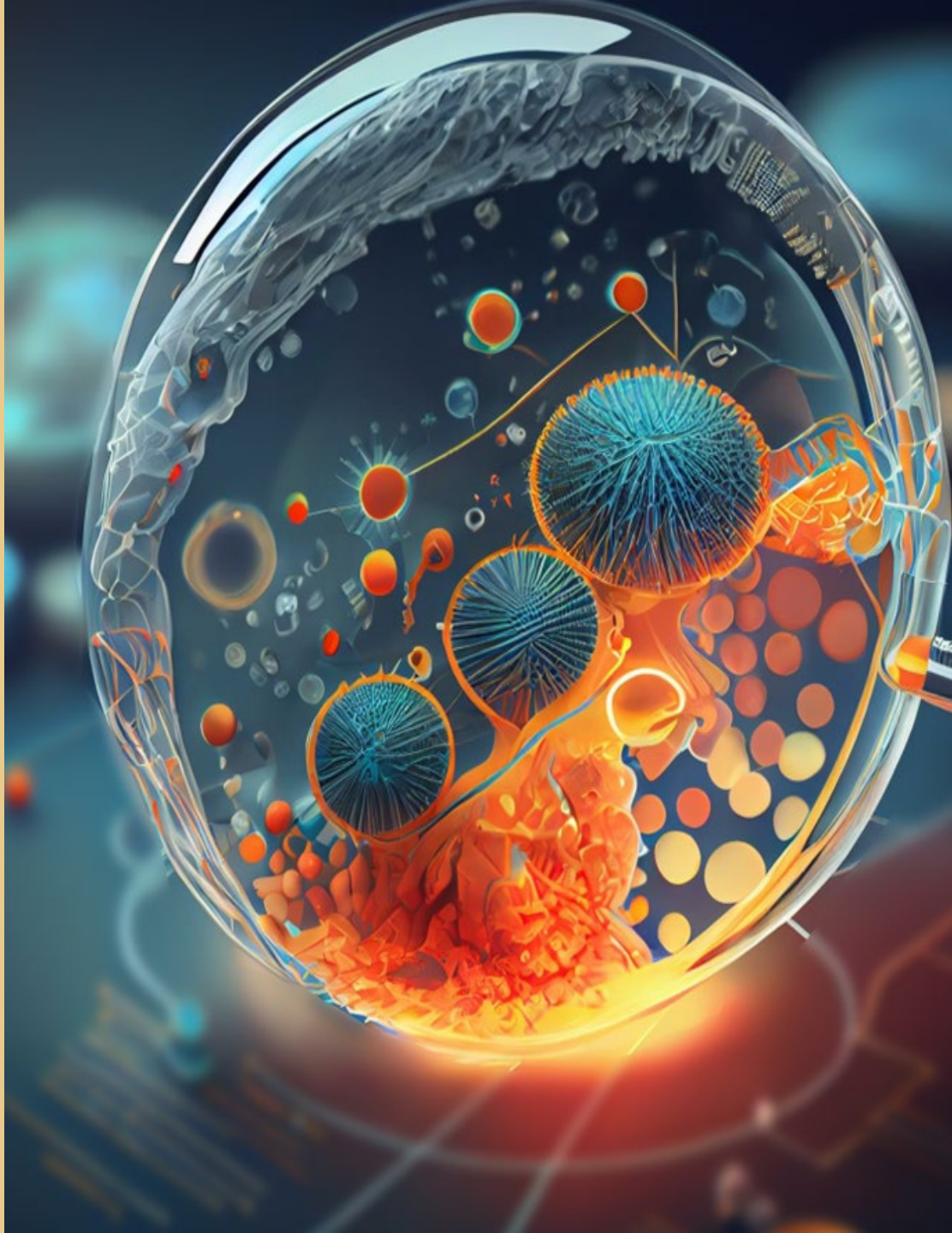
eha Sf(PM)

Using Functional Precision Medicine to Manage Cancer



Diana Azzam, PhD

Assistant Professor, Department of Environmental Health Sciences

Scientific Director, Center for Advancing Personalized Cancer Treatments (CAPCT)

Florida International University

dazzam@fiu.edu

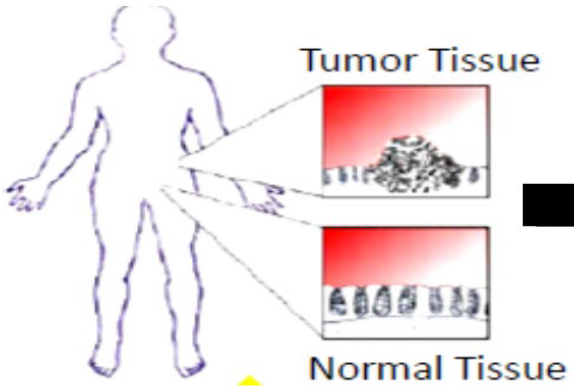
Disclosures

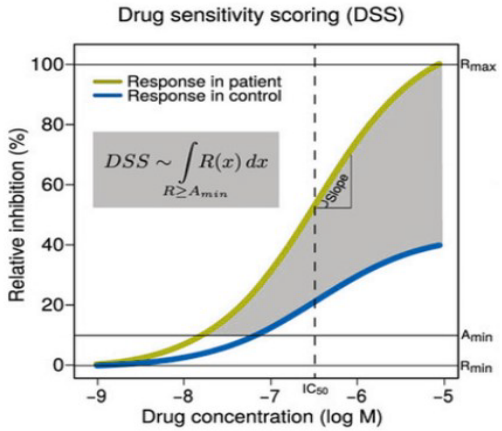
- Co-Founder & Scientific Advisor, First Ascent Biomedical, Inc

Functional Precision Medicine

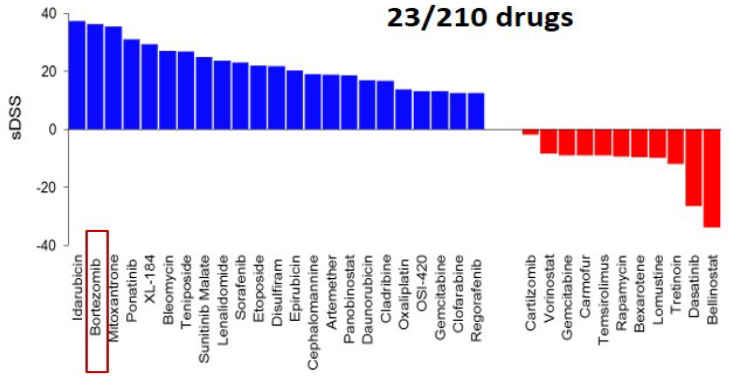
Putting Drugs on Patient Cancer Cells and Seeing What Happens!

Case Report of Highly Chemo-Resistant AML Patient

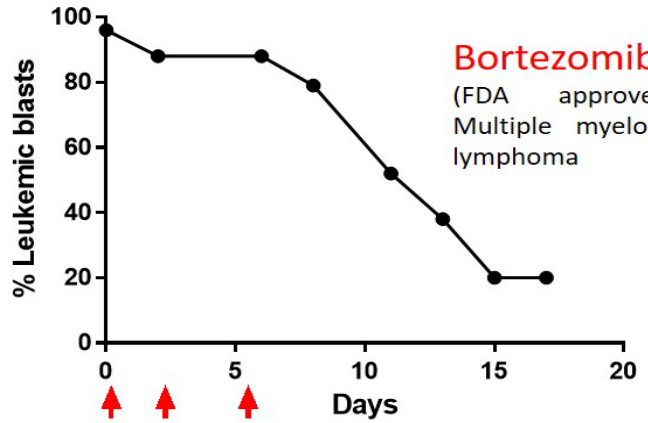




Repurposing of FDA approved oncology drugs!!!



Clinical Follow-Up on Patient



Bortezomib
(FDA approved for Multiple myeloma and lymphoma

Azzam et al. 2015 Blood 126 (23):1352

Genomics, Functional Drug Testing and Artificial Intelligence

Clinical Decision Support Tools

eha Sf(PM)

Saturday March 30, 2019 | Atlanta, GA

www.functionalprecisionmedicine.com

Functional Precision Medicine Summit

Expert speaker faculty includes:

Ned Sharpless
Director
National Cancer Institute

Reena Philip
Director, Division of Molecular Genetics & Pathology, Office of In Vitro Diagnostics & Radiological Health
CDRH, FDA

Gideon Blumenthal
Deputy Office Director of the Oncology Center of Excellence & Supervisory Associate Director for Precision Oncology
CDER, FDA

Anthony Letai
Professor of Medicine, **Dana Farber Cancer Institute** & President **SfPM**

Diane Heiser
CTO
Notable Labs

Carla Grandori
CEO
SEngine Precision Medicine

Hosted By: Sf(PM)

In collaboration with: LABCYTE, SpeciCare BICG, Inc.

