office of Data Sharing's Childhood Cancer Data Jamboree
- MCI data: pediatric STS RNA-seq, methylation, genomic data and pathology data
- CCDI: Linked clinical, demographic and outcome data
- Using Deep learning models to identify signatures of the tumor immune microenvironment



CCDI MCI Resources

MCI Data on CCDI Platforms and Tools

- CCDI Hub: ccdi.cancer.gov/MCI
- Hub Explore Dashboard MCI data: ccdi.cancer.gov/explore?study_name=Molecular%20Characterization%20Initiative
- Childhood Cancer Clinical Data Commons: https://clinicalcommons.ccdi.cancer.gov/explore?filterQuery=%7B%22study_name%22%3A%5B%22Childhood%20Cancer%20Data%20Initiative%20(CCDI)%3A%20Molecular%20Characterization%20Initiative%22%5D%2C%22upload%22%3A%5B%5D%2C%22autocomplete%22%3A%5B%5D%2C%22uploadMetadata%22%3A%7B%7D%7D
- Childhood Cancer Data Catalog: datacatalog.ccdi.cancer.gov/dataset/CCDI-phs002790
- MCI_JSON2TSV: Python-based command-line interface that converts MCI de-identified clinical report and clinical data files submitted in JSON format into tab-separated values (TSV) files. github.com/CBIIT/ChildhoodCancerDataInitiative-MCI_JSON2TSV
- H&E Stained Images: portal.imaging.datacommons.cancer.gov/explore/filters/?collection_id=ccdi_mci

Tutorials and Guides

- Hub Explore Dashboard User Guide and Access Instructions: ccdi.cancer.gov/user-guide.pdf
- CCDI Data Submission Guide: ccdi.cancer.gov/Submission_Guide.pdf
- Hub Explore Dashboard Tutorial Video: youtu.be/Eu8y1GDTszU
- How to Apply for dbGaP Controlled Access Video: youtube.com/watch?v=m0xp_cCO7kA

Team Members

- Patients and Families
- Advocacy Community
- Local treatment, pathology and surgical teams
- Children's Oncology Group Project EveryChild Team
- Children's Oncology Group Soft Tissue Sarcoma Committee
- Nationwide Biopathology Center Team
- Institute for Genomic Medicine Team
- NCI Childhood Cancer Data Initiative Team

Yassmine Akkari, Institute for Genomic Medicine
Michael A. Arnold, University of Colorado
Natalie Bir, Biopathology Center
Catherine E. Cottrell, Institute for Genomic Medicine
Avery Funkhouser, National Cancer Institute
Doug Hawkins, Seattle Children's Hospital
Subhashini Jagu, National Cancer Institute
Javed Khan, National Cancer Institute
Corinne M. Linardic, Duke School of Medicine
Elaine R. Mardis, Institute for Genomic Medicine
Mariam Mathew, Institute for Genomic Medicine
Yvonne Moyer, Biopathology Center
Sapna Oberoi, University of Manitoba
Nilsa C. Ramirez, Biopathology Center
Greg Reaman, National Cancer Institute
Erin R. Rudzinski, Seattle Children's Hospital
Kathleen Schieffer, Institute for Genomic Medicine
Malcolm Smith, National Cancer Institute
Shountea Stover, Biopathology Center
Diana Thomas, Biopathology Center
Rajkumar Venkatramani, Texas Children's Hospital
Wei Xue, University of Florida
Aaron Weiss, Maine Medical Center
Greg Wheeler, Institute for Genomic Medicine

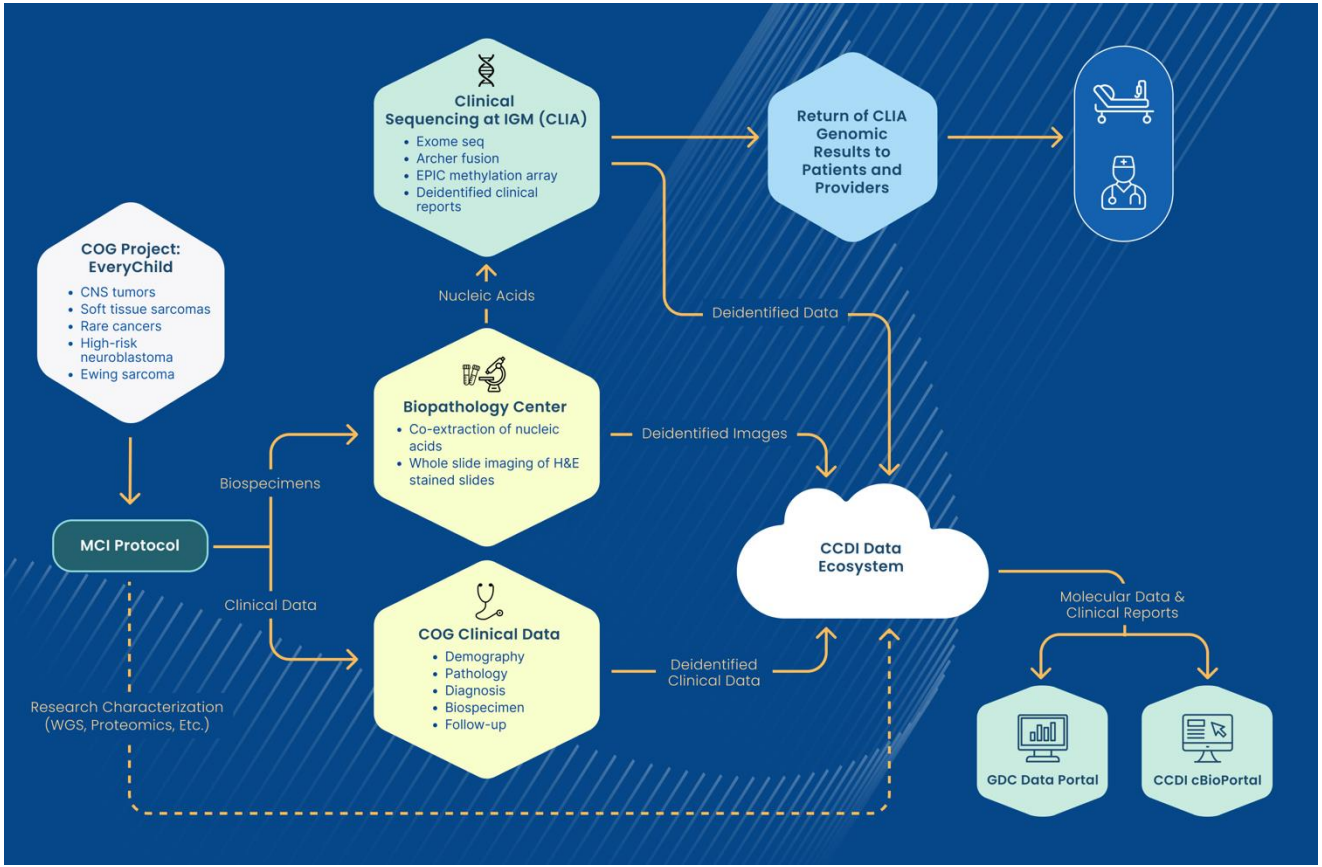
Q&A

Childhood Cancer Data Initiative Virtual Symposium Series

MCI: The Genomic Landscape of Pediatric Brain Tumors and Implications for Future Research

Diana Thomas, M.D., Ph.D. and Sarah Leary, M.D., M.S.

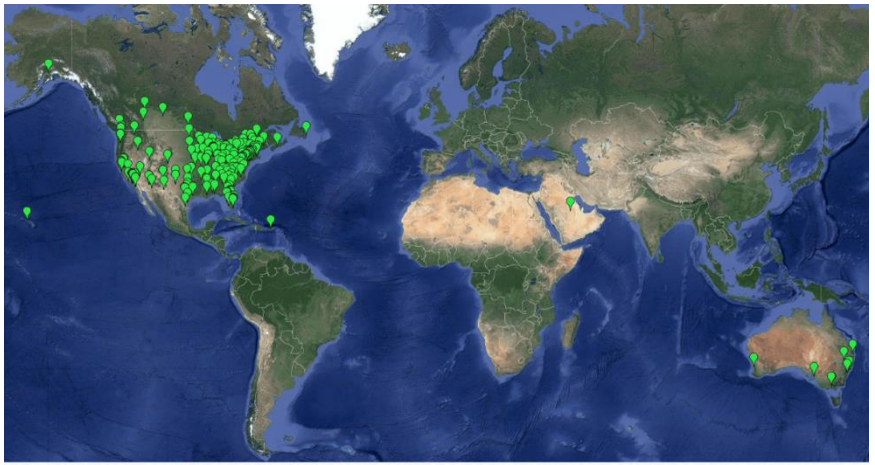
CCDI Molecular Characterization Initiative



Children's Oncology Group (COG)

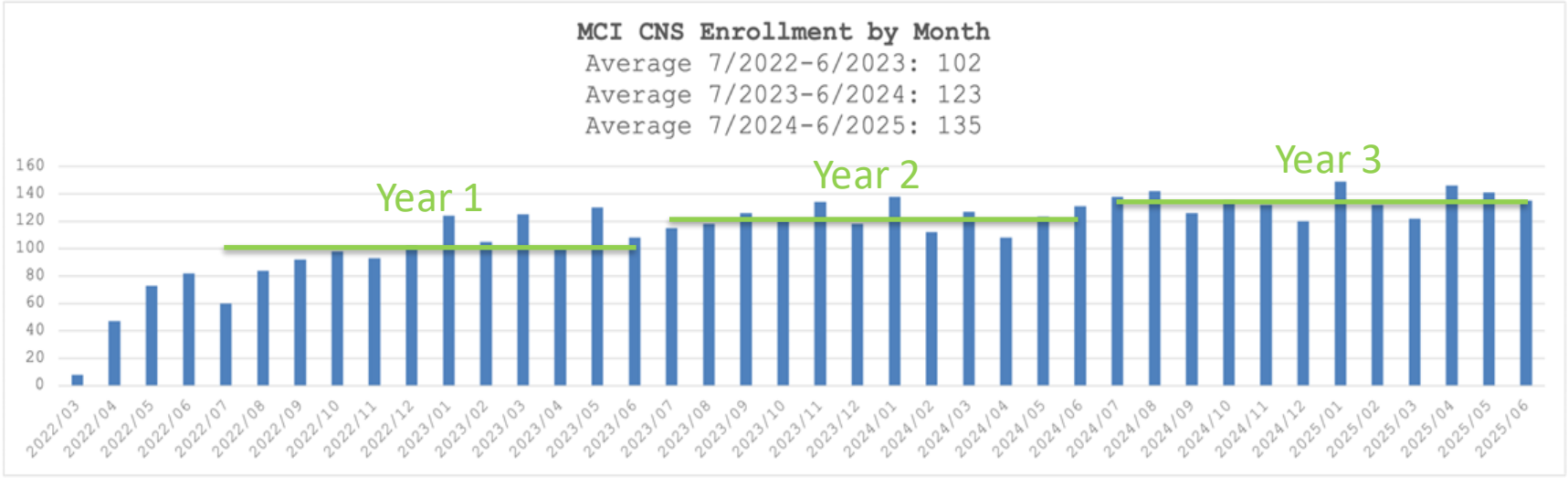
PROJECT:EVERYCHILD

- > 200 hospitals, > 10,000 members
- >90% of 16,000 children and adolescents diagnosed with cancer each year in the United States are cared for at COG member institutions
- Opened in 2015, replaced prior registry
  - 52,000 children enrolled
- Optional components: Banking, screening, MCI, outcomes, cancer registry and future contact
- Therapeutic study screening since 2017
- MCI since 2022



