

Overview of The Ottawa Hospital Transplantation and Cellular Therapy Programme

Christopher Bredeson MD MSc FRCPC FASTCT

Head, Malignant Hematology TCT

The Ottawa Hospital

Overview

- Background & History
- Oversight
- Structure
- Activities
- Special Programmes
 - CAR T Cells
 - Autoimmune Diseases
- Questions

WHY WE ARE HERE



What is a transplant? What are CAR T Cells?

- Transplants

- Collection and reinfusion of cells that can regrow the bone marrow and immune system
- Auto: uses the patients own cells to support very high dose radio/chemotherapy
 - Less complicated
- Allo: providing a new immune system to recognize and kill the bad cells
 - The pre-transplant conditioning therapy may also provide some anti-tumor benefit
 - More complicated

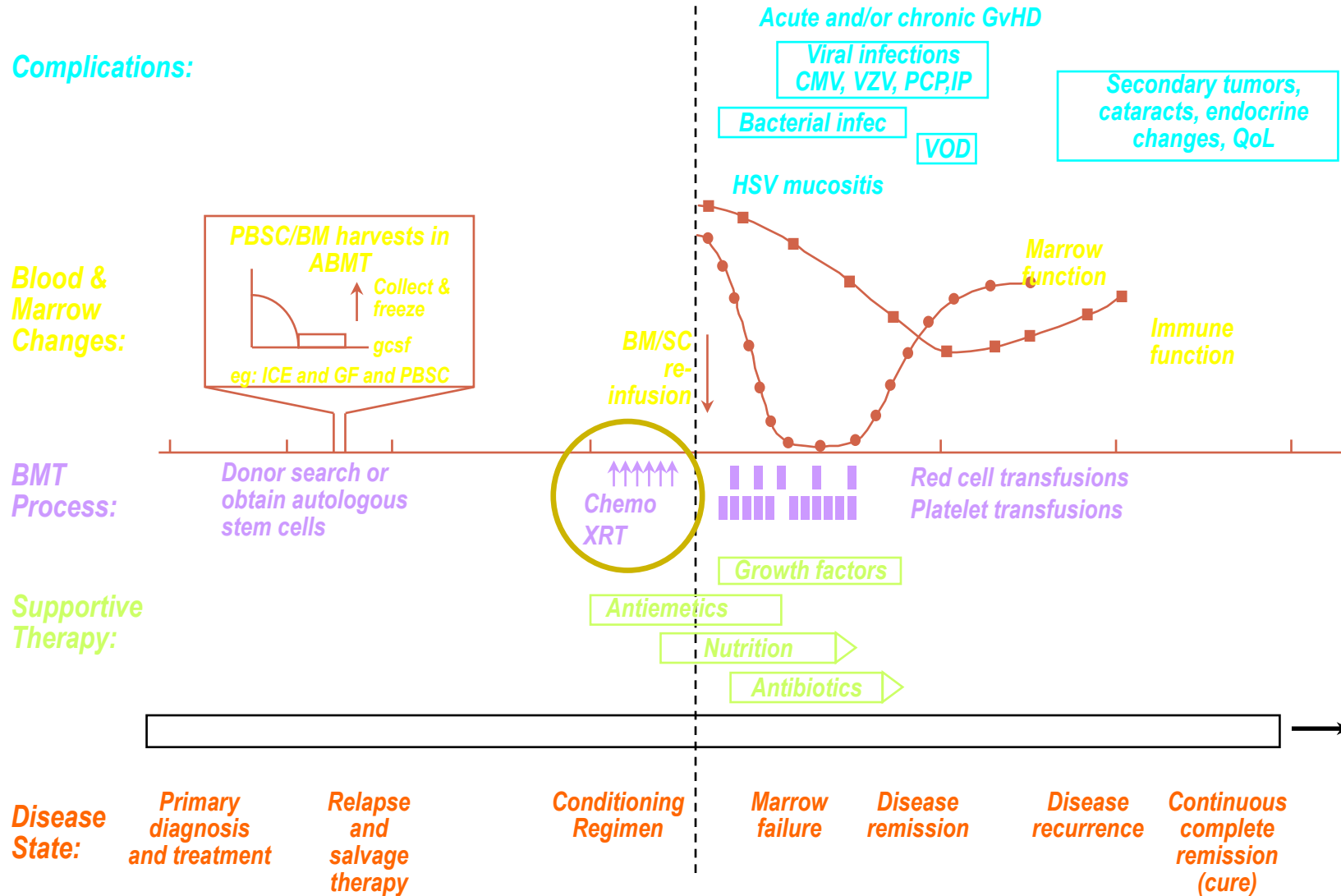
- CAR T Cells

- A “new” targeted therapy
- Uses patients own immune system cells (T cells)
- They are collected and genetically modified to recognize a marker on the patients lymphoma/leukemia
- They are expanded and reinfused into the patient
- Often called a “living drug”

When are transplants used?

- Not as a “Hail Mary”
- When the benefit to the patient (disease control/cure) outweighs the risks of the therapy
- Standard as part of first treatment strategy for many patients (AML, ALL, other bone marrow disorders, MM)
- Often as second or subsequent line of therapy when less intensive approaches have not worked (NHL, HD, germ cell tumors, some leukemia pts, some patients with autoimmune diseases etc.)

Very High Level Overview of a “Transplant”



TOH TCT PROGRAMME: HISTORY



- BMT program established in 1981
- 1st URD Transplant: 1988
- 1st Autologous Transplant: 1990
- Outpatient BMT program established in 1994
- 1st Haploidentical Transplant: 1995
- 1st FACT Accreditation: July 2000
- 1st Transplant for Multiple Sclerosis 2001
- 1st CAR-T Cell Patient: 2019



STRUCTURE



LBH started the programme
Established the culture



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d'Ottawa

ADMINISTRATIVE LEADERSHIP



Cameron Love
President



Suzanne Madore
EVP & Chief Clinical Officer



Dennis Garvin
Executive Director, Clinical Operations



Julie Renaud
Director, Regional Cancer Care



Tania Baird
Clinical Manager, TCT Inpatient & Day Hospital Units



Carey Landry TCT Coordination Unit
Program Manager, Outpatient Clinic (Module L)



Karen Lawrence
Clinical Manager, 6E Hematology Inpatient Unit & MDCU



McDiarmid, Sheryl
APN, CVAD, Therapeutic Apheresis and Hemoglobinopathy Programs, and Stem Cell Transplant Program
Manager, Collection Facility
TCT Advanced Practice RN

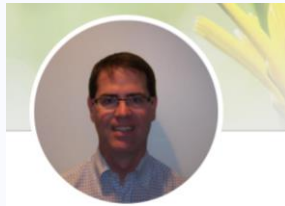


Holmes, Laurie Ann
Nurse Educator



Amber Killam
Nurse Educator

MEDICAL LEADERSHIP



Greg Knoll

Physician

Chair & Head, Department of Medicine



Cameron Love

President



Virginia Roth

Chief of Staff



Marc Carrier

Physician

Chief, Hematology



Chris Bredeson

Physician

Head, Malignant Hematology & TCT
Medical Director,
Transplant & Cellular Therapy Programme

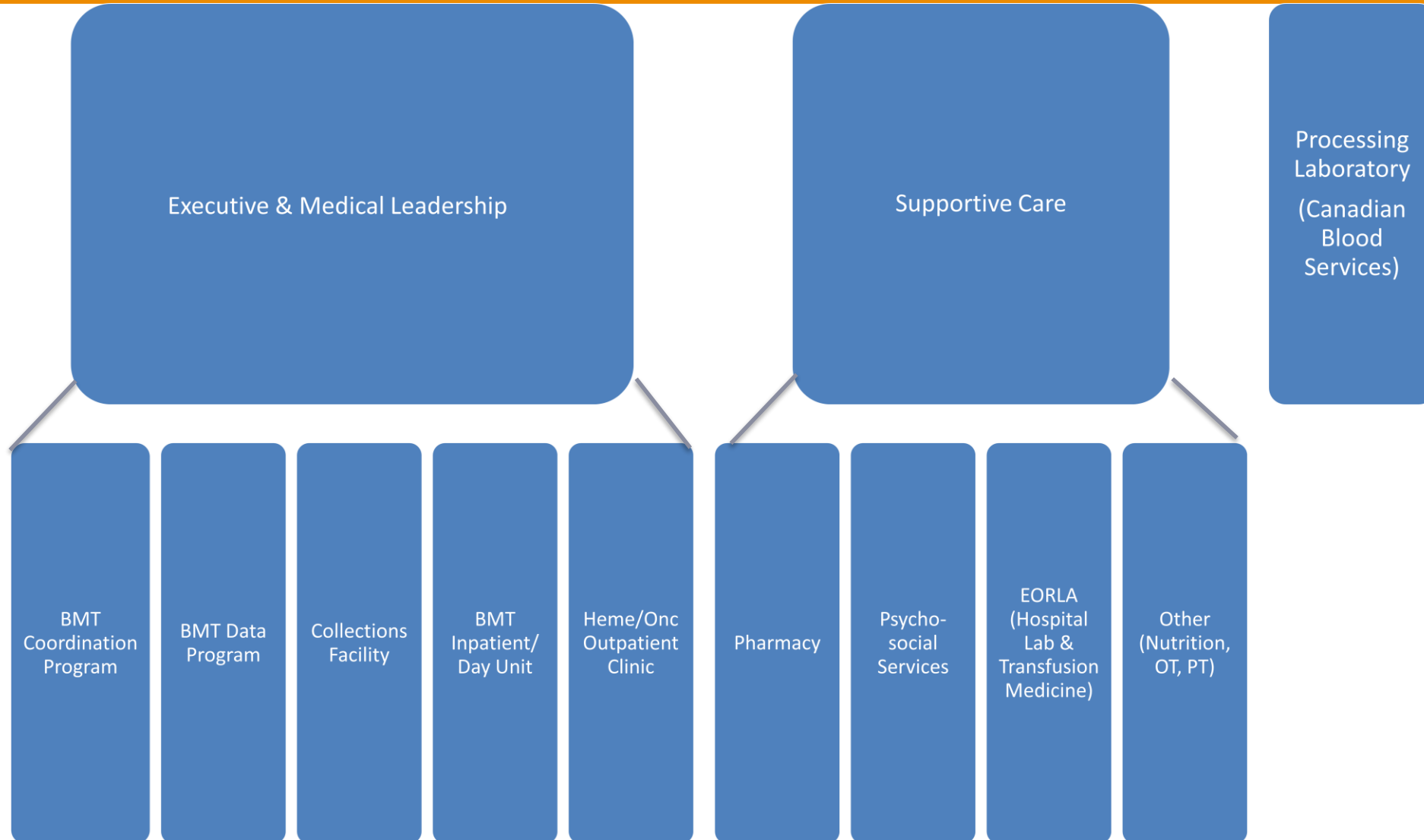
Transplant Physicians

- Dr. D. Allan**
- Dr. H. Atkins
- Dr. I. Bence-Bruckler*
- Dr. C Bredeson
- Dr. J. Fulcher*
- Dr. L. B. Huebsch
- Dr. N. Kekre
- Dr. M. Kennah
- Dr. M. Sabloff*

*Ward service/on-call rotations only

**Processing Lab Medical Director

CROSS-FUNCTIONAL ORG CHART



OVERSIGHT



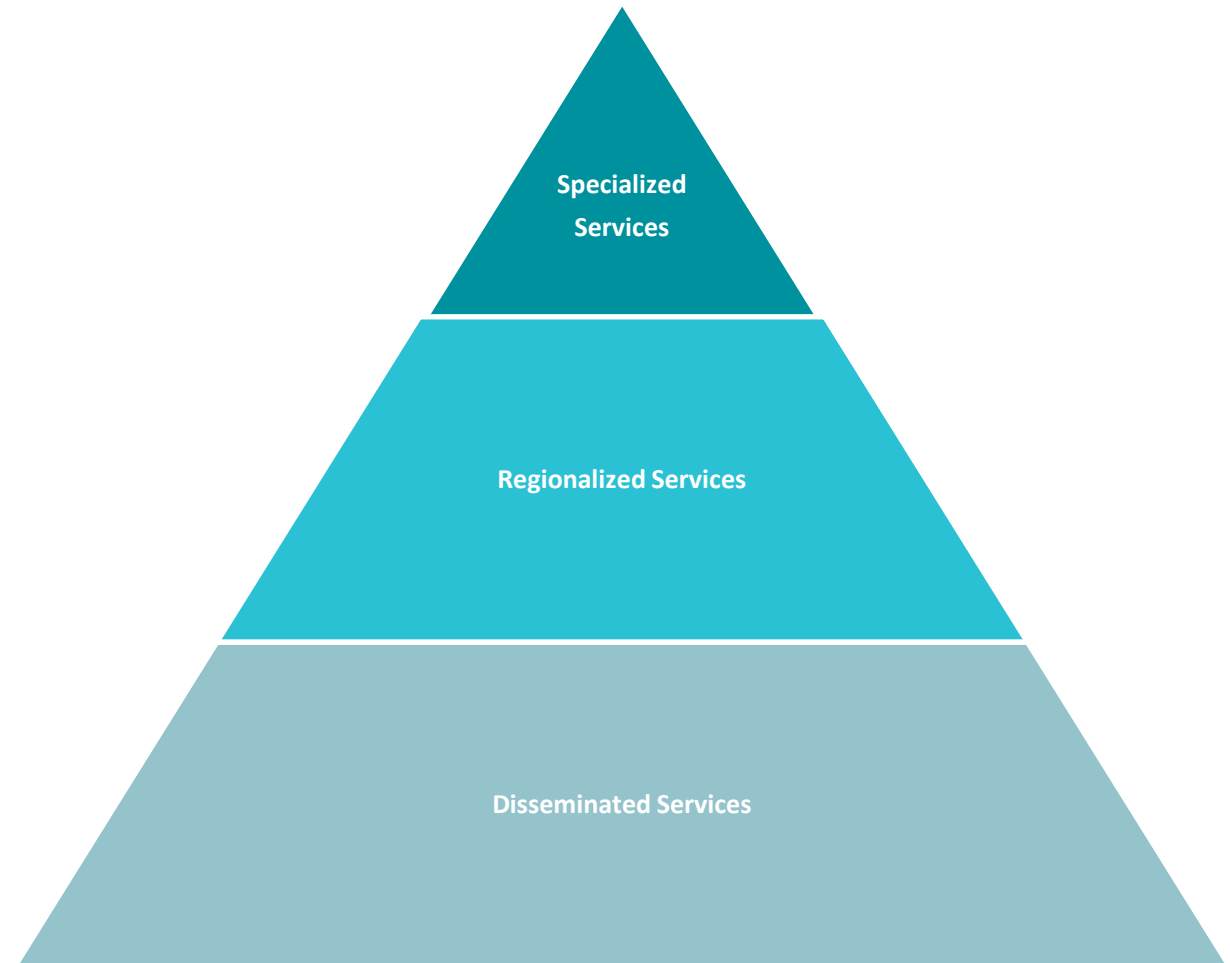
- CB inherited the programme
- Built on existing strengths

Provincial Oversight from CCO: What is Specialized Services Oversight?

What is Specialized Service?

- Low-volume
- High complexity
- High cost
- Not available in every LHIN
- Involve a rapidly evolving knowledge base and high degree of specialization

Addresses the challenge for optimization of service delivery while providing equitable access to safe, high quality, best practice care.

