WHAT'S NEW IN CLL?

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MEETING UPDATE

American Society of Hematology

ASH 2025

ASH 2025
TREATMENT-NAÏVE CLL

- **Phase III - CLL17 trial – Fixed-duration vs. continuous targeted treatment (I vs IV vs VO) (GLLSG)**
- **Phase III - Pirtobrutinib vs BR (BRUIN CLL-313) and vs IBR (BRUIN CLL-314) (Lilly)**
- **Phase III - FLAIR updates (IV vs I vs FCR) (UK CLL)**
- **Phase II - Sonrotoclax + obinutuzumab (BeOne)**
- **Phase II - Pirtobrutinib + venetoclax + obinutuzumab (PVO) (MDACC)**
- **Phase II - AV-AVO – late obinutuzumab better tolerated (MDACC)**

ASH 2025
RELAPSED/REFRACTORY CLL

- **Phase III - Pirtobrutinib vs Ibrutinib (BRUIN CLL-314) (Lilly)**
- **Phase II - Lisaftoclax (BCL2i) monotherapy (Ascentage)**
- **Phase I - Rocbrutinib (LP-168) (c/ncBTKi) (OSU)**
- **Phase I - BGB-16673 BTK-degrader (BeOne)**
- **Phase I - Bexobrutideg BTK-degrader (Nurix)**
- **Real World Experience with CD19-CAR-T cells (FHCRC)**

- **Phase II – PVO for Richter transformation (MDACC)**
- **Phase II – Tislelizumab + Zanubrutinib for Richter transformation (GCLLSG)**

UPCOMING 2026 MEETINGS

European Hematology Association

June

American Society of Clinical Oncology

June

German CLL Study Group

April

American Society of Hematology

December

THANK YOU

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"Longitudinal Trends in Vaccination and Cancer Screening Engagement Among Patients With Chronic Lymphocytic Leukemia : A prospective Cohort Study (2019–2025)"

Vanthana Bharathi, Kristofer Jennings, Jackie Broadway-Duren, Mahesh Swaminathan, Nitin Jain, William Wierda, Jan Burger, Dervy Salcedo, Stephanie Zelaya, Margaret Pace, Mariela Sivina, Alessandra Ferrajoli

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Background: Gaps in Vaccination and Screening in Patients with Chronic Lymphocytic Leukemia (CLL)

- Immune dysfunction in patients with CLL arises from both disease-related factors and treatment-related effects[1]
- Cause of death in patients with CLL - CLL progression 46%, infection 8%, other cancer 19%[2]
- Despite established guidelines, longitudinal data on preventive health uptake in CLL are lacking
- Preventive care responsibility is often unclear between PCPs and leukemia providers

[1]Arruga et al. *Int J Mol Sci.* 2020; doi: 10.3390/ijms21051825
[2]Strati et al. Br J Haematol. 2017; doi: 10.1111/bjh.14785

Study Objectives

- Evaluate 5-year trends in vaccination and cancer screening among patients with CLL followed in the Leukemia Clinic at the University of Texas MD Anderson Cancer Center
- Assess the impact of serial yearly surveys on preventive care uptake
- Identify demographic factors associated with engagement (age, sex, race, ethnicity) and explore disparities in screening

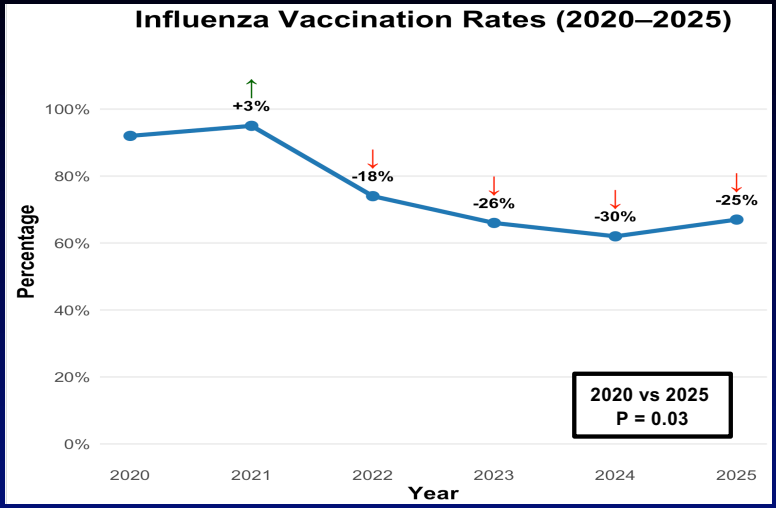
Study Design

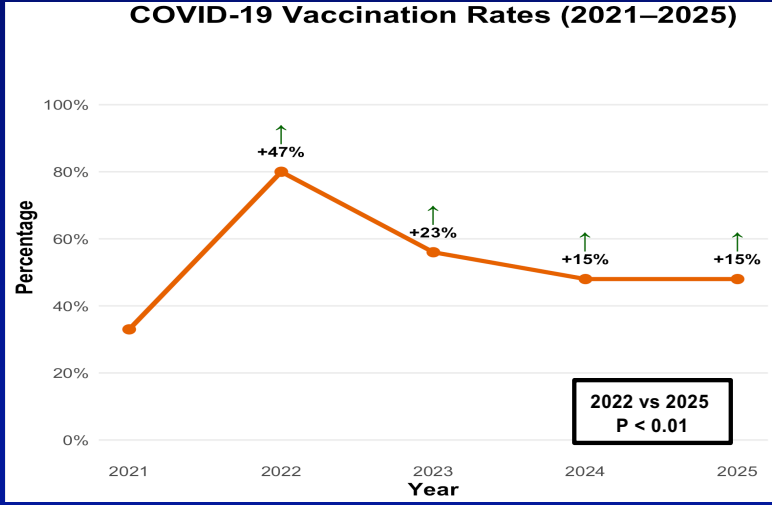
- Prospective cohort and QI initiative conducted from June 2019 to March 2025
- Patients with CLL completed a standardized yearly health-maintenance survey at each clinic visit
- Each survey collected data regarding:
  - Vaccinations: influenza, pneumococcal, shingles, COVID-19
  - Cancer screenings: mammogram, PSA, colonoscopy, skin exam
- Each survey also included reminders for recommended vaccines and cancer screenings

