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

Good Morning
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.
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
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
   - Brandi Felser (SFA)
   - Christine Heske (NCI)
   - Vidula Sukhatme (GlobalCures)
   - Andrea Gross (NCI)
   - Suanna Bruinooge (ASCO)
   - Lennie Woods (Clear Cell Sarcoma Foundation)
   - 3:15-3:45

3. Next steps
   - 4:45-5:00

4. Adjourn
   - 5:00
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 Cancer 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.
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
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

Presented by: William Tap MSKCC
Adriamycin 8 cycles (600mg/m²); Any line of treatment

PFS 4.2m vs 6.6m

OS 14.7m vs 26.5m
Presented by: William Tap MSKCC

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

624 patients
10 months

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
How Many Variable Confound a Clinical 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 clinical 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
How Have We Adapted?
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
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.
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 ~40 years 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
CSF1 receptor inhibition of tenosynovial giant cell tumor using novel disease-specific MRI measures of tumor burden

Future Oncol. (2022) 18(12), 1449–1459
Need for Placebo? Outcome assumptions? Based on ORR P1

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

PMID: 33197285
Nirogacestat, a γ-Secretase Inhibitor for Desmoid Tumors

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

#2023CDRCMeeting
nab-Sirolimus for Patients With Malignant Perivascular Epithelioid Cell Tumors

Andrew J. Wagner, MD, PhD; Vinod Ravi, MD; Richard F. Birdsell, MD; Kristen Ganjee, MD; Brian A. Van Tine, MD, PhD; Rashmi Chugh, MD; Lee Cranmer, MD, PhD; Edinosa M. Gordon, MD; Jason L. Hornick, MD, PhD; Hong Du, MD; Berenice Grigorian, BS; Anita N. Schmid, PhD; Shihou Hou, PhD; Katherine Harris, DPhD; David J. Kwiatkowski, MD, PhD; Neil P. Desai, PhD; and Mark A. Dickson, MD

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 clinical 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 clinical usage
- Mirror designs and responsive diseases through clinical trial phases (P1→P2→P3)
  appropriate controls to identify signals and define diseases
- Biomarkers and patient selection
- Iterative Correlative work
- Collaboration
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, PhD; Anna Maria Frezza, MD, PhD; Jean-Yves Blay, MD, PhD; Elizabeth H. Baldini, MD; Sylvie Bonvalot, MD, PhD; Judith V. M. G. Bovée, MD, PhD; Dario Callegaro, MD, PhD; Paolo G. Casali, MD.

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


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) 103455

Academic Consultation
Community
Treatment Community
Community

Patient Registry

Academic Consultation
Path Review
Surgery
Path Review

Accurate and Complete History

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.
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

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

Presented by: William Tap MSKCC

Silvia Stacchiotti, MD
William Tap, MD
Hugh Leonard
Nadia Zaffaroni, PhD
Giacomo G Baldi, MD

Current Treatment Options in Oncology
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!**
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 should 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

Patients Powering Research for Epithelioid Hemangioendothelioma

EHE Global Patient Registry

A Natural History Study
The EHE Global Patient Registry empowers people with Epithelioid Hemangioendothelioma (EHE) to join together to improve our understanding of this ultra-rare sarcoma.

For more information on how to register, [click here.](#)

- **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
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

Collaborators & Advisors:

The EHE Foundation Advisory Board

Critical Path Institute & CDRC for Including Patients’ & Advocacy Perspectives
THANK YOU!
c-path.org/cdrc
An EHR-connected Patient-Centric Registry for Rare Cancer Research

Mark Shapiro (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.
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)

**Inform**

- Care Summaries
- All medical records from all sites of care
- Portals for patients & providers
  - Direct communication
  - PROs
  - Clinical Decision Support
  - Program Recognizer

**Decide**

- DCTs, EAPs, EHR to EDC
- Trial matching, CDS, outcomes analysis and LTFU, RWD studies (natural history, burden of disease, etc.)
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

Integrated viewer

Hundreds of medical documents

Diverse sites of care and visit summaries: Hospital, Office, Travel, Infusion, Orders, Telephone, Etc.
Medical records received within minutes

Elapsed time <5 min
Sample automated care summary

Cancer-related diagnoses, medications, procedures automatically identified and displayed on timeline concurrently with receipt of FHIR data.
xCures Operates a Direct-to-Patient Precision Oncology Clinical Research Platform

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

- **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

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**Entire Patient Clinical Dataset Centralized and Standardized**

