



BLOOD CANCER

Connect & Learn



The Future of Blood Cancer Care

Breakthroughs in treatment and patient-centered care – Dr. Berg

The intersection of medical innovation, mental health, and quality of life – Dr. Mayo

Our Experts



Dr. Tobias Berg

Dr. Tobias Berg is an Associate Professor, Department of Oncology at McMaster University, and a Hematologist at Hamilton Health Sciences, in Hamilton, Ontario.

Our Experts

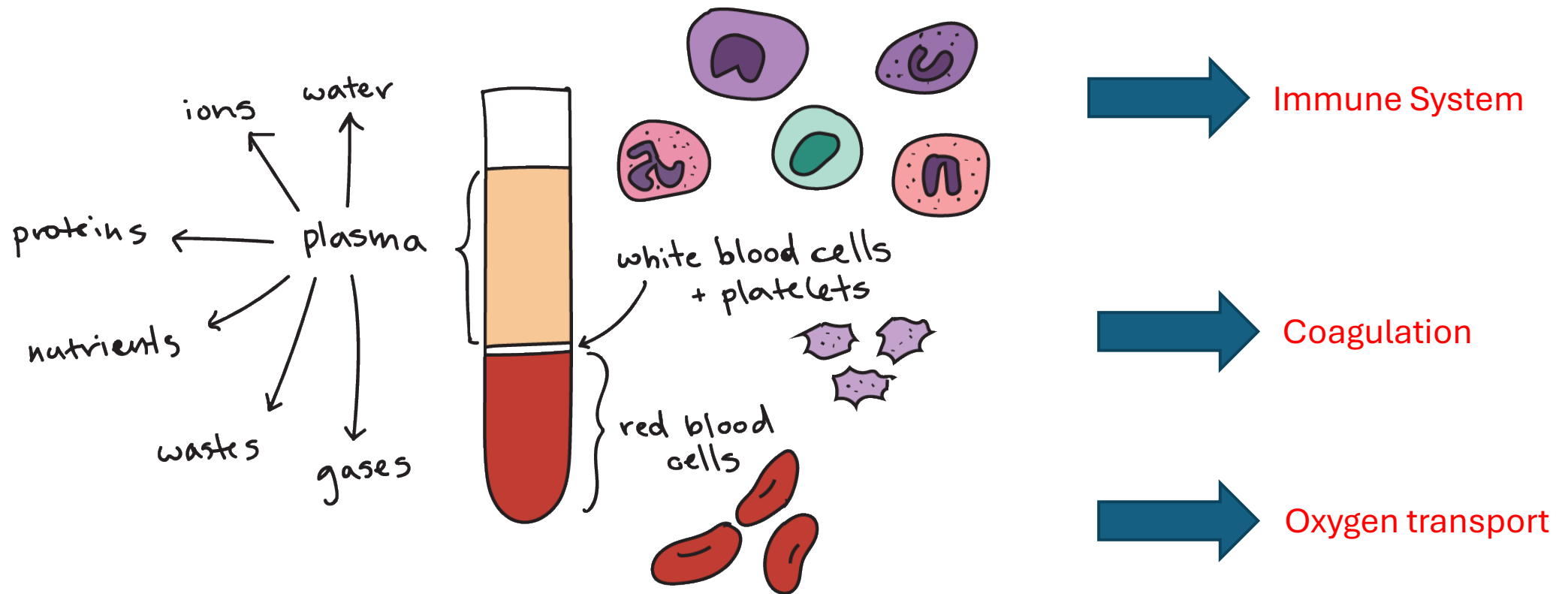


Dr. Samantha Mayo

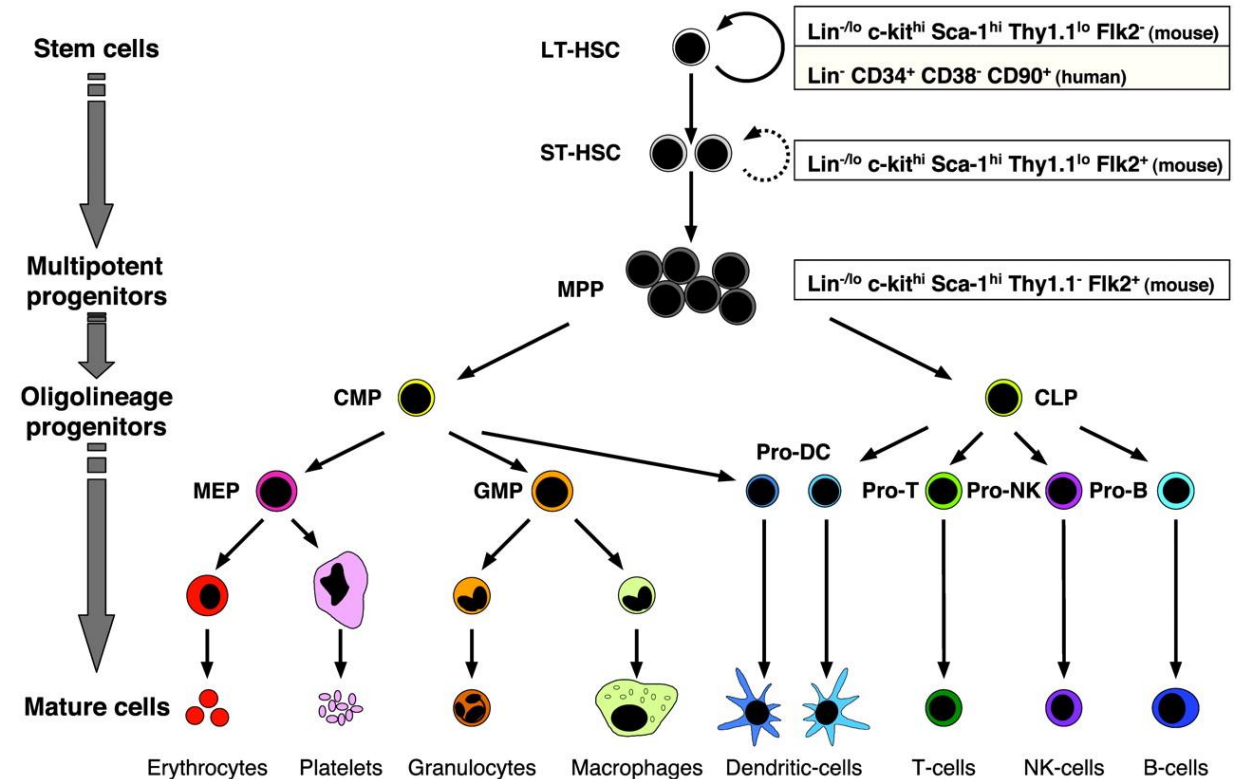
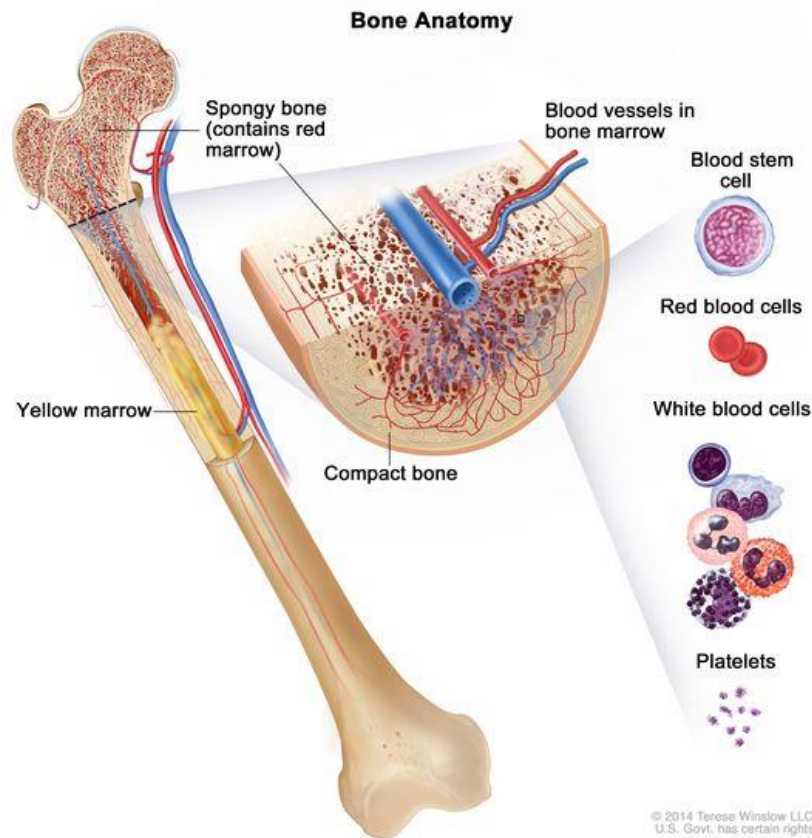
Professor Samantha Mayo RN, PhD, FAAN is an Associate Professor in the Lawrence Bloomberg Faculty of Nursing, University of Toronto. She also holds the RBC Chair in Nursing Oncology, Research & Education at the Princess Margaret Cancer Centre, where she co-leads the Oncology Nursing Research Centre of Excellence.

Breakthroughs in treatment and patient-centered care

What is our blood?



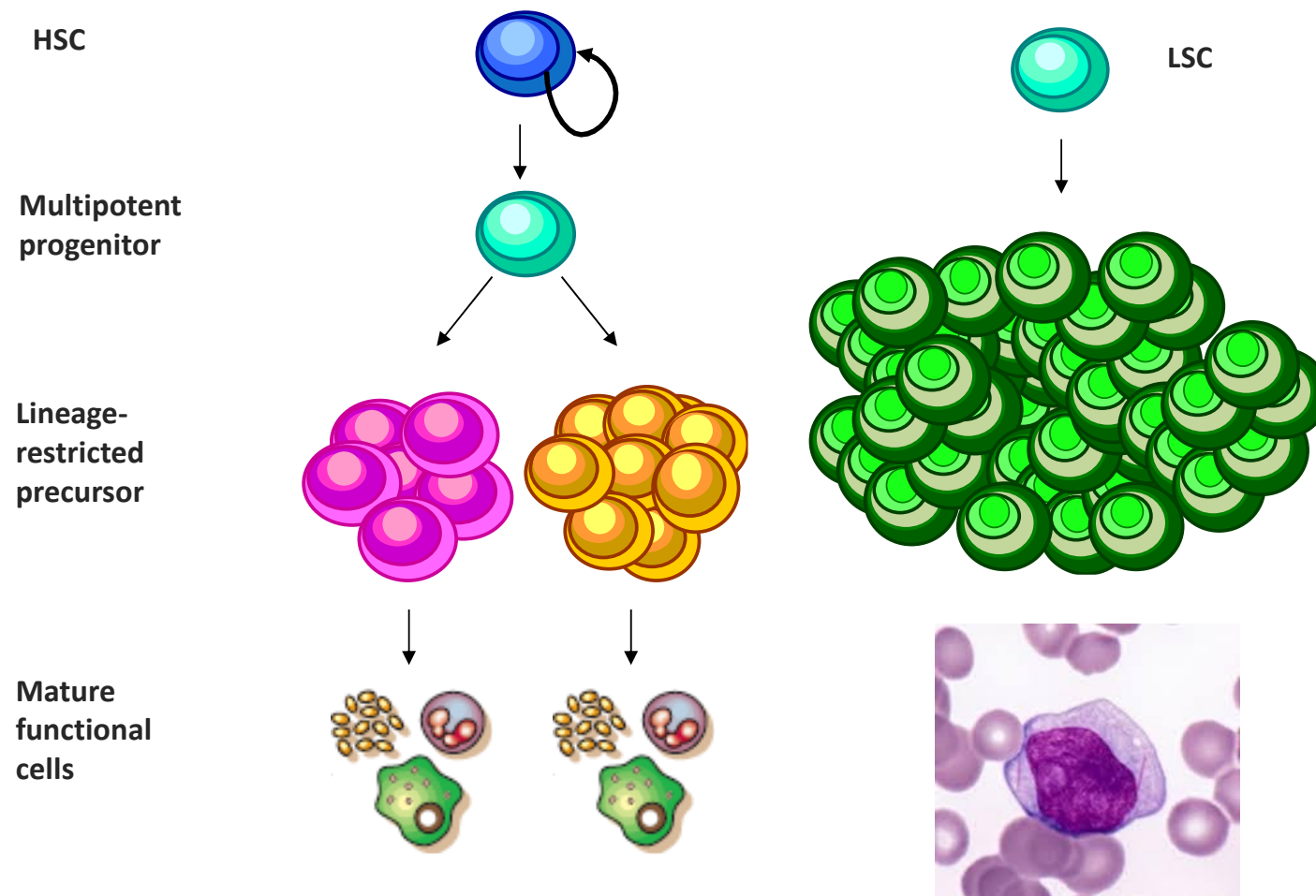
Cellular components of the blood are formed in the bone marrow



Passegué E. et.al. PNAS 2003;100:11842-11849

200,000,000,000 red cells per day
10,000,000,000 white cells per day
400,000,000,000 platelets per day

Acute Myeloid Leukemia



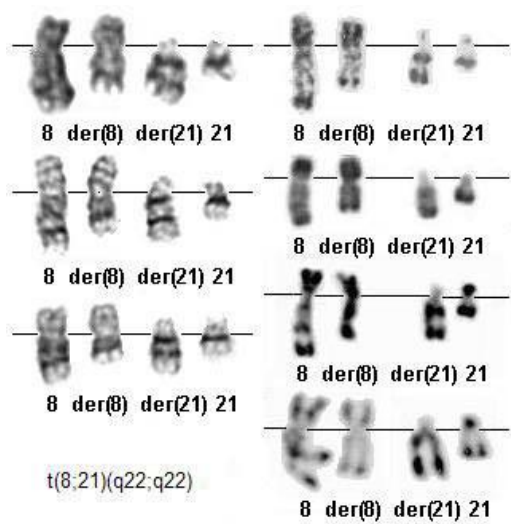
Most common acute leukemia in the adult population

Median age about 68 years

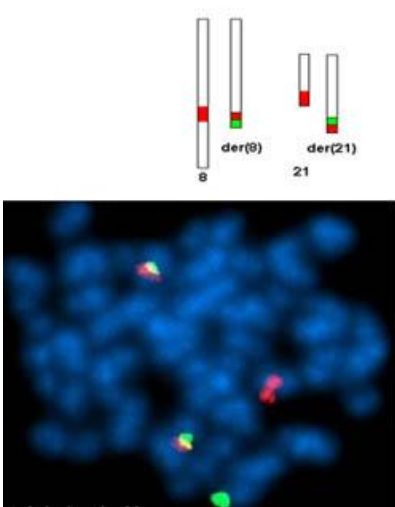
Rare disease, but unfortunately very deadly: less than 30 % of patients survive long-term

