



Guidelines and Gaps

2023 Joyce Niblack MPN Conference

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Executive Director Atrium Health Wake Forest Baptist Comprehensive Cancer Center

Enterprise Senior Vice President Atrium Health

Vice Dean for Cancer Programs – Wake Forest School of Medicine

Professor of Medicine

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Disclosures – Ruben Mesa, MD

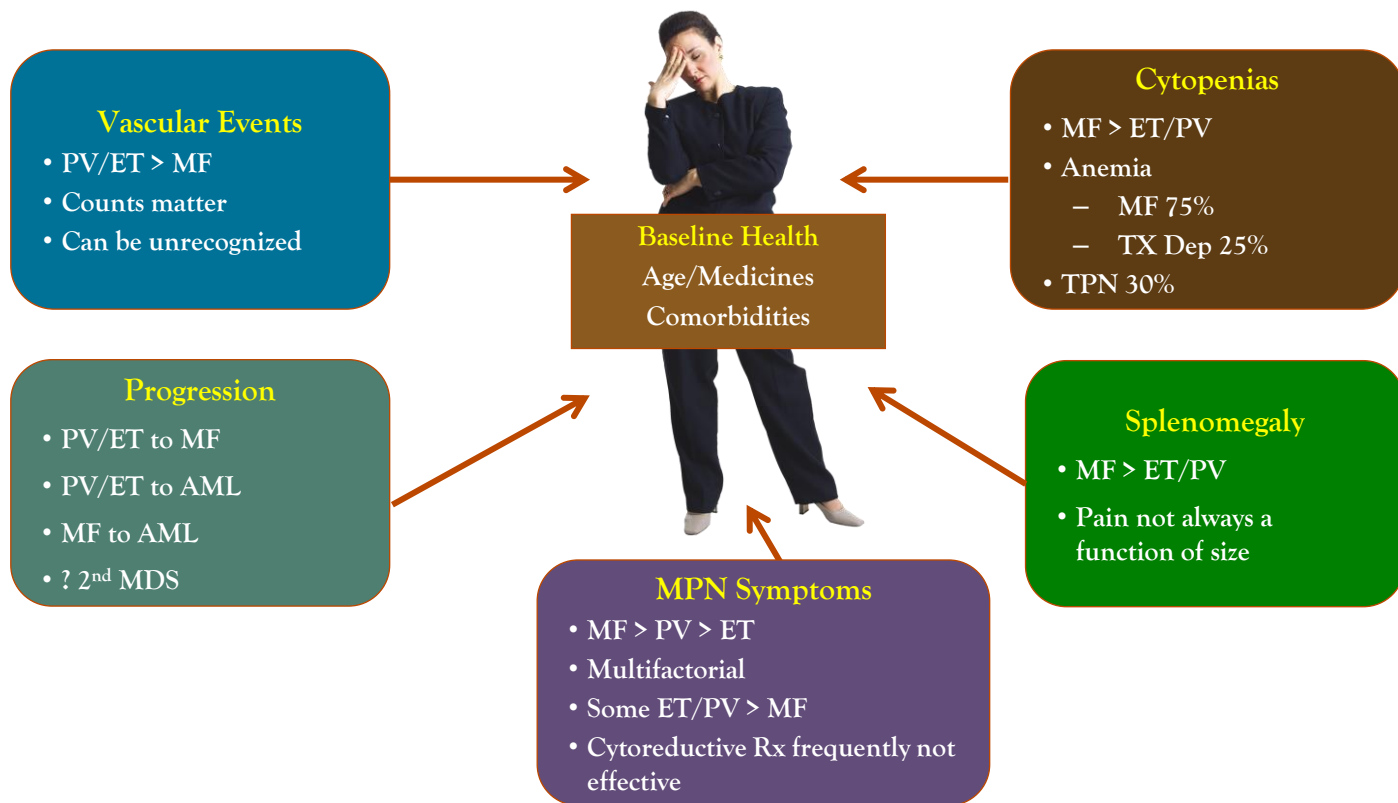
- Consultant (Honoraria) over past 3 years
 - Novartis
 - Sierra Oncology
 - Genentech
 - Sierra
 - Blueprint
 - Geron
 - Telios
 - CTI
 - Incyte
 - BMS
 - Abbvie
 - GSK
- Research Support
 - Incyte
 - Sierra
 - CTI
 - BMS
 - Abbvie
 - Genentech
 - Blueprint
 - Morphosys

Gaps and Guidelines – MPNs 2023

- Goals and Targets
- ET and PV
- JAK Inhibitors as Foundation
- Non JAKi MOA
- Other Gaps
- Putting it all Together

Assessing MPN Burden

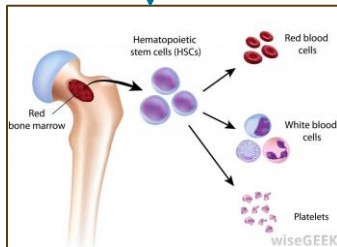
WHO Diagnosis Does Not Tell Whole Story



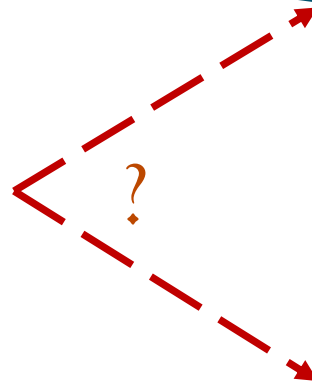
What do symptoms tell us about MPN Biology?



MPN
Symptoms

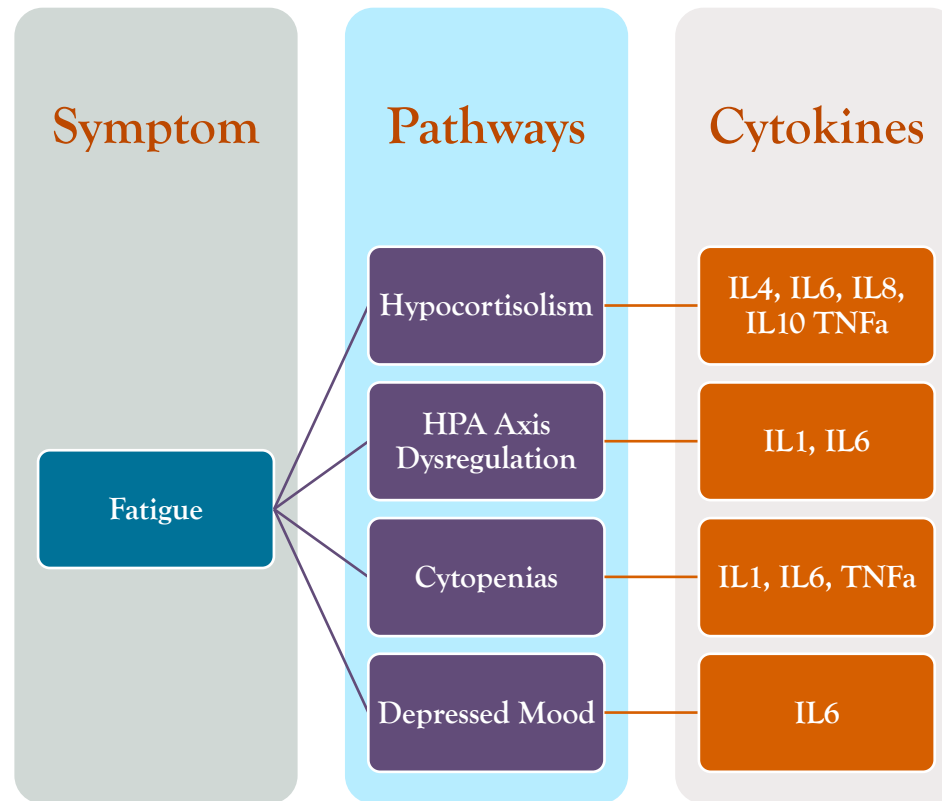


Mood Disorders
Anxiety over
Uncertainty



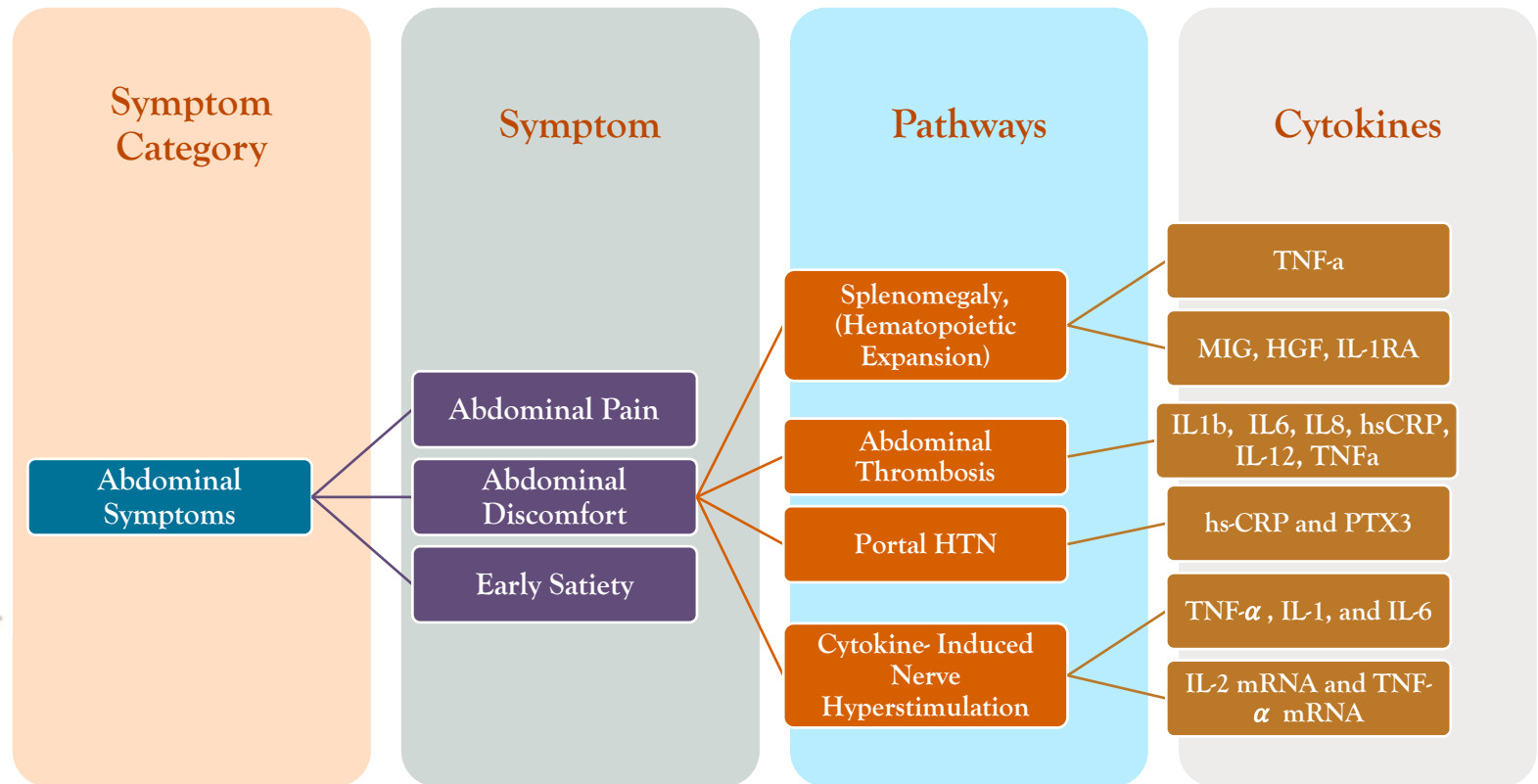
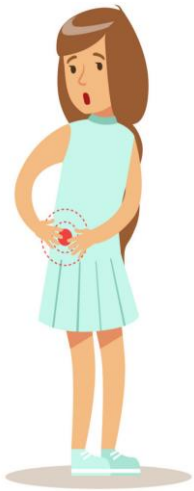
Cytokine Driven
Symptoms
Spleen/ Inflammation