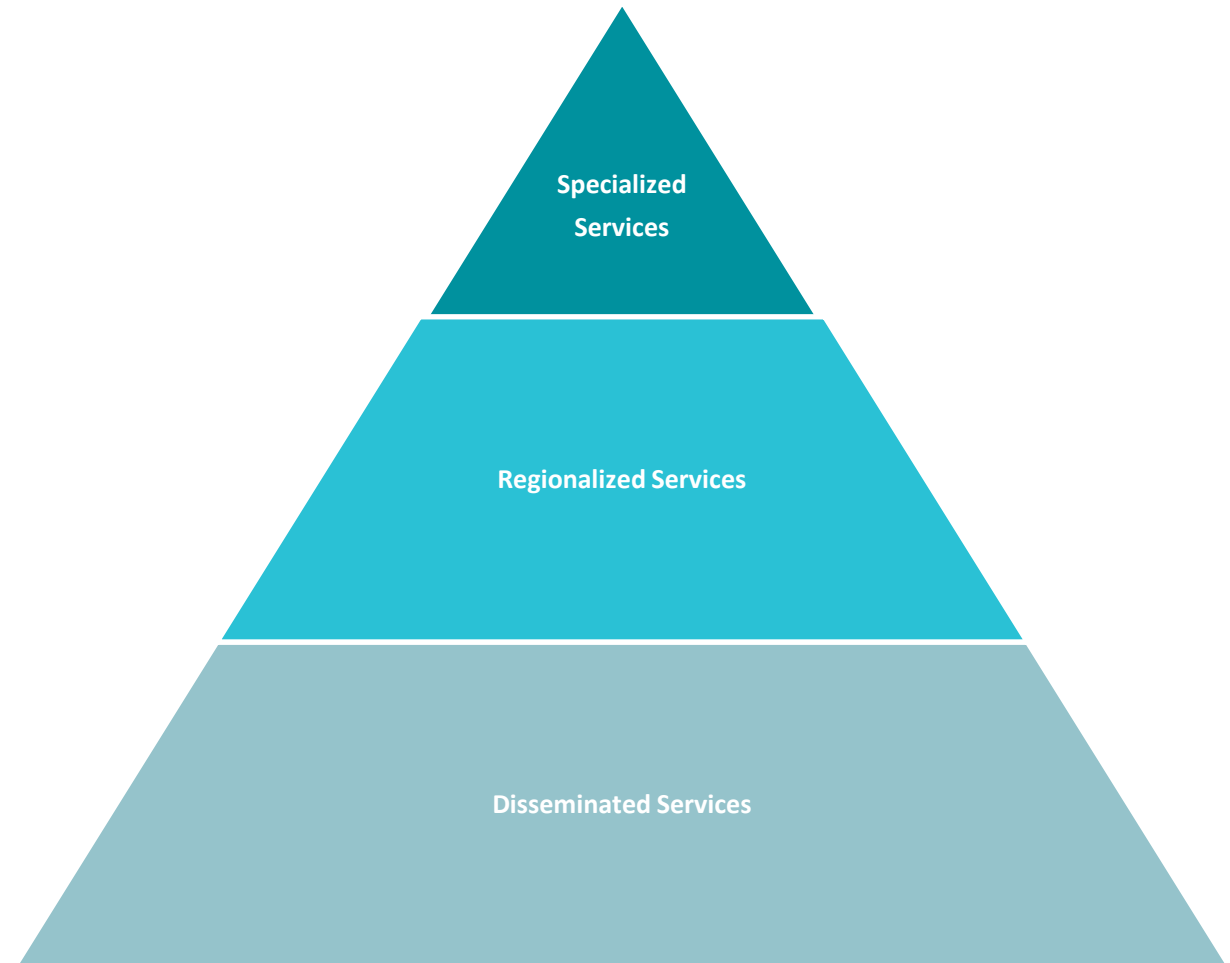


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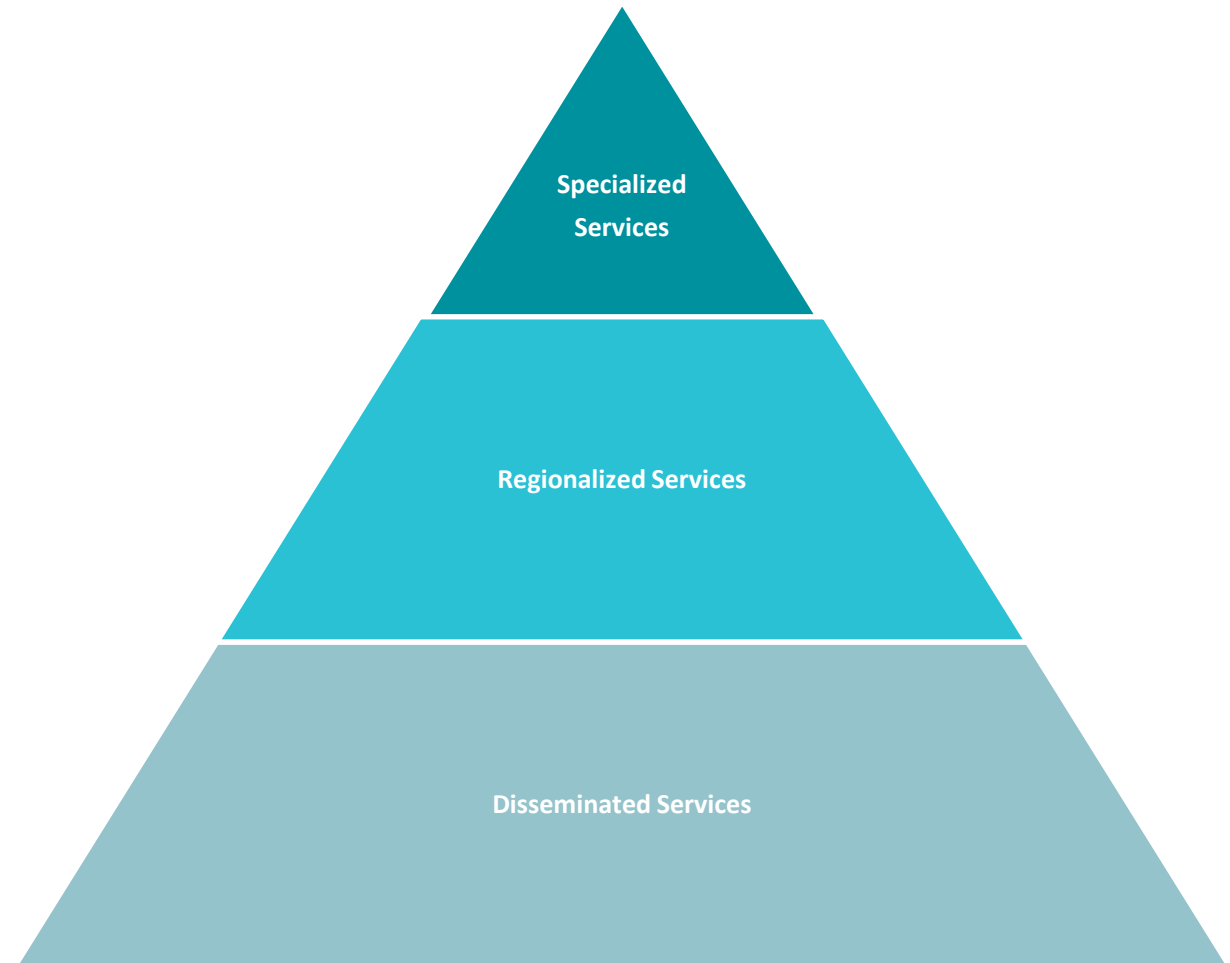


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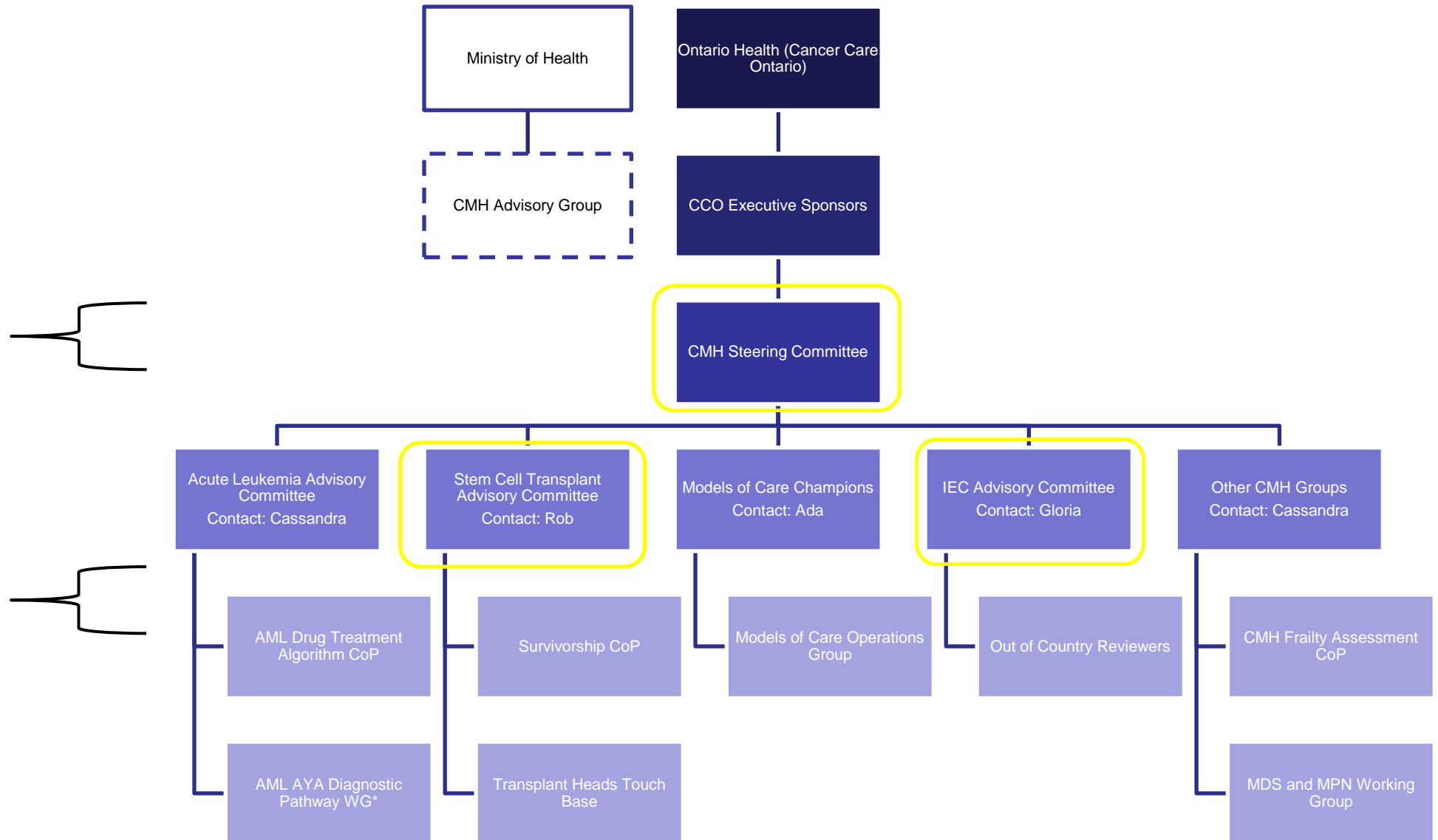
What do we accomplish at/with CCO

- Increase access to transplants
 - Capacity building
 - Day +1 transfers
 - New models of care
- Funding transplants and now CAR T therapy
 - Provincial/interprovincial activity in a regional hospital
- Enhance quality
 - Promoting FACT accreditation for all programmes in Ontario
- Facilitating Equitable Access Nationally
 - CAR T Cell therapy for out of region and out of province patients

CMH Stakeholder Engagement Model and Governance

Clinical, Administration and Patient and Family Advisory participants on Advisory and Steering Committees

Subject matter experts and those with focussed interest on Working Groups and Communities of Practice



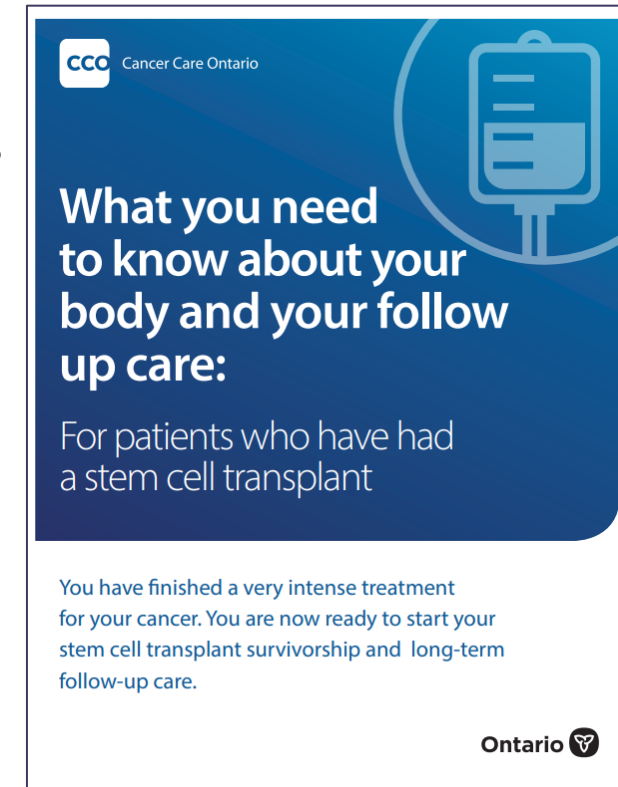
Clinical resources

Stem Cell Transplant Survivorship Care Post-Transplant

- A CCO webpage has been launched to host clinical position statements and patient education information for the unique survivorship and long-term follow-up care needs of patients following an autologous or allogeneic stem cell transplant.
- The webpage can be found [here](#).

Stem Cell Transplant Survivorship Patient Pamphlet

- A Post-Stem Cell Transplant Survivorship patient pamphlet has been developed to share with post-transplant patients.
- The pamphlet is hosted on the SCT Survivorship Care Post-Transplant [webpage](#).



The Facts About FACT

- Federation for Accreditation of Cellular Therapy
- International standard (called JACIE in Europe)
- Establishes standards programmes must meet
- Covers all aspects from infrastructure to personnel to procedures
- Annual reporting and q3yr site visits



Back to TOH Program ...

also complex

- Whether with us a short time or a long time, always family
- We like our picnics



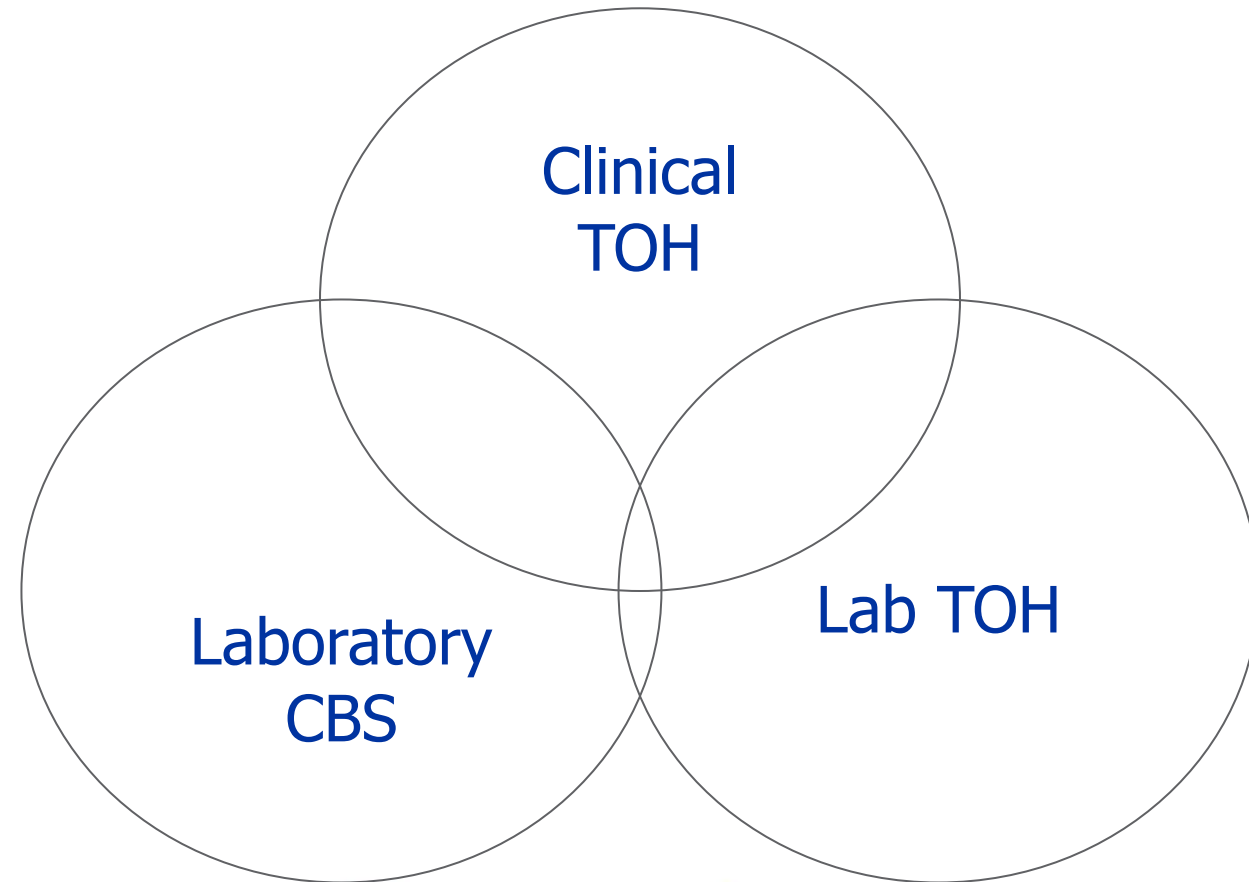
TOH BMT PROGRAM

A Collaboration of the TOH Clinical and Laboratory Programs:

- Division of Clinical Hematology
- Division of Laboratory Hematology

And the Ottawa Centre of the Canadian Blood Services

- Stem Cell Processing Laboratory
- Flow Cytometry Laboratory
- OneMatch Donor Registry