MCI Enrollment - CNS Tumors

N = 4519 from 191 COG sites (as of 6/30/25)



MCI Enrollment - CNS Tumors

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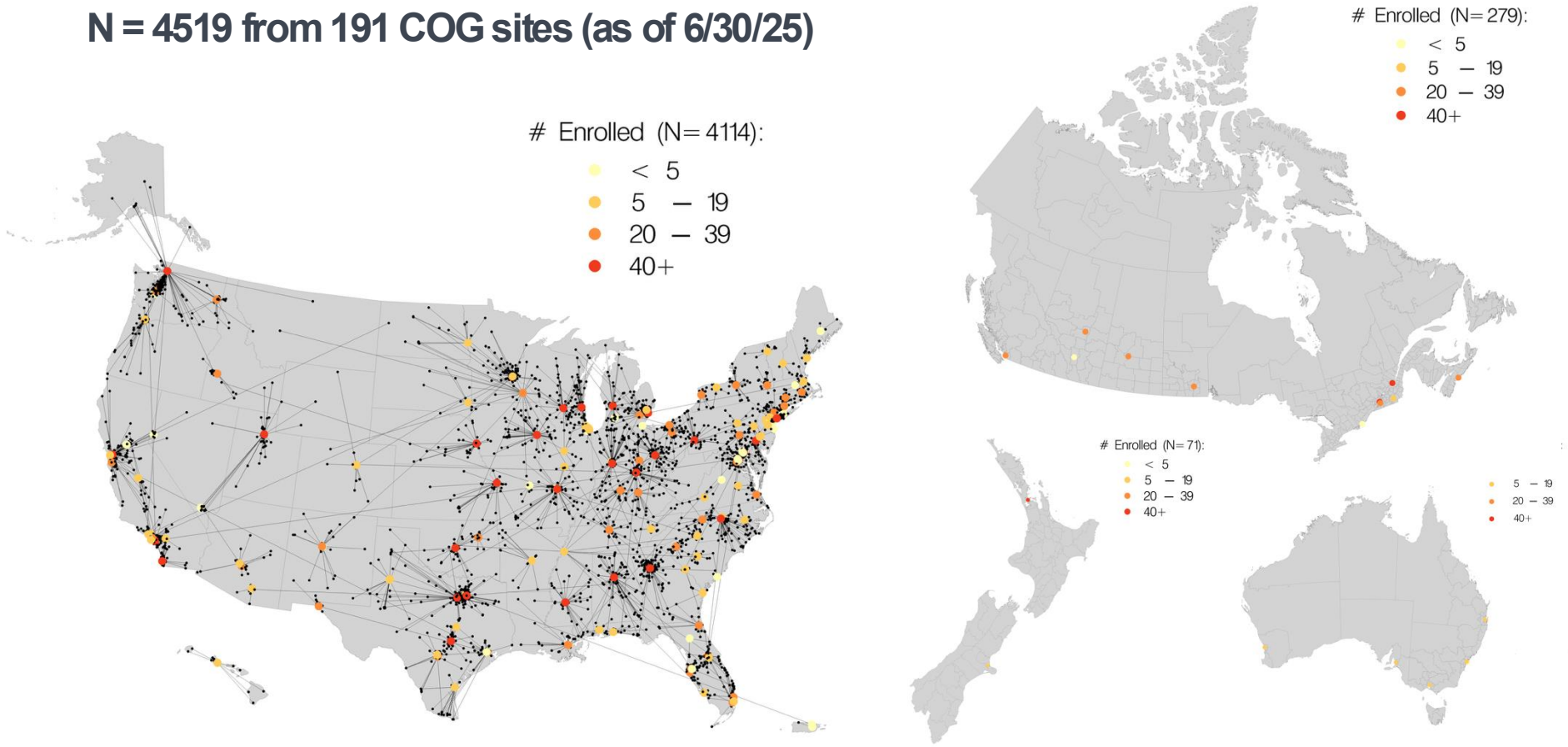
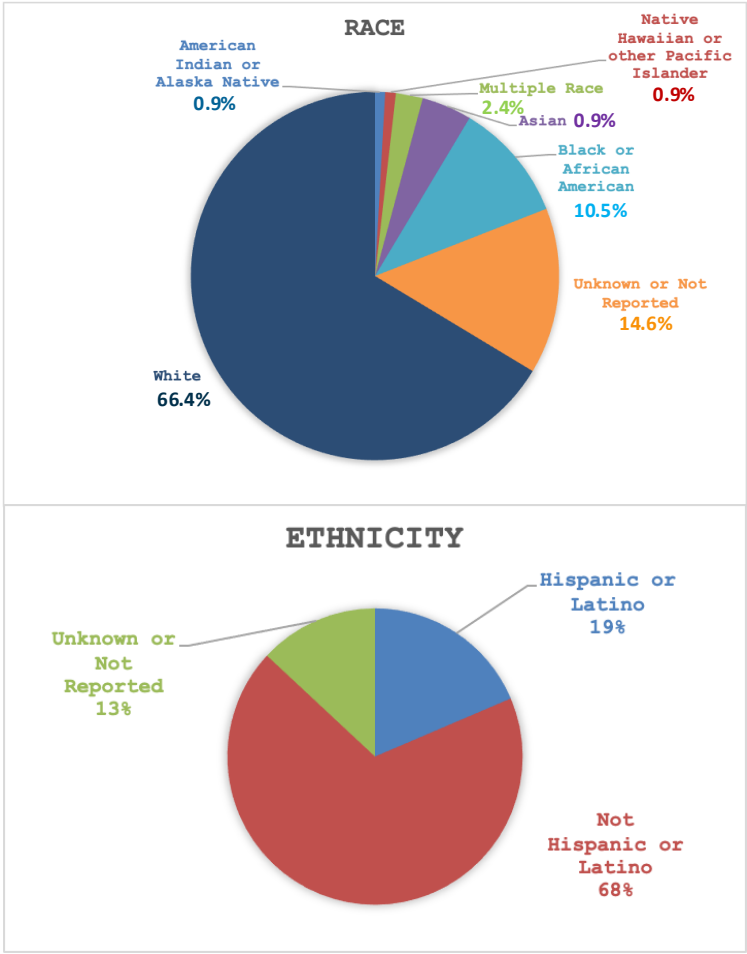


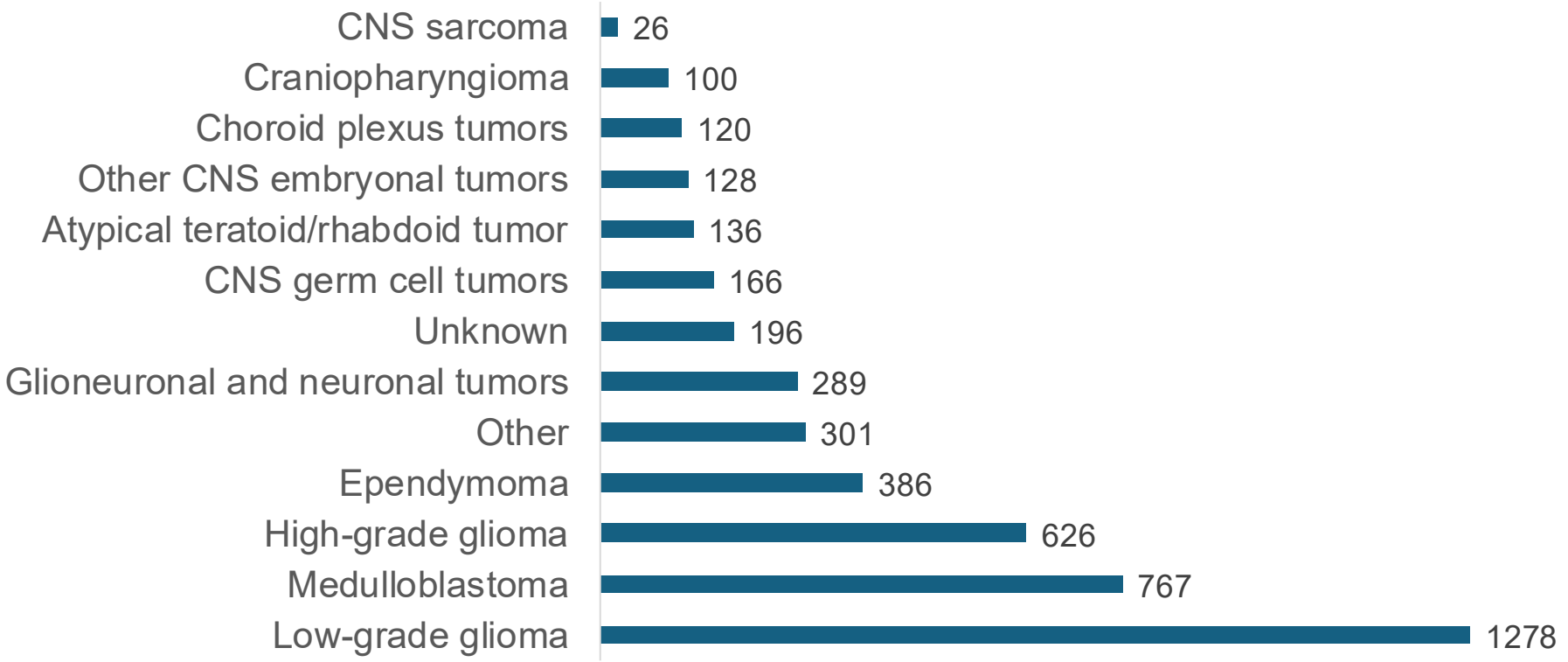
MCI Demographics – CNS Tumors
N = 4519 as of 6/30/2025

- Median age 9 (range 0-25.8 years)
- 55% male, 45% female
- Country of enrollment
  - 91% from USA
  - 9% other countries
    - 6.2% Canada
    - 2.8% Australia and New Zealand



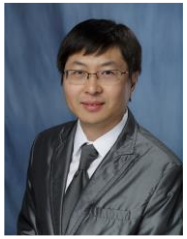
MCI CNS Tumor Diagnosis Categories

N = 4519 as of 6/30/2025



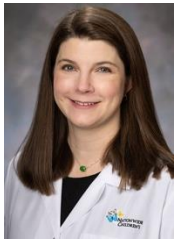
Characterization of MCI CNS Tumor Cohort

- Clinical and genomic landscape of first 2906 patients enrolled on Project:EveryChild accessed through CCDI Data Ecosystem


Yu Wang


Dr. Greg Wheeler


Dr. Sarah Leary


Dr. Diana Thomas


Dr. Katie Schieffer


Dr. Catherine Cottrell

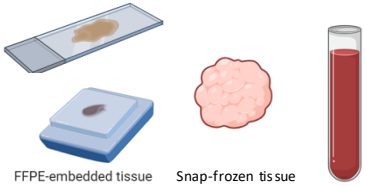
MCI CNS Cohort

(6/30/2024 enrollment cutoff)

Enrolled 2906

443 excluded (15.2%)
247 no specimens (8.5%)
141 no tumor specimen (4.8%)
55 no blood specimen (1.9%)

SPECIMEN SUBMISSION



Specimens received at BPC
2463 (85%)

