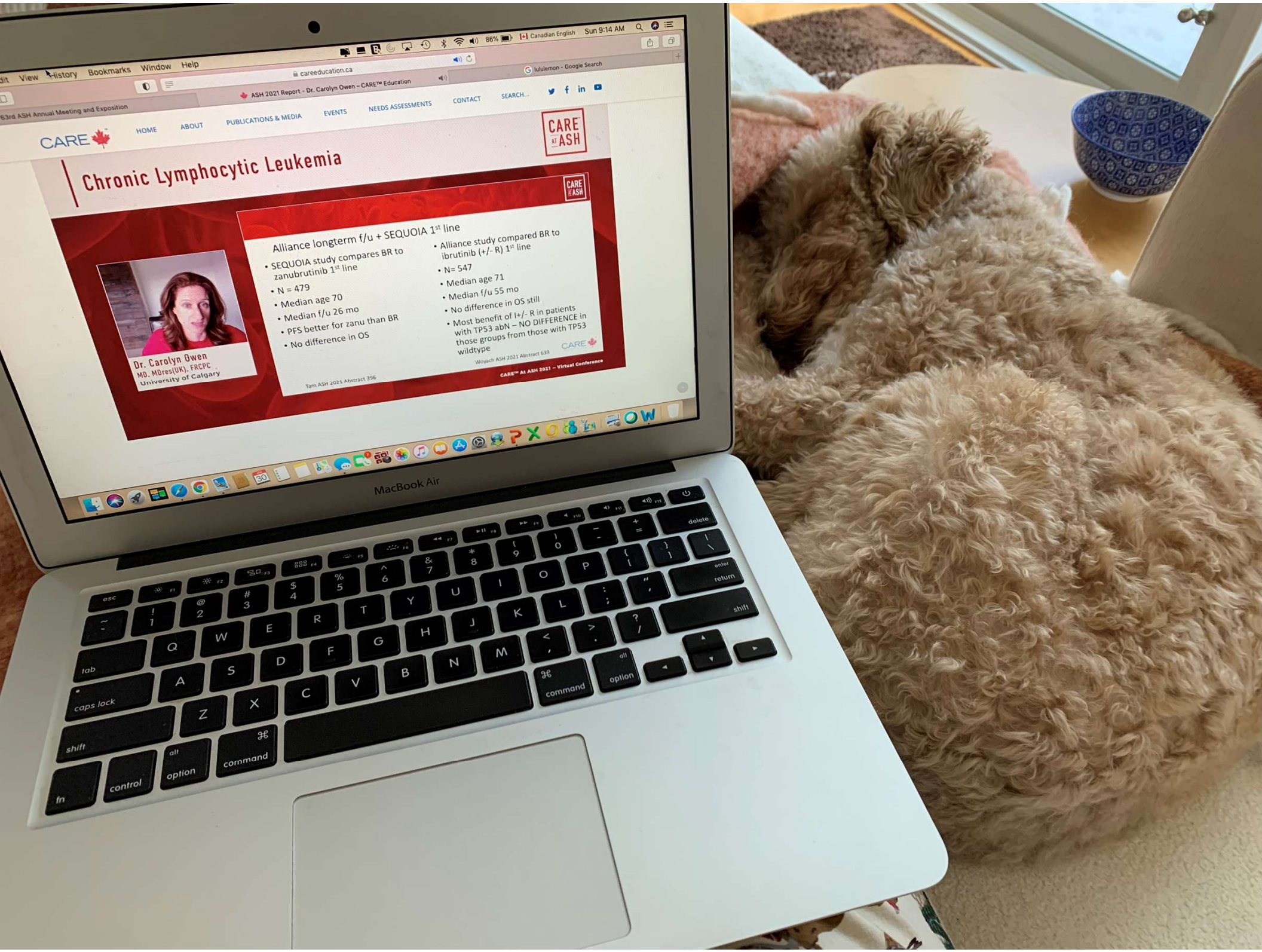
ASH 2021 - Update on Lymphoma Treatments