Demographics

Baseline Characteristics (n = 1083)	
Age in years, median (range)	69 (28 – 103)
Male, n (%)	660 (60.8%)
Race, n (%)	
White	981 (90.5%)
African American	47 (4.3%)
Asian	18 (1.7%)
American Indian/Alaska Native	5 (0.5%)
Other	32(2.9%)
Ethnicity, n (%)	
Non- Hispanic or Latino	1024 (94.7%)
Hispanic or Latino	54 (5%)
Unknown	5 (0.3%)

Vaccination Trends Over Time



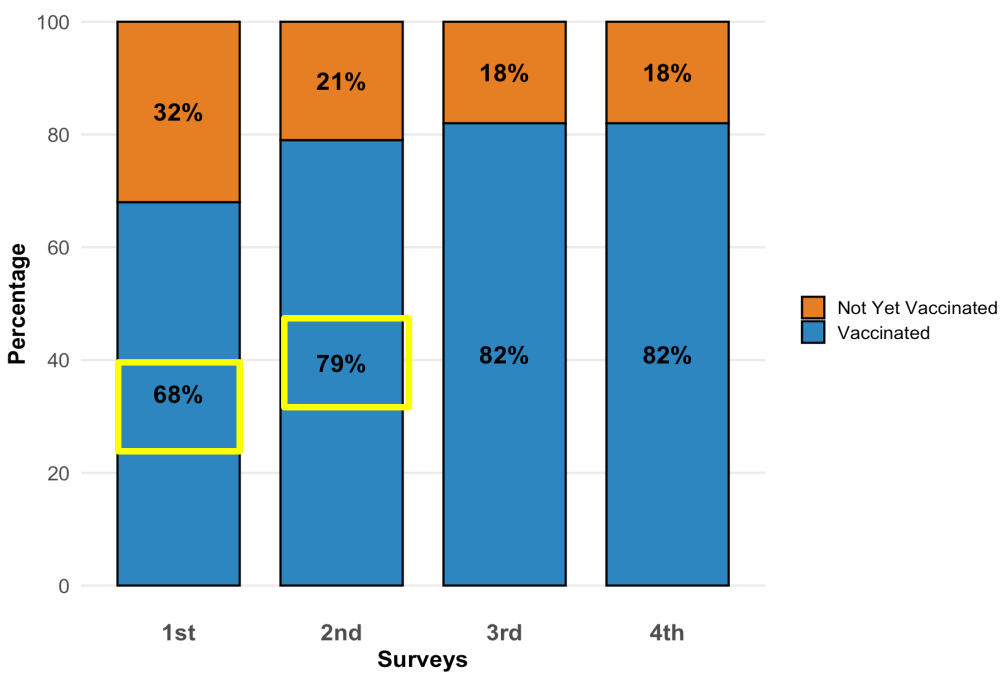


Year	Influenza	COVID-19
2020	90%	—
2021	↑93%	33%
2022	↓76%	↑80%
2023	↓67%	↓61%
2024	↓63%	↓46%
2025	↓65%	↓48%

Overall declines: Influenza −25% (2020→2025), COVID-19 −31% (2022→2025)