AML is not one disease

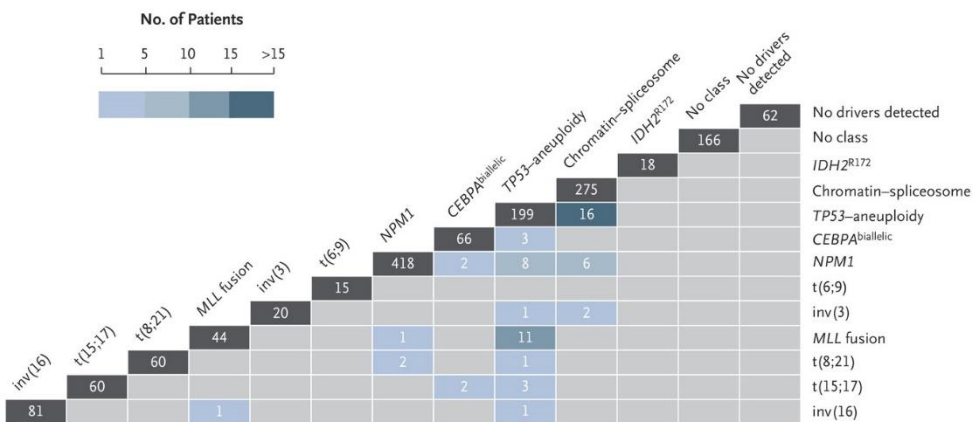
Cytogenetics



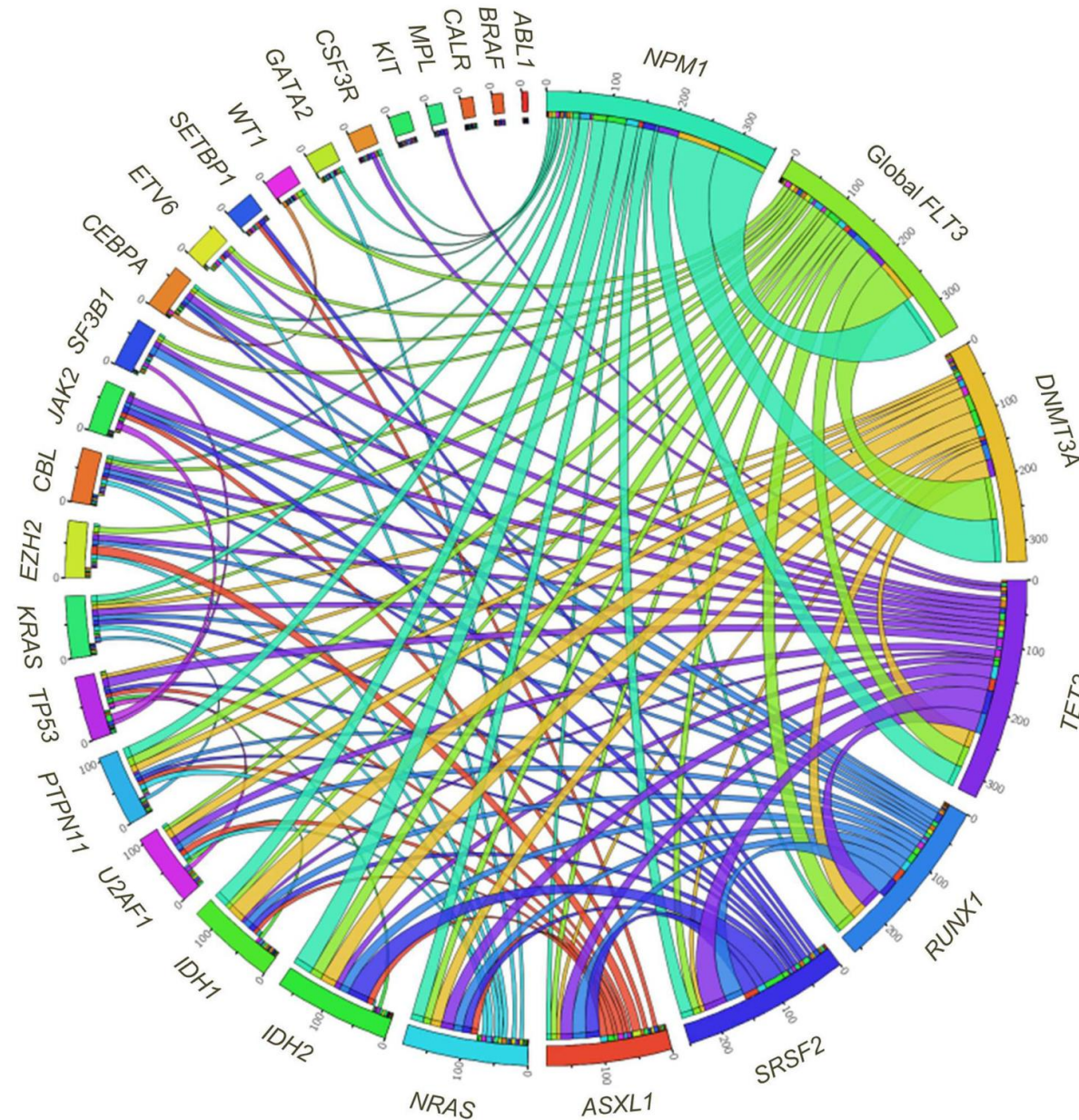
FISH



Molecular Diagnostics PCR NGS



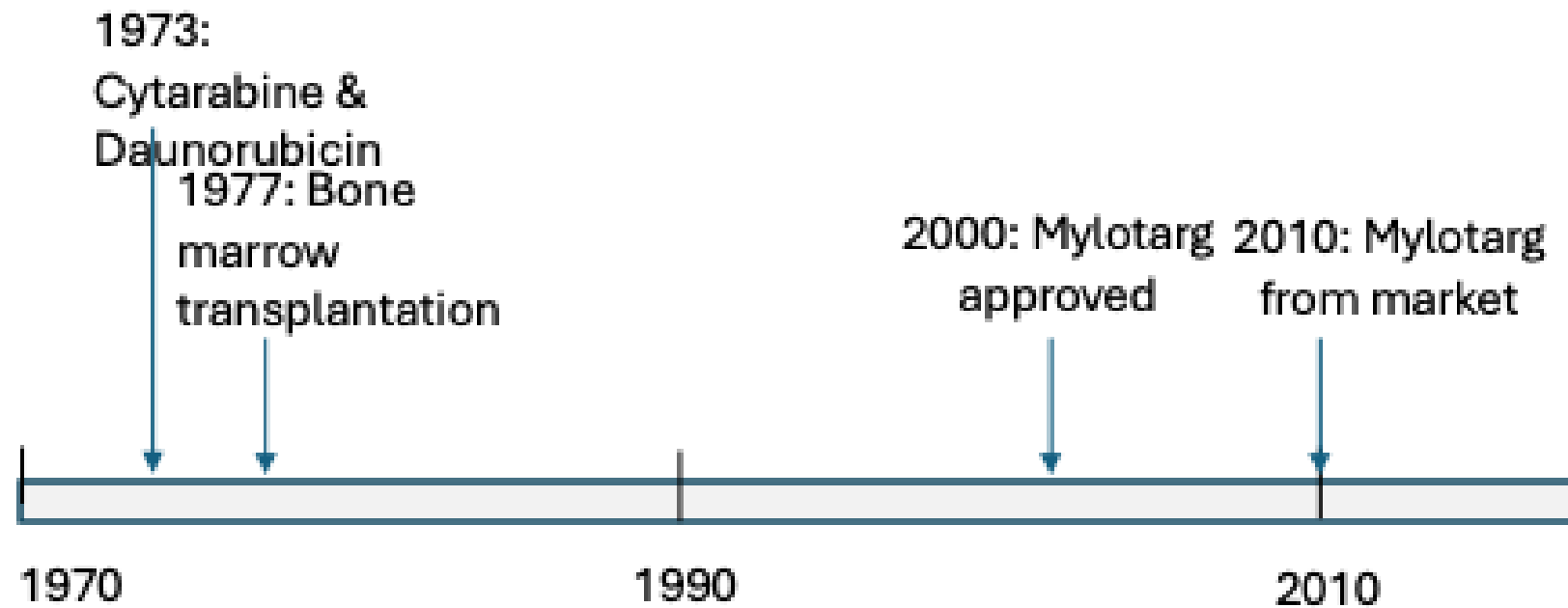
Even one type of blood cancer is many different diseases



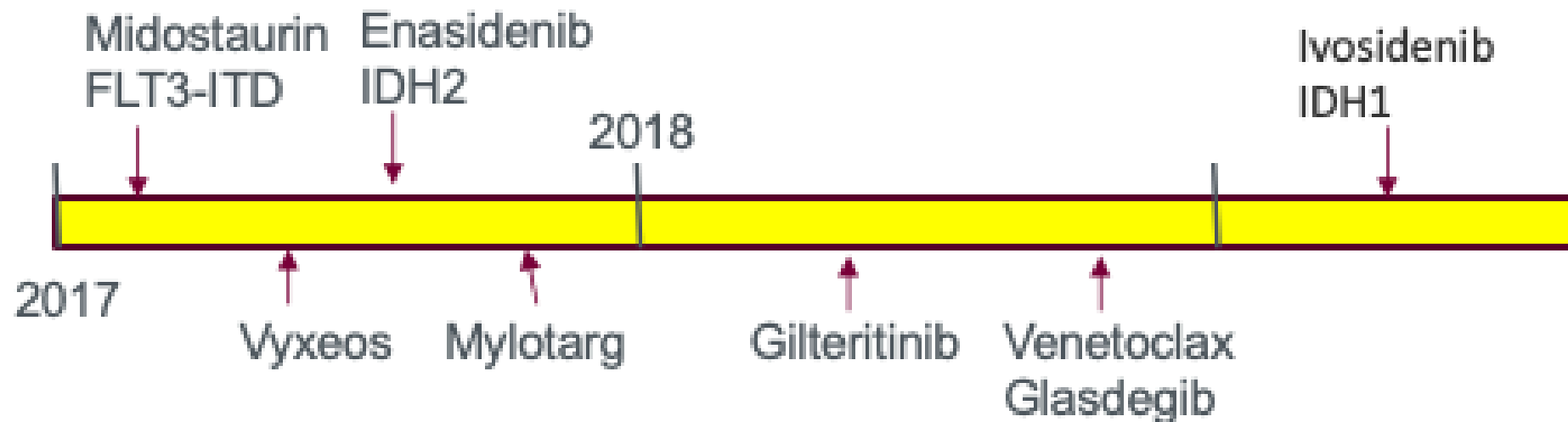
For many years there has been only one treatment in AML

7 + 3

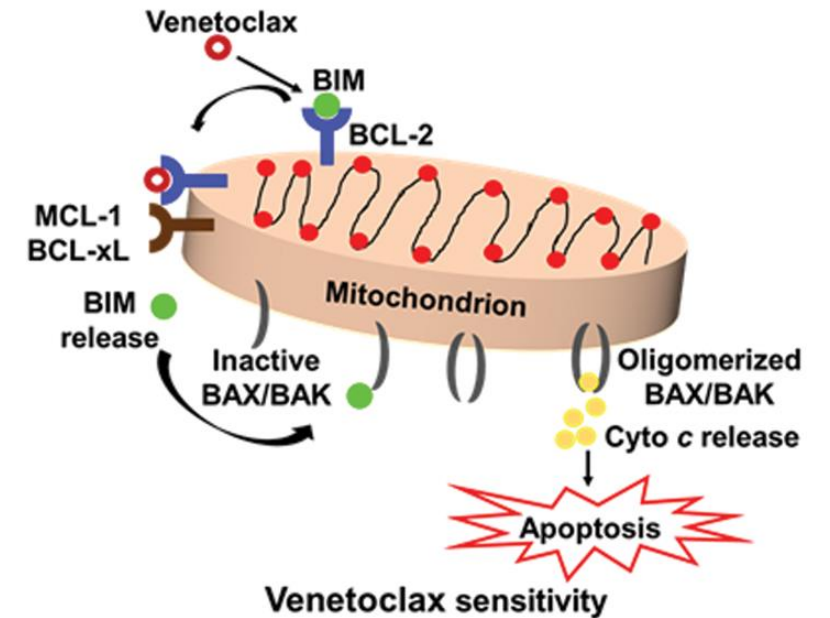
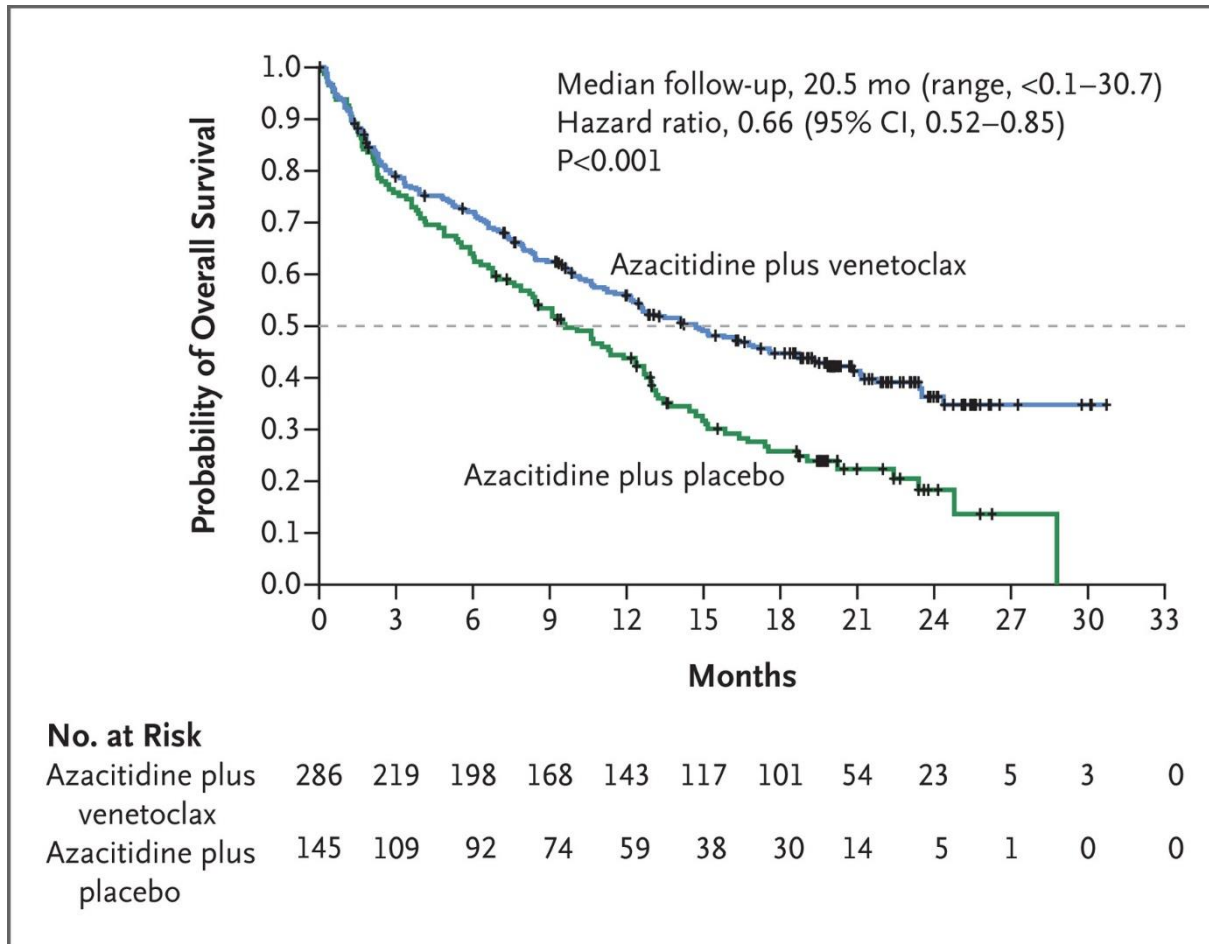
Cytarabine for 7 days
Daunorubicin for 3 days