135 excluded (5.5%)
Failed tissue or nucleic acid quality or quantity metrics

NUCLEIC ACID EXTRACTION

Nucleic acids received at IGM
2328 (95%)

107 failed methylation (5%)
121 failed exome (5%)
192 failed fusion (7%)

TESTING

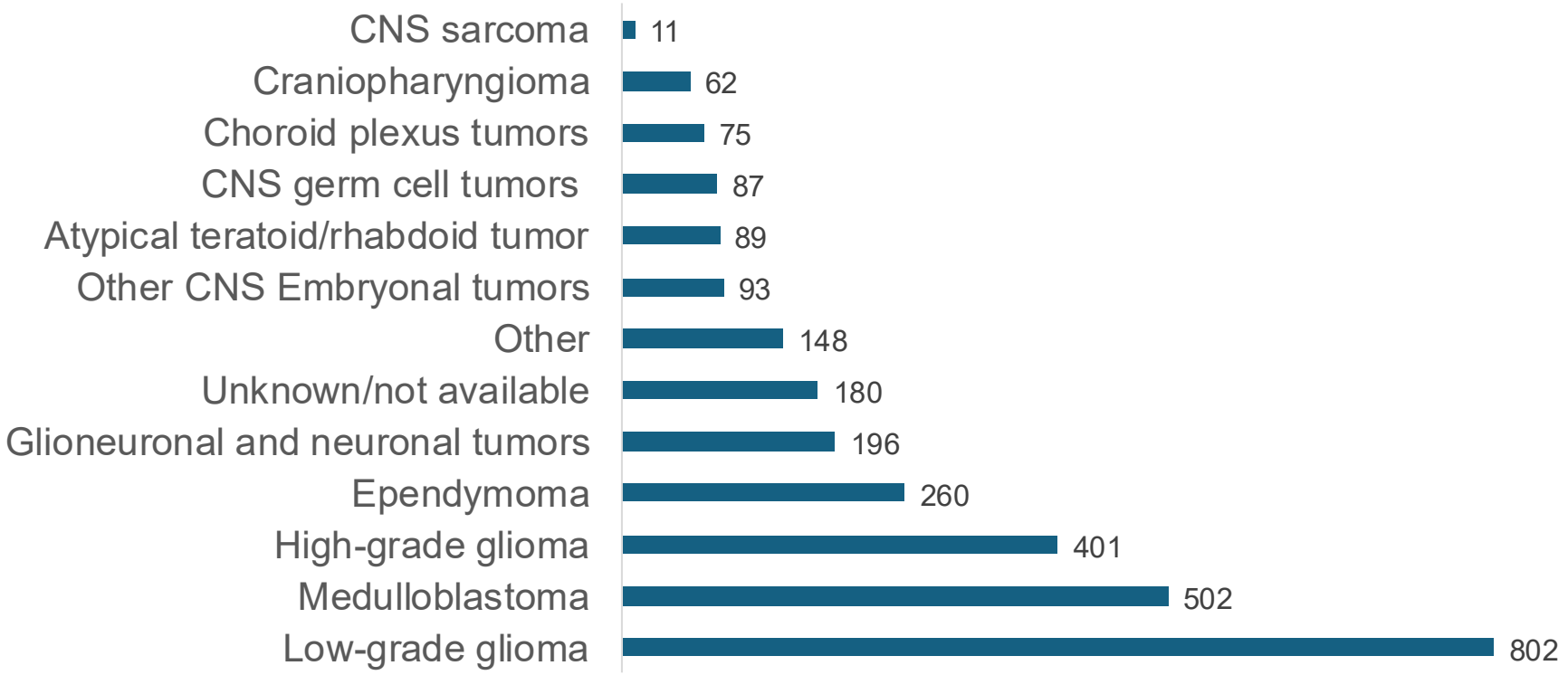
DNA Methylation resulted 2221 (95%)

Whole Exome resulted 2207 (95%)

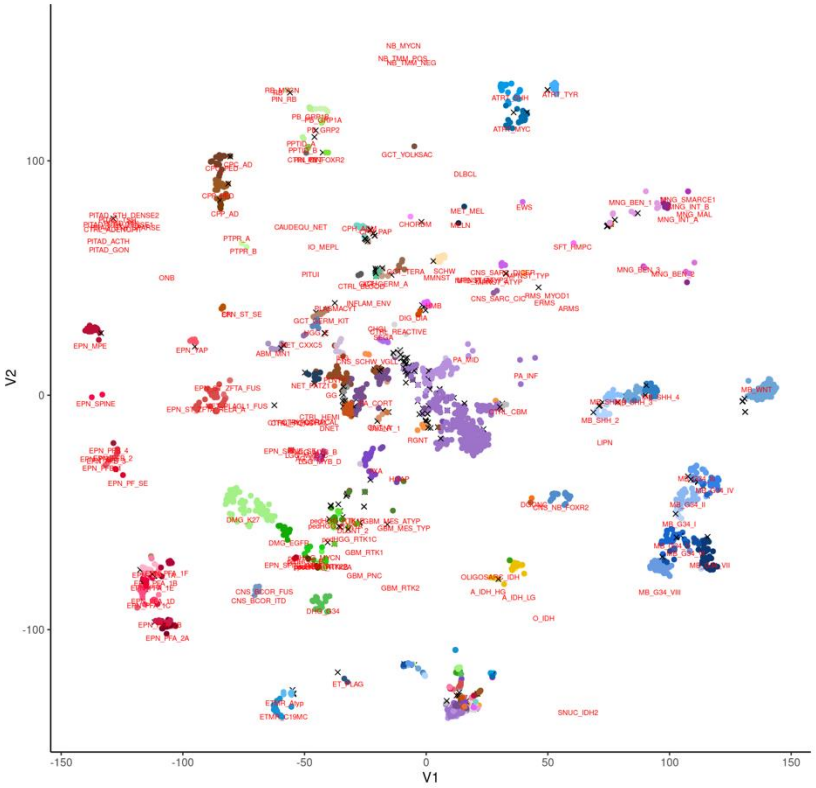
RNA Fusion Panel resulted 2136 (92%)