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COLLABORATIONS

- **Canadian Blood Services Cell Processing Lab**
 - Follows GMP guidelines; FACT, AABB Accredited;
 - >300 products processed/year;
 - Performs cryopreservation, storage, distribution, QC, testing, CD34+ selection and more...
- **OneMatch Stem Cell and Marrow Network - Donor Registry**
- **EORLA – On-site third party lab**
 - ASHI accredited HLA typing laboratory
 - Pathology, Biochemistry, Microbiology
- **VERSITI (Blood Center of Wisconsin) – Chimerism testing**
- **CHEO - Cytogenetics; Virology Laboratory**
- **Ontario Health - CCO / Provincial networks**
- **Cellular Therapy Transplant Canada (CBMTG)**
- **CIBMTR / BMTCTN**



CLINICAL PROGRAM: THE PEEPS

- Academic Program
 - Attending Hematologists
 - Clinical Associates (Hospitalists)
 - TCT and Hematology Fellows
 - Multidisciplinary Team
 - Clinical Associates, APN, NP, PAs, Trainees, Nurses, Dietician, Pharmacists, Occupational Therapist, Physiotherapist, Social Worker, Psychologist
 - Radiation Oncology
 - Hematopathology
- Consulting/Support Services
 - Infectious Diseases
 - Rapid Assessment Clinical Evaluation (RACE)
 - Intensive Care
 - Pulmonary
 - GI
 - Psychiatry
 - Palliative Care
 - Dermatology
 - etc

BMT / MALIGNANT HEMATOLOGY FOOTPRINT

Patients can transition between each location as medically required

Inpatient Unit
5 West
-20 private rooms

Intensive Care Unit

Day Hospital: 5 West
-9 single, 2 semi rooms
-12 hrs/day, 365 days/yr
MDCU
-12 + 8 beds/chairs
(chemo/supp care/procedures)
Apheresis
- Graft collections, ECP

Outpatient Clinics
-Modules L & J
(pre- and post-BMT visits)

Emergency Room

BMT PROGRAM - OVERVIEW

- Capacity >250 cellular therapy treatments / year
- In the midst of capital expansion
- Average 15-20 inpatients
- Average 10-15 day hospital patients
- Group practice model
- Average 100+ outpatient visits/week:
 - Consult
 - Planning
 - Acute follow up
 - Longterm follow up
 - Urgent CAR T referrals

The Team

- DA our link to CBS
- Active research mentor for trainees



TCT Central Activities

- TCT Office

- Giselle Villeneuve
- Shandy Jean
- Blurette Riel
- Jill Pajel
- Kelly Vien



- TCT Coordination

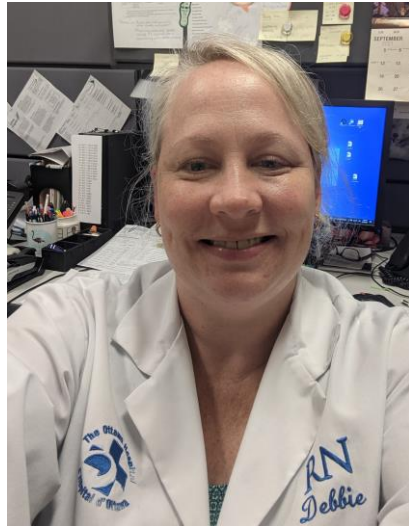
- Matt Granger

- Search Coord / FACT Guru

- Carolina Cieniak



More Central Activities



- TCT Nurses

- Nancy Agnew
- Debbie Bastien
- Matthew Paquette



- Data Management

- Hayley Mills
- Nicole Neocleous
- Kalina Abrol
- Carter Sullivan



Module L/J

- Clinic Reception

- Lama Arbach
- Marc Leblanc
- Emile Gauthier



- Clinic Nurses

- Jen Halkali (vaccines)
- Virginia Mullins
- Lana Bols
- Alana Cragg
- Amanda Plourde
- Helen Szadowski



- Clinic Care

- Elizabeth Drouin MD
- Erin Mutterback NP
- Linda Hamelin NP



5W/Out Patient TCT (apparently a shy bunch)

- Nursing Leadership 5W
 - Tania Baird
 - Katrine Richer
- Physio/OT
 - Leeanne (PT)
 - Roxanne (PT asst)
 - Nciole (OT)
- Social Workers
 - Jennifer Diamant
 - Esther Doucette
- Nutritionist
 - Dianne Marcotte
- MD Extenders
 - Michael Hodgins
 - John Cockburn
 - James Taylor
 - Kira Slivitzky
- Pharmacists
 - Michelle 1 (Boyce)
 - Michelle 2 (Delbaere)
 - Connor Prince
 - (Harry Hopkins!)
- Environmental services

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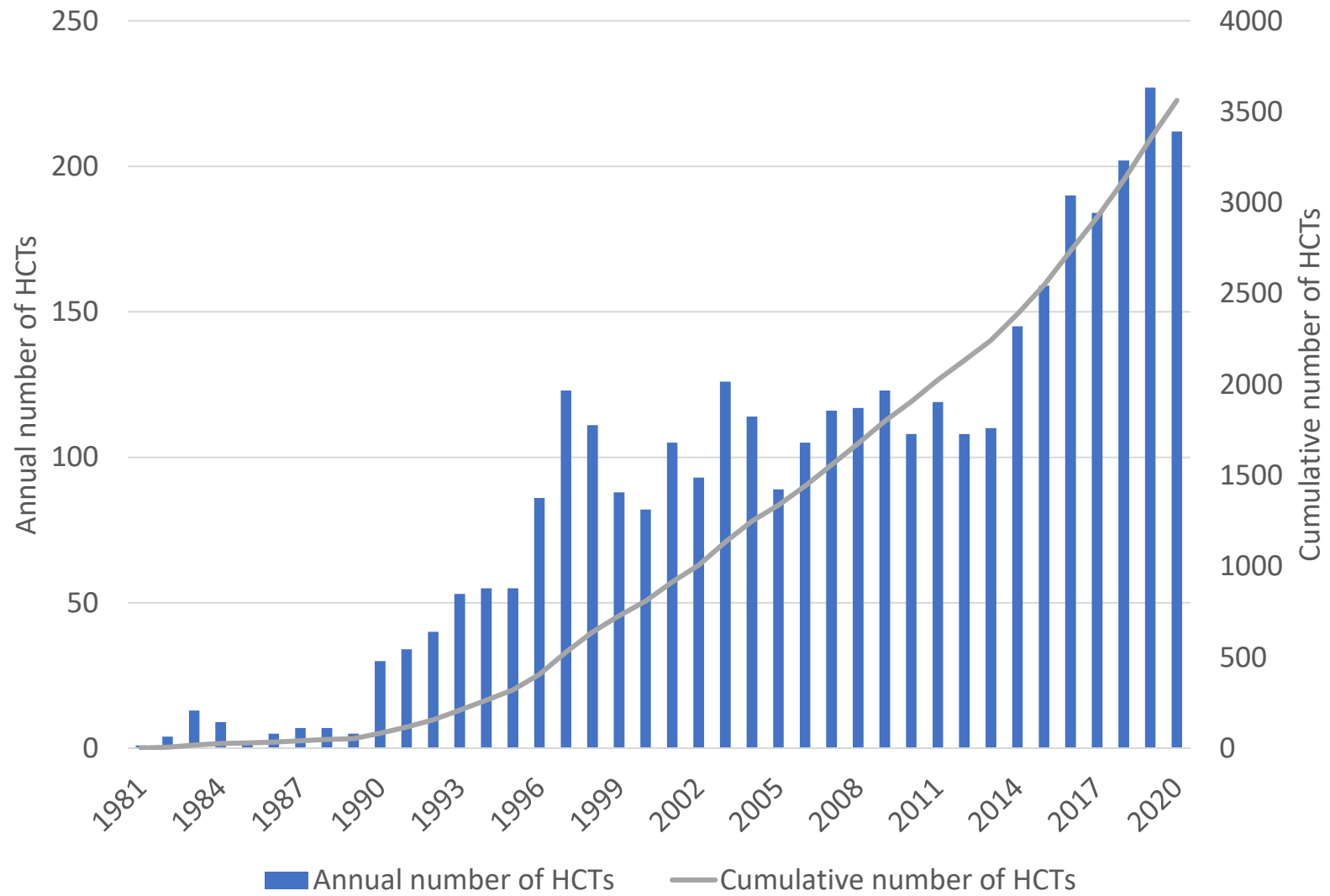


Activity

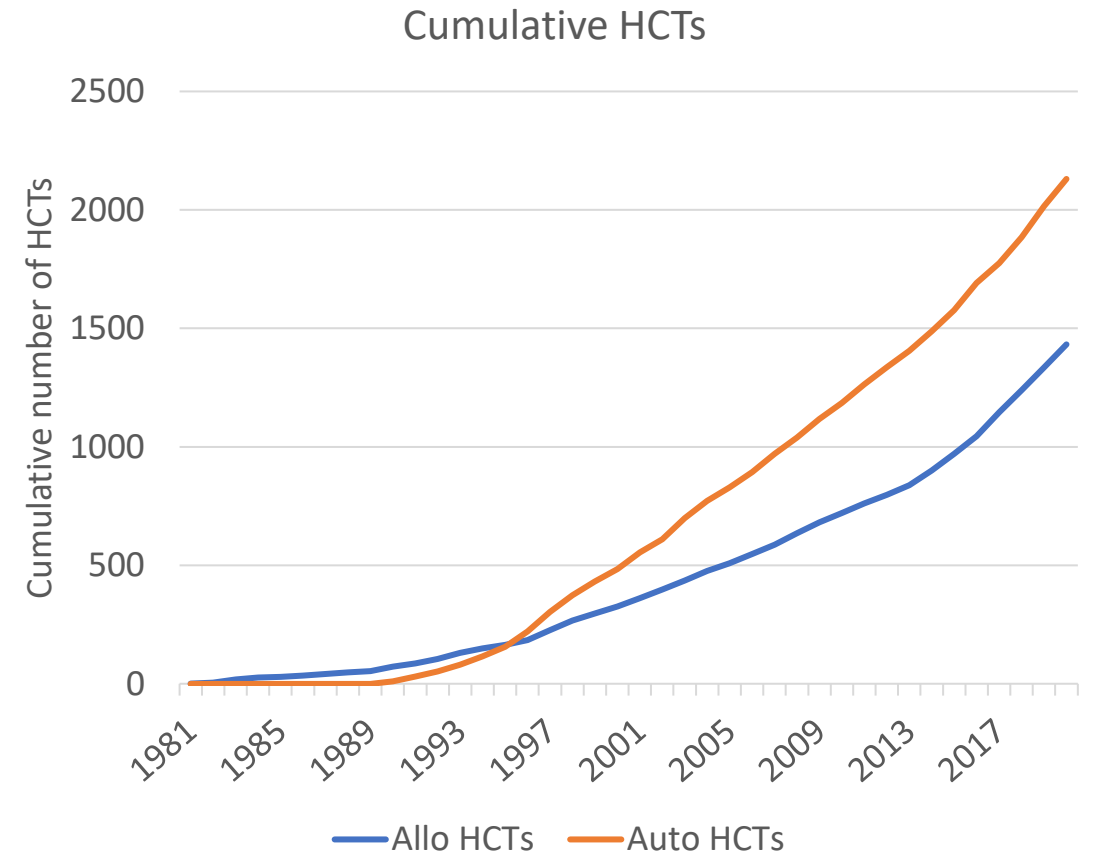
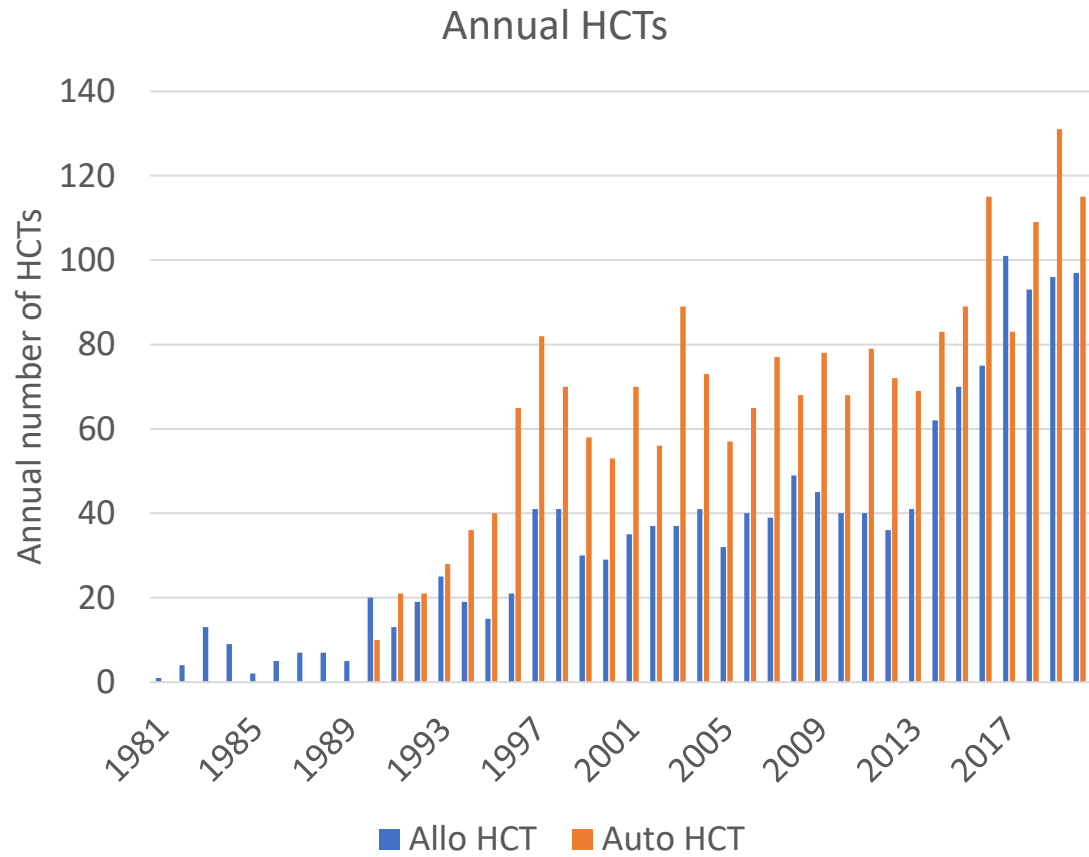
MK the future of our programme

Set up clinical CAR T Cell programme
that serves Ontario and Maritimes

Total Number of Transplants since Inception at TOH



Transplant Types since inception at TOH



Catchment Area: Come from away...



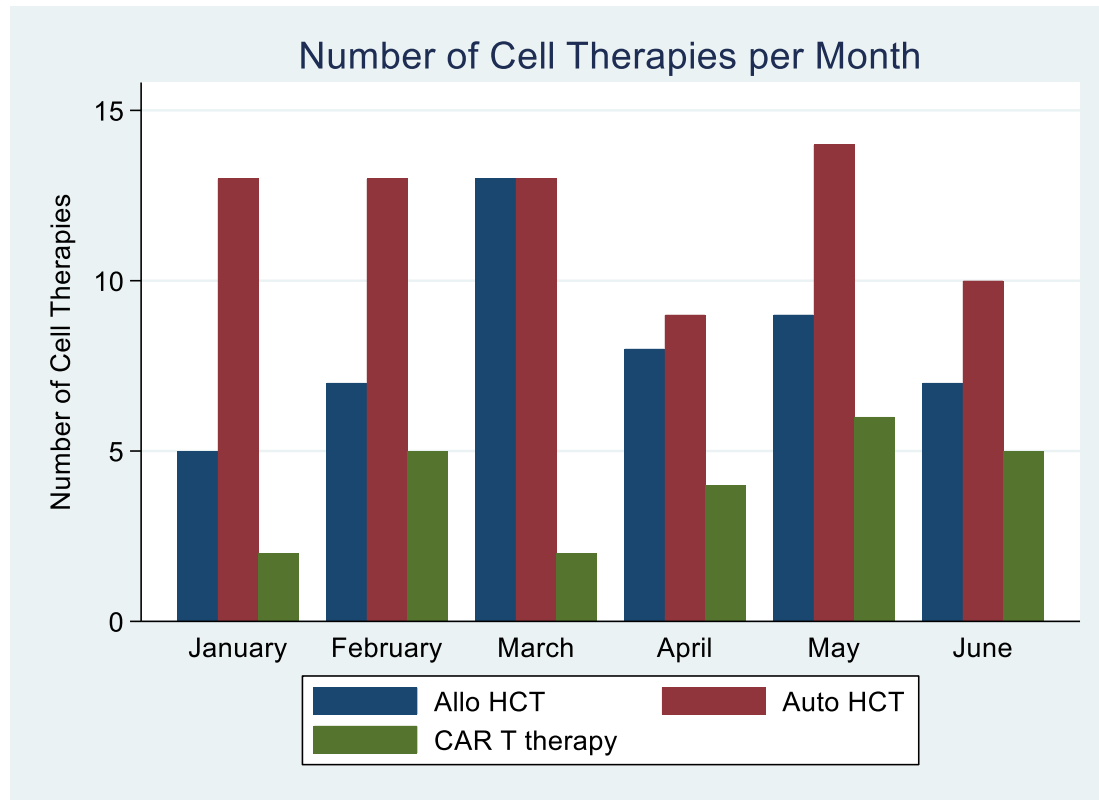
- Allos (donor transplants)
 - Eastern Ontario to ~Peterborough
 - All Northern Ontario
 - Nfld and Labrador
- Auto (self transplants)
 - Eastern Ont, T Bay, West PQ
 - All Canada for Autoimmune Pts
- CAR T Cells
 - Ont, NB, PEI, NL
- Unrelated Donors
 - All of Canada