Fatigue

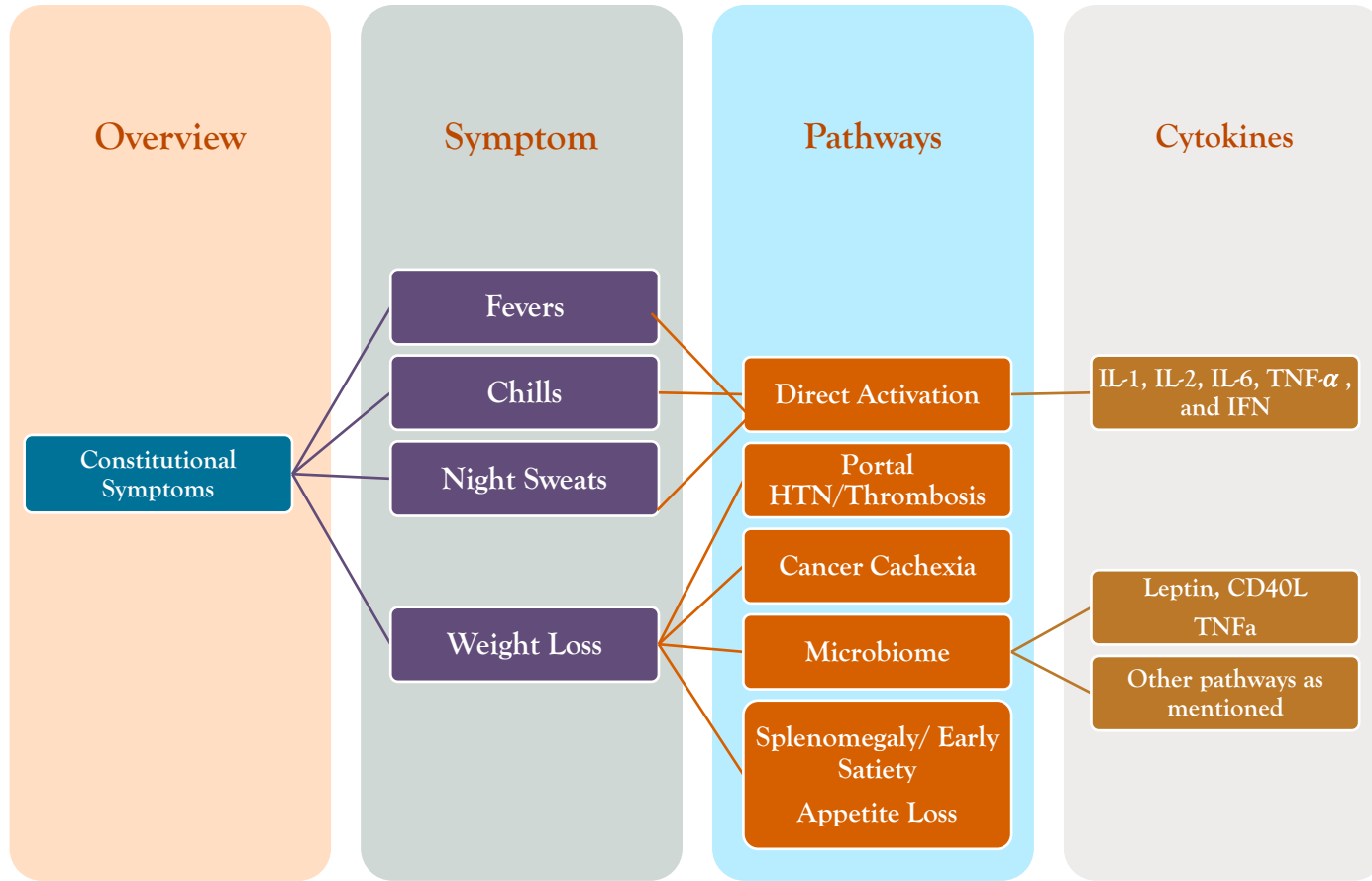


Cancer, vol. 92, no. 6, pp. 1684–1688, 2001.
Cancer, vol. 104, no. 4, pp. 788–793, 2005.
Brain, Behavior, and Immunity, vol. 21, no. 3, pp. 251–258, 2007.
Cancer, vol. 106, no. 4, pp. 751–758, 2006.
[American Journal of Psychiatry, vol. 158, no. 8, pp. 1252–1257, 2001.]

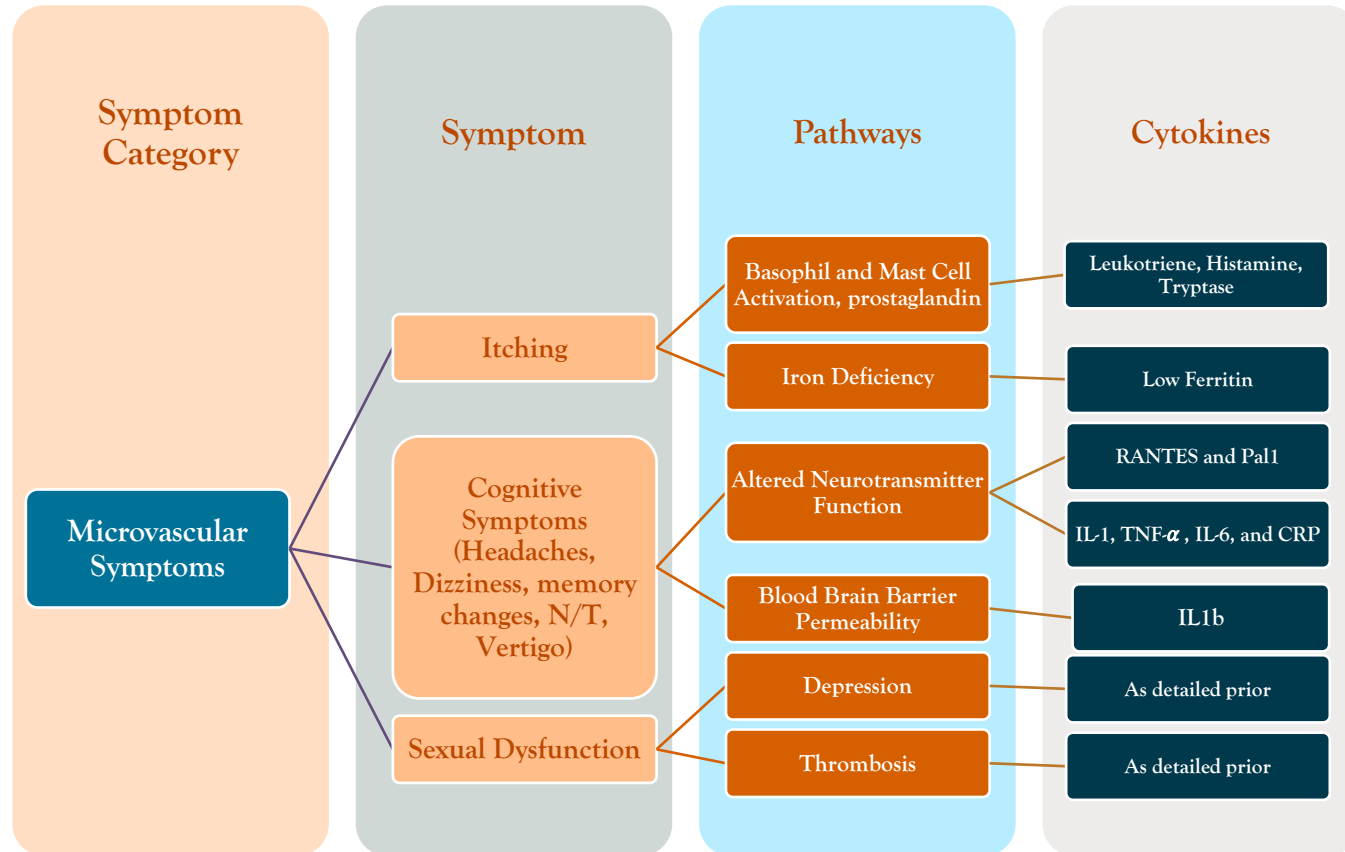
Abdominal Symptoms



Constitutional Symptoms



Microvascular Symptoms



What is Precise and Personalized Cancer Care?

