CDRC
CURE DRUG REPURPOSING COLLABORATORY
CRITICAL PATH INSTITUTE

CURE ID
Challenging cases... New approaches

2023 CDRC
Annual Meeting

April 18 - 20

Agenda

CDRC Annual Meeting and Workshop Day 3: Thursday April 20 Morning

Utility of generating real-world data for assessing repurposed drugs in rare and ultrarare cancers.

Morning: closed door meetings

1.	CDRC Advisory Committee	8:30-10:00
2.	**BREAK**	10:00-10:15
3.	Session with FDA and NIH	10:15-11:45
4.	**LUNCH**	**12:00-1:00**

Welcome

Acknowledgments

Critical Path Institute is supported by the Food and Drug Administration (FDA) of the Department of Health and Human Services (HHS) and is 55% funded by the FDA/HHS, totaling $17,612,250, and 45% funded by non-government source(s), totaling $14,203,111. The contents are those of the author(s) and do not necessarily represent the official views of, nor an endorsement by, FDA/HHS or the U.S. Government.

Agenda

CDRC Annual Meeting and Workshop Day 3: Thursday April 18 Afternoon

Afternoon: Rare Cancer (Sarcomas)

Introductions and Welcome: Marco Schito (C-Path) 1:00-1:15

Chairs: Marco Schito (C-Path) William Tap (MSKCC)

1. Sarcoma: The Evolution of Care in Rare Cancer: Establishing a Comprehensive Unified Approach - **William Tap** (MSKCC) 1:15-1:45
2. The Role of Patient Advocates in Generating Real World Data in Ultra Rare Cancer - **Denise Robinson** (EHE Foundation) 1:45-2:00
3. An EHR-connected Patient-Centric Registry for Rare Cancer Research - **Mark Shapiro** (xCures) 2:00-2:15
4. Opportunities to Catalyze Impact in Rare Cancer Clinical Repurposing Trials - **Clare Thibodeaux** (Cures within Reach) 2:15-2:30
5. Repurposed Drug Trials: Challenges and Opportunities: **Vidula Sukhatme** (GlobalCures) 2:30-2:45

Break 2:45-3:00

Agenda

CDRC Annual Meeting and Workshop Day 3: Thursday April 18 Afternoon

Afternoon: Rare Cancer (Sarcomas)
Moderators: William Tap (MSKCC) and Marco Schito (C-Path)

1. Challenges and opportunities: **Marco Schito (C-Path)**
    - Harnessing RWD to advance repurposed drugs for rare cancers 3:00-3:15
2. Panel Discussion 3:15-3:45
    - **Brandi Felser** (SFA)
    - **Christine Heske** (NCI)
    - **Vidula Sukhatme** (GlobalCures)
    - **Andrea Gross** (NCI)
    - **Suanna Bruinooge** (ASCO)
    - **Lennie Woods** (Clear Cell Sarcoma Foundation)
3. Next steps 4:45-5:00
4. **Adjourn** **5:00**

Introduction and Welcome

Stacey Simpson Duke

June 4, 1971 - February 27, 2023

Stacey was vibrant, fierce, funny, creative, resilient, filled with life and love. She loved writing, teaching, preaching, knitting, running, singing, reading, improv, cooking, baking, and being a good friend and a great mom. She had a large online following. Stacey lived with stage-four cancer (leiomyosarcoma) for 6 years, and her many posts, honest and brave, about her experience with cancer were an inspiration to many. She leaves a legacy of countless people whose lives were deeply touched by her example, her faith, and her love.

Sarcoma: The Evolution of Care in Rare Cancer: Establishing a Comprehensive Unified Approach

William Tap

(Memorial Sloan Kettering Cancer Center)

William D. Tap, MD

Chief of the Sarcoma Medical Oncology Service, Memorial Sloan Kettering Cancer Center

William D. Tap, MD is the Chief of the Sarcoma Medical Oncology Service at Memorial Sloan Kettering Cancer Center in New York. Bill has extensive experience in translational medicine and is currently in charge of the clinical, basic science, and translational aspects of the Sarcoma Medical Oncology Program at MSKCC. He is also helping to develop a comprehensive Adolescent and Young Adult Caner Program at MSKCC. Bill received his Medical Degree from Jefferson Medical College in Philadelphia, PA and performed his residency in Internal Medicine at the Vanderbilt University Medical Center in Nashville, TN and his fellowship in Hematology and Medical Oncology at the UCLA Medical Center in Los Angeles, CA. Bill also has a tremendous interest in global health care initiatives and effecting health disparities in underserved areas in the US and abroad.

Sarcoma: The Evolution of Care in Rare Cancers: Establishing a Comprehensive Unified Approach

William Tap, MD

Chief, Sarcoma Medical Oncology Service

Co-Director – Lisa and Scott Stuart Center for Adolescent and Young Adult Cancer

Memorial Sloan Kettering Cancer Center

2023 CDRC Annual Meeting

April 20, 2023

Memorial Sloan Kettering Cancer Center

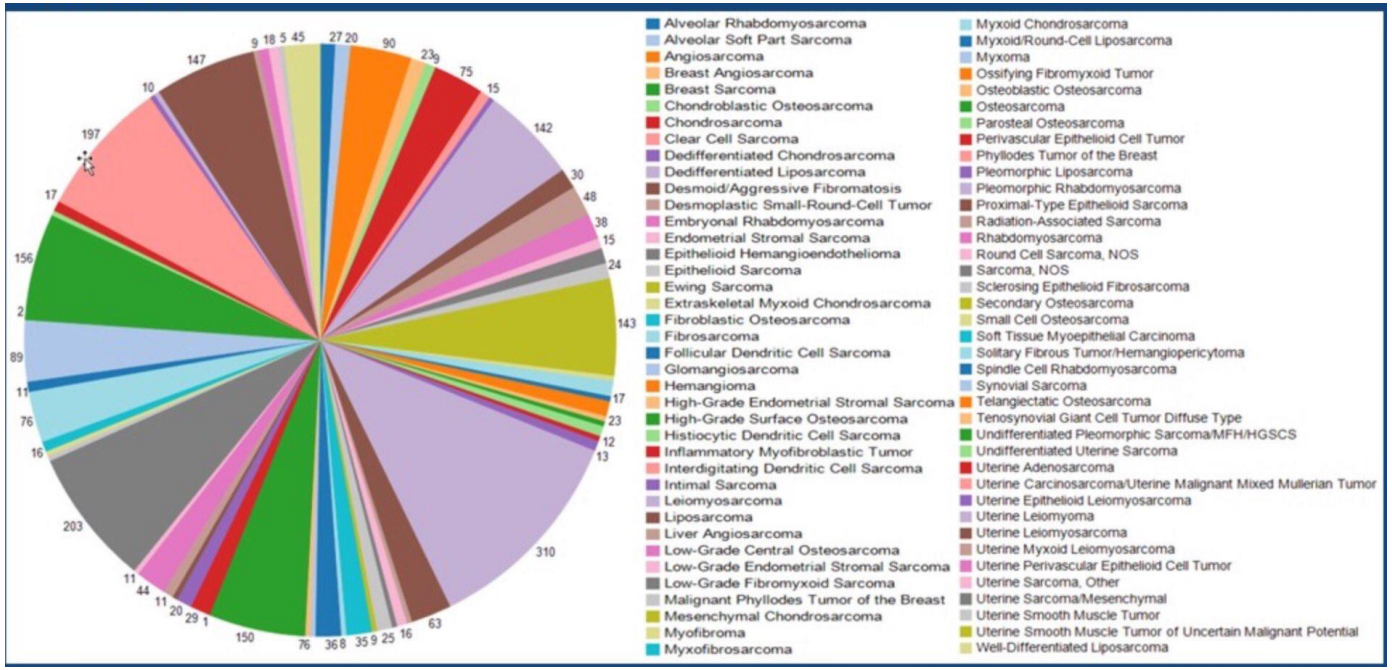
Disclosures

- I have the following financial relationships to disclose:
- Consulting for Eli Lilly, EMD Serono, Mundipharma, C4 Therapeutics, Daiichi Sankyo, Deciphera, Adcendo, Ayala, Kowa, Servier, Bayer, Epizyme, Cogent, Medpacto, Foghorn, Amgen, AmMax Bio, Boehringer Ingelheim, BioAtla, Inhibrx
- Advisory Board - Certis Oncology Solutions and Co-Founder - Atropos Therapeutics

Sarcoma: Mesenchymal Malignancies

Heterogeneous group of malignancies

- Arise from the bone and soft tissue of individuals of all ages
- 16,000 (?) new cases diagnosed in the United States per year
  - (similar to multiple myeloma, testicular cancer, esophageal cancer – well defined treatment strategies)
- 100 (?) different subtypes bone and soft tissue sarcoma



How to perform comprehensive drug development programs in rare and heterogeneous cancers

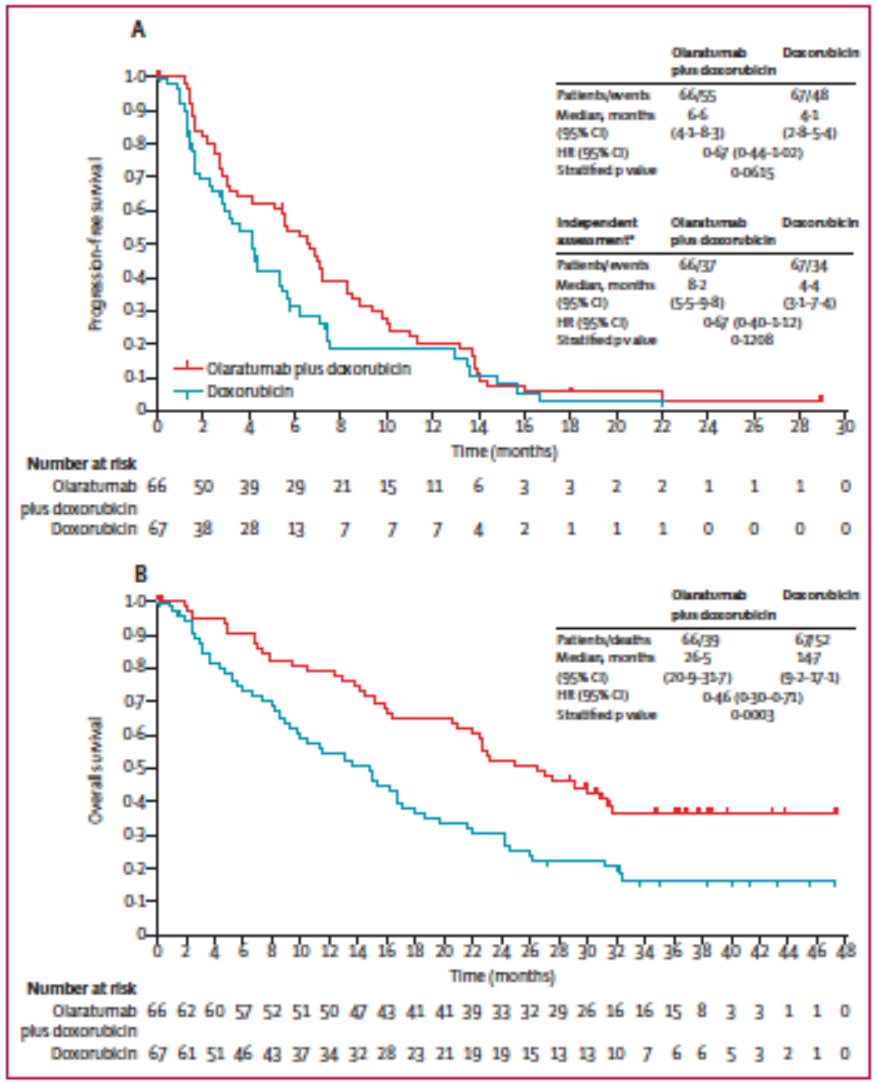
Memorial Sloan Kettering Cancer Center

Presented by: William Tap MSKCC

Olaratumab and doxorubicin versus doxorubicin alone for treatment of soft-tissue sarcoma: an open-label phase 1b and randomised phase 2 trial

Lancet 2016; 388: 488-97

Adriamycin 8 cycles (600mg/m2); Any line of treatment



PFS 4.2m vs 6.6m

OS 14.7m vs 26.5m

JAMA | Original Investigation

Effect of Doxorubicin Plus Olaratumab vs Doxorubicin Plus Placebo on Survival in Patients With Advanced Soft Tissue Sarcomas

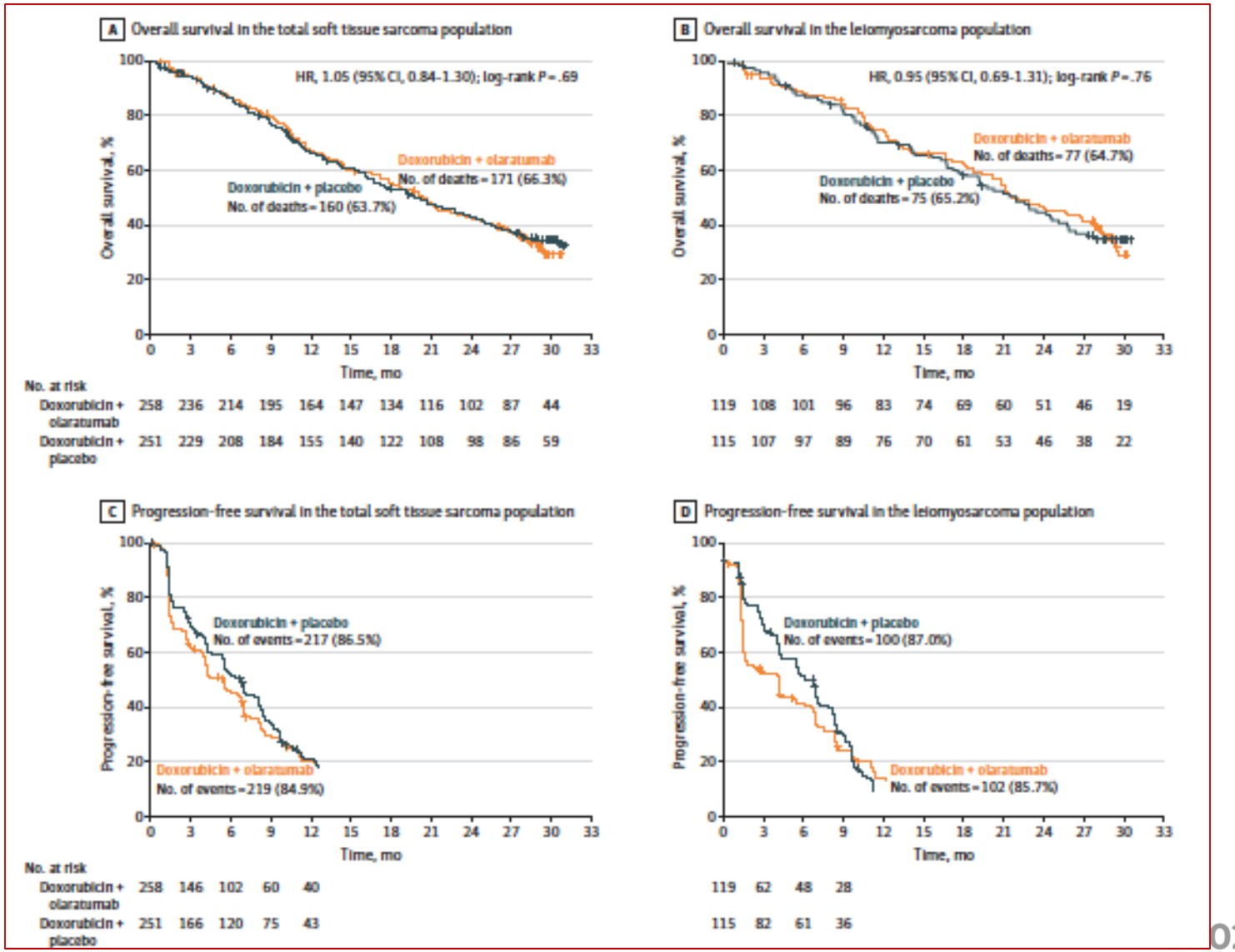
The ANNOUNCE Randomized Clinical Trial

JAMA. 2020;323(13):1266-1276.

Blinded/Placebo; OS primary endpoint
1st/2nd line stetting
Dual Primary endpoint (STS:LMS)
Olara maintenance component

624 patients
10 months

Characteristic	No. (%) Doxorubicin + olaratumab (n = 258)	Doxorubicin + placebo (n = 251)
Age, median (range), y	57.0 (23-84)	57.0 (20-82)
<65	180 (69.8)	180 (71.7)
≥65	78 (30.2)	71 (28.3)
Sex		
Male	114 (44.2)	99 (39.4)
Female	144 (55.8)	152 (60.6)
Race[a]		
White	186 (72.1)	193 (76.9)
Asian	50 (19.4)	48 (19.1)
Black or African American	12 (4.7)	2 (0.8)
Other[b]	10 (3.9)	8 (3.2)
Hispanic or Latino ethnicity[a]	26 (10.1)	29 (11.6)
Geographic region		
Europe	108 (41.9)	106 (42.2)
North America	88 (34.1)	85 (33.9)
Rest of the world	62 (24.0)	60 (23.9)
EGOG PS[c]		
0 (Capable of normal activity)	153 (59.3)	150 (59.8)
1 (Restricted in strenuous activity)	105 (40.7)	101 (40.2)
Histology		
Leiomyosarcoma	119 (46.1)	115 (45.8)
Liposarcoma	48 (18.6)	43 (17.1)
Pleomorphic sarcoma	34 (13.2)	30 (12.0)
Other[d]	57 (22.1)	63 (25.1)
Duration of disease, median (range), mo	11.3 (0-260)	11.8 (0-192)
Metastatic disease at randomization	216 (83.7)	206 (82.1)
Prior systemic therapies[e]	73 (28.3)	69 (27.5)
Neoadjuvant	1 (0.4)	1 (0.4)
Adjuvant	8 (3.1)	10 (4.0)
Locally advanced	14 (5.4)	9 (3.6)
Metastatic	59 (22.9)	54 (21.5)
Prior radiation therapy	87 (33.7)	85 (33.9)



OS 20.4 v 19.7
STS

OS 21.6 vs 21.9
LMS

PFS 5.4 v 6.8
STS

PFS 4.3 vs 6.9
LMS

Presented by: William Tap MSKCC

How Many Variable Confound a Clincial Trial

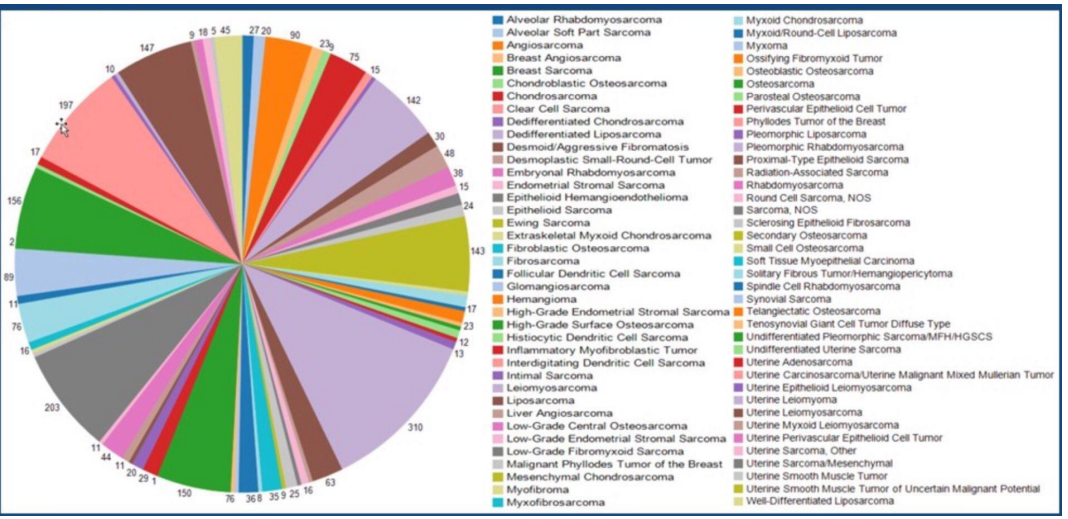
- 640 Randomized Participants
  Evofosfamide, Palifosfamide, Olaratumab, EORTC, Aldox, GeDDiS > 2000 randomized
- 40+ Disease Entities; Inter and Intra Subtype Variability
- Locally Advanced and Metastatic: Variations in clincial behavior
- 80-99 Sites Worldwide; 12+ countries
  Variations in Practice and Referral Patterns; Subsequent lines of therapy for each disease
- Inappropriate Trial Designs and Outcomes (Overall Survival)
- Lack of contemporary data sets and accurate historical controls
- ? Scientific rationale – poor understanding of MOA
- Lack of biomarkers and correlative science
- ? Pharmacodynamics

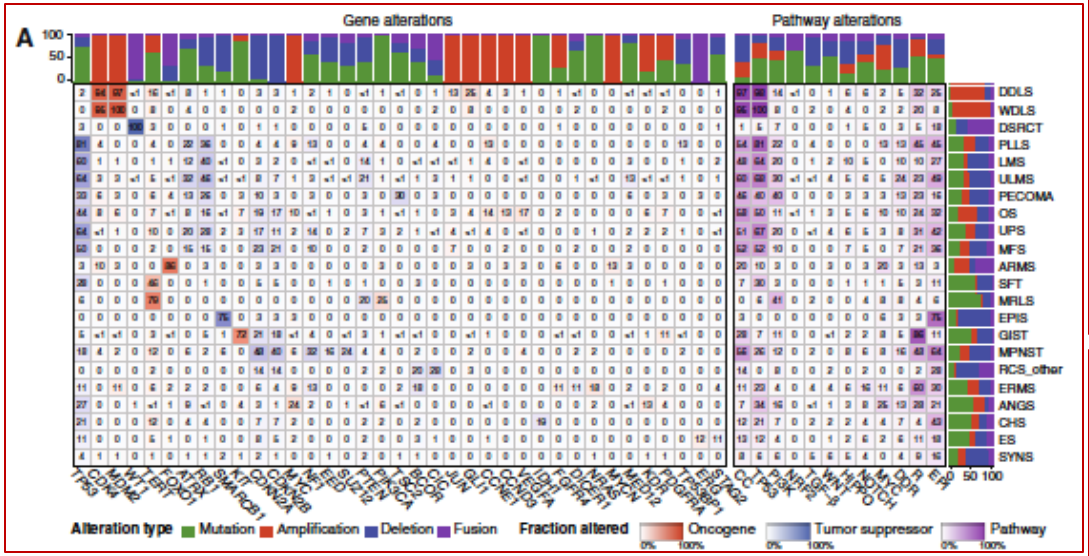
True numbers of comparable diseases (In P3; P2 vs P3)

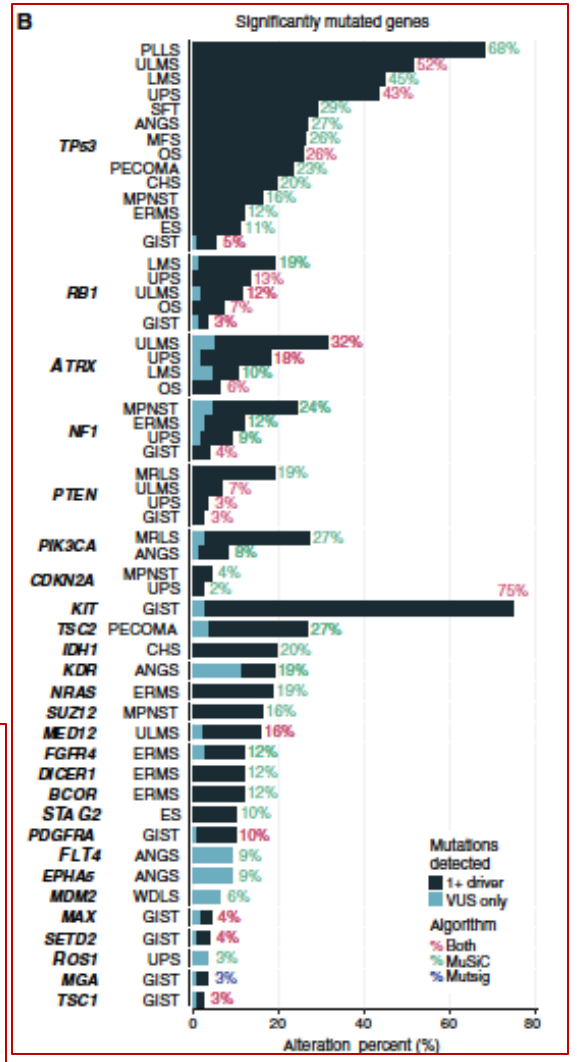
Studying different populations of those diseases in P1→ P2 → P3

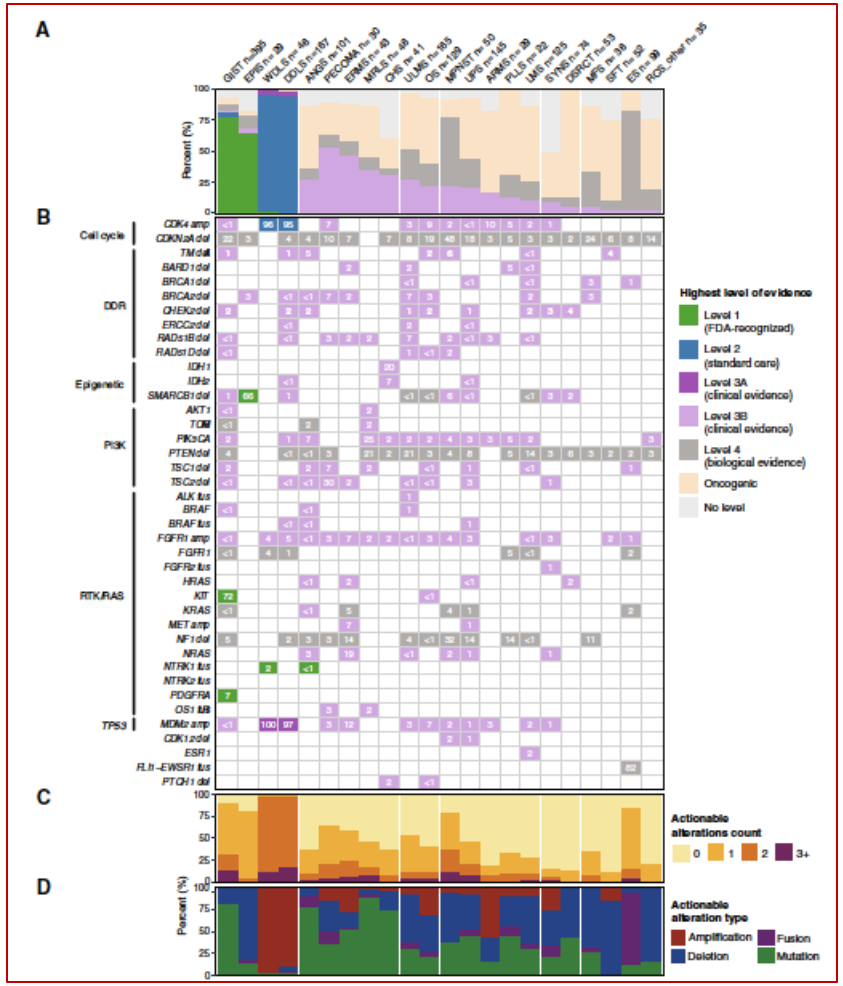
Presented by: William Tap MSKCC

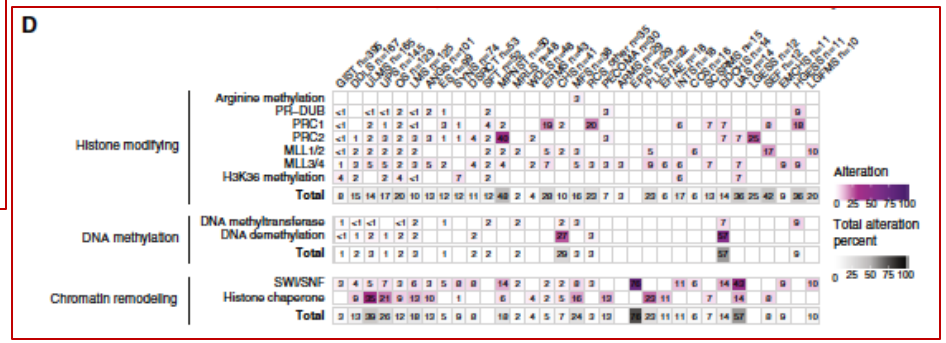
How Have We Adapted?

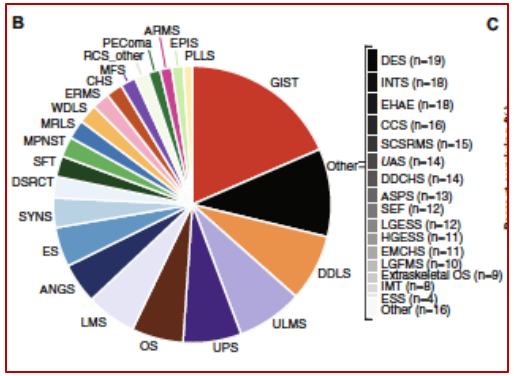












Presented by: William Tap MSKCC

Subtype Specific Clinical Trials

Understanding Ultra Rare Cancers

- Often new disease entities, recently genetically defined
- Natural history of the disease poorly understood/defined
- Genomic and clinical variability not described
- Clinical needs patient population need to be defined/measured
- Meaningful clinical and research outcome measures
- Unique features drug/technology need to be understood
- Unknown response or usage patterns for repurposed drugs

Refining Our Approach

- Early signal finding studies to pivotal efforts
- Appropriate outcomes measures
- Novel unique trial designs
- New drugs/technology – understanding of biology and MOA
- Understanding the science
- What is the correct long-term application
- Reliance on Pharma and discordant goals
- Unique Regulatory tracts
- Patient Centric

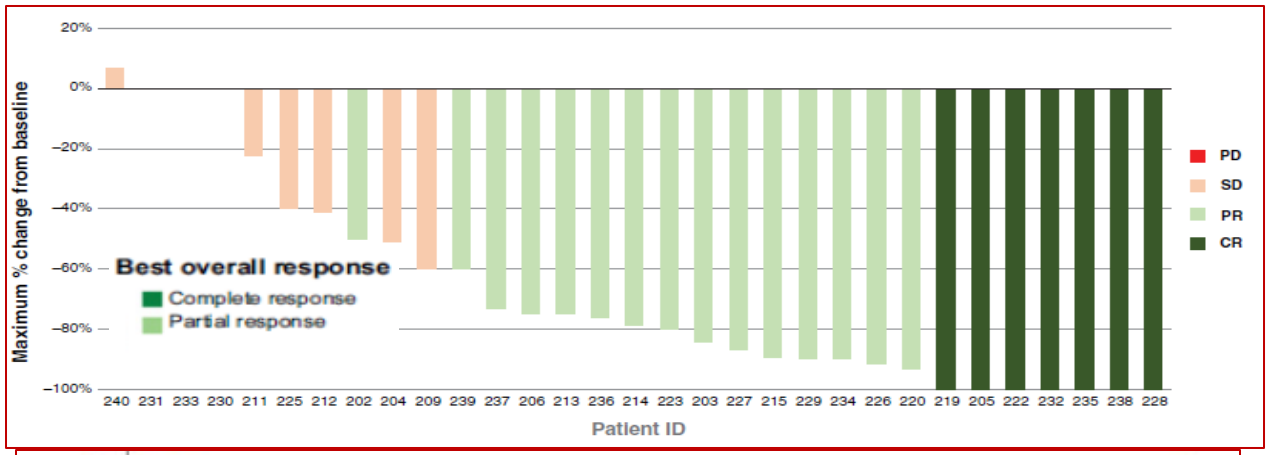
Presented by: William Tap MSKCC

ORIGINAL ARTICLE N Engl J Med 2015;373:428-37.