Lymphoma Support Group of Ottawa

Feb 1, 2022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ASH 2021 Report - Dr. Carolyn Owen – CARE™ Education
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CARE AT ASH
Chronic Lymphocytic Leukemia
Dr. Carolyn Owen
MD, MDres(UK), FRCPC
University of Calgary
Alliance longterm f/u + SEQUOIA 1st line
• SEQUOIA study compares BR to zanubrutinib 1st line
• N = 479
• Median age 70
• Median f/u 26 mo
• PFS better for zanu than BR
• No difference in OS
• Alliance study compared BR to ibrutinib (+/- R) 1st line
• N= 547
• Median age 71
• Median f/u 55 mo
• No difference in OS still
• Most benefit of I+/- R in patients with TP53 abN – NO DIFFERENCE in those groups from those with TP53 wildtype
Woyach ASH 2021 Abstract 639
Tam ASH 2021 Abstract 396
CARE™ At ASH 2021 – Virtual Conference
MacBook Air

- Advances being made across all spectrums
  - Hodgkin and non-Hodgkin lymphomas
  - Indolent and aggressive diseases
  - Frontline and relapsed setting

Profiling of Circulating Tumor DNA for Noninvasive Disease Detection, Risk Stratification, and MRD Monitoring in Patients with CNS Lymphoma

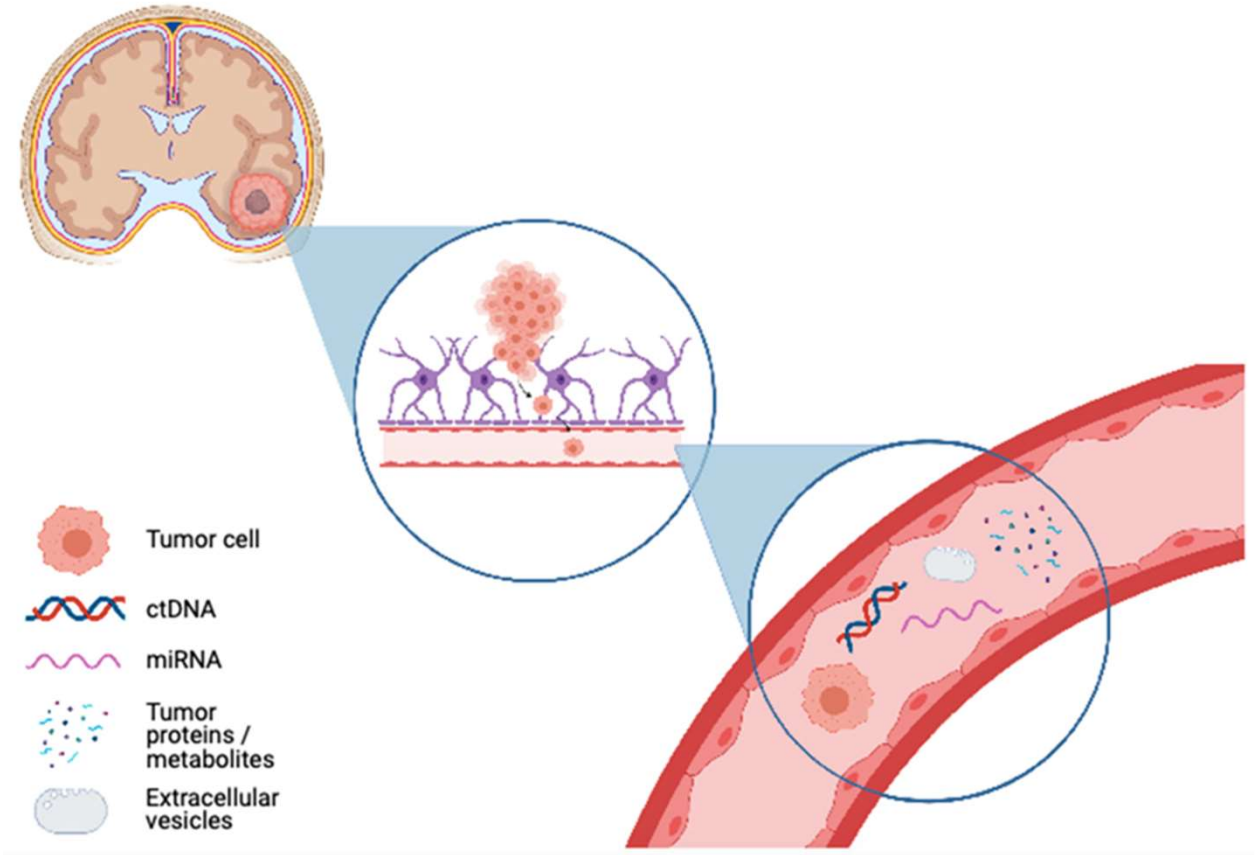
Paper Number: 6

Florian Scherer, MD ♡
University Medical Center Freiburg

Background

- Primary CNS lymphoma is an aggressive lymphoma which affects mainly the brain
- Relatively rare
- Diagnosis can be challenging and often requires very invasive procedures (eg. brain biopsy)
- Sometimes these biopsies cannot be done or are non-diagnostic