Molecular Features of
Disease

Communication
Social DOH
Health Literacy

Individual Health Factors
In Treatment
Planning?

Geography
Employment
Financial Pressures

Individualized Supportive
Care Needs?

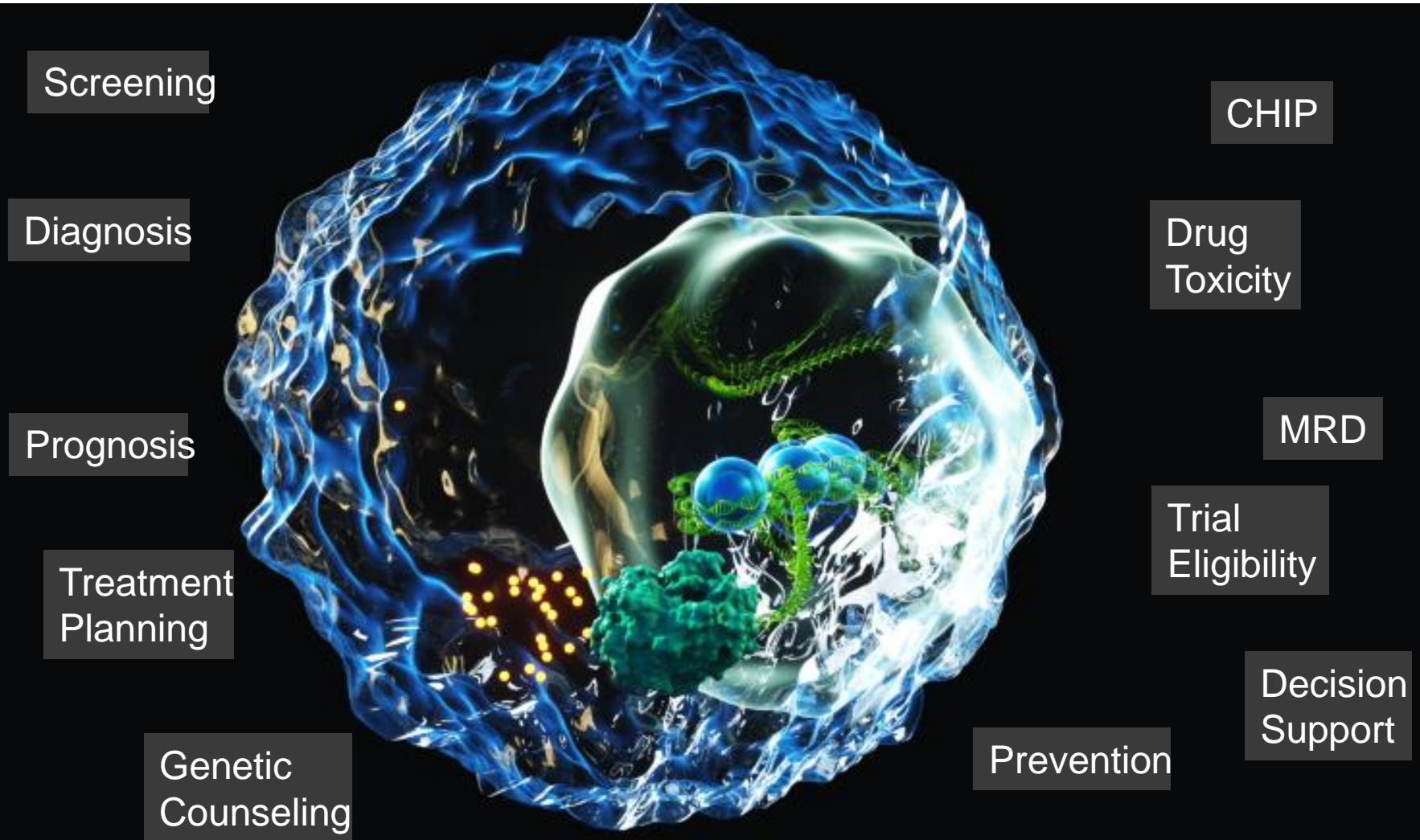
Individual Cultural
Value Factors
In Treatment
Planning?

Individualized Survivorship?

Disease impact
Symptoms
QoL?



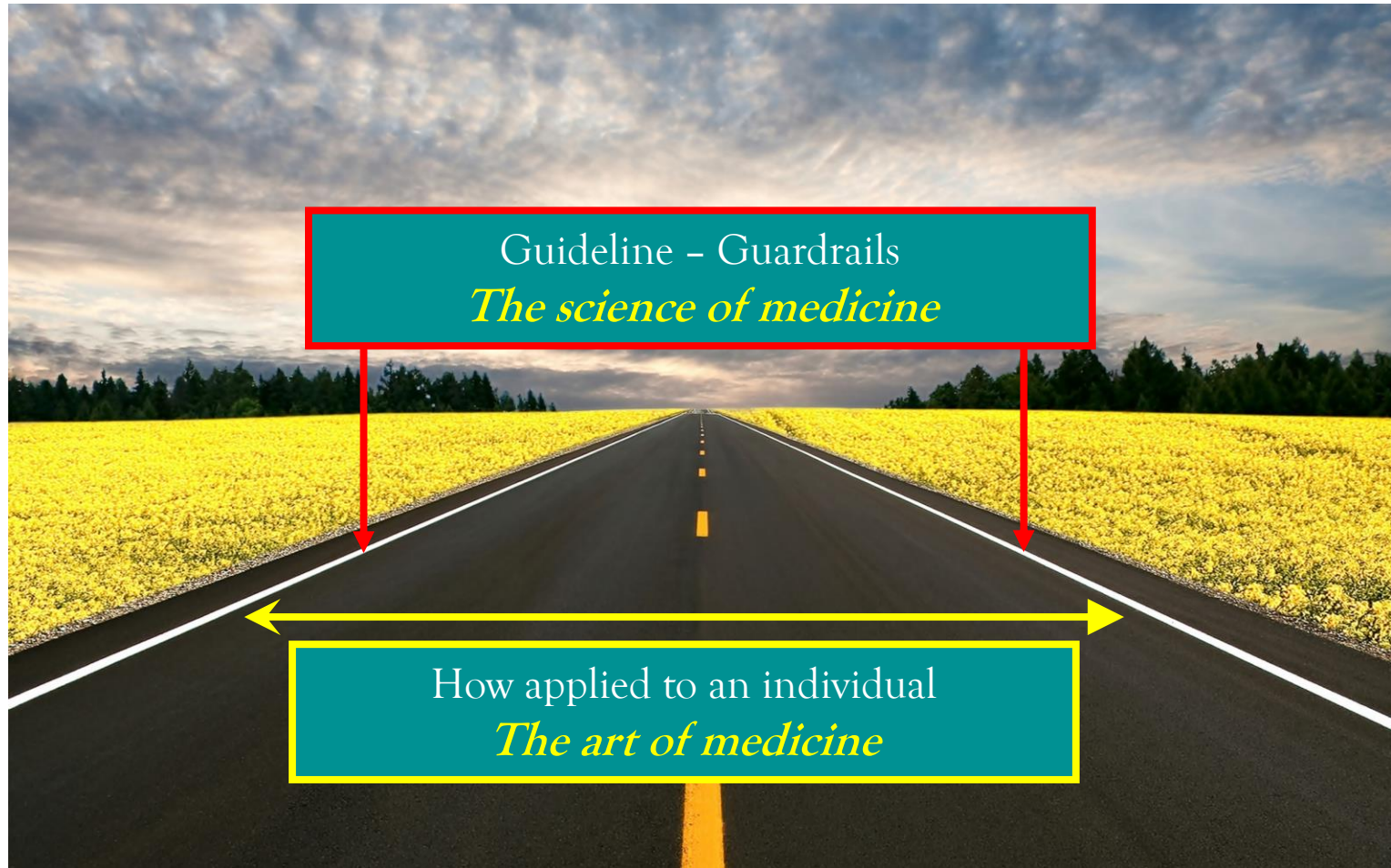
Weaving Molecular Data into Cancer Care



Therapy of MPNs 2023

- Goals and Targets
- **ET and PV**
- JAK Inhibitors as Foundation
- Non JAKi MOA
- Other Gaps
- Putting it all Together

What is a treatment guideline?



Gap 2

Do we manage CV risk well?

Gap 4

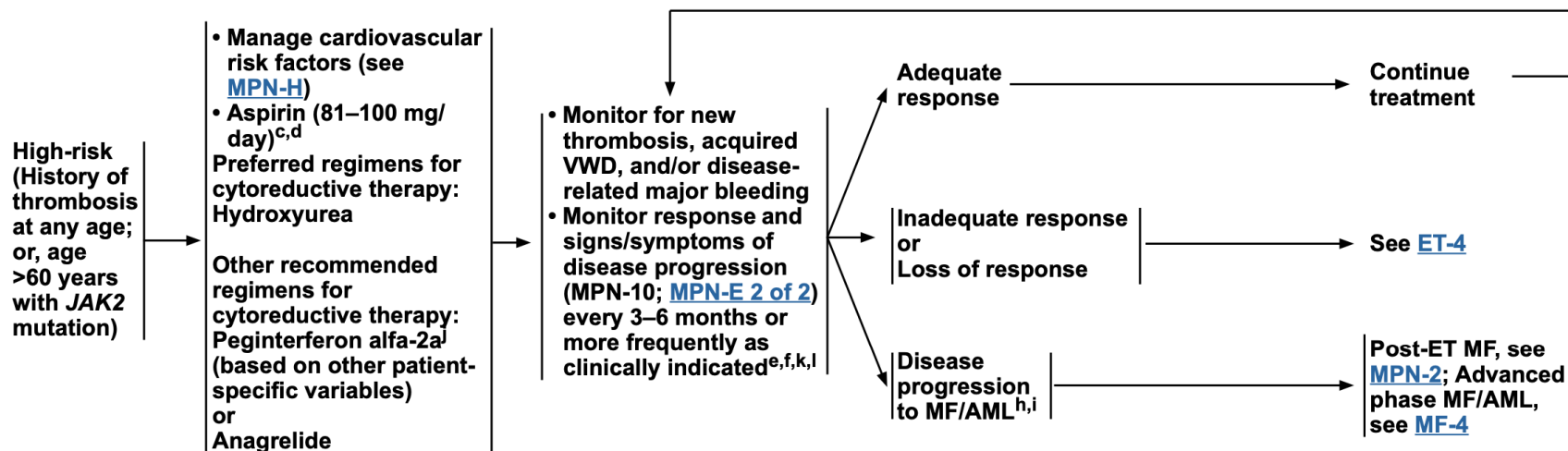
Predicting Progression and what is adequate response?