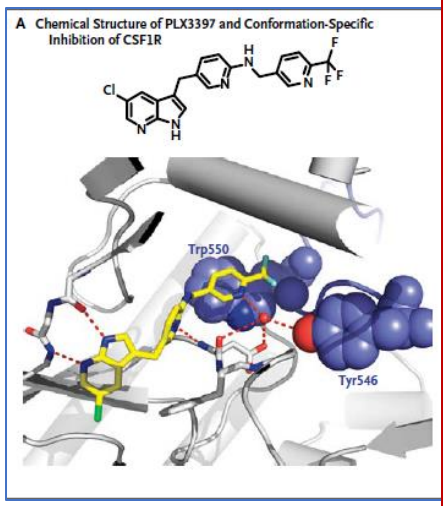
Structure-Guided Blockade of CSF1R Kinase in Tenosynovial Giant-Cell Tumor

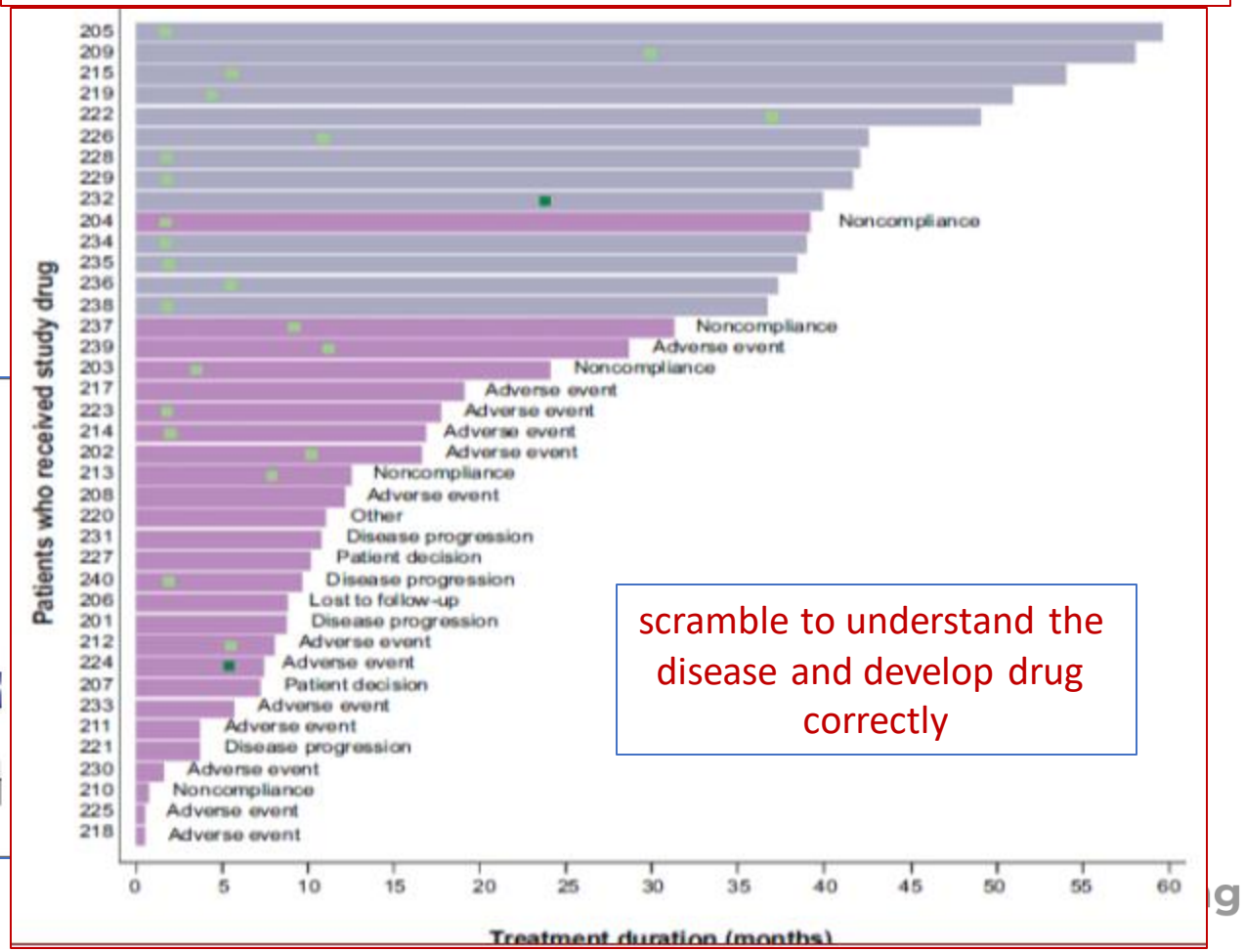
Part 2 Extension, six cohorts:

1) Mucoepidermal carcinoma salivary gland
2) Tenosynovial giant cell tumor
3) Gastrointestinal stromal tumor
4) Anaplastic thyroid carcinoma
5) Solid tumors with documented malignant pleural or peritoneal effusions, and
6) Miscellaneous tumor types, with scientific evidence supporting the involvement of CSF1R/KIT signaling in tumorigenesis



Tumor	Total treatment duration (days)	Best response
GIST	80	SD
GIST	111	SD
GIST	169	SD
GIST	345	SD
MEC	350	SD
Malignant effusion[a]	55	SD
Malignant effusion[b]	263	SD
Malignant effusion[c]	56	SD
Familial schwannomatosis	187	SD
Neurofibromatosis	199	SD
Neurofibromatosis	113	SD
ACC	57	SD
Mesothelioma	150	SD
Pancreatic neuroendocrine tumor	413	SD
Erdheim–Chester disease	494	PR
Mesothelioma	55	SD

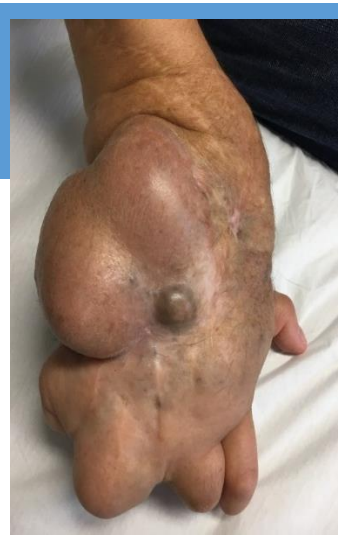




scramble to understand the disease and develop drug correctly

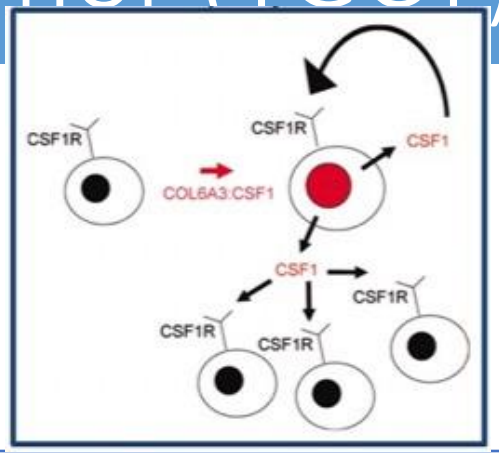
Clin Cancer Res; 28(2) January 15, 2022 PMID: 34713196

Tenosynovial Giant Cell Tumor (TGCT)



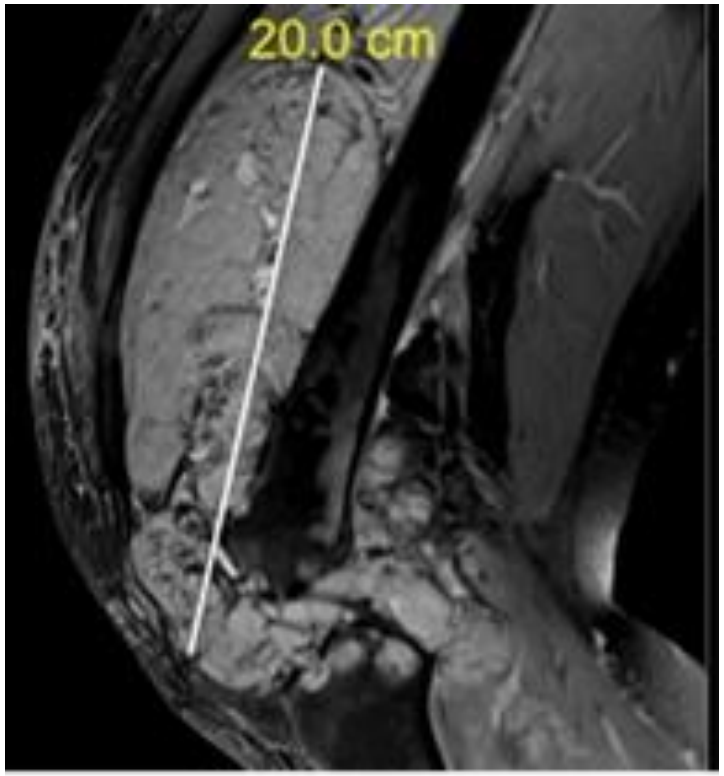
High Morbidity

- While usually not metastatic, disease is locally aggressive, and recurrence is common after surgical resection (particularly with Diffuse PVNS)
- Affects young & middle-aged adults of both sexes; no ethnic predisposition; patients are diagnosed in their 30s and 40s; and can live ~40years after diagnosis



Gross features:

- Collagen deposition
- Subchondral bone erosions
- Repeat hemarthrosis

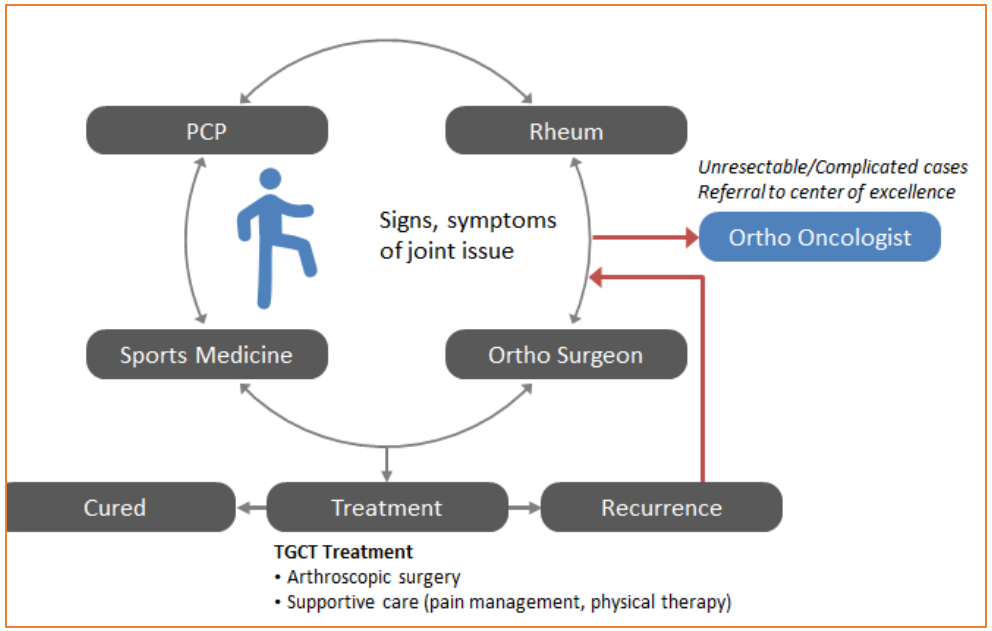


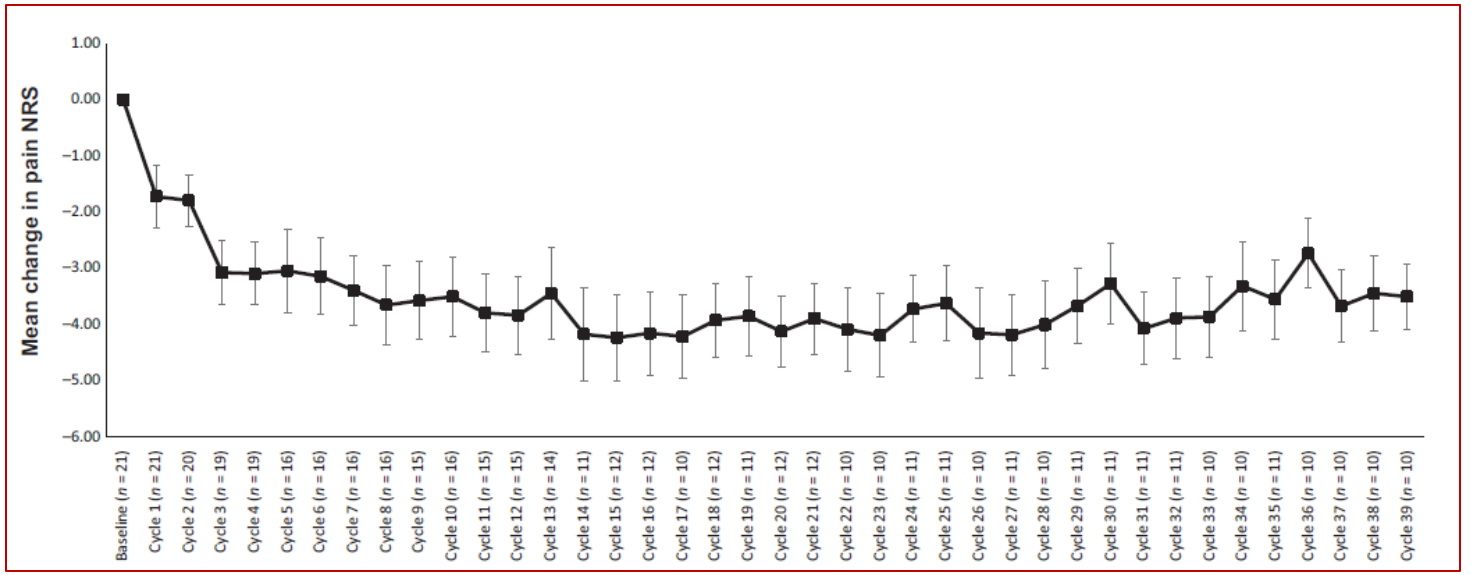
Clinical features:

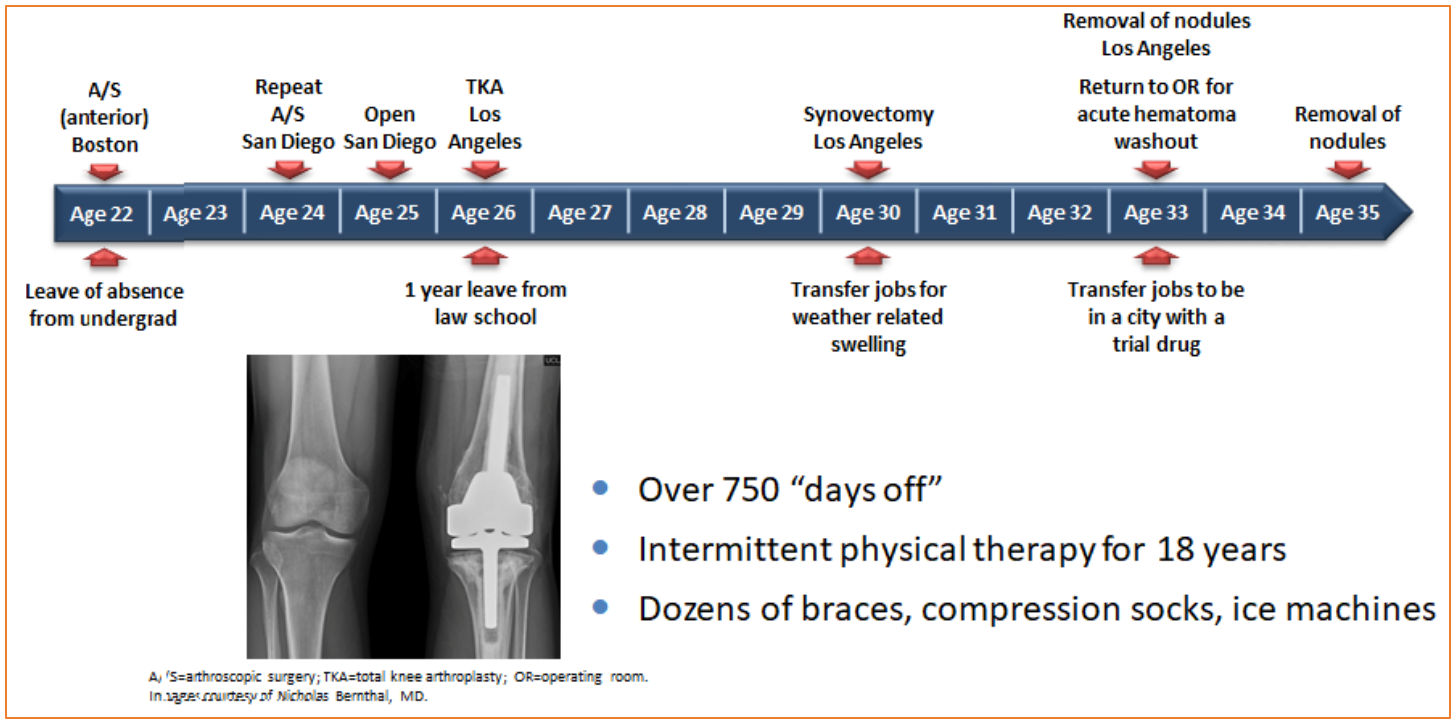
- Usually single joint:
  - Swelling
  - Pain
  - ↓ range of motion
  - Stiffness

- Functional impairment
- Narcotic use
- Disability

West, et al. (2006)
PNAS, USA 103, 690-695





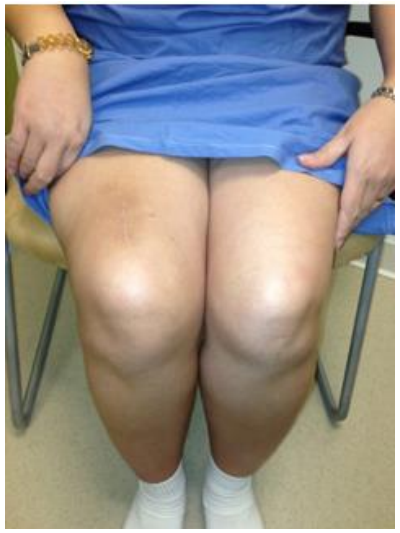


The measurement of physical functioning among patients with Tenosynovial Giant Cell Tumor (TGCT) using the Patient-Reported Outcomes Measurement Information System (PROMIS)

Journal of Patient-Reported Outcomes (2019) 3:6

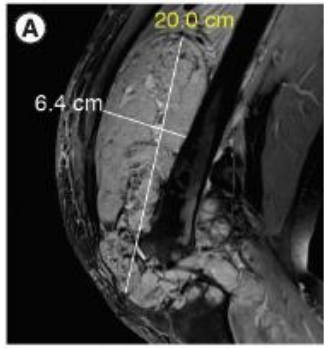
Clinical Therapeutics/Volume 8, Number 8, 2016

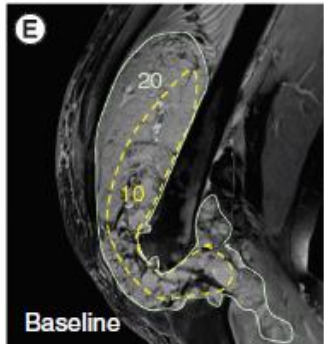
Patient-Reported Symptoms of Tenosynovial Giant Cell Tumors



CSF1 receptor inhibition of tenosynovial giant cell tumor using novel disease-specific MRI measures of tumor burden

Future Oncol. (2022) 18(12), 1449–1459

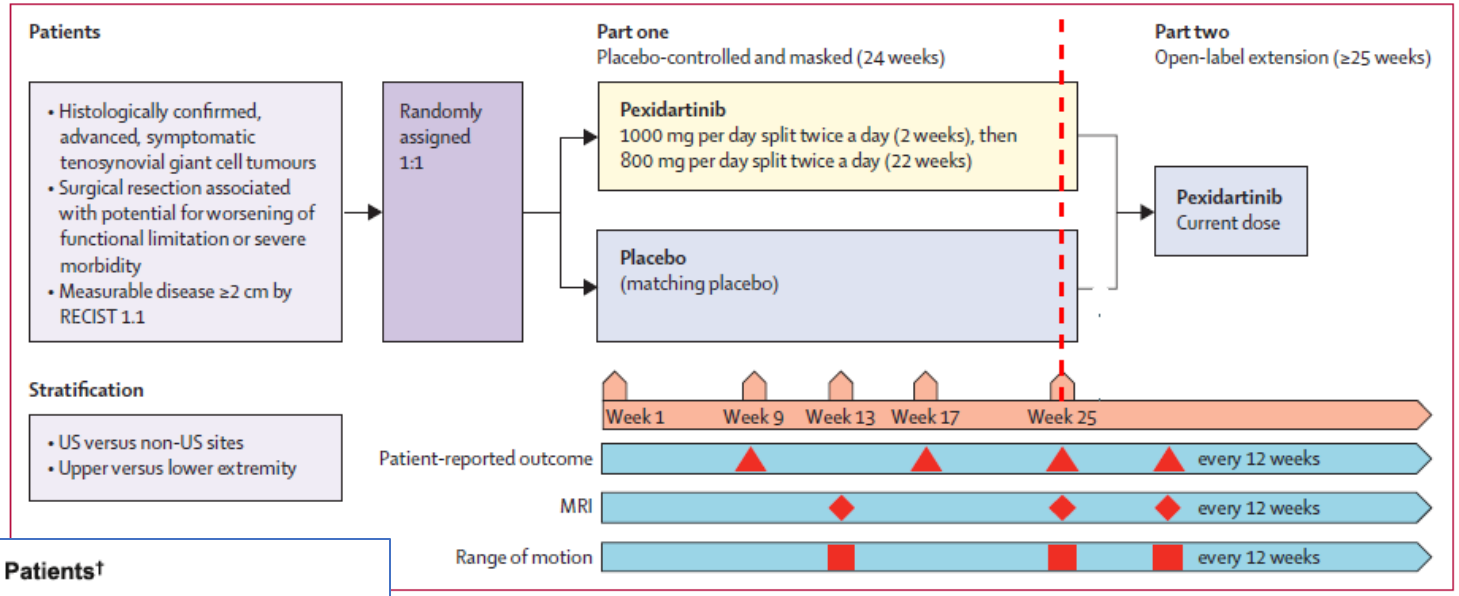


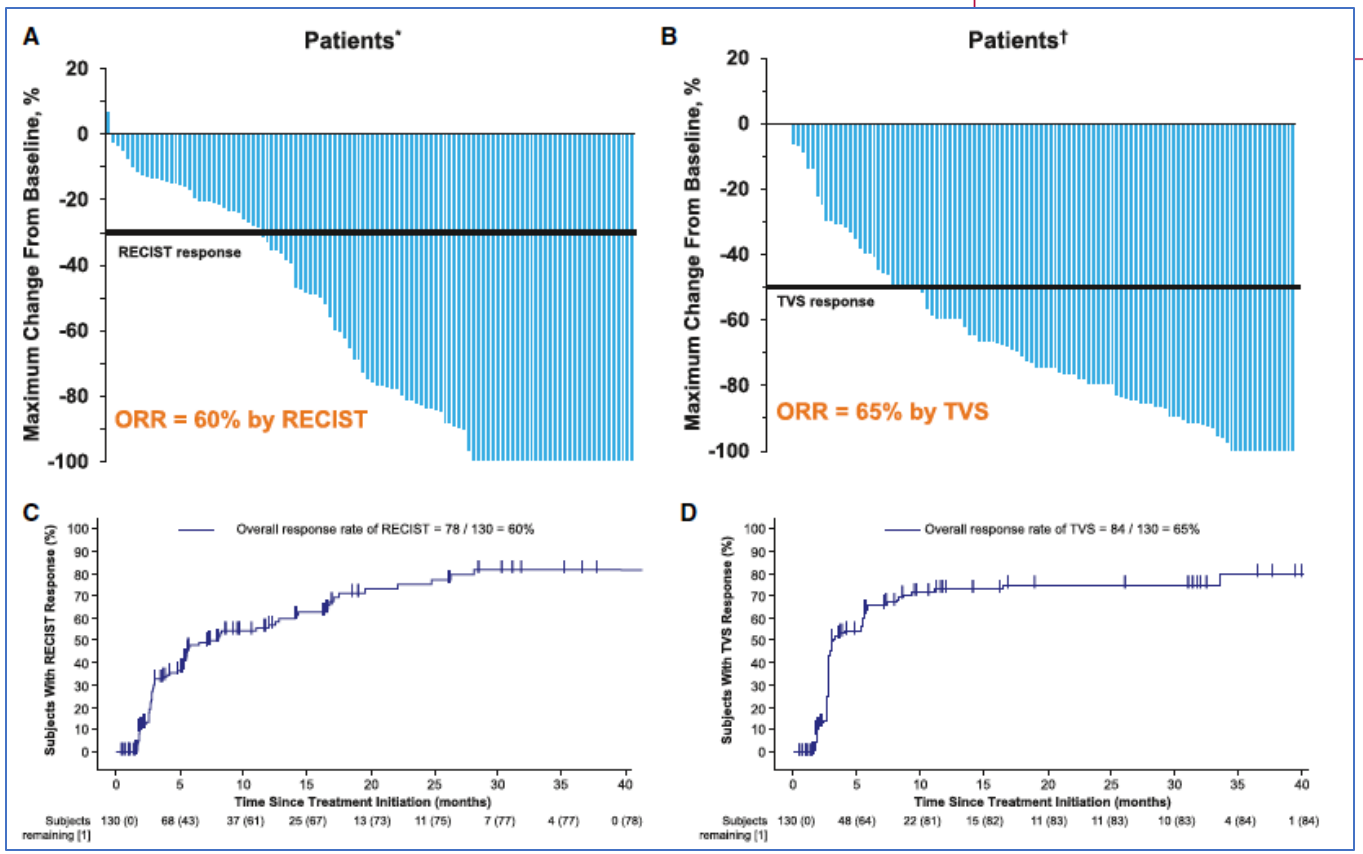


Pexidartinib versus placebo for advanced tenosynovial giant cell tumour (ENLIVEN): a randomised phase 3 trial

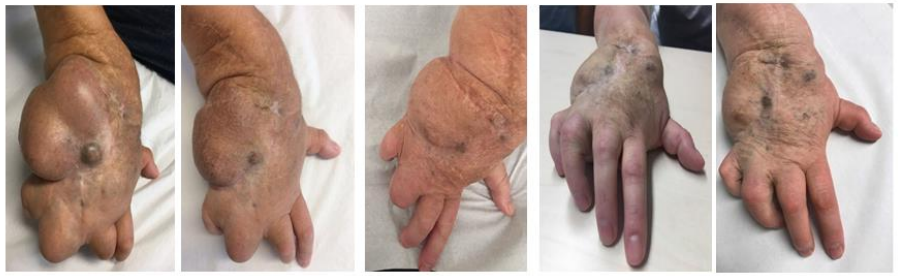
Lancet 2019; 394: 478–87

Need for Placebo?
Outcome assumptions?
Based on ORR P1





- 56-year-old female diagnosed w/TGCT Jun 10, 1988
- Multiple prior surgeries, regular RBC transfusions
- Started pexidartinib Sep 5, 2016, and still ongoing
- Baseline pain: 5.6, decreased to 0.6 at week 25



Data Missingness
Reordered endpoints
Rare but dangerous cholestatic hepatotoxicity
Vanishing Bile Duct Syndrome
ODAC and REMS

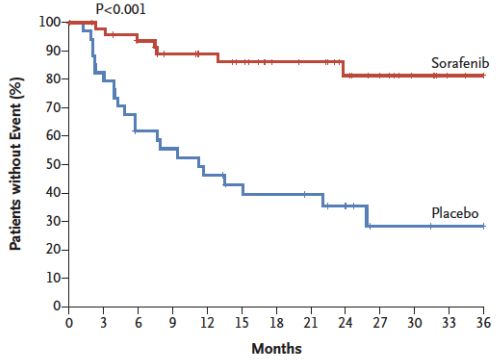
PMID: 33197285

Sorafenib for Advanced and Refractory Desmoid Tumors

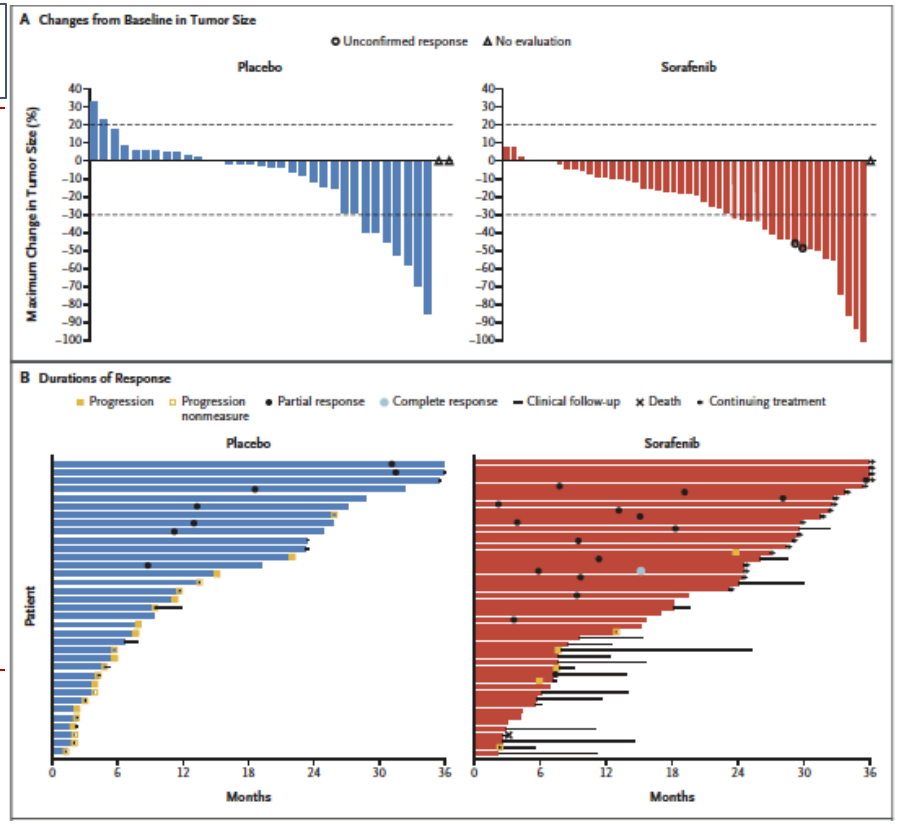
N ENGL J MED 379;25 NEJM.ORG DECEMBER 20, 2018

	No. of Patients	No. of Events	Median Progression-free Survival (95% CI)
			mo
Sorafenib	49	7	NE (NE–NE)
Placebo	35	22	11.3 (5.7–NE)

Hazard ratio for progression or death, 0.13 (95% CI, 0.05–0.31)
P<0.001



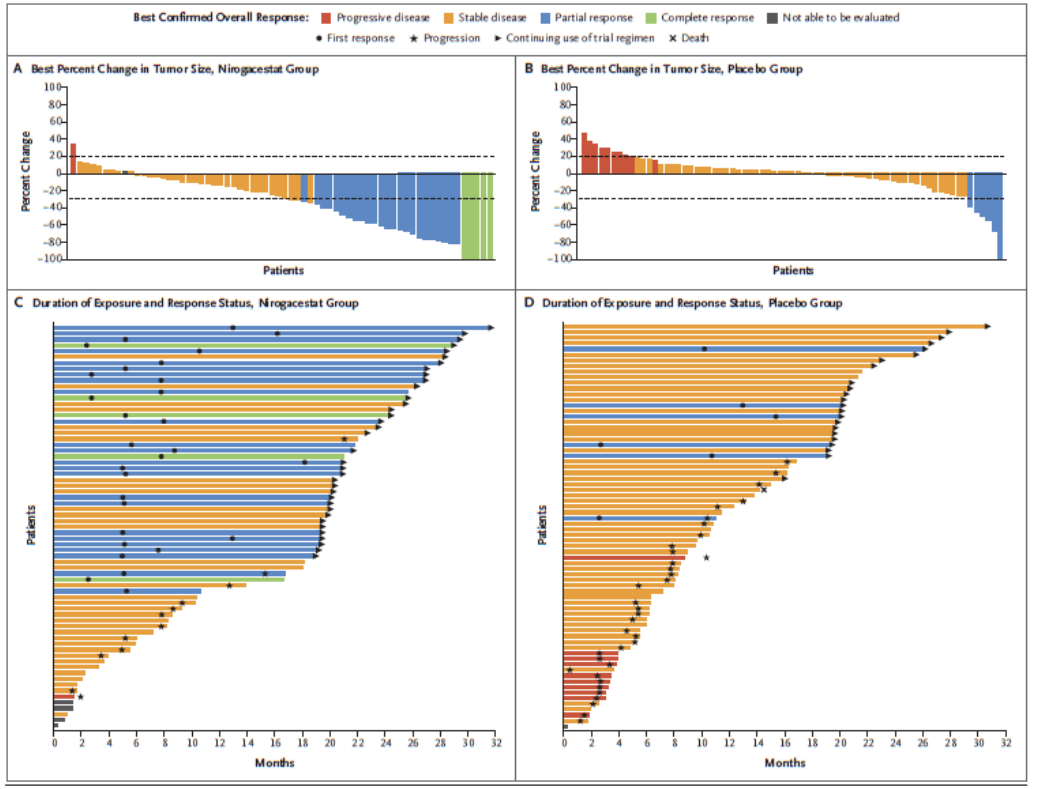
No. at Risk													
Sorafenib	49	46	41	36	32	29	23	22	17	14	8	4	3
Placebo	35	28	20	18	15	12	11	10	7	3	3	2	2

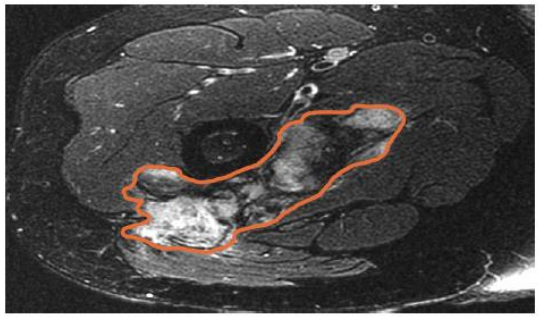


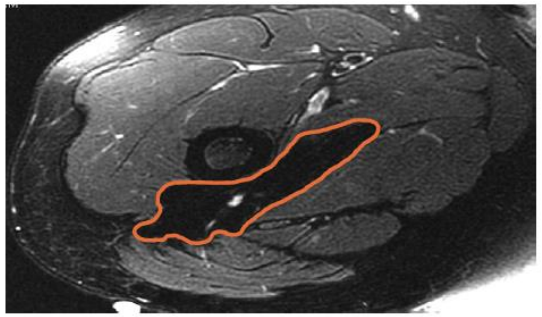
ORIGINAL ARTICLE

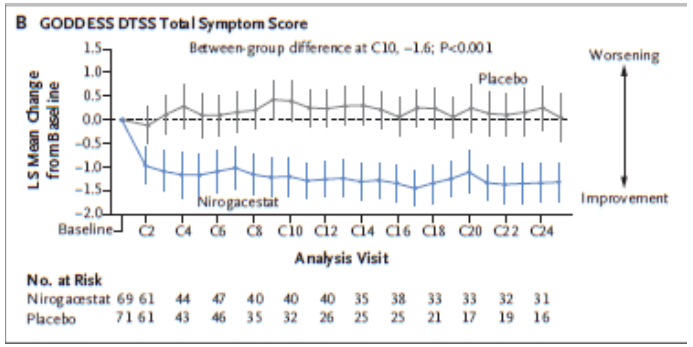
N Engl J Med 2023;388:898-912.