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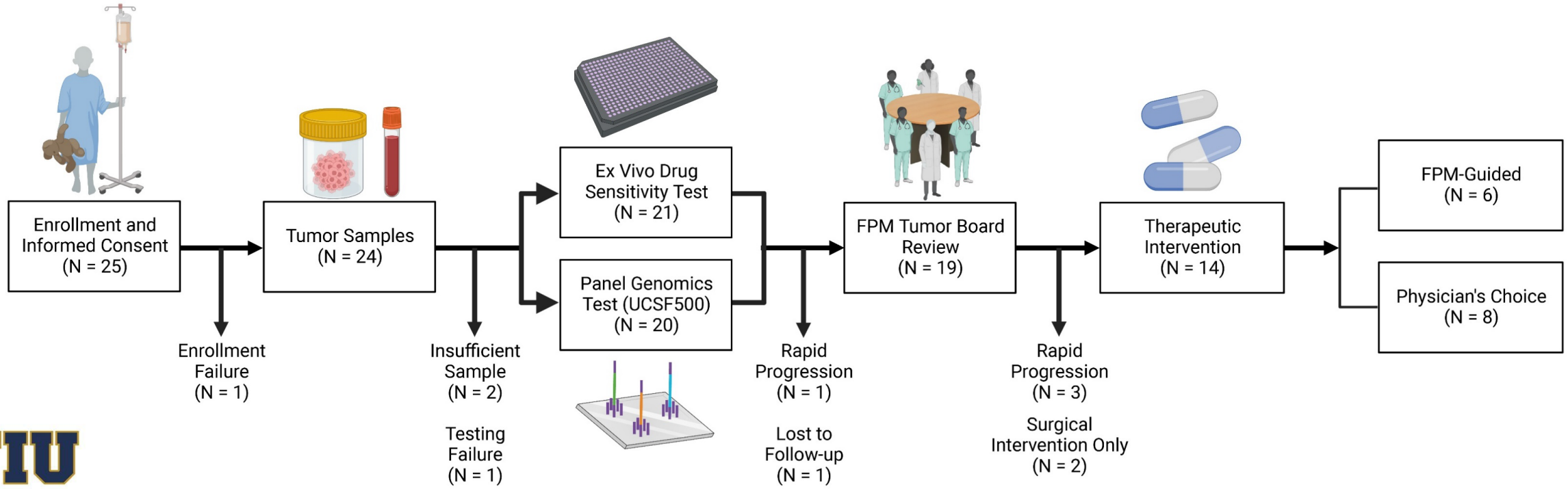
Can we use functional precision medicine to guide chemotherapy treatments in refractory pediatric cancers?

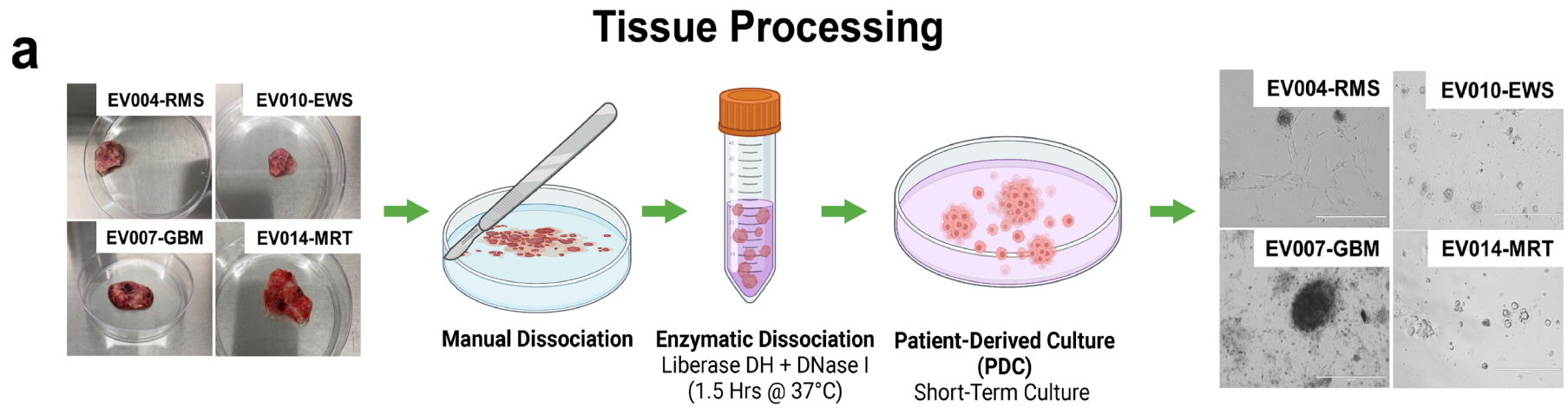
Feasibility of FPM for Guiding Treatment of Relapsed or Refractory Pediatric Cancers