National
Comprehensive
Cancer
Network®

NCCN Guidelines Version 3.2022 Essential Thrombocythemia

TREATMENT FOR HIGH-RISK ESSENTIAL THROMBOCYTHEMIA^a



Gap 1

Who needs treatment vs Risk?

Gap 3

We need more and better treatments for ET?

Gerds, AT et al. J Natl Compr Canc Netw. 2022 Sep;20(9):1033-1062.

Gap 2

Do we manage CV risk well?

Gap 4

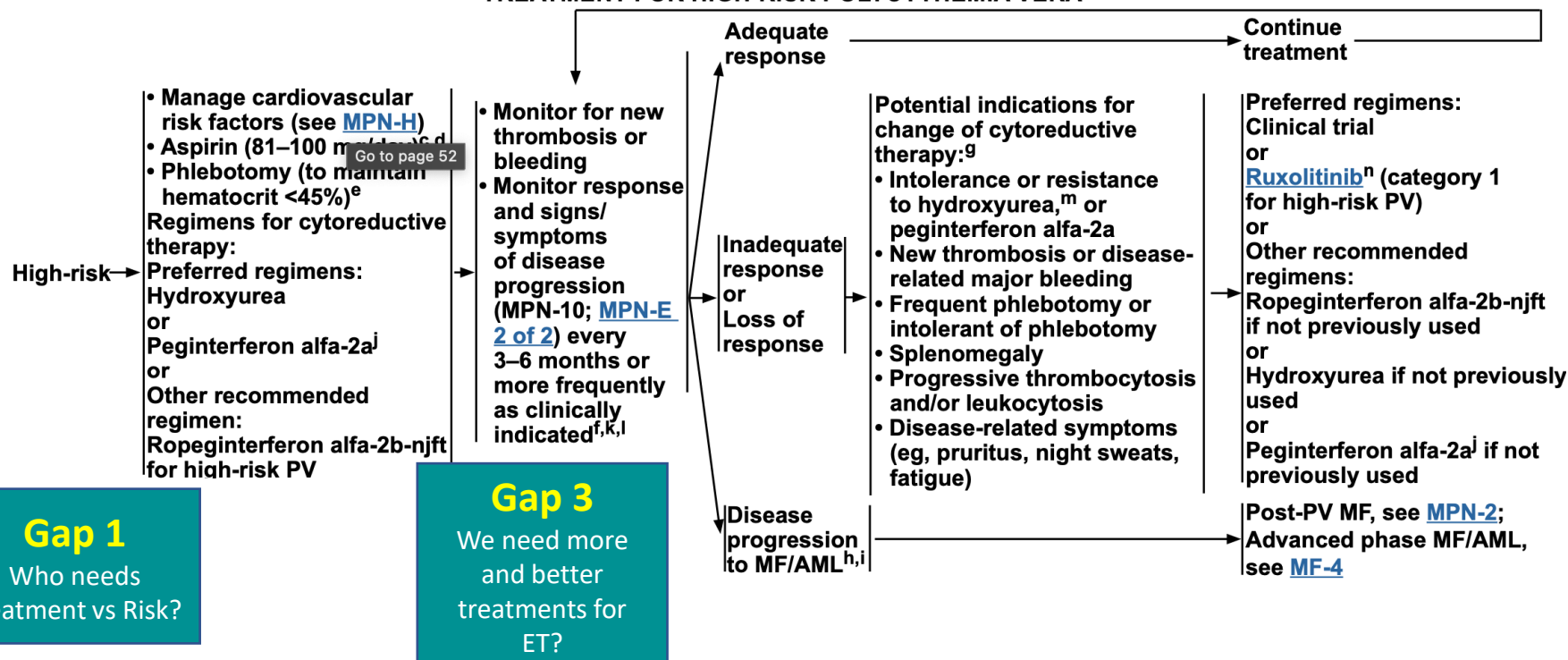
Predicting Progression and what is adequate response?

NCCN

National
Comprehensive
Cancer
Network®

NCCN Guidelines Version 3.2022 Polycythemia Vera

TREATMENT FOR HIGH-RISK POLYCYTHEMIA VERA^a

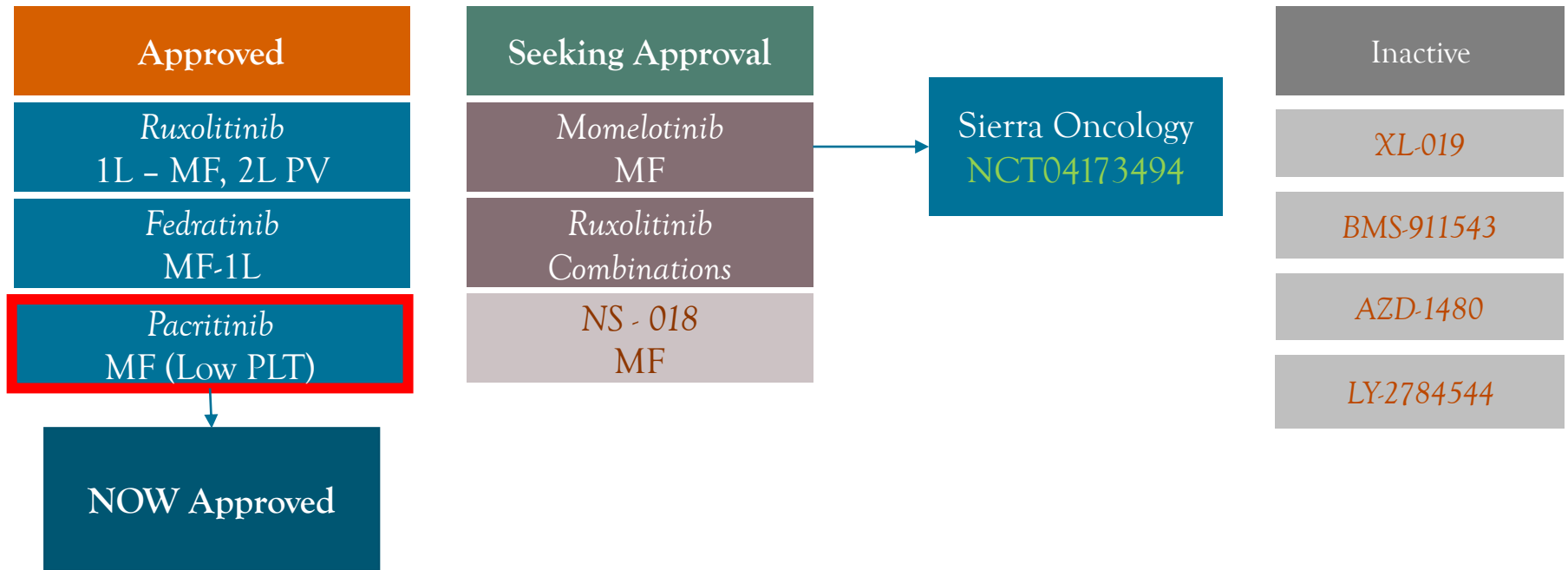


Gerds, AT et al. J Natl Compr Canc Netw. 2022 Sep;20(9):1033-1062.

Therapy of MPNs 2023

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JAK Inhibitor Landscape 2023



Gap 2

We still likely do
transplant too late
in too many

Gap 4

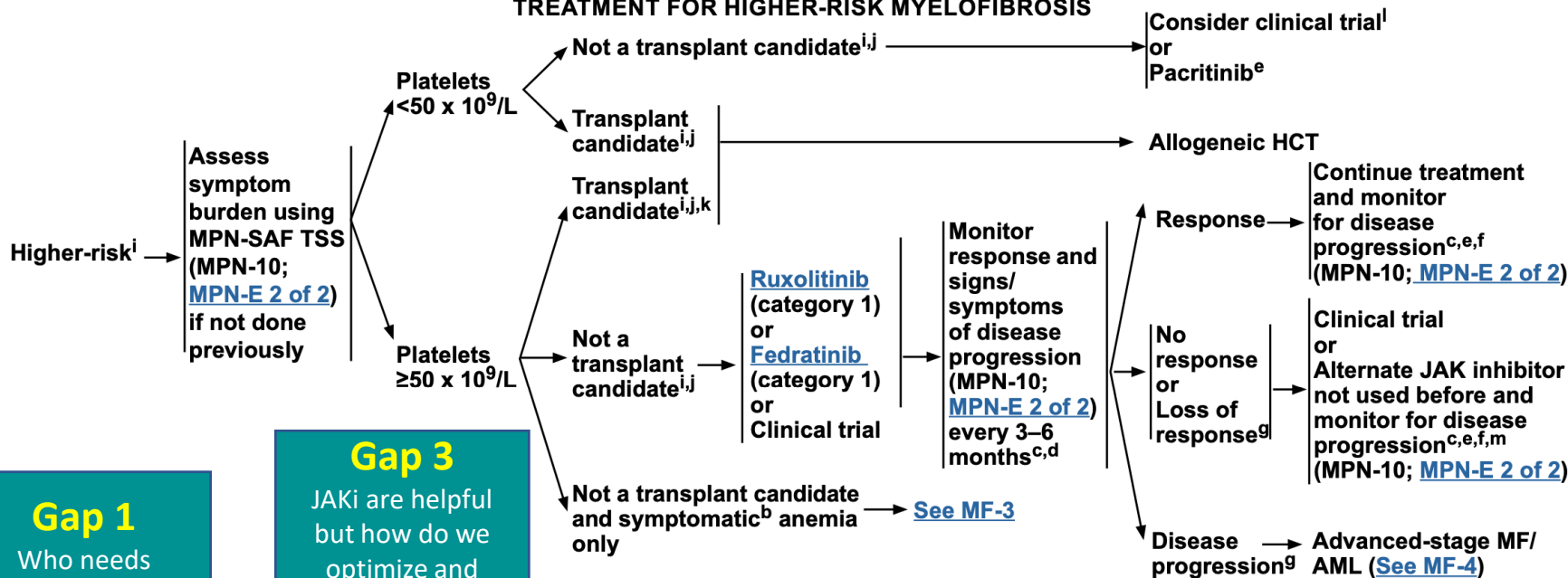
Predicting Progression and
what is adequate
response?