Nirogacestat, a γ-Secretase Inhibitor for Desmoid Tumors









No. at Risk													
Nirogacestat	69	61	44	47	40	40	40	35	38	33	33	32	31
Placebo	71	61	43	46	35	32	26	25	25	21	17	19	16

Prospective Development of a Patient-Reported Outcomes Instrument for Desmoid Tumors or Aggressive Fibromatosis

Cancer 2020;126:531-539.

Subtype Specific Approval

FDA Approved

Pexidartinib – TGCT

Olaratumab – here then gone

Avapritinib – PDGFRA GIST

Ripretinib – 4th line GIST

Tazemetostat – Epithelioid Sarcoma

Fyarro – PEComa

Atezolizumab – ASPS

Eribulin and Trabectedin – L sarcomas

Larotrectinib – NTRK Sarcomas

NCCN Compendium Listed

- Sorafenib – Desmoid Type Fibromatosis
- Checkpoint Inhibitors Angiosarcoma, DDLPS, UPS, TMB>10
- Pembro+ Axitinib – ASPS
- Palbociclib – DDLPS
- Ivosidenib – IDH1 Mutated Chondrosarcomas
- Selpercatinib – RET gene fused sarcomas
- Alectenib - IMT

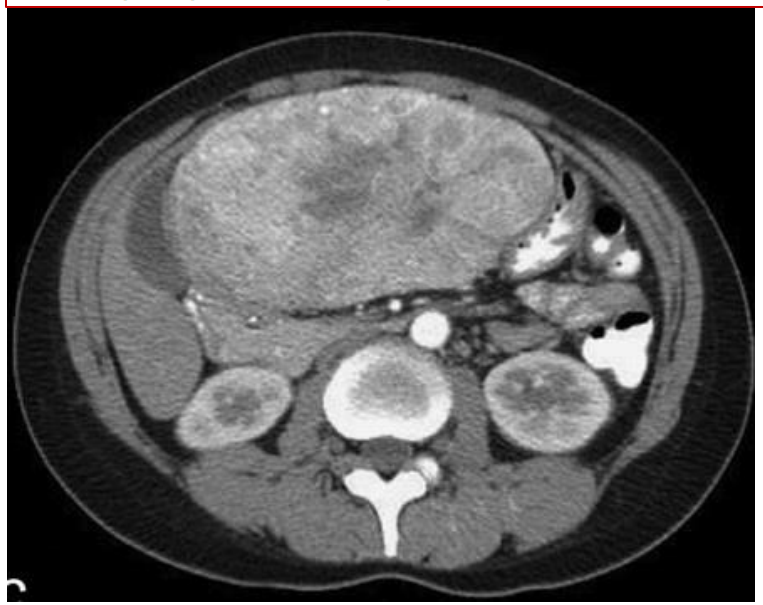
Presented by: William Tap MSKCC

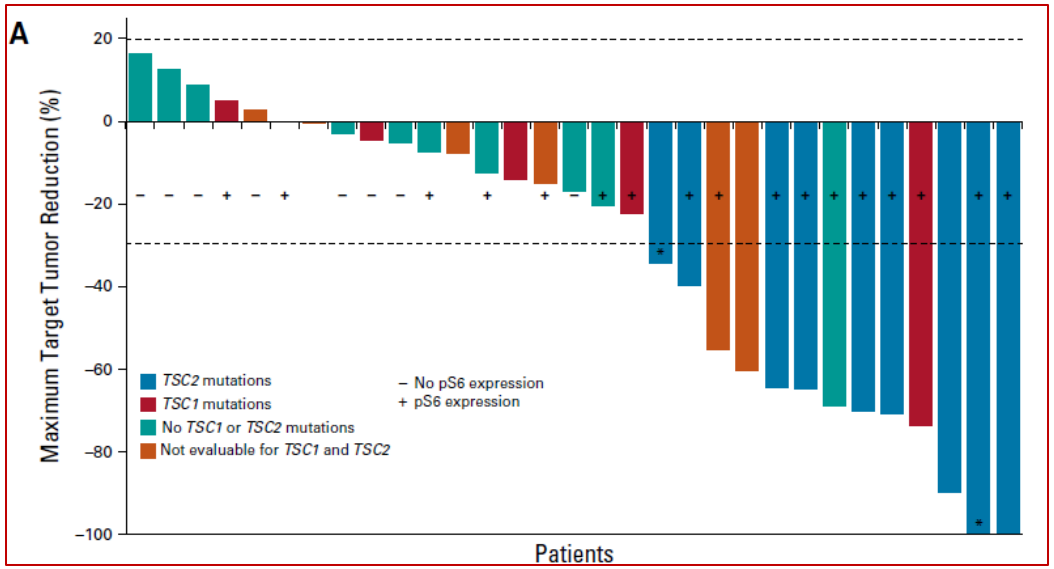
nab-Sirolimus for Patients With Malignant Perivascular Epithelioid Cell Tumors

J Clin Oncol 39:3660-3670. © 2021

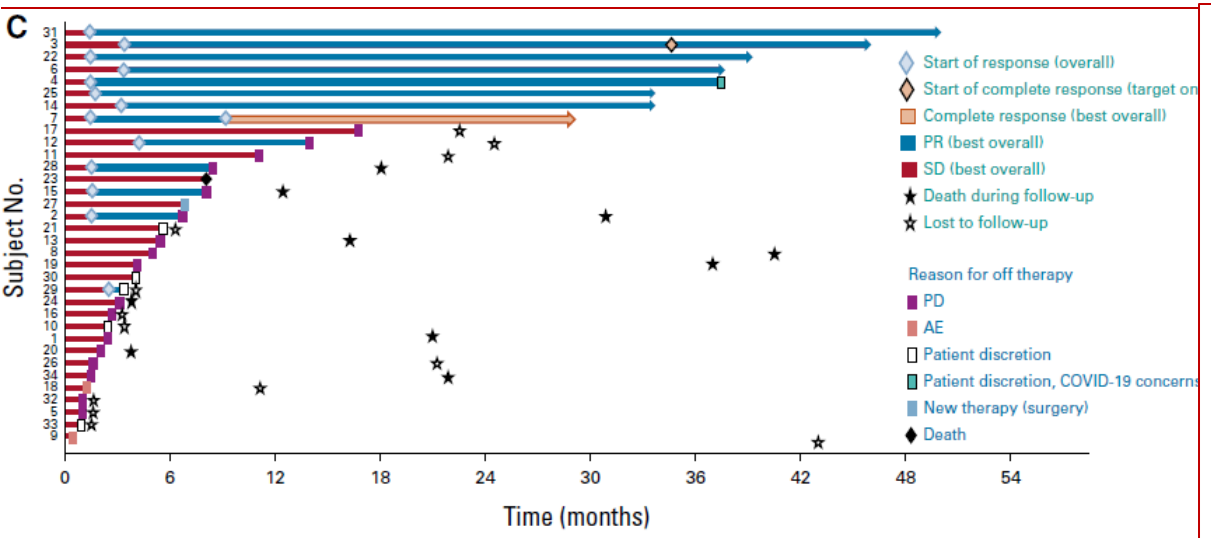
Andrew J. Wagner, MD, PhD[1]; Vinod Ravi, MD[2]; Richard F. Riedel, MD[3]; Kristen Ganjoo, MD[4]; Brian A. Van Tine, MD, PhD[5]; Rashmi Chugh, MD[6]; Lee Cranmer, MD, PhD[7]; Erlinda M. Gordon, MD[8]; Jason L. Hornick, MD, PhD[9]; Heng Du, MD[9]; Berta Grigorian, BS[10]; Anita N. Schmid, PhD[10]; Shihe Hou, PhD[10]; Katherine Harris, DrPH[10]; David J. Kwiatkowski, MD, PhD[9]; Neil P. Desai, PhD[10]; and Mark A. Dickson, MD[11]

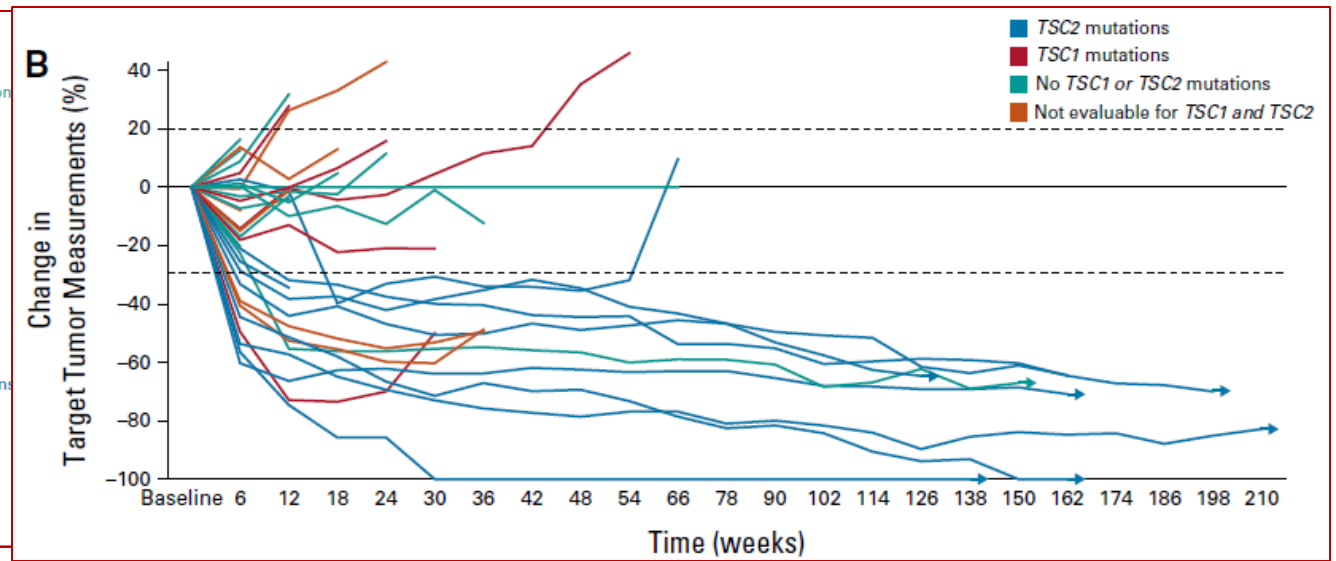
ORR 39%
mDOR NR (2.5 years f/u)
mPFS 10 months
mOS 40.8 months





Better than rapa?
Some response patterns?





The Future of Drug Development in RARE Cancers

- Strong Science and Rationale – to start or with early signals
- Early/Focused Development Strategies

  homogenous populations, deep understanding of genetic and clinical presentations for participants
- Clear understanding of the Natural History of the disease

  genomic and clincial variants, response patterns and outcomes
- Objective and Subjective measures of disease impact that is meaningful for our patients*
- Consensus trial designs – outcome measures and endpoints, PRO

  show appropriate impact and inform clincial usage
- Mirror designs and responsive diseases through clincial trial phases (P1→P2→P3)

  appropriate controls to identify signals and define diseases
- Biomarkers and patient selection
- Iterative Correlative work
- Collaboration

Presented by: William Tap MSKCC

Ultra-Rare Sarcomas: A Consensus Paper From the Connective Tissue Oncology Society Community of Experts on the Incidence Threshold and the List of Entities

Cancer
August 15, 2021

Silvia Stacchiotti, MD [1]; Anna Maria Frezza, MD [1]; Jean-Yves Blay, MD, PhD [2]; Elizabeth H. Baldini, MD[3]; Sylvie Bonvalot, MD, PhD [4]; Judith V. M. G. Bovée, MD, PhD[5]; Dario Callegaro, MD [6]; Paolo G. Casali, MD[1];

Epithelioid hemangioendothelioma, an ultra-rare cancer: a consensus paper from the community of experts

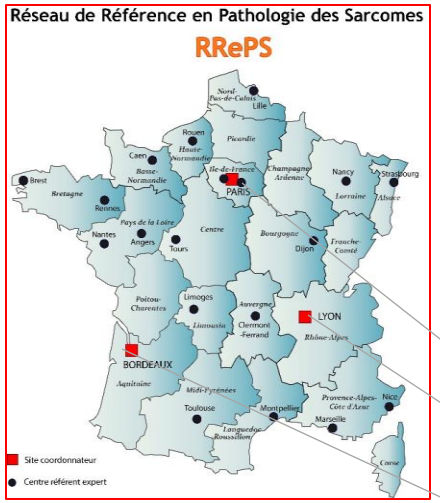
ESMO OPEN CANCER HORIZONS Volume 6 ■ Issue 3 ■ 2021

S. Stacchiotti[1*], A. B. Miah[2], A. M. Frezza[1], C. Messiou[3], C. Morosi[4], A. Caraceni[5], C. R. Antonescu[6], J. Bajpai[7], E. Baldini[8], S. Bauer[9], R. Biagini[10], S. Bielack[11], J. Y. Blay[12], S. Bonvalot[13], I. Boukovinas[14], J. V. M. G. Bovee[15], K. Boye[16], T. Brodowicz[17], D. Callegaro[18], E. De Alava[19,20], M. Deoras-Sutliff[21], A. Dufresne[12], M. Eriksson[22], C. Errani[23], A. Fedenko[24], V. Ferraresi[25], A. Ferrari[26], C. D. M. Fletcher[27], X. Garcia del Muro[28], H. Gelderblom[29], R
J. Gutkovich[21,33], R. Haas[34,35], N. Hindi[36], P. Hohenberger[37], P. Huang[38], H. J
A. Kawai[43], A. Le Cesne[44], F. Le Grange[45], A. Leithner[46], H. Leonard[47], A. L
P. Merriam[51], R. Miceli[52], O. Mir[53], M. Molinari[54], M. Montemurro[55], G.
S. Patel[59], S. Piperno-Neumann[60], C. P. Raut[61,62,63], V. Ravi[59], A. R. A. Razal
A. A. Safwat[68], C. Sangalli[69], G. Sapisochin[70], M. Sbaraglia[71], S. Scheipl[72],
K. Sundby Hall[16], W. D. Tap[76], A. Trama[77], A. Tweddle[78], W. T. A. van der Gr
G. van Oortmerssen[82], A. J. Wagner[51], M. Wartenberg[83], J. Wood[84], N. Za
A. P. Dei Tos[71] & A. Gronchi[18]

Retrospective observational studies in ultra-rare sarcomas: A consensus paper from the Connective Tissue Oncology Society (CTOS) community of experts on the minimum requirements for the evaluation of activity of systemic treatments

Cancer Treatment Reviews 110 (2022) 102455

Silvia Stacchiotti [a,*], Anna Maria Frezza [a], George D. Demetri [b], Jean-Yves Blay [c], Jyoti Bajpai [d], Giacomo G. Baldi [e], Elizabeth H. Baldini [f], Robert S. Benjamin [g], Sylvie Bonvalot [h], Judith V.M. G. Bovée [i], Dario Callegaro [j], Paolo G. Casali [a], Sandra P. D'Angelo [k], Elizabeth J. Davis [l], Angelo P. Dei Tos [m], Elizabeth G. Demicco [n], Jayesh Desai [o], Palma Dileo [p], Mikael Eriksson [q], Hans Gelderblom [r], Suzanne George [b], Rebecca A. Gladdy [s], Mrinal M. Gounder [k], Abha A. Gupta [t], Rick Haas [u], Andrea Hayes [v], Peter Hohenberger [w], Kevin B. Jones [x], Robin L. Jones [y], Bernd Kasper [z], Akira Kawai [aa], David G. Kirsch [ab], Eugenie S. Kleinerman [ac], Axel Le Cesne [ad], Roberta Maestro [ae], Javier Martin Broto [af], Robert G. Maki [ag], Aisha B. Miah [ah], Emanuela Palmerini [ai], Shreaskumar R. Patel [g], Chandrajit P. Raut [aj], Albiruni R.A. Razak [ak], Damon R. Reed [al], Piotr Rutkowski [am], Roberta G. Sanfilippo [a], Marta Sbaraglia [m], Inga-Marie Schaefer [an], Dirk C. Strauss [ao], Sandra J. Strauss [p], William D. Tap [k], David M. Thomas [ap], Annalisa Trama [aq], Jonathan C. Trent [ar], Winette T.A. van der Graaf [as], Winan J. van Houdt [at], Margaret von Mehren [au], Breelyn A. Wilky [av], Christopher D.M. Fletcher [an], Alessandro Gronchi [j], Rosalba Miceli [aw], Andrew J. Wagner [b]



Community

Treatment Community

Community

Patient Registry

HOSPITAL

HOSPITAL

Academic Consultation

Path Review

Surgery

Path Review

Accurate and Complete History

IIT Trial Database

Oncological Care

Specialty Service

Supportive Care

Images

Medications

Primary Care

Labs

Hospital Care

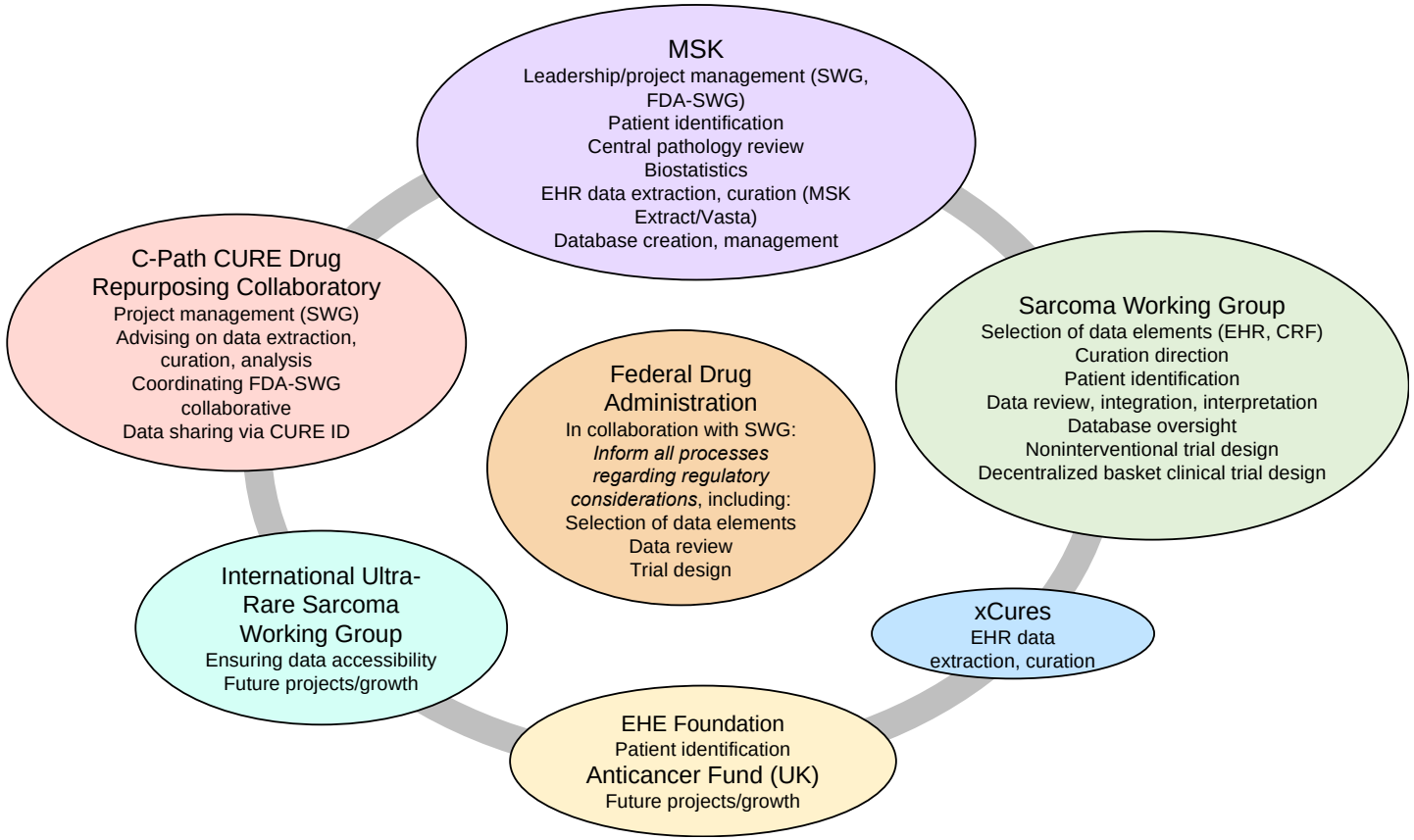
Path/ Genetics

Comprehensive Data Extraction

RWD; Nat Hx clinical and genetic variants; RWE response

Presented by: William Tap MSKCC

Using RWD from EHRs to define the natural history, identify repurposed drugs, and optimize innovative non-interventional and interventional studies in ultra-rare sarcomas



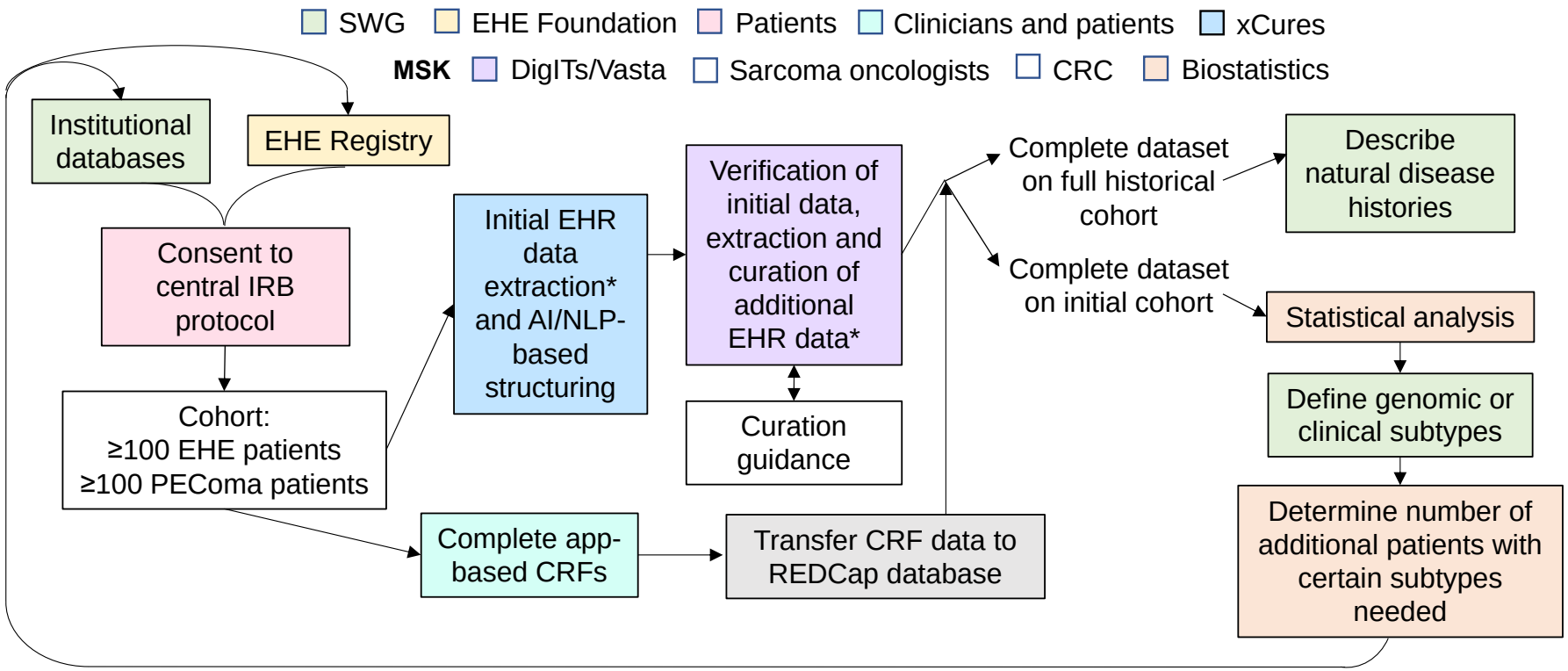
Presented by: William Tap MSKCC

Aim 1. Establish a mechanism for complete data collection from multiple sources to establish a comprehensive clinical profile of an ultra-rare cancer, using EHE and PEComa as first examples.

1a. Develop a comprehensive algorithm for extracting data from EHRs in diverse clinical settings

1b. Establish the natural history of each URS by combining individual patient courses.

1c. Create a federated database system to facilitate international access for research purposes.

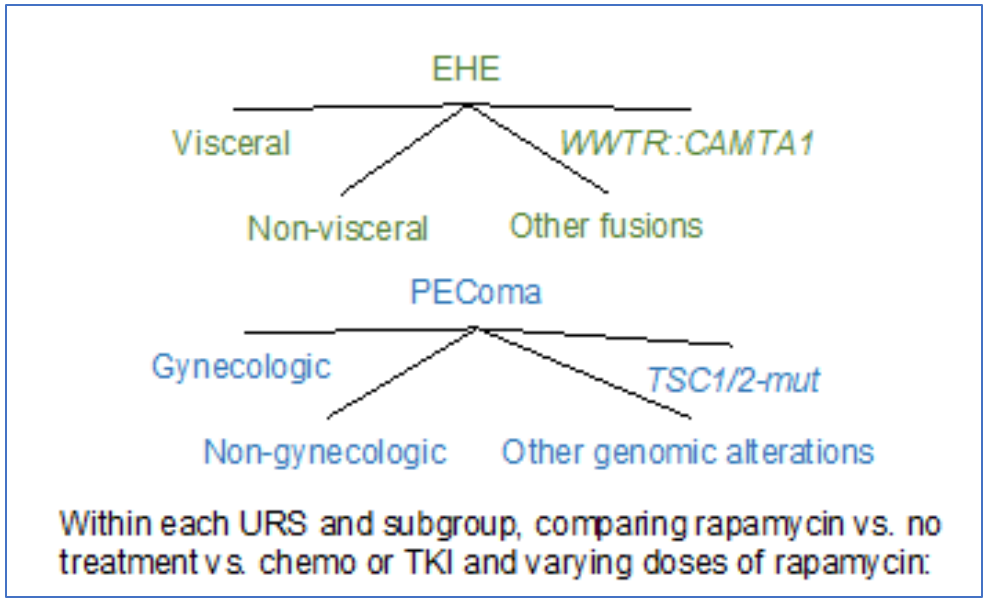


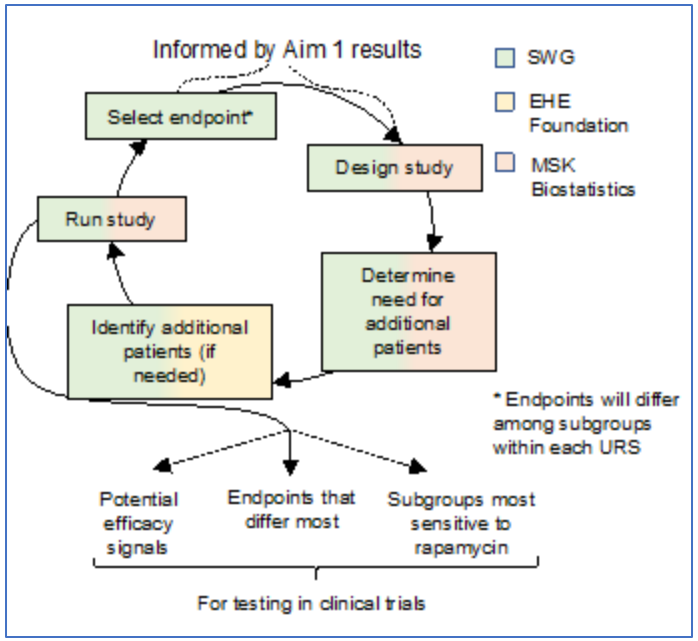
Aim 2. Establish a model for non-interventional clinical trials in ultra-rare cancers, evaluating rapamycin in EHE and PEComa as first examples.

2a. Create a comprehensive historical control dataset on the outcomes of the most common treatments

2b. Develop a comprehensive approach for performing non-interventional trials in URCs

2c. Develop drug-specific dataset + correlative database to inform regulatory interactions and clinical trials.



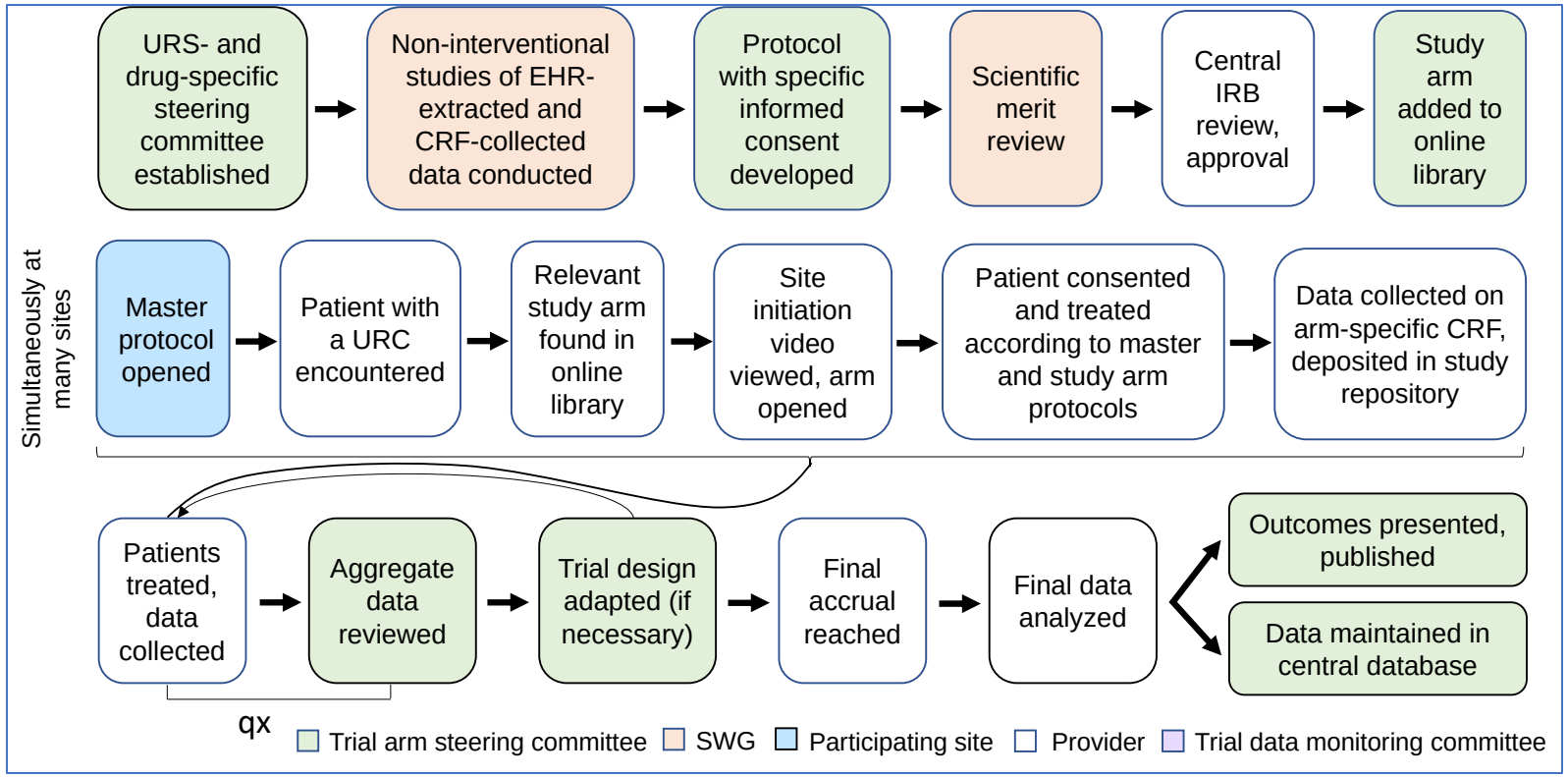


Aim 3. Establish a model for multidisciplinary collaboration with the FDA for ultra-rare cancers and develop a comprehensive, decentralized, adaptive basket clinical trial for URS.

3a. Establish an FDA-SWG collaborative team.

3b. Evaluate historical + non-interventional clinical trial data to shape data collection and analysis strategies

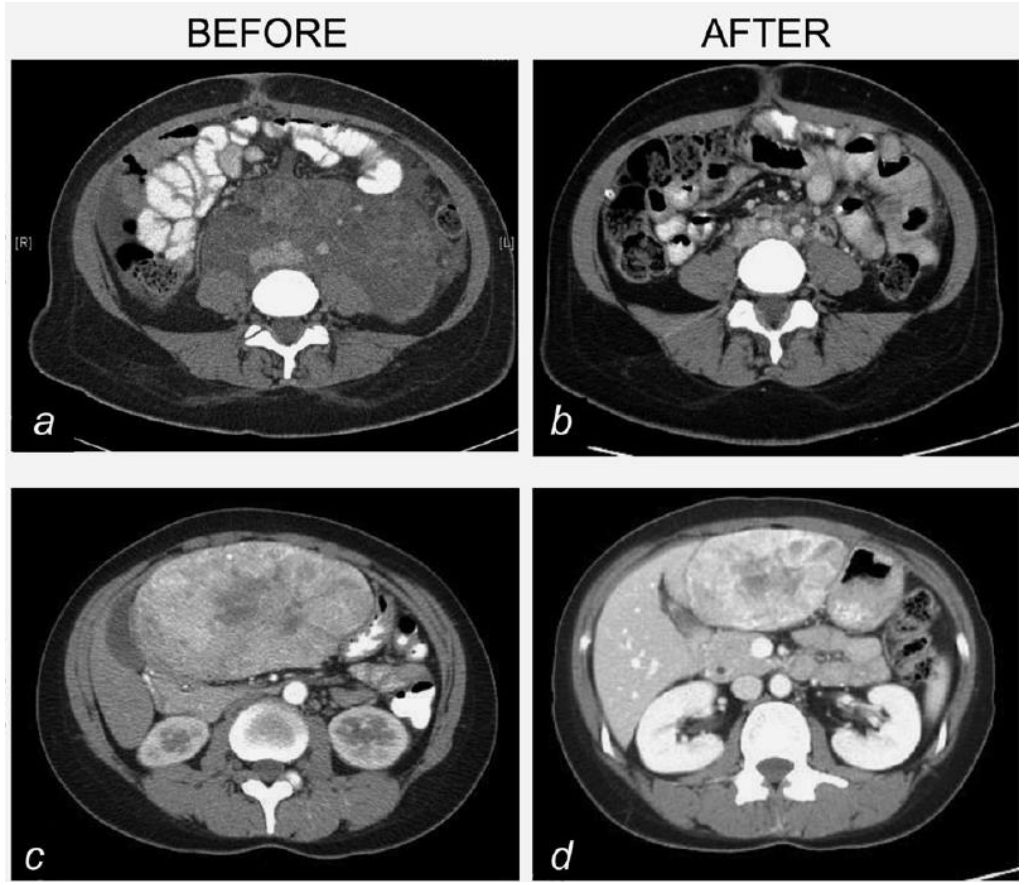
3c. Develop a master clinical trial protocol to evaluate repurposed or novel therapeutics URS.