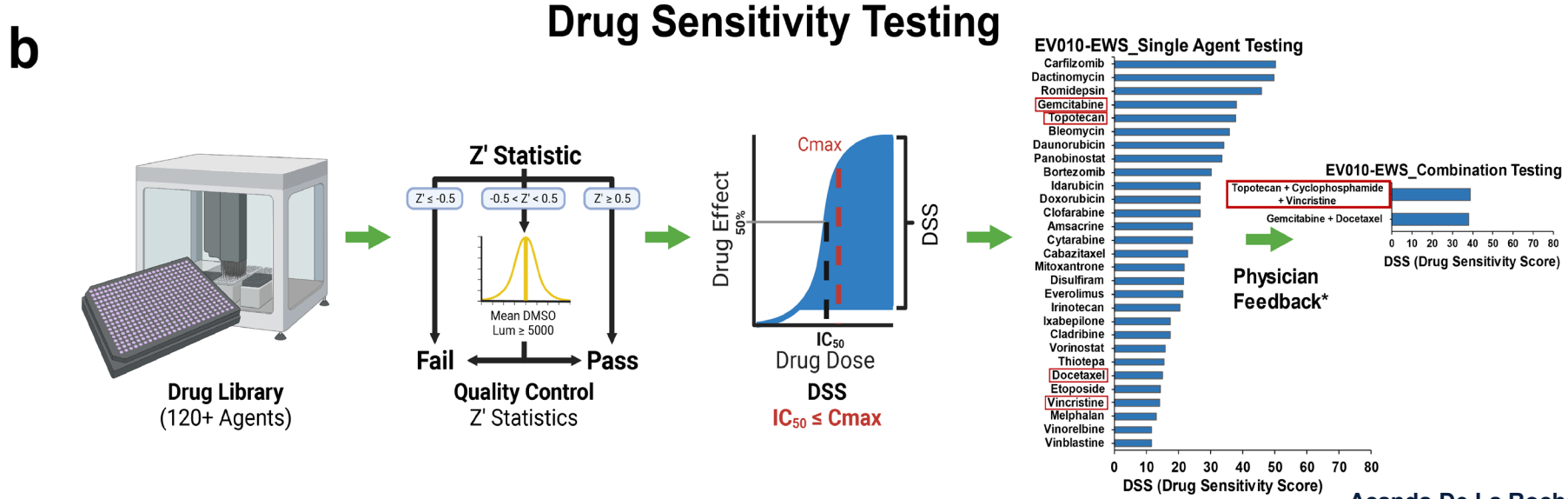


ClinicalTrials.gov number, NCT03860376

Acanda De La Rocha et al. *Nat Med 30, 990–1000 (2024)*

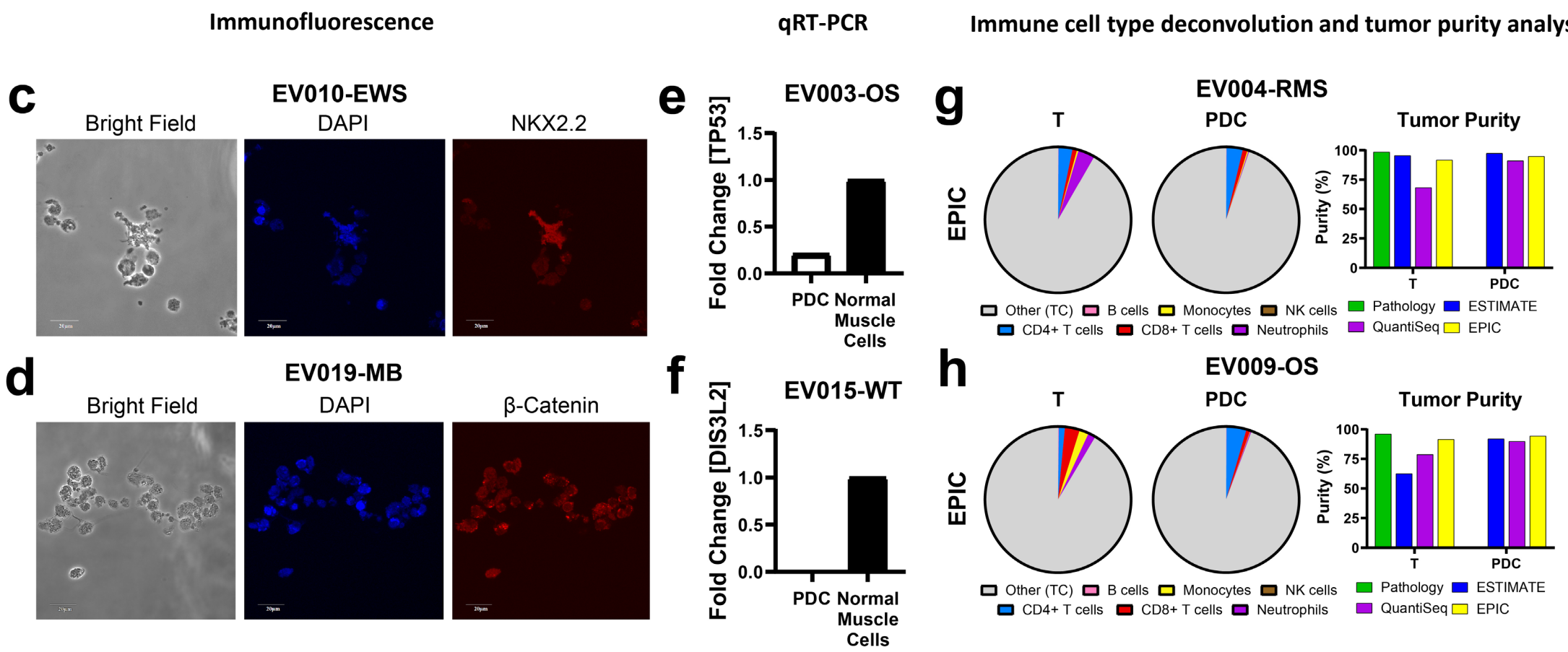
Patient-Derived Cultures and Drug Sensitivity Testing





Acanda De La Rocha et al. *Nat Med 30, 990–1000 (2024)*

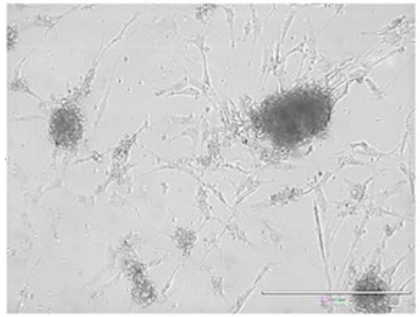
Validation of Patient-Derived Cultures



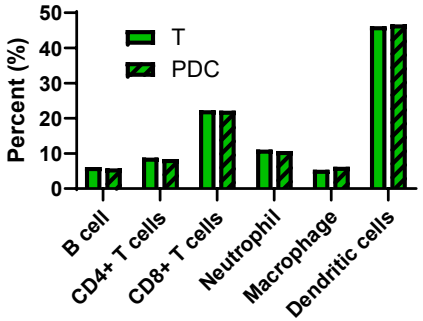
Acanda De La Rocha et al. *Nat Med 30, 990–1000 (2024)*

2D/3D Patient-Derived Cultures (PDCs)