Breakdown of Patients by Program

	2020 (Jan 1 st – Dec 30 th)	2021 (Jan 1 st – June 30 th)
Ontario	196	123
Ottawa (TOH/Ottawa)	139	82
Thunder Bay (TBRHSC)	13	14
Sudbury (HSN)	18	9
Kingston (KHSC/KGH)	18	13
Hamilton (HHS/Hamilton)	2	1
London (LHSC)	2	2
Other ON	4	2
Quebec	15	12
Gatineau	14	10
Other Quebec	1	2
Newfoundland	1	9
Prince Edward Island	0	1

Data includes all transplant and cell therapies

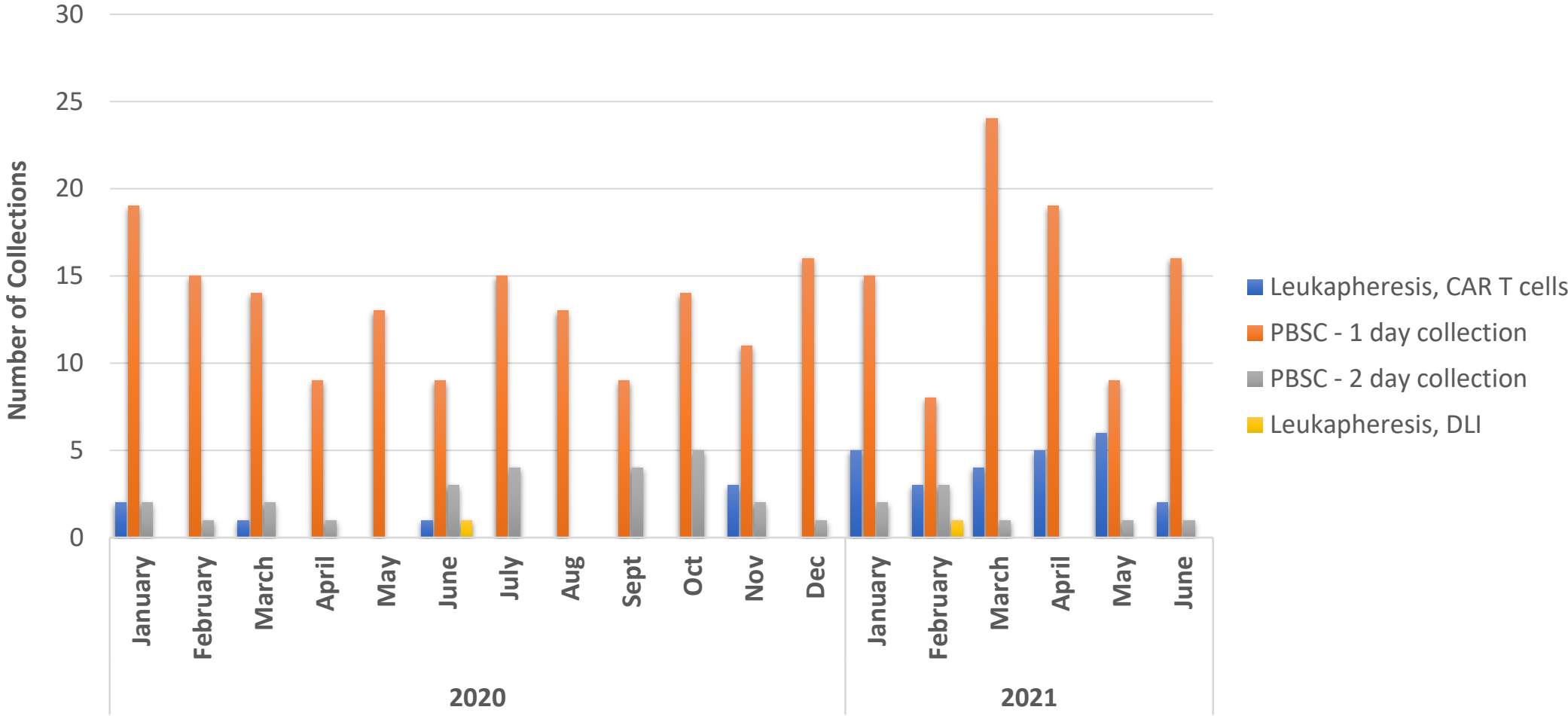
Number of Transplants and Cellular Therapies



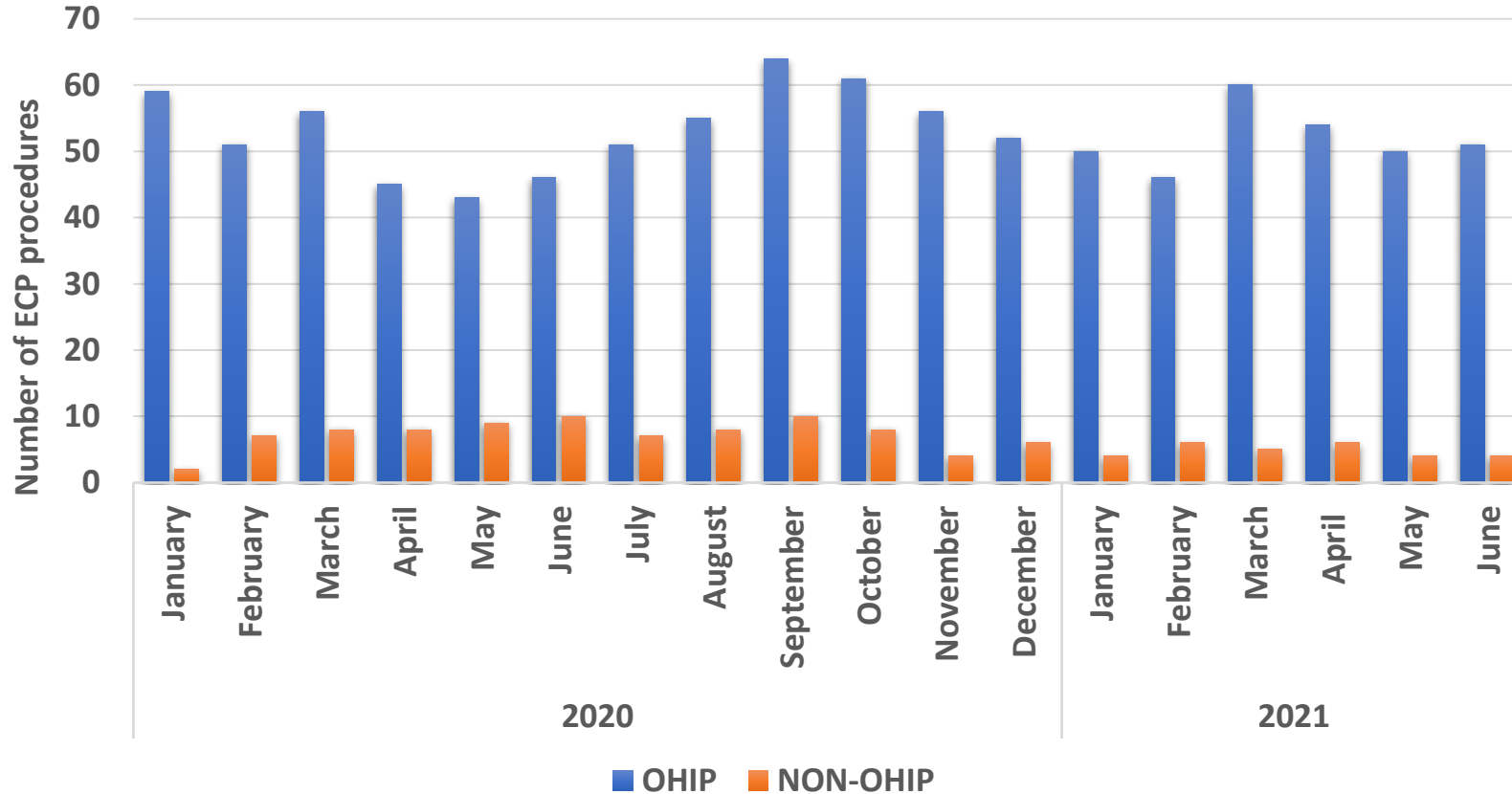
	Number of Cell Therapies			
	ALLO	AUTO	CAR T cells	Total
January	5	13	2	20
February	7	13	5	25
March	13	13	2	28
April	8	9	4	21
May	9	14	6	29
June	7	10	5	22
TOTAL	49	72	24	145

Note: Related ALLO = 11
 Unrelated ALLO = 38

Number of Collections per Month

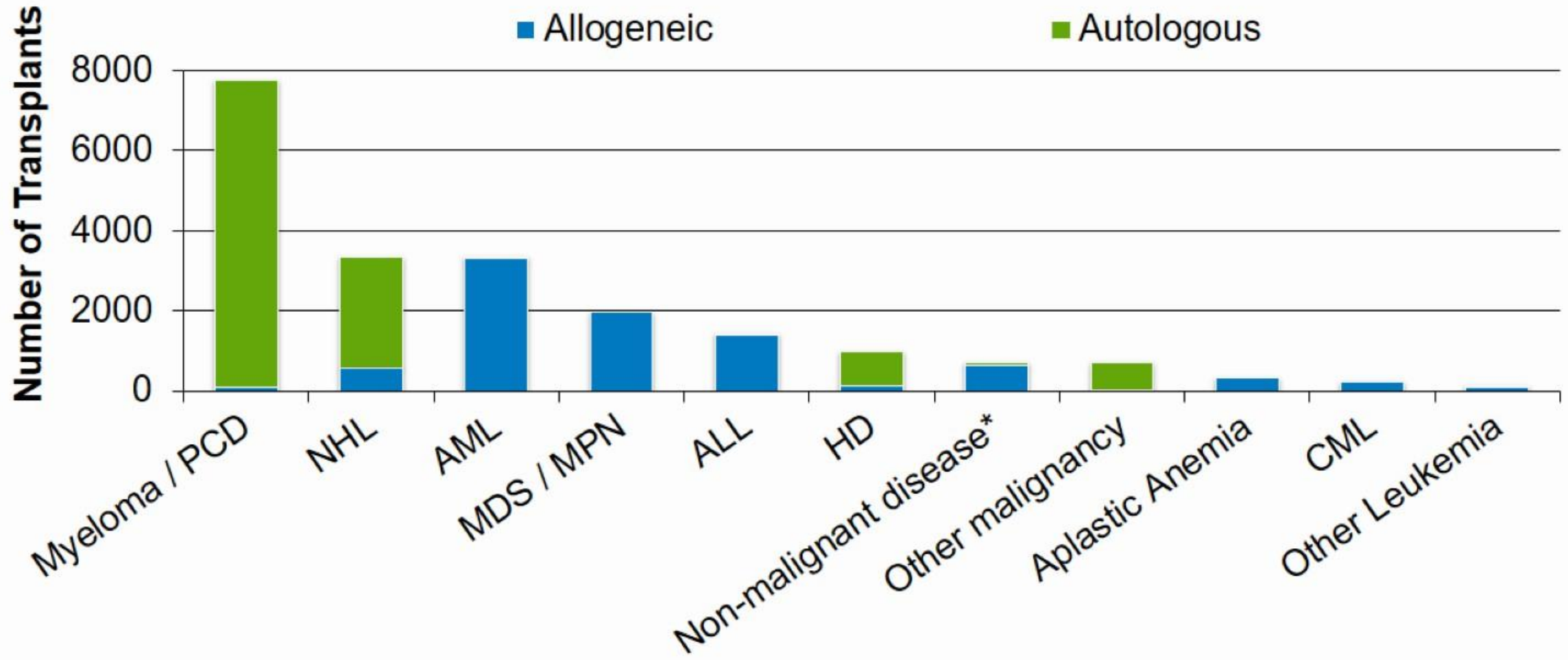


Number of ECP Procedures



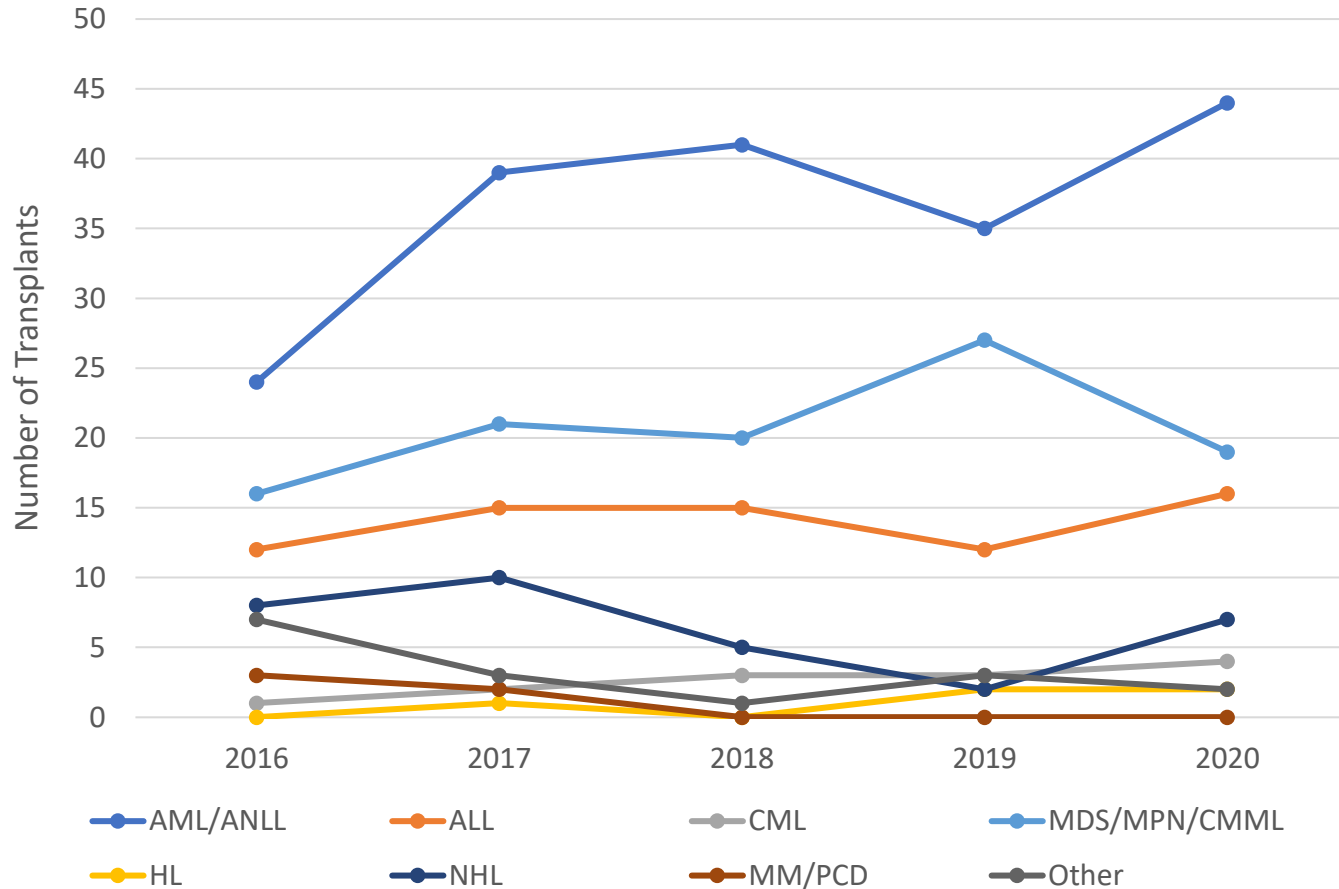
	Number of Patients		Number of Procedures	
	NHL	GVHD	NHL	GVHD
January	6	17	12	42
February	6	19	12	40
March	6	18	13	52
April	7	18	14	46
May	7	17	13	41
June	6	17	16	39

Indications for Hematopoietic Cell Transplant in the US, 2019



Trend of Allogeneic HCT infused at TOH by disease between 2016-2020

Sample size = 443



Inclusion criteria

- All age groups
- Only TOH infused recipients between 2016-2020
- Source and Type of HCT: PBSC and BM both related and unrelated
- Include both Canadian and International donors