A stellar phase in AML



Targeted therapies improving the treatment



The **NEW ENGLAND**
JOURNAL of MEDICINE

ESTABLISHED IN 1812

AUGUST 13, 2020

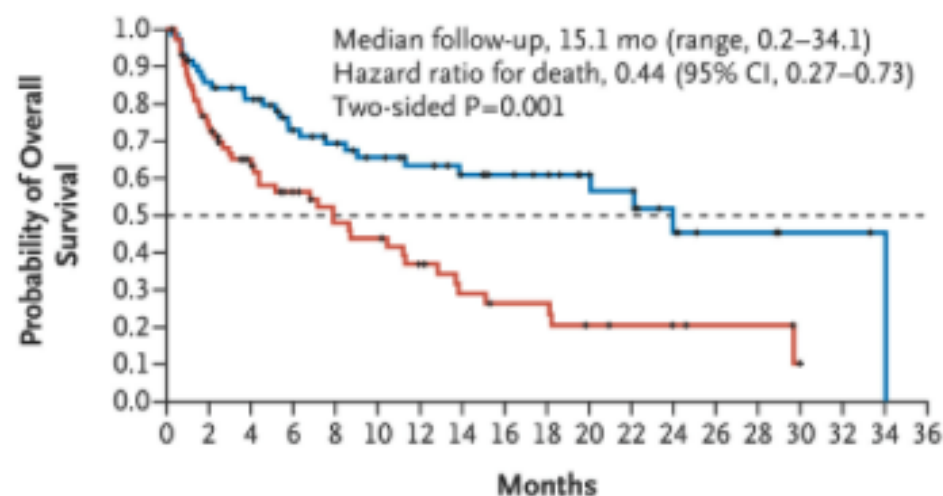
VOL. 383 NO. 7

**Azacitidine and Venetoclax in Previously Untreated
Acute Myeloid Leukemia**

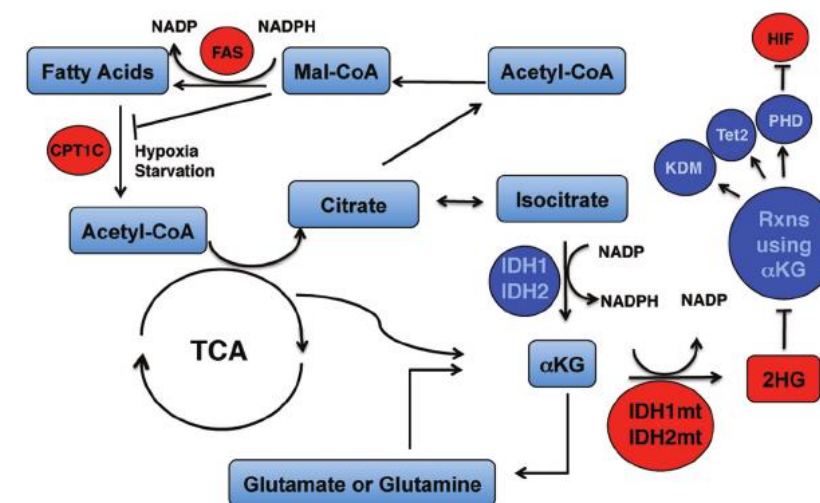
C.D. DiNardo, B.A. Jonas, V. Pullarkat, M.J. Thirman, J.S. Garcia, A.H. Wei, M. Konopleva, H. Döhner, A. Letai, P. Fenaux, E. Koller, V. Havelange, B. Leber, J. Esteve, J. Wang, V. Pejsa, R. Hájek, K. Porkka, Á. Illés, D. Lavie, R.M. Lemoli, K. Yamamoto, S.-S. Yoon, J.-H. Jang, S.-P. Yeh, M. Turgut, W.-J. Hong, Y. Zhou, J. Potluri, and K.W. Pratz

Targeted therapies improving the treatment

B Overall Survival



No. at Risk	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36
Ivosidenib+ azacitidine	72	58	53	42	38	33	29	24	21	19	15	13	7	4	4	2	2	1	
Placebo+ azacitidine	74	53	38	29	23	21	15	11	9	9	6	5	4	3	3	0			



Cold Spring Harbor Symposia on Quantitative Biology
76:299-311

ORIGINAL ARTICLE

Ivosidenib and Azacitidine in *IDH1*-Mutated Acute Myeloid Leukemia

Pau Montesinos, M.D., Ph.D., Christian Recher, M.D., Ph.D., Susana Vives, M.D.,
Ewa Zarzycka, M.D., Jianxiang Wang, M.D., Giambattista Bertani, M.D.,
Michael Heuser, M.D., Rodrigo T. Calado, M.D., Ph.D., Andre C. Schuh, M.D.,
Su-Peng Yeh, M.D., Scott R. Daigle, M.S., Jianan Hui, Ph.D., Shuchi S. Pandya, M.D.,
Diego A. Gianolio, Ph.D., Stephane de Botton, M.D., Ph.D., and Hartmut Döhner, M.D.

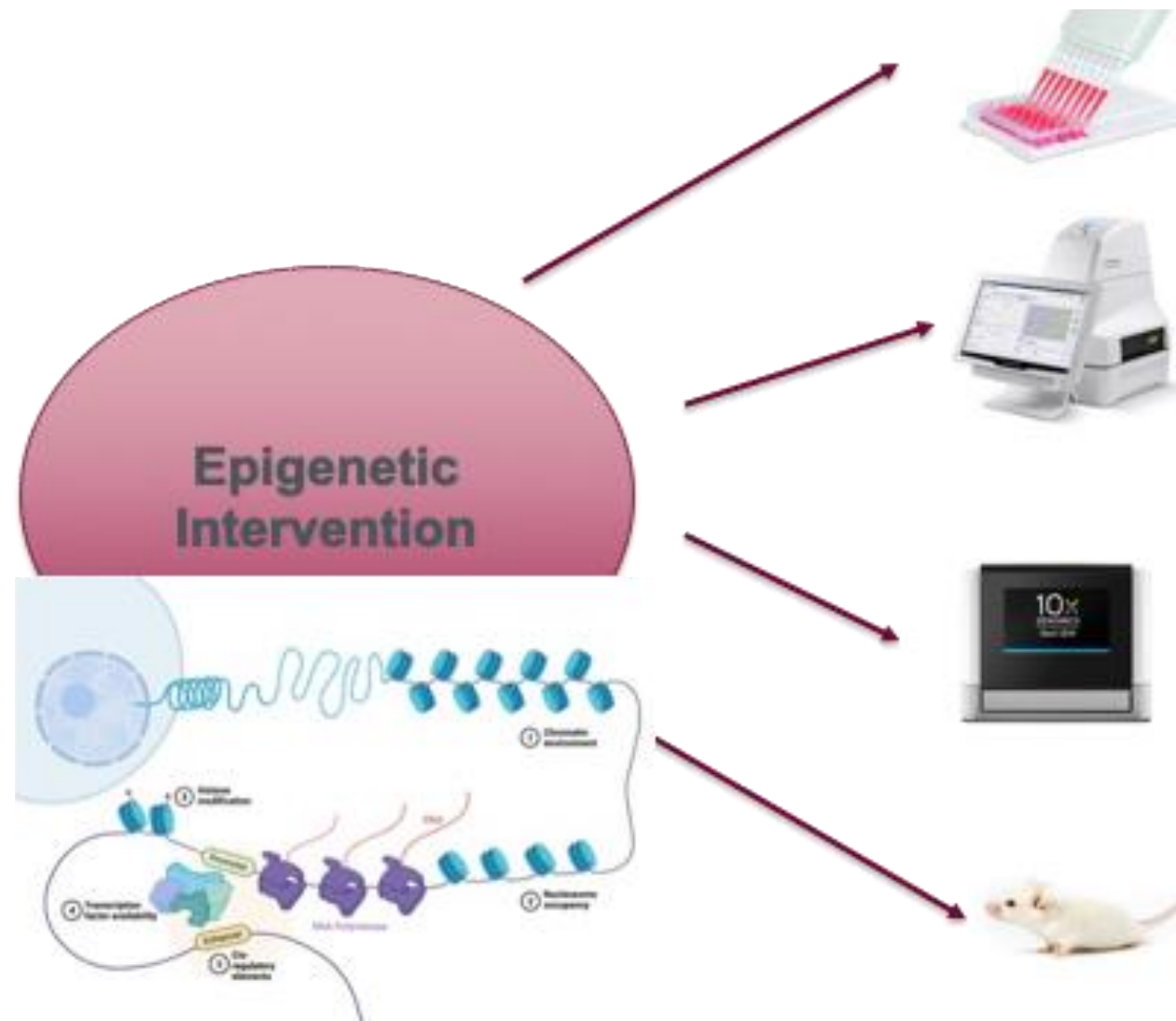
Our Research Approach

Primary Patient Material

*Live Cell Banking for
hematological malignancies
HHS McMaster Cancer
Research Stem Cell Bank*

*50 – 60 patients per year
Total > 100 AML samples*

Functional human and murine model systems



*In vitro
Screening*

*Functional
Metabolic
Profiling*

*Multiomic
Profiling*

*In vivo
Modeling*

67 year-old patient AML

Normal karyotype

NPM1 type A

FLT3-ITD+

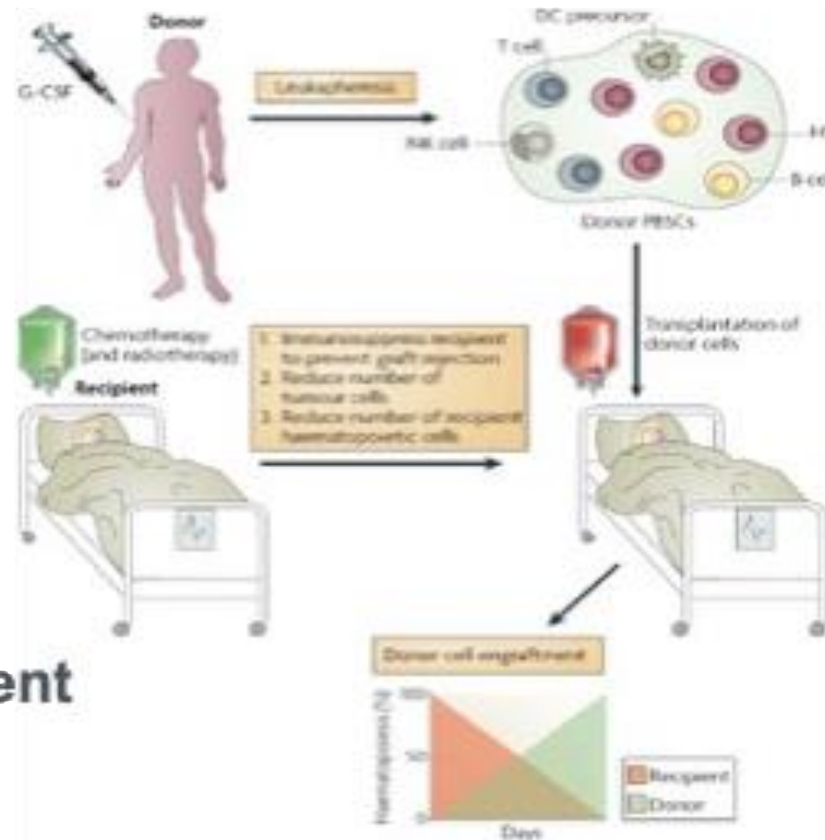
What should
we do?

- Induction with 7+3+ Midostaurin
- Disease persistence (PR)
- Received Azacitidine + Venetoclax
- CR with persistent MRD

A cure for many...