Circulating Tumor DNA



mdpi.com

-Tumor-derived fragments of DNA in the bloodstream

-”Liquid biopsies”

Abstract #6

- Used specialized DNA sequencing techniques
- 85 tumor biopsies, 131 blood samples, 62 CSF samples
- 92 patients with CNSL, 44 with other brain cancers or brain diseases
- Looked for hundreds of mutations
- Were able to demonstrate robust and sensitive detection of ctDNA at various milestones in CNSL (diagnosis, remission, relapse etc.)

The POLARIX Study: Polatuzumab Vedotin with Rituximab, Cyclophosphamide, Doxorubicin, and Prednisone (pola-R-CHP) Versus Rituximab, Cyclophosphamide, Doxorubicin, Vincristine and Prednisone (R-CHOP) Therapy in Patients with Previously Untreated Diffuse Large B-Cell Lymphoma

Paper Number: LBA-1

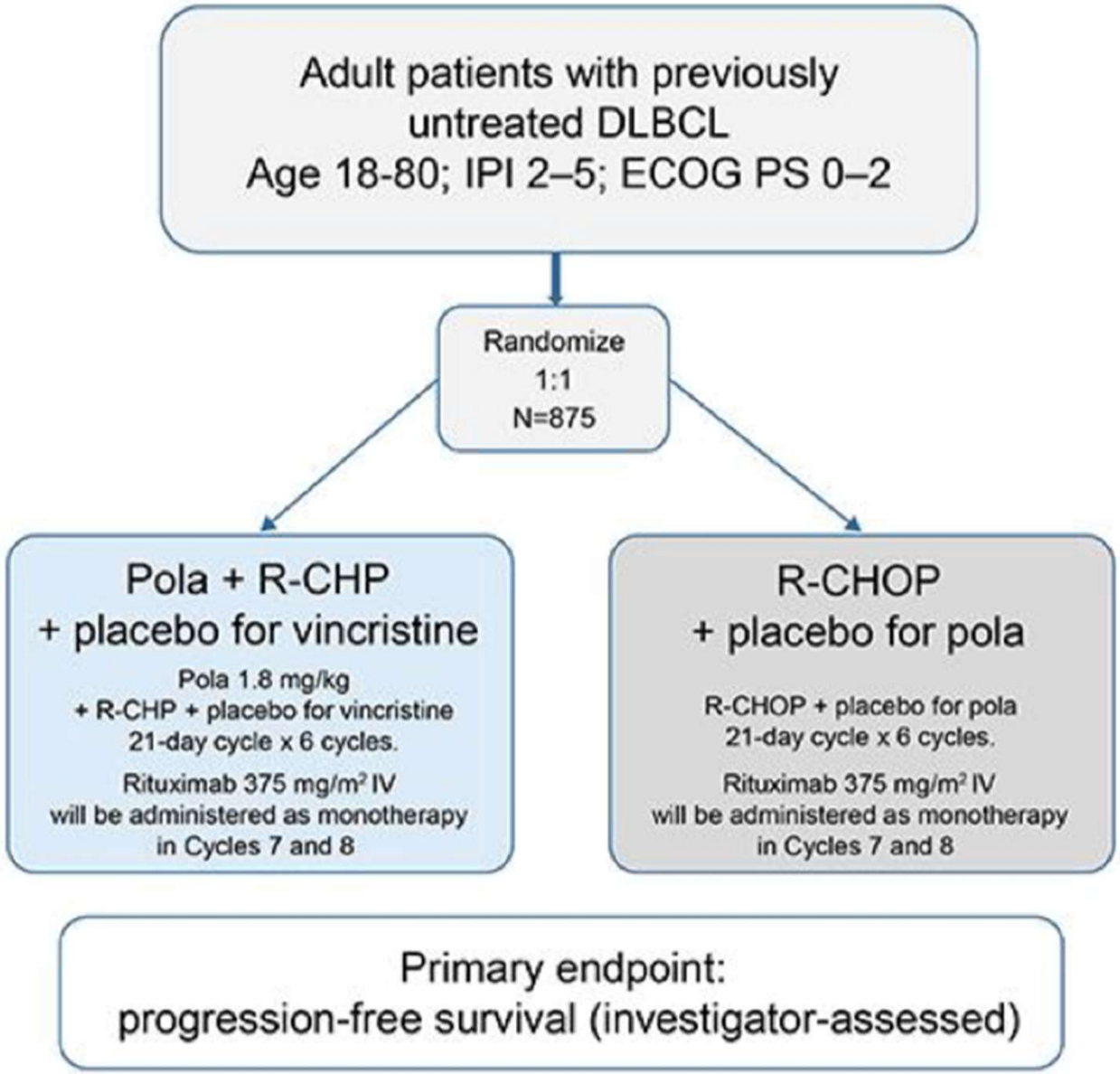
Hervé Tilly, MD ♡

Department of Hematology and U1245, Centre Henri Becquerel and University of Rouen

Background

- DLBCL is the most common type of aggressive non-Hodgkin lymphoma
- Again, approximately 60% of patients are cured with front-line therapy
- Standard therapy = R-CHOP chemotherapy
- Have been using this for years
- Many studies have tried to find regimens which would “beat” R-CHOP – none so far

POLARIX



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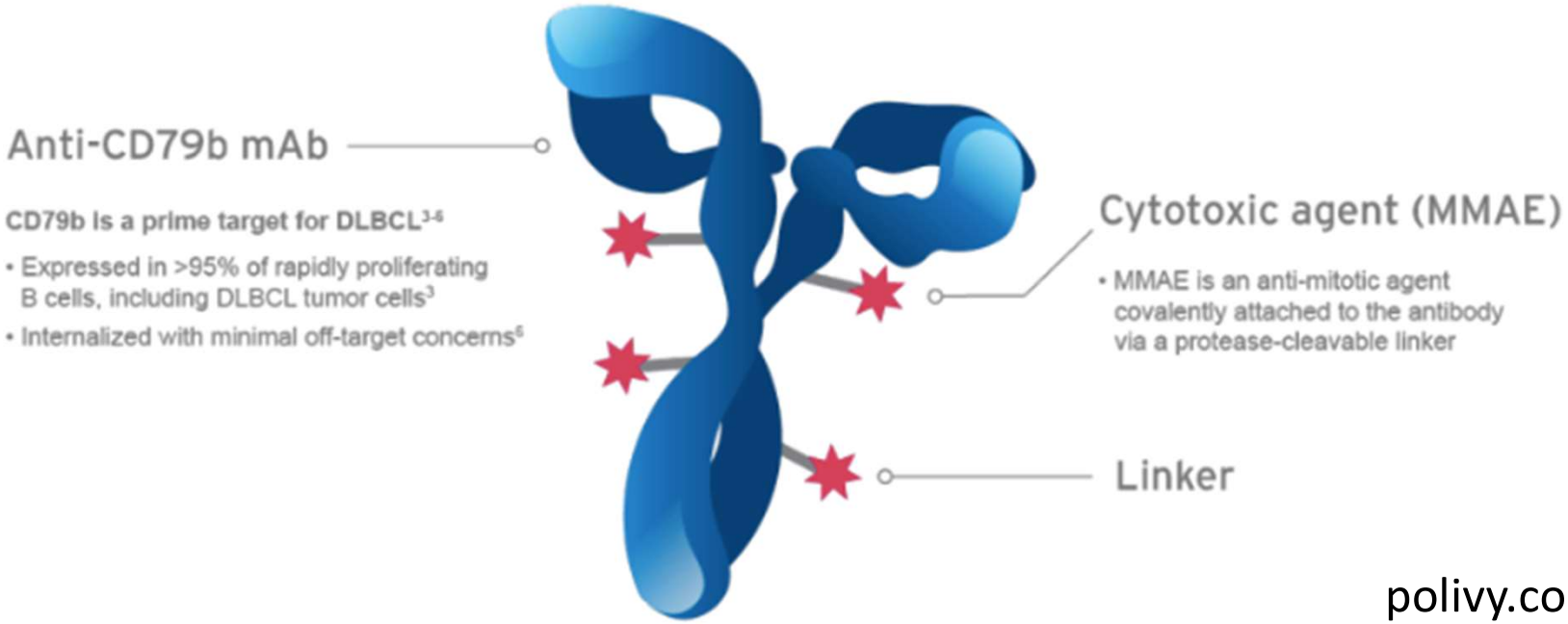
Polatuzumab