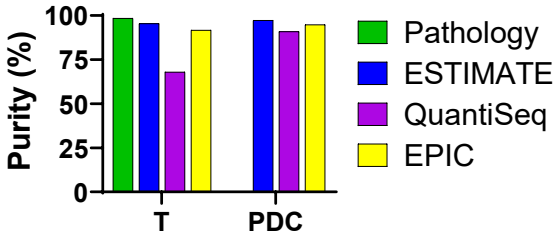
EV004



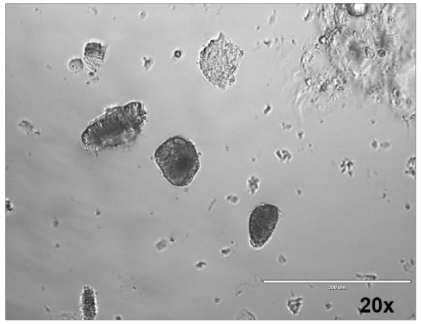
Immune Cell Composition



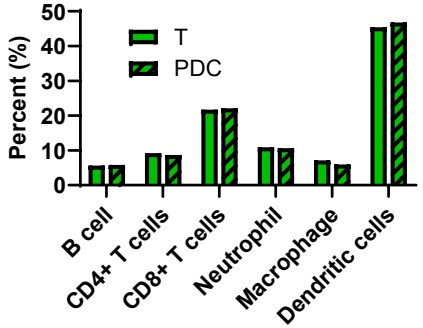
Tumor Purity



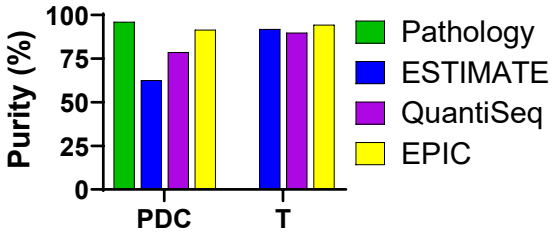
EV009



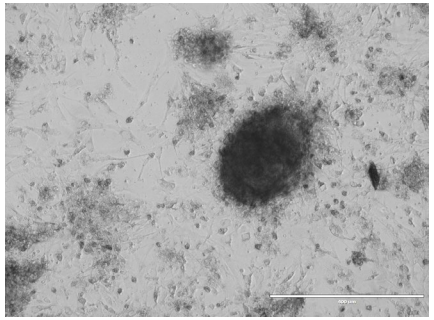
Immune Cell Composition



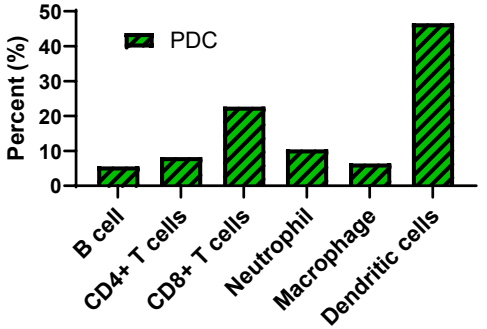
Tumor Purity



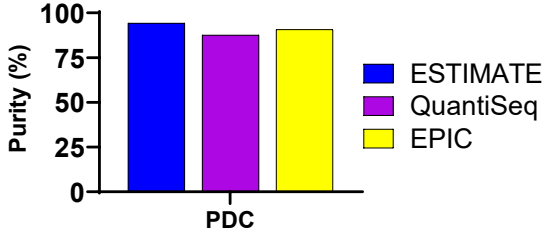
EV007



Immune Cell Composition

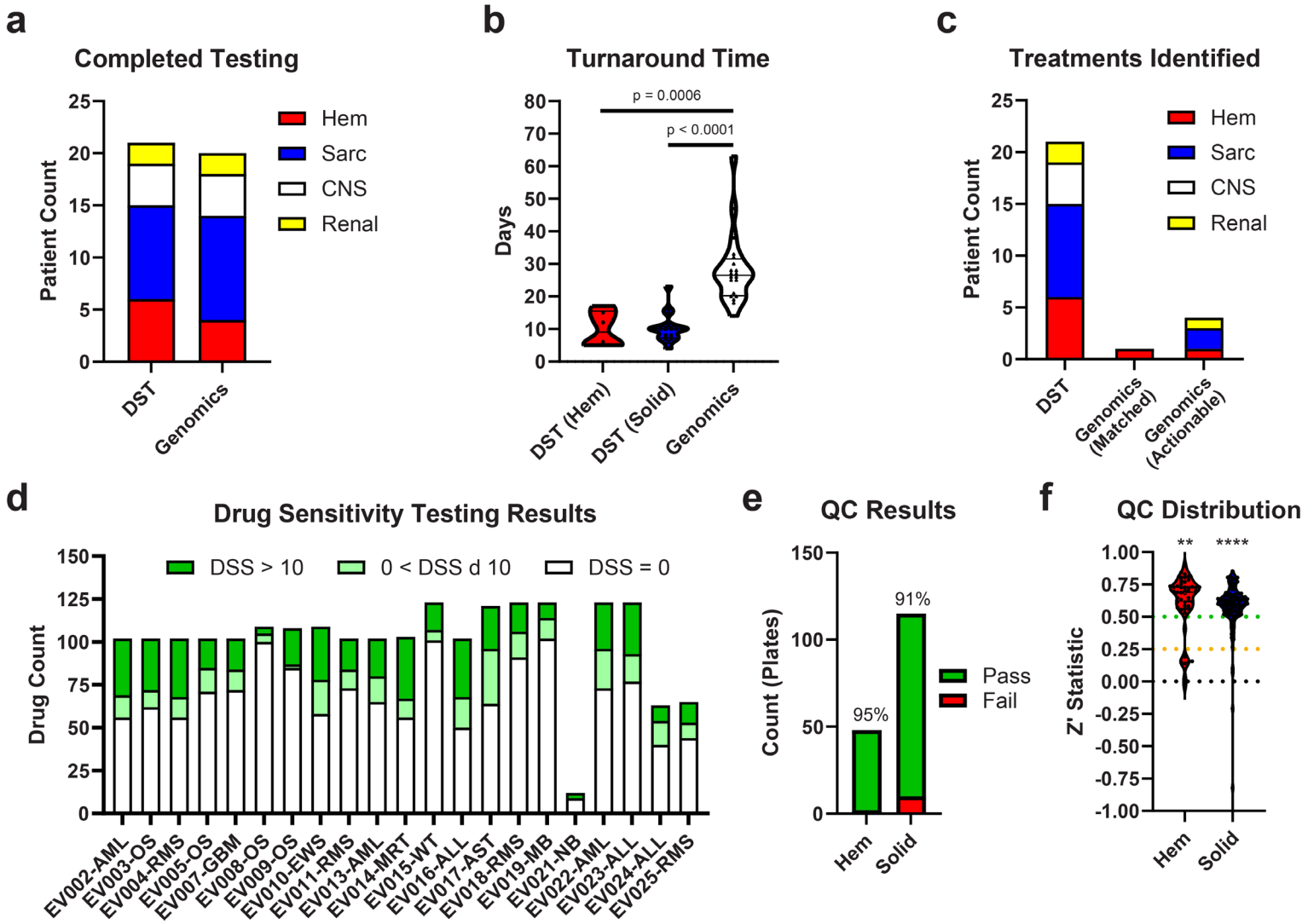


Tumor Purity



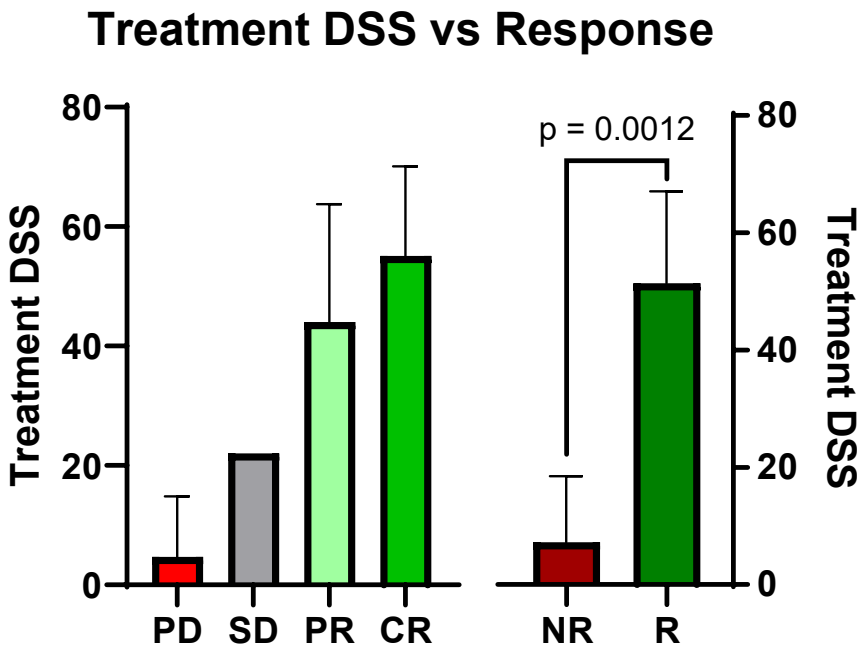
Acanda De La Rocha et al. *Nat Med 30, 990–1000 (2024)*

