Directly engaging participants in rare cancer research is feasible: The osteosarcoma and leiomyosarcoma projects

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BROAD INSTITUTE

Dana-Farber Cancer Institute

Boston Children's Hospital

HARVARD MEDICAL SCHOOL

Count Me In

Thank you to all our participants and advocacy partners!

Members of our Stakeholder Advisory Group and Hispanic/Latino Focus Groups

Study Procedures

ELIGIBILITY:
Age: Any
Stage: Any
Country: US & Canada

Online consent & assent
Baseline survey

Additional permissions:

Medical record release

Receive shared learnings from tumor sequencing

Participant receives & returns saliva and/or blood kit

Research team requests medical records **and then** tumor sample from treating institution(s)

Germline and tumor samples received

Requires an appointment with Genome Medical. Participant notified via email

Offered genetic counseling & clinical germline testing with return of results

Tumor and normal sequenced

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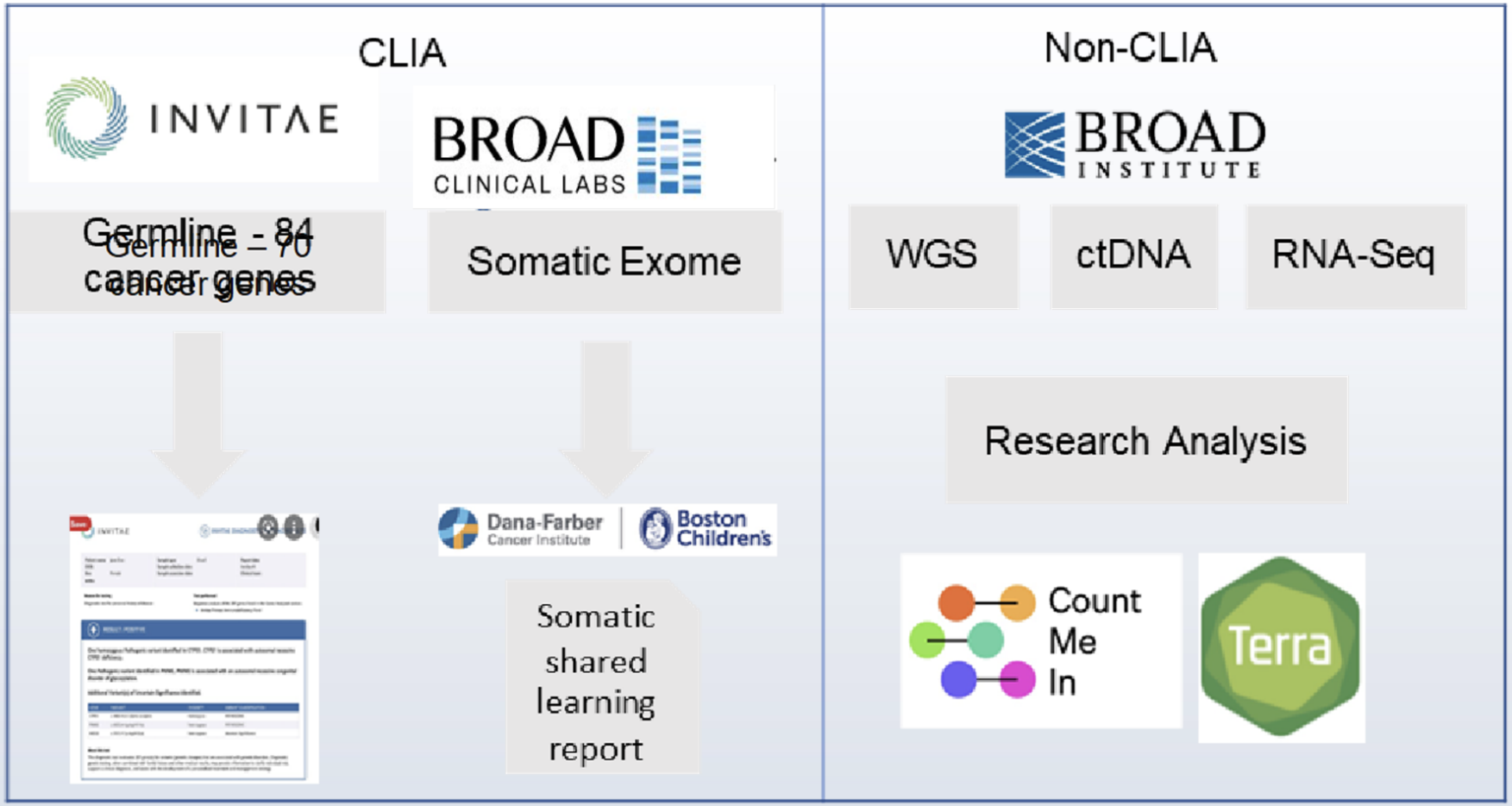
Sequencing



Additional complexity:

- Tumor only
  - Targeted NGS panel CLIA for RoR
- Germline only
  - WGS
- Wait 3 months to achieve pairing before proceeding
- NYS and Canada
  - Not eligible for Broad Clinical

Reframing "return of results" to sharing "what we are learning about your tumor genome"

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Somatic shared learnings

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Excerpt shared learning text:
We want to share with you some of the genetic information that we found within your tumor sample. Genetic changes found in your tumor that help us to learn more about how osteosarcoma develops and grows are called cancer drivers. Genetic changes found in your tumor that help us to identify new therapeutics that might be helpful for people with osteosarcoma in the future are called potential drug targets.