Extrarenal perivascular epithelioid cell tumors (PEComas) respond to mTOR inhibition: Clinical and molecular correlates

Mark A. Dickson [1], Gary K. Schwartz[1], Cristina R. Antonescu[2], David J. Kwiatkowski[3] and Izabela A. Malinowska[3]

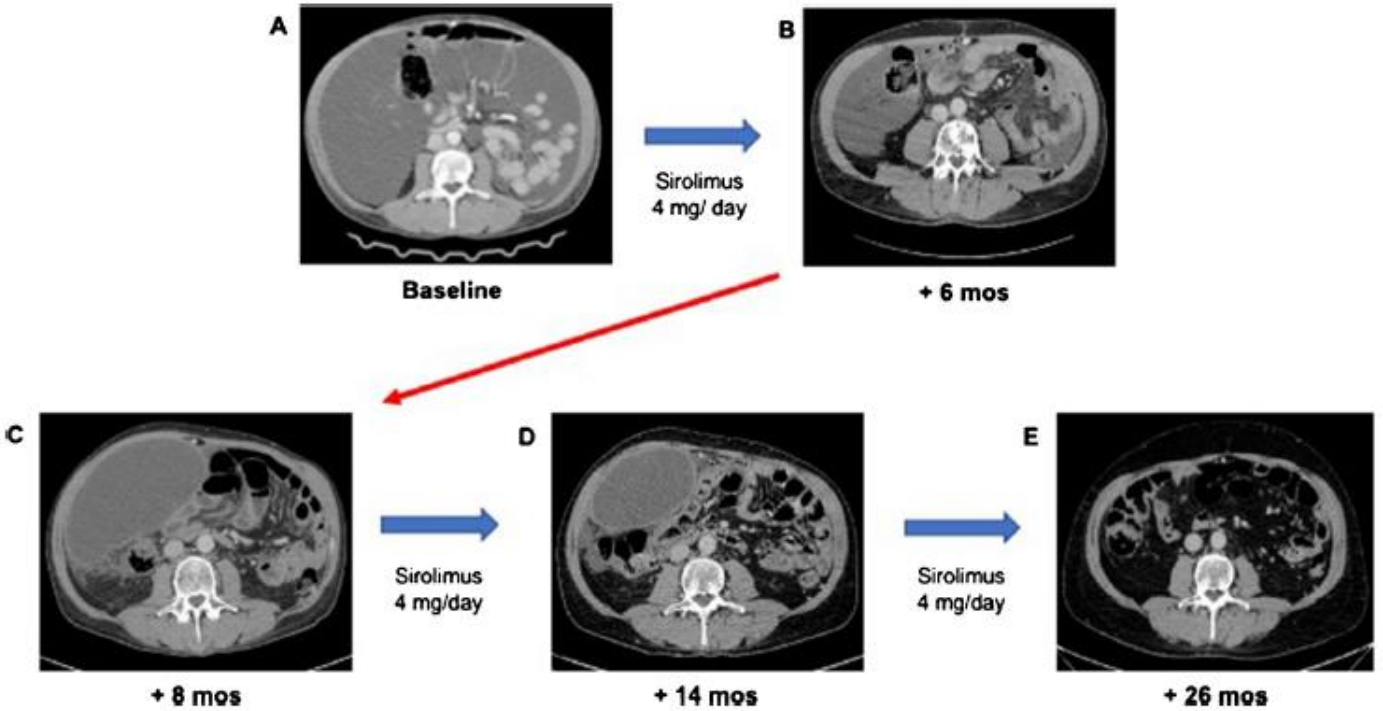
[1] Melanoma and Sarcoma Service, Department of Medicine, Memorial Sloan-Kettering Cancer Center, New York, NY
[2] Department of Pathology, Memorial Sloan-Kettering Cancer Center, New York, NY
[3] Translational Medicine Division, Brigham and Women's Hospital, Boston, MA



New Molecular Insights, and the Role of Systemic Therapies and Collaboration for Treatment of Epithelioid Hemangioendothelioma (EHE)

Silvia Stacchiotti, MD[1,]
William Tap, MD[2]
Hugh Leonard[3]
Nadia Zaffaroni, PhD[4]
Giacomo G Baldi, MD[5]

Current Treatment Options in Oncology



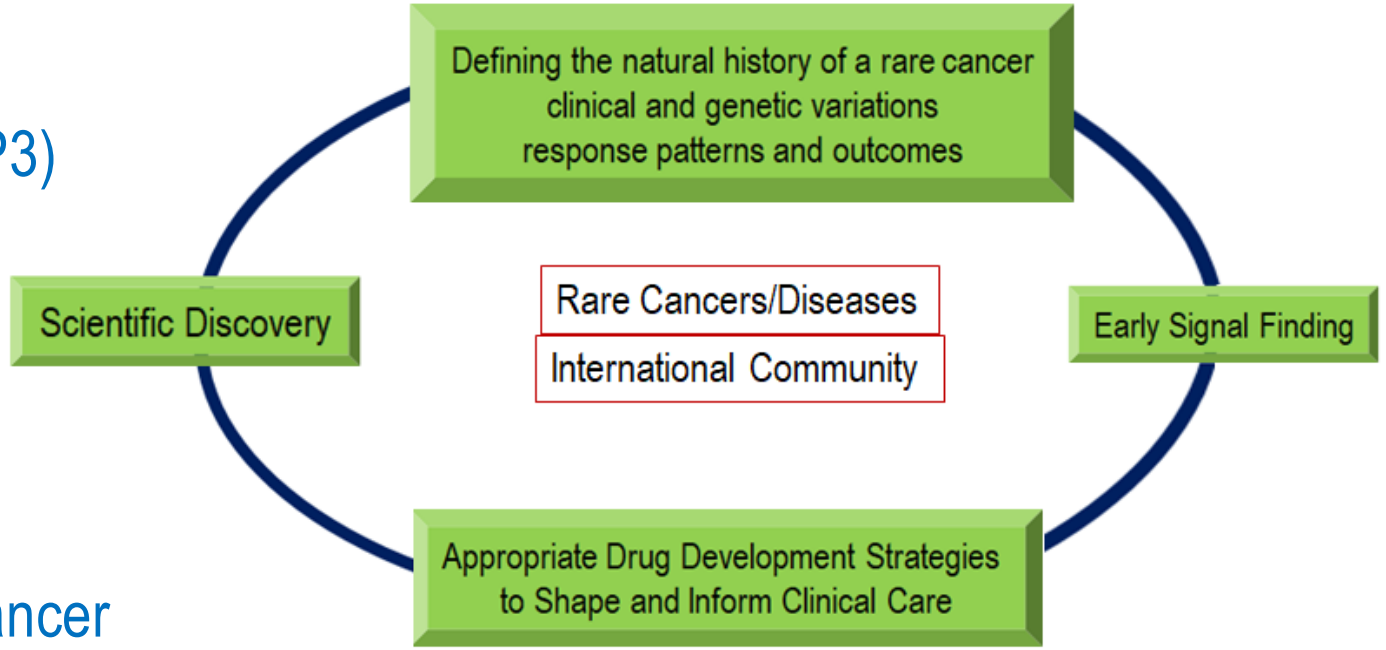
Presented by: William Tap MSKCC

Discovery and Innovation in Drug Development and Patient Care in Rare Cancers

Comprehensive Development Strategies
To ensure:

1. Successful Development Programs (P1→P3)
2. Inform Clear Clinical Application
3. Further Understanding of Biology
    1. Of Disease
    2. Response Pattern
4. Build Inclusive Collaborative Networks
5. Advance Clinical Understanding of Rare Cancer
6. Set the Paradigm for Drug Development Strategies

**Inclusive to what is important to the patient!



Presented by: William Tap MSKCC

CDRC
CURE DRUG REPURPOSING COLLABORATORY
CRITICAL PATH INSTITUTE

CURE ID
Challenging cases... New approaches

THANK YOU!

c-path.org/cdrc

The Role of Patient Advocates in Generating Real World Data in Ultra Rare Cancer

Denise Robinson (EHE Foundation)

Overview

- The EHE Foundation
- Epithelioid Hemangioendothelioma (EHE)
- Ultra Rare Cancer Challenges
- EHE Patient Powered Initiatives
- Role of Advocates in Drug Repurposing
- Ongoing & Future Needs

The EHE Foundation

Our Mission: to find treatments and a cure for Epithelioid Hemangioendothelioma (EHE)

Our Vision: a world where EHE is easily diagnosed and treatable

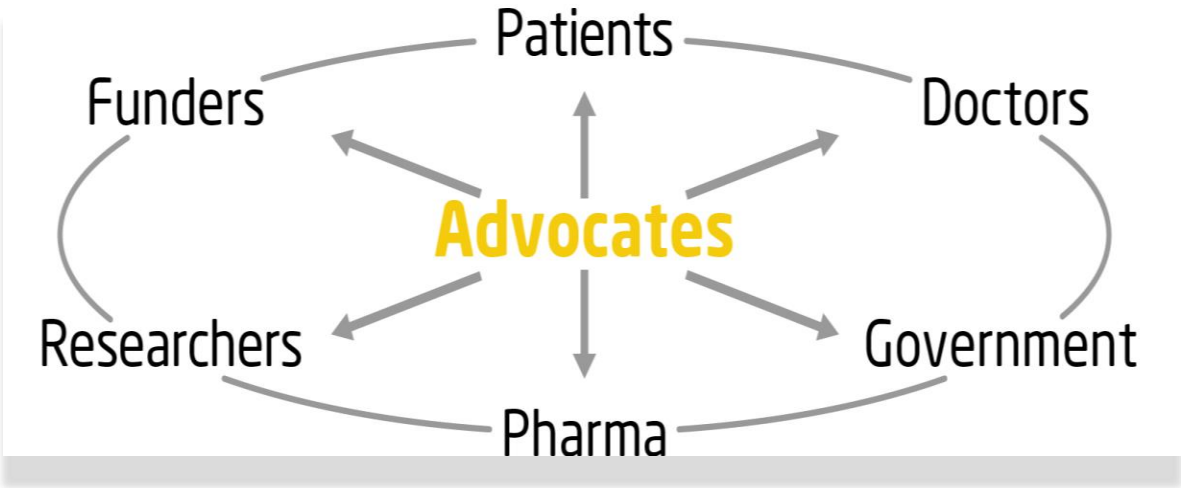
- Formed in 2015
- U.S. Based 501(c)(3) Patient Advocacy Organization supporting EHE patients and families in 80 countries
- What We Do:
  - Initiate & Support Collaborative Research
  - Provide Education & Support
  - Fundraising

Epithelioid Hemangioendothelioma (EHE)

- An ultra-rare sarcoma – incidence estimated at less than 1 in 1 million
- Marked by gene fusions: ~90% WWTR1(TAZ)-CAMTA1; ~ 10% YAP1-TFE3
- Slightly more common in women; very rare in children
- Incidence peaks at 4th – 5th decade
- Clinical course is extremely variable & hard to predict
  - Can arise in anywhere in body: most common liver; lung, and bones
  - >50% presents with metastatic disease
  - May present as indolent, often progresses and becomes aggressive causing excruciating pain and usually fatal
- No well-proven treatments; no direct targeted agents
  - 'Wait & Watch' common approach
  - Patients encouraged to seek expert sarcoma care
- Patients report significant psychological burden
- No phase II/III RCTs conducted; results from (2) phase II trials are available
- Retrospective studies / case reports limited data

Ultra Rare Cancer Challenges

- Industry has little incentive to invest in ultra-rare rare cancer
  - Hospitals also have higher scrutiny of accrual / budgets
- 80 – 100 types of sarcoma; competition to access stakeholders is high – doctors, researchers, industry, funding
  - Expert centers see most patients; are more in demand by patients, advocates, and industry
  - Government / public funding often out of reach
  - Ultra-rare = challenged fundraising = limited resources
  - Organizational capacity is limited (time, talent, funding)
- Patients <u>should</u> seek expert care, but the reality is that many cannot access experts or they become too ill to travel to a specialty center
  - Community oncology needs to educated / included

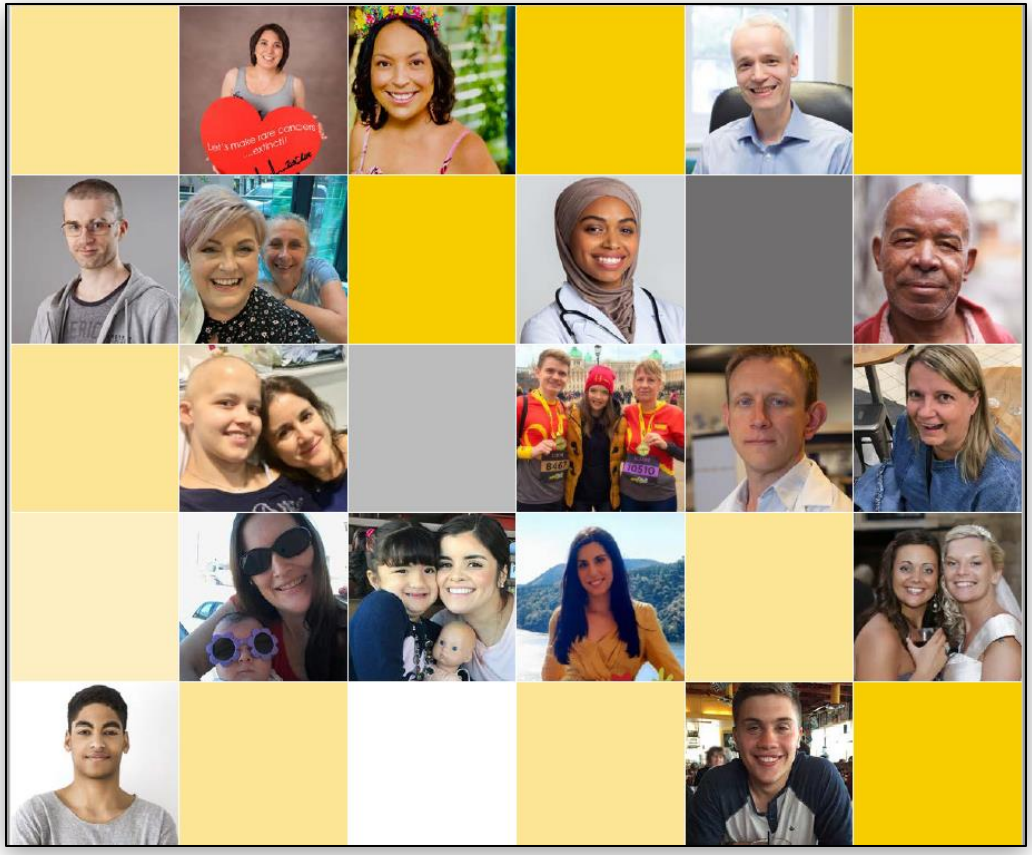


Advocates Carry a Large Burden in the Ultra-Rare Cancer Ecosystem

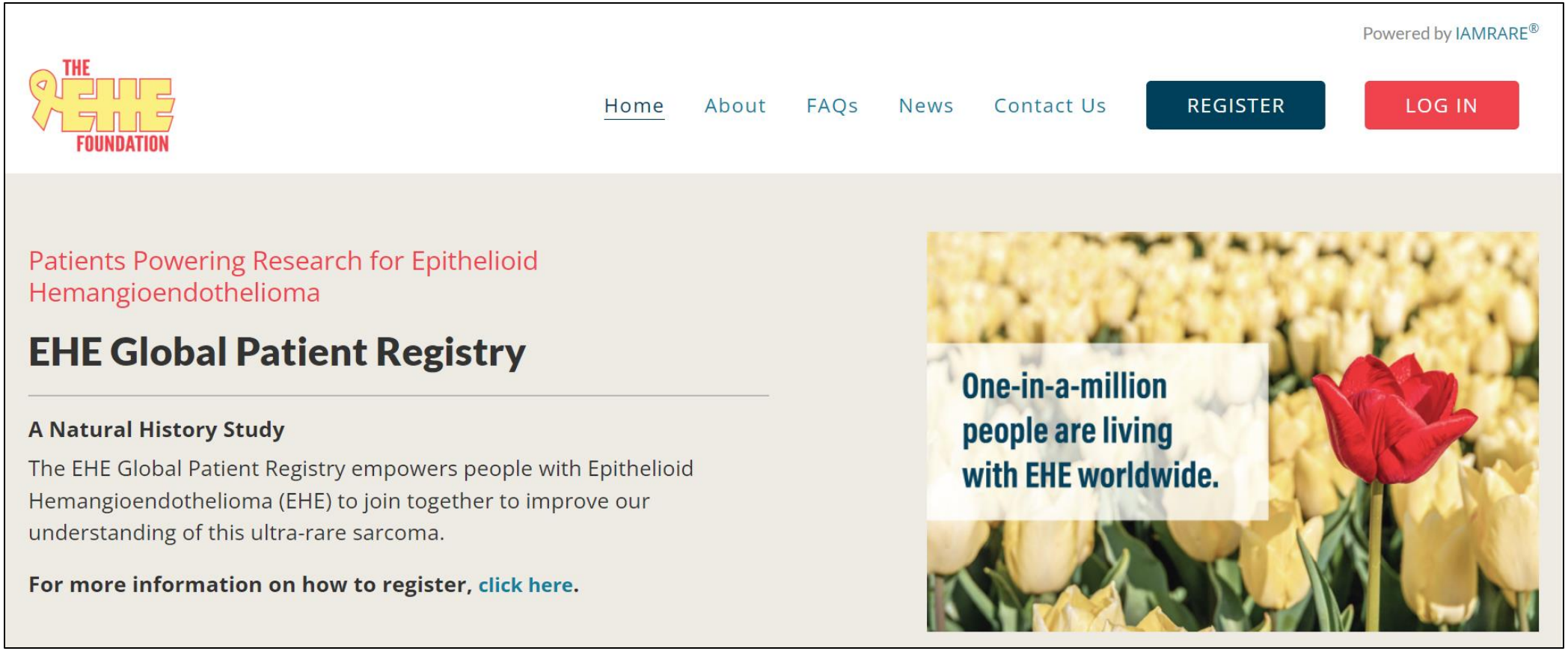
EHE Patient Powered Initiatives

Initiating & Funding Critical Projects

- EHE 360: Collaborative Research & Education
- EHE Research Grants Program
  - >$1.75M total research funding to date
- EHE Biobank (US) – initiated 2020
  - EHE Model Development
- EHE Global Patient Registry – IRB approved April 2023
- XCELSIOR: Outcomes Registry Study – launch Q2 2023



Advocacy Driving Real World Data



➢ *Soft-launch April 17th*

- Brings together ultra-rare patient experiences from around the world to answer critical questions
- Patient Self-reported Data - NORD IAMRARE® Registry Platform

EHE Global Patient Registry

- Describe people who have EHE, and better understand how EHE changes over a person's lifetime
- Learn about treatments and variations in management
- Identify doctors treating EHE
- Identify people who might be willing to take part in other ethically-approved research
- Help develop guidelines and recommendations to improve treatment outcomes for people with EHE
- Educate the EHE community
- Share data to support other research

EHE Registry: Participants & Surveys

- Patients' self-reported EHE journey
- People diagnosed with EHE anywhere in the world can contribute data
  - All ages; deceased patients included
- IAMRARE Platform - eConsent of Legal Adults, LARs, and Designated Representatives
- Self-report of EHE diagnosis; supporting evidence of diagnosis requested, not required

Baseline Surveys

XCELSIOR: Outcomes Registry Study

- A prospective, longitudinal database of clinical outcomes from past and present EHE patients
- Gathers data on effectiveness of treatments over time
- Will inform and serve the patient community, clinicians, researchers, and pharmaceutical companies
- Patients provide Consent & sign HIPAA release for access to all past and current treating hospitals
- Platform captures clinical data in a HIPAA-compliant database
- Builds a comprehensive cancer history
- Patients can view and download their data

Recent Patient Perspectives Survey

Simple global survey of patients' perspectives on Sirolimus for EHE to support EMA application for label expansion

- 122 patients responded
  - 42 patients were either on or had taken sirolimus
    - 27 patients were still on sirolimus
    - 17 without transplant
    - 10 post-transplant
  - 14 patients had stopped taking sirolimus
  - 1 patient survey was incomplete
  - 80 patients were not on sirolimus – reported it was important to them to be able to have access / their doctor choose to prescribe

Role of Advocates in Drug Repurposing

Bridging Patients, Clinicians, and Researchers

- Ensure patients are aware of and have access to research – invite participation directly
- Generate data leveraging *Patients' Voices* – fill clinical data gaps
- Share knowledge to instigate new studies
- Be a bridge for researchers/investigators & patients – provide continuous awareness and feedback to keep interest & information forefront
- Leverage, share, or use patient-derived data to support or collaborate across stakeholders
- Advocate for and seek funding for rare cancer
- Continue to seek & foster, share capacity-building opportunities – do not re-invent the wheel with each rare cancer

Ongoing & Future Needs

- Natural History & Prospective Clinical Data
- Improved Outcome Measures for Clinical Trials
- Persistent Sharing Across Stakeholders
- Availability of Genomic Testing
- Increased Access to Funding Mechanisms
- Rare Cancer Awareness
- Collaboration Nationally and Internationally
- Industry Collaboration & Support

Acknowledgements

Thank You to Patients, Clinicians & Researchers Who Contribute to and Advance EHE Research!

Funding & Support Provided by:

The Margie & Robert E. Petersen Foundation

Chan Zuckerberg Initiative

Rare As One

Collaborators & Advisors:

NORD

EHE RARE CANCER CHARITY (UK)

EHE Rare Cancer Foundation Australia

The EHE Foundation Advisory Board

Critical Path Institute & CDRC for Including Patients' & Advocacy Perspectives

CDRC
CURE DRUG REPURPOSING COLLABORATORY
CRITICAL PATH INSTITUTE

CURE ID
Challenging cases... New approaches

THANK YOU!

c-path.org/cdrc

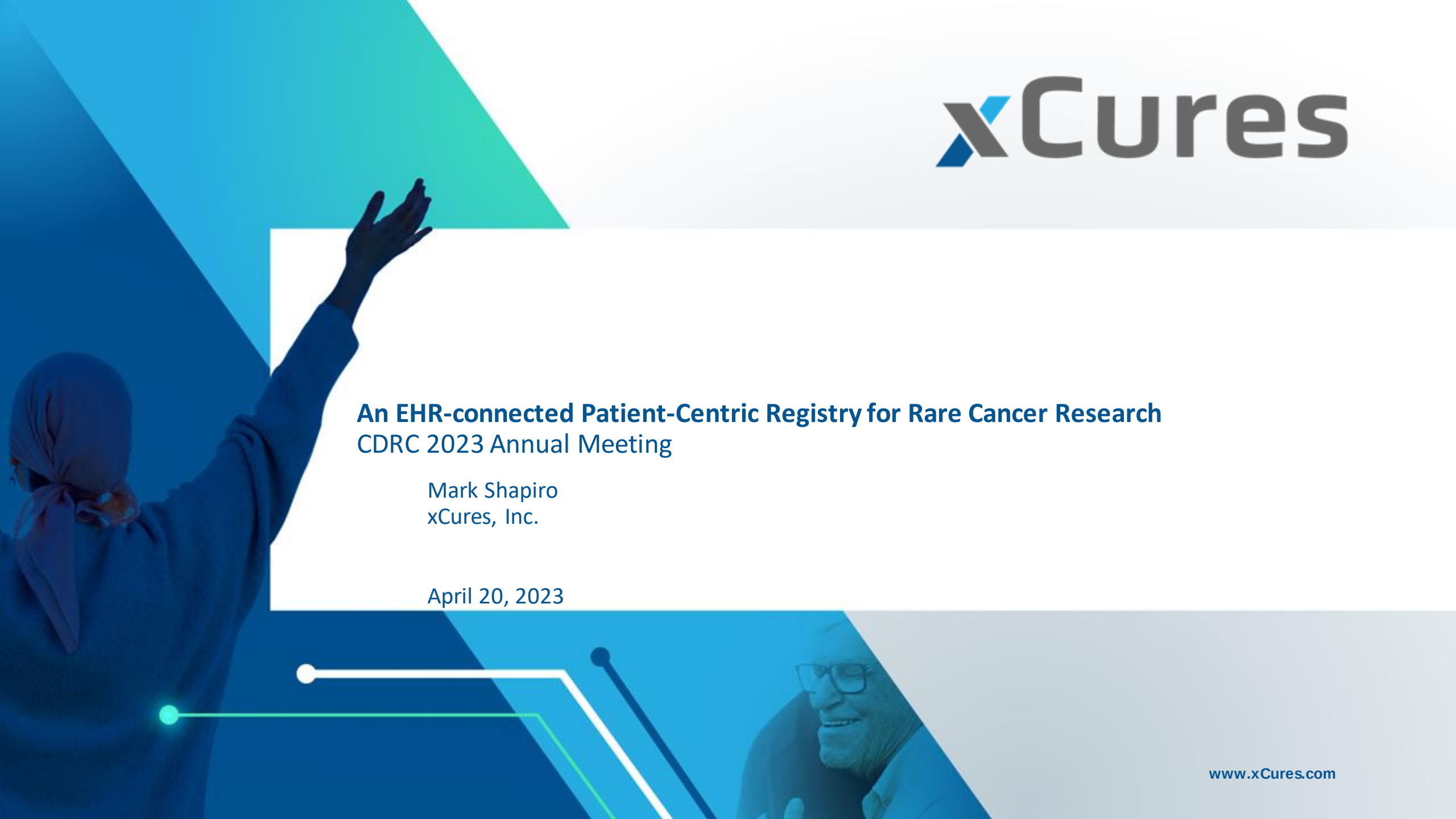
An EHR-connected Patient-Centric Registry for Rare Cancer Research

Mark Shapiro (xCures)

Mark Shapiro

COO, xCures

Mark Shapiro is the COO of xCures and principal investigator for XCELSIOR a patient-powered real-world data and outcomes registry in cancer. Prior to joining xCures, Mr. Shapiro was SVP, Operations at a global oncology CRO, where he was responsible for a team of about 500 drug development professionals in 30 countries, and a portfolio of more than 100 active clinical trials. He was previously a management consultant in the Clinical Development and Medical Affairs consulting practice at Syneos Health Consulting. He also managed a pediatric clinical trials network coordinating center at Duke University focused on clinical, pharmacogenomic, and psychometric research. He has published many peer-reviewed articles and patent applications related to clinical research and the use of AI/ML in clinical research and medicine. Mr. Shapiro is a graduate of the Fuqua School of Business at Duke University and holds a master's degree in Pharmacology from the Boston University, School of Medicine.



An EHR-connected Patient-Centric Registry for Rare Cancer Research

CDRC 2023 Annual Meeting

Mark Shapiro
xCures, Inc.

April 20, 2023

Mission

Improve cancer outcomes – one patient, one doctor, and one treatment at a time.

Vision

To accelerate cancer research and care by continuously learning in real time from every patient's journey, the experience of leading oncologists, and the best available knowledge

A Direct-to-Patient/Physician Web-based Platform

xCures

1. Patient consents to xCures or an xCures partner

2. Perpetual data access via Health Information Exchanges & directly from sites

3. Data processed via rules engines and AI/ML

4. Automated data structuring

5. Searchable structured data & Meta-data catalogue

6. Fit for purpose dataset built to spec (Regulatory-grade)

All medical records from all sites of care

Care Summaries

xINFORM

xDECIDE

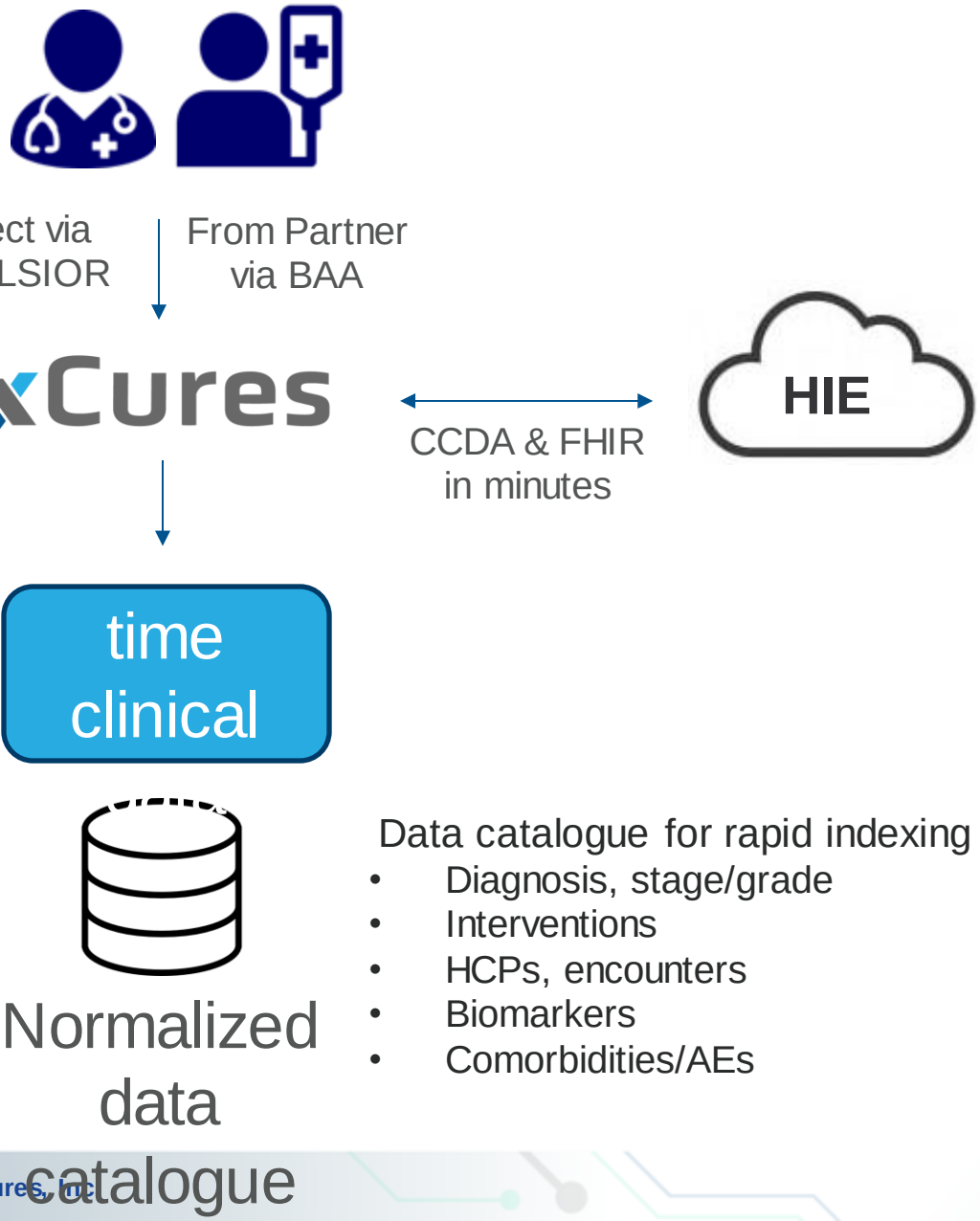
Portals for patients & providers

- Direct communication
- PROs
- Clinical Decision Support
- Program Recognizer

Trial matching, CDS, outcomes analysis and LTFU, RWD studies (nautral history, burden of disease, etc.)