POLIVY is composed of the potent cytotoxin monomethyl auristatin E (MMAE) and a CD79b-targeted monoclonal antibody (mAb)[1,3-6]



polivy.com

-Antibody-drug conjugate (ADC)
-Anti-CD79b monoclonal antibody
-Delivers MMAE into the cancer cell

Polarix

- 2 year PFS 76% with pola-R-CHP, compared to 70% with R-CHOP
- Pola-R-CHP led to a 27% relative risk reduction in disease progression, relapse or death
- ?Cost-effectiveness of this approach

Frontline Treatment with Single Agent Pembrolizumab (PEM) Followed By AVD Chemotherapy for Classic Hodgkin Lymphoma: Updated Results and Correlative Analysis

Paper Number: 231

Pamela Allen, MD ♡

Winship Cancer Institute at Emory University

Mosunetuzumab Monotherapy Is an Effective and Well-Tolerated Treatment Option for Patients with Relapsed/Refractory (R/R) Follicular Lymphoma (FL) Who Have Received ≥2 Prior Lines of Therapy: Pivotal Results from a Phase I/II Study

Paper Number: 127

L. Budde ♡
City of Hope

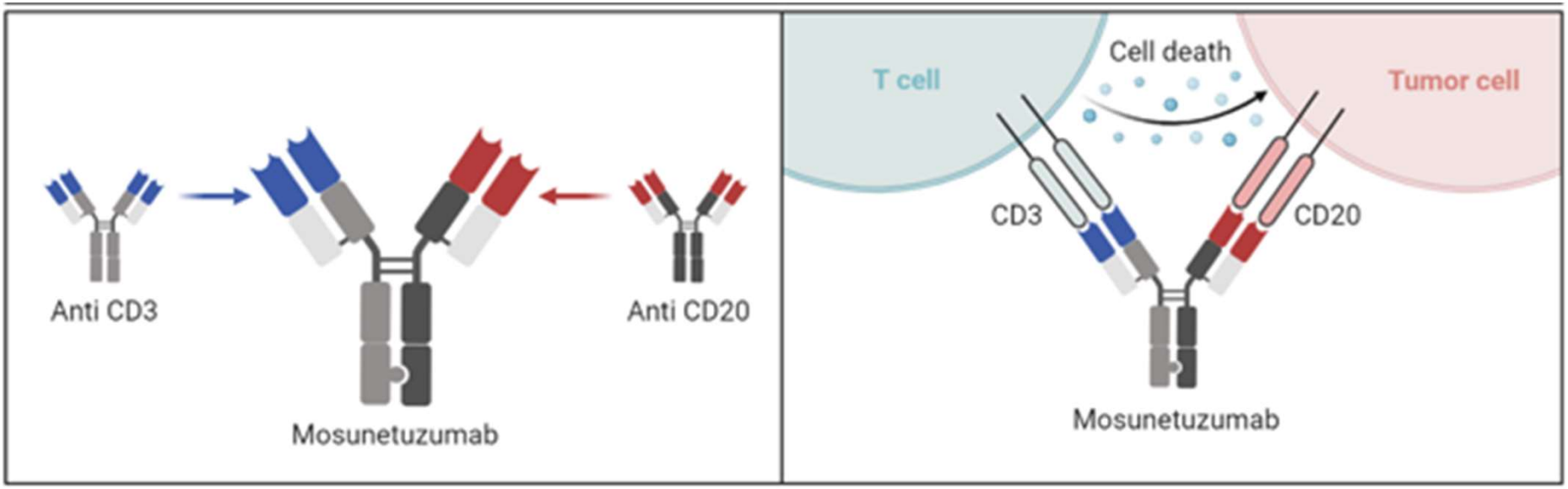
Background

- Follicular lymphoma is the most common indolent (non-aggressive) non-Hodgkin lymphoma
- Median survival today is 18-20 years
- Some patients will initially be placed on watchful waiting
- Some will need treatment on repeat occasions throughout their lives
- Some patients relapse early after receiving therapy (POD24)

Background

- Most patients today in Ontario will receive bendamustine-rituximab (BR) as their first line of therapy (immunochemotherapy)
- Numerous options for time of relapse
  - Immunochemotherapy
  - Novel (oral) agents
  - Bone marrow transplant
  - Experimental: CAR-T, BITE