Stem Cell Transplantation

Stem Cell
Mobilization



Transplant
Stem Cells
Immune Cells

2-4 weeks wait until
new blood cells are made

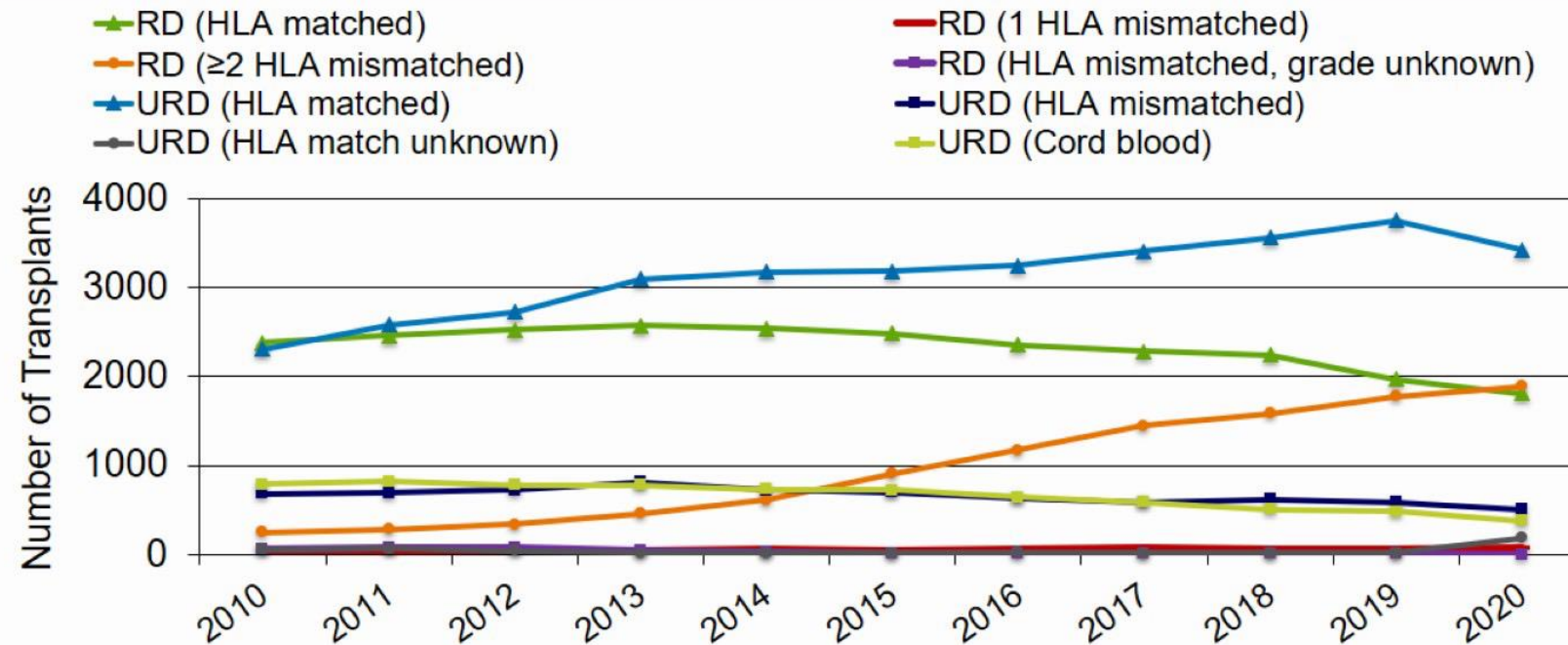
Most effective treatment
for AML

Shlomchik – Nat Rev Immunol, 2007

Who can be a donor?

- Matched related donor = Siblings
- Matched unrelated donors
- Haploidentical donors = Other siblings, kids, parents

Number of Allogeneic HCTs in the US by Donor Type



Who can get a transplant?



No strict age limit...

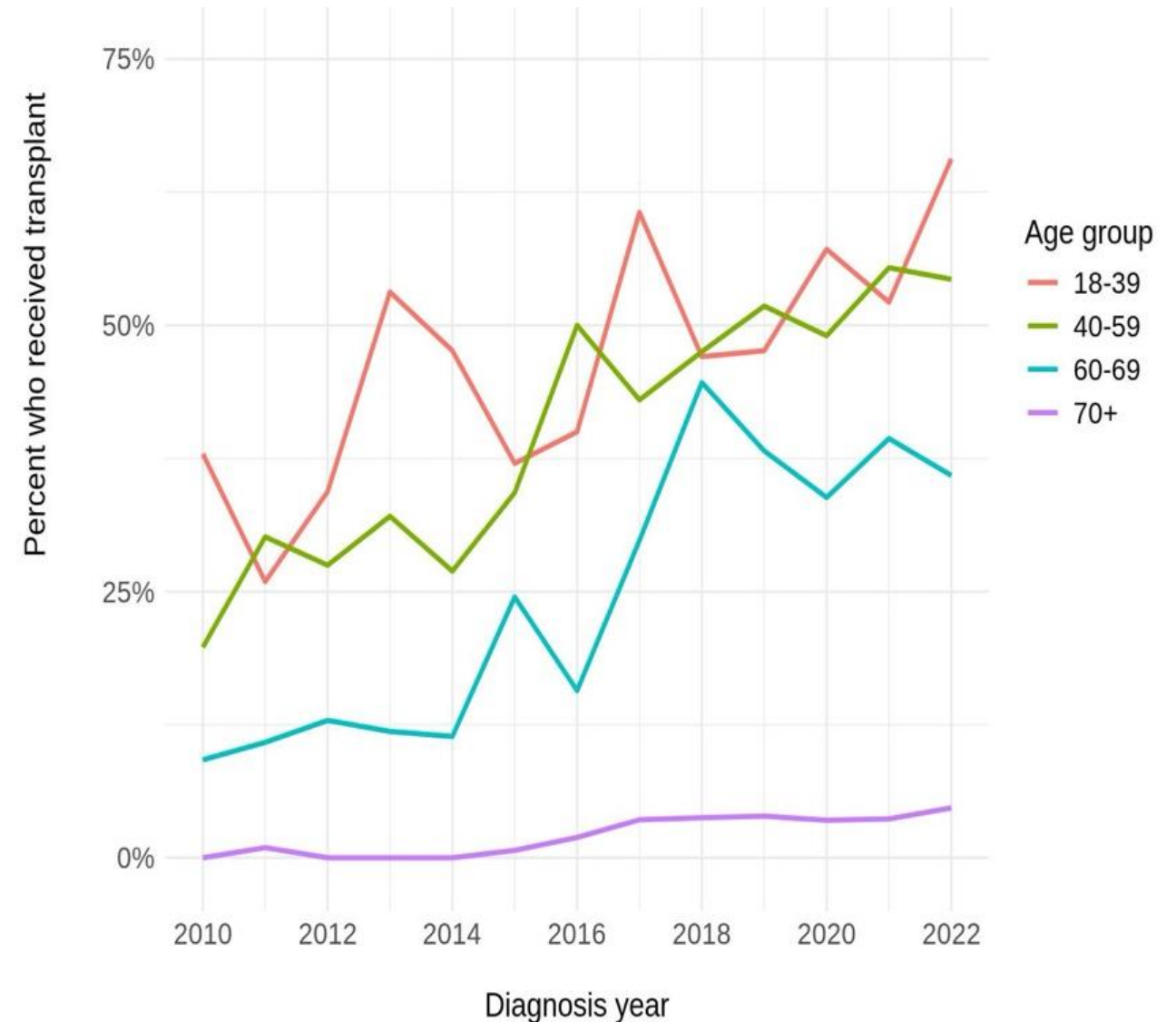
”Biological Age less than 75...”

**Because:
Comorbidities
are important!**

How many patients with AML get a transplant?

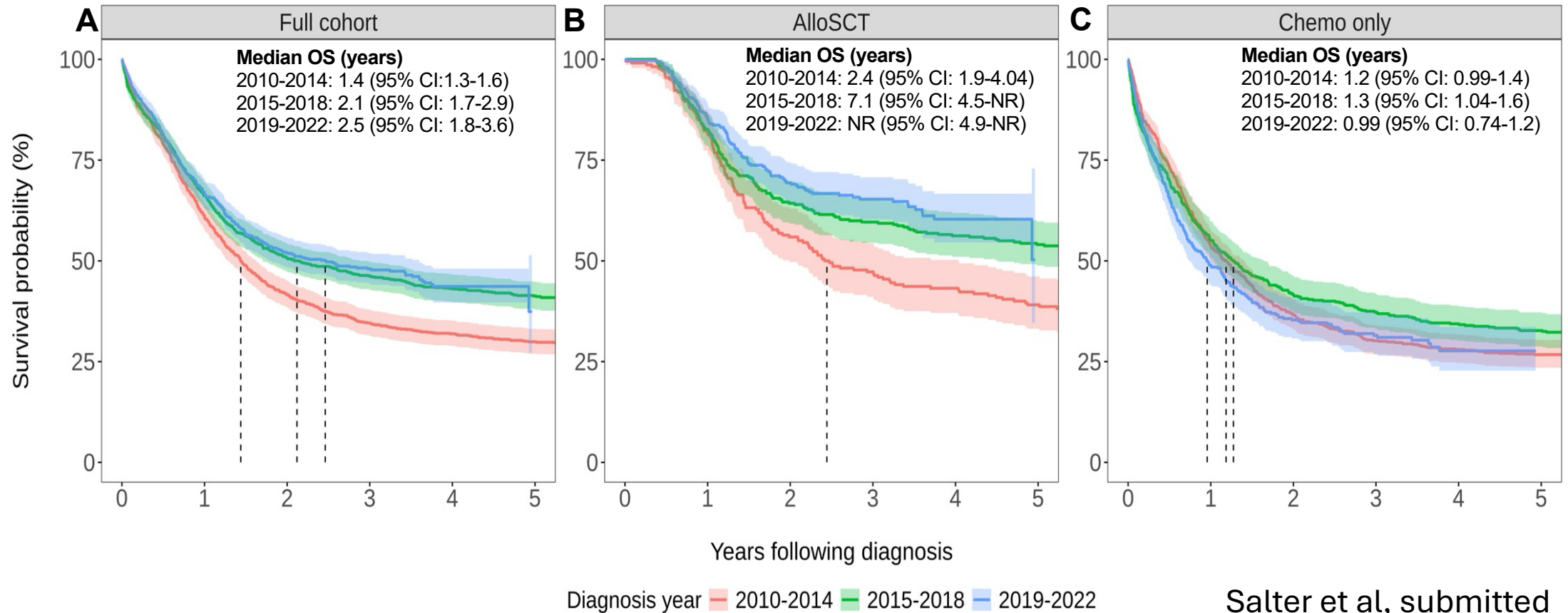


Laura Hillier, 2016
From CBC Global News



Salter et al, submitted

Transplant has become better over time

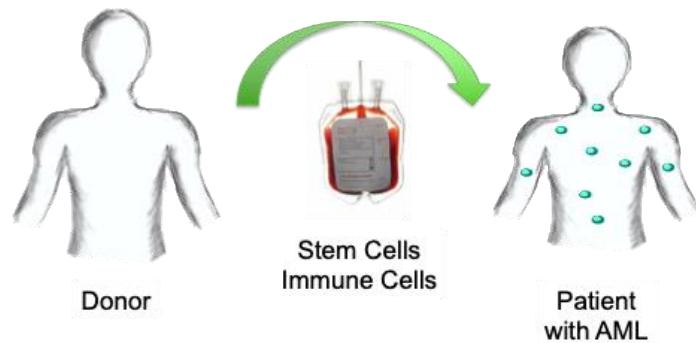


More and better
matching donors

Better transplant
protocols

Better supportive
therapies

Problems after transplant



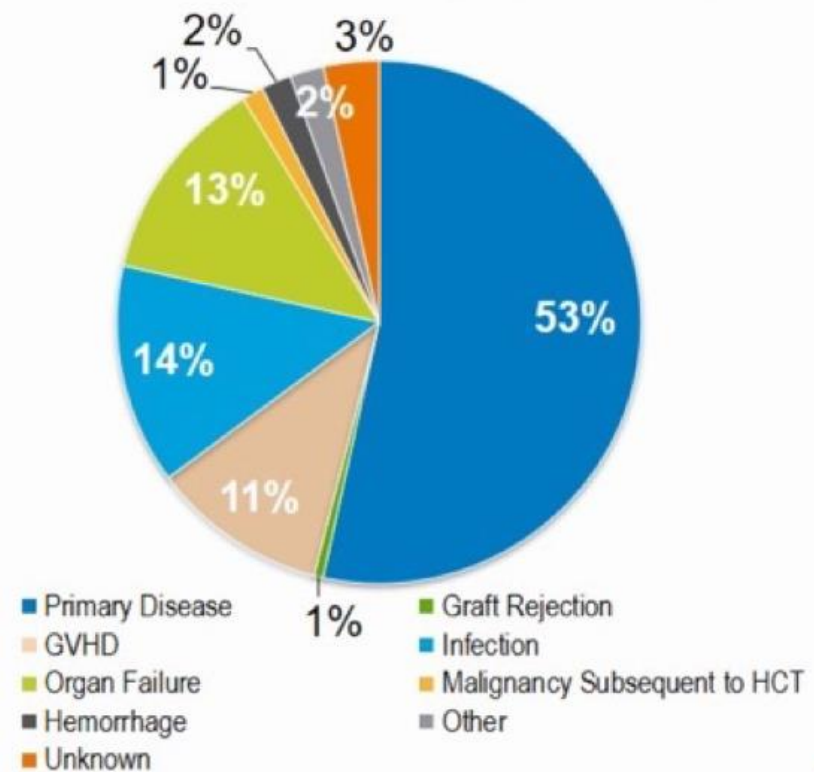
Problems after allogeneic stem cell transplantation

- Relapse
- GVHD

NEED:

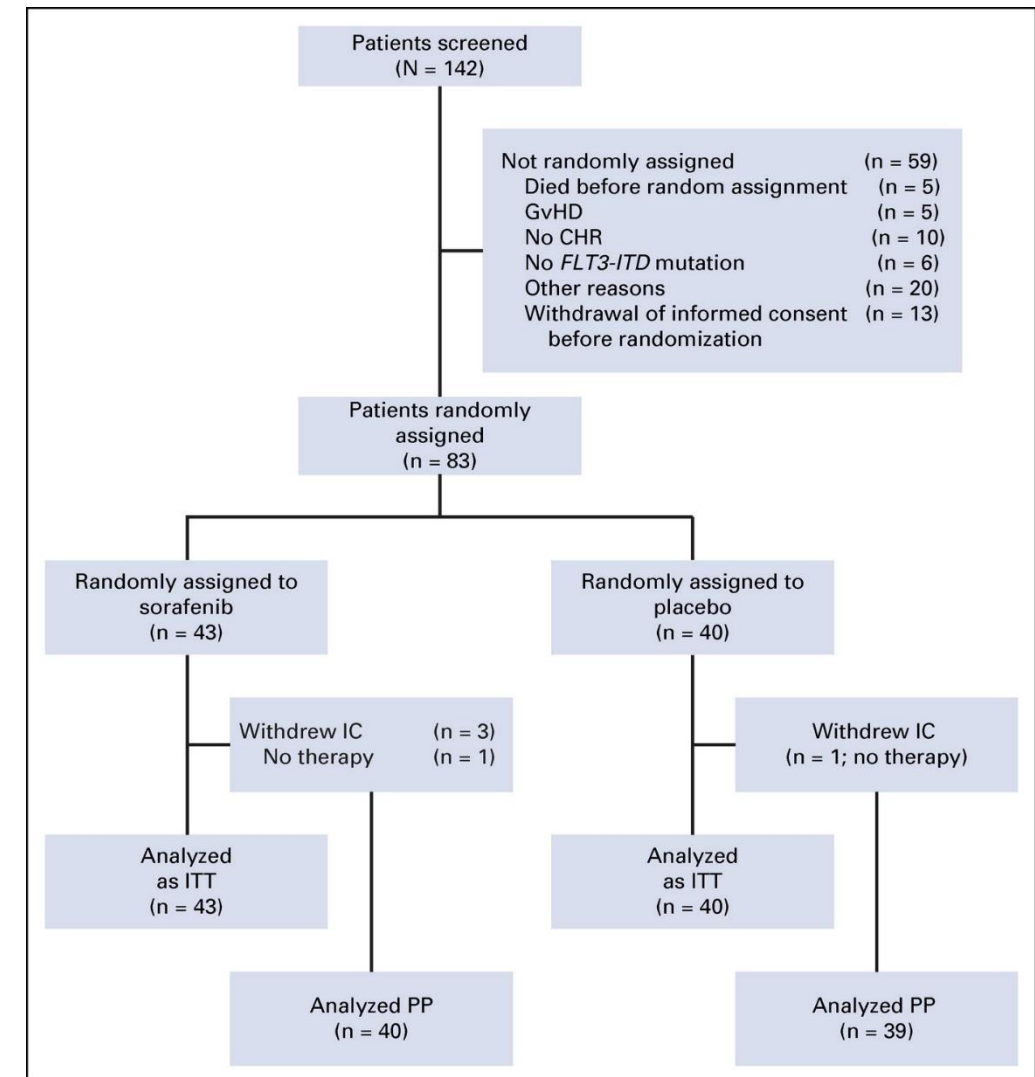
Strategies that favor GVL over GVHD!