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

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**xCESIOR PLATFORM**

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

**NCT0379388**
Efficient Data Structuring from Health Records
Integrating structured data from HIEs with xCures NER / NLP technology

Data Sources
- Fax/Email
- HIE
- EMR/My Chart
- NGS Labs (FM, Caris, TEMPUS, etc.)
- Imaging

Structured Data
- Labs, demographics

Unstructured Data
- Clinic notes, pathology, radiology

~80% of relevant data is unstructured

PATIENT DATA PRE-PROCESSING
- Files Received into HIPAA Compliant Document Server
- Optical Character Recognition Applied
- Document Classification & Standardization Process

PATIENT DATA PROCESSING
- Ontology Annotation (Parsing and NER)*
- NLP Assisted Data Extraction

QC & QA
- Source Data Verification

OUT

Creates regulatory-grade RWD
Structured and Unstructured Data Processing
NER & NLP Assisted Data Extraction

*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.
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

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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

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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*

*Only patients who definitively did not receive ONC201 are included in control group.

mOS = 19.6 mo vs. 11.4 mo
p = 0.028
GBM Patient DICOM Analysis

Tumor Isolated on MRI

Mass Effect Quantification
Validation of Precision Oncology Algorithms
Platform enables deployment of point-of-care solutions

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

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

For Clinician 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)

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

Subject Map

Encounter Map
### Overview of sarcoma patients

<table>
<thead>
<tr>
<th>Subjects</th>
<th>Subjects with Records</th>
<th>Average Record Count</th>
<th>Conditions</th>
<th>Medications</th>
<th>Procedures</th>
<th>Observations</th>
<th>Encounters</th>
<th>Unique Locations</th>
</tr>
</thead>
<tbody>
<tr>
<td>400</td>
<td>400</td>
<td>3,876</td>
<td>15,143</td>
<td>115,649</td>
<td>95,687</td>
<td>804,446</td>
<td>291,811</td>
<td>9,005</td>
</tr>
</tbody>
</table>

**Subjects**

- Vancouver
- Seattle
- Los Angeles
- Chicago
- New York

**Encounters**

- Vancouver
- Seattle
- Los Angeles
- Chicago
- New York
Preliminary Overview of Sarcoma Data

### Subjects by Organ

<table>
<thead>
<tr>
<th>Organ</th>
<th>Subject ID</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lymphoid</td>
<td>34</td>
</tr>
<tr>
<td>Uterus</td>
<td>30</td>
</tr>
<tr>
<td>Other</td>
<td>25</td>
</tr>
<tr>
<td>Bone</td>
<td>19</td>
</tr>
<tr>
<td>Soft Tissue</td>
<td>13</td>
</tr>
<tr>
<td>CNS/Brain</td>
<td>7</td>
</tr>
<tr>
<td>Ovary/Fallopian Tube</td>
<td>7</td>
</tr>
<tr>
<td>Skin</td>
<td>7</td>
</tr>
<tr>
<td>Head and Neck</td>
<td>2</td>
</tr>
<tr>
<td>Lung</td>
<td>1</td>
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</table>