MCI CNS Tumor Diagnosis Categories

N = 2906 as of 6/30/2024

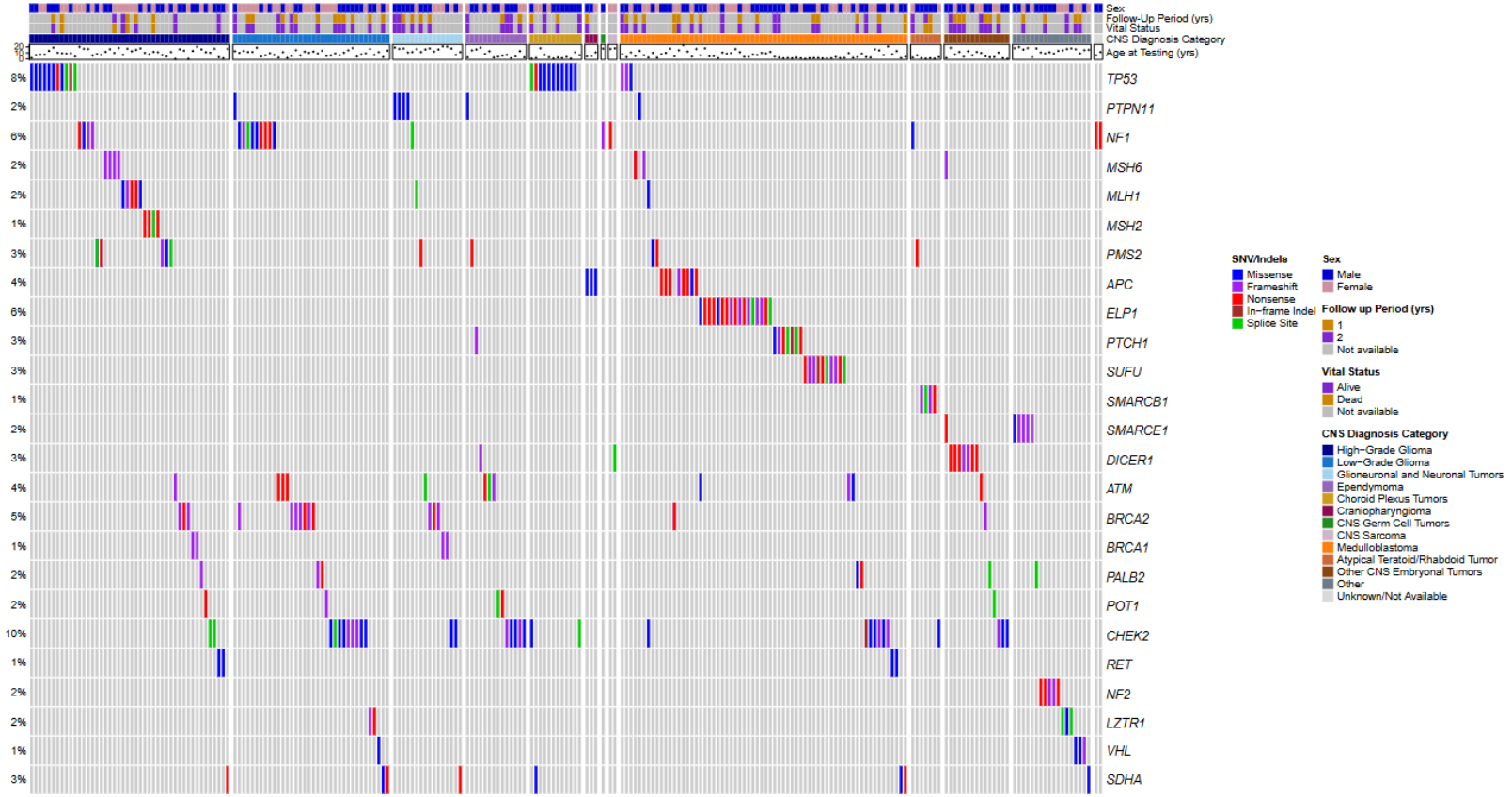


> 100 Distinct CNS Tumor Classes by DNA Methylation

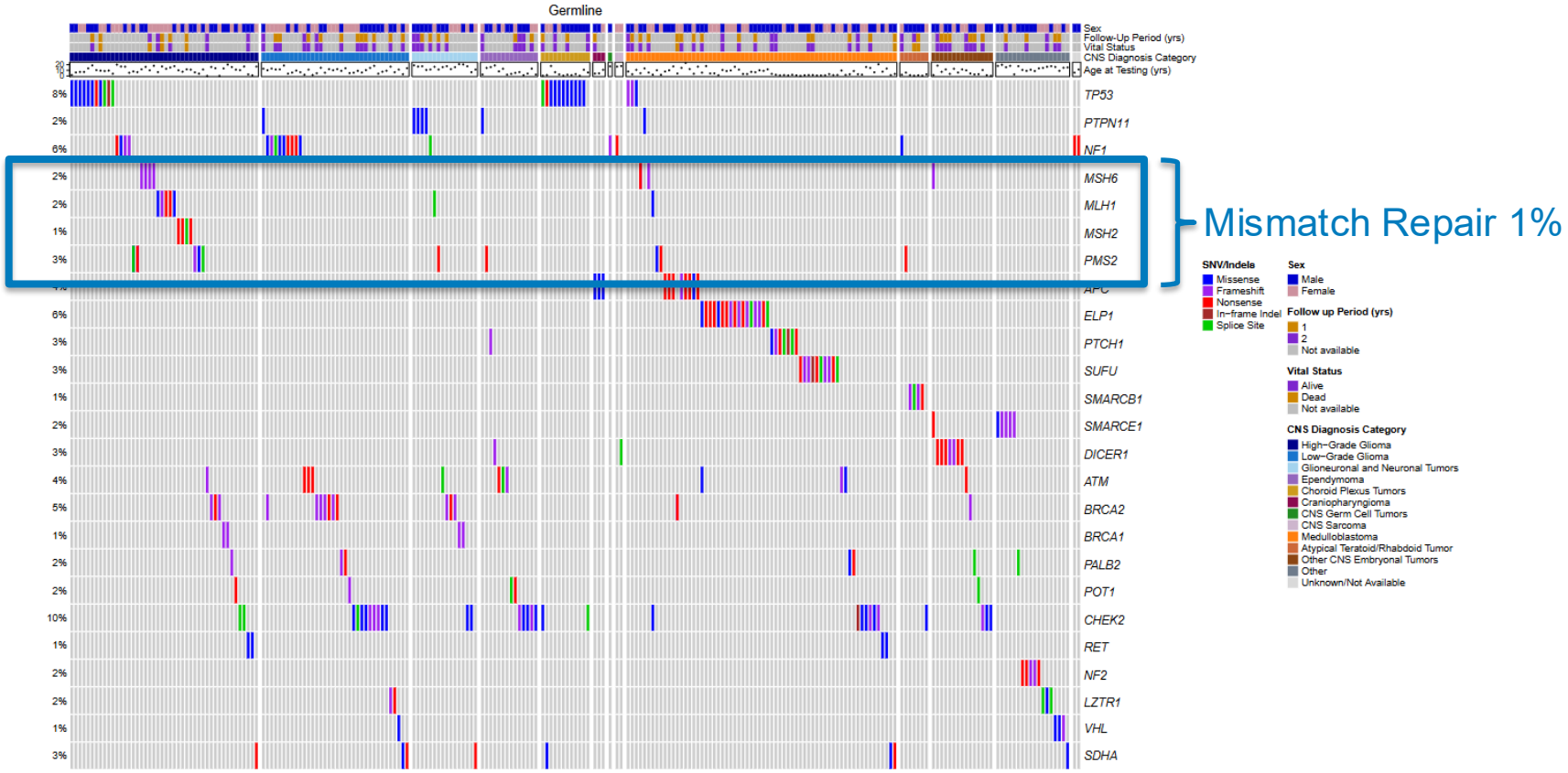


Methylation Classification	Frequency	Percent (%)
Match	1783	80.3%
Suggestive	206	9.3%
Not Determined	232	10.4%
Total Tested	2221	100%

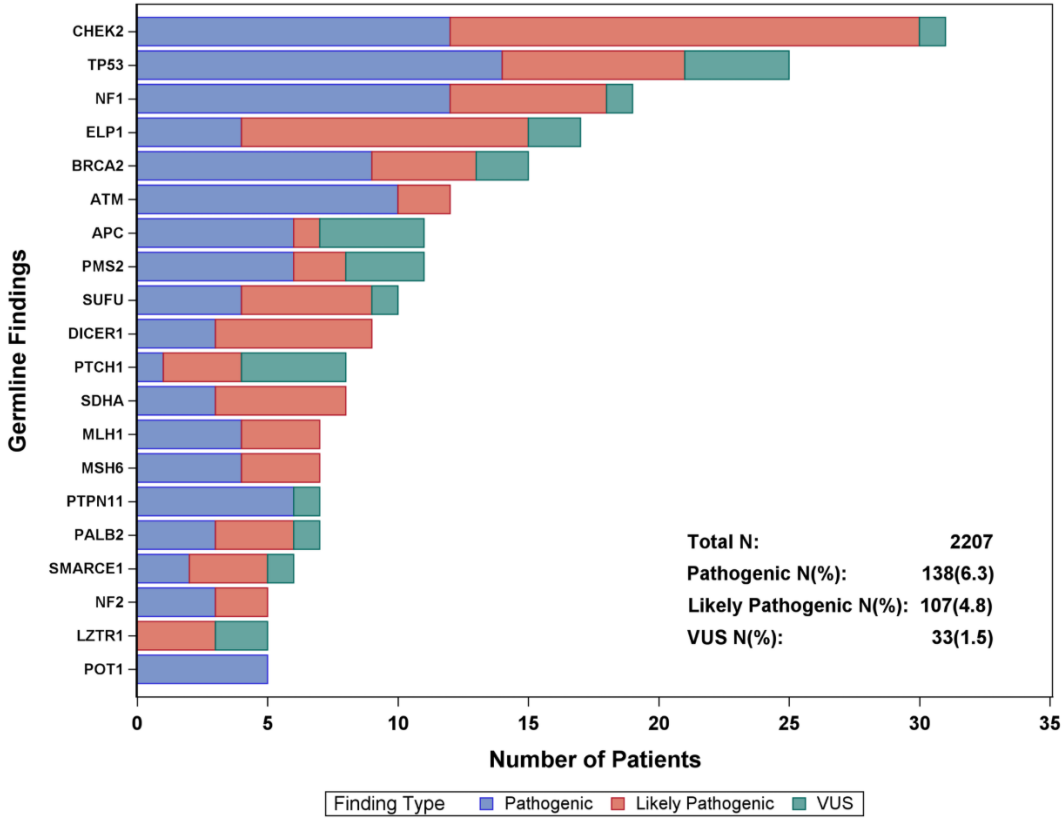
Germline Cancer Predisposition in 13% of Patients with CNS Tumors
N = 297/2207



Germline Cancer Predisposition in ~13% of Patients with CNS Tumors
N = 297/2207

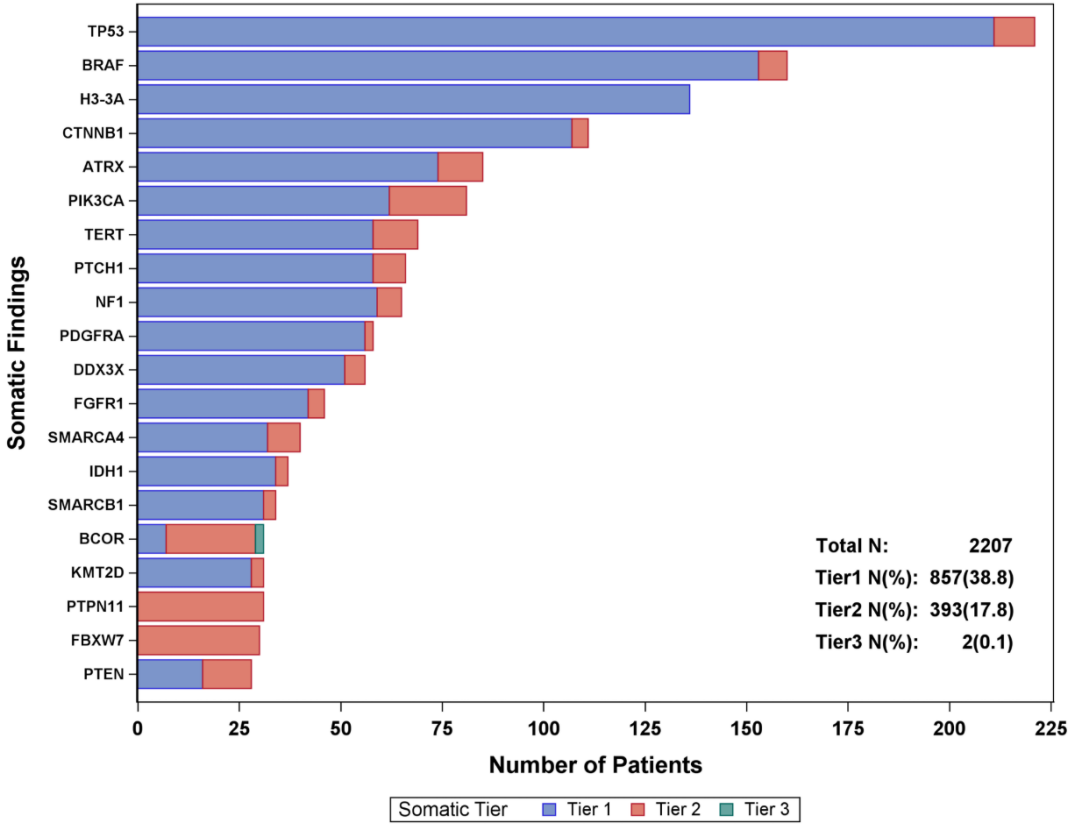


Germline Landscape of CNS Tumors in Cohort



12.6% of patients tested

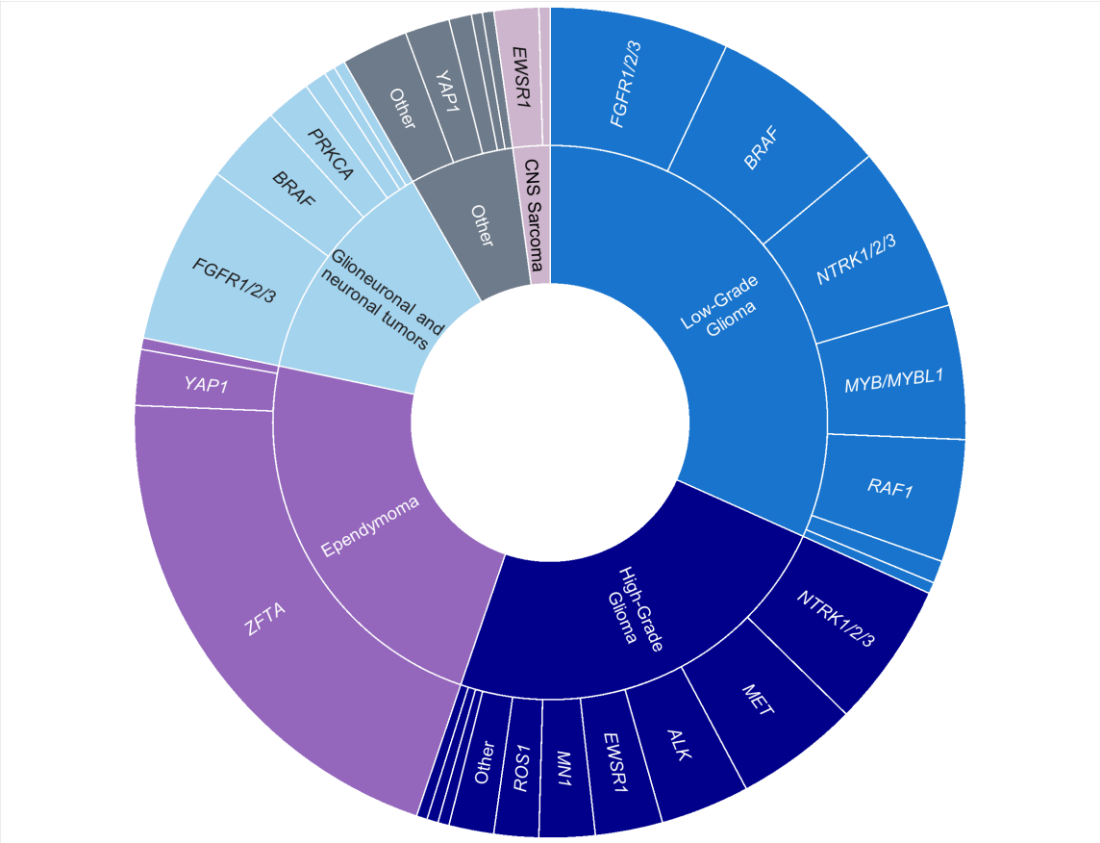
Somatic Landscape of CNS Tumors in Cohort