Died at or beyond 100 days post-transplant*

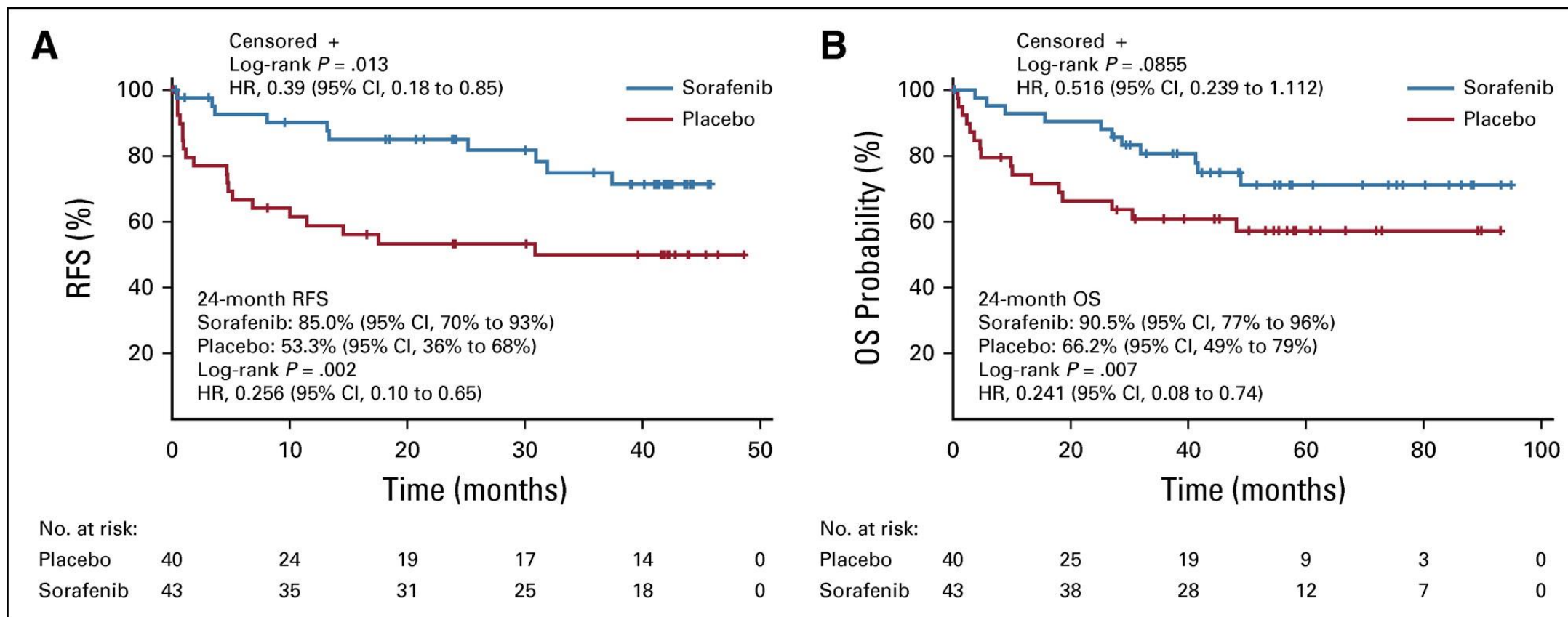


Sorafenib Maintenance After Allogeneic Hematopoietic Stem Cell Transplantation for Acute Myeloid Leukemia With *FLT3*–Internal Tandem Duplication Mutation (SORMAIN)

Andreas Burchert, MD¹; Gesine Bug, MD²; Lea V. Fritz, MSc¹; Jürgen Finke, MD³; Matthias Stelljes, MD⁴; Christoph Röhlig, MD, MSc⁵; Ellen Wollmer, MD¹; Ralph Wäsch, MD³; Martin Bornhäuser, MD⁵; Tobias Berg, MD²; Fabian Lang, MD²; Gerhard Ehninger, MD⁵; Hubert Serve, MD²; Robert Zeiser, MD³; Eva-Maria Wagner, MD⁶; Nicolaus Kröger, MD⁷; Christine Wolschke, MD⁷; Michael Schleuning, MD⁸; Katharina S. Götze, MD⁹; Christoph Schmid, MD¹⁰; Martina Cysandt, MD¹¹; Eva Eßeling, MD⁴; Dominik Wolf, MD¹²; Ying Wang, MD¹; Alexandra Böhm, MD¹³; Christian Thiede, MD⁵; Torsten Haferlach, MD¹⁴; Christian Michel, MD¹; Wolfgang Bethge, MD¹⁵; Thomas Wündisch, MD¹; Christian Brandts, MD²; Susanne Harnisch, DiplHumanbiol¹⁶; Michael Wittenberg, PhD¹⁶; Heinz-Gert Hoeffkes, MD¹⁷; Susanne Rospleszcz, PhD¹⁸; Alexander Burchardt, MD¹⁹; Andreas Neubauer, MD¹; Markus Brugger, DiplHumanbiol, MSc²⁰; Konstantin Strauch, PhD^{20,21}; Carmen Schade-Brittinger¹⁶; and Stephan K. Metzelder, MD¹



Burchert et al, 2020



Burchert et al, 2020

Patient was started on
Sorafenib Maintenance

Ongoing **molecular CR**

- Mild hypertension
- Hand-Foot syndrome



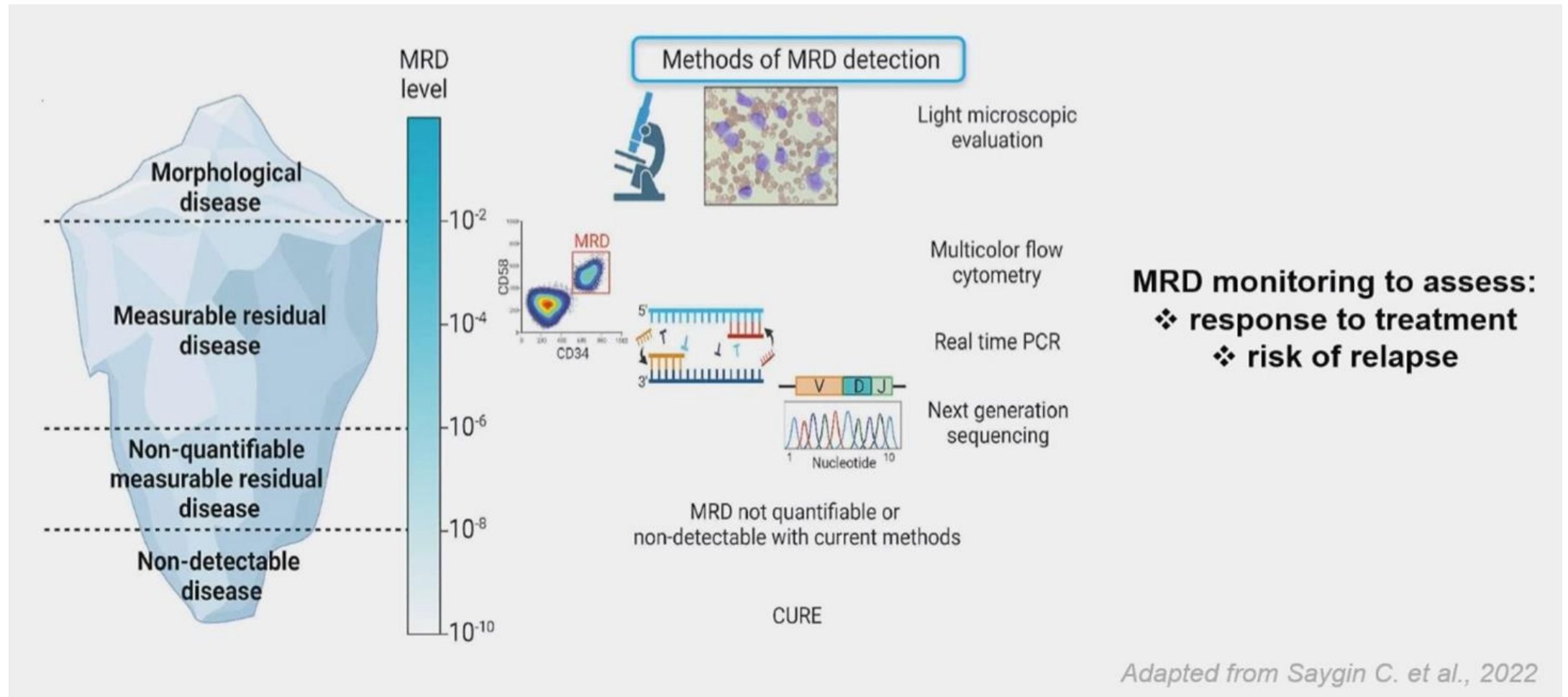
**Can we find out early if
something starts to go wrong?**

MRD = Minimal Residual Disease

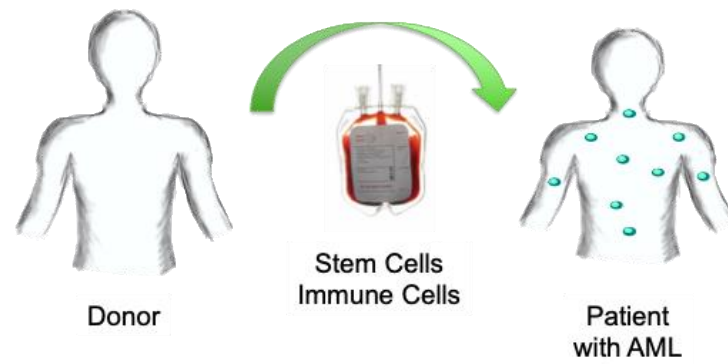


Can we find out early if something starts to go wrong?

MRD = Minimal Measurable Residual Disease



Can we find out early if something starts to go wrong?

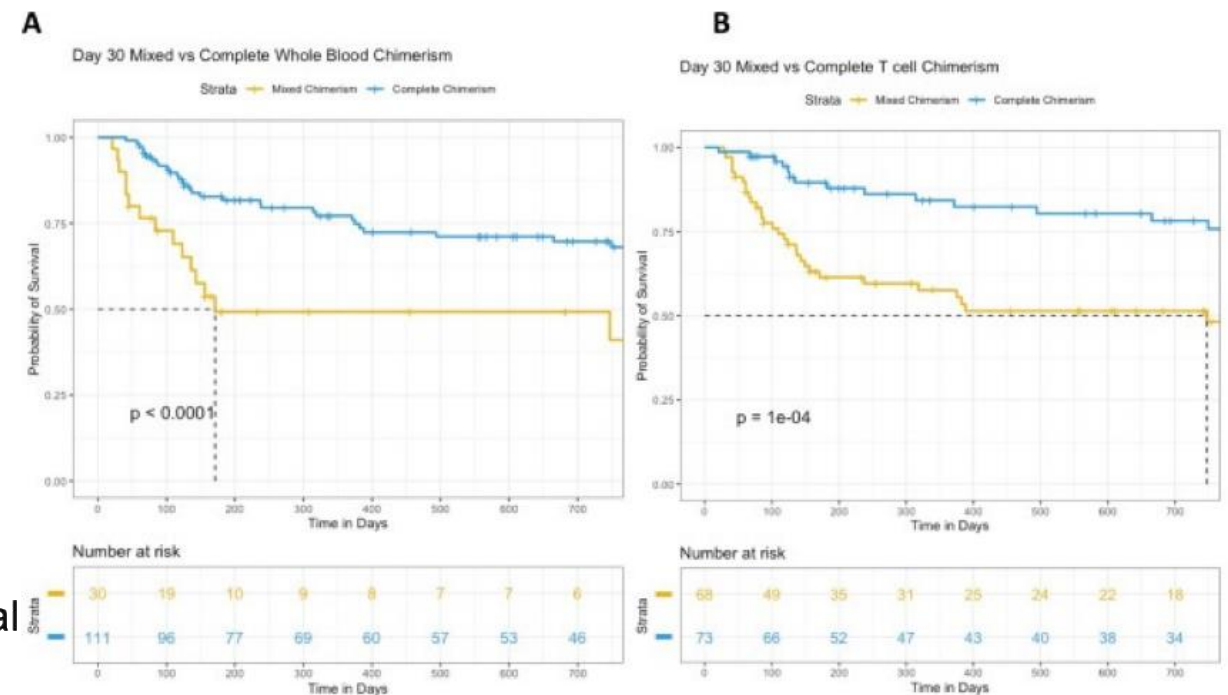


Chimerism Analysis:

- Investigate how many cells are derived from donor?
- Complete Chimerism: all cells from donor
- Mixed Chimerism: significant fraction of residual recipient cells

Early Mixed Donor Chimerism is a Strong Negative Prognostic Indicator in Allogeneic Stem Cell Transplant for AML and MDS

Michael Radford^{1,*}, Alejandro Garcia-Horton¹, Rohail Badami², Elaine Jin³, Nida Usmani⁴, Daria Grafodatskaya^{5,6}, Elizabeth McCready^{5,6}, Dina Khalaf¹, Irwin Walker³, Brian Leber³, Kylie Lepic¹, Gregory Pond^{1,7}, Tobias Berg^{1,7,8}



What do we do if we find something?