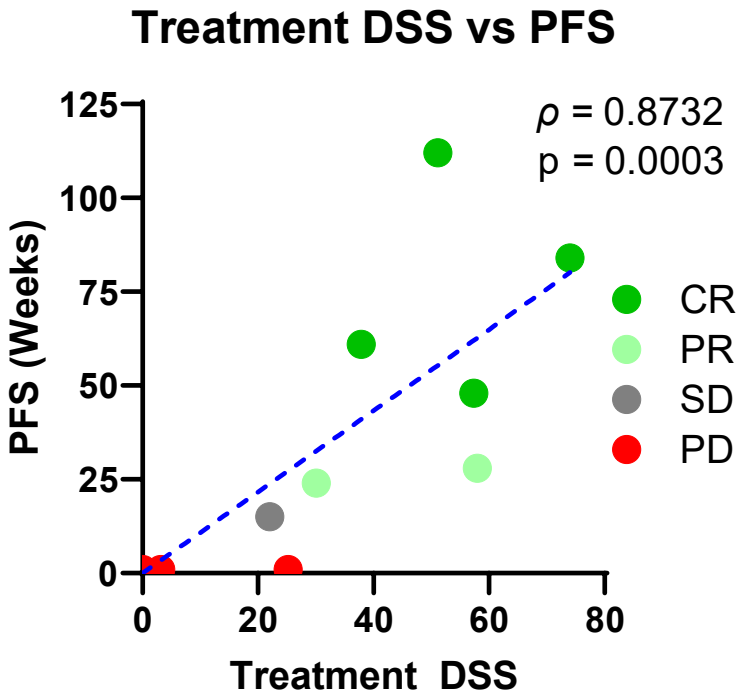
Testing Outcomes



Acanda De La Rocha et al. *Nat Med 30, 990–1000 (2024)*

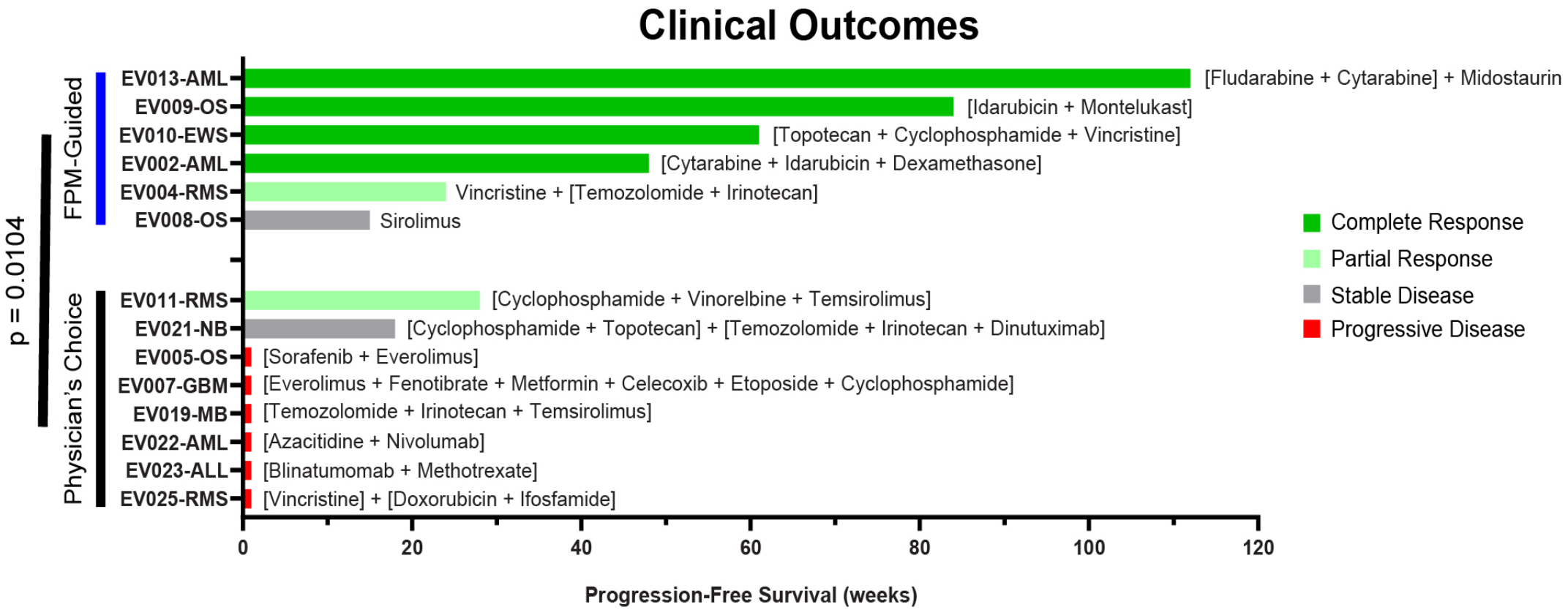
Correlation of DST with Clinical Outcomes





Acanda De La Rocha et al. *Nat Med 30, 990–1000 (2024)*

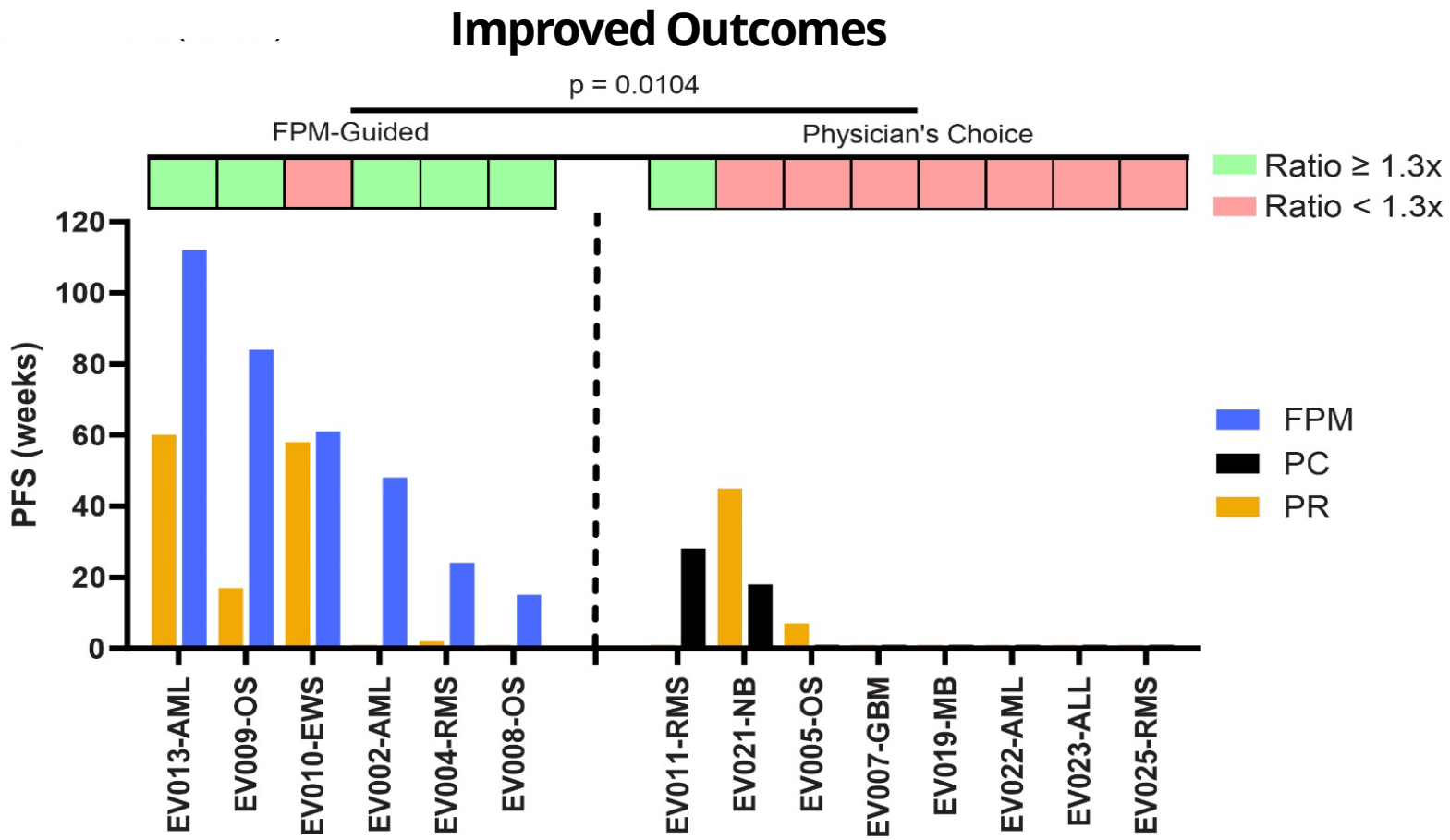
Patients guided by FPM have Improved Clinical Outcomes



Acanda De La Rocha et al. *Nat Med 30, 990–1000 (2024)*

ClinicalTrials.gov number, NCT03860376

Patients guided by FPM have Improved Clinical Outcomes



83%

13%

$$\frac{\text{PFS(Trial)}}{\text{PFS(Previous)}} > 1.3$$

Acanda De La Rocha et al. *Nat Med 30, 990–1000 (2024)*

Patient 13: The power of combining genomics and DST

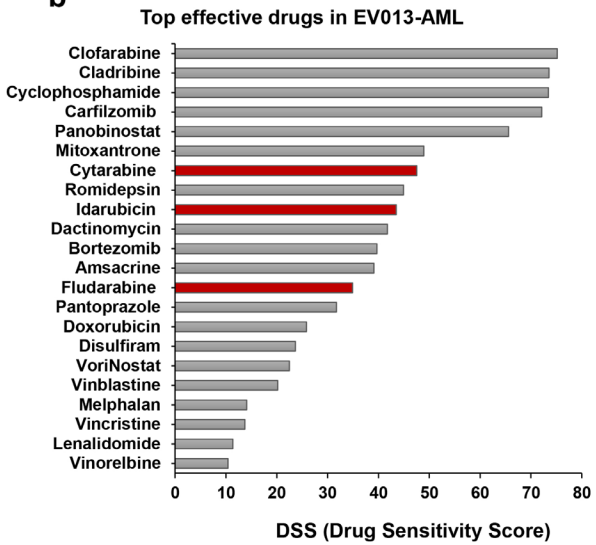
5-year-old boy at Nicklaus Children's Hospital