DCTs, EAPs, EHR to EDC

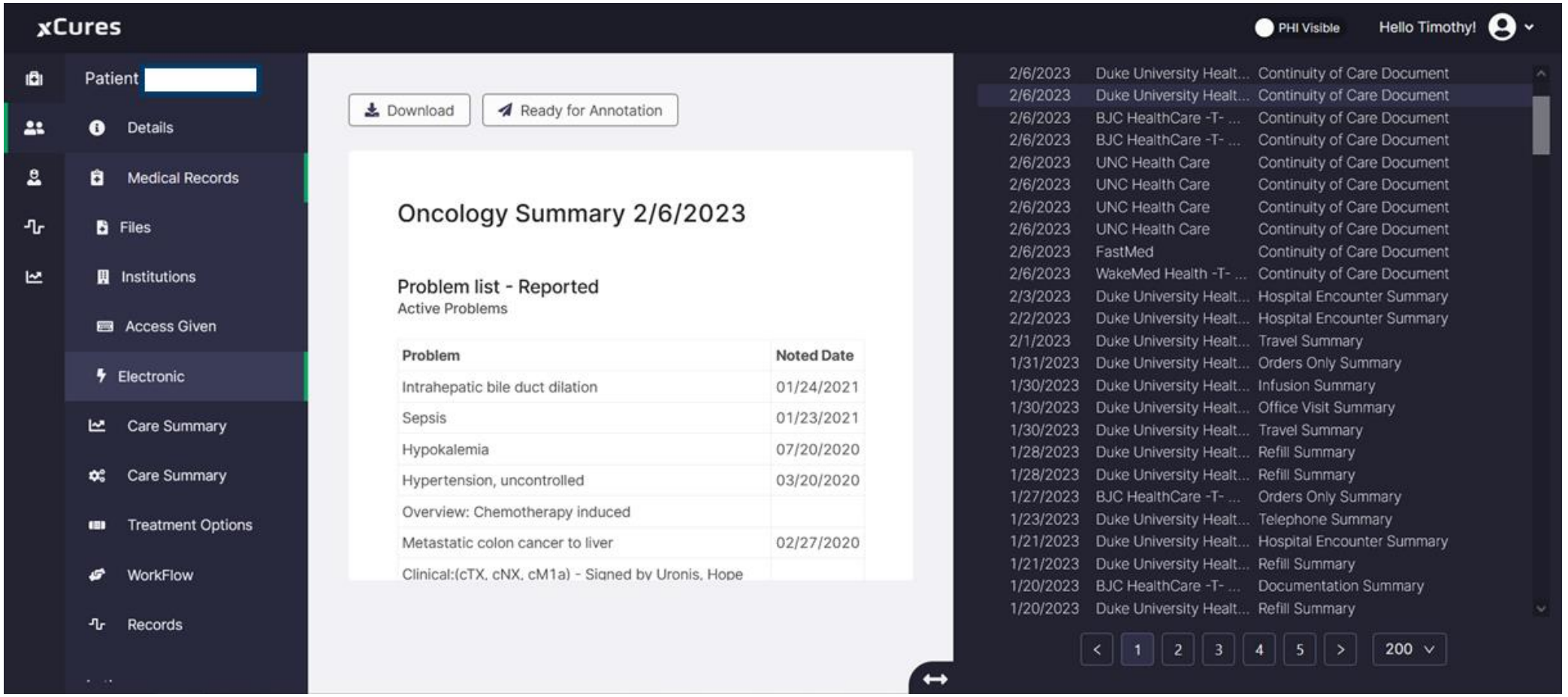
HIE connection completely automated workflows



Health Information Exchange integration

- Within minutes, xCures can gather and structure medical records from any institution on the exchange
  - >90% of academic medical centers
  - ~60% of health systems
  - = >70% of all cancer patients
  - **Rapidly growing due to Medicare Promoting Interoperability Program**
- CCDA and FHIR format
- Automated structuring of FHIR endpoints into longitudinal care summary
- Ongoing work mapping CCDA to FHIR
- Data can be refreshed within minutes

Sample medical records returned from HIE

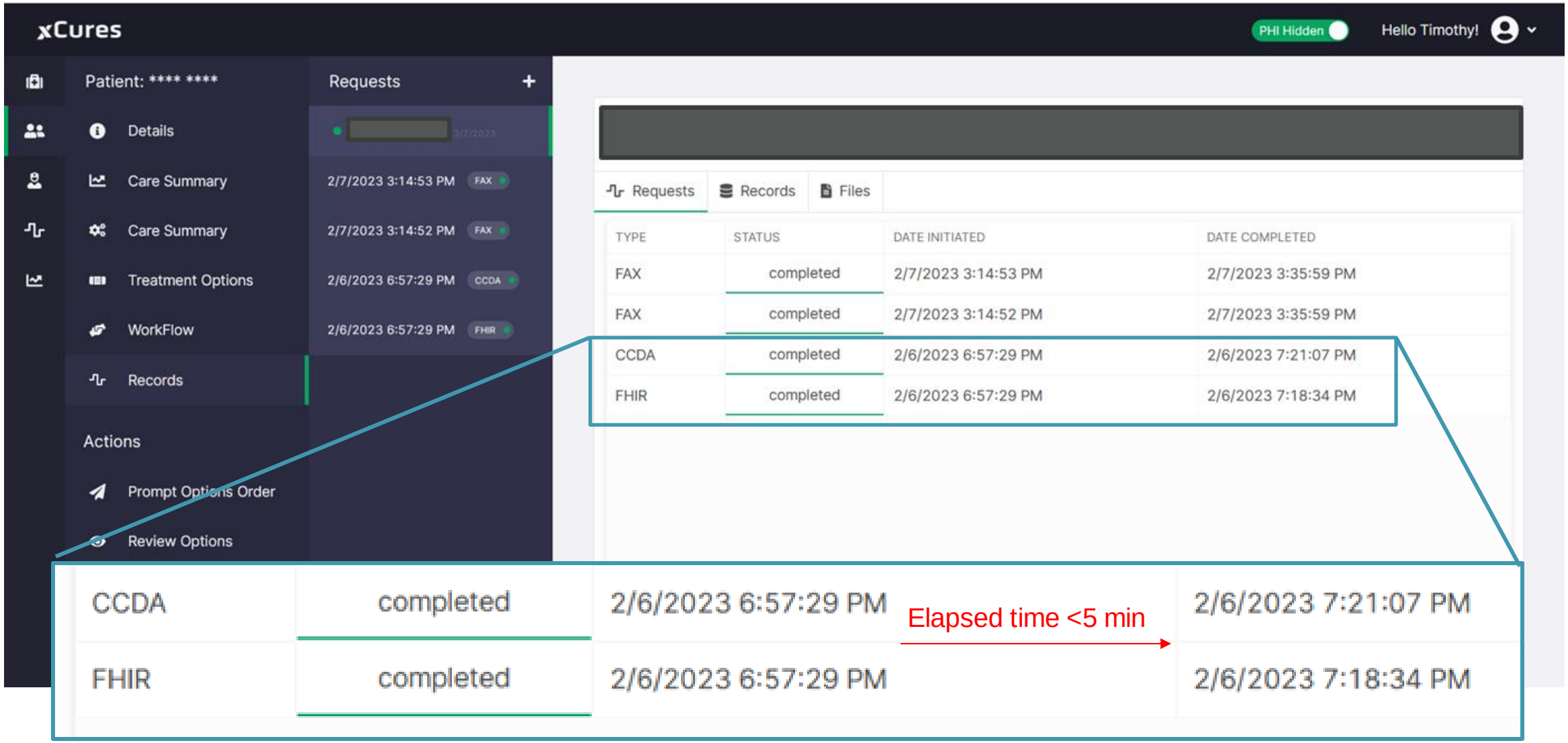


Diverse sites of care and visit summaries: Hospital, Office, Travel, Infusion, Orders, Telephone, Etc.

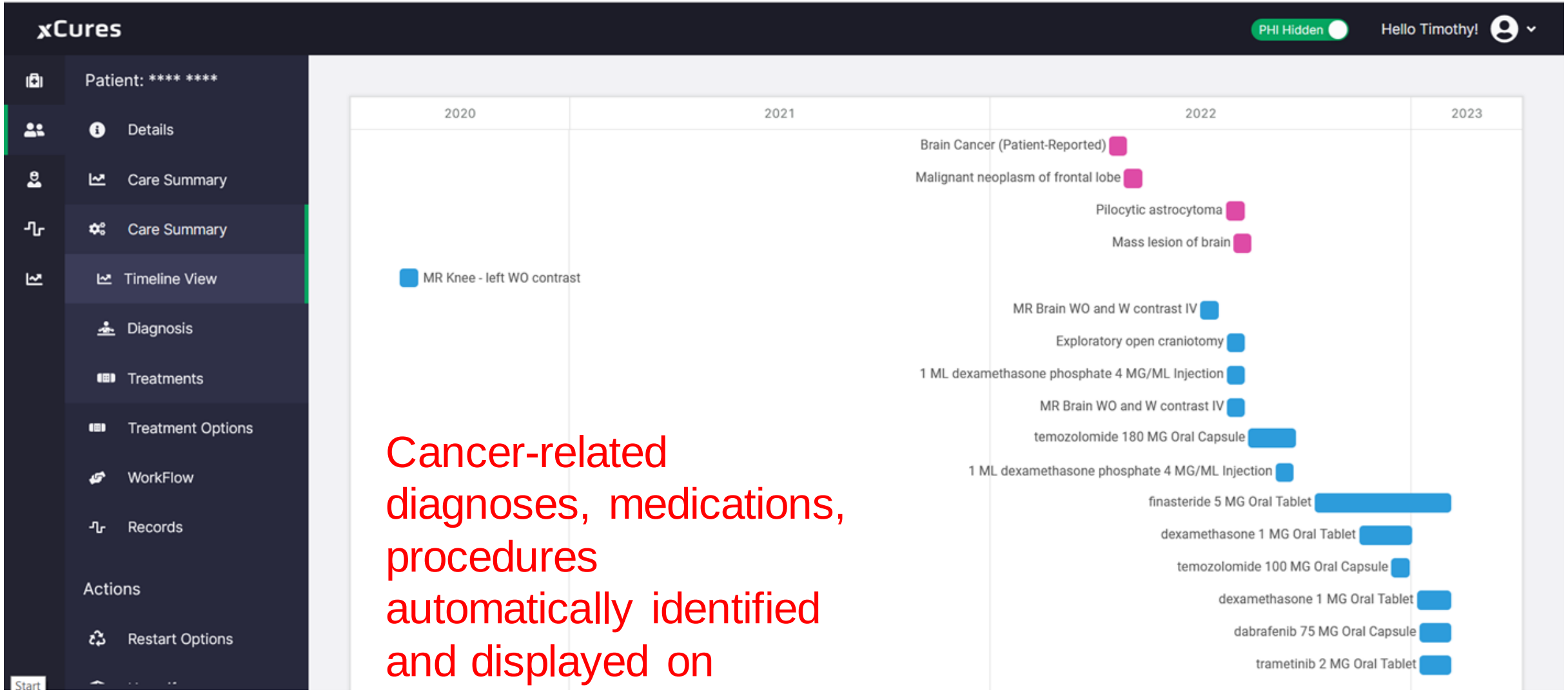
Integrated viewer

Hundreds of medical documents

Medical records received within minutes



Sample automated care summary



Cancer-related diagnoses, medications, procedures automatically identified and displayed on timeline concurrently with receipt of FHIR

xCures Operates a Direct-to-Patient Precision Oncology Clinical Research Platform

NCT03793088

- Nationwide pan-cancer observational research protocol
- eConsent, completely virtual
- Direct access to medical records

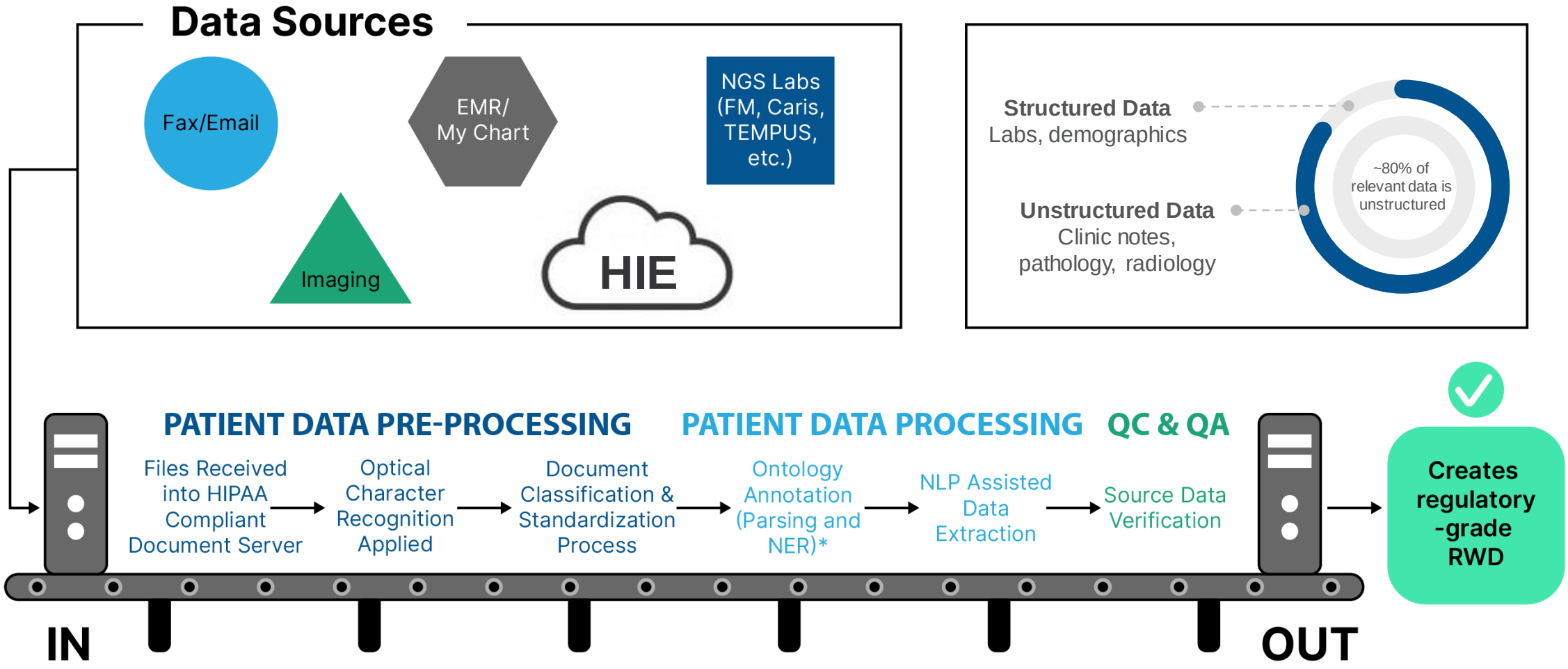
- **Novel patient-centric platform**
  - Direct patient relationship and navigation
- **Part 11-compliant EHR-to-EDC**
  - Longitudinal, uninterrupted clinical data
- **Decentralized clinical trial capabilities**
  - Nationwide reach; bring the study to the patient

Entire Patient Clinical Dataset Centralized and Standardized

Clinic notes	Pathology	Radiology reports	Labs and Genomics	Raw Imaging (DICOMs)	Raw Sequencing (FASTQs)

Efficient Data Structuring from Health Records

Integrating structured data from HIEs with xCures NER / NLP technology

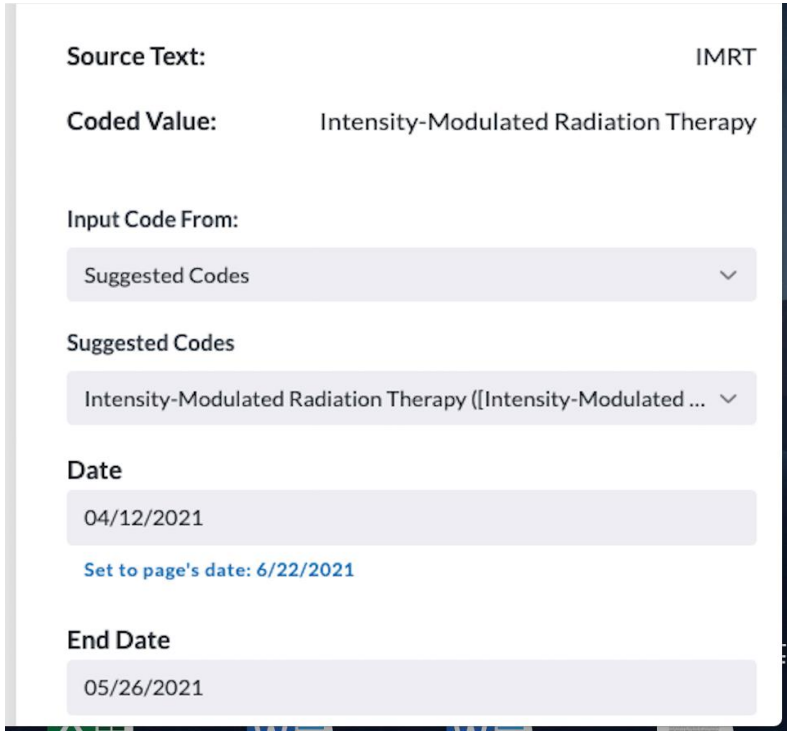


Structured and Unstructured Data Processing

NER & NLP Assisted Data Extraction

[redacted] who underwent a left steoreotactic brain biopsy on March 18, 2020 at Rhode Island Hospital. Pathology revealed Glioblastoma, IDH1-wildtype, with focal small-cell component, WHO grade IV, MGMT-methylated. He underwent IMRT from 4/12/2021-5/26/2021 and Adjuvant temozolomide. He has has weaned off of decadron. He remains on Keppra 1500mg BID although feels some dizziness which he attributes to Keppra. His last seizure Was on March 21st. He notes generalized weakness in the extremities, however feels his leg Strength has improved. He feels his energy has improved since weaning off the decadron. He feels best first thing in the morning. He has increased mobility in the legs. He feels he Has difficulty speaking as clearly as he used to be able to. He has some difficulty with short Term memory. He has occasionally headaches on the left supraorbital region. He recently Developed left side tinnitus and loss of hearing. He is seeing an ENT this month. He takes Meclizine for dizziness with good improvement. He was recently started on eliquis for Management of a PE. He denies any facial or extremity weakness, numbness, tingling, Swallowing difficulty, vision changes, bowel or bladder incontinence.

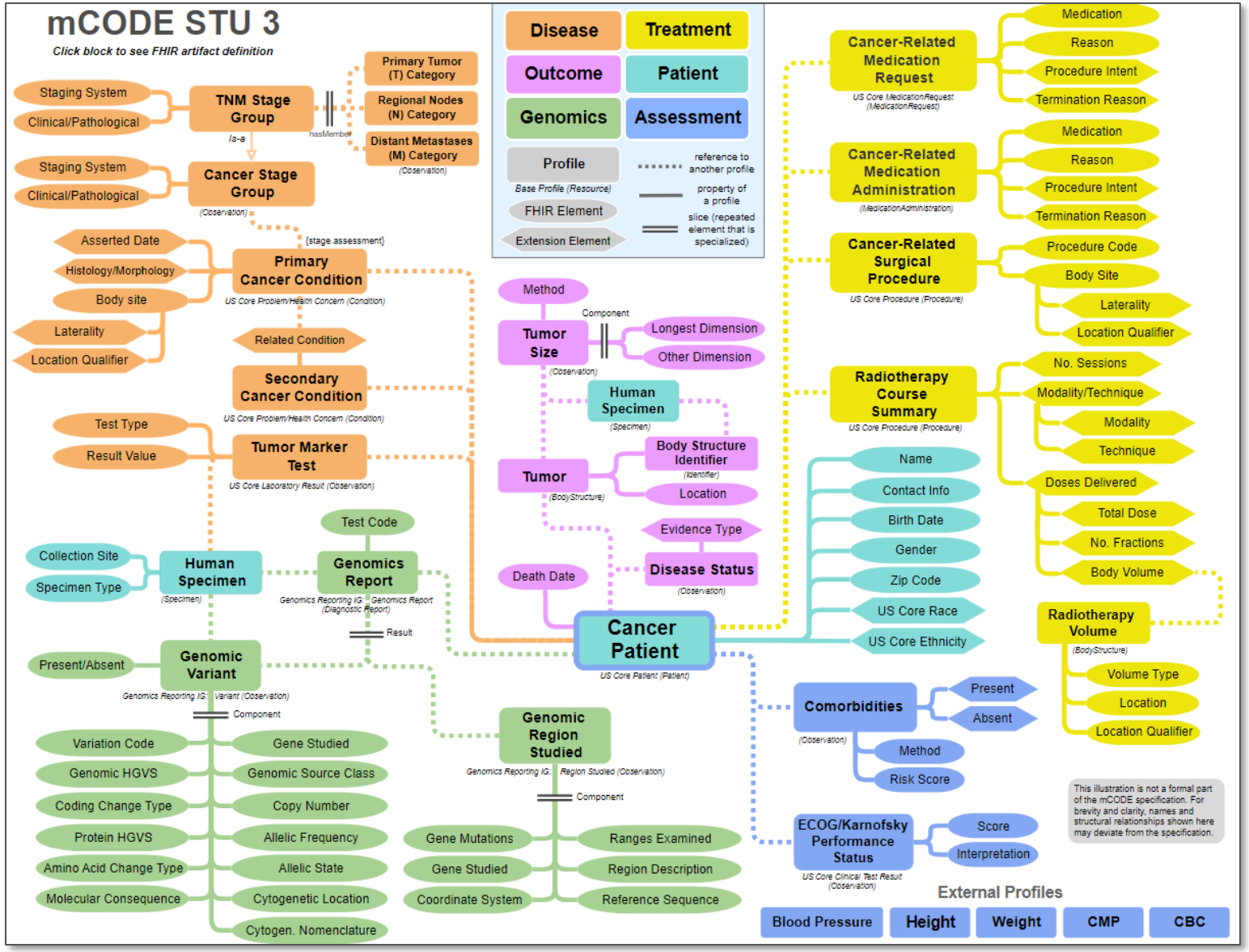
*Source = Clinic note from 22JUN2021



- Entities correspond to fields in Data Model (CRFs) and flow directly to EDC system from the source.
- Source Data Verification processes are run without ever losing the provenance of the data.

xCures CDM – Fax or FHIR to mCODE and OMOP

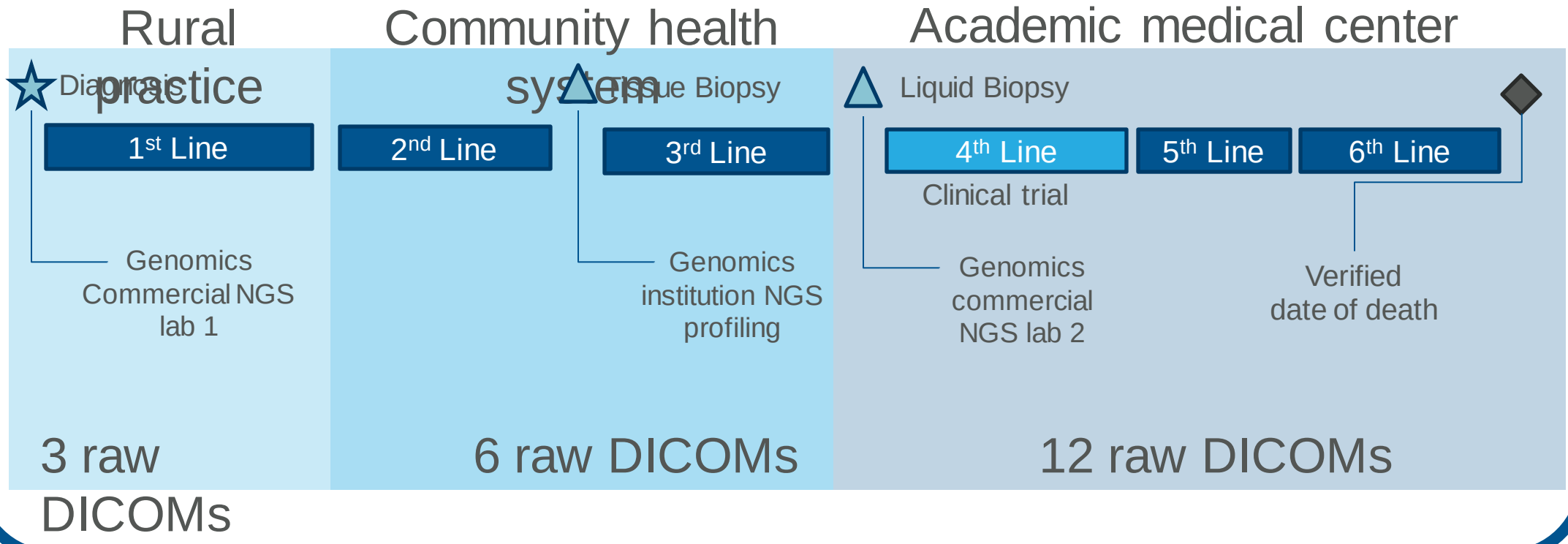
Mapped to several dictionaries and data models for interoperability with different clients



- Source file
- Source type
- Source location tag
- Institution
- NPIs
- SDoH
- QoL (EQ-5D)
- PRO-CTCAE
- DICOM image files
- Verbatim term(s)
- Coded terms(s)
  - Dictionary
- Imputed term(s)
  - Is_a
- Derived term(s)
  - Regimen
  - Line of Tx

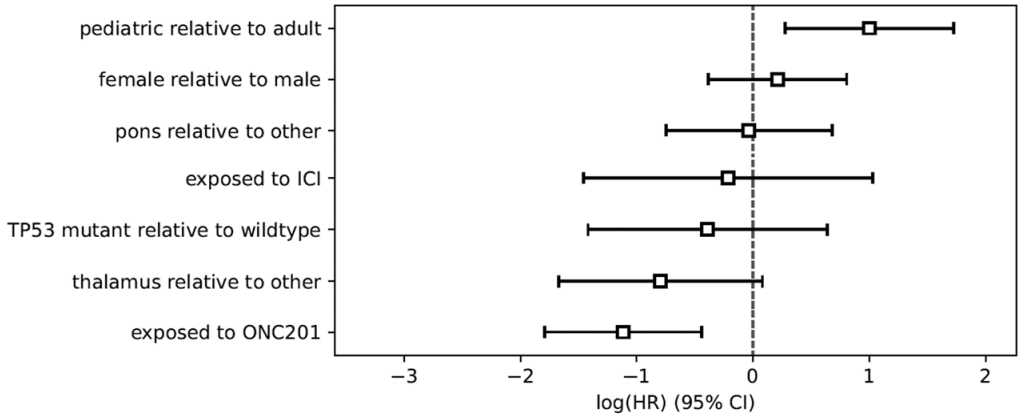
Complete, uninterrupted longitudinal clinical data

Real-time Regulatory-grade Clinical data (RRC) from xCures



Core findings from 2022 SNO DMG abstract

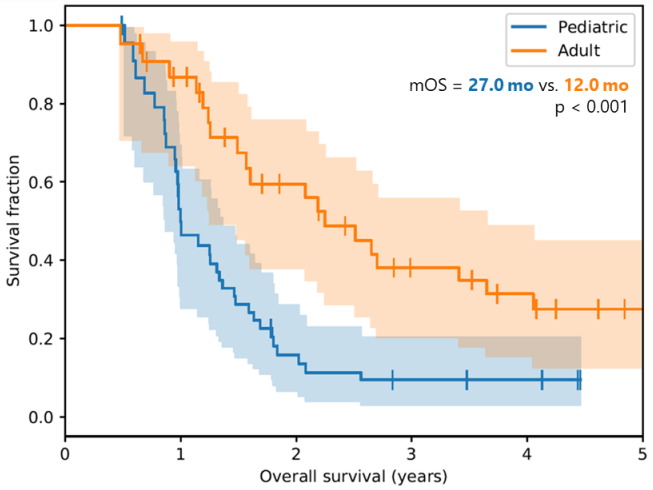
1A **Cox Proportional Hazard analysis identifies adult age at diagnosis and exposure to ONC201 as associated with better overall survival**



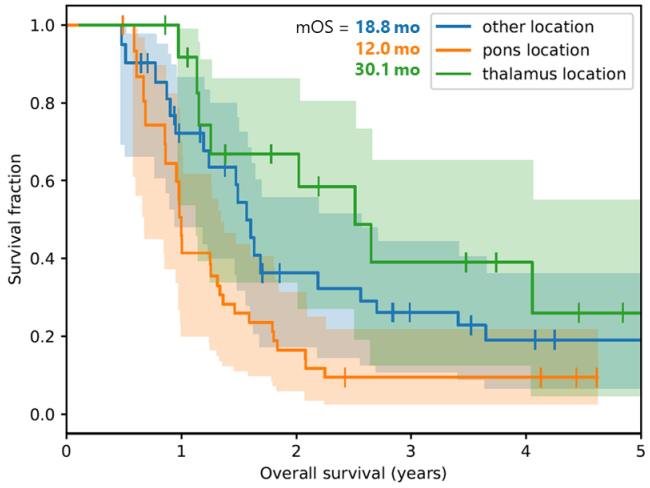
1B

log(HR) [95% confidence]	p-value
1.0 [0.28-1.72][a]	0.01
0.21 [-0.38-0.81]	0.48
-0.03 [-0.75-0.68]	0.93
-0.21 [-1.46-1.03]	0.74
-0.39 [-1.42-0.64]	0.46
-0.79 [-1.67-0.08]	0.08
-1.12 [-1.79--0.44][b]	<0.001

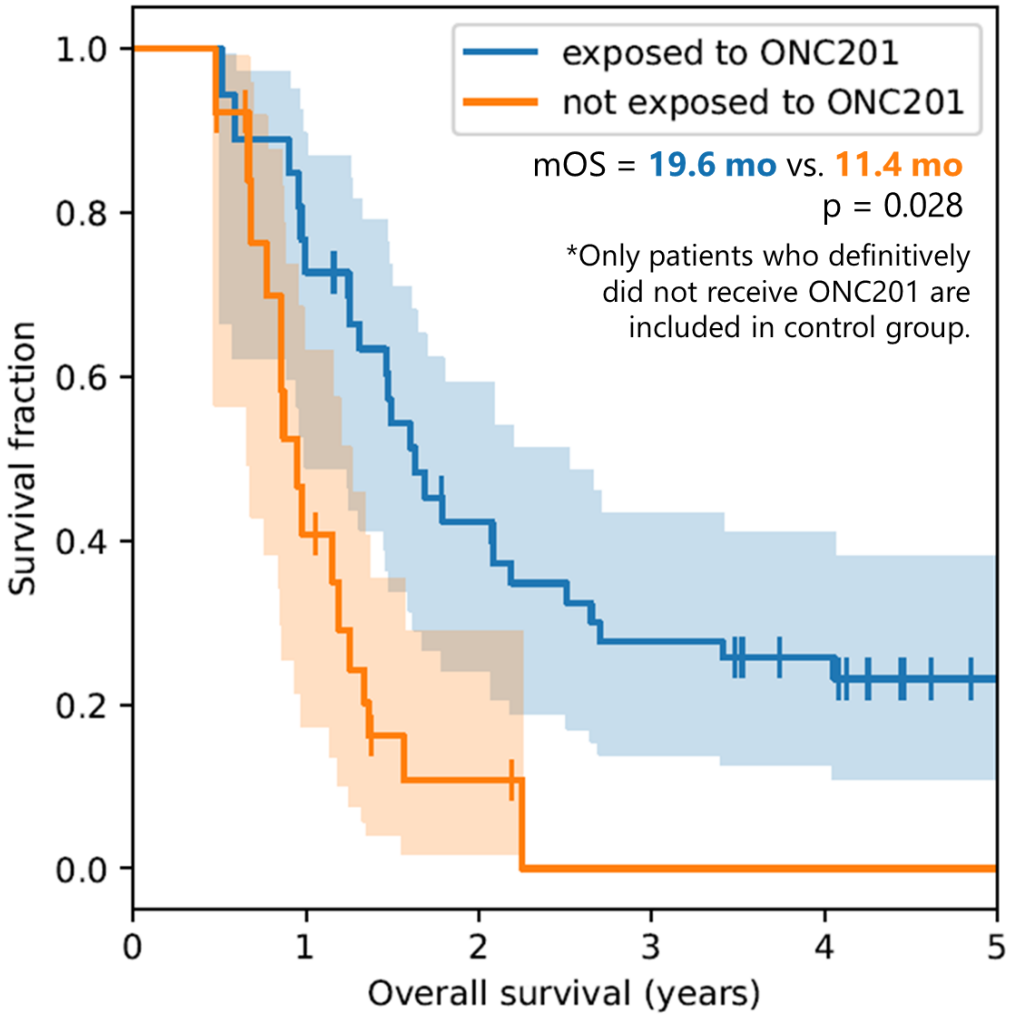
1C **Pediatric age at diagnosis is associated with worse overall survival**



1D **Pons location is associated with worst overall survival; thalamus location is associated with best overall survival**



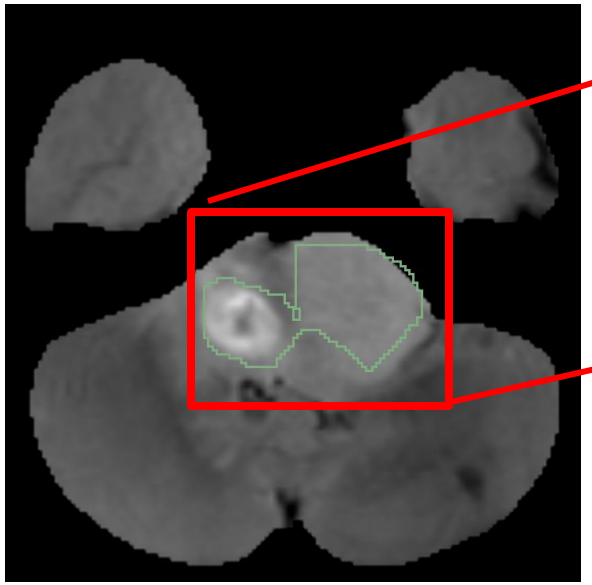
3A **ONC201 significantly extends OS vs. a cohort of patients who did not receive ONC201 during their treatment***