“Ordering a diagnostic test is like picking your nose in public. You must first consider what you will do if you find something.”

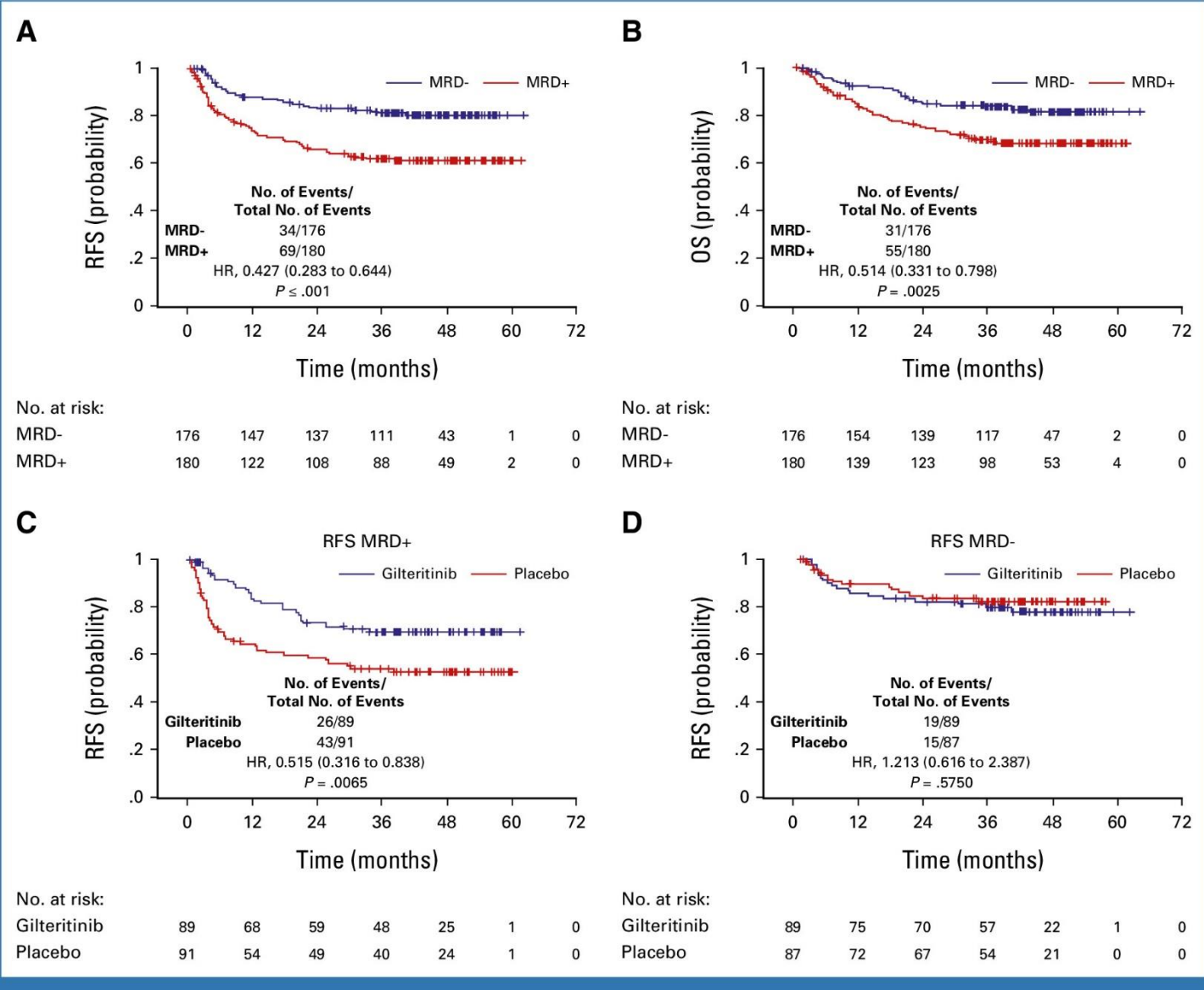
Catherine D. DeAngelis, MD, MPH
Pediatrician and Editor-in-chief of
the *Journal of the American Medical Association* (JAMA)



From Wikipedia, the free encyclopedia

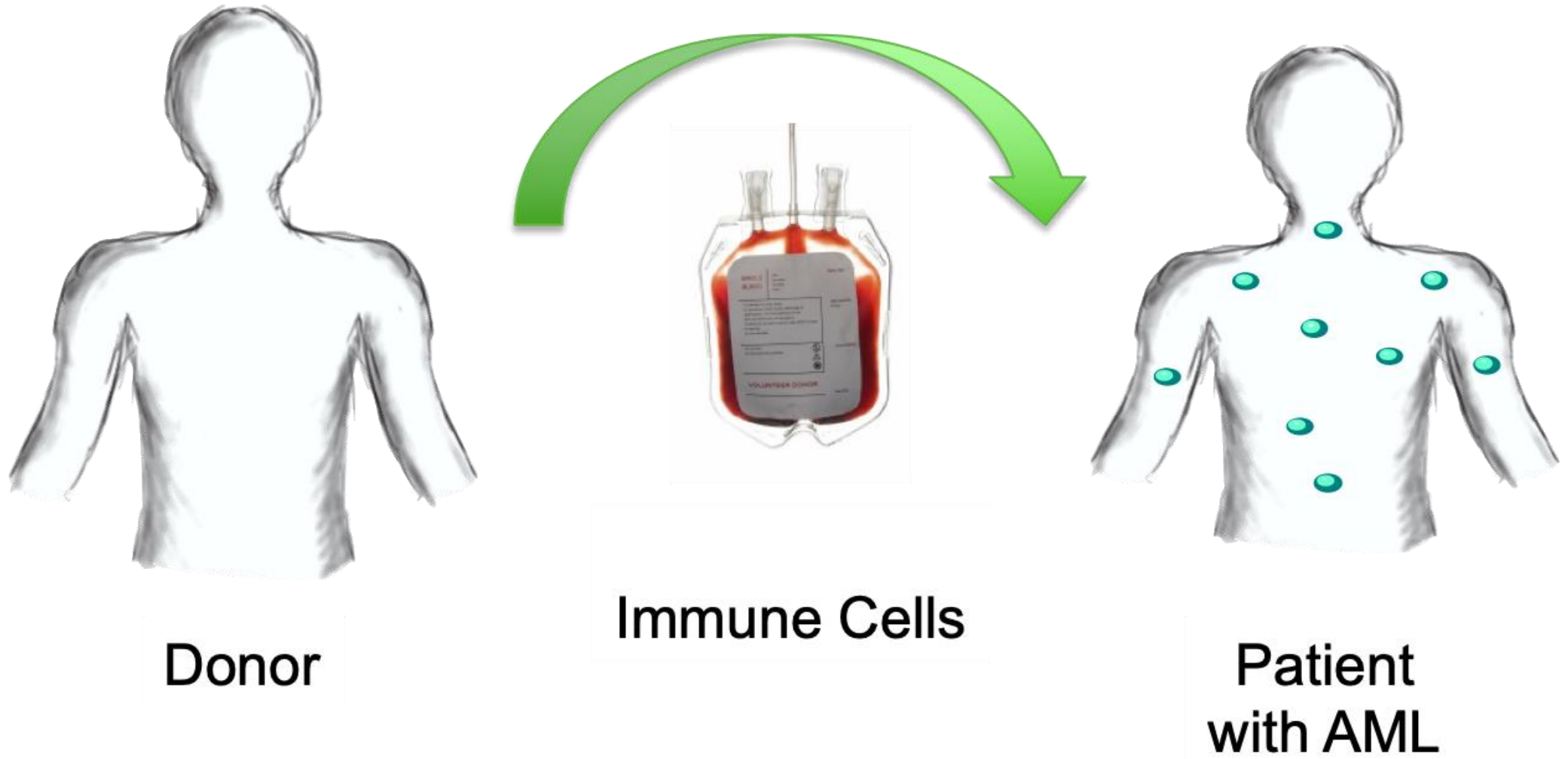
Maintenance treatment

Gilteritinib as Post Transplant Maintenance – BMT-CTN 1506 MORPHO Study



<https://www.cambridgebutterfly.com/the-famous-blue-morpho/>

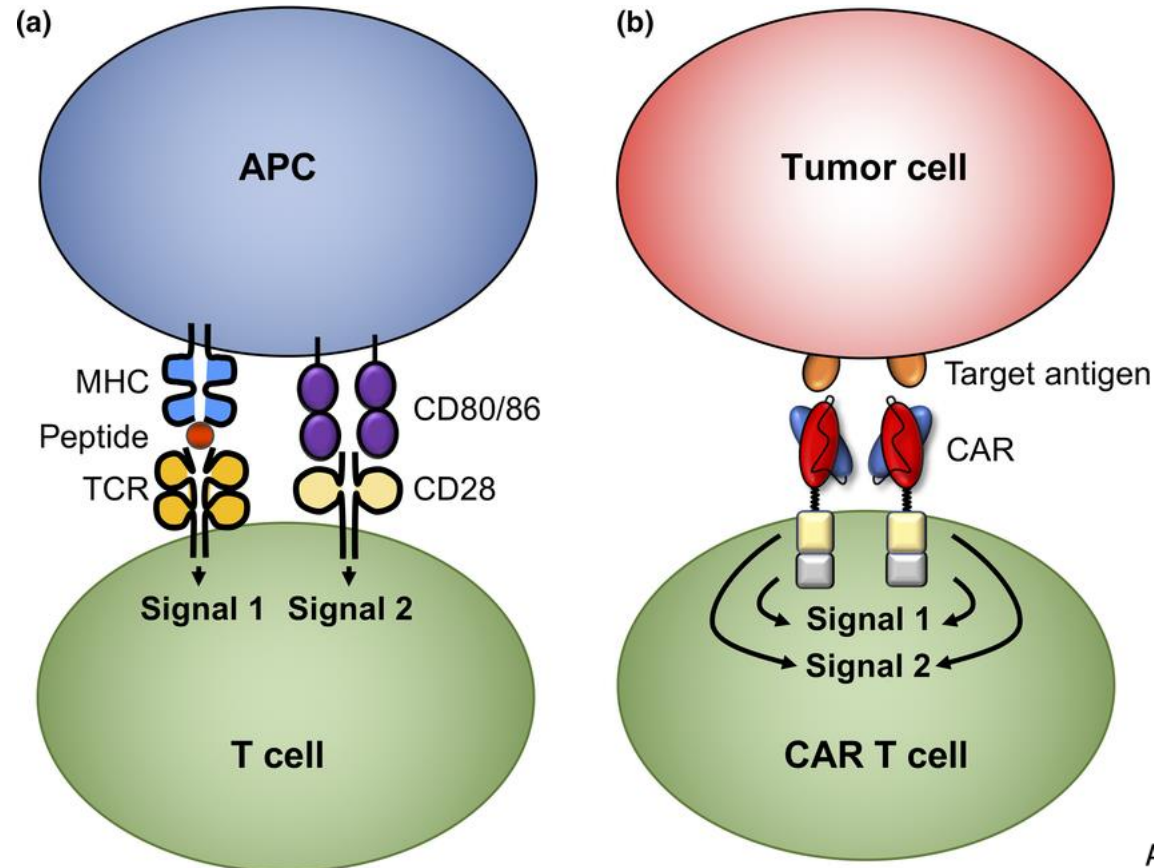
Donor lymphocyte infusion



**Can we use immune cells
without the risk for GVHD?**

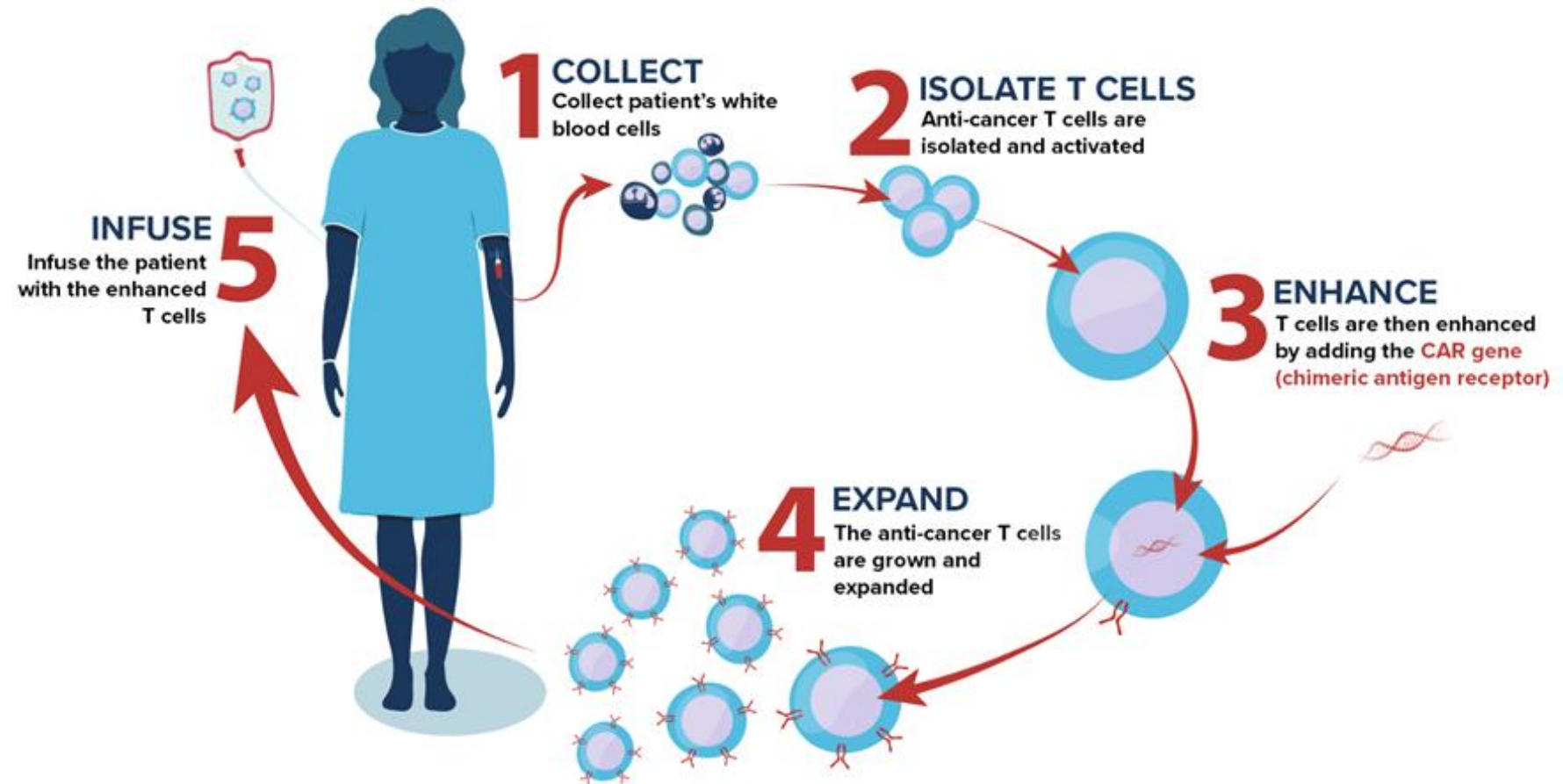


CAR T has been made possible by a deep understanding of the immune system...