Mosunetuzumab



molecularcloud.org

-Bispecific antibody
-T-cell engager
-”BITE”

Abstract #127

- Early phase study
- Patients with relapsed/refractory follicular lymphoma, who have received at least 2 prior lines of therapy
- Mosun administered IV every 21 days

Abstract #127

Population	ORR, % (95% CI)	CR rate, % (95% CI)
All 3L+ R/R FL pts, n=90	79 (69–87)	58 (47–68)
Pts with POD24, n=47	83 (69–92)	55 (40–70)
Pts with 2 prior lines of therapy, n=34	85 (69–95)	68 (49–83)
Pts with ≥3 prior lines of therapy, n=56	75 (62–86)	52 (38–65)
Pts with disease refractory to any prior anti-CD20 Ab therapy, n=71	76 (64–85)	52 (40–64)
Pts with disease refractory to any prior anti-CD20 Ab therapy and an alkylator (double refractory), n=48	69 (54–81)	48 (33–63)
Pts with disease refractory to their last prior therapy, n=62	76 (63–86)	48 (35–61)

Primary Analysis of ZUMA-7: A Phase 3 Randomized Trial of Axicabtagene Ciloleucel (Axi-Cel) Versus Standard-of-Care Therapy in Patients with Relapsed/Refractory Large B-Cell Lymphoma

Paper Number: 2

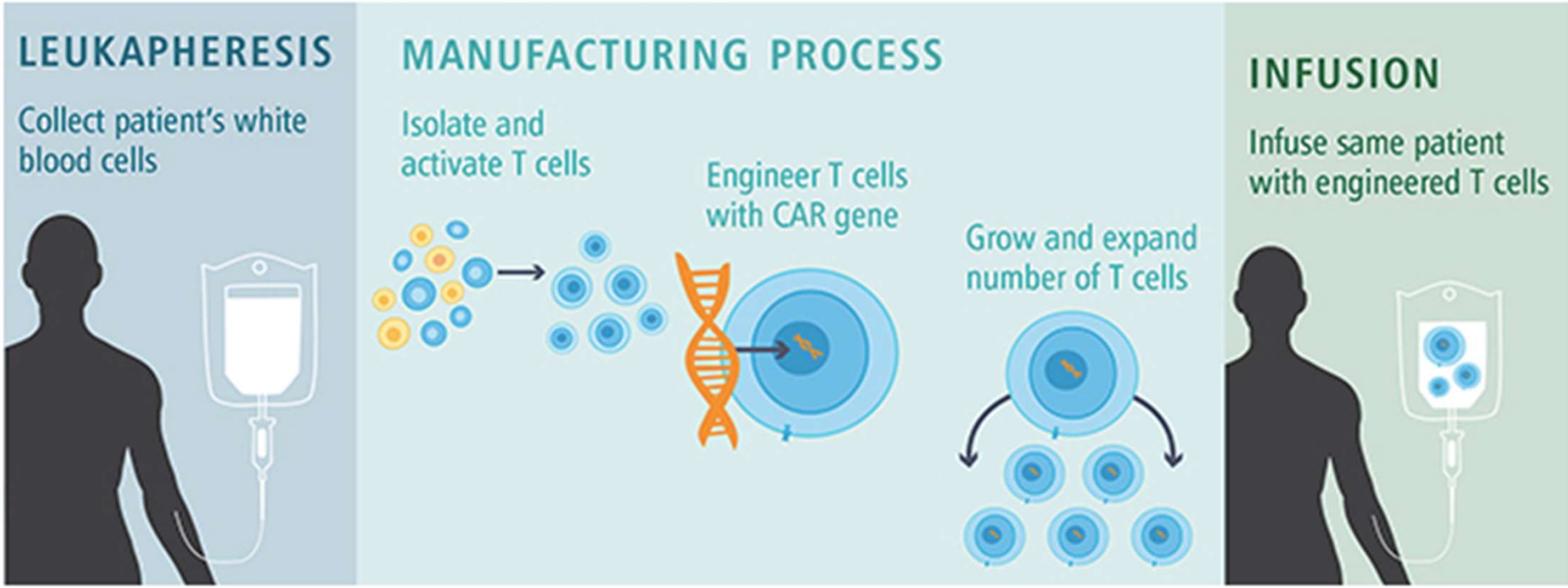
Frederick Locke, MD ♡

Moffitt Cancer Center

Background

- Aggressive non-Hodgkin lymphomas (DLBCL)
- Currently most patients treated with R-CHOP
- About 60% will be cured with this
- This means that 40% either do not go into remission or relapse
- Currently if someone is not in remission or relapses, the first step is to administer more chemotherapy → autologous bone marrow transplant