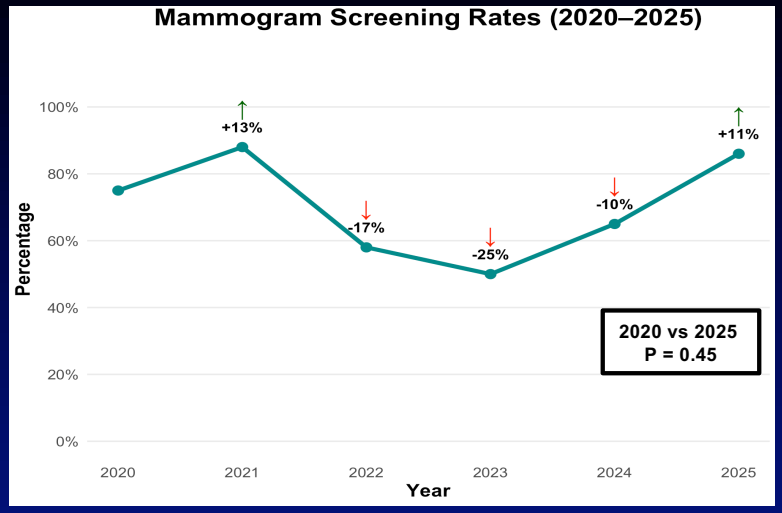
Cumulative Uptake with Serial Surveys

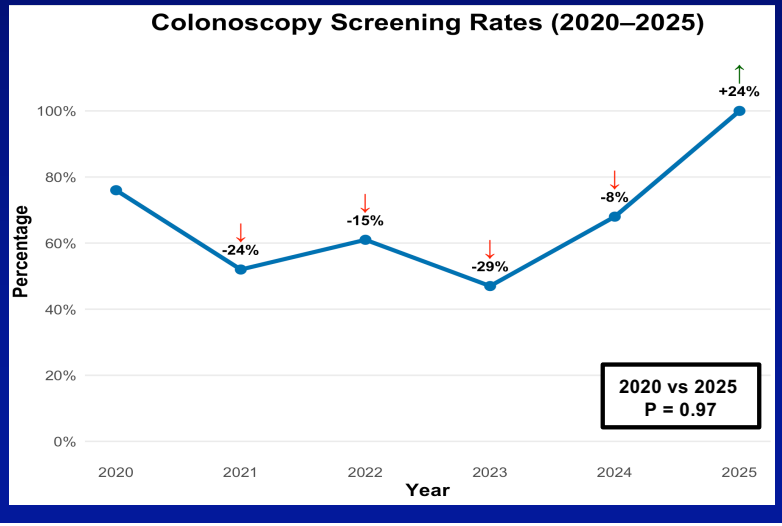
Influenza



Serial engagement improves vaccination uptake

Cancer Screening Trends Over Time



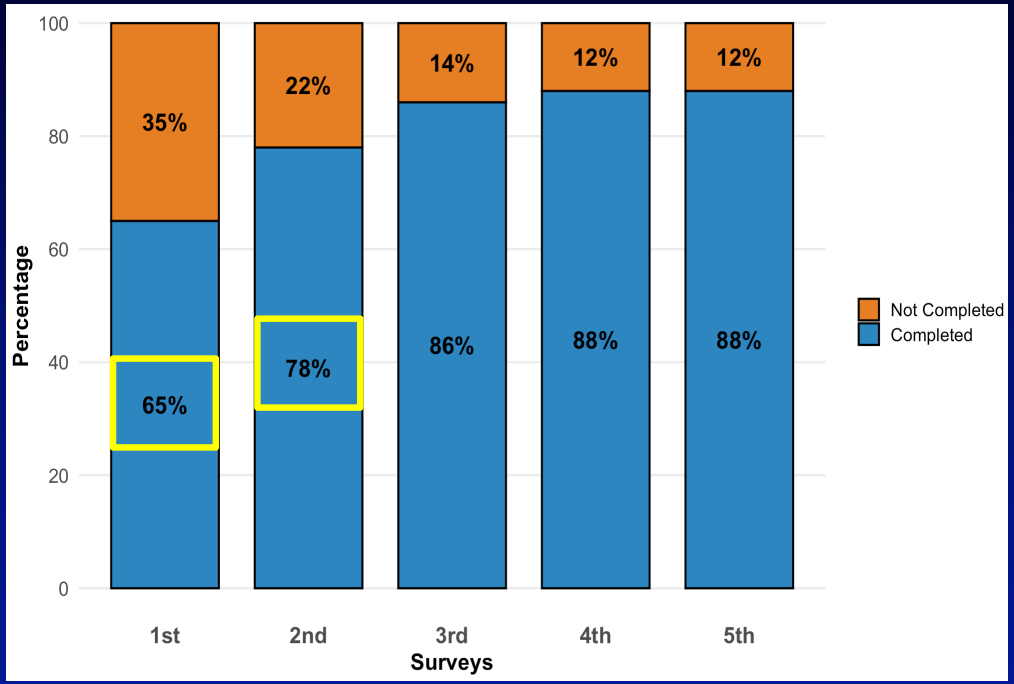


Year	Mammogram	Colonoscopy
2020	75%	76%
2021	↑88%	↓52%
2022	↓58%	↓61%
2023	↓50%	↓47%
2024	↓65%	↓68%
2025	↑86%	↑100%

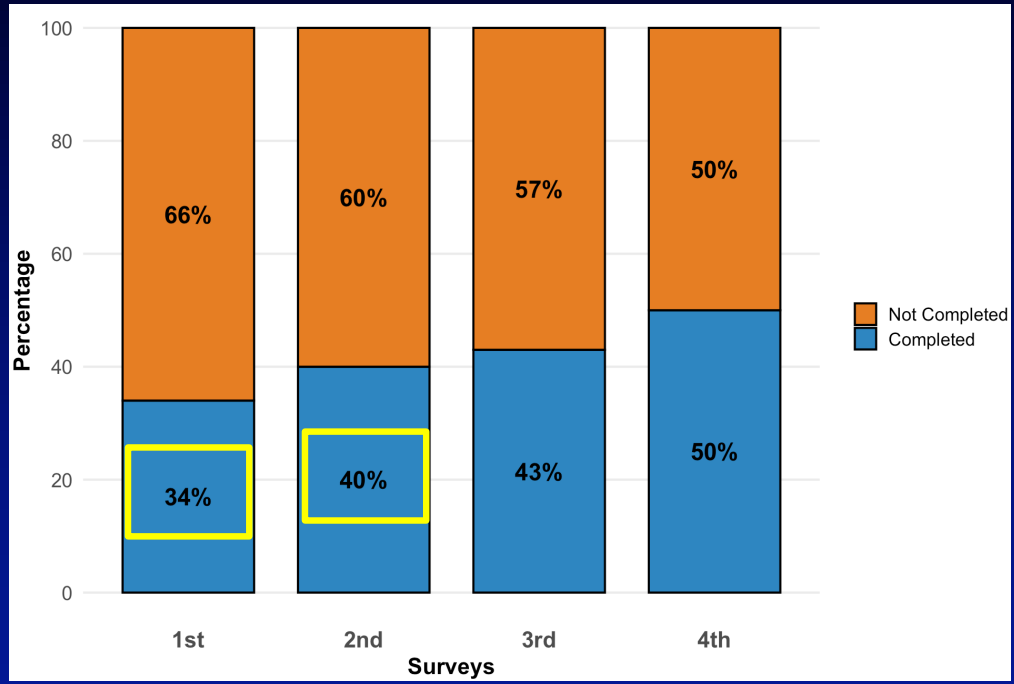
2020 → 2025 change: Mammogram +11%, Colonoscopy +24%

Cumulative Uptake with Serial Surveys

Skin cancer screening



PSA screening



Serial engagement improves cancer screening uptake

Conclusions

- A simple, repeatable health-maintenance survey proved to be a scalable intervention to improve vaccination and cancer screening in patients with CLL
- This project included the period of the COVID-19 pandemic and showed a decline in preventive care, particularly for vaccinations
- Age was the only consistent independent predictor of adherence (older=better adherence); most sex, race, and ethnicity differences were not significant after adjustment
- Skin cancer and PSA screening showed the strongest racial disparities, identifying a key area for targeted intervention