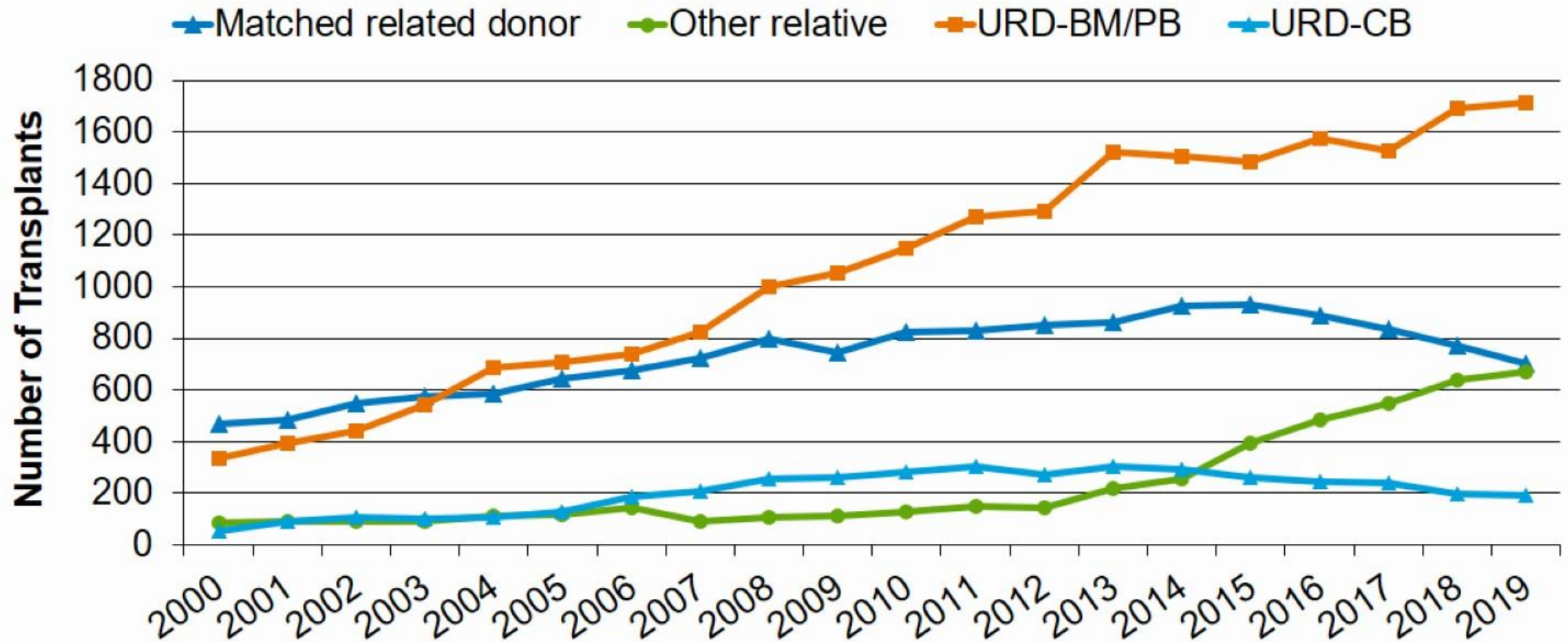
Exclusion criteria

- Infusions at other centers
- Source of HCT: exclude DLI

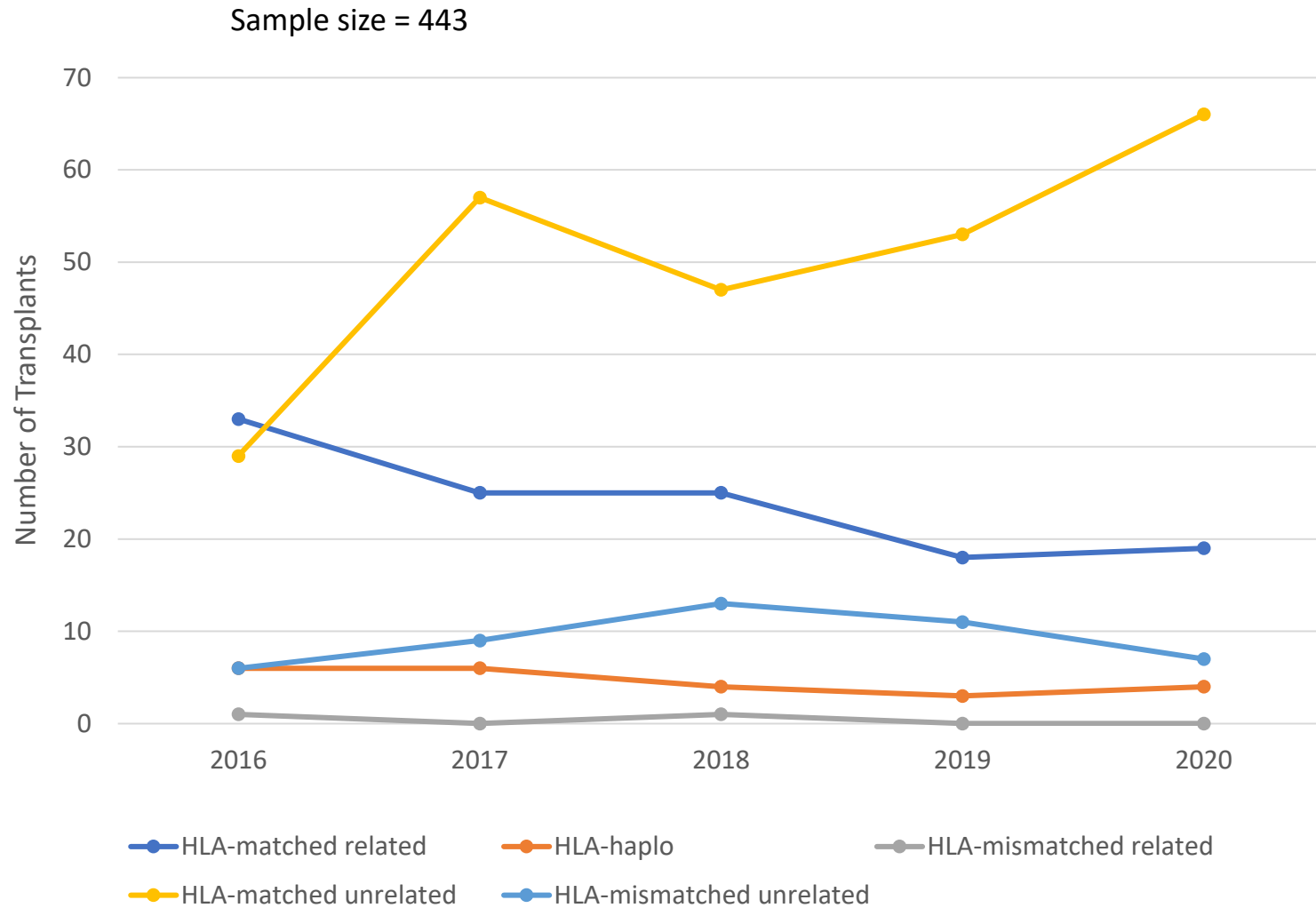
Note: others includes SAA and inherited disorders of metabolism

Summary: Relative change in number of allo HCTs is greatest for AML (83.3% increase)

Trends in allogeneic HCT for Acute Myelogenous Leukemia (AML) by Donor Type in the US

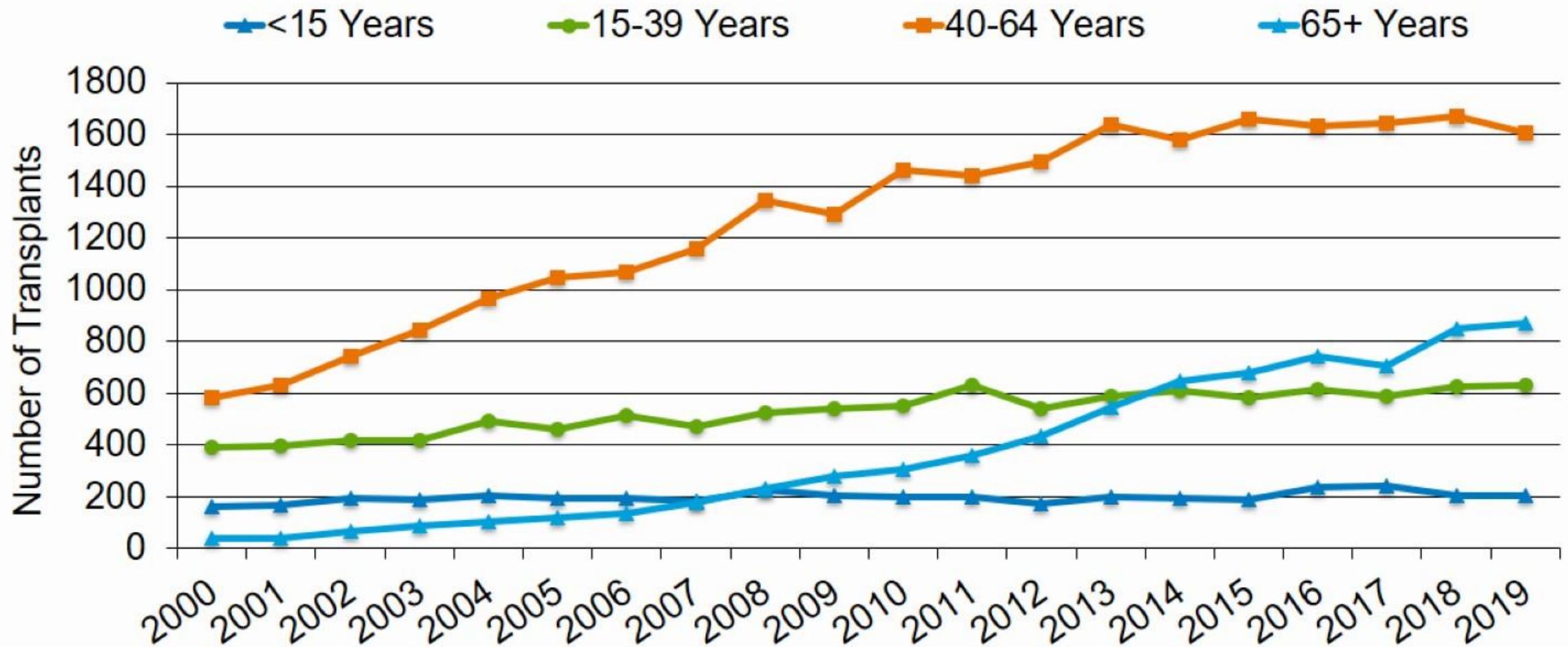


Trend of Allogeneic HCT infused at TOH by donor type between 2016-2020



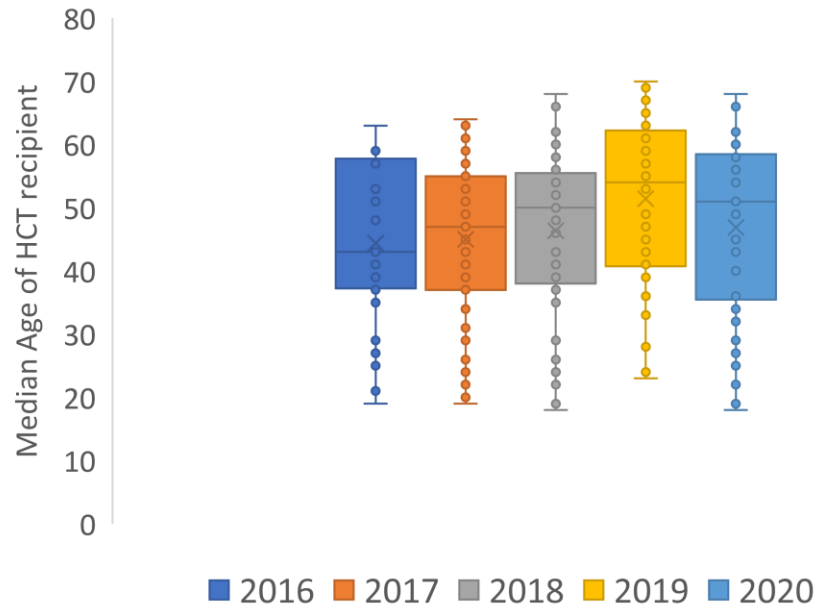
Summary: Allo transplants with HLA-matched unrelated donors have increased over the years whereas all other donor types have decreased.

Trends in allogeneic HCT for Acute Myelogenous Leukemia (AML) by Recipient Age in the US

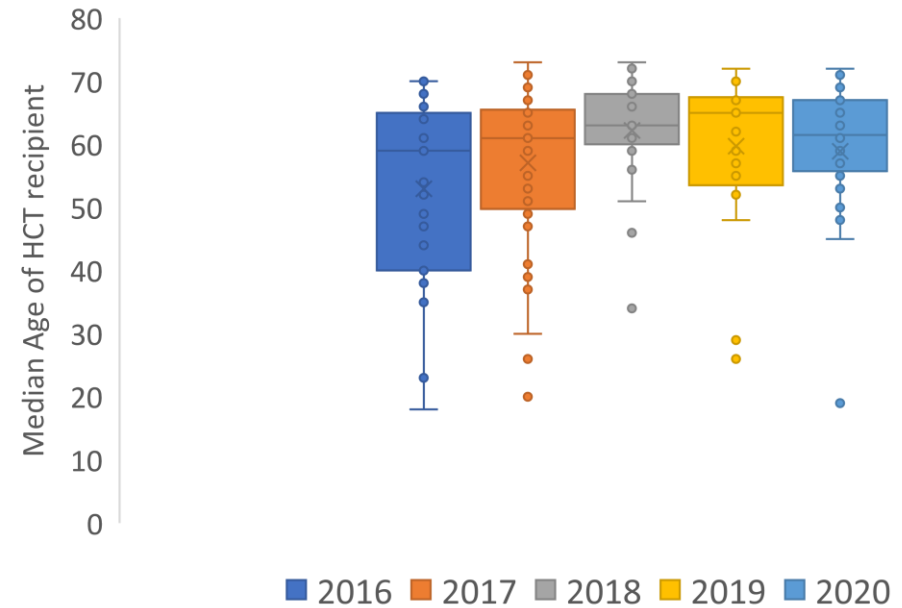


Median Age of Allogeneic HCT Recipient following myeloablative or reduced intensity conditioning regimen by year

Median Age of HCT recipient for myeloablative conditioning



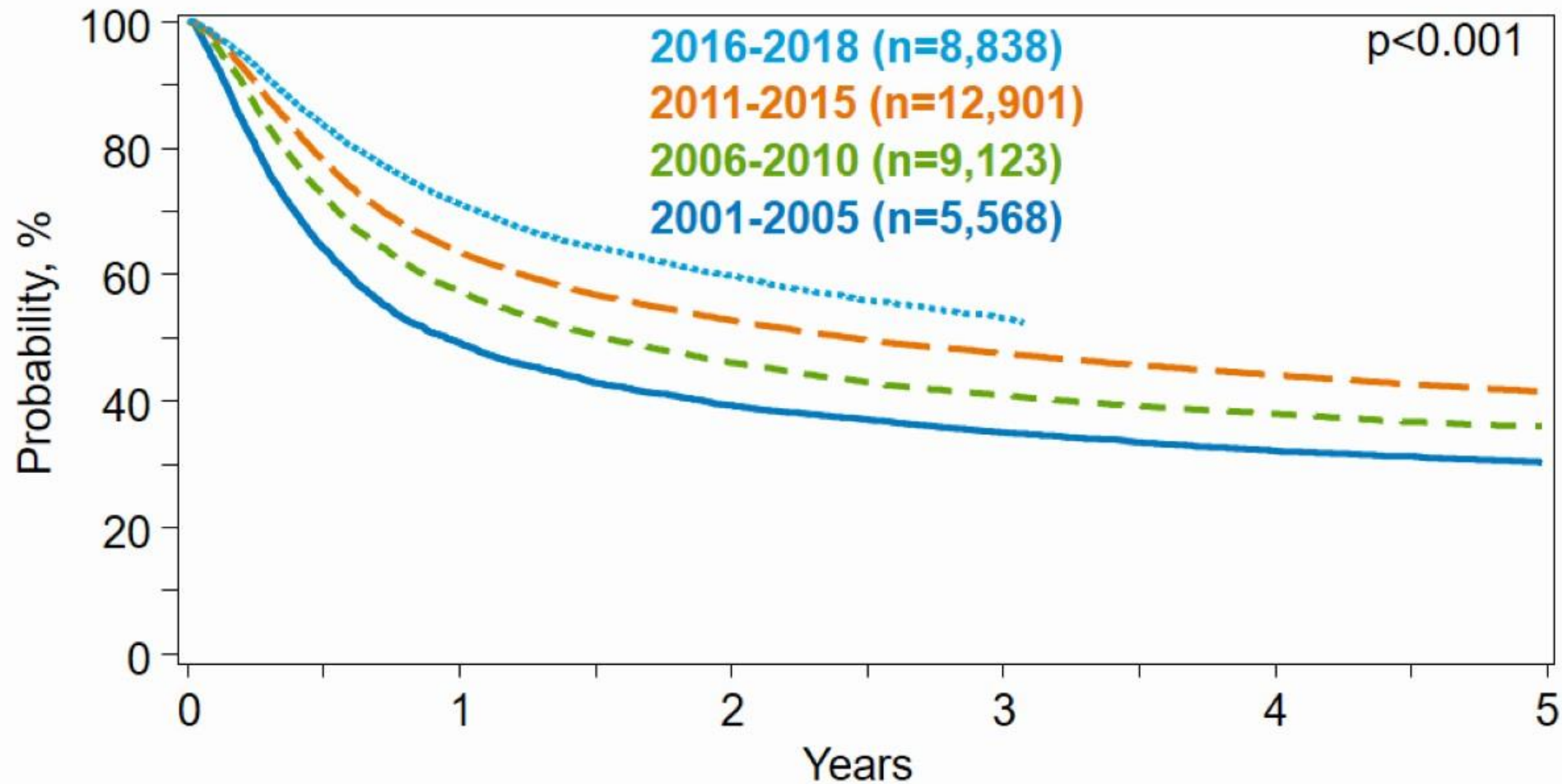
Median Age of HCT recipient for reduced intensity conditioning