### Subjects by Condition

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

<table>
<thead>
<tr>
<th>Conditions</th>
<th>Subjects</th>
<th>Condition Medication Combos</th>
<th>Unique Conditions</th>
<th>Unique Medications</th>
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<tr>
<td>Malignant neoplastic disease</td>
<td>211</td>
<td>111,553</td>
<td>621</td>
<td>376</td>
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<tr>
<td>Primary malignant neoplasm of soft tissues</td>
<td>50</td>
<td>46</td>
<td>40</td>
<td>36</td>
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<tr>
<td>Sarcoma</td>
<td>46</td>
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<td>31</td>
<td>28</td>
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<tr>
<td>Primary malignant neoplasm of female breast</td>
<td>30</td>
<td>30</td>
<td>28</td>
<td>28</td>
</tr>
<tr>
<td>Primary malignant neoplasm of uterus</td>
<td>25</td>
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<td>20</td>
<td>20</td>
</tr>
<tr>
<td>Malignant tumor of breast</td>
<td>32</td>
<td></td>
<td>31</td>
<td>25</td>
</tr>
<tr>
<td>Primary malignant neoplasm of endometrium</td>
<td>30</td>
<td>30</td>
<td>28</td>
<td>28</td>
</tr>
<tr>
<td>Malignant neoplasm of corpus uteri, excluding isthmus</td>
<td>26</td>
<td>26</td>
<td>25</td>
<td>25</td>
</tr>
<tr>
<td>Malignant neoplasm of endometrium of corpus uteri</td>
<td>26</td>
<td>26</td>
<td>25</td>
<td>25</td>
</tr>
<tr>
<td>Secondary malignant neoplasm of bone</td>
<td>26</td>
<td>26</td>
<td>25</td>
<td>25</td>
</tr>
<tr>
<td>Malignant neoplasm of female breast</td>
<td>31</td>
<td>31</td>
<td>28</td>
<td>28</td>
</tr>
<tr>
<td>Secondary malignant neoplasm of lung</td>
<td>26</td>
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<td>25</td>
<td>25</td>
</tr>
<tr>
<td>Malignant lymphoma</td>
<td>20</td>
<td></td>
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<tr>
<td>Primary malignant neoplasm</td>
<td>20</td>
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<td>20</td>
<td>20</td>
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<tr>
<td>Secondary malignant neoplasm of liver</td>
<td>18</td>
<td></td>
<td>18</td>
<td>18</td>
</tr>
<tr>
<td>Leiomyosarcoma</td>
<td>20</td>
<td>18</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neoplasm of uncertain behavior of soft tissues</td>
<td>18</td>
<td>18</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Secondary malignant neoplastic disease</td>
<td>18</td>
<td>18</td>
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<td></td>
</tr>
<tr>
<td>Medications</td>
<td></td>
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</tr>
<tr>
<td>Medication Name</td>
<td></td>
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</tr>
<tr>
<td>anastrozole 1 MG Oral Tablet</td>
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<tr>
<td>doxorubicin</td>
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<td></td>
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<tr>
<td>25 ML doxorubicin hydrochloride 2 MG/mL Injection</td>
<td></td>
<td></td>
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<tr>
<td>medroxyprogesterone acetate 10 MG Oral Tablet</td>
<td></td>
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<tr>
<td>docetaxel</td>
<td></td>
<td></td>
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<tr>
<td>letrozole 2.5 MG Oral Tablet</td>
<td></td>
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<td></td>
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<tr>
<td>pazopanib 200 MG Oral Tablet</td>
<td></td>
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<tr>
<td>pembrolizumab</td>
<td></td>
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<tr>
<td>tamoxifen 20 MG Oral Tablet</td>
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<tr>
<td>500 ML mannitol 200 MG/mL Injection</td>
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<td></td>
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</tr>
<tr>
<td>paclitaxel</td>
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<td></td>
</tr>
<tr>
<td>pazopanib</td>
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<td></td>
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</tr>
<tr>
<td>capecitabine 500 MG Oral Tablet</td>
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</tr>
</tbody>
</table>
Sarcoma Patients with Genomic Sequencing

Subjects with somatic NGS

194

Subjects with germline testing

141
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

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
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.**
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's funding considerations:

- **Basic Research**
  - Animal Studies
  - CWR funding only when donor-directed

- **Late Stage Animal**
  - Final prep for next phase
  - CWR may consider funding at this stage

- **Proof of Concept or Phase I**
  - CWR funds when others say ‘come back when you have first-in-human data’

- **Phase II**
  - Leverage of follow-on funding
  - CWR may fund at this stage

**Funding Focus:**

- **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

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

18 ongoing clinical trials in rare diseases

as of 4.1.2023
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
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76% adult, 24% pediatric
97% clinical, 3% pre-clinical
79% US, 21% outside of US
79% drug, 21% device/other

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

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

- 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

- 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 health disparities
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.
Repurposed Drug Trials: Challenges and Opportunities

Vidula Sukhatme (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
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