T cell receptor signaling

...and gene therapy



Remarkably successful...

Emily Whitehead was diagnosed with acute lymphoblastic leukemia (ALL) in May 2010 when she was five years old.

Incredibly, the T-cell therapy worked, and Emily has remained cancer-free.



<https://emilywhiteheadfoundation.org/our-journey/>

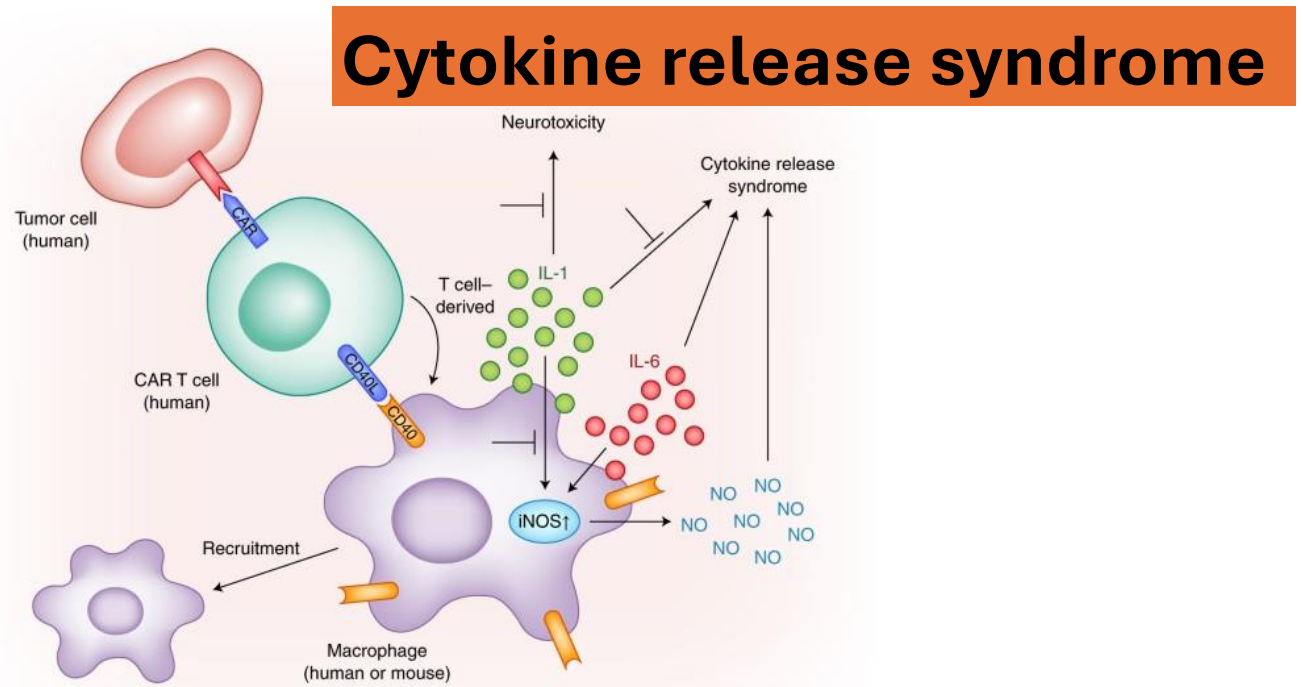
Carl June



Stephan Grupp



... but not free of side effects



Nature Medicine volume 24, pages 705–706 (2018)



Which diseases can we treat with CAR-T cell therapy

• B cell ALL	tisagenlecleucel	2018
• B cell lymphoma	axicabtagene ciloleucel	2019
• Multiple Myeloma	ciltacabtagene autoleucel	2024

Maybe also AML? In the future ...


The future of blood cancer treatment is now

- Targeted therapies are selected based on genetic mutations and drug sensitivity testing
- Use of MRD testing to decide about treatment and employ intervening strategies
- Engineering of more and more sophisticated cellular therapies to improve outcomes of even very difficult-to-treat leukemias and lymphomas

The Intersection of Medical Innovation, Mental Health and Quality of Life



LEUKEMIA &
LYMPHOMA
SOCIETY OF
CANADA



Mental Health in the Era of Medical Innovation

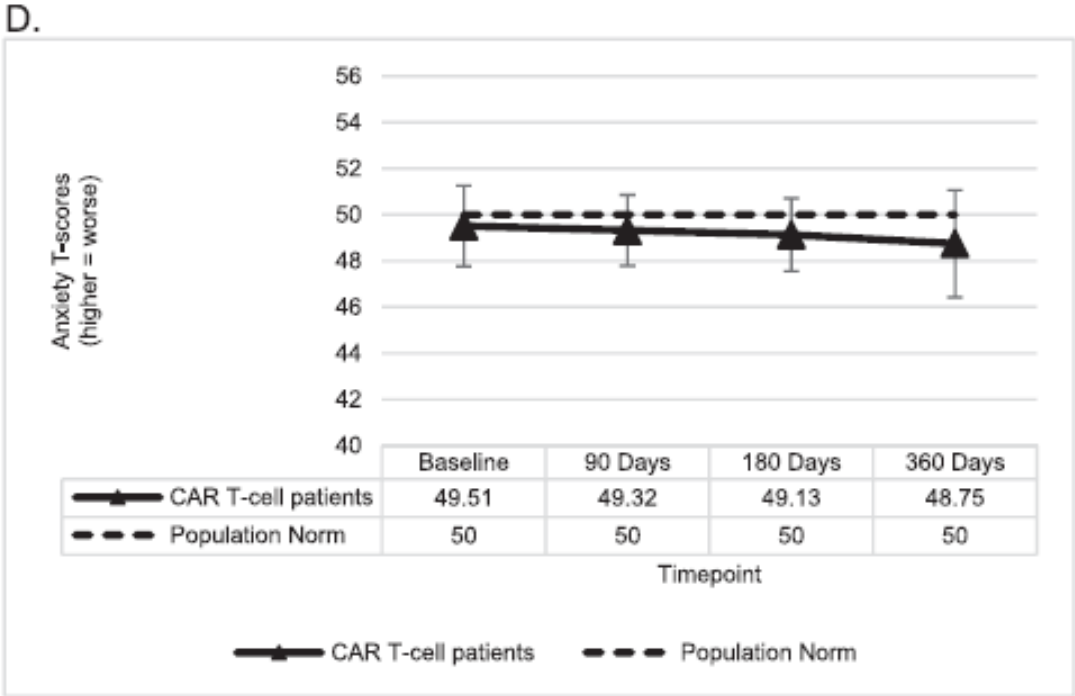
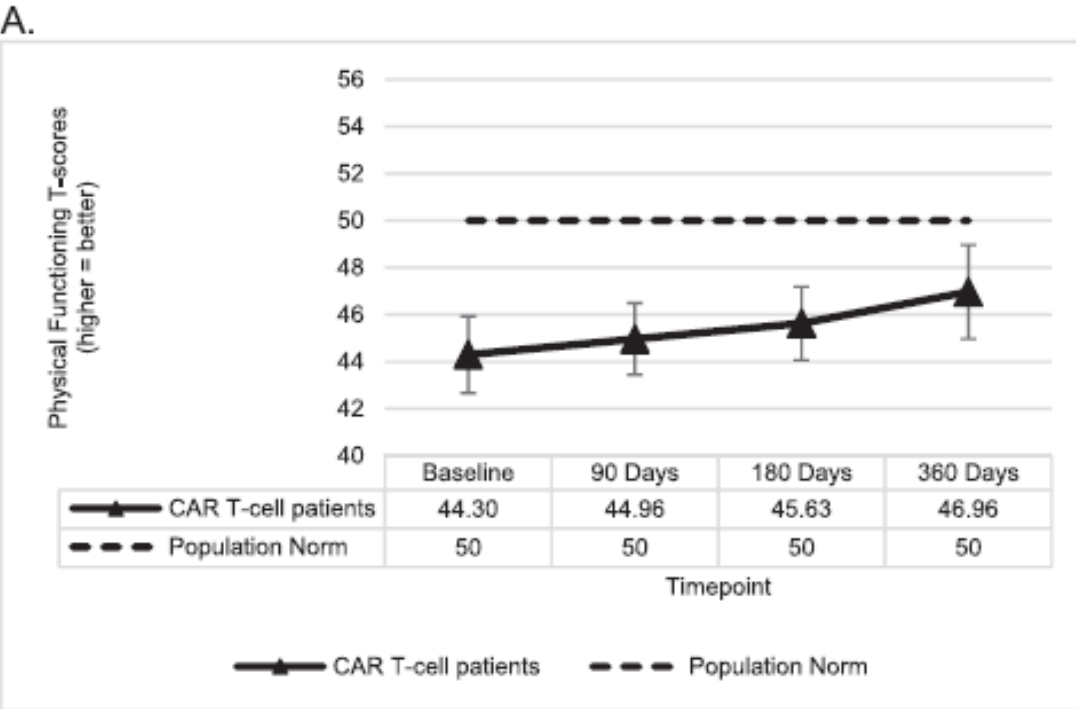


LEUKEMIA &
LYMPHOMA
SOCIETY OF
CANADA

Quality of Life

- QoL is more than “being alive” — it’s about how we live
- New therapies may reduce physical side effects — but can still have physical impacts, such as:
 - Disrupt sleep, appetite, concentration
 - Require long-term monitoring or lifestyle change
- Emotional and social dimensions of QoL:
 - Impact on work, identity, relationships, finances
 - Family caregiver stress

During the first year after CAR T-Cell therapy, Quality of Life improves or remains similar to pre-CAR T-Cell therapy levels

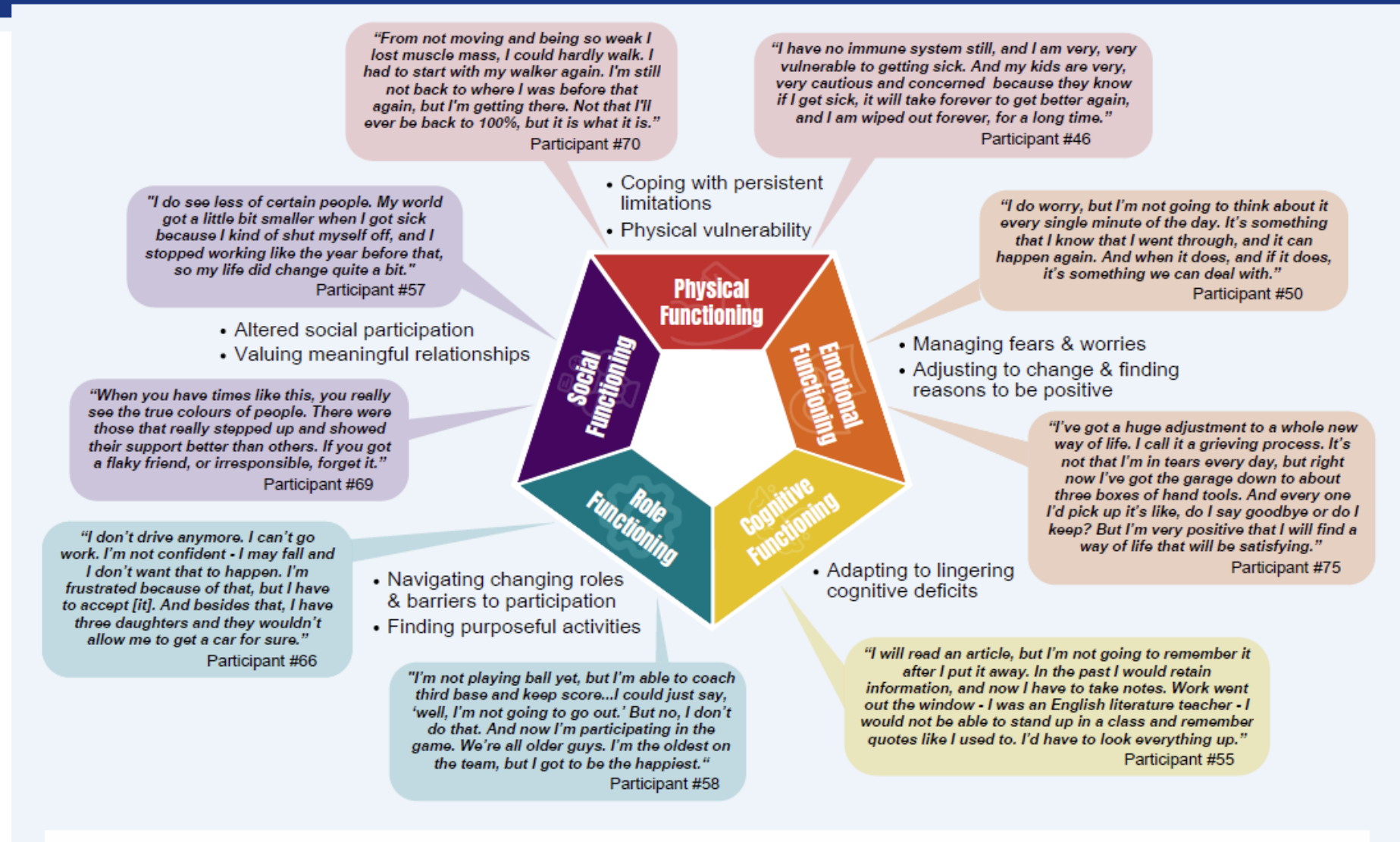


“Qualitative methods are needed to understand patient experience”