NCCN

National
Comprehensive
Cancer
Network®

NCCN Guidelines Version 3.2022 Myelofibrosis

TREATMENT FOR HIGHER-RISK MYELOFIBROSIS



Gap 1

Who needs
treatment vs Risk?

Gap 3

JAKi are helpful
but how do we
optimize and
which agent
when?

Gap 5

How do we get to deeper
and broader impact?

Gerds, AT et al. J Natl Compr Canc Netw. 2022 Sep;20(9):1033-1062.

Therapy of MPNs 2023

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Current Phase III trials in MF

SINGLE

- Pacritinib (JAKi) NCT03165734 (PACIFICA)

Combination RX

- Pelabresib (BETi) NCT04603495 (MANIFEST II)
- Navitoclax (Bcl-XL) NCT04472598 (TRANSFORM I)
- Parsiclisib (PI3K Inhib) NCT04551053 (LIMBER 313)

Ruxolitinib

SubOpt JAKi
ADD-ON

- Luspatercept (Activin) NCT04717414 (INDEPENDENCE)
- Navitoclax (BCL-Xli) NCT04468984 (TRANSFORM II)
- Parsiclisib (PI3Ki) NCT04551053 (LIMBER304)
- KRT-232 (HDM2) NCT03662126 (BOREAS)

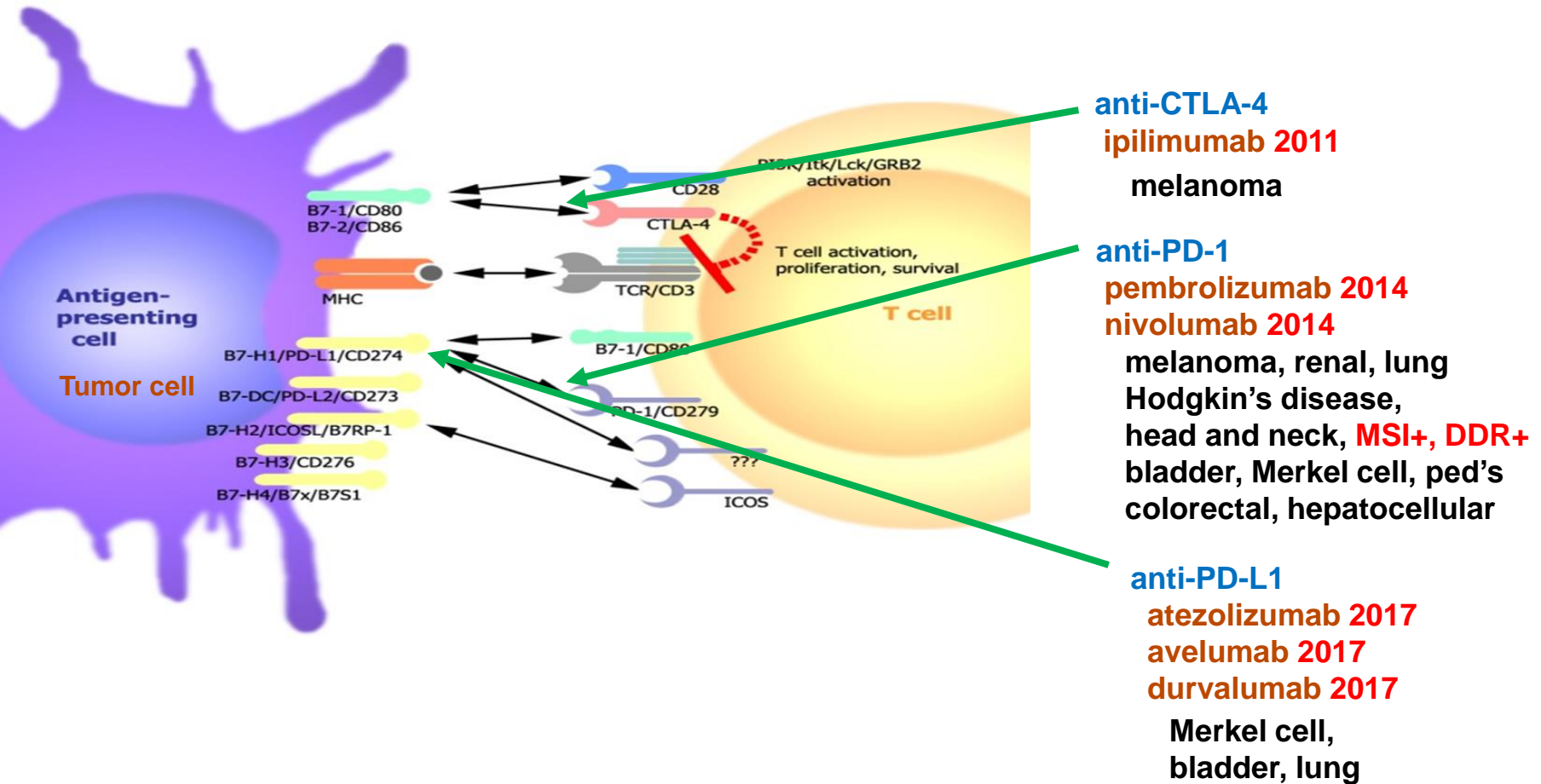
Ruxolitinib

JAKi Fail

Ruxolitinib

- Imetelstat (TelomeraseI) NCT04576156
- Momelotinib (JAKi) NCT04173494 (MOMENTUM)

Immune Therapies



Target MF Stem Cell: NCI Funded MPN RC

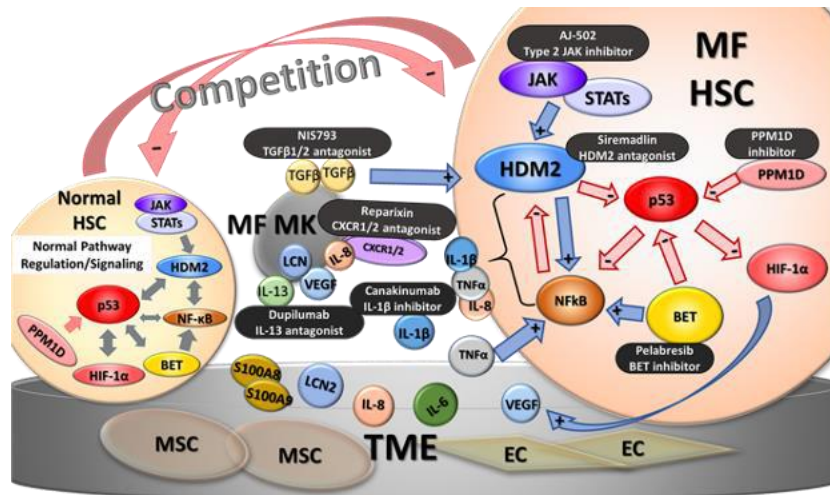


Figure 1. Bench to bed strategy to deplete MF stem cells.

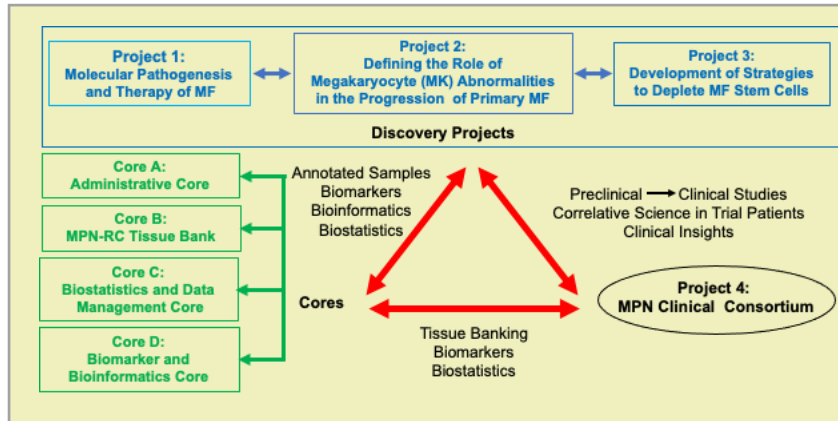


Table 1. Members of the MPN-RC

Institutions	Members
Icahn School of Medicine at Mount Sinai, NY, NY*	Ronald Hoffman, MD (PI)
Cedars-Sinai Medical Center, Los Angeles, CA*	Ronald L. Paquette, MD*
Cleveland Clinic Lerner College of Medicine of CWRU, Cleveland, OH*	Aaron Gerds, MD*
Mayo Clinic Arizona, Scottsdale, AZ*	Amylou Dueck, PhD
Mays Cancer Center; University of Texas Health Science Center, San Antonio, TX*	Ruben Mesa, MD*
Moffitt Cancer Center, Tampa FL*	Andrew Kuykendall, MD*
St. Jude Children's Research Hospital, Inc.	John Crispino, PhD
Sloan Kettering Institute for Cancer Research, NY, NY*	Ross Levine, MD
University of Kansas Medical Center Research Institute, Westwood, KS*	Abdulraheem Yacoub, MD*
Wake Forest University Health Sciences, Winston-Salem, NC*	Rupali Bhavne*
Roswell Park Comprehensive Cancer Center, Buffalo, NY*	Eunice Wang, MD*
Canada	
University Health Network, Toronto, Canada*	Vikas Gupta, MD*