Limited list of genes reported

AKT1	**CDK12**	**IDH2**	**NOTCH1**	**RECQL4**
AKT2	CDK4	IGF1R	**NOTCH2**	**RET**
ALK	CDK6	**JAK1**	**NRAS**	**ROS1**
APC	**CDKN2A**	**JAK2**	**NTRK1**	SETD2
ARID1A	CDKN2B	**JAK3**	**NTRK2**	**SMARCB1**
ARID1B	**CHEK1**	KDR	**NTRK3**	**STK11**
ATM	**CHEK2**	**KIT**	**PALB2**	**TERT**
ATR	**CTNNB1**	**KRAS**	**PDGFRA**	**TET2**
ATRX	**DICER1**	**MAP2K1**	**PDGFRB**	**TP53**
AURKB	**EGFR**	**MAP2K4**	**PIK3CA**	**TSC1**
BARD1	**ERBB2**	**MAP3K1**	PIK3R1	**TSC2**
BLM	**EZH2**	MCL1	**PMS2**	VEGFA
BRAF	**FANCL**	**MDM2**	**PTEN**	WRN
BRCA1	**FGFR1**	**MET**	**PTPN11**	
BRCA2	**FGFR2**	**MLH1**	RAD21	
BRIP1	**FGFR3**	**MSH2**	**RAD51B**	
CCND1	**FIP1L1**	**MSH6**	**RAD51C**	
CCND2	GNAS	MYC	**RAD51D**	
CCND3	**HRAS**	**NF1**	**RAD54L**	
CCNE1	**IDH1**	**NF2**	**RB1**	

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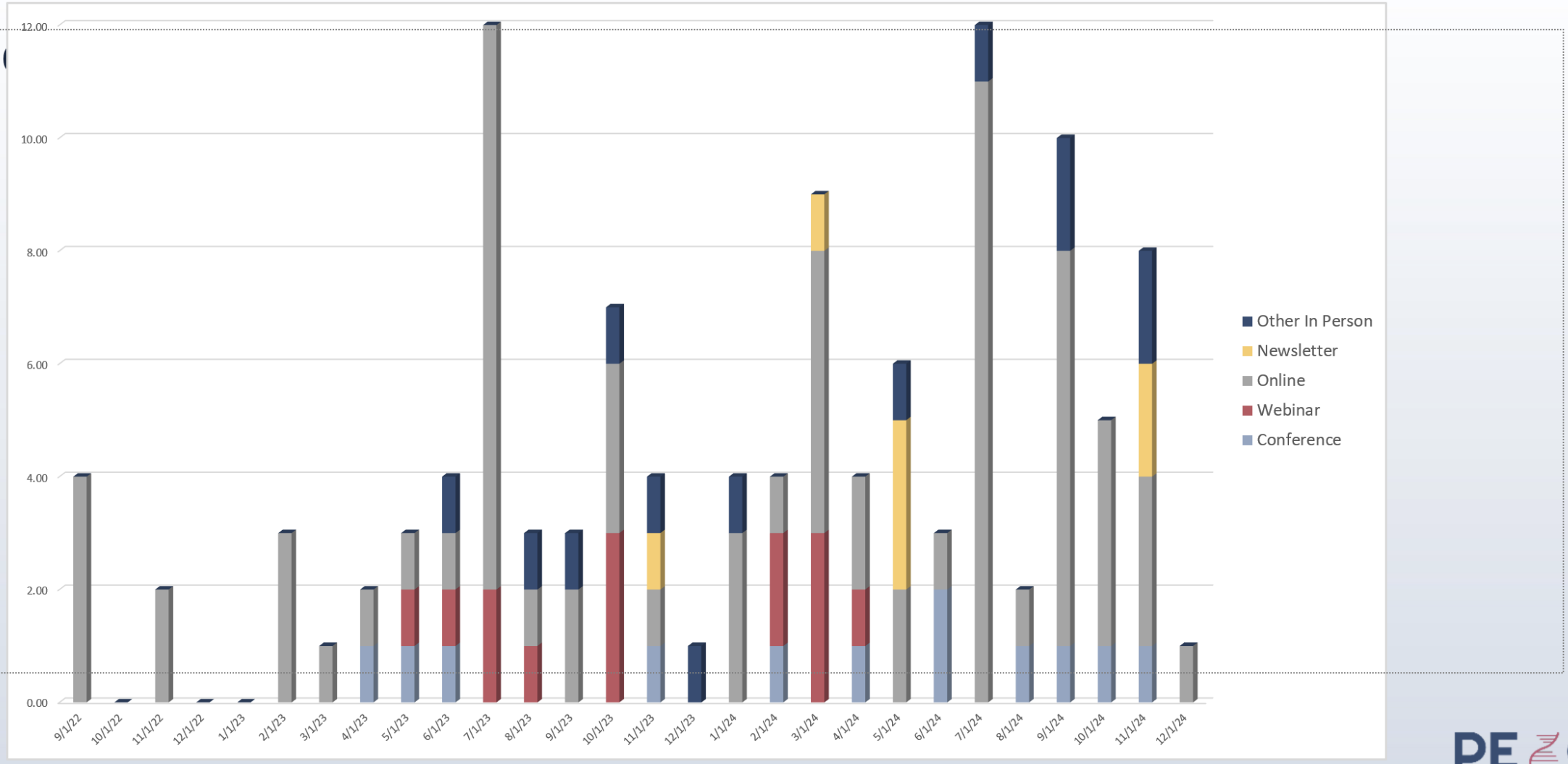
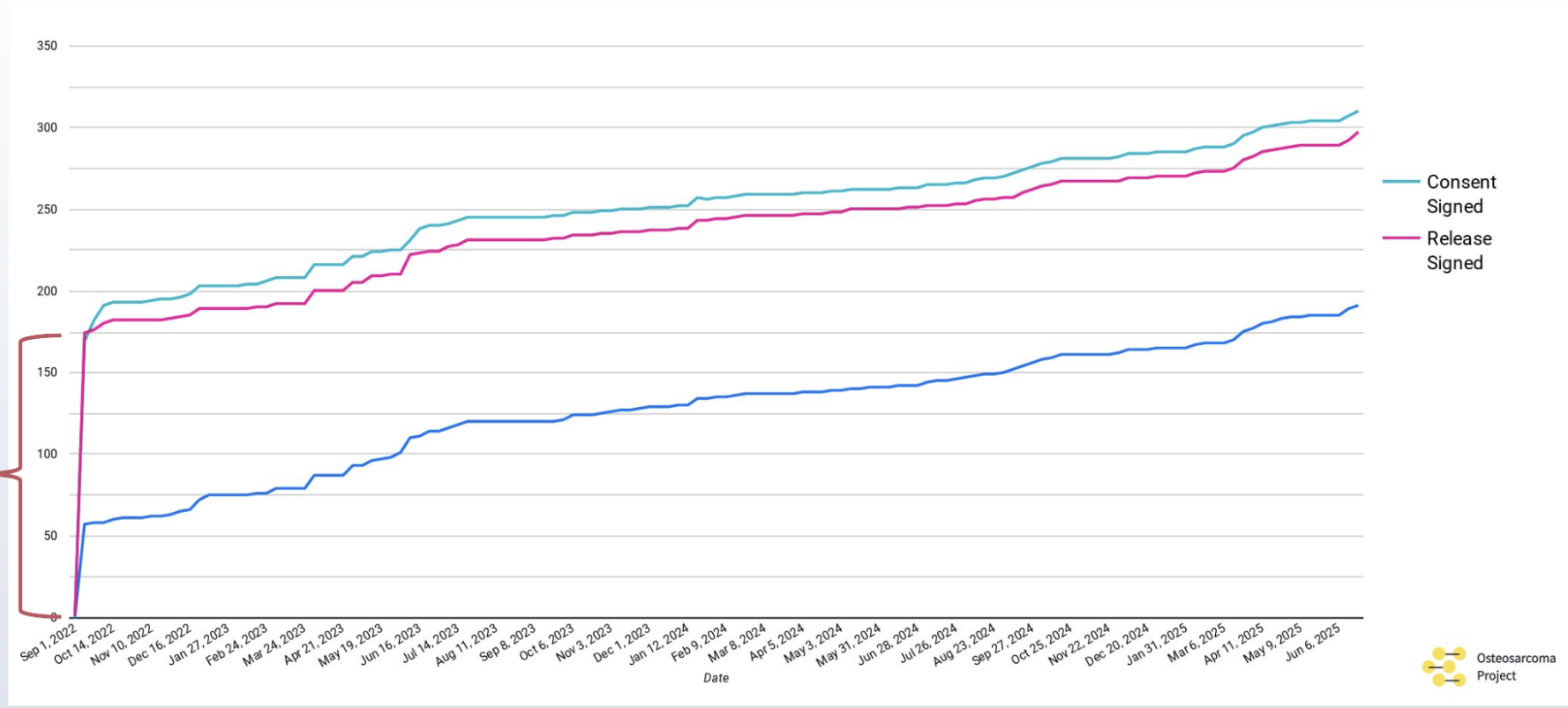
Communications / Recruitment