Patient EV013-AML: Refractory AML with FLT3-ITD Mutation

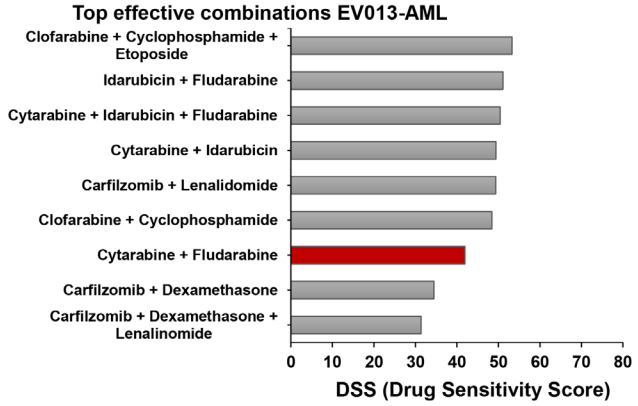
a

FLT3 Inhibitor	DSS
Midostaurin	5.97
Sorafenib	1.81
Ponatinib	0

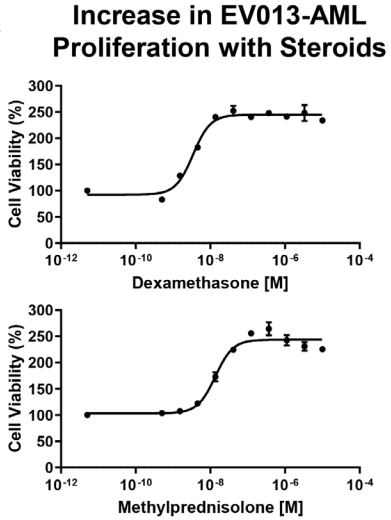
b



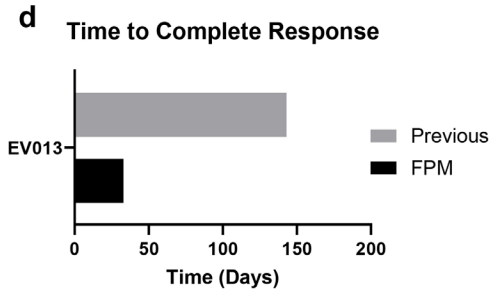
Physician feedback ↓



c



d

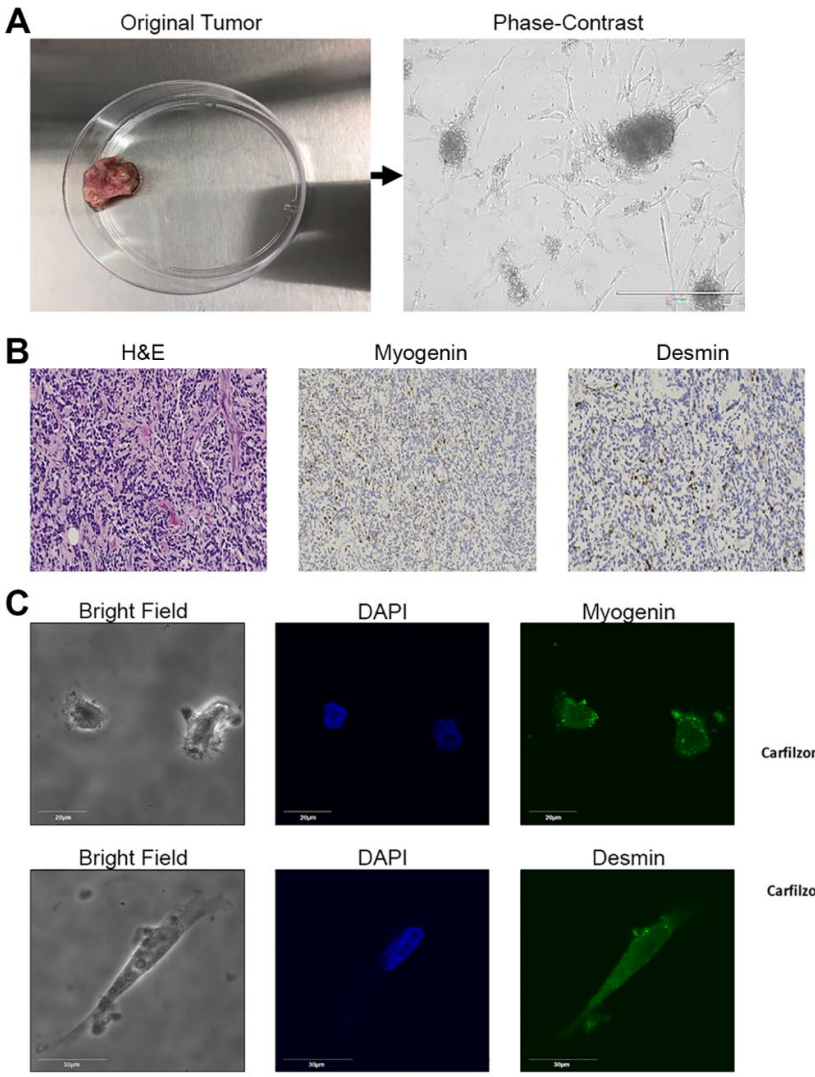


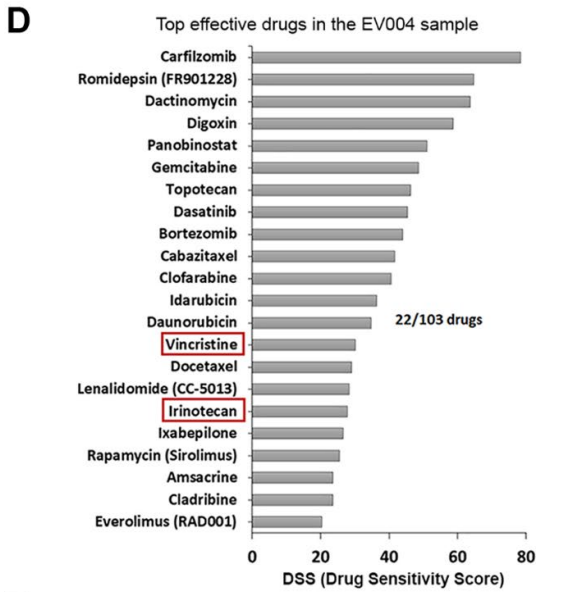
Acanda De La Rocha et al. *Nat Med 30, 990–1000 (2024)*

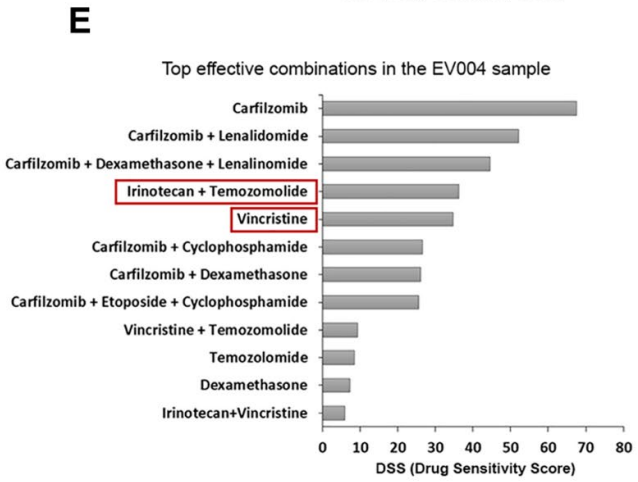
Patient 4: DST implicated previously used regimen

7-year-old girl at Nicklaus Children's Hospital

Metastatic Rhabdomyosarcoma







Acanda De La Rocha et al.
JCO Precision Oncology, 2021

Patient 4: DST implicated previously used regimen

7-year-old girl at Nicklaus Children's Hospital

Metastatic Rhabdomyosarcoma

January 2019 — Metastatic Relapse

Physician Choice Therapy
3rd Regimen:
- SBRT (Radiation)
- Pazopanib (daily)
- Nivolumab IVQ

March 2019 — Stable Disease (PFS~2 weeks)

April 2019 — Tumor Progression

Enrolled in Functional Precision Medicine Study (Nicklaus – FIU)

Molecular Tumor Analysis

Variant	Transcript ID	Allele Frequency
CDKN2A, CDKN2B	Deep deletion	N/A
GNAS	p.R202C	96%
NRAS	p.Q61K	46%

DST-Guided Therapy
4th Regimen:
- Cycle 1:
  - Vincristine
  - Irinotecan
  - Temozolomide (D1-5)
- Cycle 2:
  - Vincristine (D8 + D15)
  - Irinotecan
  - Temozolomide (D1-5)

June 2019 — Partial Response Improved Quality of life (PFS~24 weeks)