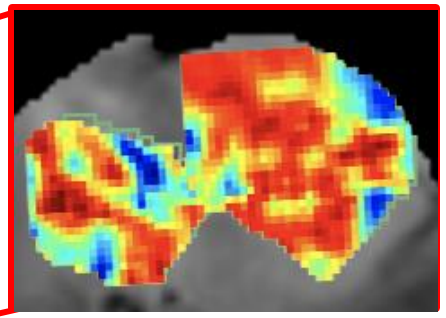
GBM Patient DICOM Analysis

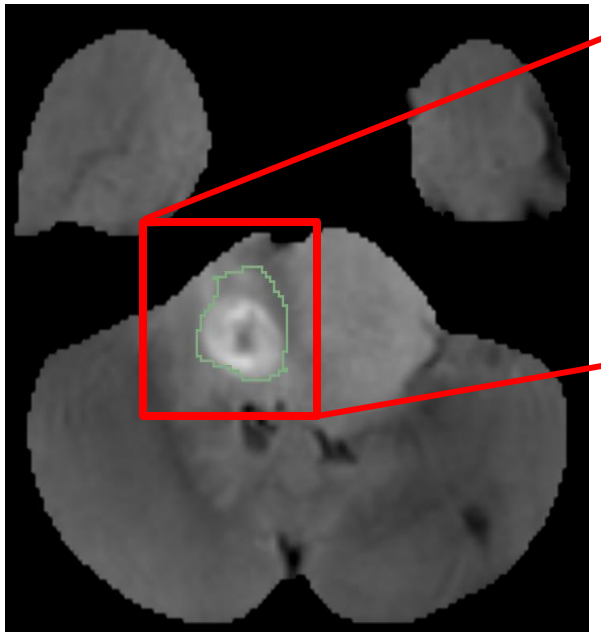
xCures

Tumor Isolated on MRI

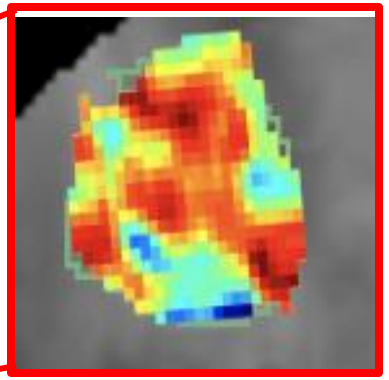


Tumor core + Edema

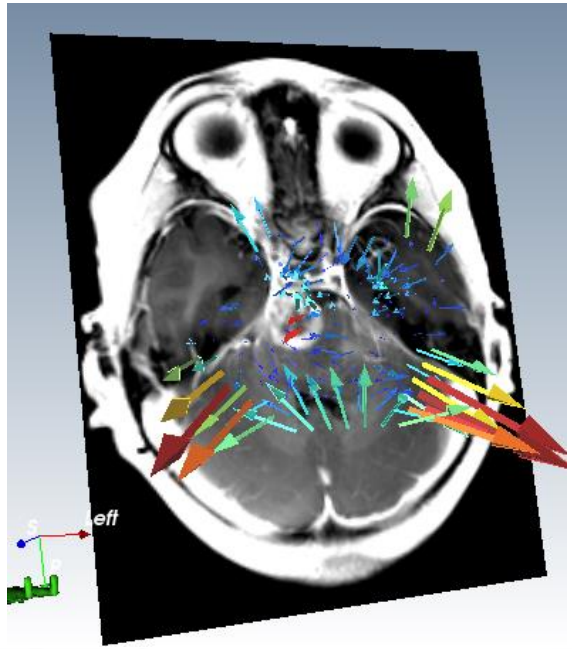




Tumor core



Mass Effect Quantification

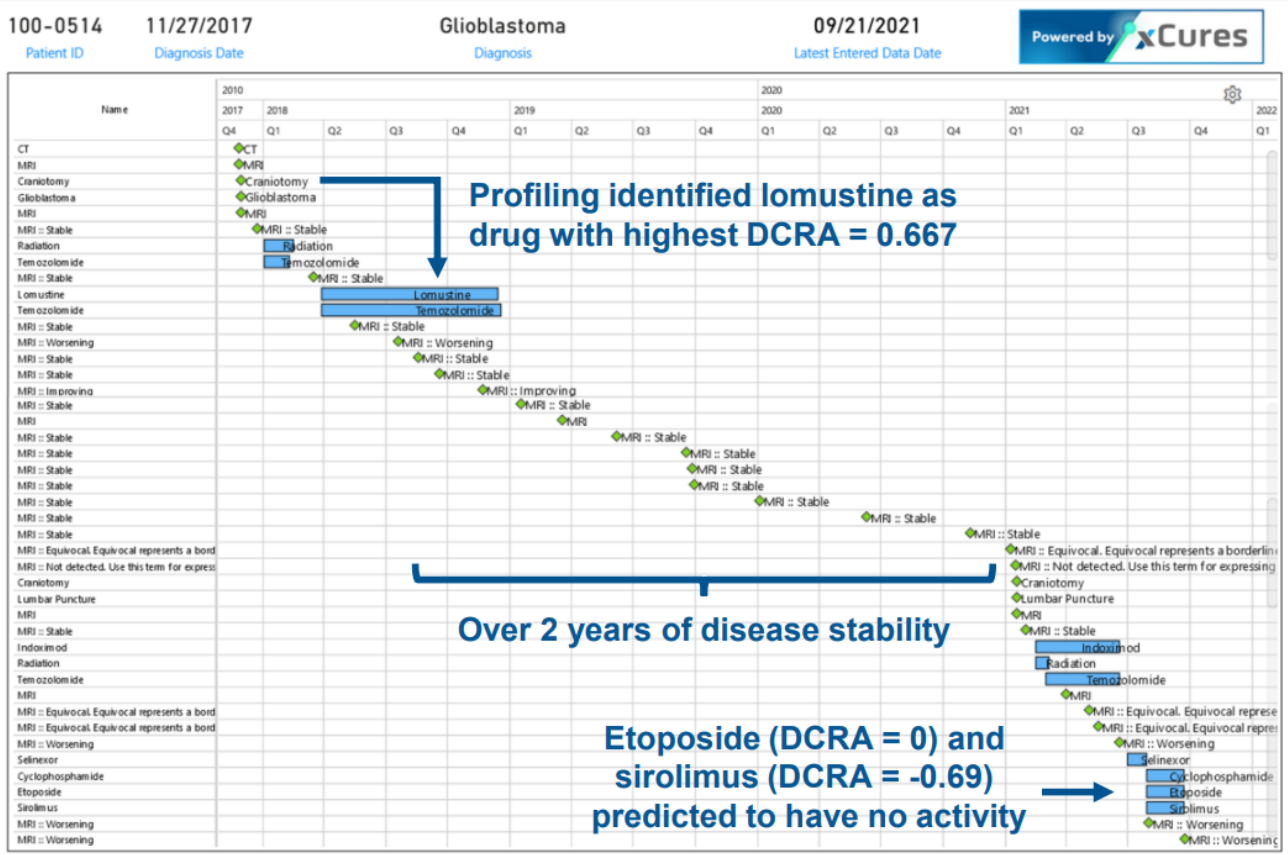


Validation of Precision Oncology Algorithms

Platform enables deployment of point-of-care solutions

xCures

C Case example of lomustine activity



Genomics

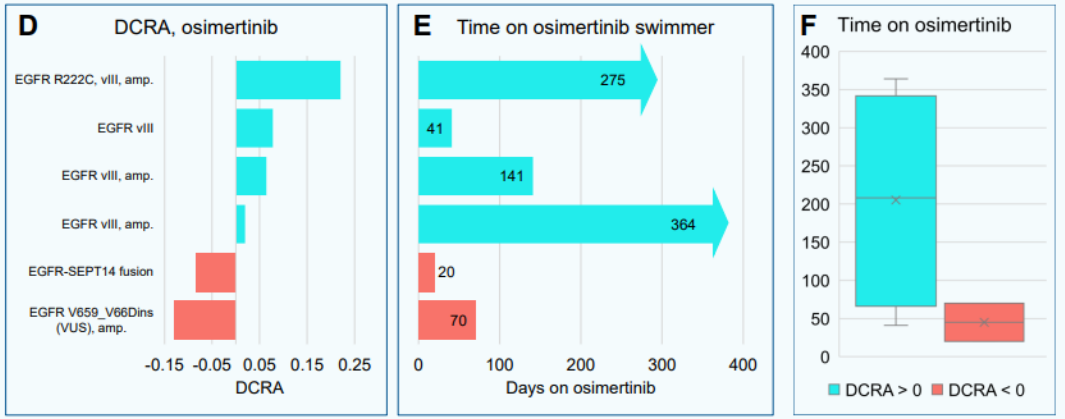
MGMT equivocal
IDH1 wild type
ATRX E886fs
BCOR C1329fs
H3F3A G35R
TP53 R273H

PD-L1 negative
MSI stable
MMR proficient
TMB low, 6 Mut/Mb

- Partnership with Institute for Systems Biology to run precision oncology drug sensitivity models for patients with hard-to-treat cancers
- Retrospective analysis validates ISB systems biology model for many approved treatments used in a precision medicine model

Treatment recommender, trial matching, and precision oncology algorithms can be delivered to physicians within the platform at the point-of-care.

Osimertinib time-on-treatment clinical correlations with DCRA



RWD Replication of an RCT
SOC +/- Optune in glioblastoma

xCures

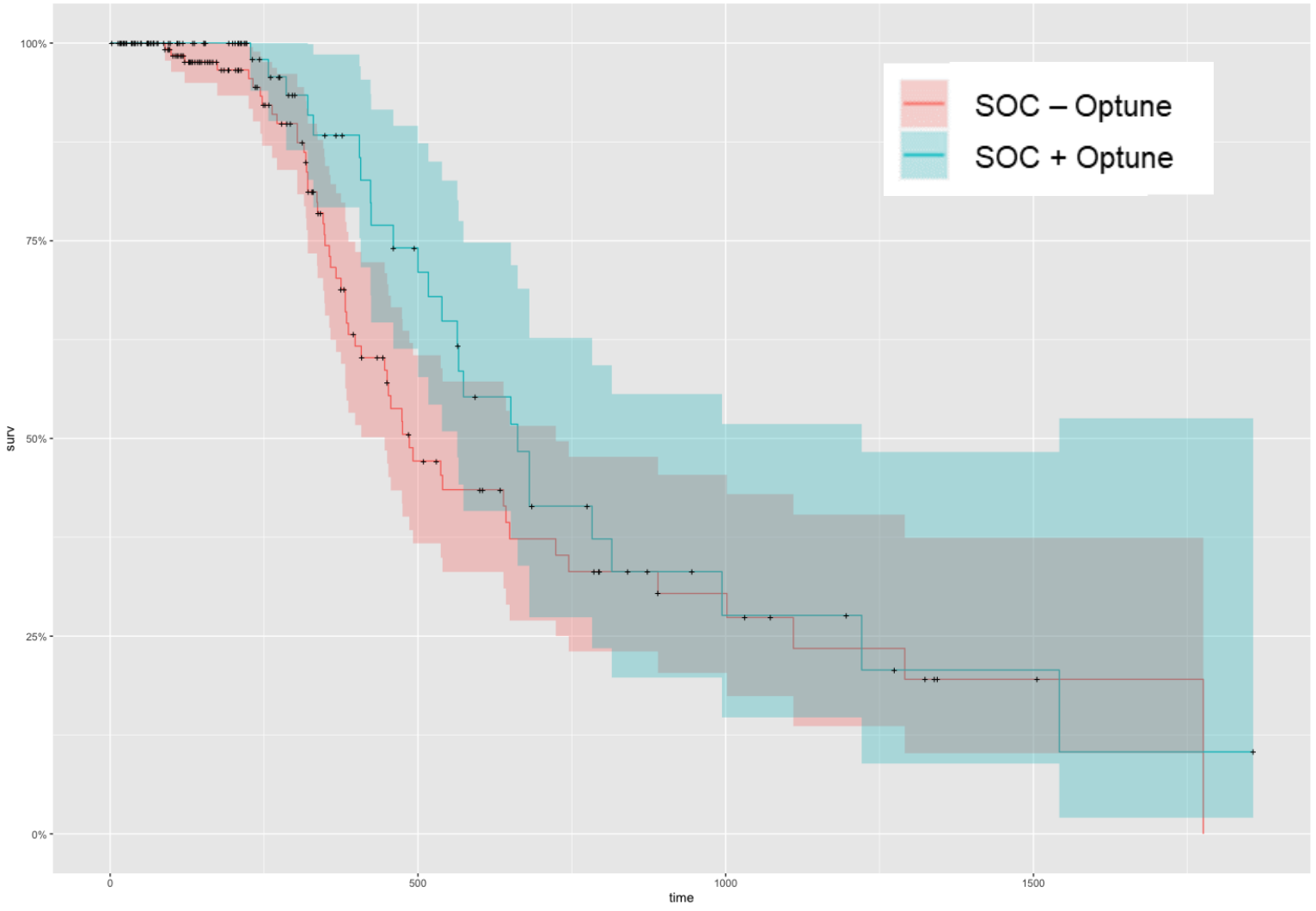
Overall survival from diagnosis

Population (N=246)

- Glioblastoma diagnosis (primary or secondary) on or after 1/1/2016
- Treated only with SOC agents (TMZ, radiation, lomustine, bevacizumab, other chemo)

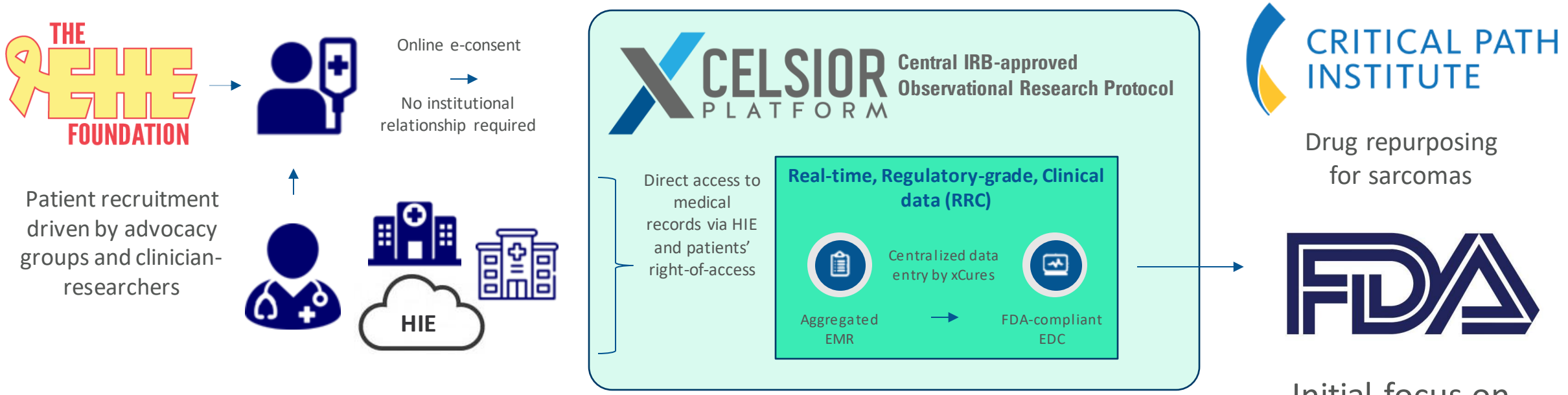
Medial Overall Survival

- RW - SOC + Optune (blue, N=73) vs. SOC – Optune (red, N=173)
  - **21.8 mo vs. 16.0 mo (p < 0.01)**
  - Survival at 2 years = 42% vs. 37%
- RCT – TMZ + Optune 20.9 mo (n=466) vs. TMZ ((n = 229)
  - **20.9 mo vs. 16.0 mo (p < 0.001)**



CDRC Pilot for Sarcoma Drug Repurposing

xCures



For Clinican Researchers:

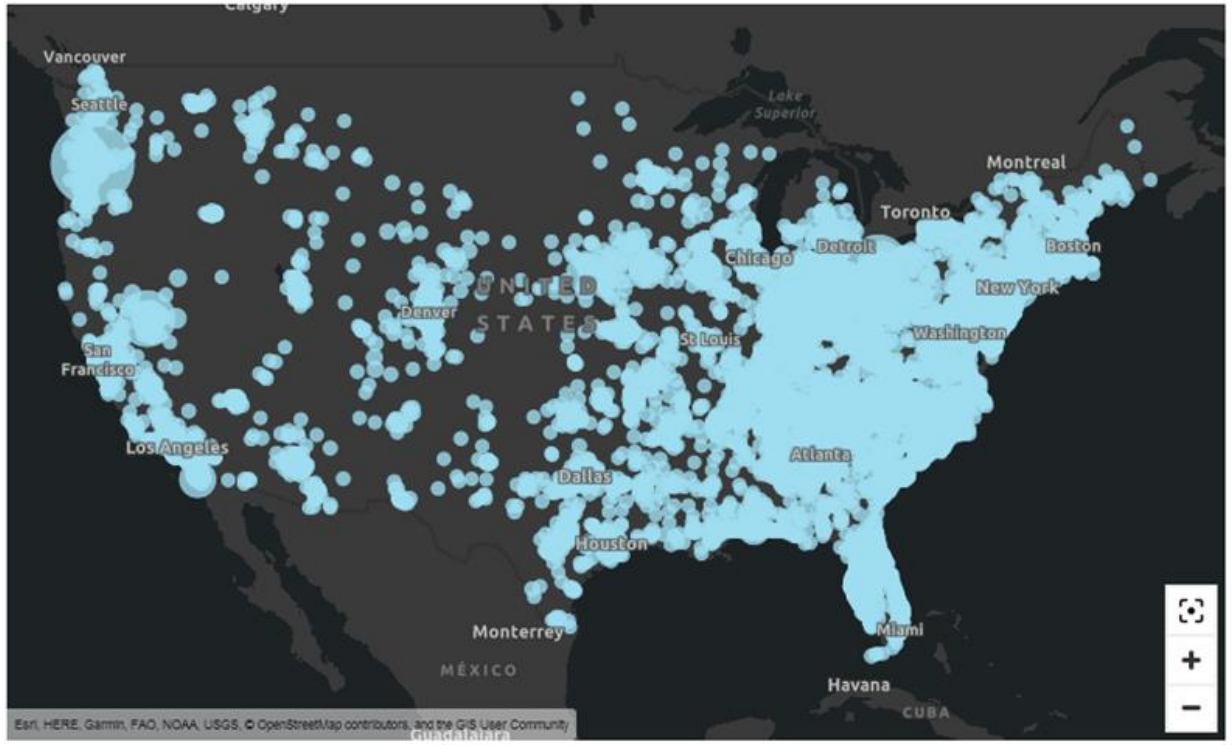
- Collaboration opportunities
- Data for design of prospective trials
- Publish case series with RWD
- Understand treatment landscape
- Real-time medical records and care summaries for patients across sites of care

Patient Data Overview (4/14/2023)

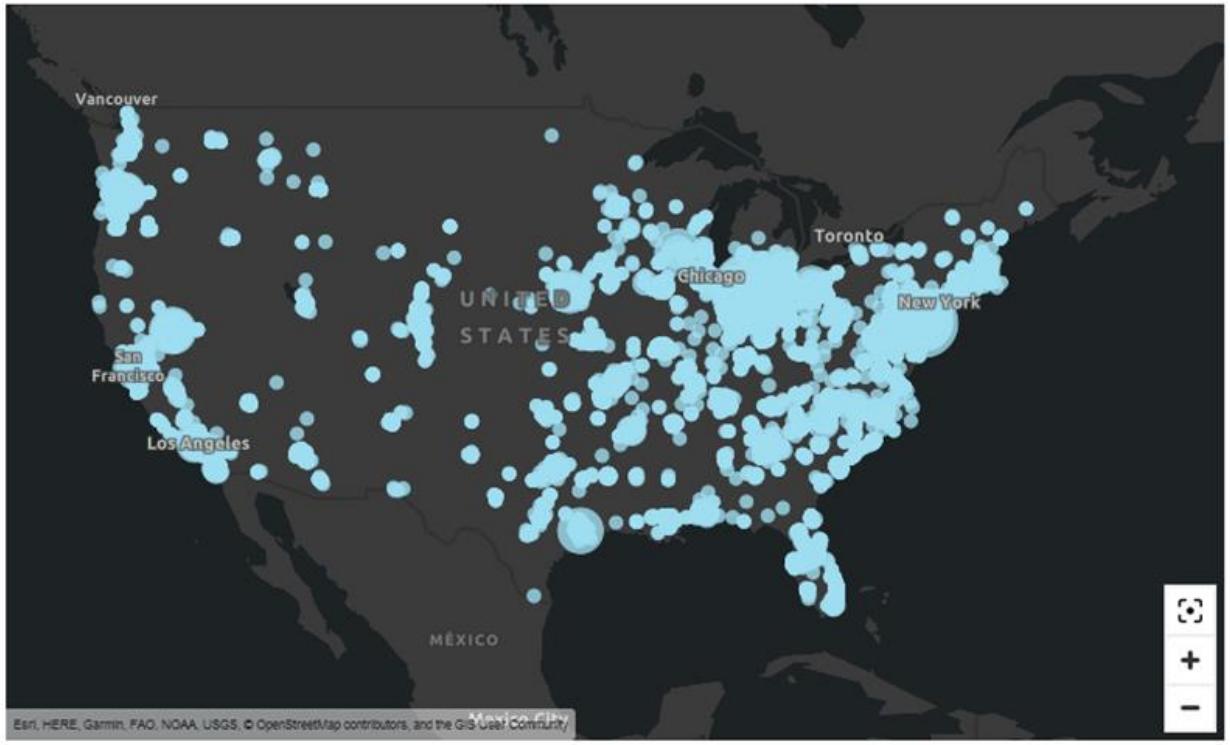
xCures

Subjects	Subjects with Records	Average Record Count	Conditions	Medications	Procedures	Observations	Encounters	Unique Locations
56,776	46,277	1,456	443,213	4,763,591	3,725,085	32,436,836	13,631,963	133,829

Subjects



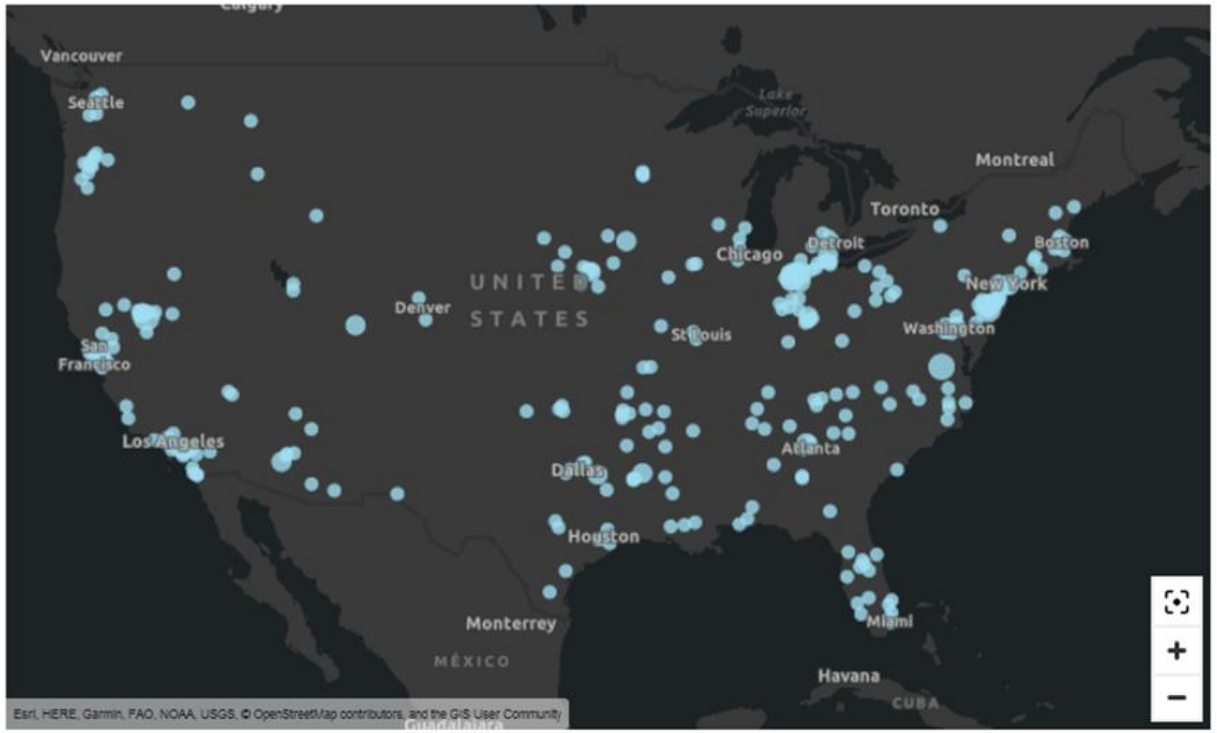
Encounters



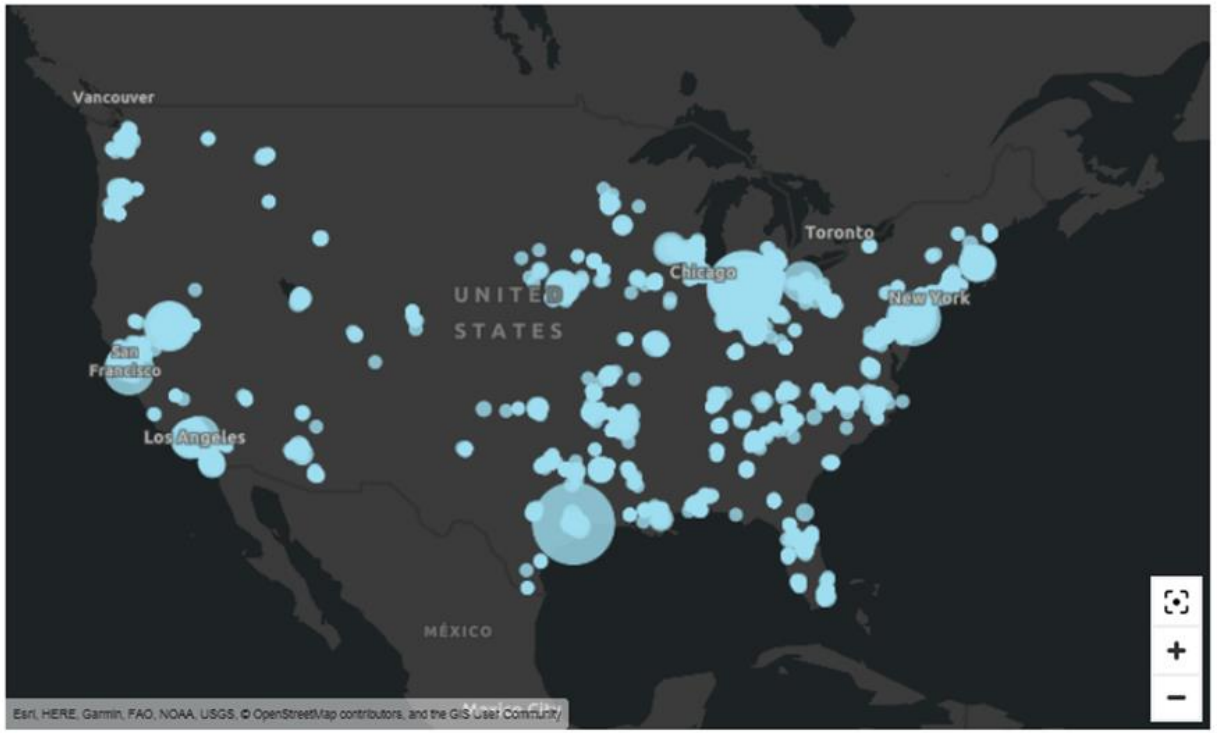
Overview of sarcoma patients

Subjects	Subjects with Records	Average Record Count	Conditions	Medications	Procedures	Observations	Encounters	Unique Locations
400	400	3,876	15,143	115,649	95,687	804,446	291,811	9,005

Subjects



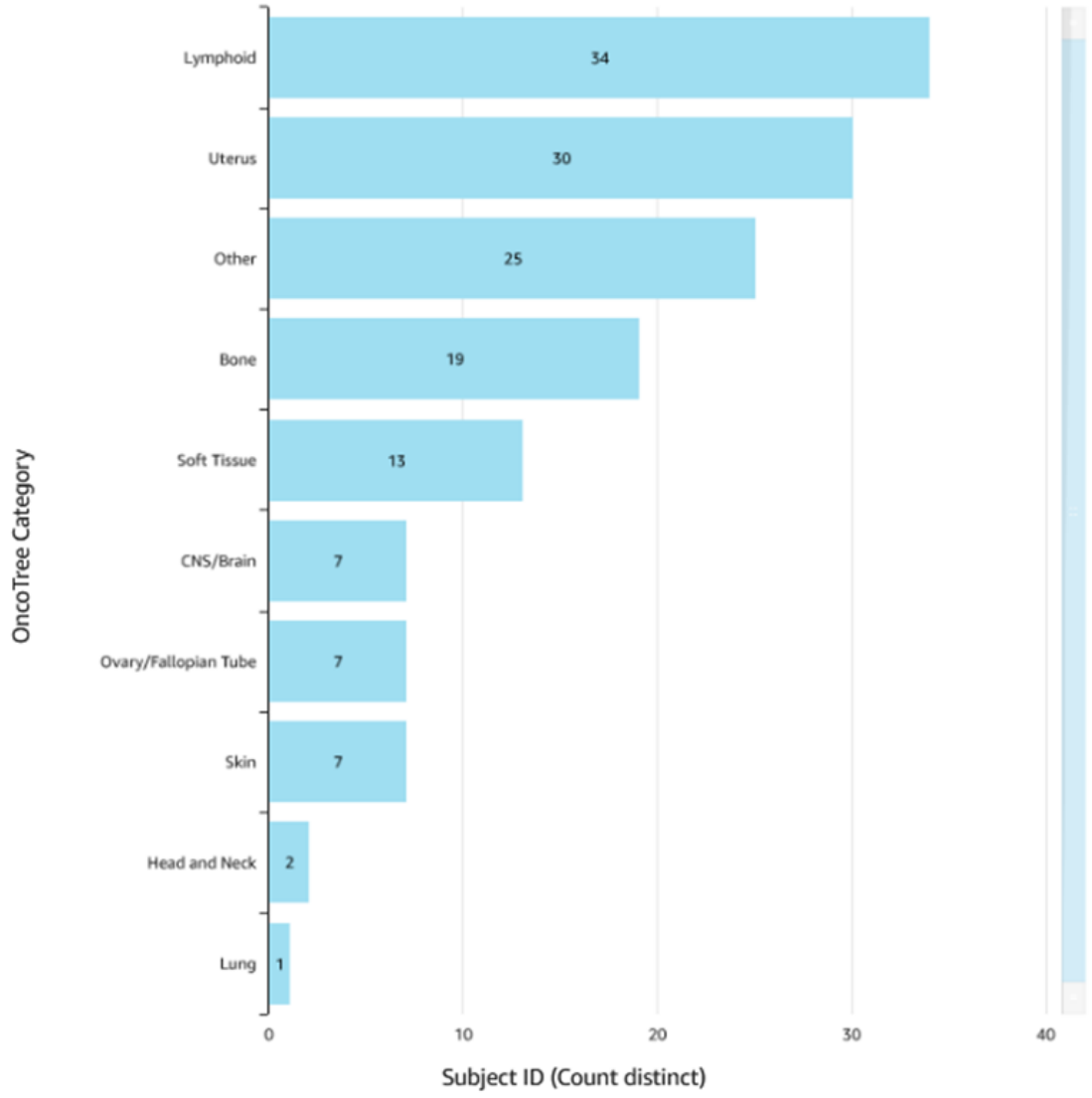
Encounters



Preliminary Overview of Sarcoma Data

xCures

Subjects by Organ



Subjects by Condition

Condition Name	Subject ID
Sarcoma	93
Sarcoma of endometrium	45
Leiomyosarcoma	31
Sarcoma of soft tissue	30
Sarcoma of uterus	24
Carcinosarcoma of uterus	18
Sarcoma (HCC)	17
History of sarcoma	16
Endometrial stromal sarcoma, high grade	15
Sarcoma (CMS/HCC)	15
Leiomyosarcoma of uterus	14
Carcinosarcoma of corpus uteri	13
Osteosarcoma of bone	13
Soft tissue sarcoma	13
Endometrial sarcoma (HCC)	12
Lymphosarcoma	12
Liposarcoma	11
Lymphosarcoma and reticulosarcoma	11
Angiosarcoma	10
Chondrosarcoma	10
Endometrial carcinosarcoma	10
Leiomyosarcoma (HCC)	10
Metastatic sarcoma	10
Sarcoma (CMS-HCC)	10
Gliosarcoma	9
Carcinosarcoma of body of uterus	8
Reticulosarcoma	8

Sarcoma Condition/Medication Combinations

xCures

Subjects	Condition Medication Combos	Unique Conditions	Unique Medications
211	111,553	621	376

Conditions

Condition Name	Subject ID
Malignant neoplastic disease	78
Primary malignant neoplasm of soft tissues	50
Sarcoma	46
Primary malignant neoplasm of female breast	40
Primary malignant neoplasm of uterus	36
Malignant tumor of breast	32
Primary malignant neoplasm of endometrium	31
Malignant neoplasm of corpus uteri, excluding isthmus	30
Malignant neoplasm of endometrium of corpus uteri	28
Secondary malignant neoplasm of bone	28
Malignant neoplasm of female breast	26
Secondary malignant neoplasm of lung	25
Malignant lymphoma	20
Primary malignant neoplasm	20
Secondary malignant neoplasm of liver	20
Leiomyosarcoma	18
Neoplasm of uncertain behavior of soft tissues	18
Secondary malignant neoplastic disease	18

Medications

Medication Name	Subject ID
anastrozole 1 MG Oral Tablet	22
doxorubicin	14
25 ML doxorubicin hydrochloride 2 MG/ML Injection	13
medroxyprogesterone acetate 10 MG Oral Tablet	13
docetaxel	12
letrozole 2.5 MG Oral Tablet	12
pazopanib 200 MG Oral Tablet	12
pembrolizumab	12
temozolomide	12
cyclophosphamide	11
Gemcitabine-containing product	10
anastrozole 1 MG Oral Tablet [Arimidex]	10
medroxyprogesterone	10
tamoxifen 20 MG Oral Tablet	10
500 ML mannitol 200 MG/ML Injection	9
paclitaxel	9
pazopanib	9
capecitabine 500 MG Oral Tablet	8