	2016	2017	2018	2019	2020
N	40	55	57	58	57
Median Age	43	47	50	54	51

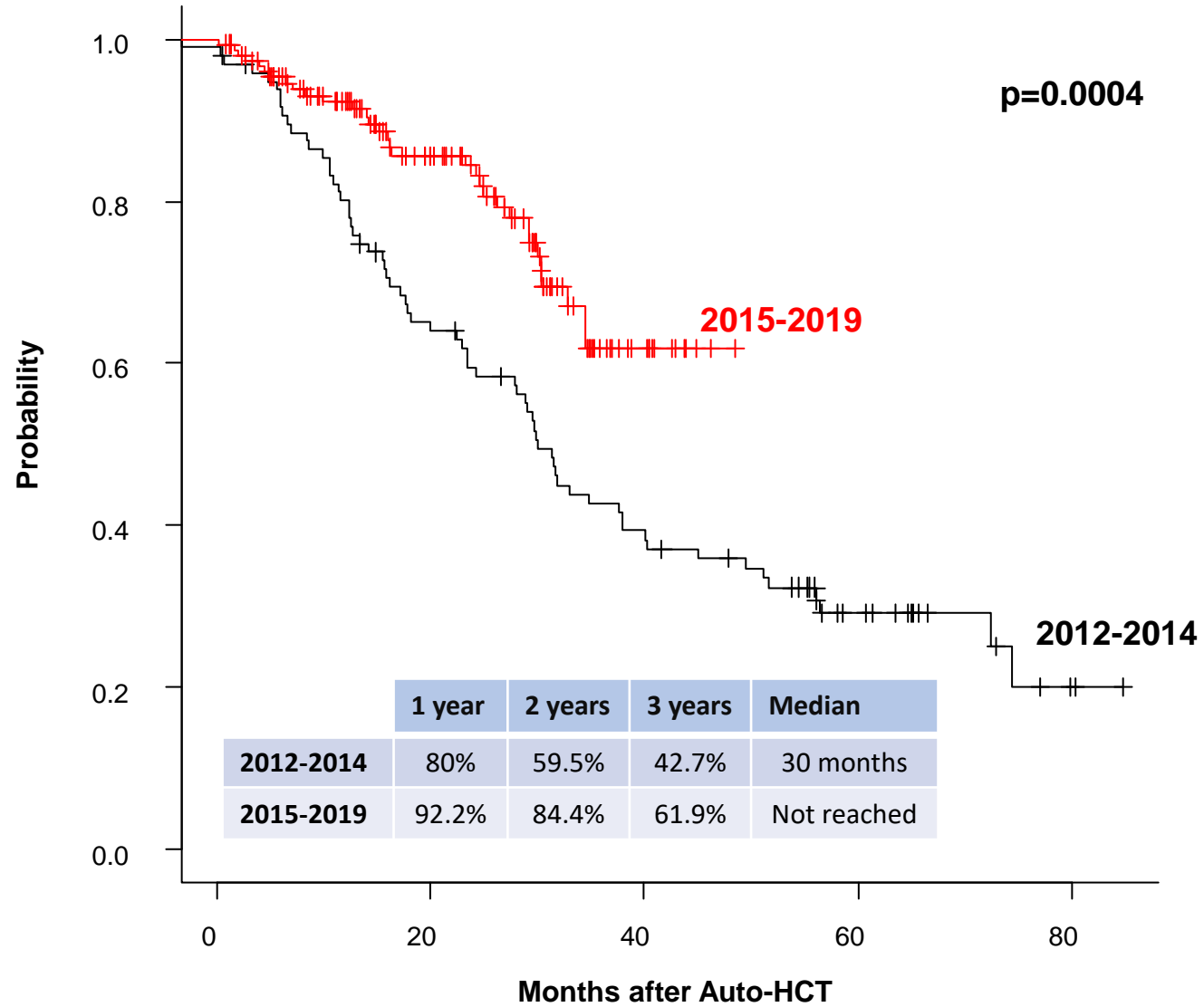
	2016	2017	2018	2019	2020
N	35	42	33	25	38
Median Age	59	61	63	65	61.5

Trends in Survival after Allogeneic HCT for Acute Myelogenous Leukemia (AML), Age ≥ 18 Years, in the US, 2001-2018

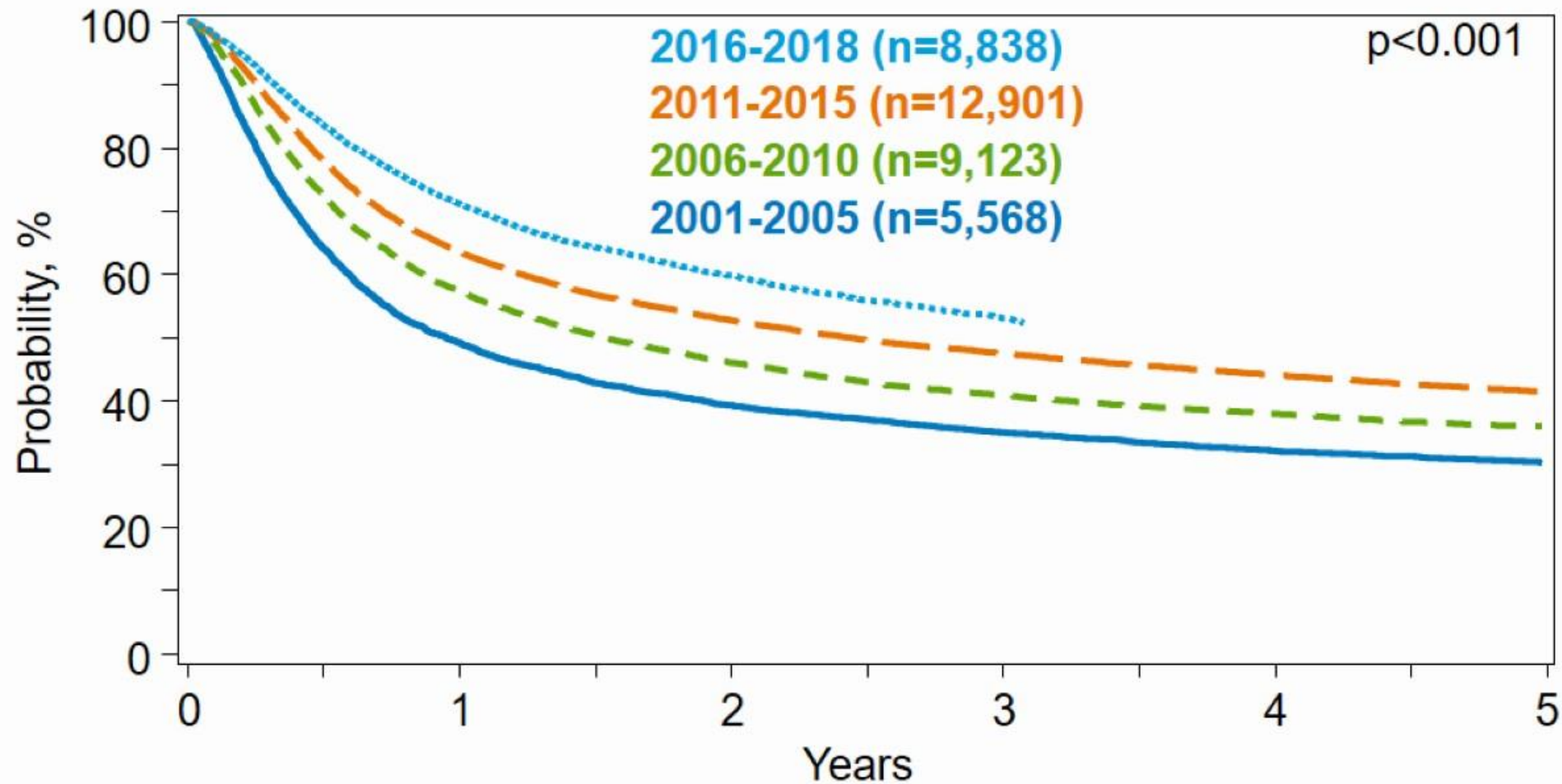


ALL AUTO-HCT FOR MULTIPLE MYELOMA (2012-2019)

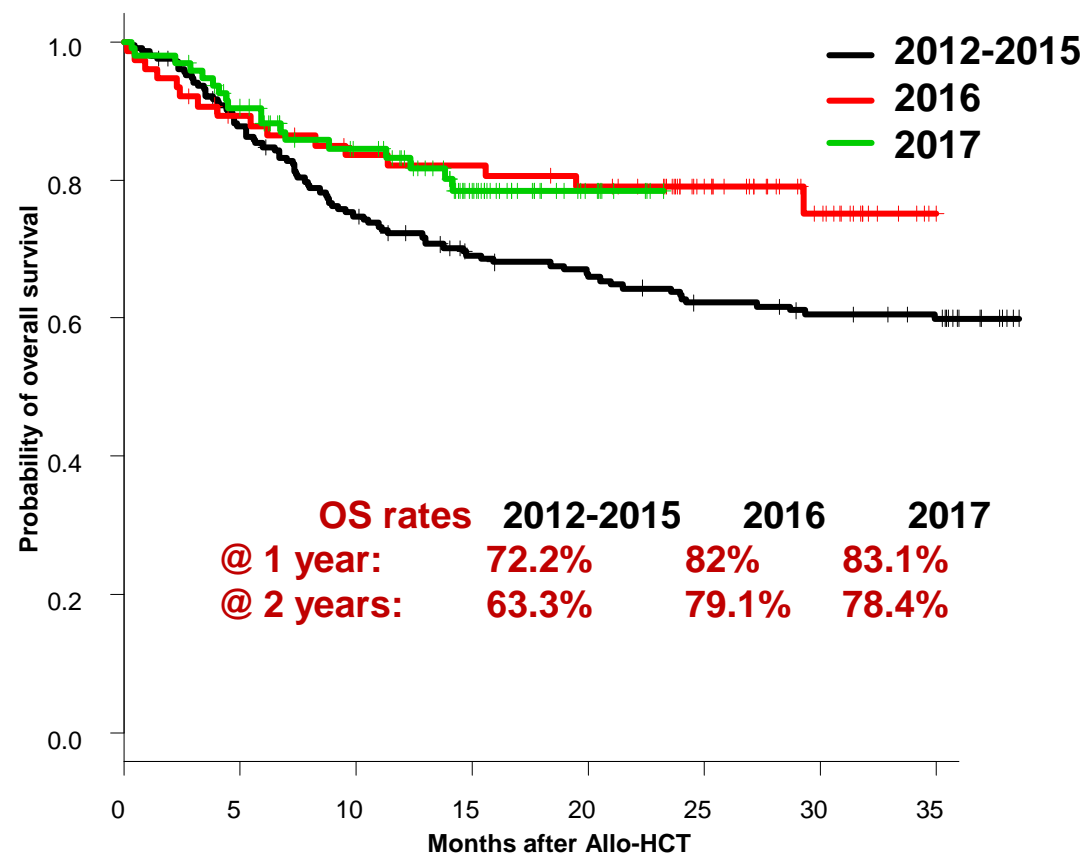
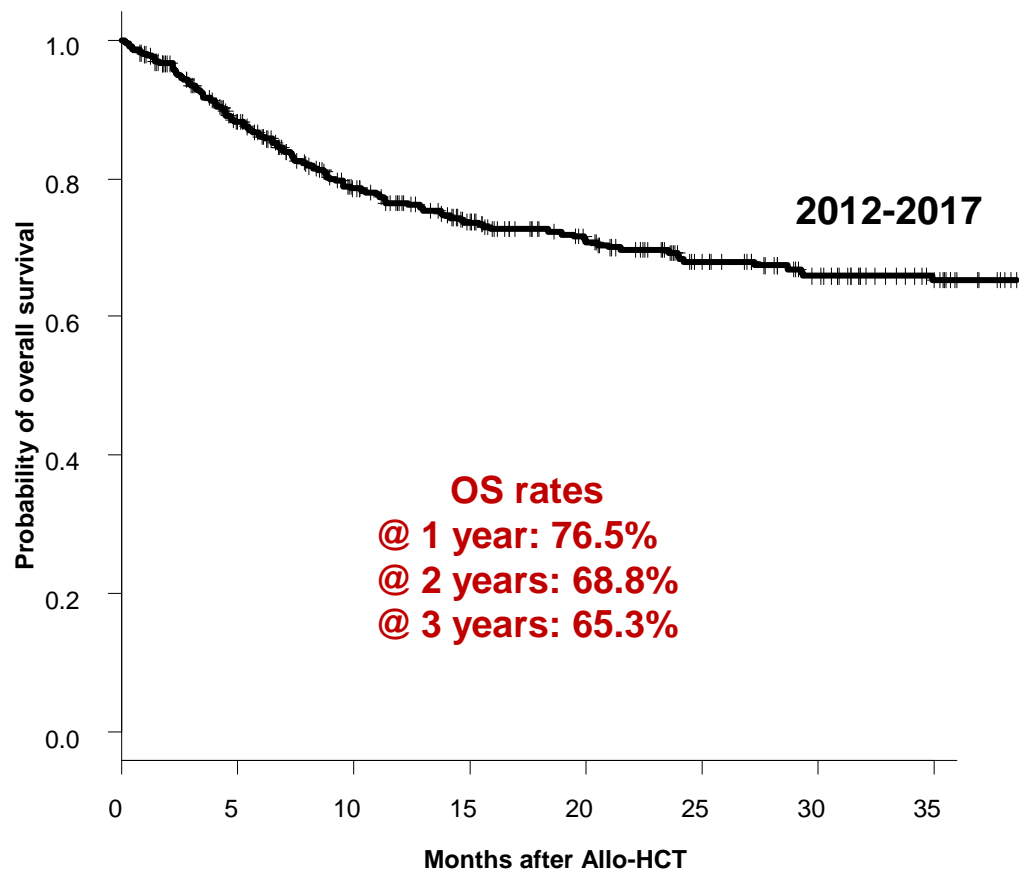
PFS



Trends in Survival after Allogeneic HCT for Acute Myelogenous Leukemia (AML), Age ≥ 18 Years, in the US, 2001-2018