* Denotes PI of Clinical Sites

Projects 1-3:
Laboratory
investigations

Project 4:
Translation to
the clinic

Characterizing
MF Stem Cells
and Microenvironment

Depletion of
MF Stem Cells
and Dampening of
Tumor Microenvironment

Novel MPN
Therapeutic
Approaches/
Combination Therapies



American Society of Hematology

Helping hematologists conquer blood diseases worldwide

Discovery of INCA033989, a Monoclonal Antibody That Selectively Antagonizes Mutant Calreticulin Oncogenic Function in Myeloproliferative Neoplasms

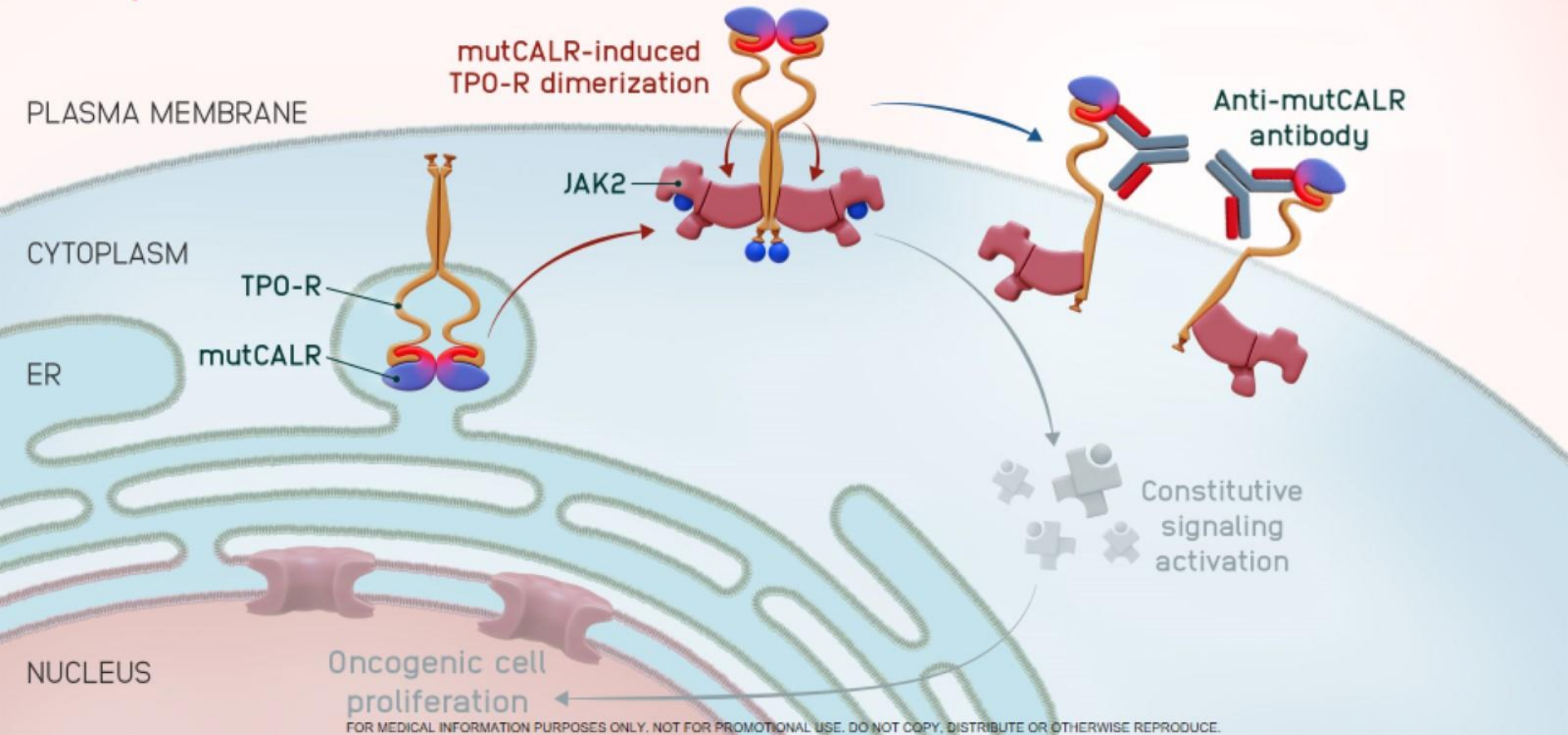
Edimara Reis¹, Rebecca Buonpane¹, Hamza Celik¹, Caroline Marty², Angela Lei¹, Fatoumata Jobe¹, Mark Rupar¹, Yue Zhang¹, Darlise DiMatteo¹, Rahel Awdew¹, William Vainchenker², Jing Zhou¹, Ian Hitchcock³, Isabelle Plo², Horacio Nastri¹, Patrick Mayes¹

¹Incyte Corporation, Wilmington, DE, USA; ²INSERM UMR 1287, Université Paris-Saclay, Gustave Roussy, Villejuif, France;

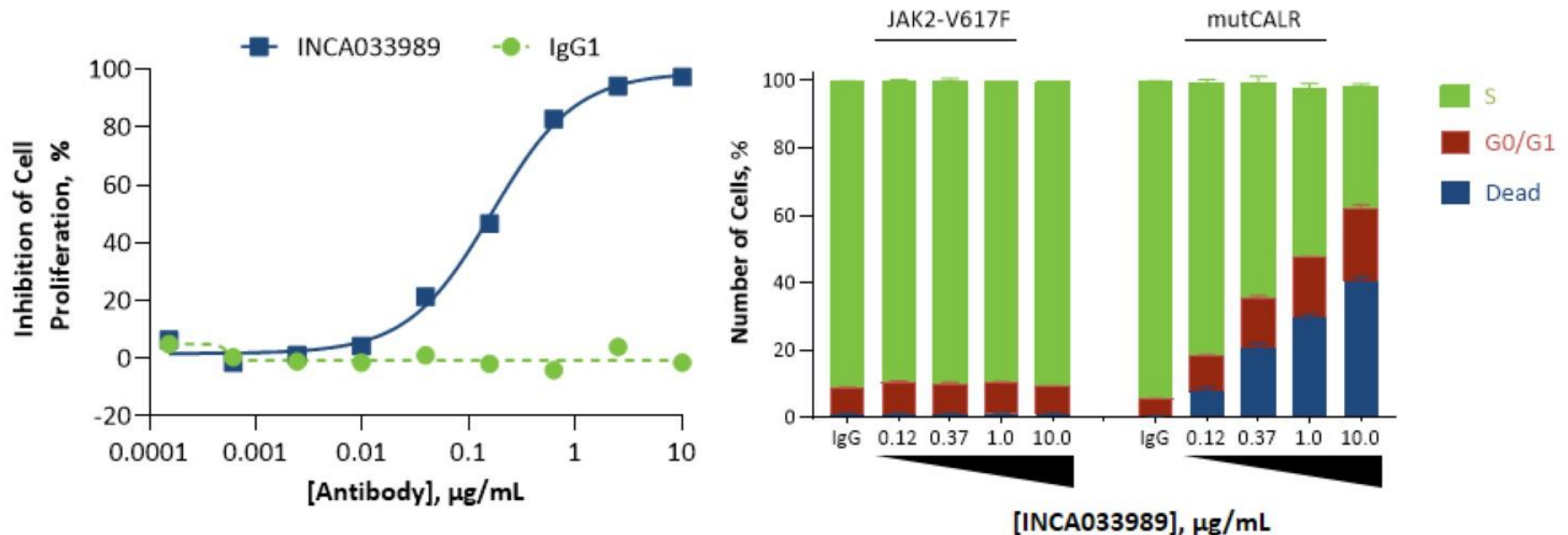
³York Biomedical Research Institute, Department of Biology, University of York, York, UK

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Anti-mutCALR antibody selectivity inhibits oncogenic cell proliferation



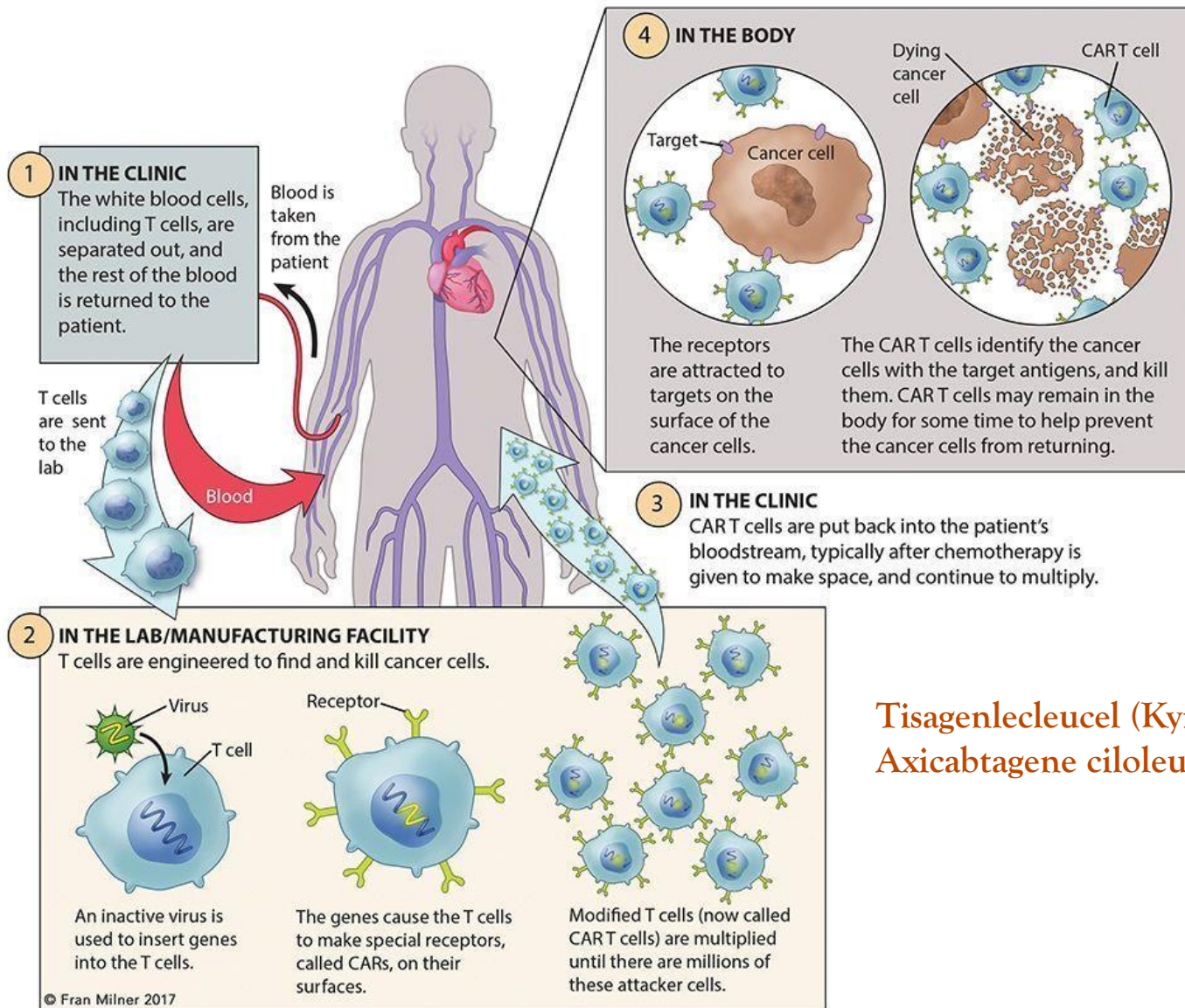
INCA033989 selectively inhibits cell proliferation and induces death of mutCALR⁺ cells