Sarcoma Patients with Genomic Sequencing

xCures

Subjects with somatic NGS

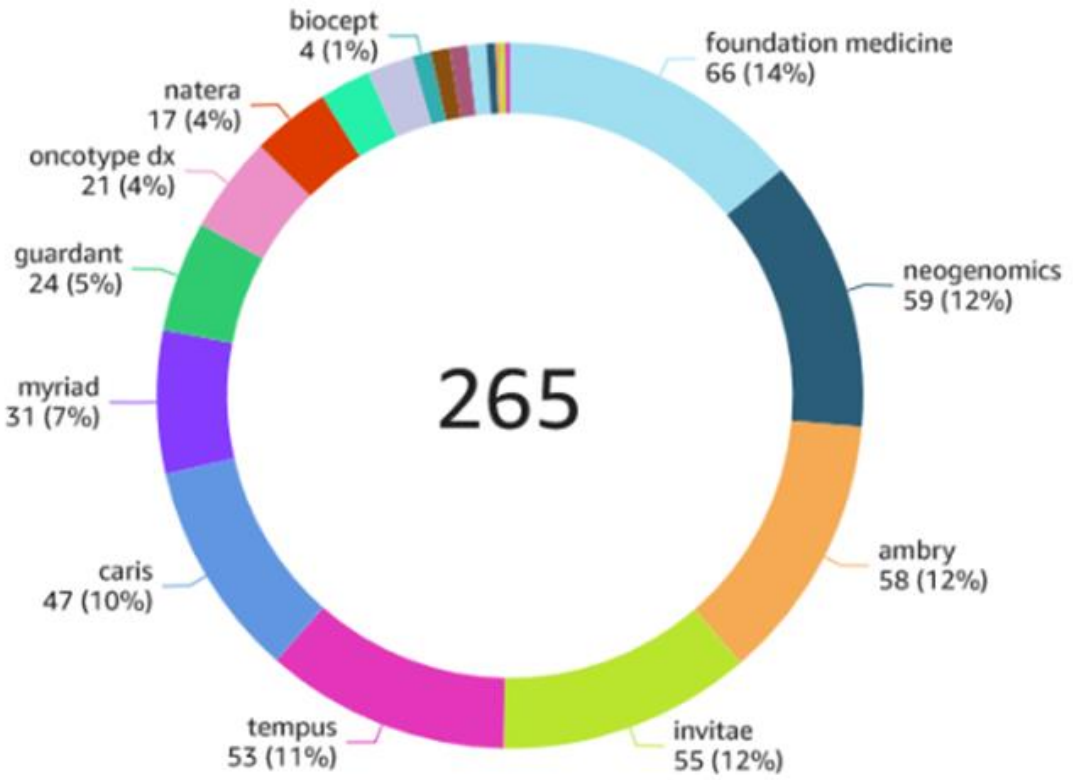
194

Subjects with germline testing

141

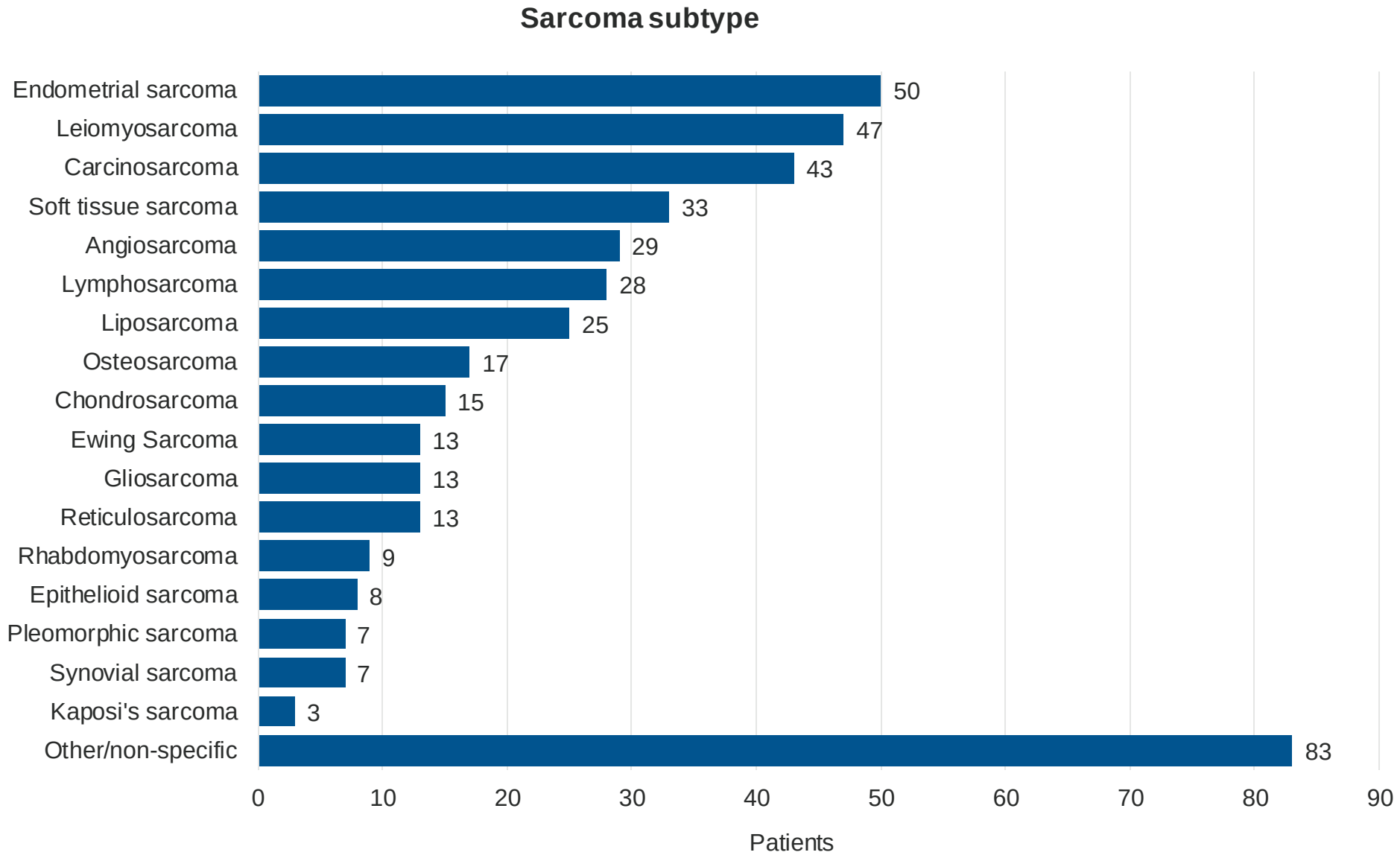
Subjects with genomic profiling

SHOWING TOP 20 IN TERM OCCURRENCE LABEL



Group By: Term Occurrence Label
Size: Subject ID (Count distinct)

Sarcoma Patients by Subtype



Opportunities to Catalyze Impact in Rare Cancer Clinical Repurposing Trials

Clare Thibodeaux
(Cures within Reach)

Clare Thibodeaux, PhD

Vice President, Scientific Affairs with Cures Within Reach

Clare Thibodeaux, PhD is the Vice President, Scientific Affairs with Cures Within Reach and has over 20 years of scientific research and philanthropic experience. Clare joined the Cures Within Reach team in November 2015, and collaborates with key opinion leaders, research institution partners, industry representatives and patient advocates from any disease area globally to identify, centralize and vet clinical repurposing research for funding. She is responsible for leading scientific initiatives at Cures Within Reach, managing Cures Within Reach's scientific grant outreach and review process, leading the Science Advisory Board and developing research and patient education events. Clare also serves on the Advisory Board for the Critical Path Institute's CURE Drug Repurposing Collaboratory. She holds a PhD in Tumor Biology from Georgetown University and an MBA from George Mason University.

Opportunities to Catalyze Impact in Rare Cancer Clinical Repurposing Trials

2023 CDRC Annual Meeting
April 20, 2023

CuresWithinReach

Clare Thibodeaux, PhD
Vice President, Scientific Affairs

- **Repurposing**: finding a new disease indication for a drug, device or nutraceutical already approved for human use
- **Repositioning / Rescue**: finding an indication for a human-safe, still-in-the-pipeline compound
- **Philanthropic**: able to be used by physicians and patients but not likely able to generate a profit in the market
- **Commercial**: able to generate a profit for an organization by bringing it to market through regulatory approval

CuresWithinReach

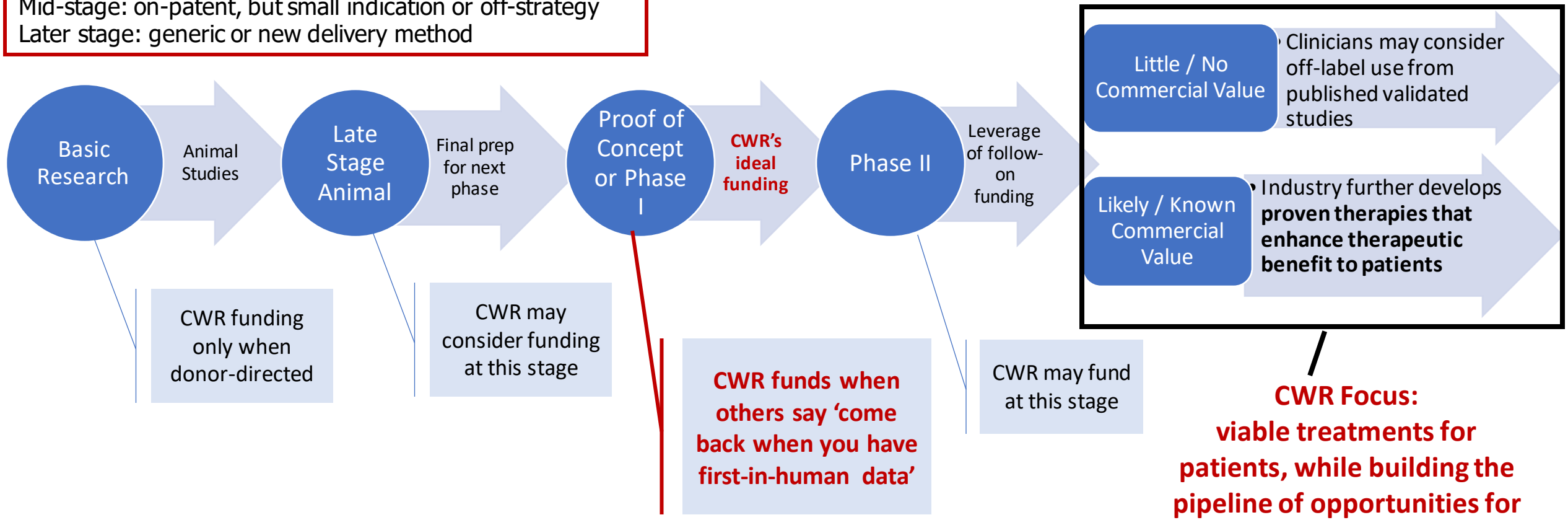
Mission:

To leverage the speed, safety and cost-effectiveness of **testing already approved therapies for new indications** that improve patient quality and length of life, serving philanthropic and/or commercial uses – **driving more treatments to more patients more quickly.**

Disease agnostic, Geography agnostic, Institution agnostic

We Enable Clinical Trial Funding at a Critical Stage of Therapy Development

Additive to Life Cycle Management:
Mid-stage: on-patent, but small indication or off-strategy
Later stage: generic or new delivery method



CWR Focus:
viable treatments for patients, while building the pipeline of opportunities for investors and partners

CWR isn't funding to the finish line, but providing enough
seed funds to achieve catalytic effect

38 trials at 33 institutions in 27 diseases in 7 countries

47% rare diseases
21% ear nose throat
21% oncology
21% neurology
(neurodegenerative, mental health, pain)
13% infectious diseases
11% immune disorders / diabetes
8% ophthalmic
8% other

76% adult, 24% pediatric
97% clinical, 3% pre-clinical
79% US, 21% outside of US
79% drug, 21% device/other

18 ongoing clinical trials in rare diseases

Our ongoing projects are also in:
Germany, India, Kenya, Nigeria, Spain, Vietnam

as of 4.1.2023

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as of 4.1.2023

CWR Cancer Success Stories

- **Thalidomide** in **Multiple Myeloma**:
  FDA approval

- **Laser Device** in **Prostate Cancer**: *follow-on funding and additional clinical trials*

- **Ablation Device** in **Pancreatic Cancer**: *online training tool and expansion to liver cancer*

- **Combination Therapy** in **Lung Cancer**: *support from industry for follow-on trial*

Leveraging Existing Funding

- Co-winner of 2021 CureAccelerator Live! for Rare Diseases pitch event
- Ongoing trial adding hydroxychloroquine to chemotherapy
- **Additional funding supports a biomarker study** to identify any differences between responders and non-responders to repurposed therapy

Leveraging Existing Funding

- Ongoing trial adding metal reduction therapy to chemotherapy
- Additional funding expands the adult clinical trial to include pediatric, adolescent and young adult patients
- **Allows for a wider age range of patients in the study** and potential data comparison across age groups

Attracting Follow-On Support

Principal Investigator: Dr. Alix Seif

Disease: Acute Lymphoblastic Leukemia

Research Description: Pediatric acute lymphoblastic leukemia (ALL) affects approximately 3,000 children per year, and while rare, it is the sixth most common pediatric cancer. Children with ALL who need bone marrow transplants have a high risk of relapse after transplant, and these relapses are usually incurable. New ways to prevent relapse after transplant are urgently needed. Highly sensitive tests that use a fast method of identifying genetic fingerprints called "next generation sequencing" (NGS) can find very low levels of leukemia cells called "measurable residual disease" (MRD), and NGS MRD testing can find 1 leukemia cell in a million blood cells. The team will use NGS MRD testing after transplant to find those children with the highest chances of relapse. They will then match patients to personalized repurposed immune treatments based on features of each child's leukemia. The treatments include daratumumab (approved for multiple myeloma) and blinatumomab (approved to treat already relapsed ALL). If this highly sensitive testing is successfully in providing pediatric ALL patients with personalized, repurposed treatment to prevent relapse in

Current Research

Children's Hospital of Philadelphia
RESEARCH INSTITUTE

Read more in the CureAccelerator Live! poster

- Originally a single site pilot trial, **now expanded to 7 total sites across U.S.** following CWR funding
- Increased target enrollment over originally funded study
- Securing study drug donation from pharma
- Challenge: increased time for FDA approval and coordinating multiple IRB processes

Engaging Underserved Patients/Researchers

Principal Investigator: Dr. H. Steven Sims

Disease: Esophageal cancer

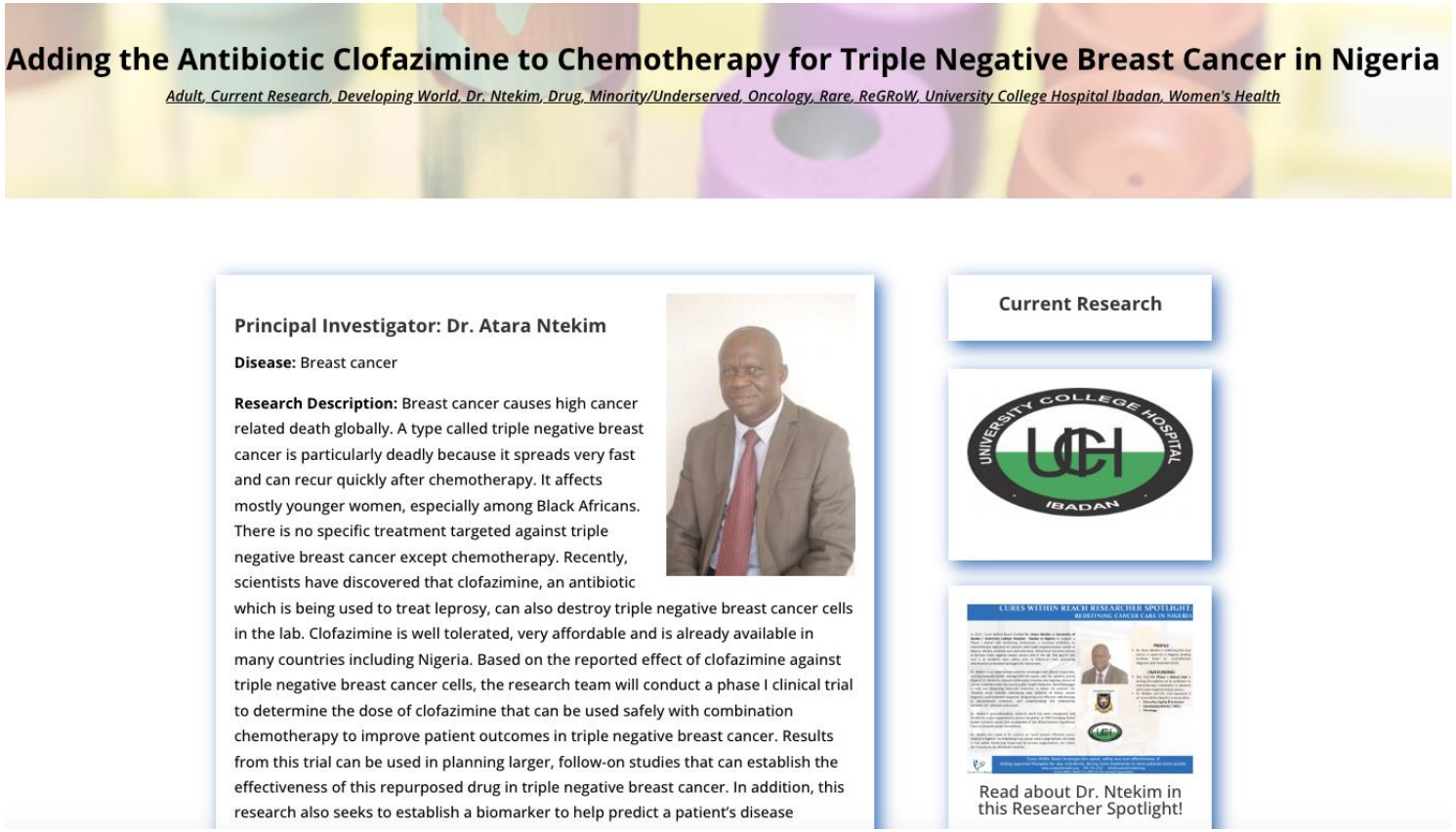
Research Description: Esophageal cancer can be divided into two types: adenocarcinoma (the majority of diagnoses in White patients) and squamous cell carcinoma (SCCA, the majority of diagnoses in Black patients). Black males in particular have poorer outcomes from esophageal cancer. Transnasal esophagoscopy (TNE) uses a flexible endoscope device to identify conditions that are risk factors for adenocarcinoma, such as Barrett's esophagus, and to monitor for adenocarcinoma through routine screenings. However, TNE is not currently used for SCCA routine screening. This community-based study will survey the population at community health centers to inquire about risk factors for SCCA (primarily tobacco and alcohol consumption). The research team will then use TNE on those with self-reported risk factors to screen for SCCA, focusing on Black males. Those patients with positive

Current Research

UIC UNIVERSITY OF ILLINOIS CHICAGO

- Squamous cell esophageal cancer more common in Black patients; Black patients have poorer outcomes
- Repurposing a device typically used to screen for adenocarcinoma to develop a routine screening program for squamous cell carcinoma
- **Working with community-based organizations to engage, enroll and share results and address heath disparites**

Engaging Underserved Patients/Researchers



- Higher cancer burden in low and lower-middle income countries (LMICs)
- **Repurposing generic, accessible drugs**; adding an antibiotic to chemotherapy in TNBC to improve outcomes
- Opportunity to engage stakeholders already working in LMICs to increase research in rare cancers globally

Summary: Catalytic Opportunities

- Researchers and clinicians can collaborate and be additive with funding sources to increase patient impact
- Expand patient engagement to include underserved patients and look for opportunities to address health disparities in rare cancers
    - Sarcoma example: pediatric osteosarcoma more common in minority patients, especially Blacks
- Rare cancers are a global problem; include researchers, patients and stakeholders from LMICs

Clare Thibodeaux, PhD

Clare@cureswithinreach.org

For more information:

www.cureswithinreach.org

Twitter: @CuresWReach

Facebook: CuresWithinReach

Repurposed Drug Trials: Challenges and Opportunities

Vidula Sukhatme (GlobalCures)

Ms. Vidula Sukhatme

CEO, GlobalCures

Ms. Vidula Sukhatme is the Co-founder and CEO of GlobalCures, Inc. Additionally, she played a role in founding the Morningside Center for Innovative and Affordable Medicine at Emory University. She has earned two master of science degrees: one in mathematics from Northeastern University and another in epidemiology from the Harvard T.H. Chan School of Public Health. She also has two decades of experience working with information systems in healthcare settings.

Repurposed Drug Trials: Challenges and Opportunities

Vidula V. Sukhatme MS

Co-Founder & CEO, GlobalCures, Inc.

Co-founder, Emory University Morningside Center for Innovative and Affordable Medicine

April 20, 2023

globalcures

Morningside Center for Innovative and Affordable Medicine

Why we exist:

To rapidly develop new, effective and affordable treatments for unmet medical needs (initially cancer)

How we do it:

By “adopting financial orphans”, scientifically promising treatments lacking financial reward

What we do:

- Identify promising financial orphan interventions (ReMedy Database)
- Prioritize treatments ready for testing and facilitate and fund clinical trials.
- Fund critical pre-clinical experiments, for ideas not ready for clinical studies
- Educate and advocate for adoption of “financial orphans”

Emory University Morningside Center for Innovative and Affordable Medicine

ReMedy-Cancer

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Home

ReMedy (Repurposed Medicines)-Cancer Database aims to make the process of finding repurposed drug data related to cancer easier for patients, physicians and potential investigators.

There are currently unmet needs in medicine due to expensive, toxic, and only moderately effective therapies. However, there are also scientifically promising ideas for new treatments which are not being developed largely because they lack sufficient financial incentive. Many of these potential treatments include FDA approved drugs that could be repurposed for other indications, such as cancer.

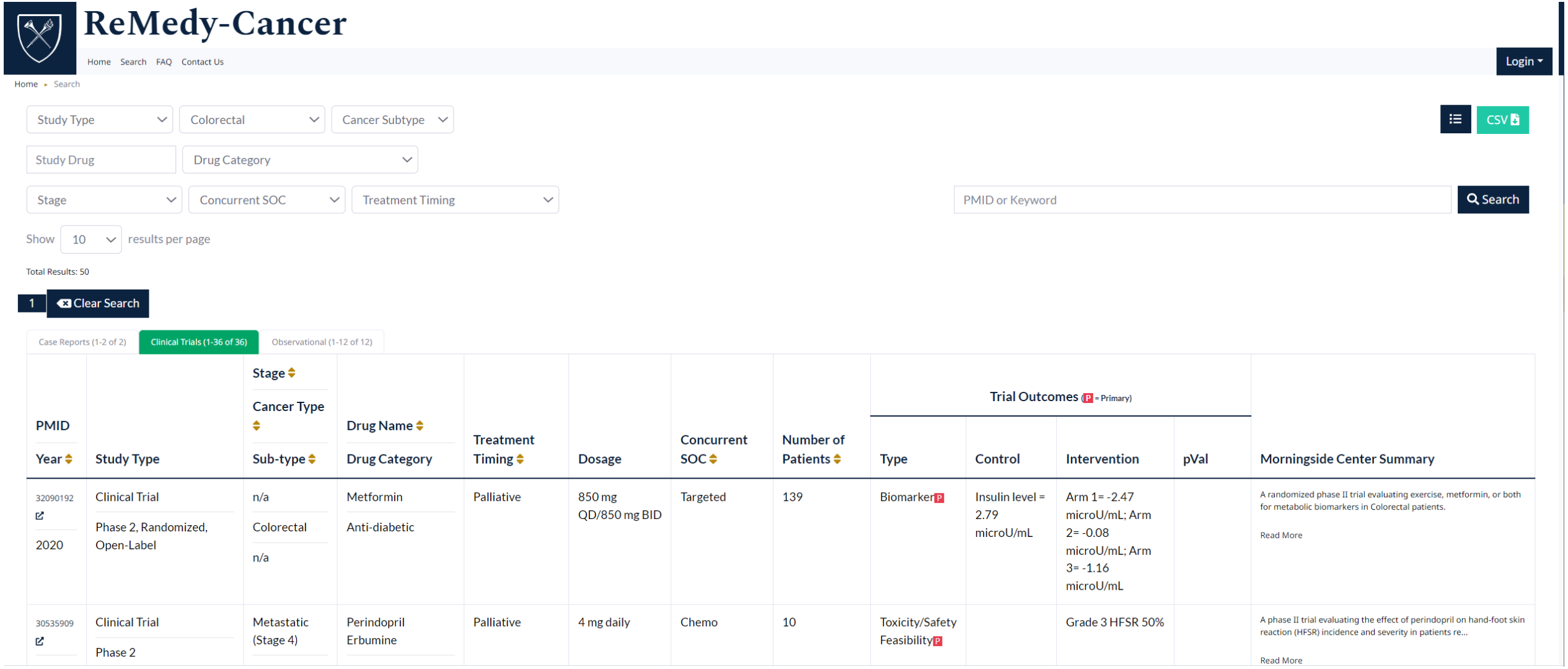
ReMedy-Cancer Database allows users to search for this information by Cancer Type, Drug Name, and Study Type. Users can also refine their results by Cancer Subtype, Cancer Stage, Drug Category, Concurrent Standard of Care Treatment (SOC), and Treatment Timing.

ReMedy-Cancer Database

Repurposed drug knowledgebase related to cancer treatments

ReMedy-Cancer Database is supported by the Morningside Center for Innovative and Affordable Medicine, an interdisciplinary unit located within the Woodruff Health Sciences Center at Emory University. Extending the vision of GlobalCures Inc., a non-profit medical research organization, the Morningside Center was created to promote research, education, and advocacy for effective and affordable medical treatments that are not being pursued because of a lack of financial return.

Emory University Morningside Center for Innovative and Affordable Medicine



Morningside Center Clinical Trials

Study Name	Principal Investigator
Pilot Study of Biomarker Evaluation and Safety of Pre-Incisional Ketorolac for Patients Undergoing Surgical Resection for Non-Small Cell Lung Cancer and Renal Cell Carcinoma	Viraj Master, MD, PhD
Paricalcitol and hydroxychloroquine (PH) combination with gemcitabine and nab-paclitaxel in advanced pancreatic cancer	Olatunji Alese, MD
Propranolol Hydrochloride and Pembrolizumab in Patients with Recurrent or Metastatic Urothelial Carcinoma: A Single-Institute Phase II Trial	Bassel Nazha, MD, MPH
A Phase Ib/II Study of Propranolol with Fixed-dose Pembrolizumab in Patients with Unresectable Stage III and Stage IV Melanoma (Collaborative Trial with Roswell Park)	Melinda Yushak, MD, MPH
Neoadjuvant simvastatin and letrazole in early-stage hormone positive breast cancer	Ruth Sacks, MD
Treatment of Brain Metastases with Arginine Supplementation	Lisa Sudmeier, MD, PhD

Clinical Trials in Development

Study Name	Principal Investigator	Working Group
Phase Ib Study of diclofenac salvage in patients metastatic non-small cell lung cancer with early signs of progression on single agent PD(L)-1 blockade	Jennifer Carlisle, MD	*Lung*
Treatment of ovarian cancer with atovaquone	Namita Khanna, MD & Jane Meisel, MD	*Gynecologic Oncology*
Treatment of pediatric brain cancer with atovaquone	Tobey MacDonald, MD	*Aflac Cancer and Blood Disorders Center, Children's Healthcare of Atlanta*
A phase II trial of T3 replacement for hypothyroidism induced by immune checkpoint blockade	TBD	*Melanoma, Lung, GU*

Challenges: Recruiting Clinical Investigators

Generic repurposed drug trials do not have pharma **Sponsors** and are considered as **Investigator-initiated trials** (IITs).

For IITS, the clinician is both the Sponsor and the Principal Investigator (PI) and responsible for all tasks below.

Major Tasks for Clinical Trials	Sponsor	Principal Investigator
Develop trial concept and protocol (drug, disease, clinical setting, statistics, etc)	√ √ √	√
File IND application or obtain exemption	√ √ √	√
Secure funding	√ √ √ √	
IRB process	√ √	√ √
Conduct trial		√ √ √ √
Patient recruitment	√ √	√ √
Regulatory process (monitor/report/etc)	√ √ √	√

Challenges: Recruiting Clinical Investigators

- PIs do not have formal training for sponsor tasks
- Sponsor tasks require a substantial amount of time.
- Small repurposed drug trial budgets include only about 2-3% (40-60 hours) of PI's salary. No incentives (financial or reputational) to become a PI on a small trial if opportunities exist for enrolling patients on industry sponsored trials.
- Most PIs available for repurposed drug trials are 'Young Investigators' or 'Investigators in training' who need mentorship and institutional infrastructure to help with sponsor tasks.

Challenges: Funding

Philanthropic or government grants:

Scientific reviewers perceive the supporting data for new drugs as much stronger than supporting data for repurposed drugs. Hard to compete for funding available to both types of trials.

Data	New Drugs	Repurposed Drugs
Pre-clinical data	*Focused strong data*	*Fragmented, multi-user data*
Mechanism of action	*Single, well defined*	*Pleotropic, perception: "Dirty Drug"*
Dose response – new indication	*Well defined*	*Not well explored – supporting data in the form of retrospective studies*
Human Data	*None*	*Retrospective, case reports, small non-randomized studies*

Challenges: Funding

There are many small pilot, phase I or Phase II single arm trials done with repurposed drugs. However, the study design is not always optimal.

Reason: Inadequate funding

Most trials have funding in the amounts of $50K to $300K. Often, this amount is insufficient to include control arms, placebos, multiple doses, randomization or biomarkers.

Challenges: Successful Completion

Slow Accrual, End of Funding or PI no longer at the institution!

Metformin Hydrochloride in Treating Women With Stage I or Stage II Breast Cancer That Can Be Removed By Surgery

ClinicalTrials.gov Identifier: NCT00984490

Recruitment Status : Terminated (slow accrual)
First Posted : September 25, 2009
Results First Posted : July 13, 2012
Last Update Posted : July 13, 2012

Metformin as a Chemoprevention Agent in Non-small Cell Lung Cancer

ClinicalTrials.gov Identifier: NCT01717482

Recruitment Status : Terminated (Poor accrual and funding ended)
First Posted : October 30, 2012
Results First Posted : June 19, 2019
Last Update Posted : March 10, 2020

Metformin and Carbohydrate Restriction With Platinum Based Chemotherapy In Stage IIIB/IV Non-Squamous Non-Small Cell Lung Cancer (NS-NSCLC) (METRO)

ClinicalTrials.gov Identifier: NCT02019979

Recruitment Status : Terminated (PI left the institution)
First Posted : December 24, 2013
Results First Posted : May 4, 2018
Last Update Posted : May 4, 2018

Metformin in Non Small Cell Lung Cancer (NSCLC):

ClinicalTrials.gov Identifier: NCT02285855

Recruitment Status : Terminated (Poor Accrual)
First Posted : November 7, 2014
Results First Posted : January 6, 2020
Last Update Posted : January 6, 2020

Challenges - Summary and Next Steps

- **Recruitment of Clinical Investigators**
  - National agency to provide training/mentorship to clinical investigators
  - Financial incentives and recognition for clinical investigators willing to work on financial orphans
  - National agency to act as ‘SPONSOR’ for financial orphans
- **Successful Completion of the trial**
  - National agency to recruit patients and help with accruals
  - Innovation in multi-center trial design
- **Funding**
  - Separate track for evaluation and funding of financial orphans

Repurposed Drug Trials: The Opportunity!

Rapidly develop New, Effective and Affordable treatments for unmet medical needs!

Thanks

Break

Challenges and opportunities

CDRC CRITICAL PATH INSTITUTE | CURE ID Challenging cases... New approaches

Harnessing RWD to advance repurposed drugs for rare cancers

Panel

Panel Discussion

- **Brandi Felser** (SFA)
- **Christine Heske** (NCI)
- **Vidula Sukhatme** (GlobalCures)
- **Andrea Gross** (NCI)
- **Suanna Bruinooge** (ASCO)
- **Lennie Woods** (Clear Cell Sarcoma Foundation)

Brandi Felser

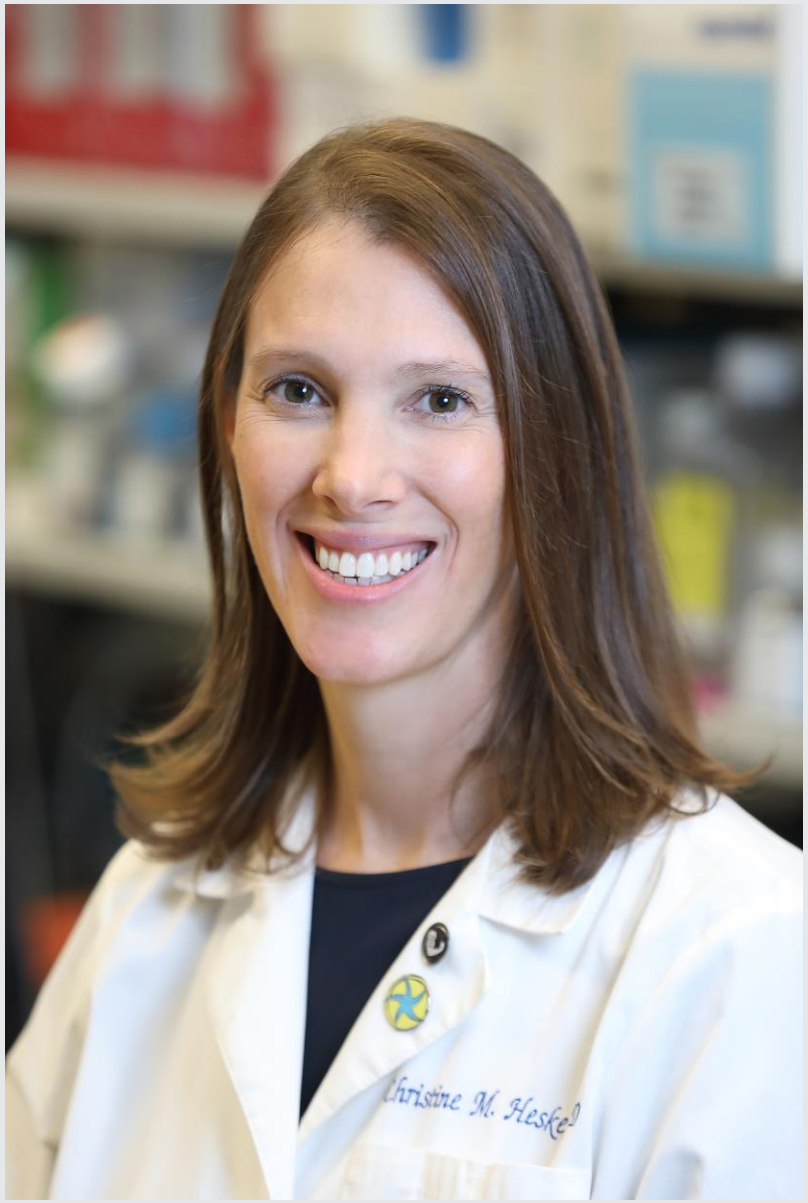
Chief Executive Officer, Sarcoma Foundation of America (SFA)

Brandi Felser joined the Sarcoma Foundation of America (SFA) as the Chief Executive Officer in December 2019. She has more than 20 years' non-profit senior leadership experience, most recently serving as the Chief Operating Officer – Chief of Staff at the National Breast Cancer Coalition. Brandi has a strong background in patient advocacy and education, as well as advancing cancer research and public policy initiatives. Having lost both of her parents to cancer, Brandi uses her passion and personal experience to elevate the voices of sarcoma patients and family members and to fund meaningful research that will ultimately lead to better outcomes for people diagnosed with sarcoma. She has a Master of Business Administration (MBA) from The George Washington University, and is completing a Master in Liberal Arts, Clinical Psychology, from the Harvard University Extension School.