ALLO-HCT: OVERALL SURVIVAL

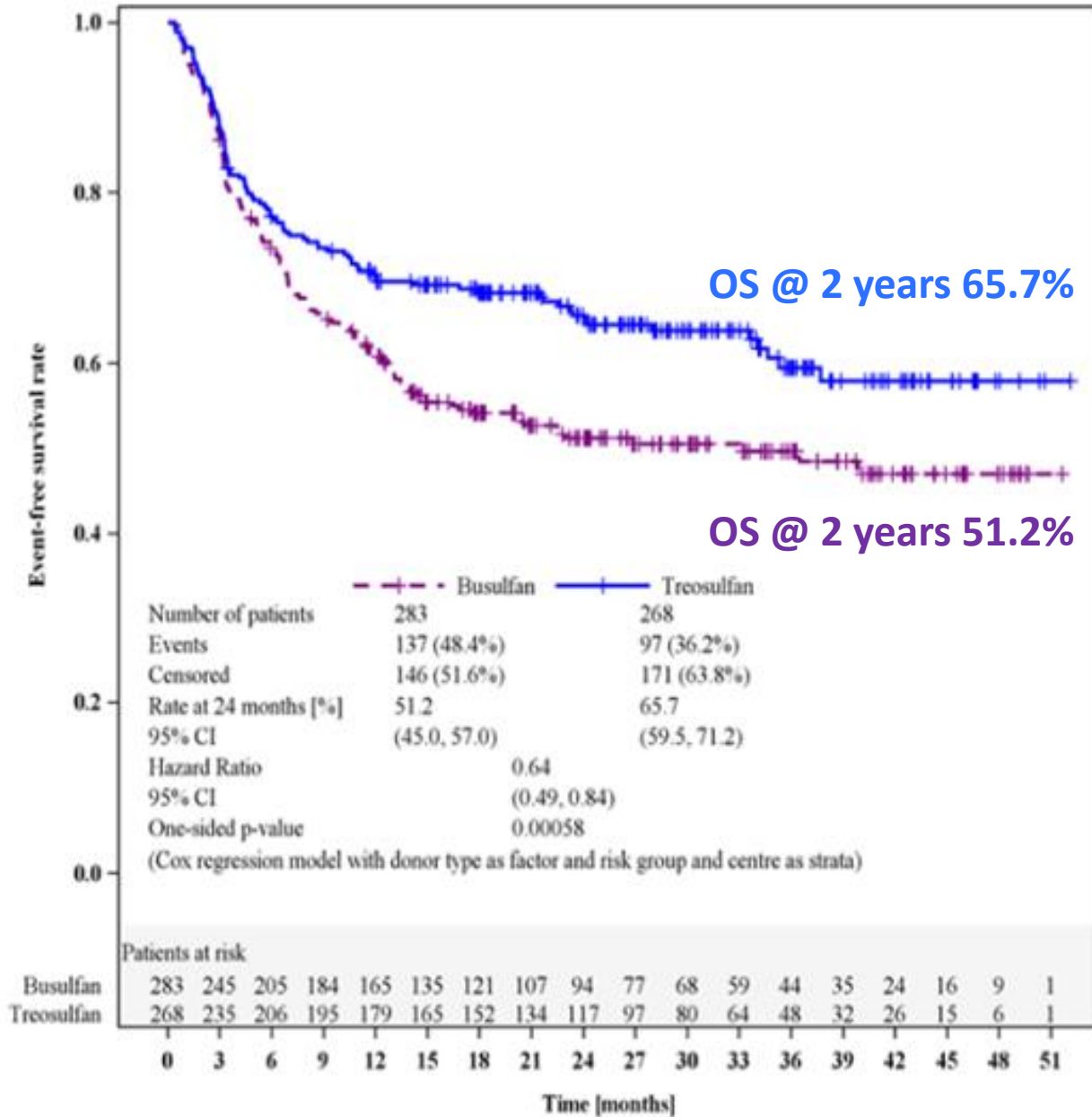


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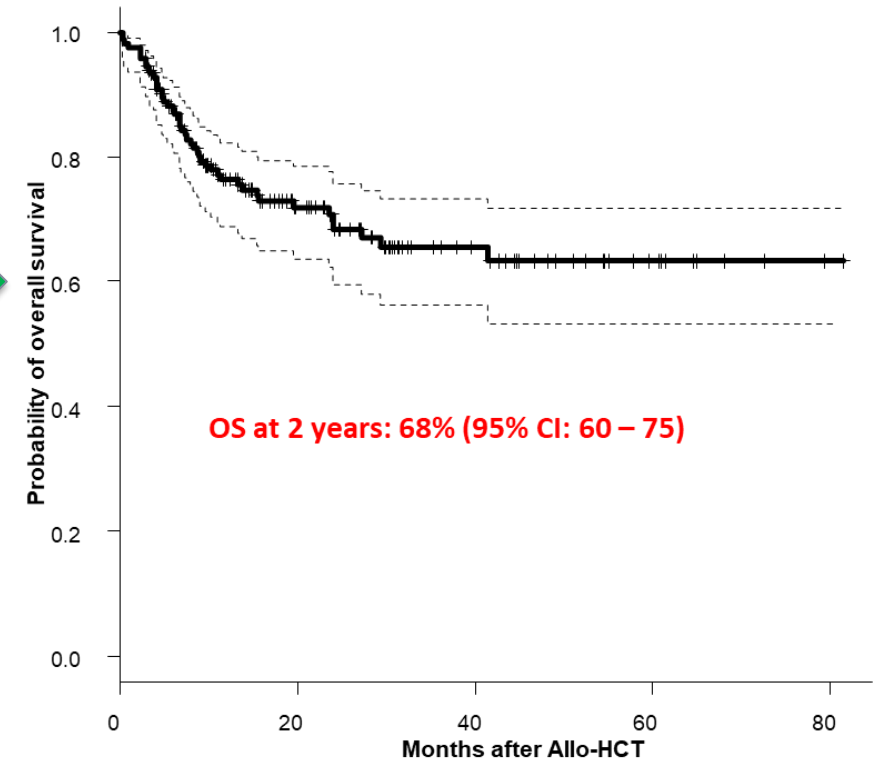
ADVANCES IN THE CONDITIONING SETTINGS

IMPROVED SURVIVAL OF AML- AND MDS-PATIENTS AFTER TREOSULFAN-BASED COMPARED TO REDUCED-INTENSITY BUSULFAN-BASED CONDITIONING-REGIMEN FOR ALLOGENEIC HAEMATOPOIETIC CELL TRANSPLANTATION: FINAL RESULTS OF A PROSPECTIVE RANDOMISED PHASE-III-TRIAL

Dietrich Beelen¹ et al. EBMT 2019



TOH TCT PROGRAMME RESULTS – OS MDS + AL IN CR

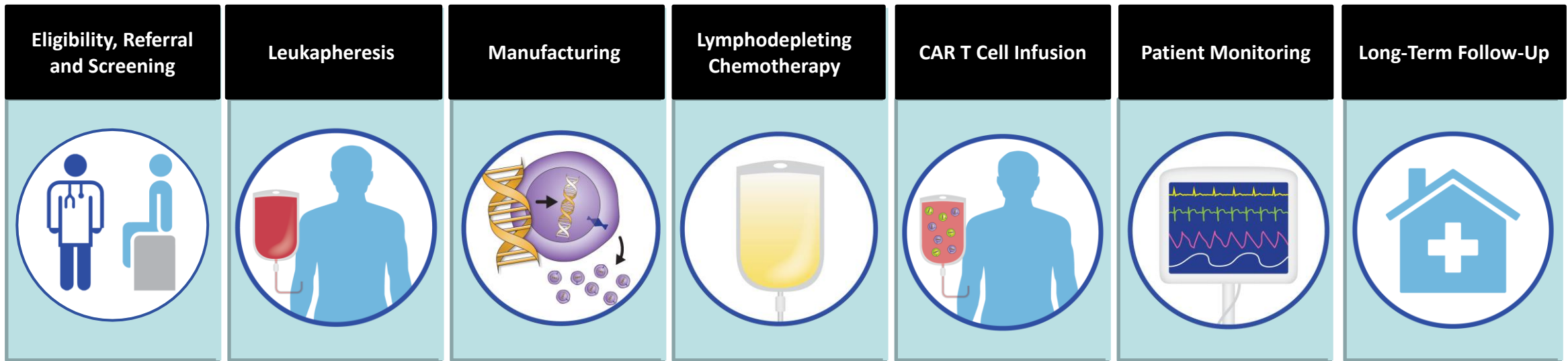


CAR T CELLS

- NK also the future of our programme
- Nationally recognized for developing made in Canada CAR T Cells with BIOCANRx



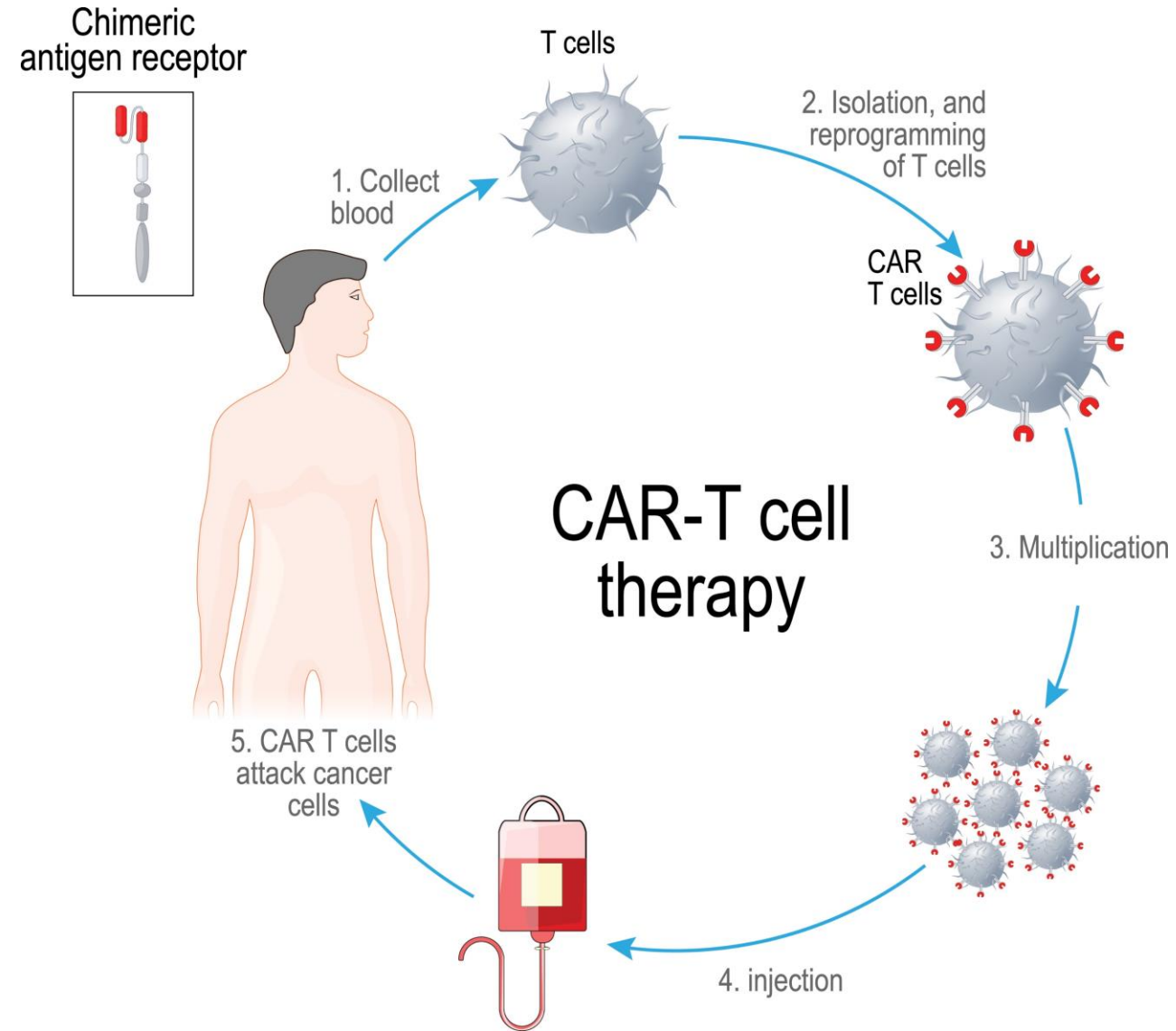
CAR-T Cell Treatment Journey Overview



Path for referring centre:

- Begins with referral to an approved treatment centre
- Referring site plays active role in salvage, bridging therapy and long-term patient care and monitoring
- Repatriation back to referring physician for follow up expected 4 weeks after infusion

CAR T CELLS



Lymphoma Indications: Yescarta & Kymriah

- Diffuse large B-cell lymphoma (DLBCL) not otherwise specified
- High grade B-cell lymphoma with MYC and BCL2 and/or BCL6 rearrangements (double or triple hit by FISH) or not otherwise specified
- DLBCL arising from follicular lymphoma
- Primary mediastinal large B-cell lymphoma (PMBCL) – axicabtagene ciloleucel

Exclusions:

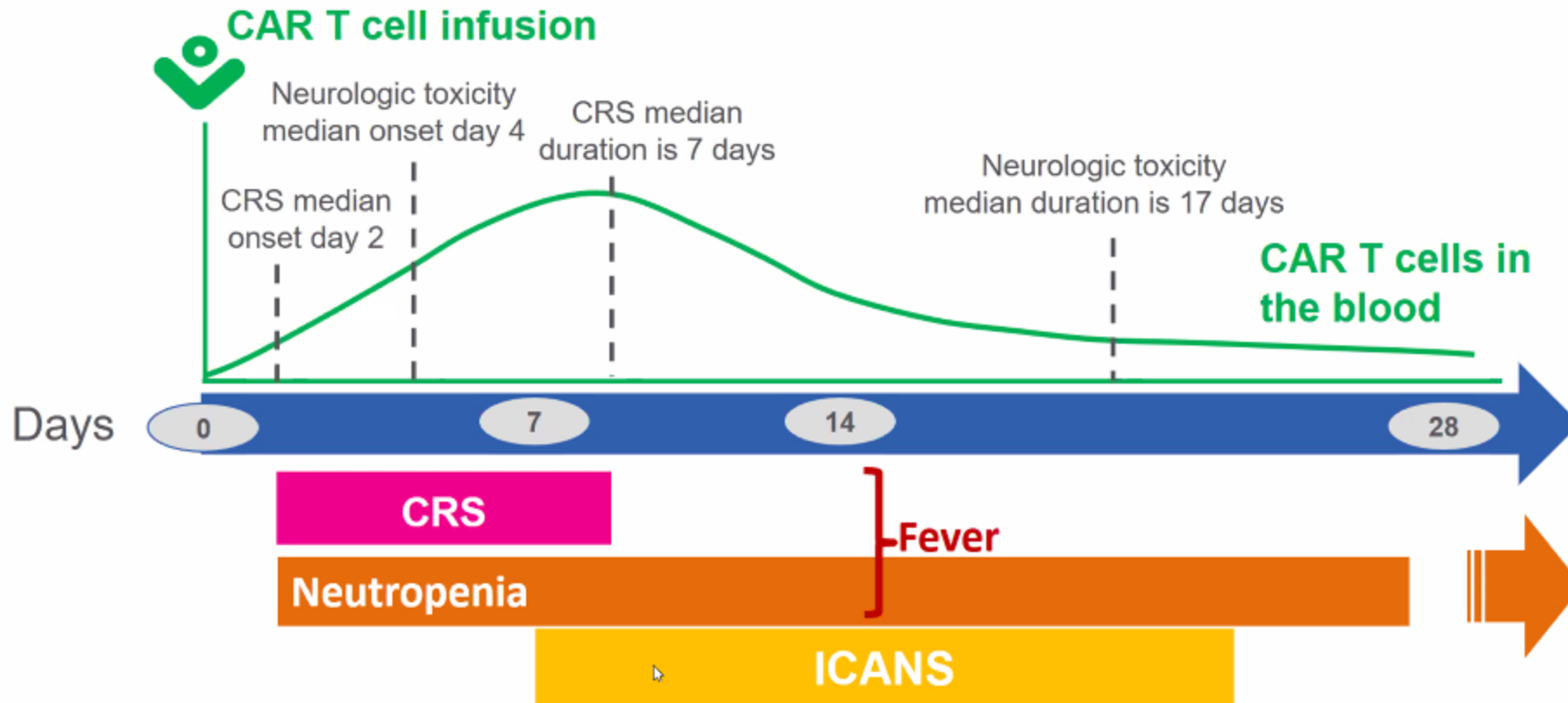
- Richter transformation (DLBCL from CLL), mantle cell lymphoma, Burkitt lymphoma, follicular lymphoma

Leukemia Indication: Kymriah

- Patient has CD19+ B-cell acute lymphoblastic leukemia (ALL)
- Patient is 25 years of age or younger
- Disease status is refractory, relapsed after allogeneic stem cell transplant (SCT), is ineligible for SCT, or has experienced second or later relapse.



Toxicities related to CAR T-cells infusion



98% of all patients recovered from neurologic adverse reactions

98% of all patients recovered from CRS

Adapted from Lee DW, et al. *Blood*. 2014;124:188-195. 2.