Nicklaus Children's Hospital
MIAMI CHILDREN'S HEALTH SYSTEM

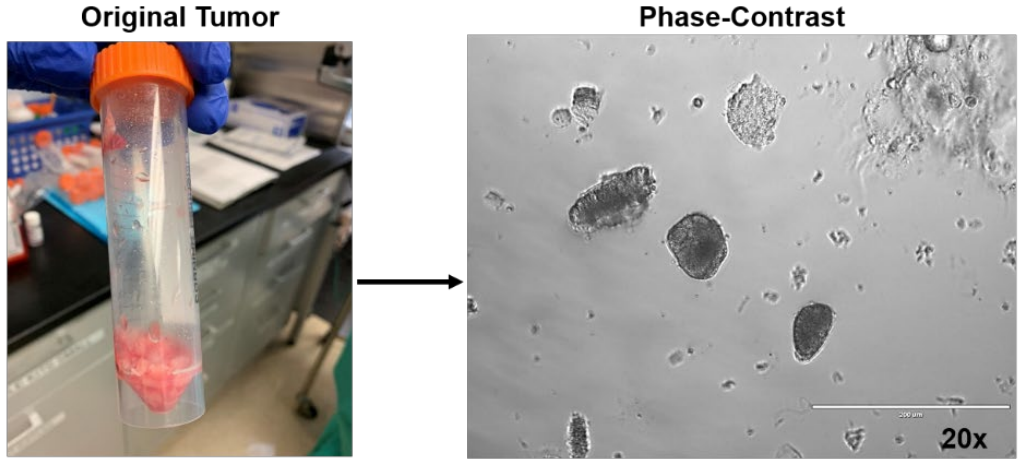
FIU FLORIDA INTERNATIONAL UNIVERSITY

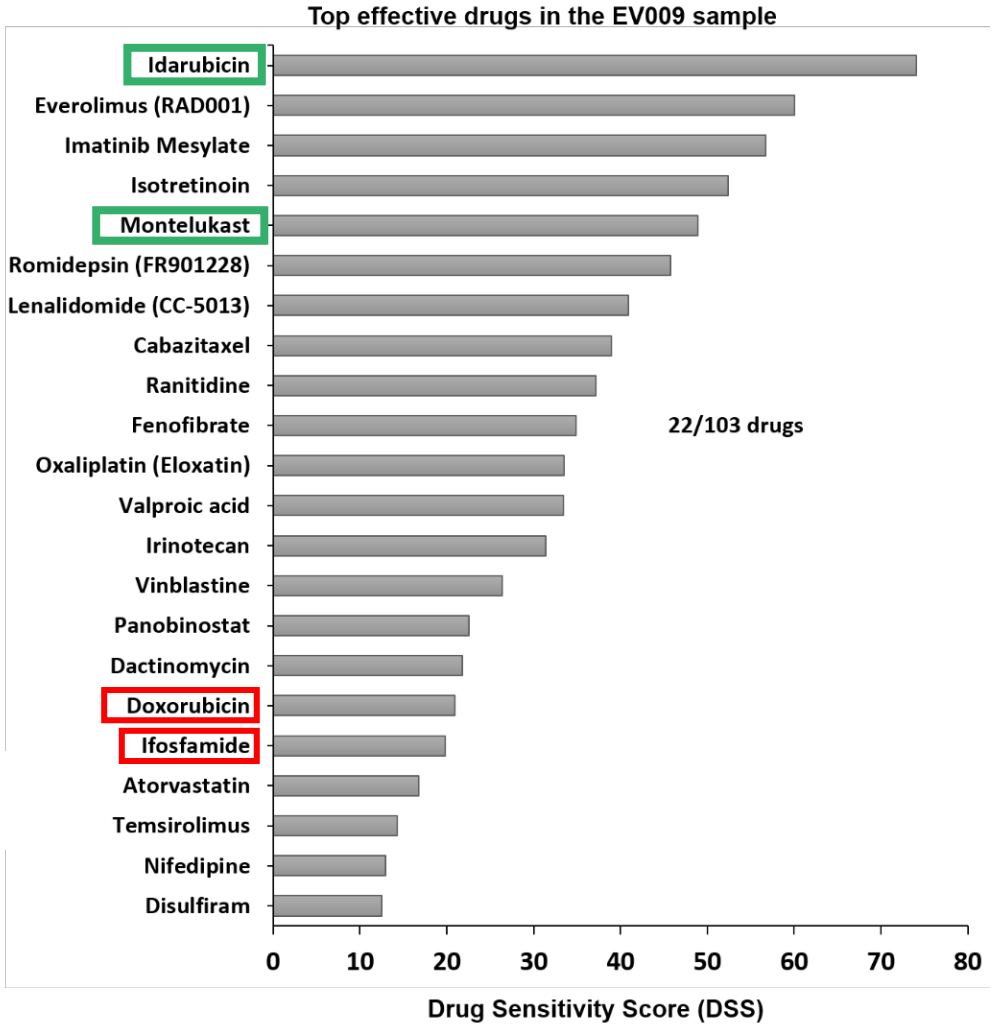
Acanda De La Rocha et al. JCO Precis Oncol 2021

Patient 9: DST provided cheaper and readily accessible drugs

9-year-old girl at Nicklaus Children's Hospital

Metastatic Osteosarcoma





NCCN Guidelines - Osteosarcoma

Osteosarcoma			
First-line therapy (primary/ neoadjuvant/adjuvant therapy or metastatic disease)	**Preferred Regimens** • Cisplatin and doxorubicin[47-49] (category 1) • MAP (high-dose methotrexate, cisplatin, and doxorubicin)[49-52] (category 1)[h,i]	**Other Recommended Regimens** • Doxorubicin, cisplatin, ifosfamide, and high-dose methotrexate[57,h]	
Second-line therapy (relapsed/ refractory or metastatic disease)	**Preferred Regimens** • Ifosfamide (high dose) ± etoposide[53,54] • Regorafenib[55] (category 1) • Sorafenib[56]	**Other Recommended Regimens** • Cabozantinib[38] • Cyclophosphamide and topotecan[29-30] • Docetaxel and gemcitabine[39] • Gemcitabine[58] • Sorafenib + everolimus (category 2B)[59]	**Useful in Certain Circumstances** • Cyclophosphamide and etoposide[60] • Ifosfamide, carboplatin, and etoposide[40] • High-dose methotrexate[h] • High-dose methotrexate, etoposide, and ifosfamide[61,h] • Sm^{153}-EDTMP for relapsed or refractory disease beyond second-line therapy[62]

Manuscript in preparation.