Accrual

136 participants enrolled in legacy study only
50 participants converted from legacy study to PE-CGS study



Participant interviews

Motivation is advance science & help others

Hard to take on additional burden during illness

Examples
"It's not for me, but for the ones that follow me."
“I want to find a cure.”
“It's telling me that I'm a partner in this.”

Accrual 5 patients per month

296 participants consented & release signed
Help us get to 300!

Scan the QR today, and help change the future of osteosarcoma.
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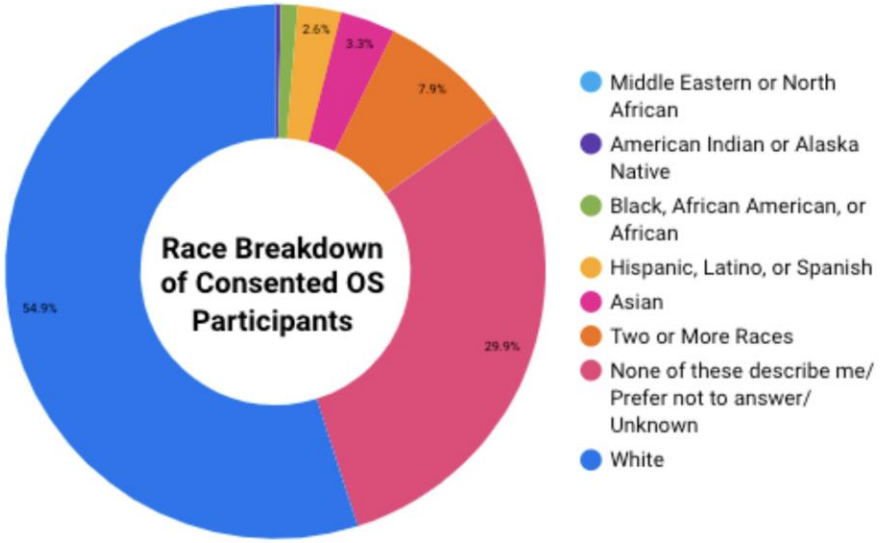
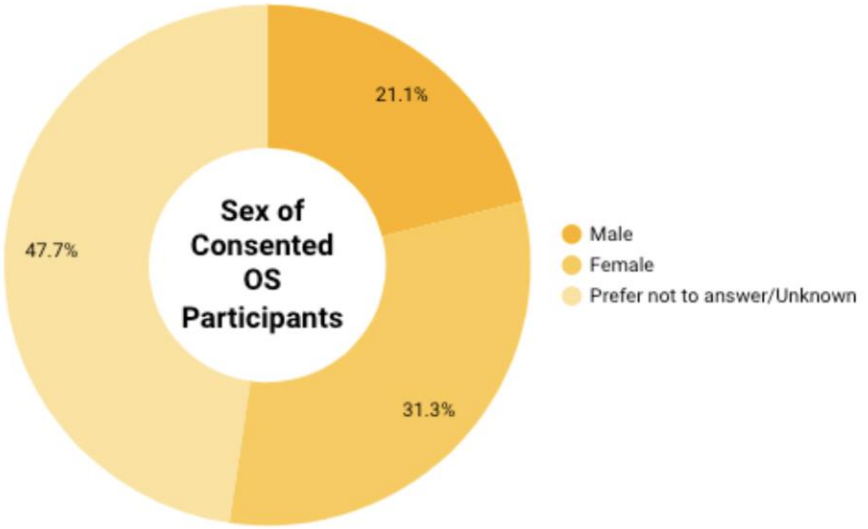
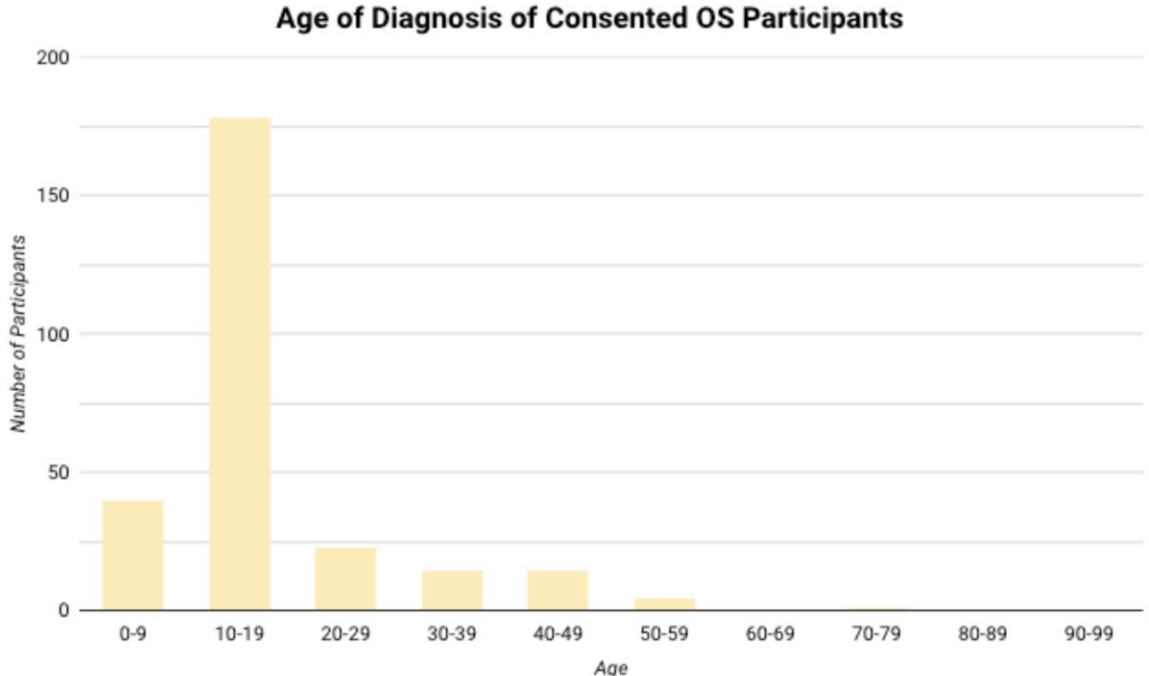
OS PE-CGS Demographic Data

Last Updated: 06/02/2025







Osteosarcoma Project

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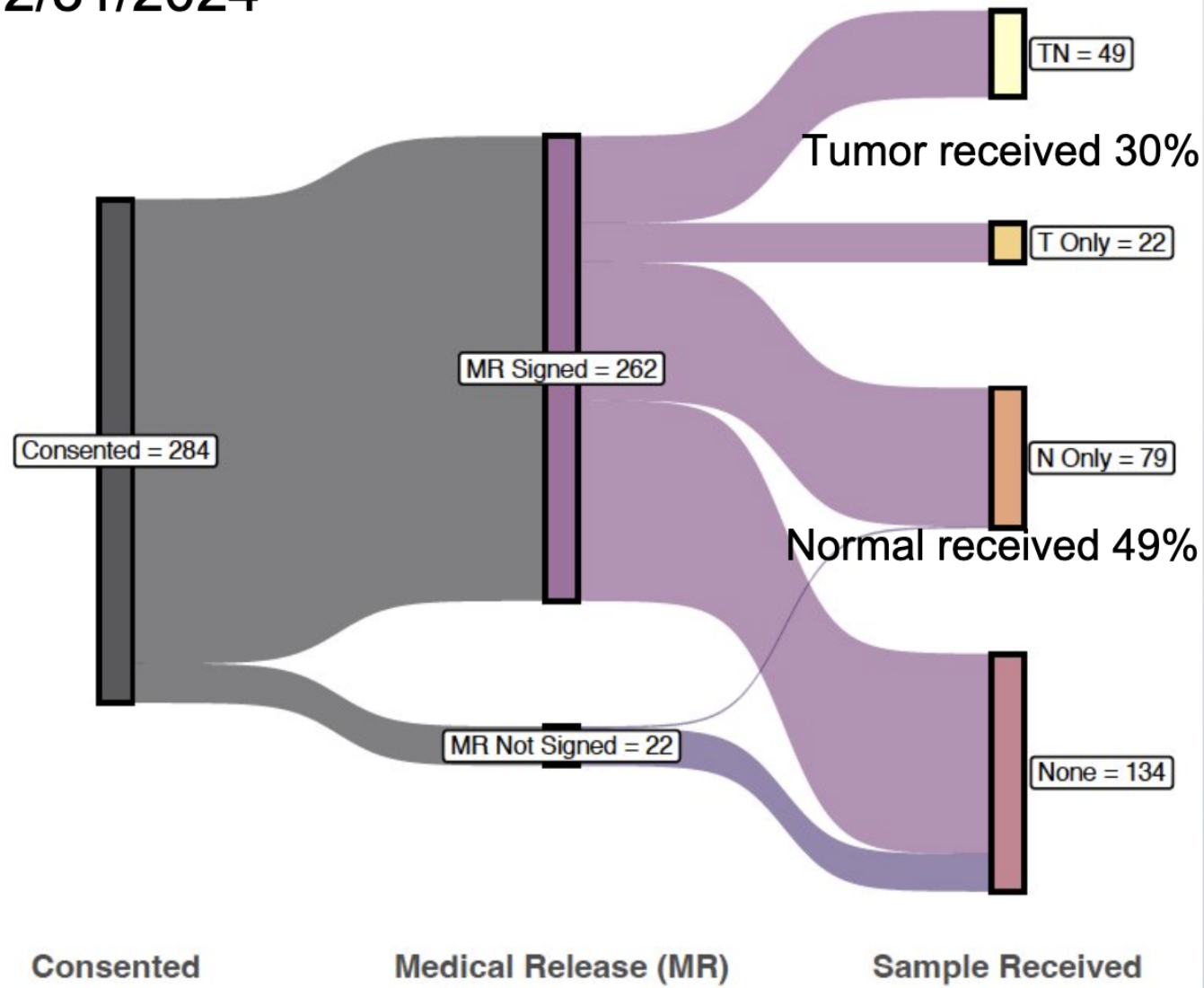
Patients and samples