American Society of Hematology

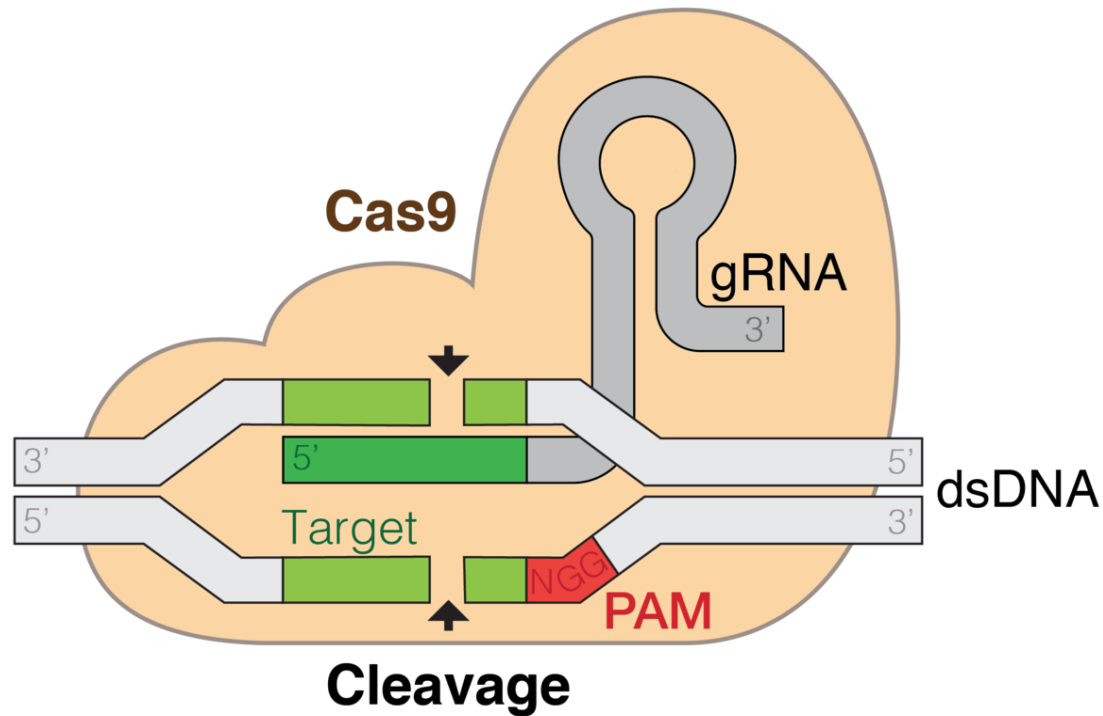
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Cellular Therapies



Tisagenlecleucel (Kymriah™) – ALL, DLBCL
Axicabtagene ciloleucel (Yescarta™) - Lymphoma

Click to edit Master title style



Consumer-based meditation app, calm, for treatment of sleep disturbance in hematological cancer patients



Consumer-based meditation app, calm, for treatment of sleep disturbance in hematological cancer patients

- NIH NCI-Funded (1R01CA262041-01A1)
- 5-year project period (2022-2027)
- Target enrollment = 276 heme cancer patients actively undergoing treatment
- 20-wk RCT comparing Calm meditation app to health education podcast app (8-wk intervention + 12-wk follow-up)
- **Primary outcomes:** Oura Ring sleep; PROMIS sleep, sleep diary
- **Secondary outcomes:** fatigue, anxiety, depression, and QoL (PROMIS); inflammatory biomarkers (TNF- α ; IL-6; IL-8; CRP)



2021

R01 Grant Funded w/ Perfect Score!!!

R01 project kicked off in April 2022

2027

Study preparation and planning

- First ~6-9 months of project
- Prepare study documents and materials
- Receive regulatory approvals
- Establish partnerships and contracts
- Develop recruitment materials
- Setup and finalize meditation and podcast apps for study implementation

Recruitment and enrollment

- Begins at ~9 months into project
- Kickoff recruitment with project partners
- Primary recruitment methods include sharing of study on social media sites, partner websites and email listservs
- Targeted enrollment of 276 heme cancer patients over ~3.5 years

Study implementation and data collection

- Months ~9-54 of the project
- Rolling enrollment of ~10 participants/month
- 20-wk study = 8-wk intervention + 12-wk follow-up
- Outcome measures at baseline, wk 8, and wk 20
- Remote blood draws for inflammatory biomarkers
- Oura ring to capture sleep
- Online surveys via Qualtrics to capture self-report outcomes

Data analysis and manuscript development

- Final ~6 months of project
- Complete data analysis
- Develop manuscripts for publication

Therapy of MPNs 2023

- Goals and Targets
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- **Other Gaps**
- Putting it all Together

We lack effective early detection approaches to diagnose many types of cancer.

We have curative therapies that come at the cost of serious side effects.

We have too few methods to prevent cancer.

We leave too many patients and families to navigate the disease on their own.

Cancer as we know it today



We have stark inequities in diagnosis, treatment and trial access, and patient outcomes, based on race, region and resources.

Cancer kills 600,000 people per year in the United States, including close to 1,800 aged 19 and under.

We have limited success in some of the toughest to treat and rare cancers.

What it will take to end cancer as we know it



Reignition of the Cancer Moonshot 2022



7 Pillars – Progress for

1. Cancer Early Detection
2. Prevention
3. Equity
4. Precision Medicine
5. Rare & Childhood Cancers
6. Supporting Patients & Caregivers
7. Learning From Patients

Priority Actions

- Close the Screening Gap
- Understand & Address Environmental/Toxic Exposures
- Decrease Preventable Cancers
- Bring Cutting Edge Research Through Pipeline to Patients & Communities
- Support Patients and Caregivers

A Team Based Approach for Care

Helping Cancer Patients RISE Beyond Their Cancer!



CANCER MEDICAL SPECIALTIES

- Cardio-Oncology
- Onco-Nephrology
- Optho-Oncology
- Palliative Medicine
- Survivorship Clinics
- Endocrine
- Medical Management Clinic

PATIENT & CAREGIVER SERVICES

- Nutrition
- Genetic Counseling
- Psycho-Social Support
- Social Work
- Transportation
- Holistic Support Programs
- Financial Counseling



Standardizing MPN Data Collection

Pre MPN History

- Complete Demographics
- Co-morbidities
- Meds
- Fam Hx
- Prior Events/ Symptoms