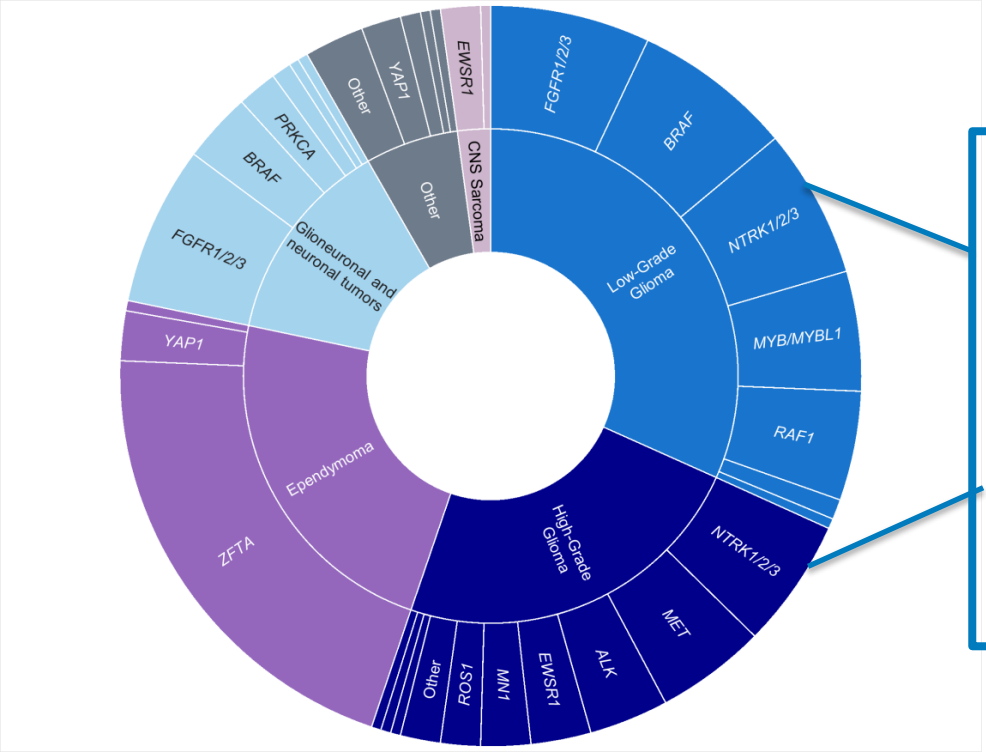
57% of patients tested

Gene Fusions Identified in 28% of CNS Tumors

N = 598/2136



Fusion-Driven CNS Tumors – Potentially Targetable

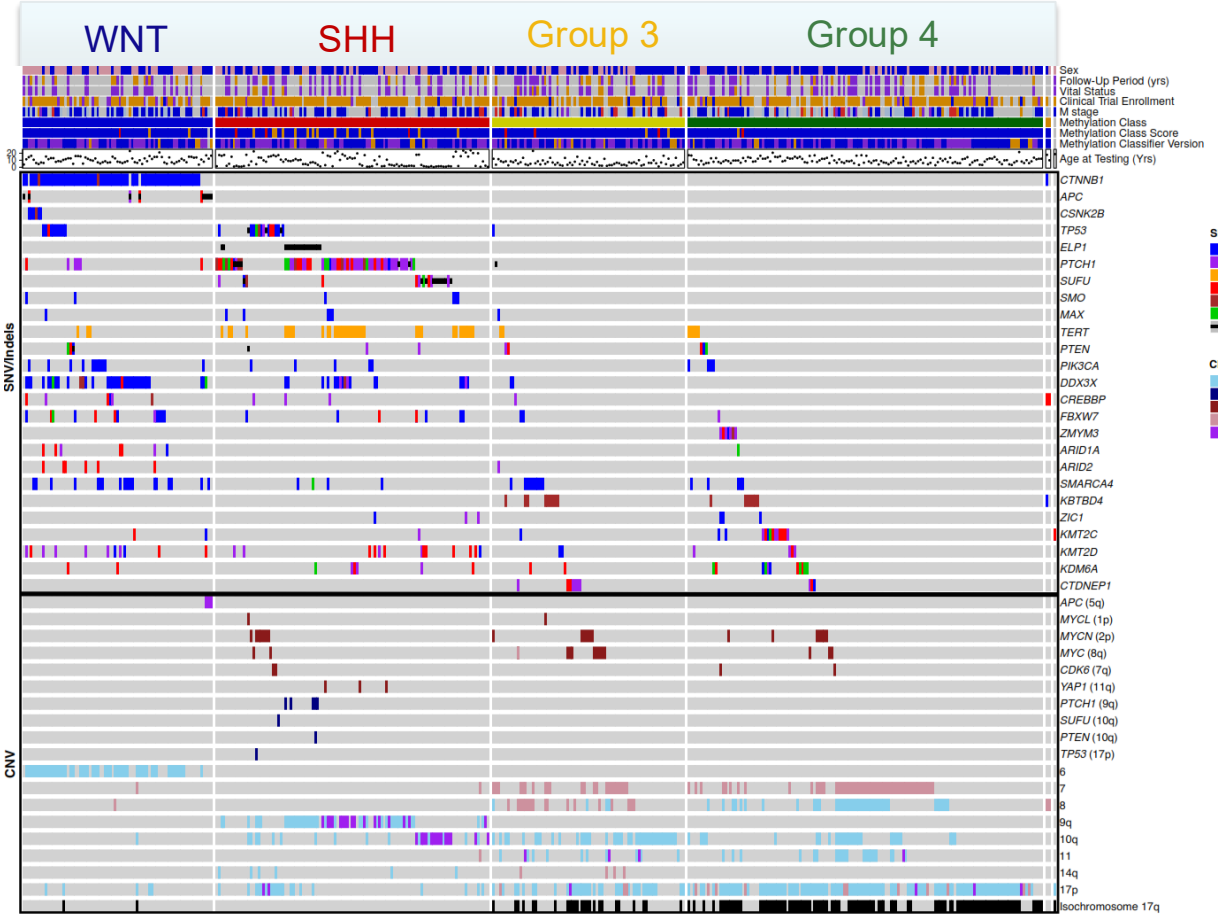


*NTRK*1/2/3 fusion (1.5%)
N = 32/2136

- Pleomorphic xanthoastrocytoma
- Ganglioglioma
- Infant-type hemispheric glioma
- Low-grade glioma, NOS/NEC
- Pilocytic astrocytoma
- Diffuse midline glioma, H3 K27-altered
- Glioneuronal and neuronal tumors, NOS/NEC
- High-grade glioma, NOS/NEC

Molecular Landscape of Medulloblastoma

N = 496/2207



CNS WHO classification 5th ed.

SNV/Indels
- Missense
- Frameshift
- Promoter
- Nonsense
- In–frame indel
- Splice site
- Germline

CNV
- Loss
- Biallelic loss
- Amplification
- Gain
- LOH

Sex
- Male
- Female

Follow-Up Period (yrs)
- 1
- 2
- Not reported

Vital Status
- Alive
- Dead
- Not reported

Clinical Trial Enrollment
- COG
- Non–COG
- No
- Not reported

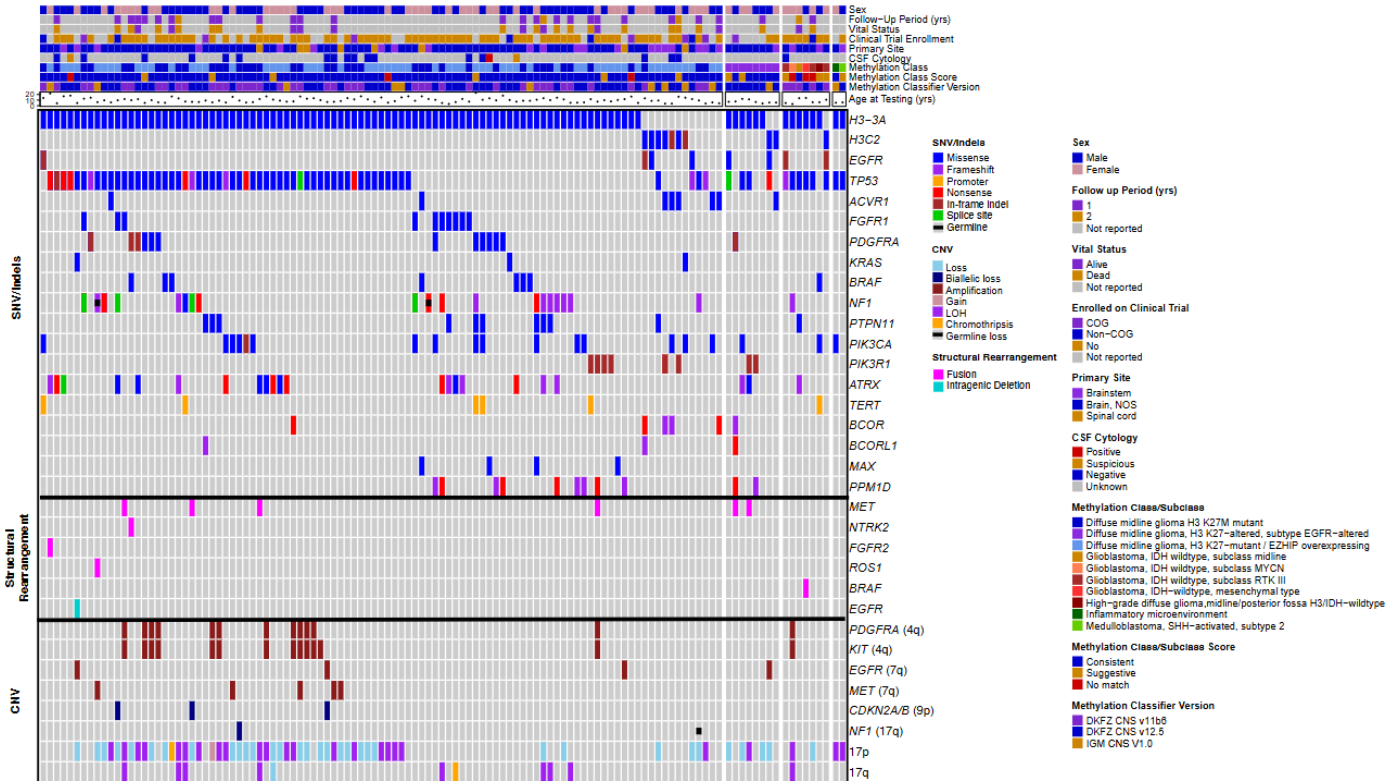
M Stage
- M0
- M1
- M2
- M3
- Unknown/Not applicable
- Not reported

MB Group by Methylation Class
- WNT
- SHH
- Group 3
- Group 4
- Medulloymoblastoma
- Other
- Not available

Methylation Class Score
- Consistent with
- No match, but suggestive of
- Not determined
- Not available

Methylation Classifier Version
- DKFZ CNS v11b6
- DKFZ CNS v12.5
- IGM CNS V1.0
- Not available