12/31/2024

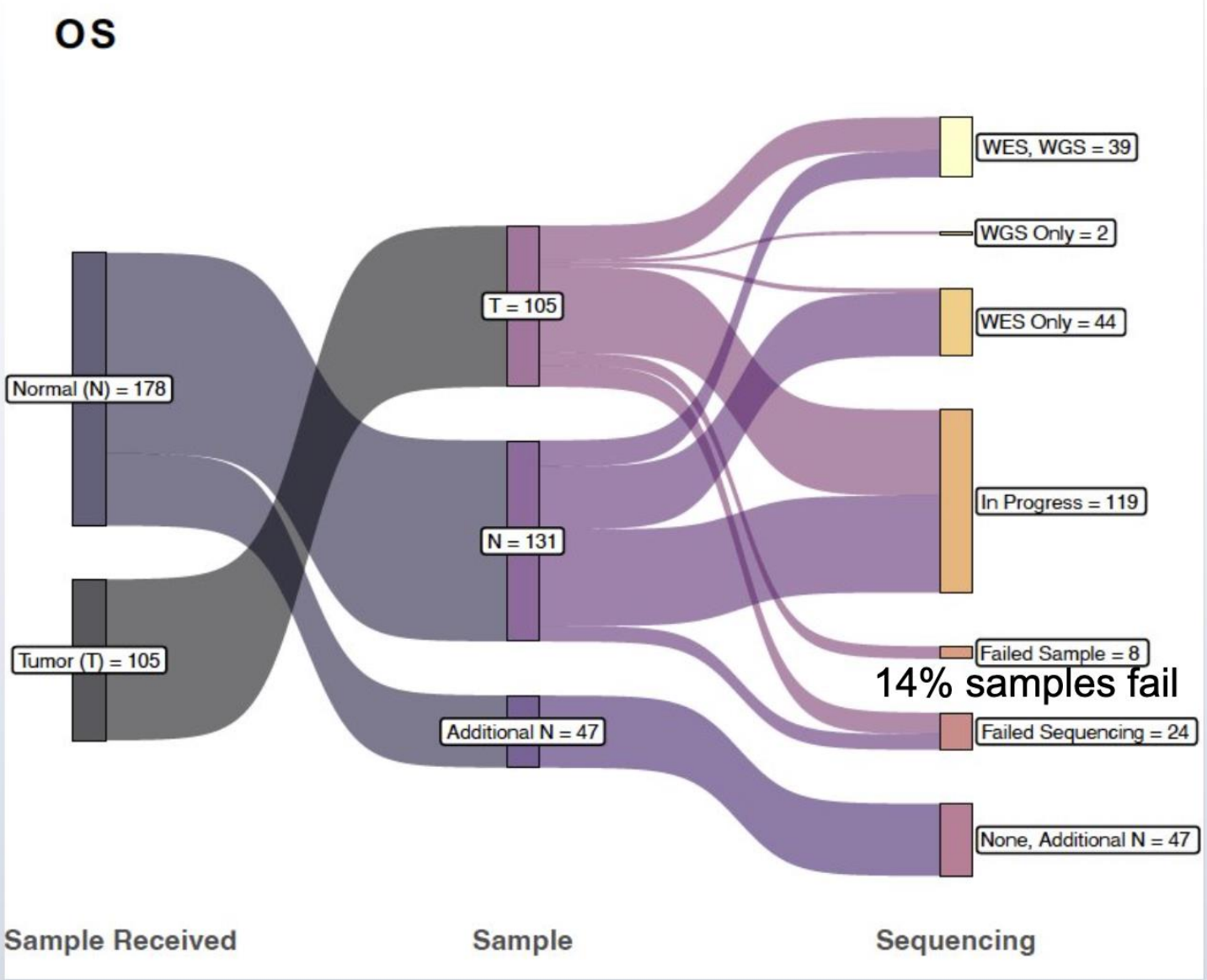


Currently, patient level:

141 pts with germline sample

136 tumor samples from 85 patients
1.6 tumors/pt

Sequencing



Tumor Sequencing	N
Tumor Sample Received	136
Successful WES	38
Successful WGS	32
Successful RNAseq	25
In Progress	78