MPN Presentation

- Labs/ Exam
- MPN SAF
- Marrow and NGS

MPN Course

- Meds/ Toxicities (inc \$)
- Events
- Serial Labs/ MPN SAF
- Repeat Marrow NGS

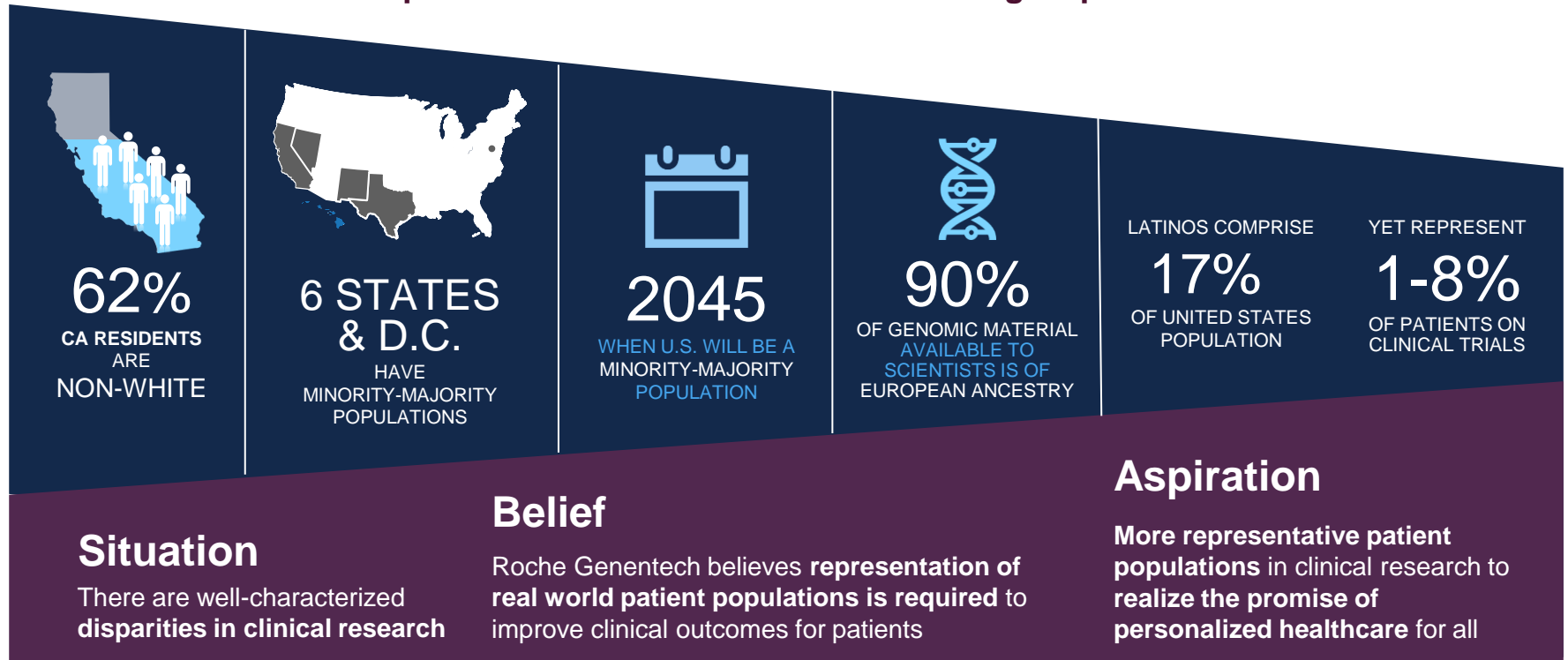
Outcomes

- Events
- Progression
- Co-Morbidities
- Mortality



Advancing Inclusive Research®

Enterprise-wide initiative focused on tackling disparities in clinical research



Sources: <https://www.census.gov/quickfacts/fact/table/US/PST045216>; https://i0.wp.com/www.brookings.edu/wp-content/uploads/2018/03/20180910_metro_Frey_census-datacharts-revised-Fig1.png?w=768&crop=0%2C0px%2C100%2C9999px&ssl=1, *Nature* 538, 161–164 (13 October 2016) doi:10.1038/538161a
<https://statisticalatlas.com/state/California/Race-and-Ethnicity>: US Census Bureau, specifically from the 2010 census, and from the 2012-2016 American Community Survey.
Coakley M, Fadiran EO, Parrish LJ, Griffith RA, Weiss E, Carter C. *J Womens Health (Larchmt)*. 2012;21(7):713-716.
Mills, M.C., Rahal, C. *Nat Genet* 52, 242–243 (2020).
<https://www.appliedclinicaltrialsonline.com/view/special-populations-underrepresented-oncology-research-challenges-and-solutions-engage-hispanic-popu>

What is inclusivity?

- 1) Race?
- 2) Ethnicity?
- 3) Gender?
- 4) Age span (across the lifespan)?
- 5) Sexual Orientation?
- 6) Basically a trial should reflect the population, not a subset

Cancer Focus: Testimony on Diversity for Clinical Trials

Mays Cancer Center



117th US Congress: Energy & Commerce March 17, 2022

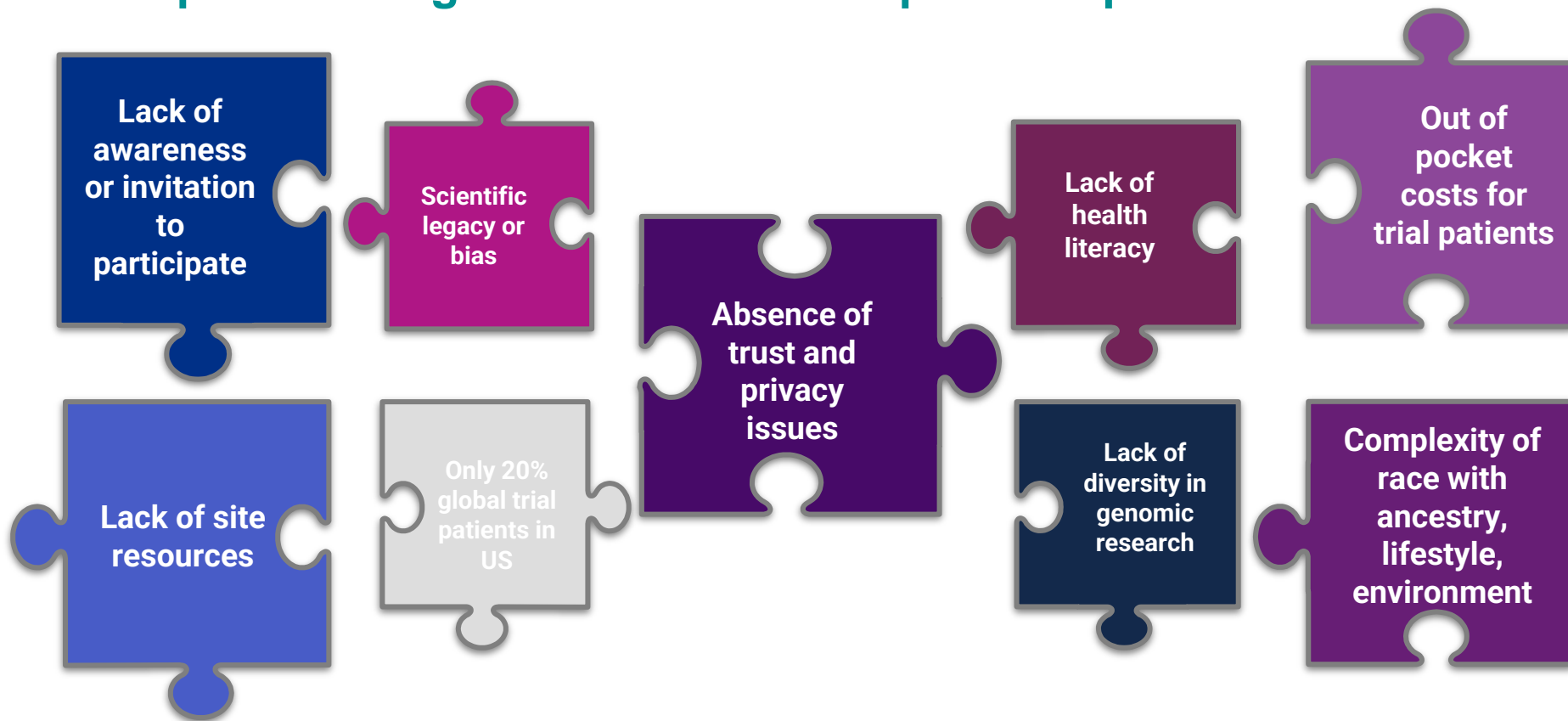


REP Anna Eshoo (CA-18)



TOPIC: Diversity on Clinical Trials in setting of FDA User Fee Reauthorization Bills

Multiple Challenges to Address to Improve Representation



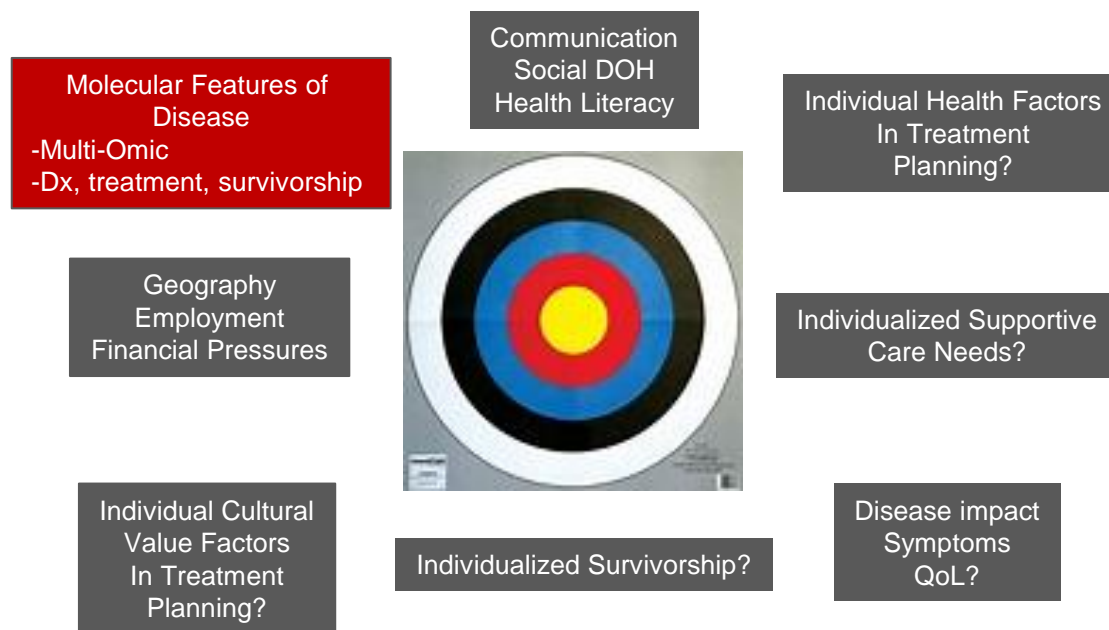
Why make a trial inclusive?

- 1) All patients should have a chance to benefit from the benefits of a trial (JUSTICE)
- 2) Inclusive trials help identify differences in efficacy between subgroups that might better lead to treatment planning (GOOD SCIENCE)
- 3) Inclusive trials might help to identify differences between subgroups in terms of toxicity that might lead to more precise dosing and use (GOOD PATIENT CARE)

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What is Precise and Personalized Cancer Care?



MPN Patient Community

MPN Group	Focus	Website
MPN Research Foundation	RES-ED-ADV	www.Mpnresearchfoundation.org
Leukemia and Lymphoma Society*	RES-ED-ADV	www.lls.org
MPN Advocacy & Education International*	ED-ADV	www.mpnadvocacy.com
MPN Education Foundation*	ED-COMM	www.mpninfo.org
AAMDS Foundation	ED	www.aamds.org
MPN Voice	ED	www.mpnvoice.org.uk
MPN HUB*	ED	www.mpn-hub.com
MPN Advocates Network	ED-ADV	www.mpn-advocates.net
Global MPN Scientific Foundation*	RES-ED-ADV	www.gmpnsf.org
MPN Forum Facebook Group	ED-COMM	https://www.facebook.com/groups/ourmpnforum/