An Interpretive Description of Quality of Life After Treatment of Relapsed & Refractory B-Cell Lymphoma

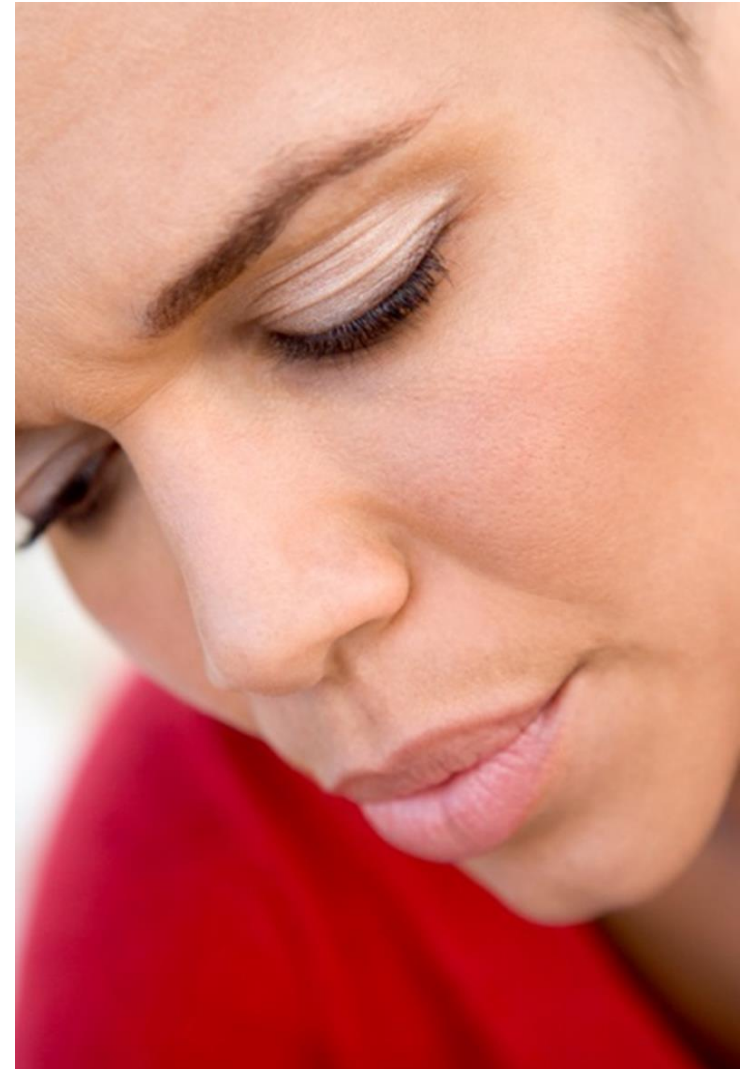
Samantha Mayo^{1,2} Jeus Cabaluna³ Stacey Morrison¹ Shanelle Racine¹ Medha Surajpal¹ Anca Prica^{1,2} John Kuruvilla^{1,2}

1 Princess Margaret Cancer Centre, Toronto, Canada; 2 University of Toronto, Toronto, Canada; 3 University Health Network, Toronto, Canada

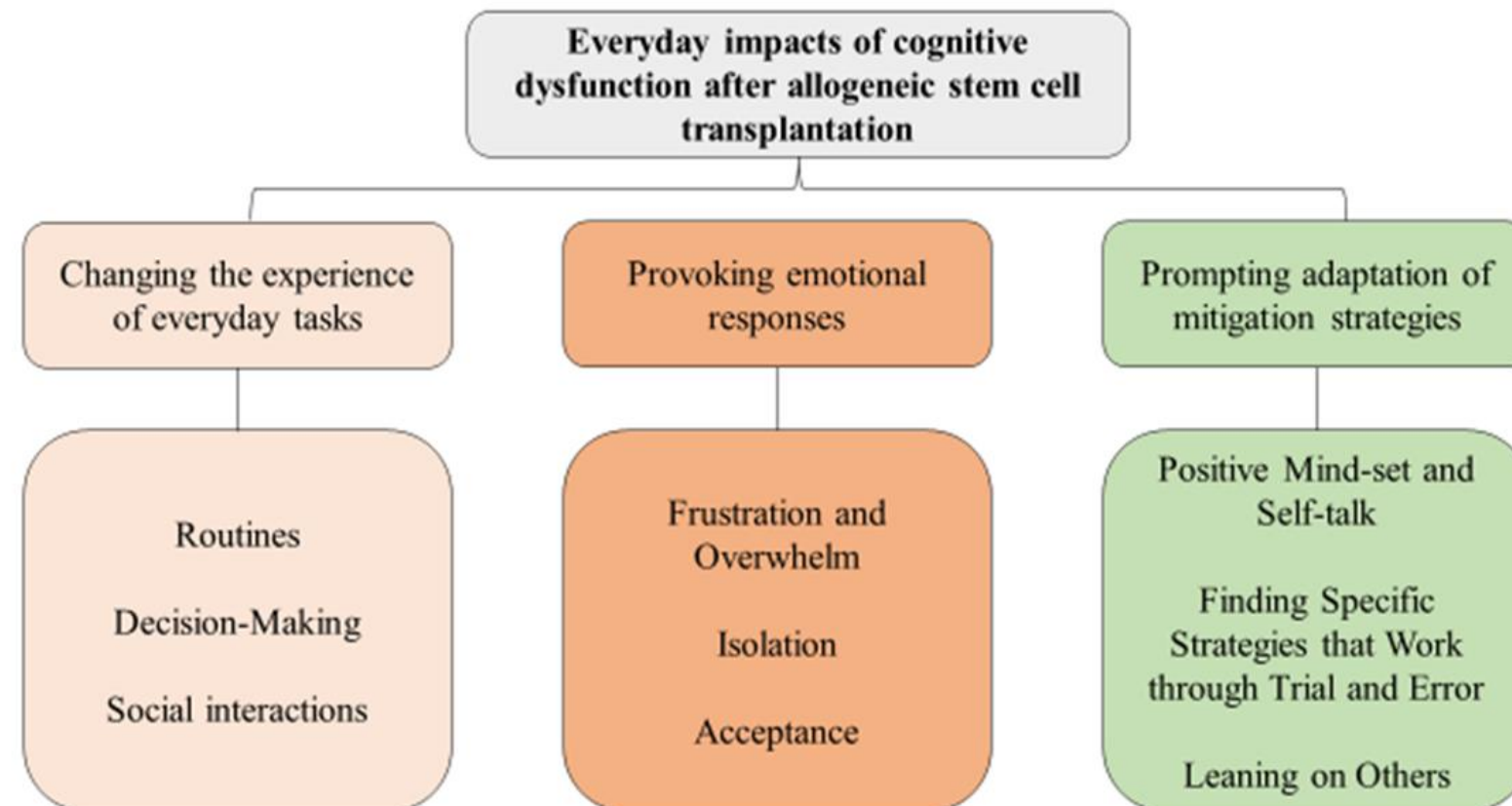


Cancer-Related Cognitive Impairment

- Decreased short-term memory
- Difficulty finding the right words
- Trouble paying attention or concentrating
- Feeling disorganized
- Taking longer to do tasks
- Feeling “foggy”



Everyday Impacts of Cognitive Difficulties



“The way I best described it was it’s like a pencil. You can still write with a pencil, but it just wasn’t quite as sharp. So, I was able to get the things done, but just not with the precision that I was used to.” (ID:3)

Neurocognitive outcomes after treatment with autologous stem cell transplantation or CAR-T cell therapy for relapsed or refractory b-cell lymphoma

S J Mayo¹, K Edelstein¹, L J Bernstein¹, S Morrison¹, S Racine¹, M Surajpal¹, A Haghayegh¹, E Atenafu³, A Prica², and J Kuruvilla²

¹ Department of Supportive Care, ² Division of Medical Oncology & Hematology, ³ Department of Biostatistics
Princess Margaret Cancer Centre, University Health Network, Toronto, Canada

Table 1. Frequency of neurocognitive impairment

Neurocognitive Battery Test	n (%) Impaired
HVLT-R Trial 1	6 (9.8%)
HVLT-R Total Recall (Immediate)	15 (24.6%)
HVLT-R Delayed Recall	16 (26.2%)
HVLT-R Retention	6 (9.8%)
HVLT-R Recognition Discrimination Index	6 (9.8%)
Oral Trail-Making Test A	8 (13.1%)
Oral Trail-Making Test B	3 (5.4%)
COWAT	7 (11.5%)
Overall Impaired	21 (34.4%)

Table 2. Self-reported cognitive function

EORTC QLQ-C30 CF Score	
Mean ± SD	79.0 ± 22.1
Range	0 - 100
Clinically Important Score (≤ 75)	31%

Impairment rates across domains ranged from about 10% (attention span), 25% (verbal memory), 13% (processing speed), and 5% to 12% (executive functioning).

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Co-designing New Models of Care

Supportive Care in Cancer
<https://doi.org/10.1007/s00520-020-05860-9>

REVIEW ARTICLE



Cancer-related cognitive impairment in patients with non-central nervous system malignancies: an overview for oncology providers from the MASCC Neurological Complications Study Group

Samantha J. Mayo^{1,2} • Maryam Lustberg³ • Haryana M. Dhillon⁴ • Zev M. Nakamura⁵ • Deborah H. Allen⁶ • Diane Von Ah⁷ • Michelle C. Janelins^{8,9,10} • Alexandre Chan¹¹ • Karin Olson¹² • Chia Jie Tan¹³ • Yi Long Toh¹³ • Jeong Oh¹⁴ • Lisa Grech^{15,16,17,18} • Yin Ting Cheung¹⁹ • Ishwaria Mohan Subbiah¹⁴ • Duska Petranovic²⁰ • James D'Olimpio²¹ • Margherita Gobbo^{22,23} • Susanne Koeppen²⁴ • Charles L. Loprinzi²⁵ • Linda Pang²⁶ • Shivani Shinde²⁷ • Olanipekun Ntukidem²⁸ • Katherine B. Peters²⁹

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Abstract

Cancer-related cognitive impairment (CRCI) is commonly experienced by individuals throughout the disease and treatment trajectory. CRCI can have a substantial impact on patients and their families. To mitigate the impact, oncology providers must know about CRCI and its management. The objective of this review is to provide oncology clinicians with non-central nervous system cancers, with a particular focus on current management.

COPING WITH CHEMO BRAIN

Cancer-Related Brain Fog

Princess Margaret

Information for cancer patients and caregivers about cancer-related brain fog

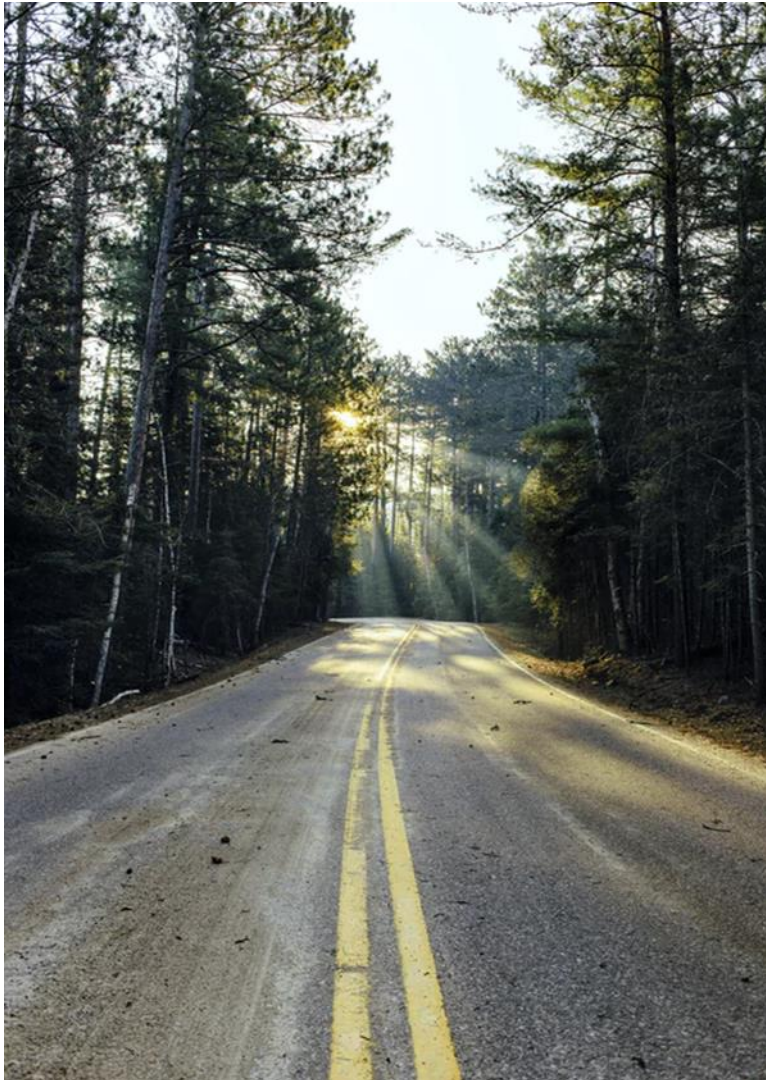
Also called "Chemo-Fog", "Chemo-Brain", or "Cancer-Related Cognitive Dysfunction"



LEUKEMIA & LYMPHOMA SOCIETY OF CANADA
fighting blood cancers



Understanding the patient and caregiver experience over time



Our current studies are examining the experience of people impacted by:

- Non-Hodgkin Lymphoma
 - Relapsed Refractory B-Cell Lymphoma
 - Relapsed Refractory Acute Leukemia
 - Critical Illness and Hematological Malignancy
 - Transplant as an Adolescent/Young Adult
 - Caregiving in the setting of Blood Cancers
-
- Findings will support tailored and effective approaches for meeting their needs

Goal: Support for the Whole Self

- Greater integration of psychosocial and supportive care into cancer care
- Better understanding of the impacts of new treatments on quality of life and how these impacts differ among people
- Health systems that advocate for equitable access to care, trials, and mental health resources

Caregiver Well-being and Supports



Closing thoughts

- Novel treatments may be associated with a range of psychosocial and functional challenges that may impact quality of life over the long-term.
- Quality of life may be optimized through tailored approaches to address factors that impact overall health and well-being.
- There is a need for real-world data to inform the design of health services that comprise the right interventions, provided at the right time, to the right people.