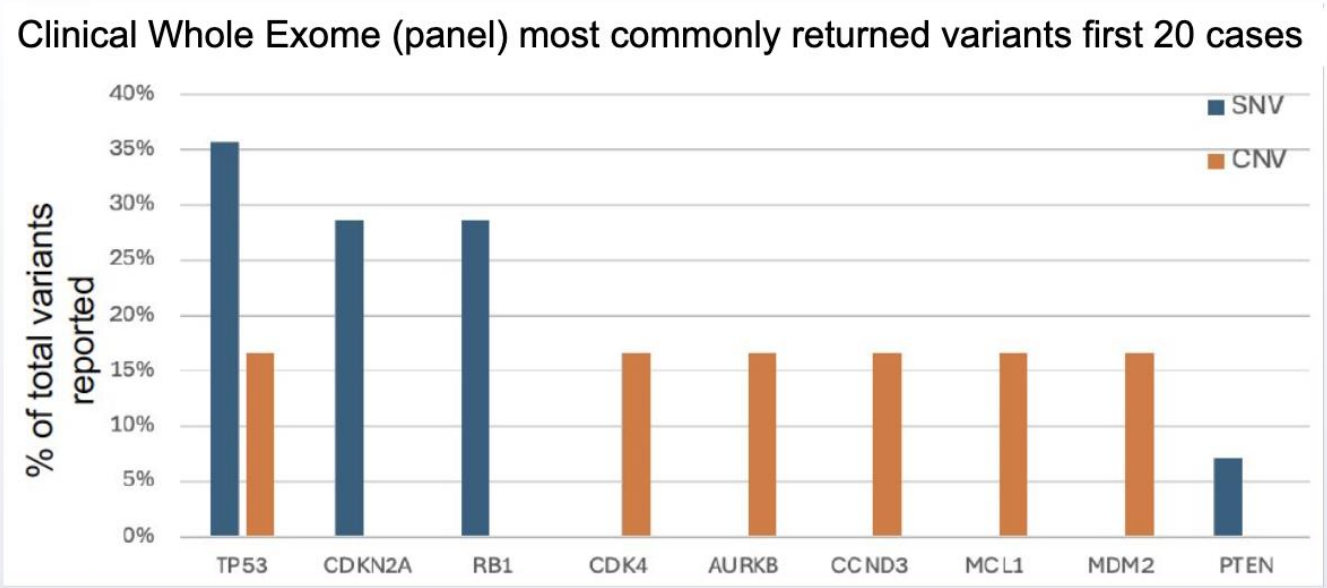
Germline Sequencing	N
Germline Sample Received**	232
Successful WES	103
Successful WGS***	117
In Progress	16

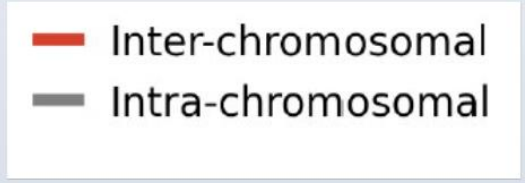
Genomic Data Freeze 12/31/2024: Clinical Features

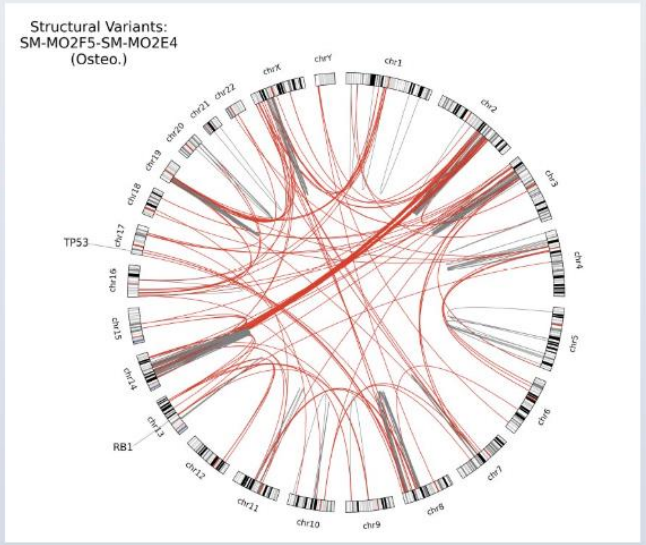
Patients	N=19
Age at diagnosis mean (range)	22 (4-74)
Sex, N (%) M F	 10 (53%) **9 (47%)**
Stage @ dx, N (%) Localized Metastatic	 **15 (79%)** 4 (21%)
Grade @ dx, N (%) Low Int High Unk	 0 0 18 (95%) 1 (5%)
Progression, N (%) None Local only Metastatic only Both local AND metastatic	 **8 (42%)** 1 (5%) 5 (26%) 5 (26%)