How CAR T-Cell Therapy Works



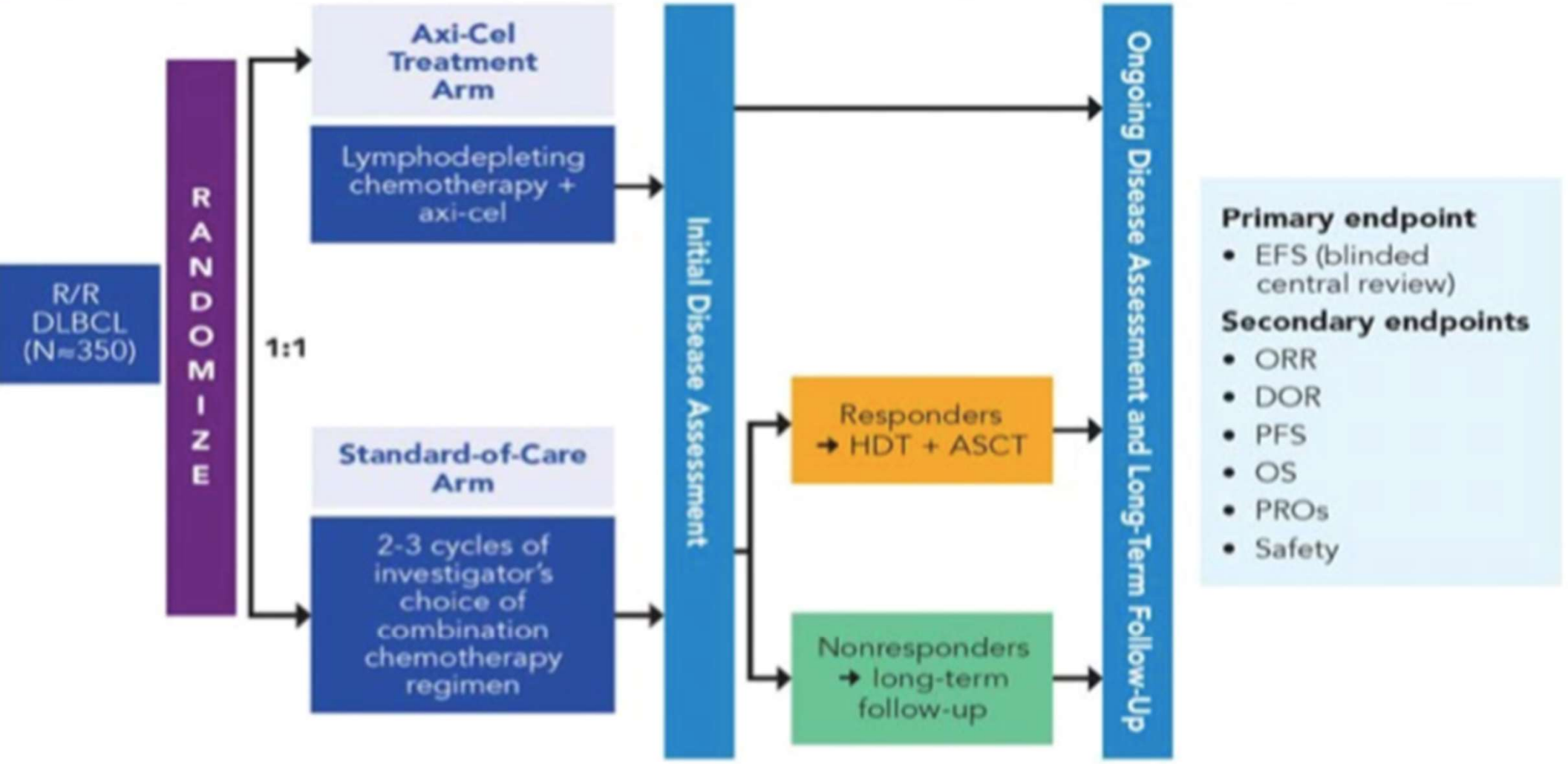
Dana-farber.org

CURRENTLY IN ONTARIO

-**Approved for**: DLBCL/high grade lymphomas which have failed two lines of therapy; B-ALL