Patient 9: DST provided cheaper and readily accessible drugs

9-year-old girl at Nicklaus Children's Hospital

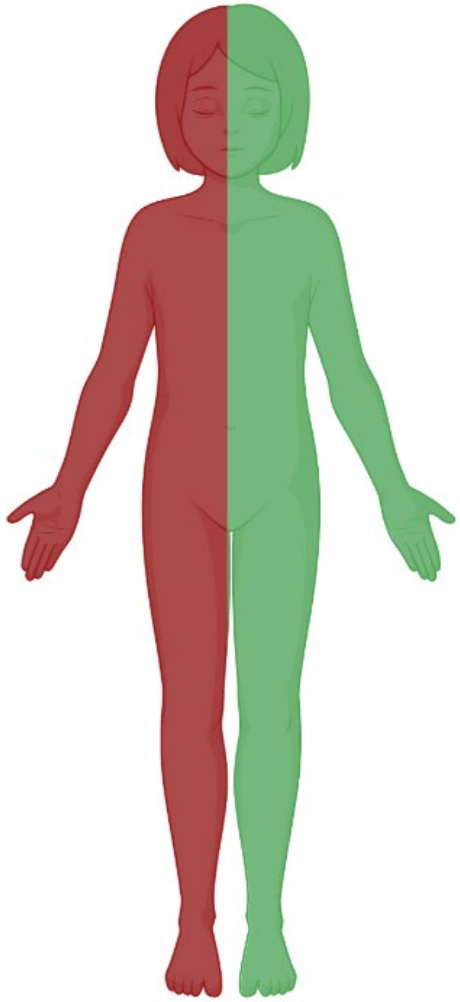
Metastatic Osteosarcoma

Physician Choice

Ifosfamide + Larotrectinib

Outcome: SD, **17 Weeks PFS**

Drug Cost: $12k+/month



FPM-Guided

Idarubicin + Montelukast

Outcome: **CR**, **84 Weeks PFS**

No evidence of osteo recurrence

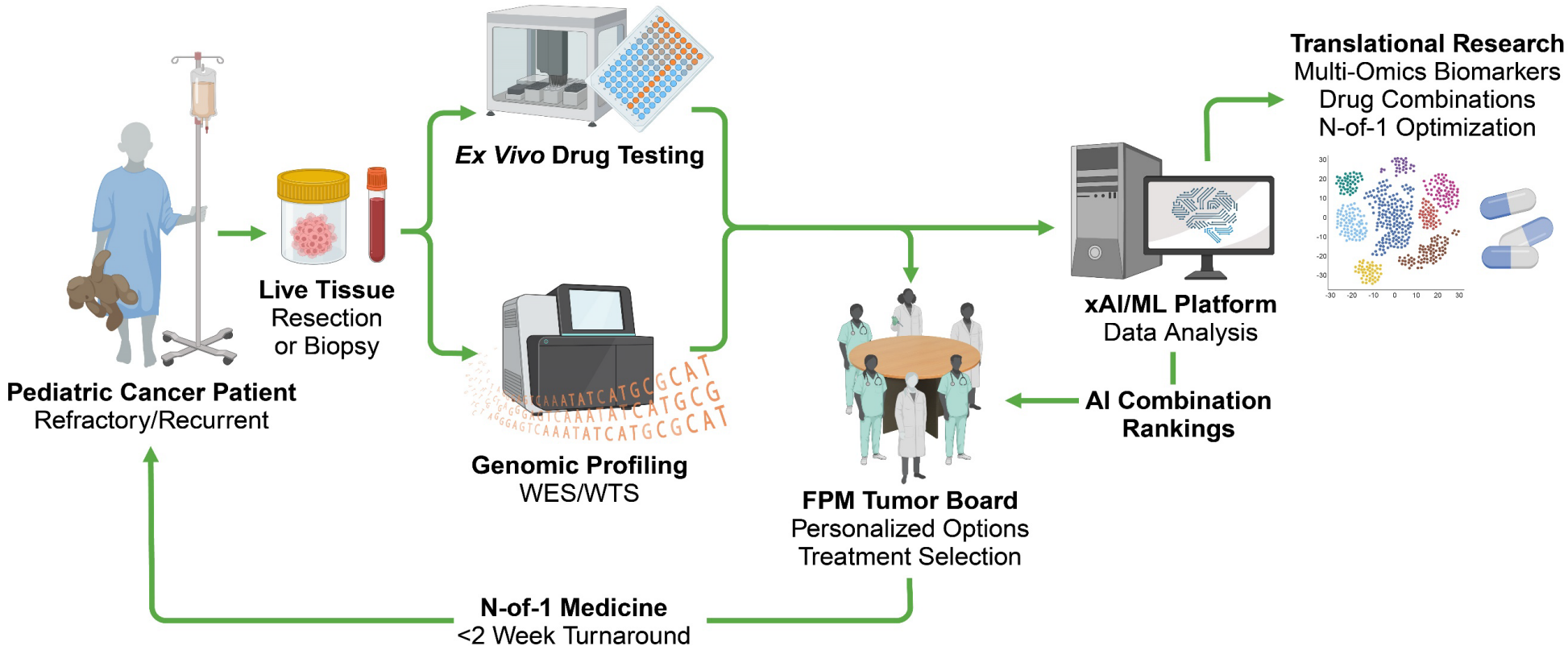
Drug Cost: $100s/month

Off-Label Use of Approved Agent

Manuscript in preparation.

National Institute on Minority Health and Health Disparities

Integrating FPM with Artificial Intelligence for Biomarker Discovery and Advancing Personalized Medicine Workflows



FIU FLORIDA INTERNATIONAL UNIVERSITY

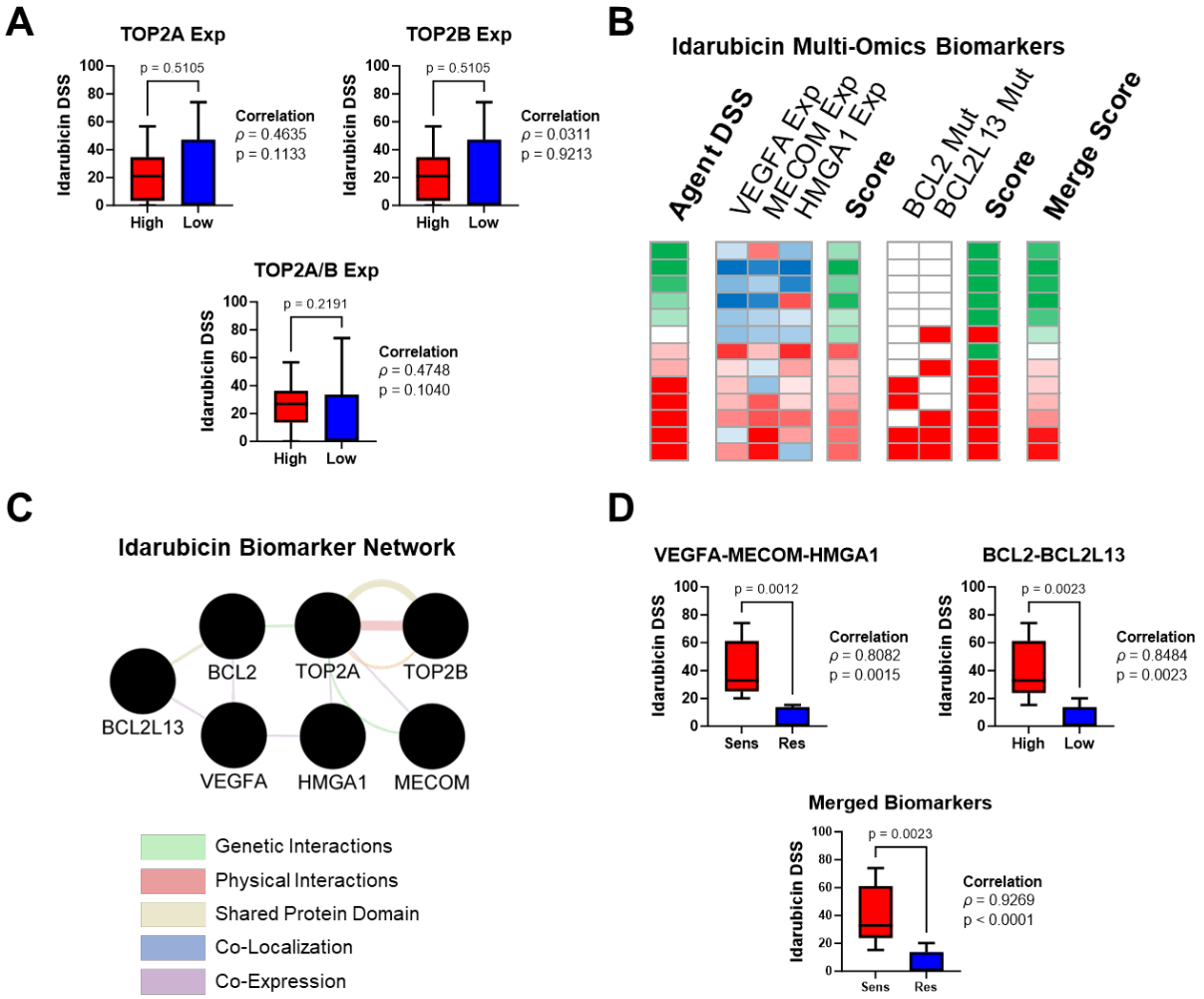
Nicklaus Children's Hospital

FIRST ASCENT BIOMEDICAL

ClinicalTrials.gov number, NCT05857969

National Institute on Minority Health and Health Disparities

Identification of Idarubicin Response Biomarkers Specific to Minority Pediatric Cancer Patients



Establishing a CLIA-Certified Lab for Functional DST in the State of Florida

$2M

in funding for the center for advancing personalized cancer treatments from the State of Florida

The **goal** is to launch large-scale prospective **multi-center randomized clinical trials** to better assess clinical utility of functional precision medicine approaches in the treatment of refractory/relapsed cancers

Ongoing Studies in Pediatric and Adult Refractory Cancers

Refractory Pediatric Cancer

65 Patients – Now Enrolling

NCT05857969

Number of patients enrolled to date: 23

Patients with Multiple DST: 7

Number of patients guided by FPM : 23 (100%)

Clinical Outcomes pending

Nicklaus Children's Hospital

NIH National Institute on Minority Health and Health Disparities

Refractory Adult Cancer

36 Patients – Now Enrolling

NCT06024603

Number of patients enrolled to date: 24

Patients with Multiple DST : 4

Number of patients guided by FPM: 3 (13%)

Clinical Outcomes pending

Cleveland Clinic

COMMUNITY FOUNDATION OF BROWARD

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