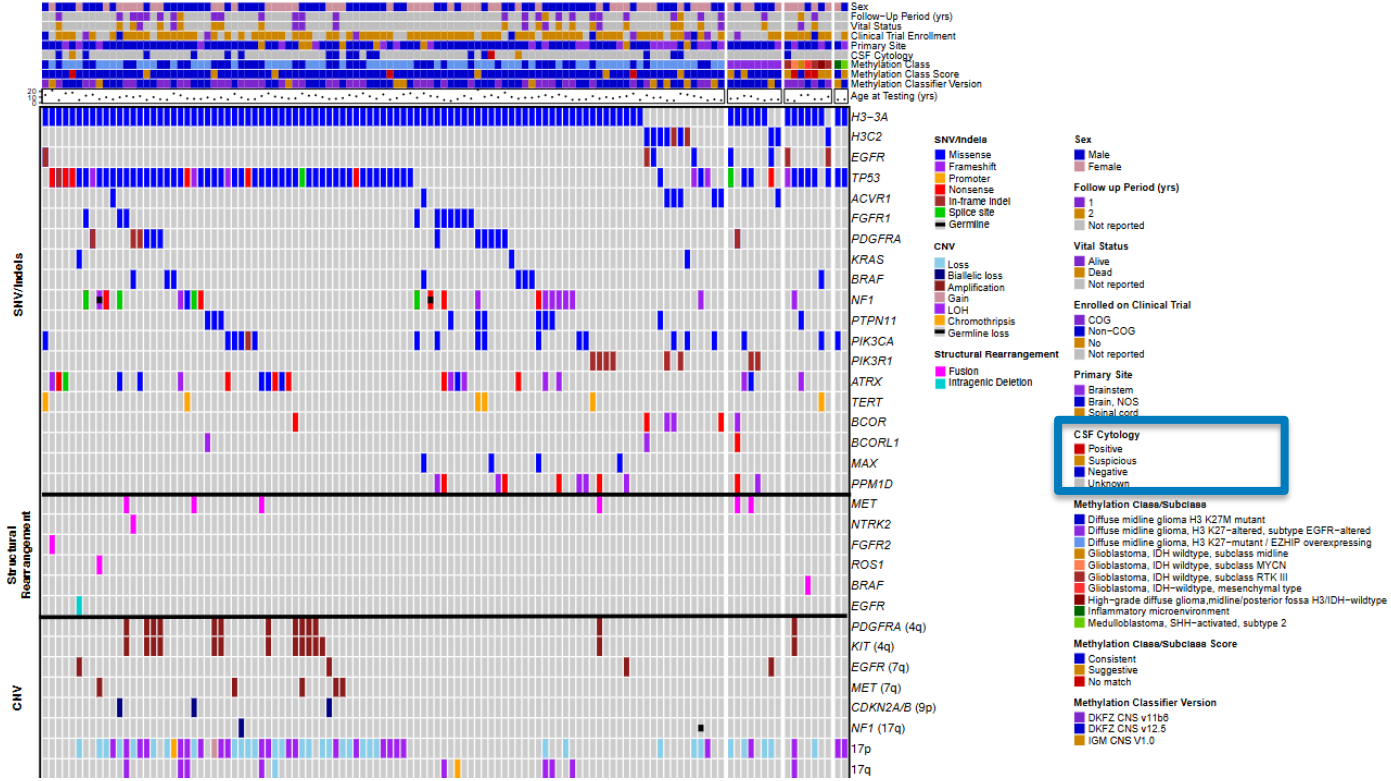
Molecular Landscape of Diffuse Midline Glioma (DMG), H3 K27-Altered
N = 120/2207



CNS WHO classification 5th ed.

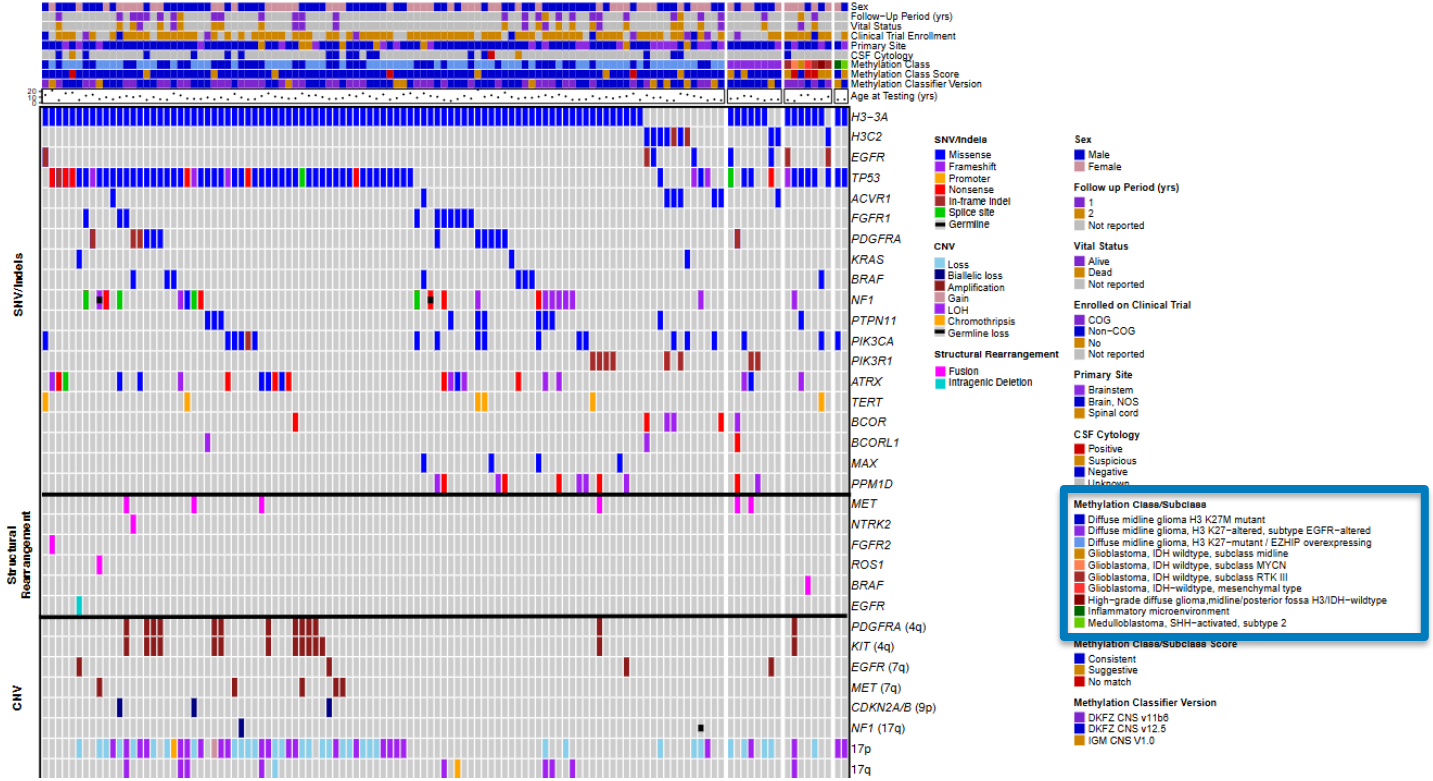
Molecular Landscape of Diffuse Midline Glioma (DMG), H3 K27-Altered

N = 120/2207



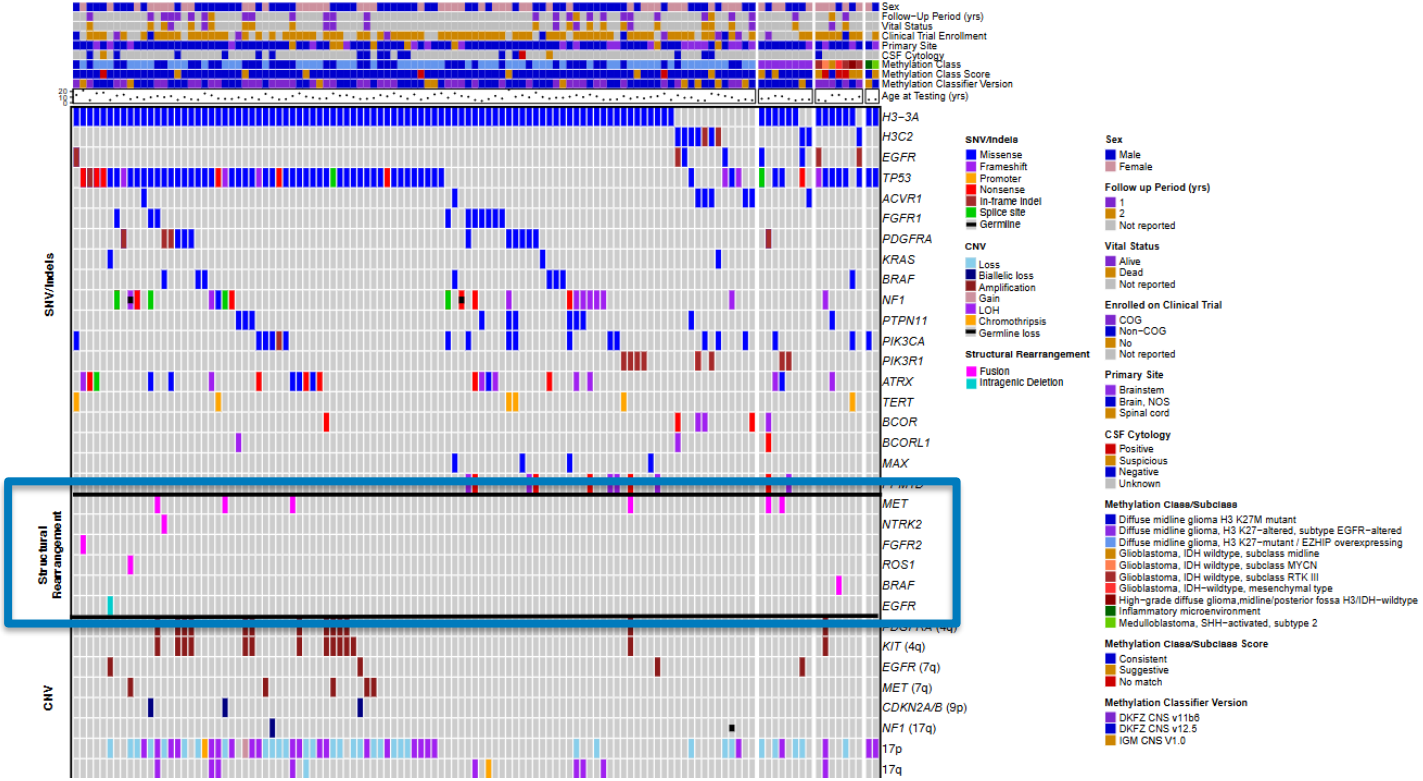
Molecular Landscape of Diffuse Midline Glioma (DMG), H3 K27-Altered