Autologous HCT for Autoimmune Diseases

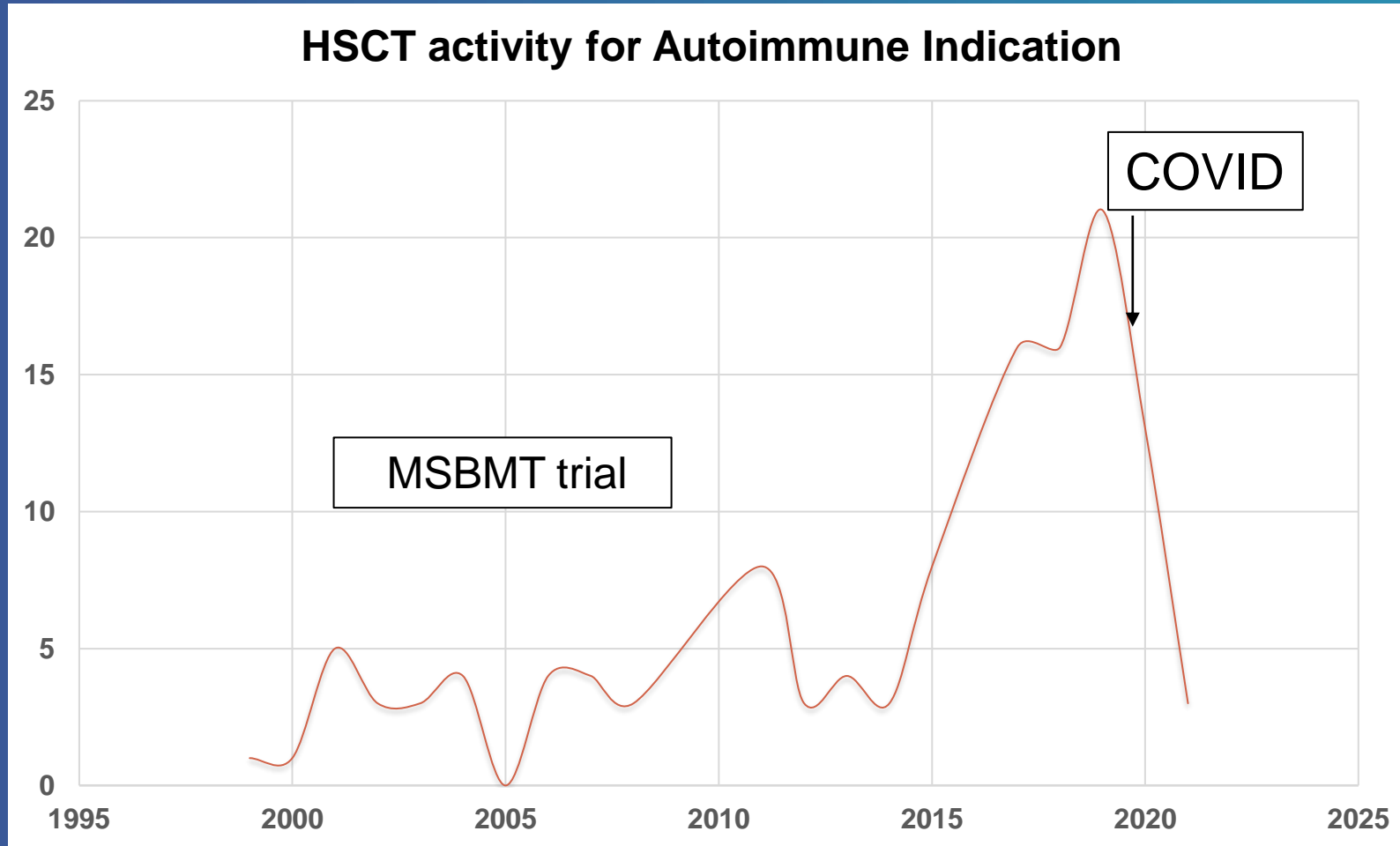
- HA an internationally recognized innovator
- Has a fondness for Hawaiian shirts





HSCT for AID – slow adoption but accelerating

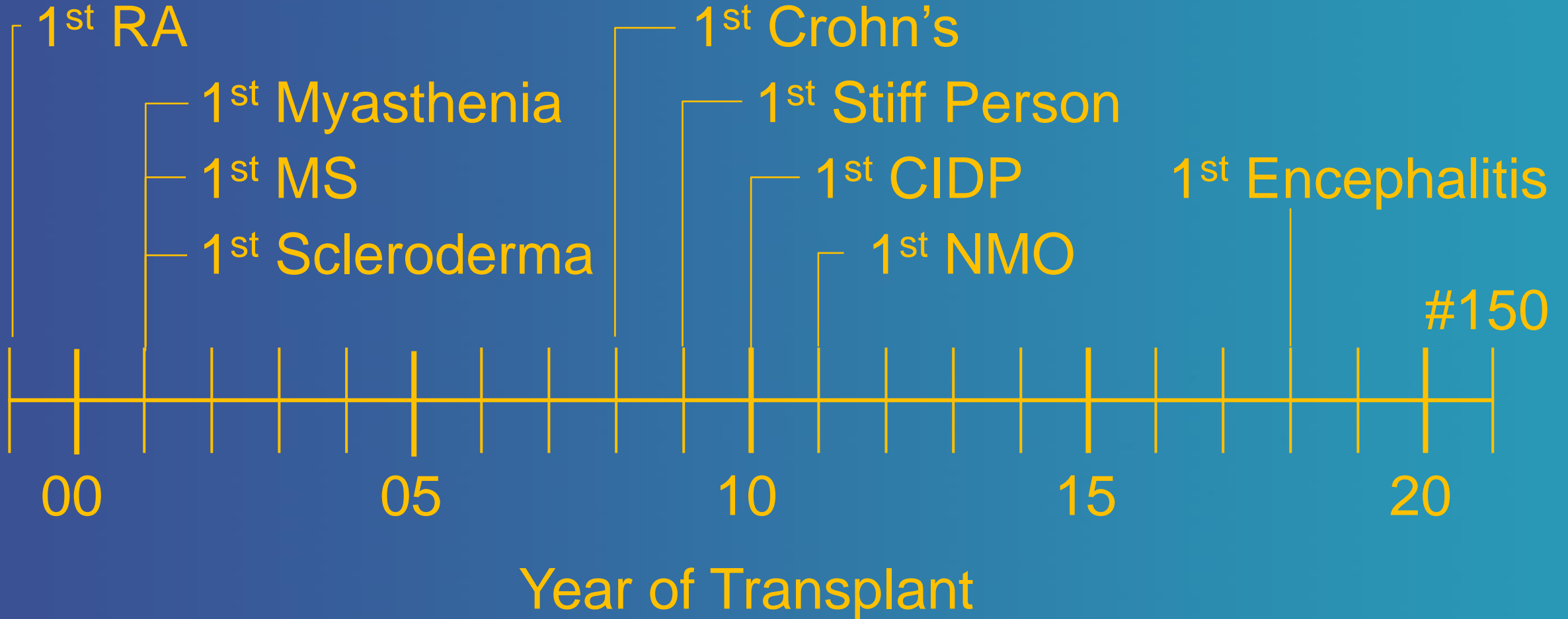
Number
Of
HSCT



Updated Feb 2021



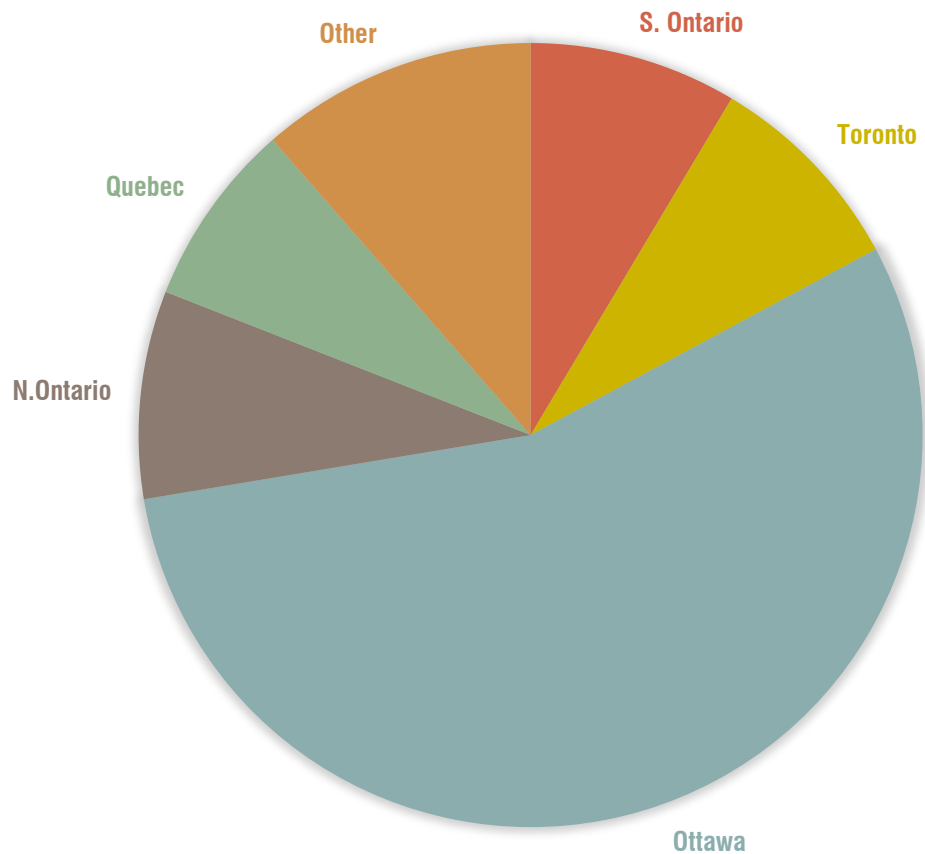
“Build it and they will come?” or “nothing left to try?”



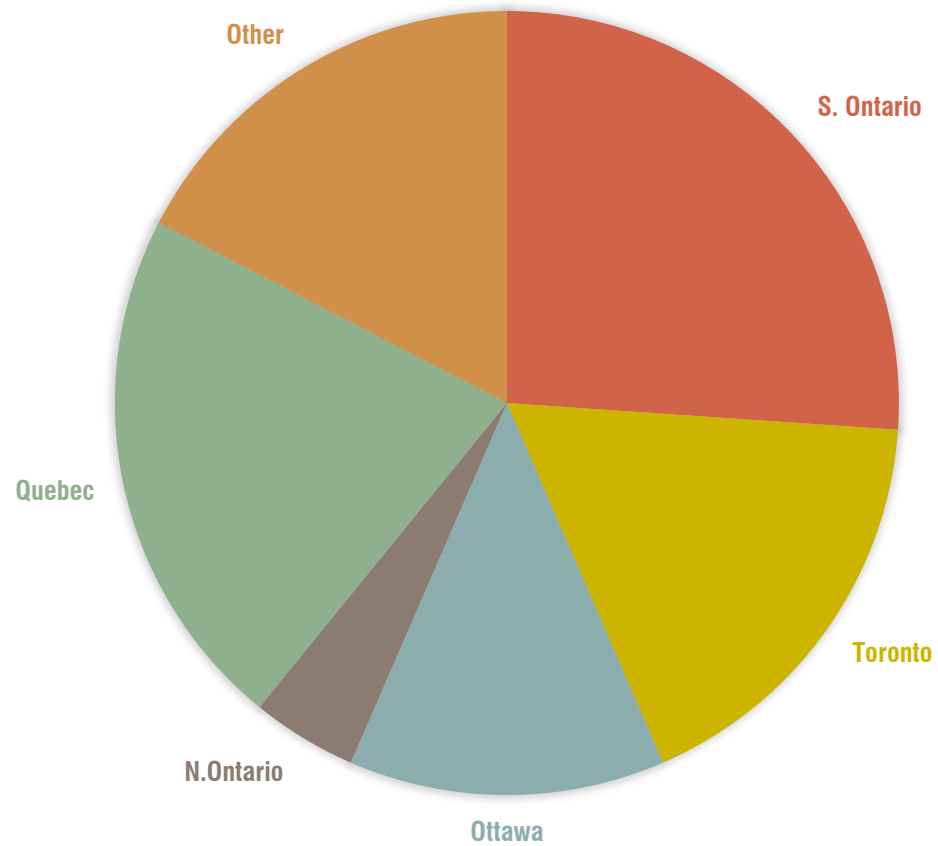


Geographic Region of Patients.

NEURO-AID



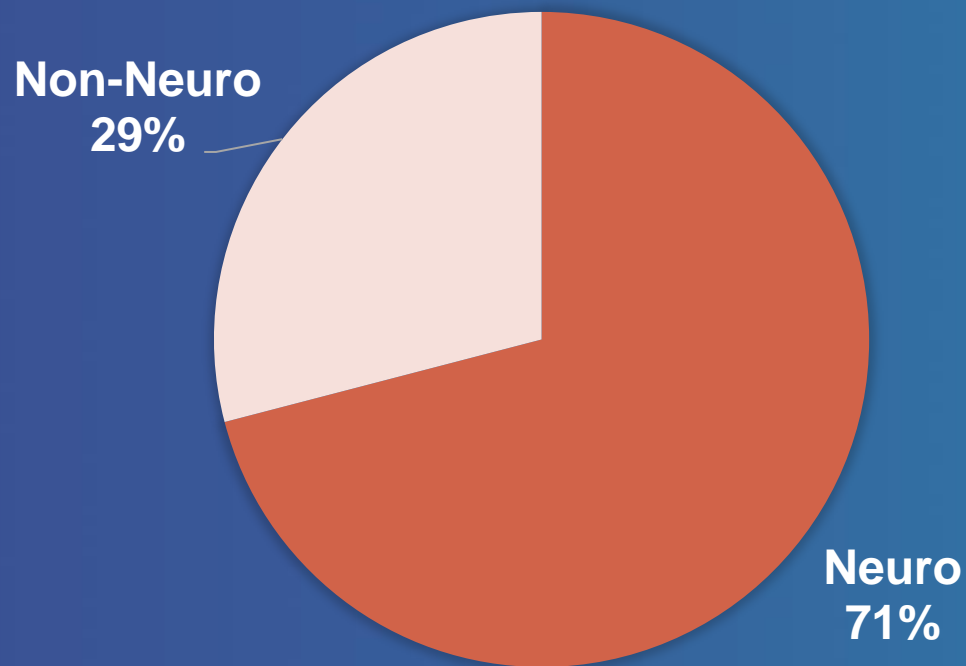
RHEUM-AID





Stem Cell Transplant Indication – Neuro AID

INDICATION



Indication	
Multiple Sclerosis	72
Myasthenia Gravis	12
CIDP	7
Stiff Person Syndrome	7
Neuromyelitis Optica	6
Autoimmune Encephalitis	3
Total	107



AutoHSCT for MS – Clinical Relapse

Before HSCT

Clinical Data on 42 pts

- 195.9 pt-years follow-up
- 206 relapse
- 1.1 relapses/pt/year

MRI Data on 53 pts

- 283 scans
- 108 scans with new or enhancing lesions

After HSCT

Clinical Data on 42 pts

- 288 pt-years follow-up
- 0 relapses
- 0 relapses/pt/year

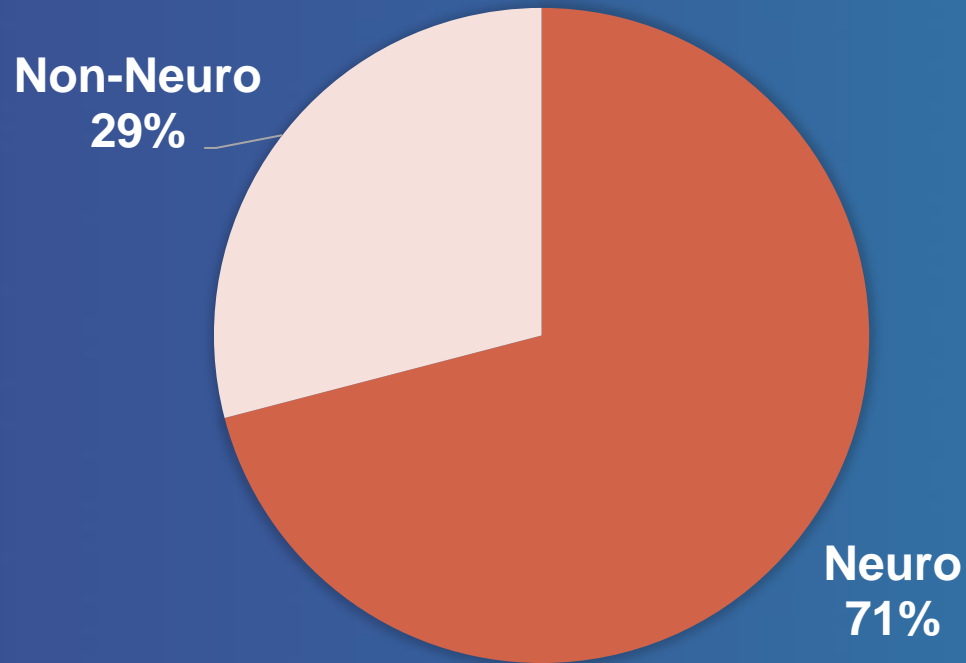
MRI Data on 52 pts

- 650 scans
- 2 scan with new or enhancing lesion



Stem Cell Transplant Indication – Non-Neuro AID

INDICATION

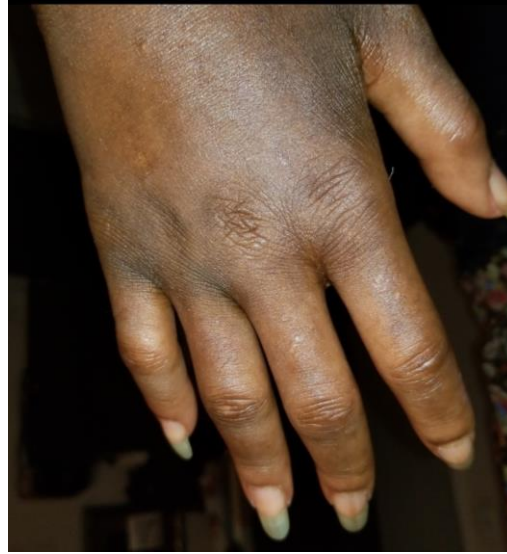


Indication	
Scleroderma	26
Rheumatoid Arthritis	4
PSC	5
Crohn's Disease	6
ITP	1
APLS	1
Total	44



Scleroderma - Skin Remodeling

Prior to
HSCT



6 weeks
after HSCT





Questions?



- My happy place...