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.
<table>
<thead>
<tr>
<th>PMID</th>
<th>Year</th>
<th>Study Type</th>
<th>Cancer Type</th>
<th>Study Type</th>
<th>Drug Name</th>
<th>Treatment Timing</th>
<th>Dosage</th>
<th>Concurrent SOC</th>
<th>Number of Patients</th>
<th>Morningside Center Summary</th>
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<tbody>
<tr>
<td>20201902</td>
<td>2020</td>
<td>Clinical Trial</td>
<td>n/a</td>
<td>n/a</td>
<td>Metformin</td>
<td>Palliative</td>
<td>850 mg QD/850 mg BID</td>
<td>Targeted</td>
<td>199</td>
<td>Biomarker (P) = 2.79 microU/mL, Arm 1 = 2.47 microU/mL, Arm 2 = 0.08 microU/mL, Arm 3 = 1.16 microU/mL</td>
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<tr>
<td>36303999</td>
<td>2019</td>
<td>Clinical Trial</td>
<td>Metastatic</td>
<td>Stage 4</td>
<td>Perindopril</td>
<td>Palliative</td>
<td>4 mg daily</td>
<td>Chemo</td>
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<td>Toxicity/Safety Feasibility (SF) = 3 HFSR 50%</td>
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<tr>
<td>Study Name</td>
<td>Principal Investigator</td>
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<tr>
<td>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</td>
<td>Viraj Master, MD, PhD</td>
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<tr>
<td>Paricalcitol and hydroxychloroquine (PH) combination with gemcitabine and nab-paclitaxel in advanced pancreatic cancer</td>
<td>Olutunji Alese, MD</td>
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<tr>
<td>Propranolol Hydrochloride and Pembrolizumab in Patients with Recurrent or Metastatic Urothelial Carcinoma: A Single-Institute Phase II Trial</td>
<td>Bassel Nazha, MD, MPH</td>
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<tr>
<td>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)</td>
<td>Melinda Yushak, MD, MPH</td>
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<td>Neoadjuvant simvastatin and letrozole in early-stage hormone positive breast cancer</td>
<td>Ruth Sacks, MD</td>
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<tr>
<td>Treatment of Brain Metastases with Arginine Supplementation</td>
<td>Lisa Sudmeier, MD, PhD</td>
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</table>
## Clinical Trials in Development

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

<table>
<thead>
<tr>
<th>Major Tasks for Clinical Trials</th>
<th>Sponsor</th>
<th>Principal Investigator</th>
</tr>
</thead>
<tbody>
<tr>
<td>Develop trial concept and protocol (drug, disease, clinical setting, statistics, etc)</td>
<td>✔✔✔</td>
<td>✔</td>
</tr>
<tr>
<td>File IND application or obtain exemption</td>
<td>✔✔✔</td>
<td>✔</td>
</tr>
<tr>
<td>Secure funding</td>
<td>✔✔✔✔</td>
<td></td>
</tr>
<tr>
<td>IRB process</td>
<td>✔✔</td>
<td>✔</td>
</tr>
<tr>
<td>Conduct trial</td>
<td></td>
<td>✔✔✔✔</td>
</tr>
<tr>
<td>Patient recruitment</td>
<td>✔✔</td>
<td>✔</td>
</tr>
<tr>
<td>Regulatory process (monitor/report/etc)</td>
<td>✔✔✔✔</td>
<td>✔</td>
</tr>
</tbody>
</table>
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.

<table>
<thead>
<tr>
<th>Data</th>
<th>New Drugs</th>
<th>Repurposed Drugs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-clinical data</td>
<td><em>Focused strong data</em></td>
<td><em>Fragmented, multi-user data</em></td>
</tr>
<tr>
<td>Mechanism of action</td>
<td><em>Single, well defined</em></td>
<td><em>Pleotropic, perception: “Dirty Drug”</em></td>
</tr>
<tr>
<td>Dose response – new indication</td>
<td><em>Well defined</em></td>
<td><em>Not well explored – supporting data in the form of retrospective studies</em></td>
</tr>
<tr>
<td>Human Data</td>
<td><em>None</em></td>
<td><em>Retrospective, case reports, small non-randomized studies</em></td>
</tr>
</tbody>
</table>
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!
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

Harnessing RWD to advance repurposed drugs for rare cancers
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 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

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).

Unesbulin (second-generation BMI-1 inhibitor) for soft tissue sarcoma (Orphan drug designation by EMA)
EHRs to systematically collect RWD for sarcoma subtypes

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)
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

4 months
- Data Analysis
  - Bioinformatic pipeline
  - Statistical analysis plan

CURE ID
- Host data at NCATS
- Open access
- Deidentified
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

**Chart**
- Complete stakeholder review of clinical CRF
- NCATS App development
- Clinical Data Collection
- Develop patient CRF
- Patient Data Collection
- Onc App Launch
Pilot study: Draft of data flow

- Health information exchange
- EHRs
- Financial records
- Insurance
- Labs/images...
- ePRO

- Access to larger data set
- Clinicians
- Design RCTs

- Defined data elements from CRF

- Clinical CRF
- Patient CRF?

- NCATS/FDA CURE Database

- Curated EHR data
  - Angiosarcoma

- cBioPortal

- CURE Platform
  - Open access
  - Clinical and patient deidentified data linked

- xCures Platform

- PEComa Patient

- Clinicians and Patient Advocates

- CDRC Education Campaign
  - Who
  - What
  - Why
  - How
  - Security

- 3rd party right of access

- IC
- IRB
- Protocol
Wrap up and next steps
Goodbye and Thank You

Thank You
THANK YOU!

c-path.org/cdrc