N = 120/2207



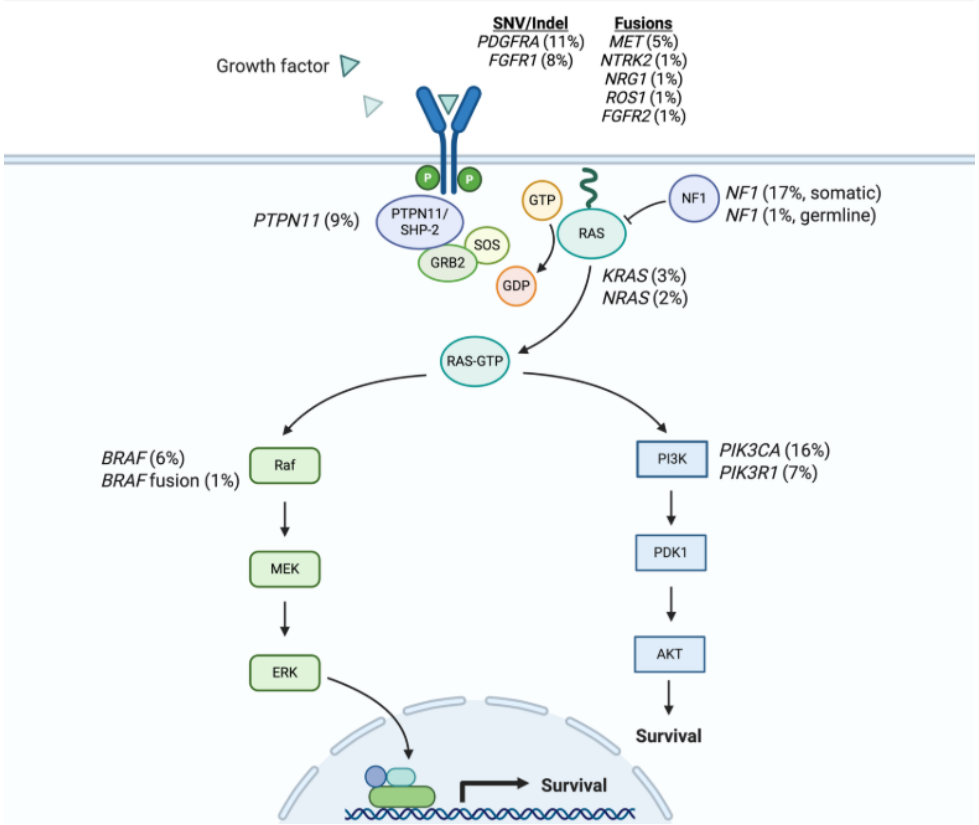
Molecular Landscape of Diffuse Midline Glioma (DMG), H3 K27-Altered

N = 120/2207



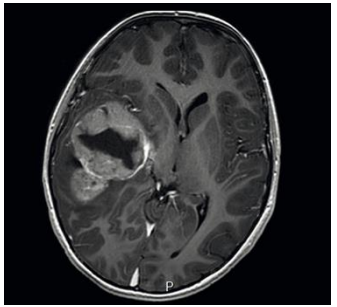
Molecular Landscape of Diffuse Midline Glioma, H3 K27-Altered

- Alterations in the RAS/MAPK and PI3K/AKT signaling pathway were observed
  - *NF1* and *PIK3CA* most common
- Activating fusions were observed in 10/118 (8.5%) of individuals
  - *MET* fusion most common

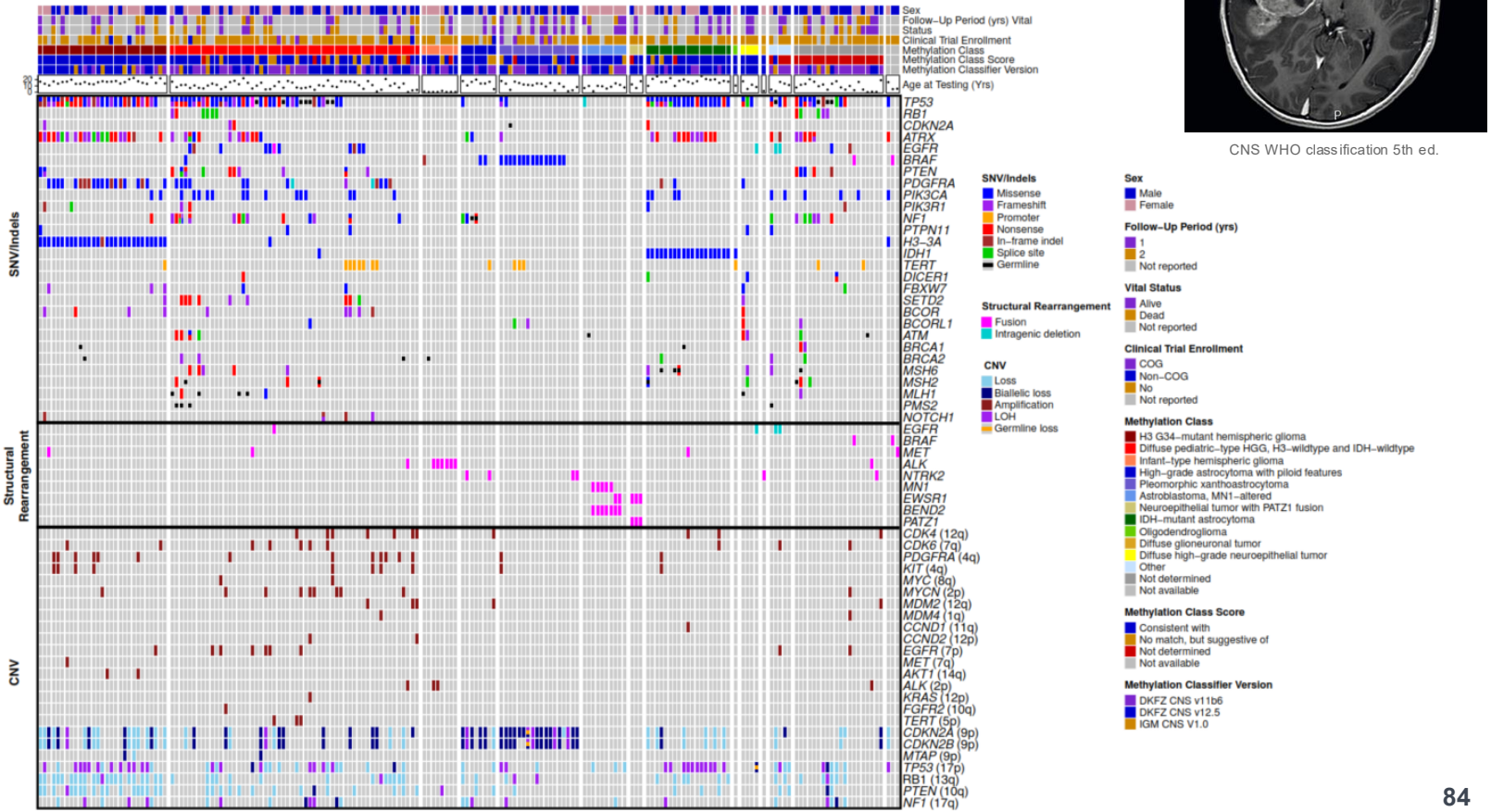


Molecular Landscape of Non-DMG High-Grade Glioma

N = 293/2207

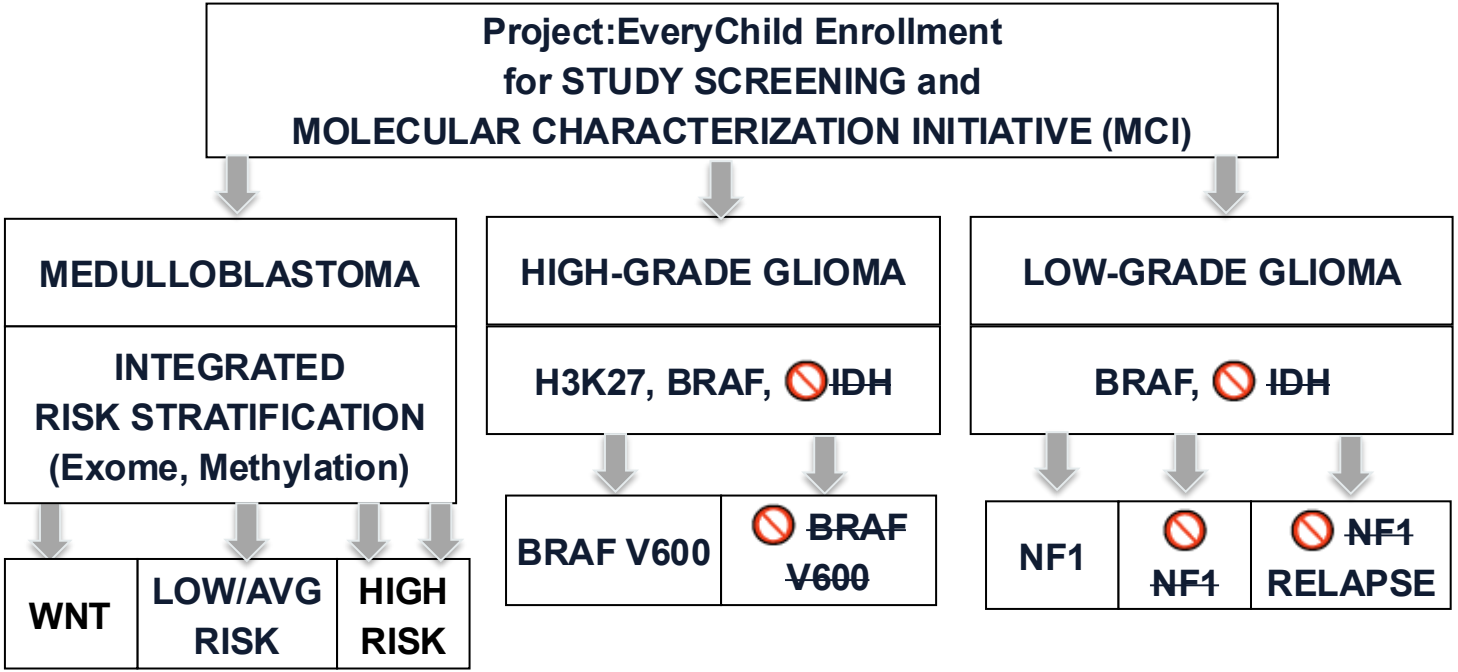


CNS WHO classification 5th ed.