-**Still experimental**: follicular lymphoma, mantle cell lymphoma, CLL, etc

ZUMA-7



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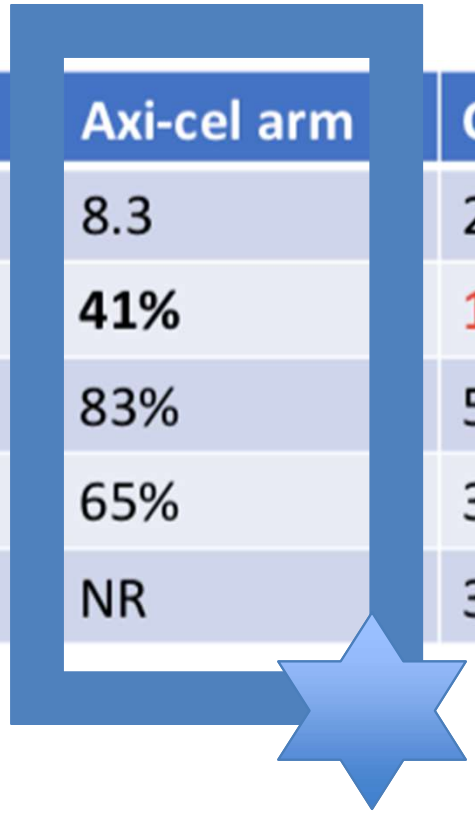
ZUMA-7

	Axi-cel arm	CIT and autoHCT arm	Stats
mEFS (months)	8.3	2.0	HR 0.398, p<.0001
24-month EFS	**41%**	16%	
ORR	83%	50%	OR 5.31, p<.0001
CR	65%	32%	
mOS (months)	NR	35.1	HR 0.730, p=.027



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A Randomized Phase III Study of Venetoclax-Based Time-Limited Combination Treatments (RVe, GVe, GIVe) Vs Standard Chemoimmunotherapy (CIT: FCR/BR) in Frontline Chronic Lymphocytic Leukemia (CLL) of Fit Patients: First Co-Primary Endpoint Analysis of the International Intergroup GAIA (CLL13) Trial

Paper Number: 71

Barbara Eichhorst, MD ♡

Department I of Internal Medicine and Center of Integrated Oncology Cologne Bonn, University Hospital

Background

- CLL is the most common leukemia in adults
- Behaves very much like an indolent non-Hodgkin lymphoma
- The field of CLL therapeutics has exploded over the last 5-10 years
- Watchful waiting still standard of care for asymptomatic patients
- Numerous options for patients needing therapy

Publicly funded treatment options in Ontario (constantly evolving)

- **Upfront – mutated IgHV**
  - FCR, bendamustine, GA101-chlorambucil
- **Upfront – unmutated IgHV, 17p del, TP53 mut**
  - Ibrutinib*
- **Relapsed**
  - Ibrutinib*, venetoclax*, R-venetoclax

CLL13 (GAIA)

- Large randomized trial
- “Fit” patients
- Frontline therapy
- Primary endpoint - uMRD

CLL13 (GAIA)

- Winning combinations were:
  - GVe
  - GIVe

- However more adverse events with GIVe

Humoral Response to mRNA Vaccines BNT162b2 and mRNA-1273 COVID-19 in Chronic Lymphocytic Leukemia Patients

Paper Number: 637

Cristina Bagacean, MD,PhD ♡
Inserm UMR1227

Abstract #637

- 530 patients with CLL
- 71% Pfizer, 14% Moderna, 15% mixed
- 40% untreated, 26% prior treatment, 34% on treatment

- Response rates to vaccines:
  - 27% after 1st dose (all comers)
  - 52% after 2nd dose (all comers)

  - 35% after 3rd dose (this was in patients who had no response after 2nd dose)

Response rates according to treatment status

- 1st dose
  - 34% untreated, 33% prior treatment, 15% on treatment
- 2nd dose
  - 72% untreated, 60% prior treatment, 22% on treatment

Response rates for those on treatment, according to type

- BTKi – 22%
- Venetoclax – 52% (significantly higher)
- Monoclonal antibody – 0%
- Venetoclax + ibrutinib – 0%