Acknowledgements

Patients and Families

Leukemia Clinic staff, APPs, and research coordinators

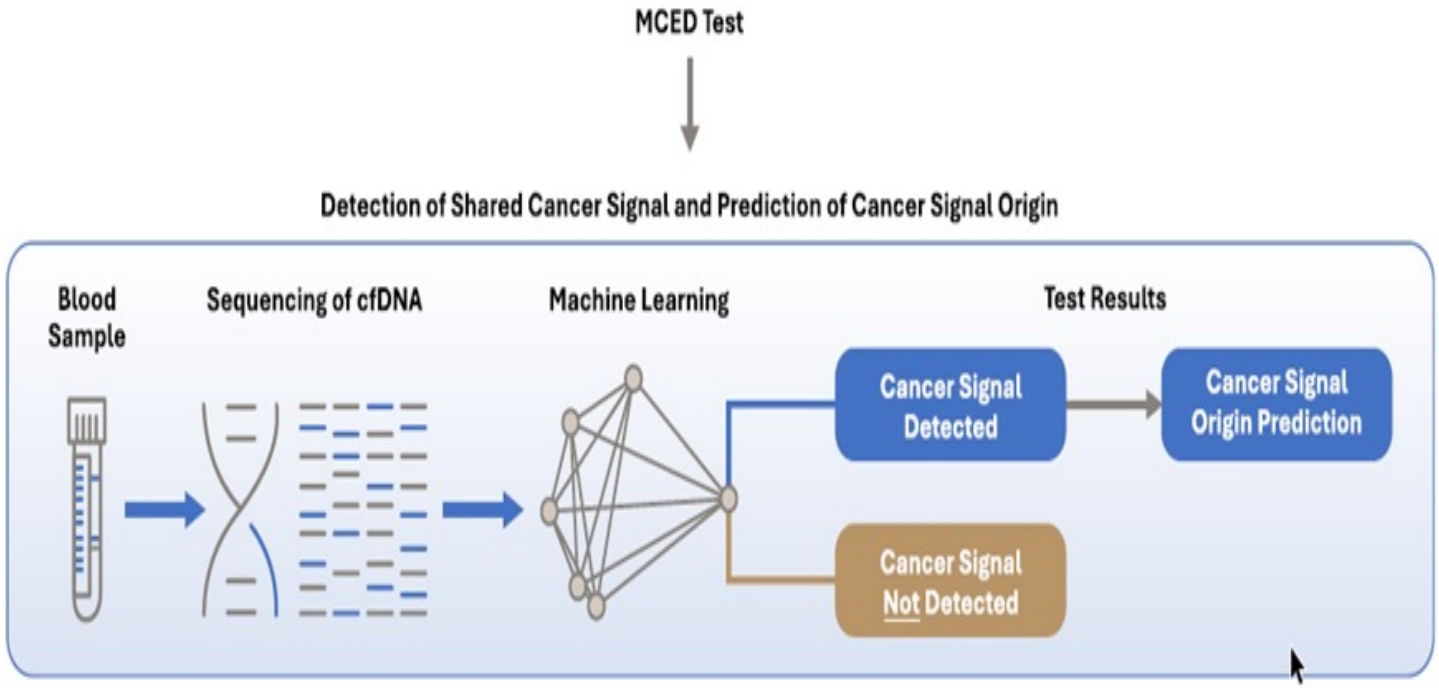
Statistics and data management team

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center

FUNDING:

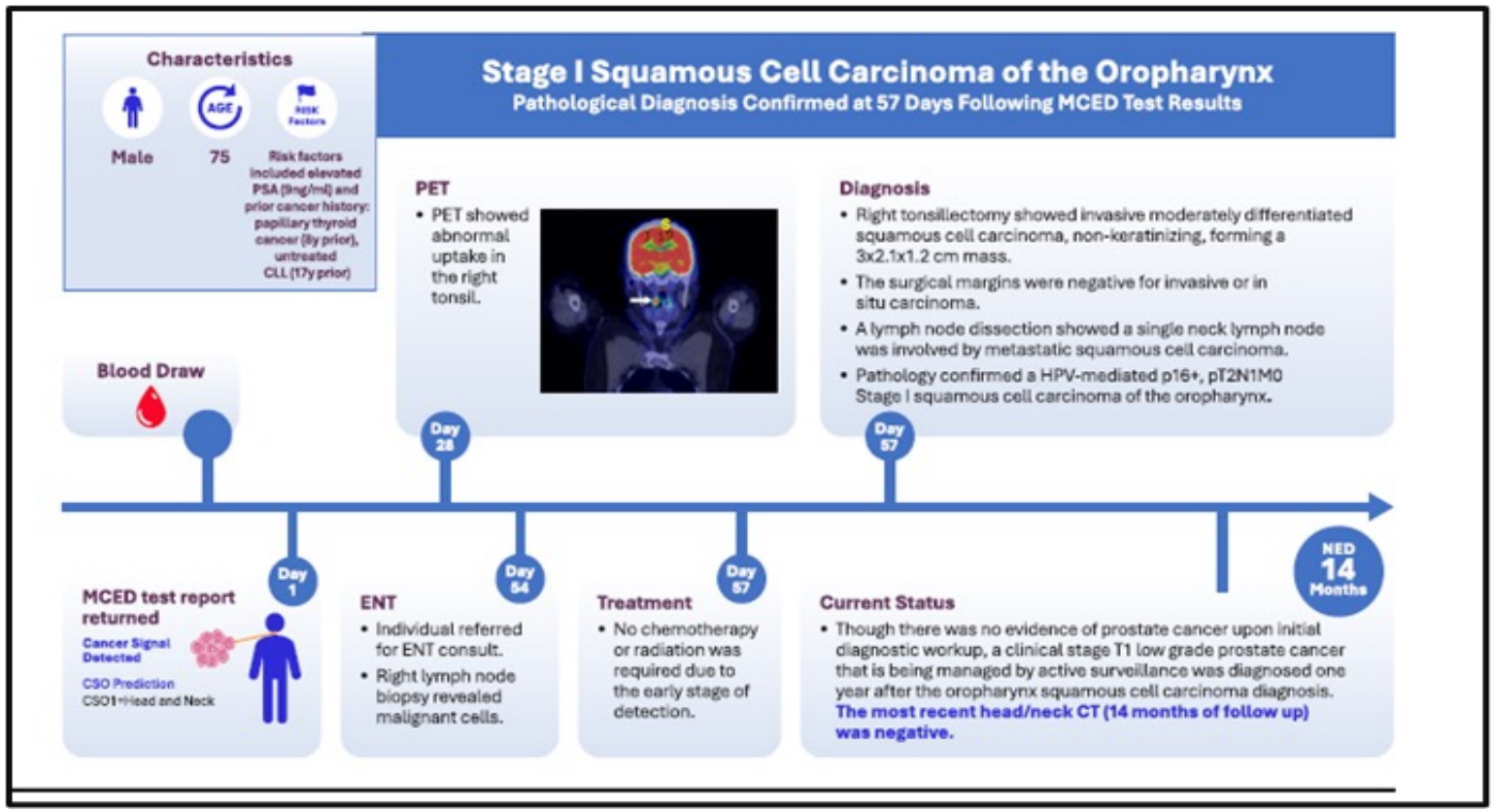
CLL GLOBAL RESEARCH FOUNDATION®
• CHRONIC LYMPHOCYTIC LEUKEMIA •

NCCN Sponsored Prospective Study: Improving the Detection of Other Cancers in Patients with CLL Using Multicancer Early Detection Testing - MCED in CLL



GRAIL Galleri, FDA breakthrough device designation application in process

A Multi-cancer Early Detection Blood Test Using Machine Learning Detects Early-stage Cancers Lacking USPSTF-recommended Screening in Patient with CLL



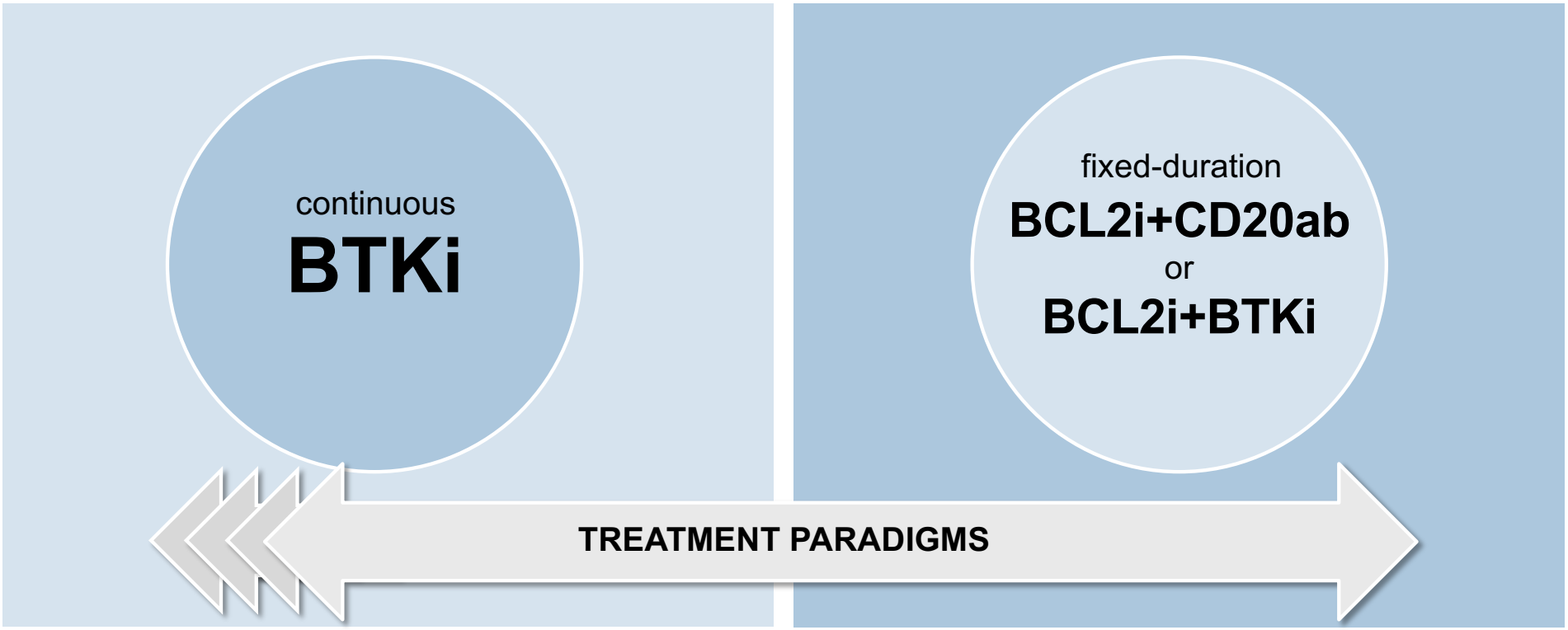
Vittone J, Gill D, Goldsmith A, Klein EA. *Prec Oncol*. 2024

Fixed-duration versus continuous targeted treatment for previously untreated chronic lymphocytic leukemia: Results from the randomized CLL17 trial