Christine Heske

Investigator, National Cancer Institute

Dr. Christine Heske is a clinician and physician-scientist with an active translational and clinical research program focused on sarcoma treatments. Her goal is to improve outcomes for patients with pediatric sarcomas by understanding mechanisms of resistance and identifying and evaluating new therapeutic targets. After completing her undergraduate work at Harvard University, Dr. Heske received her M.D. from The George Washington University School of Medicine and Health Sciences. She completed her pediatric internship and residency at Brown University/Hasbro Children's Hospital, followed by her fellowship training at the combined National Cancer Institute Johns Hopkins University Pediatric Hematology and Oncology program, where she served as Chief Fellow. In 2016, Dr. Heske began her own group as a Physician-Scientist Early Investigator in the Pediatric Oncology Branch. She was promoted to Investigator in 2021 and currently leads the Translational Sarcoma Biology Group. Dr. Heske holds board certifications in General Pediatrics and Pediatric Hematology/Oncology.



Ms. Vidula Sukhatme

CEO, GlobalCures

Ms. Vidula Sukhatme is the Co-founder and CEO of GlobalCures, Inc. Additionally, she played a role in founding the Morningside Center for Innovative and Affordable Medicine at Emory University. She has earned two master of science degrees: one in mathematics from Northeastern University and another in epidemiology from the Harvard T.H. Chan School of Public Health. She also has two decades of experience working with information systems in healthcare settings.

Andrea Gross

Assistant Research Physician, Center for Cancer Research

Dr. Andrea Gross is a board-certified pediatrician and pediatric oncologist who earned her medical degree at the University of Connecticut and completed pediatric residency at Cincinnati Children's Hospital Medical Center. She completed a pediatric hematology/oncology fellowship at Children's National Medical Center and is currently an Assistant Research Physician working in the Pediatric Oncology Branch at the National Cancer Institute in the lab of Dr. Brigitte Widemann. Dr. Gross has been the lead associate investigator on the phase 2 trial of selumetinib for patients with neurofibromatosis type 1 (NF1) and inoperable plexiform neurofibromas since 2015, which led to the first FDA approved medication for NF1 in 2020. Her research focuses on clinical trials for tumor predisposition syndromes. Her areas of interest include developing and utilizing functional outcome measures to define clinical benefit of therapies for tumor predisposition syndromes like NF1, designing and running clinical trials for rare disease populations and working with patient advocates to increase patient engagement in clinical trial design.

Suanna Bruinooge, MPH

Division Director of Research Strategy and Operations, ASCO's Center for Research and Analytics (CENTRA)

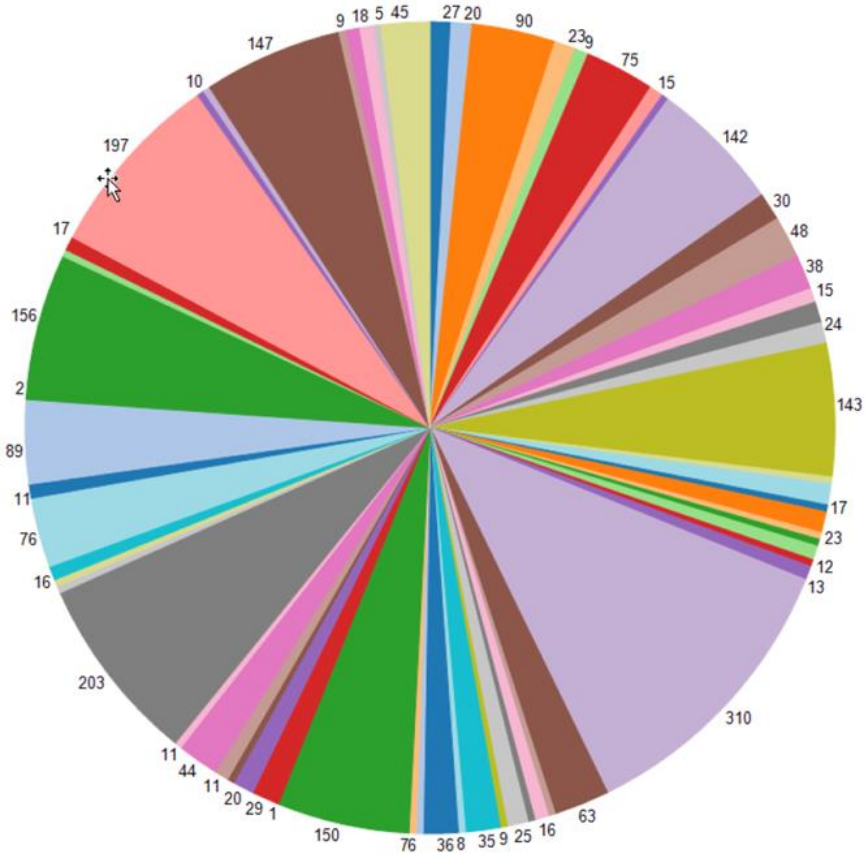
Suanna Bruinooge, MPH, is the Division Director of Research Strategy and Operations in ASCO's Center for Research and Analytics (CENTRA). CENTRA generates, integrates, analyzes, and shares oncology data to foster innovation in research and patient care and help develop and evaluate ASCO's policy positions. CENTRA develops and implements ASCO's research priorities, including the Targeted Agent Profiling and Utilization (TAPUR) clinical trial and projects to advance clinical trial design and methodology. CENTRA also staffs ASCO's Cancer Research Committee and Research Community Forum. Prior to joining ASCO, Suanna worked for seven and a half years in the U.S. House of Representatives, working for Congresswoman Nancy Johnson (R-CT) and Congressman Vernon Ehlers (R-MI). Ms. Bruinooge earned a Master of Public Health in Health Policy at The George Washington University's Milken Institute School of Public Health in 2015. Suanna also has a B.A. in political science from Calvin College in Grand Rapids, MI.

Lennie Woods

Executive Director and Co- Founder, Clear Cell Sarcoma Foundation

Lennie Woods is executive director and co- founder of the Clear Cell Sarcoma Foundation (formerly Sara's Cure) along with her husband of 30 years, Denny. As a Charleston native and college of Charleston graduate, she was able to build a successful career in Real Estate until life's direction took a drastic change in when her daughter, Sara, was diagnosed with Clear Cell Sarcoma during a church mission trip to Guatemala. After flying home Lennie and Denny were told Sara was metastatic and there was no treatment or cure, they immediately decided that this was not acceptable for their daughter or anyone suffering from this ultra-rare cancer. Lennie is blessed with a drive to get answers and make the connections needed for success. The CCSF was established for the purpose of finding the right treatment for clear cell sarcoma by bringing the patients and their experiences together, so CCS has a bigger voice within the cancer research community. Thanks to some amazing doctors and aggressive surgery, Sara has been NED since 2018.

Sarcoma subtypes

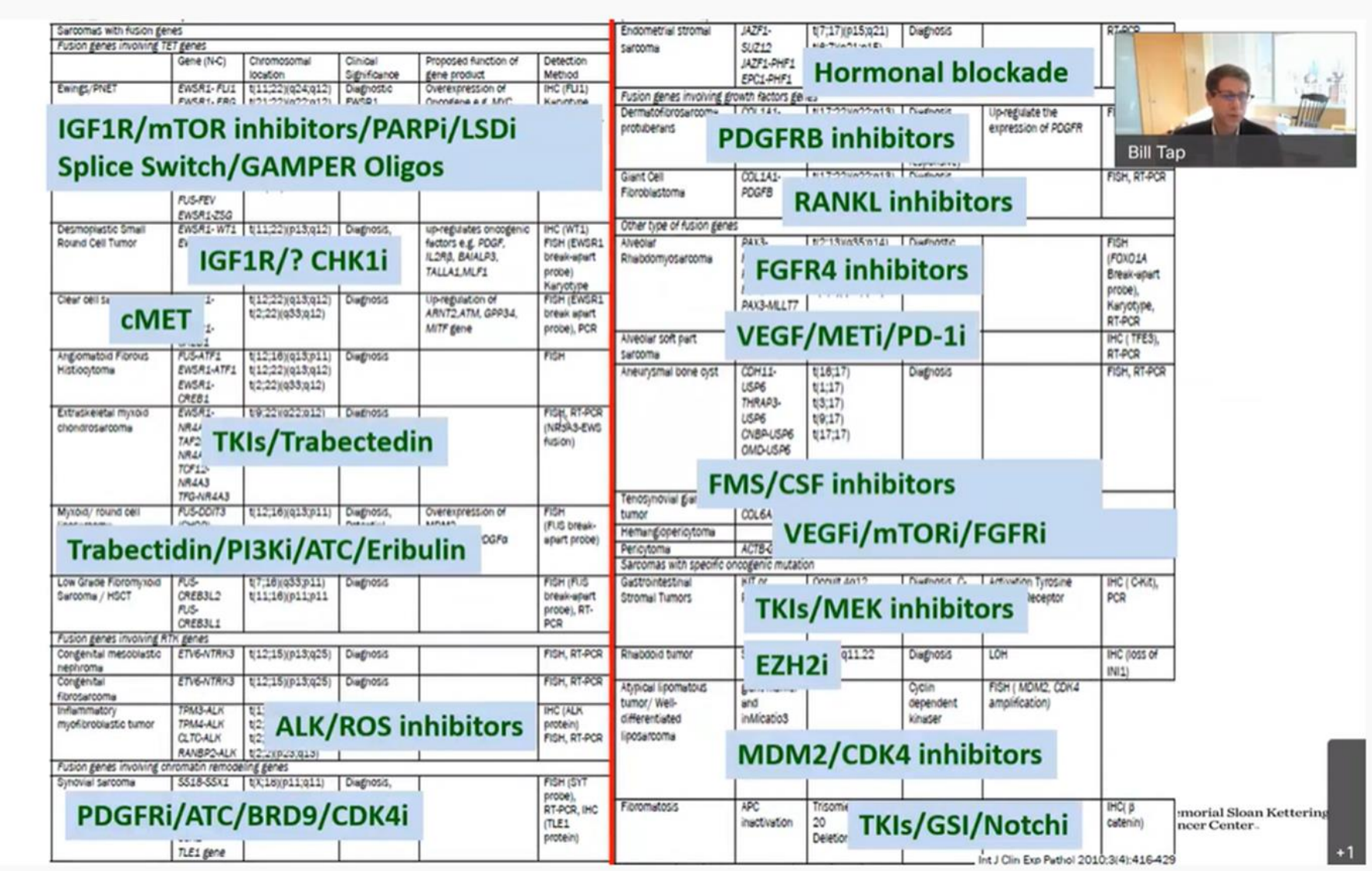


- Alveolar Rhabdomyosarcoma
- Alveolar Soft Part Sarcoma
- Angiosarcoma
- Breast Angiosarcoma
- Breast Sarcoma
- Chondroblastic Osteosarcoma
- Chondrosarcoma
- Clear Cell Sarcoma
- Dedifferentiated Chondrosarcoma
- Dedifferentiated Liposarcoma
- Desmoid/Aggressive Fibromatosis
- Desmoplastic Small-Round-Cell Tumor
- Embryonal Rhabdomyosarcoma
- Endometrial Stromal Sarcoma
- Epithelioid Hemangioendothelioma
- Epithelioid Sarcoma
- Ewing Sarcoma
- Extraskeletal Myxoid Chondrosarcoma
- Fibroblastic Osteosarcoma
- Fibrosarcoma
- Follicular Dendritic Cell Sarcoma
- Glomangiosarcoma
- Hemangioma
- High-Grade Endometrial Stromal Sarcoma
- High-Grade Surface Osteosarcoma
- Histiocytic Dendritic Cell Sarcoma
- Inflammatory Myofibroblastic Tumor
- Interdigitating Dendritic Cell Sarcoma
- Intimal Sarcoma
- Leiomyosarcoma
- Liposarcoma
- Liver Angiosarcoma
- Low-Grade Central Osteosarcoma
- Low-Grade Endometrial Stromal Sarcoma
- Low-Grade Fibromyxoid Sarcoma
- Malignant Phyllodes Tumor of the Breast
- Mesenchymal Chondrosarcoma
- Myofibroma
- Myxofibrosarcoma
- Myxoid Chondrosarcoma
- Myxoid/Round-Cell Liposarcoma
- Myxoma
- Ossifying Fibromyxoid Tumor
- Osteoblastic Osteosarcoma
- Osteosarcoma
- Parosteal Osteosarcoma
- Perivascular Epithelioid Cell Tumor
- Phyllodes Tumor of the Breast
- Pleomorphic Liposarcoma
- Pleomorphic Rhabdomyosarcoma
- Proximal-Type Epithelioid Sarcoma
- Radiation-Associated Sarcoma
- Rhabdomyosarcoma
- Round Cell Sarcoma, NOS
- Sarcoma, NOS
- Sclerosing Epithelioid Fibrosarcoma
- Secondary Osteosarcoma
- Small Cell Osteosarcoma
- Soft Tissue Myoepithelial Carcinoma
- Solitary Fibrous Tumor/Hemangiopericytoma
- Spindle Cell Rhabdomyosarcoma
- Synovial Sarcoma
- Telangiectatic Osteosarcoma
- Tenosynovial Giant Cell Tumor Diffuse Type
- Undifferentiated Pleomorphic Sarcoma/MFH/HGSCS
- Undifferentiated Uterine Sarcoma
- Uterine Adenosarcoma
- Uterine Carcinosarcoma/Uterine Malignant Mixed Mullerian Tumor
- Uterine Epithelioid Leiomyosarcoma
- Uterine Leiomyoma
- Uterine Leiomyosarcoma
- Uterine Myxoid Leiomyosarcoma
- Uterine Perivascular Epithelioid Cell Tumor
- Uterine Sarcoma, Other
- Uterine Sarcoma/Mesenchymal
- Uterine Smooth Muscle Tumor
- Uterine Smooth Muscle Tumor of Uncertain Malignant Potential
- Well-Differentiated Liposarcoma

Anticancer Fund

The Anticancer Fund supports rare sarcoma trials

Genetic and molecular drivers for different Sarcomas



Personalized medicine?

- Genomic
- Epigenetic
- Transcriptomic perturbations

Drug resistance

- Classical
- Tumor acidosis
- Dormancy and reoccurrence

Biomarkers

- Cytokines
- miRNAs
- Extracellular vesicles
- Circulating Tumor Cells
- cfDNA

Treatment likely is multifactorial

- Combination therapy

Capture RWD being generated every day regarding repurposed drugs

- How can we harness existing clinical experience to generate hypothesis using RWD (clinician submitted reports or EHR data extraction) that can be tested in RCTs?

E.g., checkpoint inhibitors in Sarcomas

High response rates were seen in classic Kaposi sarcoma (CKS), with ORR of 0.69 (95% CI 0.51–0.82).

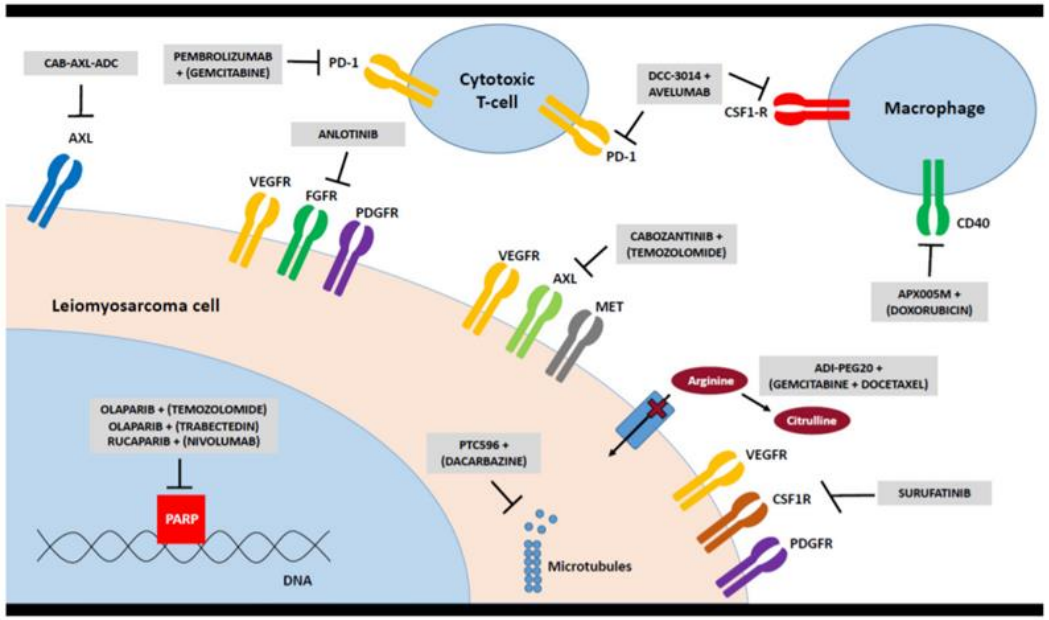


Figure 1. New possible treatment strategies and their mode of action for patients with LMS.

ELSEVIER

European Journal of Cancer
Volume 152, July 2021, Pages 165-182

Review

Immune checkpoint inhibitors in treatment of soft-tissue sarcoma: A systematic review and meta-analysis

Michael Saerens [a], Nele Brusselaers [b, c, d], Sylvie Rottey [a, e, g], Alexander Decruyenaere [a], David Creytens [f, g], Lore Lapeire [a, g]

[a] Department of Medical Oncology, Ghent University Hospital, Ghent, Belgium
[b] Global Health Institute, Antwerp University, Antwerp Belgium
[c] Centre for Translational Microbiome Research, Karolinska Institutet, Stockholm, Sweden
[d] Department of Head and Skin, Ghent University Hospital, Ghent, Belgium
[e] Drug Research Unit Ghent, Ghent University Hospital, Ghent, Belgium
[f] Department of Pathology, Ghent University Hospital, Ghent, Belgium
[g] Cancer Research Institute Ghent, Ghent University, Ghent, Belgium

Received 10 March 2021, Revised 12 April 2021, Accepted 22 April 2021, Available online 6 June 2021.

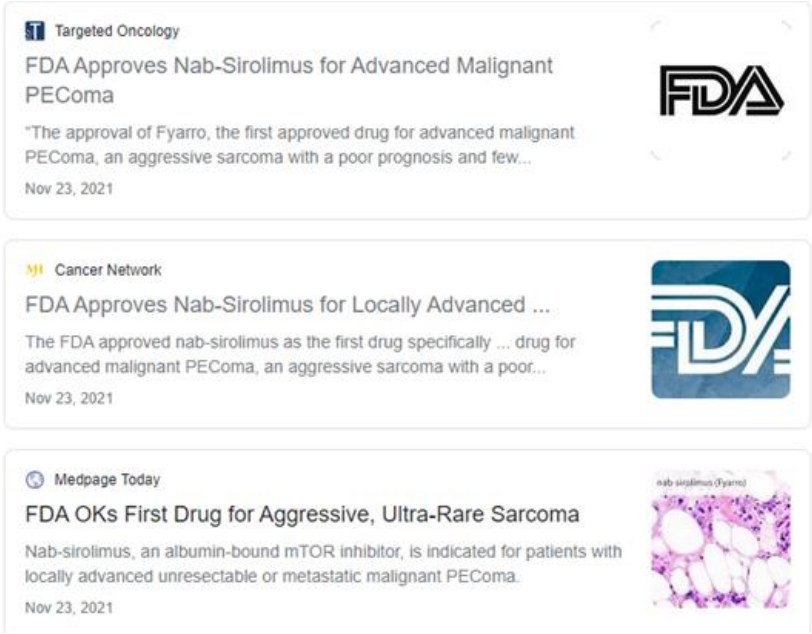
Unesbulin (second-generation BMI-1 inhibitor) for soft tissue sarcoma (Orphan drug designation by EMA)

EHRs to systematically collect RWD for sarcoma subtypes

CDRC CRITICAL PATH INSTITUTE | CURE ID Challenging cases... New approaches

Opportunities…gold nuggets?

1. Imatinib Mesylate used in GIST
   - Potential for tyrosine kinase inhibitors for other sarcoma subtypes?
2. Rapamycin used in PEComa
   - Can also use mTOR inhib for Epithelioid Hemangioendothelioma (EHE)
3. Immunotherapy used in Angiosarcomas
   - β-blockers (+/- propranolol) checkpoint inhibitors
4. Others?
   - Antibiotics for liposarcoma
   - Systematically capture off-label use in practice of medicine

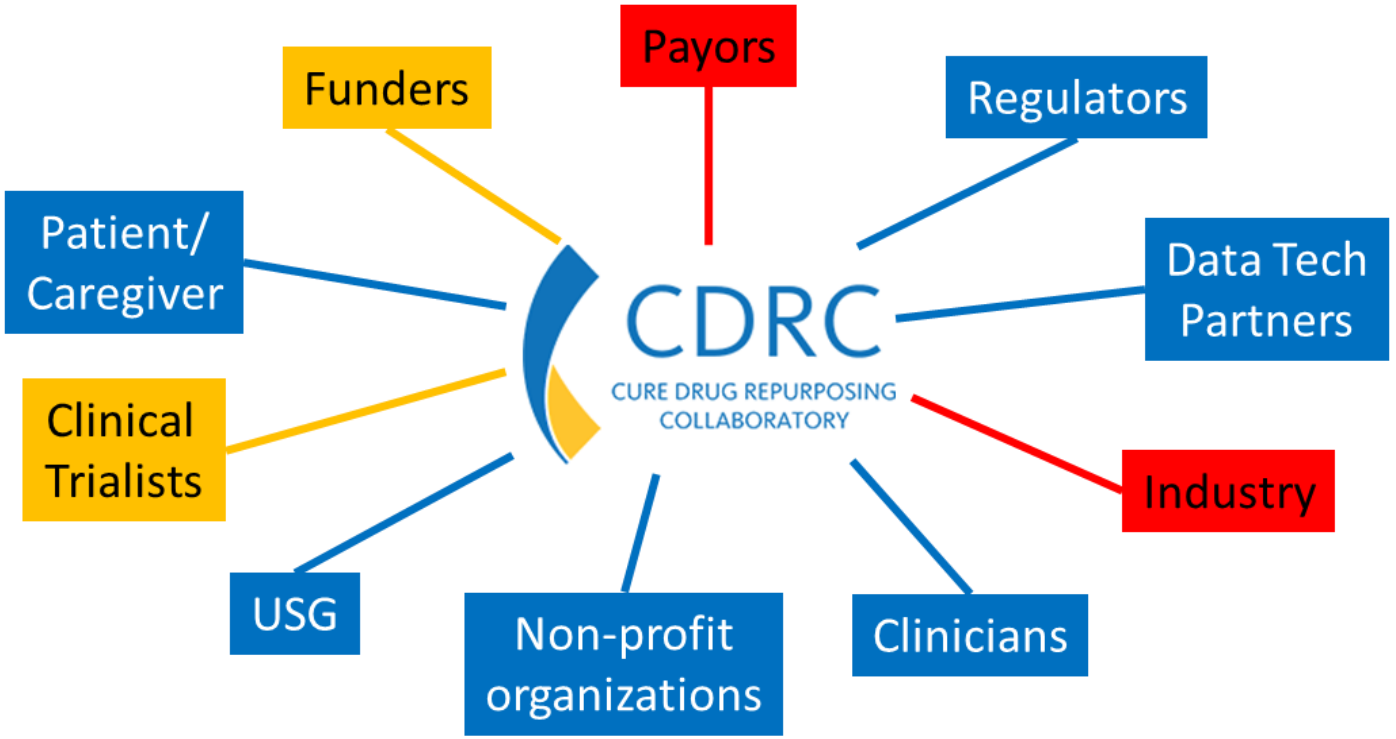


- ✓ What's in the pipeline and is there sufficient data on off-label usage?
- ✓ Use of molecular markers to identify genomic correlates of response

Engage all stakeholders

Patient advocacy groups

- Denise Reinke stood up the Patient Drug Repurposing Task Force
  - Lennie Woods (Clear Cell)
- Leiomyosarcoma drug repurposing task force presentation by CDRC
- Sarcoma coalition (Denise and Leslie are panel members)



cancers
MDPI

Review

Unmet Medical Needs and Future Perspectives for Leiomyosarcoma Patients—A Position Paper from the National LeioMyoSarcoma Foundation (NLMSF) and Sarcoma Patients EuroNet (SPAEN)

Bernd Kasper [1,*], Annie Achee [2], Kathrin Schuster [3], Roger Wilson [3], Gerard van Oortmerssen [3], Rebecca A. Gladdy [4], Matthew L. Hemming [5], Paul Huang [6], Matthew Ingham [7], Robin L. Jones [6,8], Seth M. Pollack [9], Denise Reinke [10], Roberta Sanfilippo [11], Scott M. Schuetze [12], Neeta Somaiah [13], Brian A. Van Tine [14], Breelyn Wilky [15], Scott Okuno [16] and Jonathan Trent [17]

CDRC sarcoma timeline

1 month

Landscape Analysis

- Review subtypes
- Pathway groupings
- Data sources
  - Preclinical
  - Literature
  - Trials
  - Registries
- Future pharma trials
- Centers of excellence
- Patient groups

2 months

Disease Subtype

- Criteria?
- Lack of drug development
- Off-label use
- Data availability (US, EU…)
- Q. Hypothesis generation
- **Angiosarcoma**
- **PEComa and EHE**
- Stakeholders
- Patient portal

6 months

Case Report Form

- **Data sources (EHRs)**
- **Define data variables**
- **Covariates of interest**
- **Stakeholder buy in**

- Explore **patient portal** to supplement clinical data
- Comparator group
- Causal inference
- Propensity matching
- Historical controls

6 months

Partnerships

- Define process of securing data
- SOWs
- Legal agreements
- Clinical CRF finalized
- Secure data

CURE ID

- Host data at NCATS
- Open access
- Deidentified

4 months

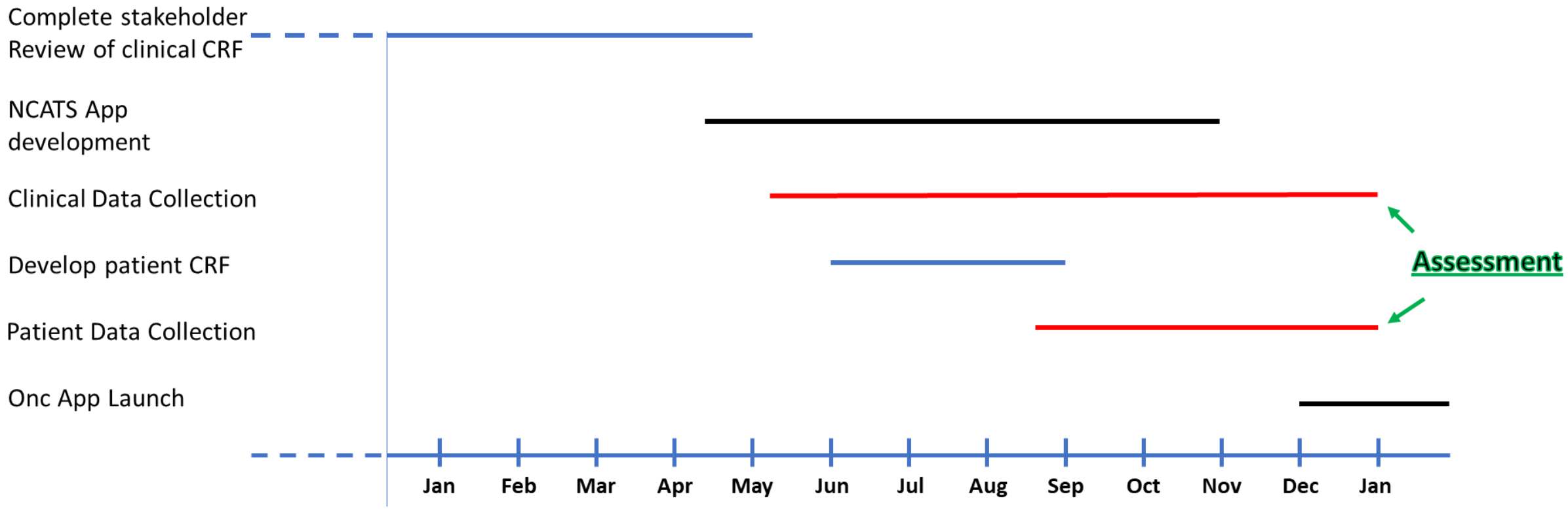
Data Analysis

- Bioinformatic pipeline
- Statistical analysis plan

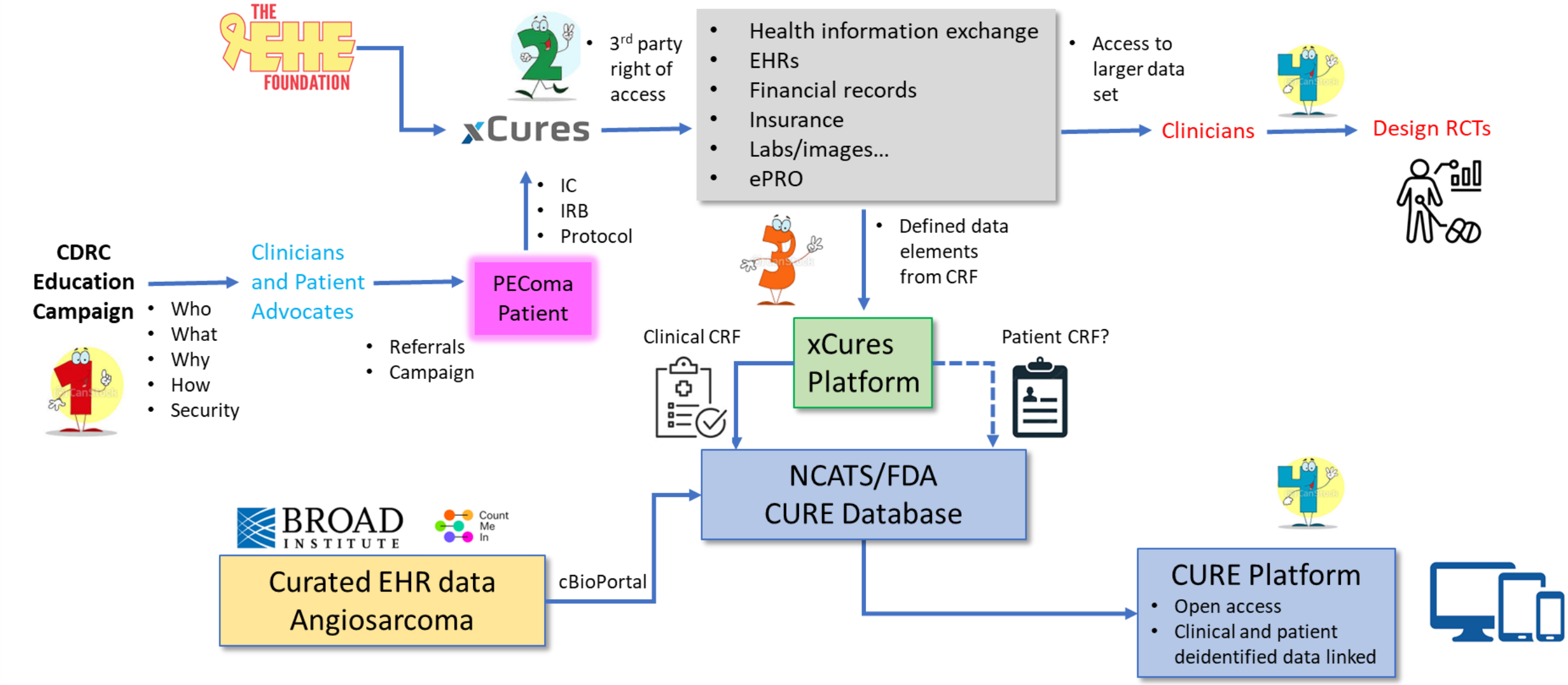
Next steps

Goals

- Capture key data elements using RWD and share deidentified CRF publicly
- Identify potential FDA approved drugs that improve outcomes but have not been labeled for the indication
- Insights for clinical trials



Pilot study: Draft of data flow



Question & Answer

Wrap up and next steps

Goodbye and Thank You

CDRC
CURE DRUG REPURPOSING COLLABORATORY
CRITICAL PATH INSTITUTE

CURE ID
Challenging cases... New approaches

THANK YOU!

c-path.org/cdrc