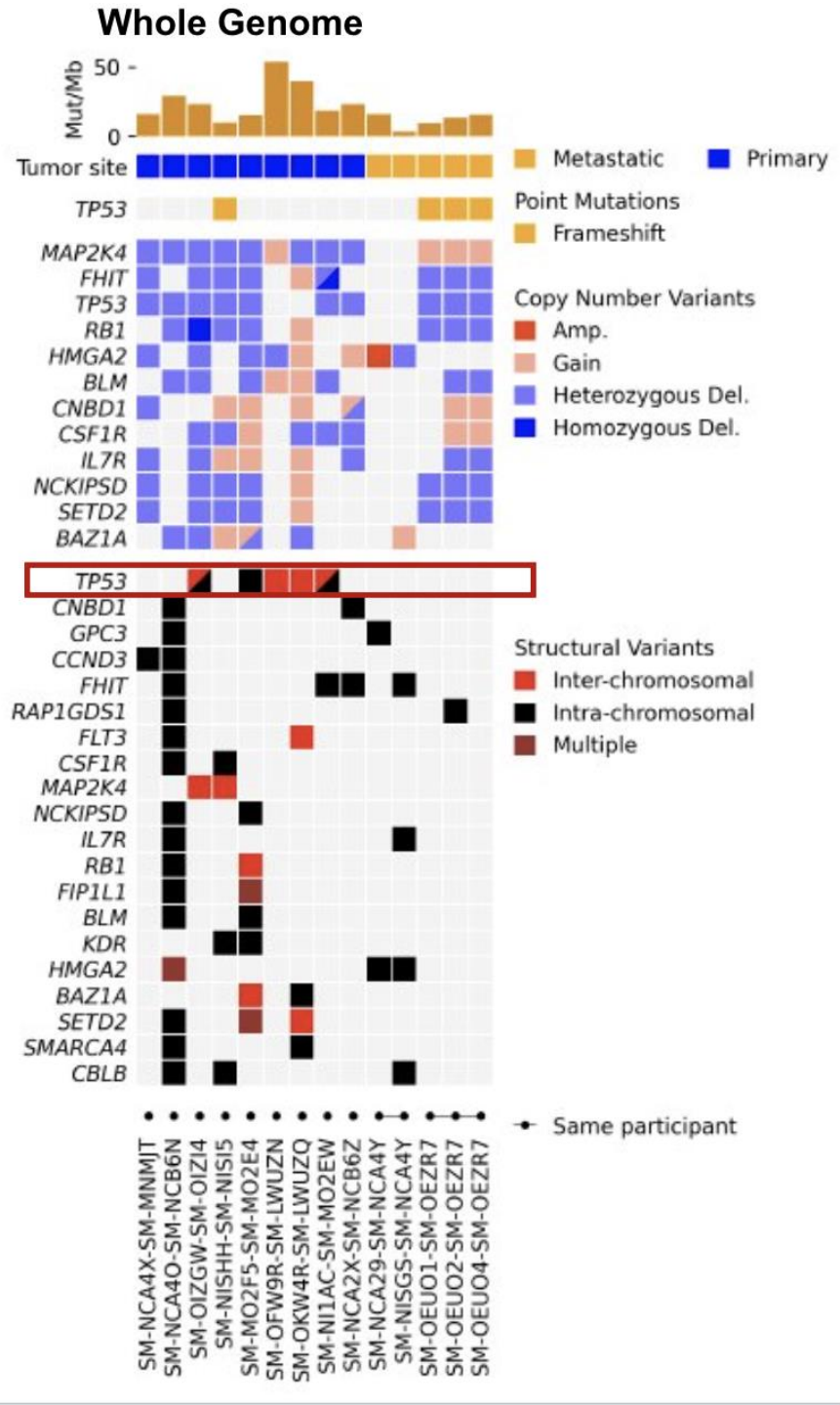
Tumor Samples	N = 27
Tumor timepoint, N (%) Diagnosis Recurrence Unk	 12 (44%) **15 (56%)** 0
Tumor sample site, N (%) Primary Metastatic	 14 (52%) **13 (48%)**

Expected variants identified









Germline Return of Results Case

- Female diagnosed with osteosarcoma of the distal femur at age 5 in 2016
  - Received MAP chemotherapy and local control with rotationplasty, alive, no recurrence
  - Saw a genetic counselor and had genetic testing: TP53 and APC without alterations
  - Consented to germline addendum, provided with Genome Medical information but had not made an appointment

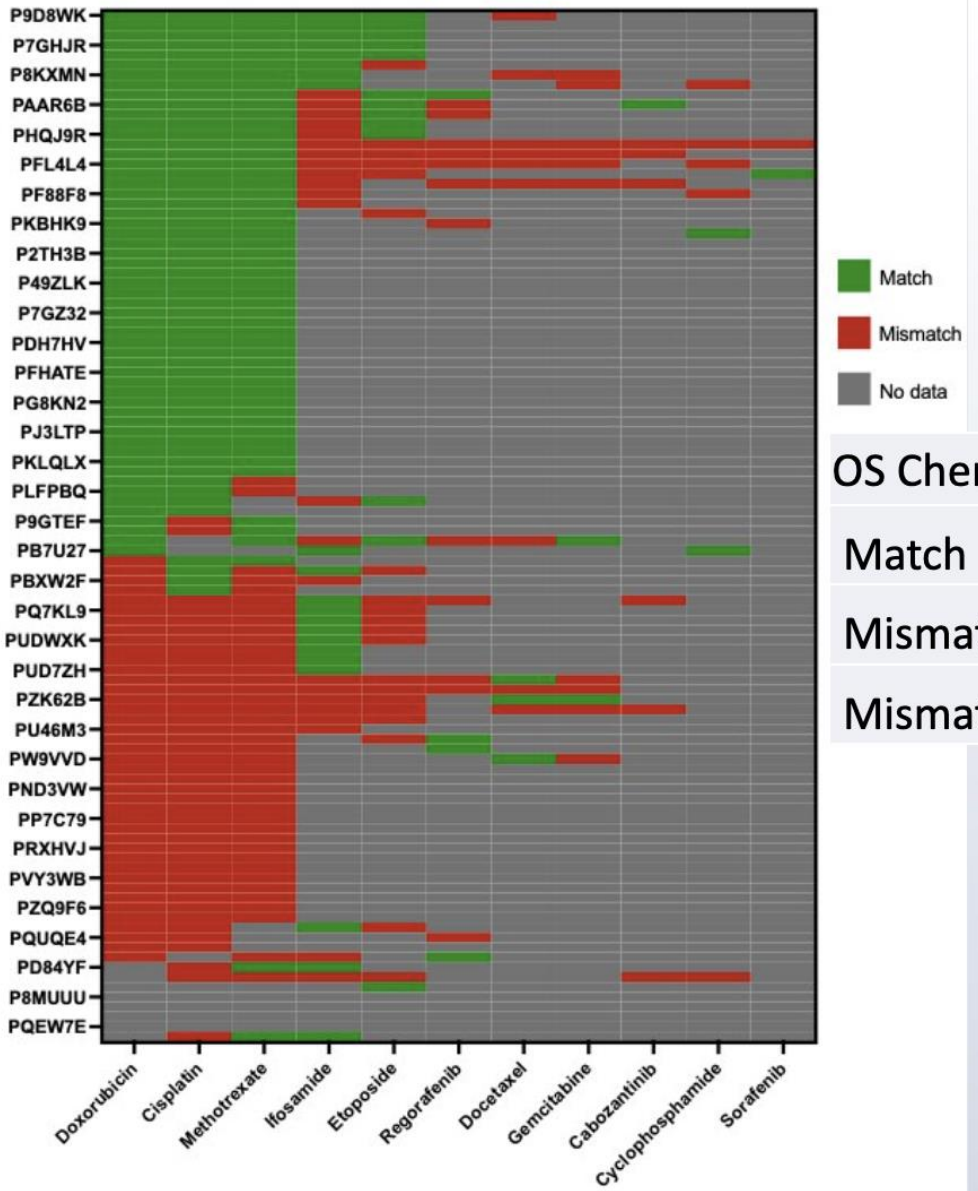
- Identified germline LoF variant on the germline clinical WES: NM_000059.4(BRCA2):c.7617+1G>A