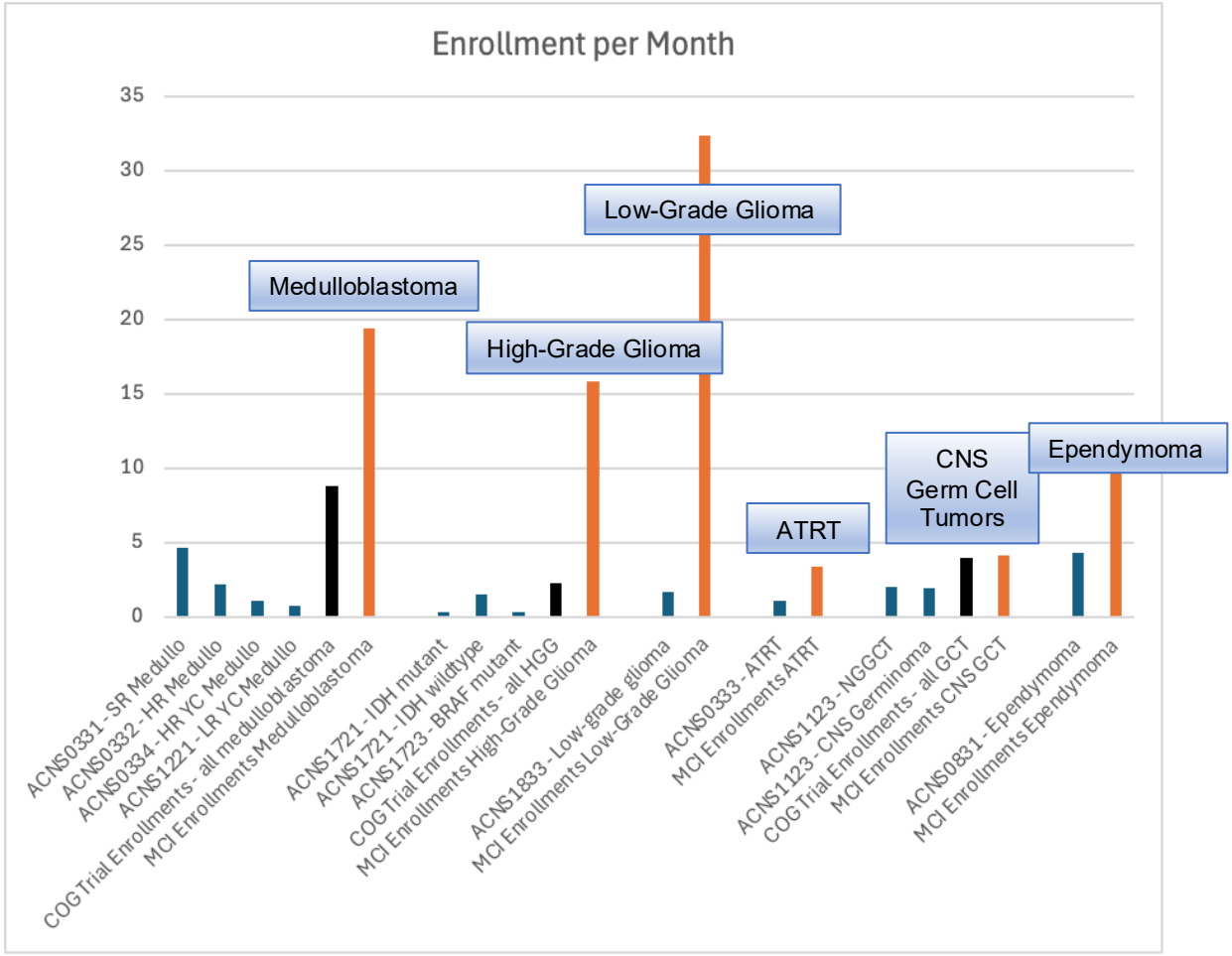
MCI CNS Clinical Applications and Opportunities

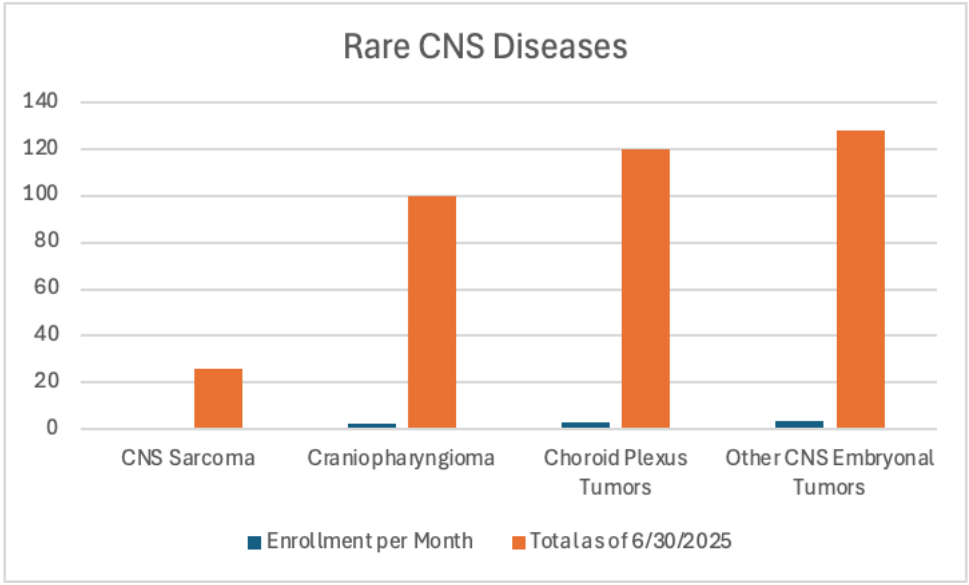
Applications of MCI Data - Screening



COG CNS Therapeutic Trials

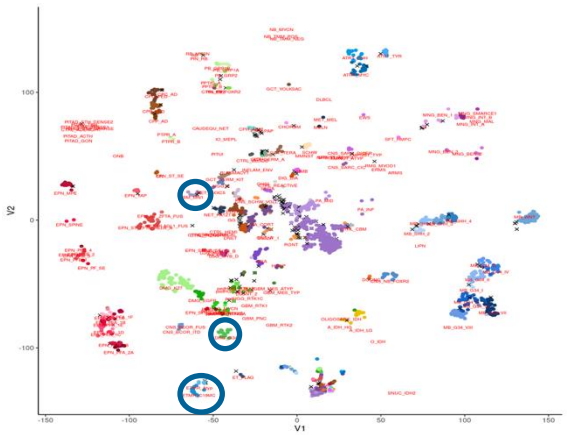
MCI

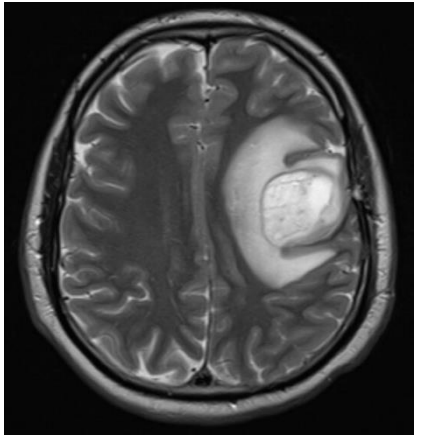



Rare CNS Diseases
140
120
100
80
60
40
20
0
CNS Sarcoma
Craniopharyngioma
Choroid Plexus Tumors
Other CNS Embryonal Tumors
Enrollment per Month
Total as of 6/30/2025

Examples of Ultra-Rare Disease (as of 6/30/2024)

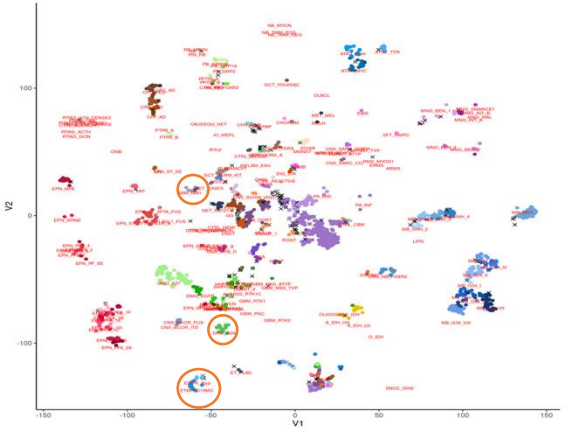
- ETMR: 31
- HGG G34 mutant: 30
- Astroblastoma: 18
- Infantile Hemispheric Glioma: 16
- Tumors in children with constitutional mismatch repair defects: 24

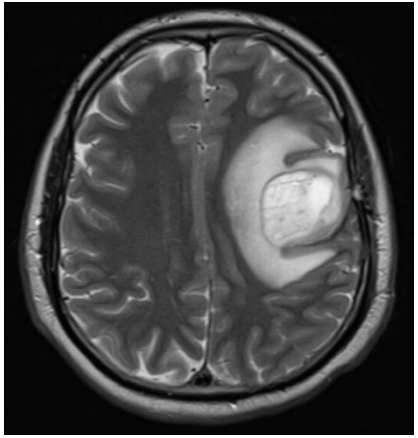




Examples of Ultra-Rare Disease (as of 6/30/2024)

- ETMR: 31
  - Nijmegen Breakage Syndrome
  - PALB2-Related Cancer Predisposition Syndrome
  - POT1 and Shelterin-Related Tumor Predisposition Syndrome
  - MBD4-Associated Neoplasia Syndrome
- HGG G34 mutant: 30
- Astroblastoma: 18
- Infantile Hemispheric Glioma: 16
- Tumors in children with constitutional mismatch repair defects: 24





Examples of Ultra-Rare Disease (as of 6/30/2024)

- ETMR: 31
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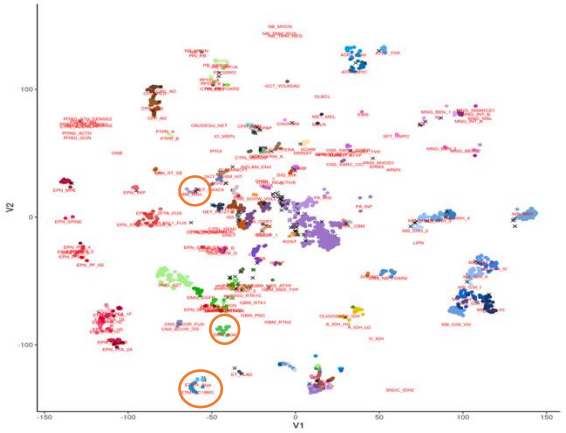
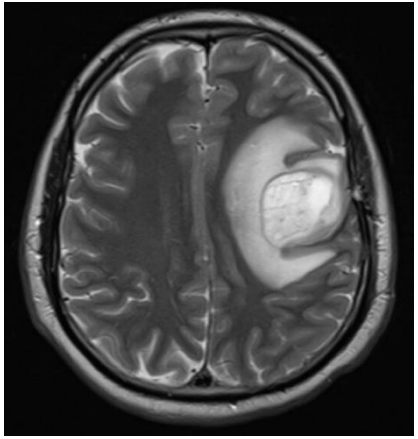
- 16p11.2 Deletion Syndrome
- Breast/Ovarian/Pancreatic Tumor Predisposition Syndrome





Examples of Ultra-Rare Disease (as of 6/30/2024)

- ETMR: 31
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- Infant-type Hemispheric Glioma: 16
- Tumors in children with constitutional mismatch repair defects: 24

- Pheochromocytoma/
- Paraganglioma Syndrome
- BRCA-Related Cancer Predisposition Syndrome

BRAF p.Val600Asp

KANK1::NTRK3
BEND5::NTRK2
GAB1::ABL2;GAB1::ABL2
SPECC1L::ALK
SNRNP70::ALK
PPP1CB::ALK
KANK1::NTRK2
BCR::NTRK2
MYO5A::NTRK3
EML4::ALK
TRIM24::NTRK2
TPM3::NTRK1
GOPC::ROS1
PPP1CB::ALK
PRKAR2A::ALK

Implications for Future Research

- Identification of rare therapeutic targets
- External control cohorts
- Pragmatic trials
- Tumor predisposition and prevention

The impact of molecular data is dependent on connection to clinical data – particularly treatment and outcomes

CCDI
CHILDHOOD CANCER DATA INITIATIVE

Children's Brain Tumor Network

Rare Brain Tumor consortium
Translating knowledge to cures for orphan tumors

DATA FOR THE COMMON GOOD

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- Sarah Leary (Seattle, Washington)
- Diana Thomas (Columbus, Ohio)

Q&A

Join Us For Our Upcoming CCDI Virtual Symposium Series Events!

March 18

March 25

April 2

April 7

April 8

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Thank you for attending!

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