Othman Al-Sawaf, Janina Stumpf, Can Zhang, Florian Simon, Francesc Bosch, Emadoldin Feyzi, Paolo Ghia, Michael Gregor, Arnon Kater, Vesa Lindstrom, Mattias Mattsson, Carsten U Niemann, Philipp Staber, Tamar Tadmor, Patrick Thornton, Clemens Wendtner, Ann Janssens, Thomas Nösslinger, Jan-Paul Bohn, Casper da Cunha-Bang, Christian Poulsen, Juha Ranti, Thomas Illmer, Björn Schöttker, Sebastian Böttcher, Tobias Gaska, Elisabeth Vandenberghe, Ruth Clifford, Ohad Benjamini, Anna Maria Frustaci, Lydia Scarfo, Paolo Sportoletti, John Schreurs, Mark David Levin, H.M. van der Straaten, Marjolein van der Klift, Hoa Thi Tuyet, Javier de la Serna Torroba, Javier Loscertales, Oscar Lindblad, Anna Bergendahl Sandstedt, Jeroen Goede, Michael Baumann, Anna Fink, Kirsten Fischer, Matthias Ritgen, Karl-Anton Kreuzer, Christof Schneider, Eugen Tausch, Stephan Stilgenbauer, Sandra Robrecht, Barbara Eichhorst, Michael Hallek

Sunday, December 7th, 2025, ASH Annual Meeting, Orlando, USA

RATIONALE



So far, these two paradigms have not been directly compared in a randomized trial.

CLL17 STUDY DESIGN

Patients with previously untreated CLL

1:1:1 randomization
Stratification according to fitness, del17p/*TP53*, IGHV

Ibrutinib 420 mg po daily until PD

Venetoclax 400 mg po daily (c1 d22 – c12)
Obinutuzumab 1000 mg iv (c1 d1(2)/8/15, c 2-6 d1)

Venetoclax 400 mg po daily (c4 d1 – c15)
Ibrutinib 420 mg po daily (c1 d1 – c15)

976 patients screened, in 174 sites, across 13 countries.

Patient enrollment from February 2021 to November 2022.

Median observation time: 34.2 months (IQR 30.3-39.3)

OBJECTIVES AND ENDPOINTS

Primary objective:

Testing PFS non-inferiority of **fixed-duration venetoclax-obinutuzumab (VO) versus continuous ibrutinib (I)** and **fixed-duration venetoclax-ibrutinib (VI) versus continuous I**.

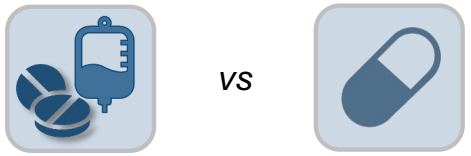
Hypothesis:

A ≤ 8% reduction in 3-yr PFS rates was considered clinically not meaningful.

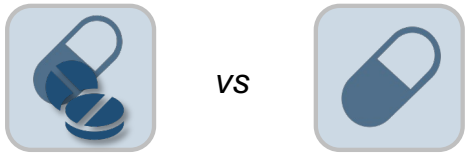
A non-inferiority margin of a HR = 1.608 was defined for each hypothesis test, based on available literature in 2020.

In clinical terms:

A short-term combination treatment (VO, VI) **is non-inferior (i.e. clinically equally effective)** to a long-term monotherapy (I).