  Classified as pathogenic in ClinVar with review by an expert panel→ **disruption of this splice site induces altered splicing; may result in an absent or disrupted protein product.**

- Issue: Broad pipeline not validated for RoR from germline but this finding has clinical significance
- Reminded participant about Genome Medical but no uptake
- Prospective deviation to return results from the paired germline WES from the Broad, IRB approved
- Study genetic counselor spoke with family, results provided, clinical testing recommended
  - Multiple attempts, including phone, mail and email required

Medical Record Review and Abstraction

- Medical record
  - Demographics
  - Baseline clinical features
  - Treatment
  - Outcome
  - Sample data
- Survey
  - Sites of disease
  - Recurrence
  - Treatment
  - Surgery



OS Chemotherapy Drugs Received (n=486)	
Match	221 (47.2%)
Mismatch (not in MR)	209 (44.7%)
Mismatch (not in survey)	38 (8.1%)

Future Work

- Study ramp-down
  - Funding ends August, 2025
  - End enrollment planned for 12/12/2025
  - Messaging and virtual enrollment event planned
  - Current estimates:
    - 330 enrolled
    - 175 tumors from 110 patients
    - 200 germline
    - 85% with clinical annotation
- Other components
  - Understanding genetic testing in family members
  - snRNASeq, spatial transcriptomics and proteomics (pending funding approval)
  - Innovation in ctDNA

Please signup (if you haven't already)

Scan the QR today, and help change the future of osteosarcoma.
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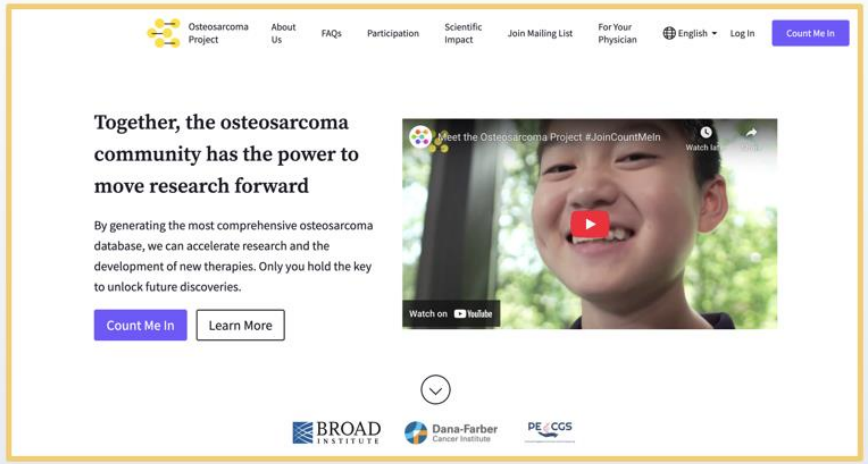

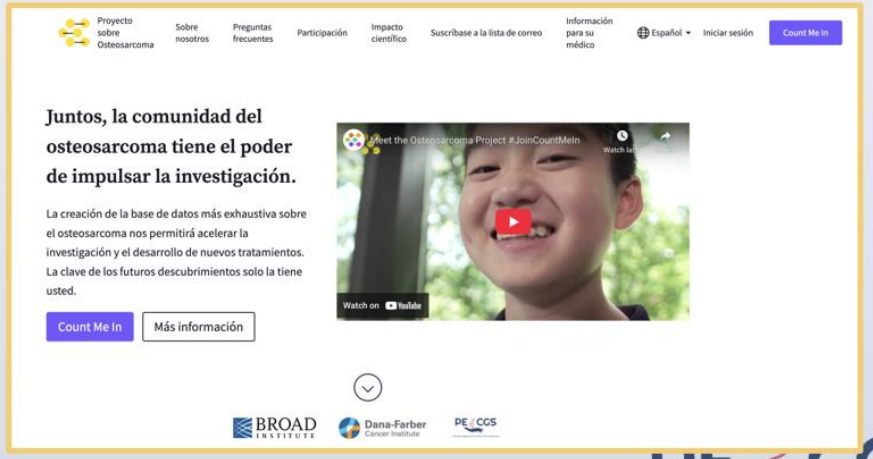

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Count Me In PE-CGS Center Team

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