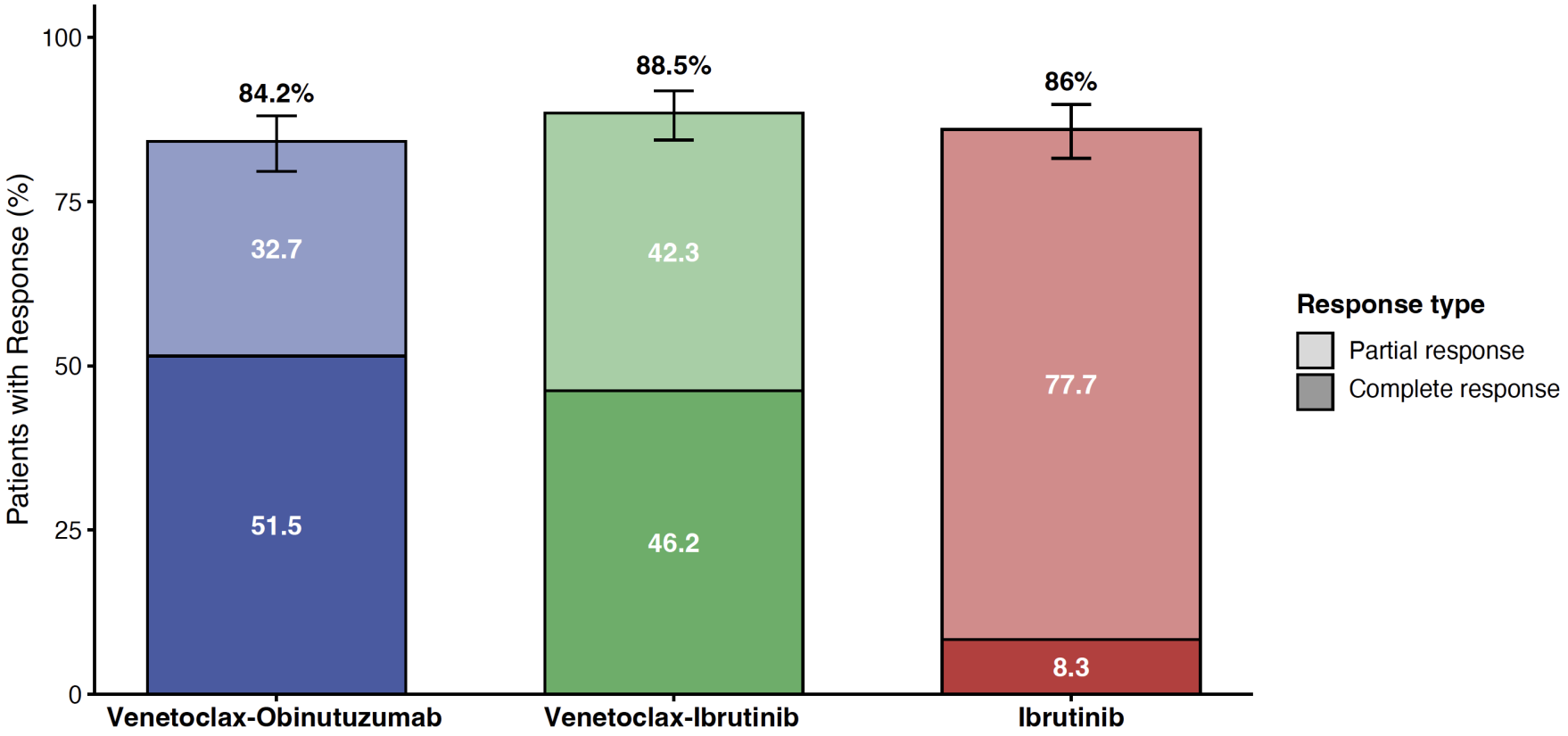
VO **I**



VI **I**

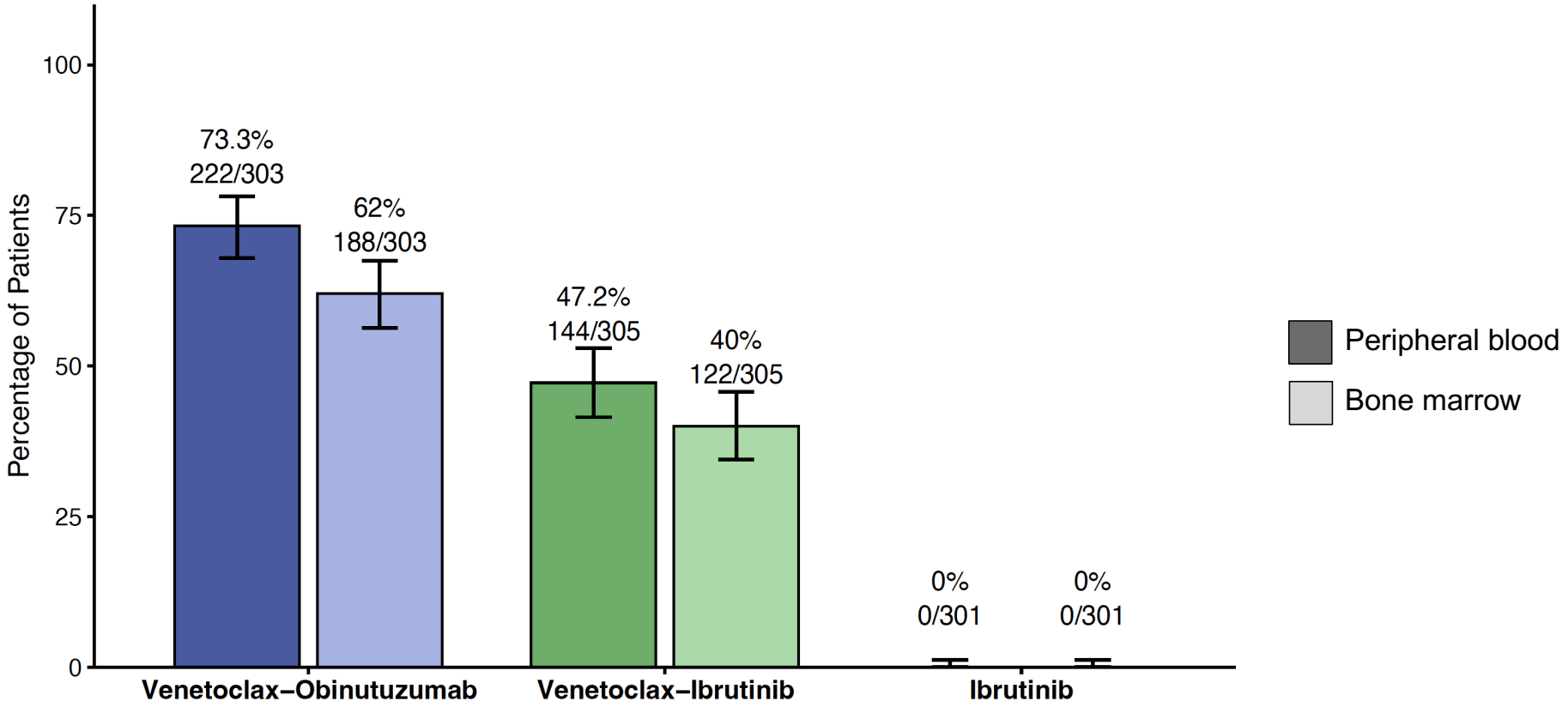
RESPONSE TO TREATMENT

iwCLL response at final restaging (C18D1)

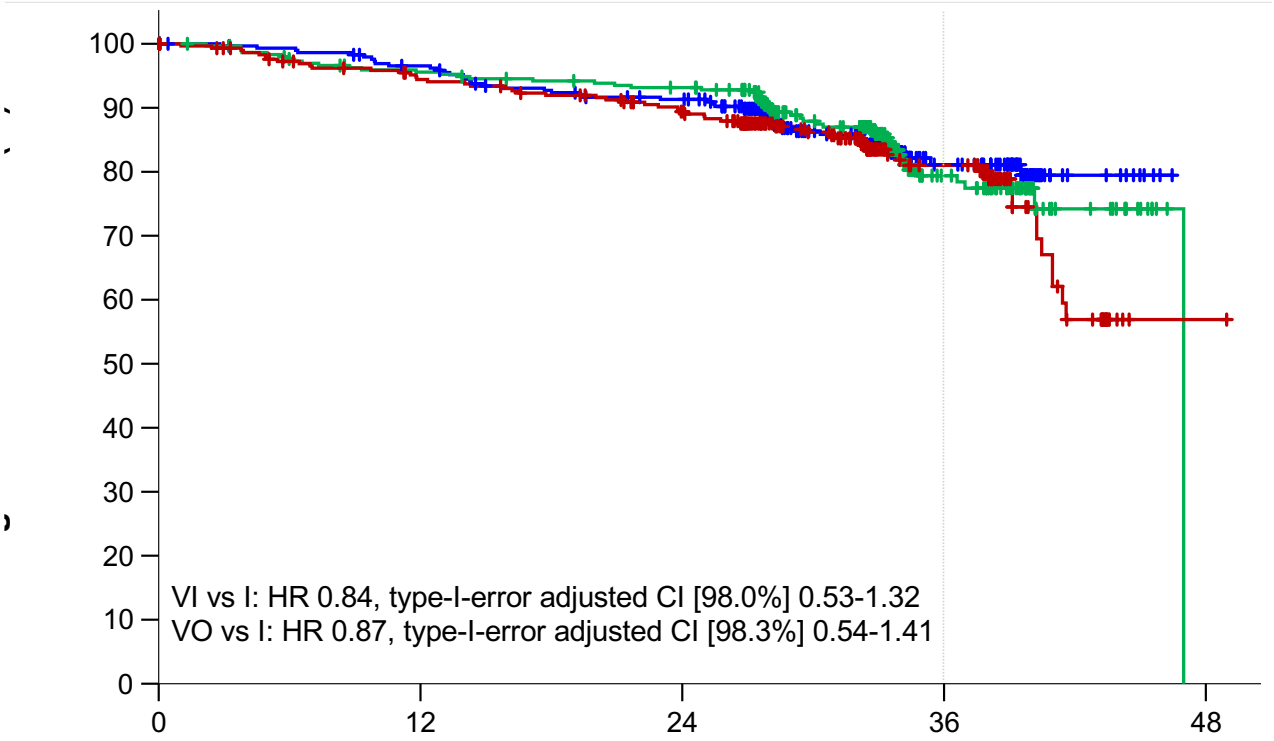


RESPONSE TO TREATMENT

uMRD $<10^{-4}$ in **peripheral blood** and **bone marrow**, by flow cytometry, at final restaging



PROGRESSION-FREE SURVIVAL



Patients at risk

VO	303	278	256	77	0
VI	305	278	267	82	0
I	301	267	243	94	1

3-year-PFS

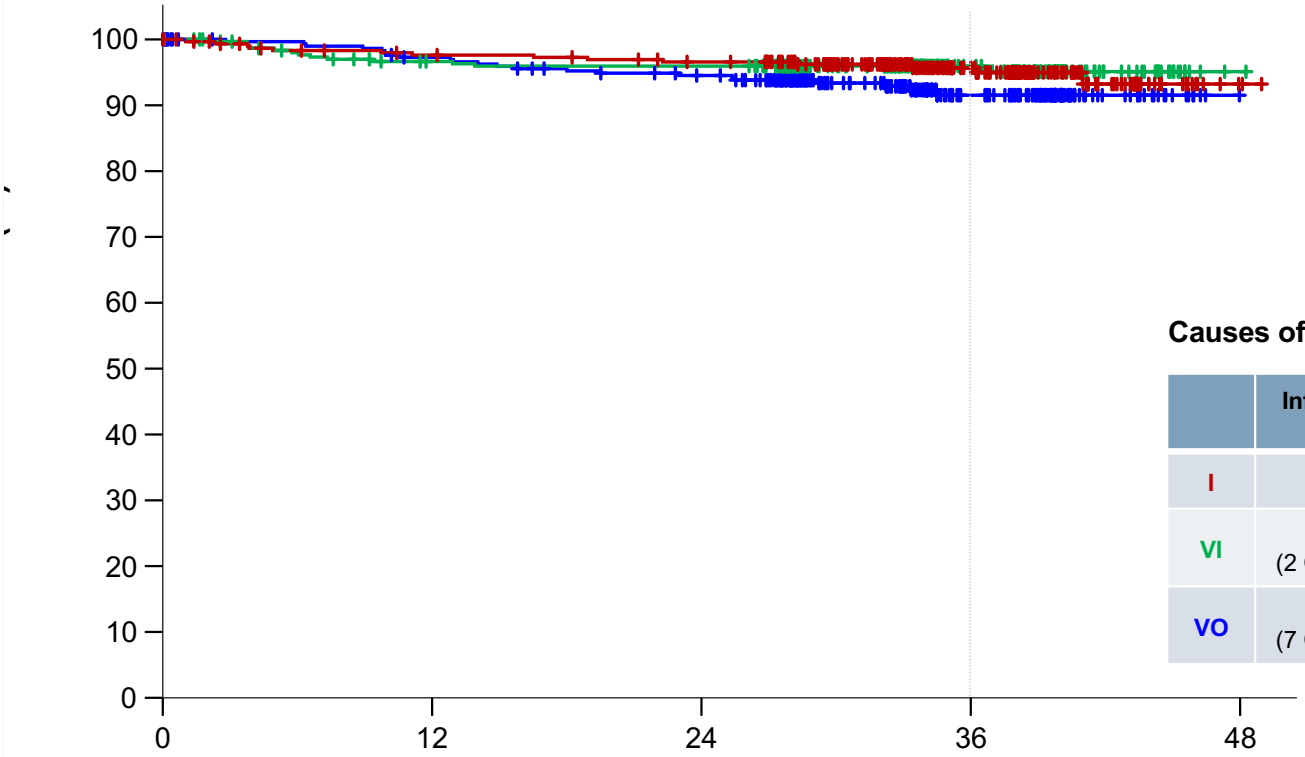
I 81.0%

VI 79.4 %

VO 81.1%

	PD	Death
I	46	11
VI	37	13
VO	25	21

OVERALL SURVIVAL



Patients at risk					
VO	303	284	269	102	0
VI	305	281	279	114	1
I	301	284	276	141	2

3-year-OS

I 95.7%

VI 96.0%

VO 91.5%

Causes of death

	Infection	Cardio-vascular	PD/RT	SPM	Other	Total
I	3	5	0	2	4	14
VI	7 (2 Covid)	3	0	2	1	13
VO	12 (7 Covid)	5	1	4	0	22

VI vs I: HR 0.96, 95% CI 0.45-2.05

VO vs I: HR 1.67, 95% CI 0.86-3.28