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# ASH 2025 COMES TO YOU

**JANUARY 14, 2026**

9:00 AM PT, 10:00 AM MT

11:00 PM CT, 12:00 PM ET

# THIS PROGRAM IS MADE POSSIBLE THROUGH GENEROUS DONORS AND GRANT SUPPORT

# SPEAKERS

## Adam Kittai

**MD**
**(SPEAKER)**

Associate Professor, Division of Hematology and Medical Oncology, Assistant Director of Lymphoma Clinical Research, CLL Clinical Research Leader, Icahn School of Medicine at Mount Sinai Hospital, New York, NY

## Brian Koffman

**MDCM (retired) MS Ed**
**(SPEAKER & MODERATOR)**

Co-Founder and Chief Medical Officer Emeritus
CLL Society

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# ASH 2025 COMES TO YOU!

**Dr. Adam Kittai**
Associate Professor, Division of Hematology and Medical Oncology
Assistant Director of Lymphoma Clinical Research
CLL Clinical Research Leader
Icahn School of Medicine at Mount Sinai Hospital
New York, NY

# 3 PRACTICE-CHANGING ABSTRACTS AT ASH

- **CLL17 Study – Ibrutinib vs. venetoclax + obinutuzumab (VO) vs. ibrutinib + venetoclax (IV)**
  - First randomized study of continuous therapy vs. time-limited therapy

- **BRUIN CLL-314 – Pirtobrutinib vs. Ibrutinib – non-covalent BTKi vs. covalent BTKi**

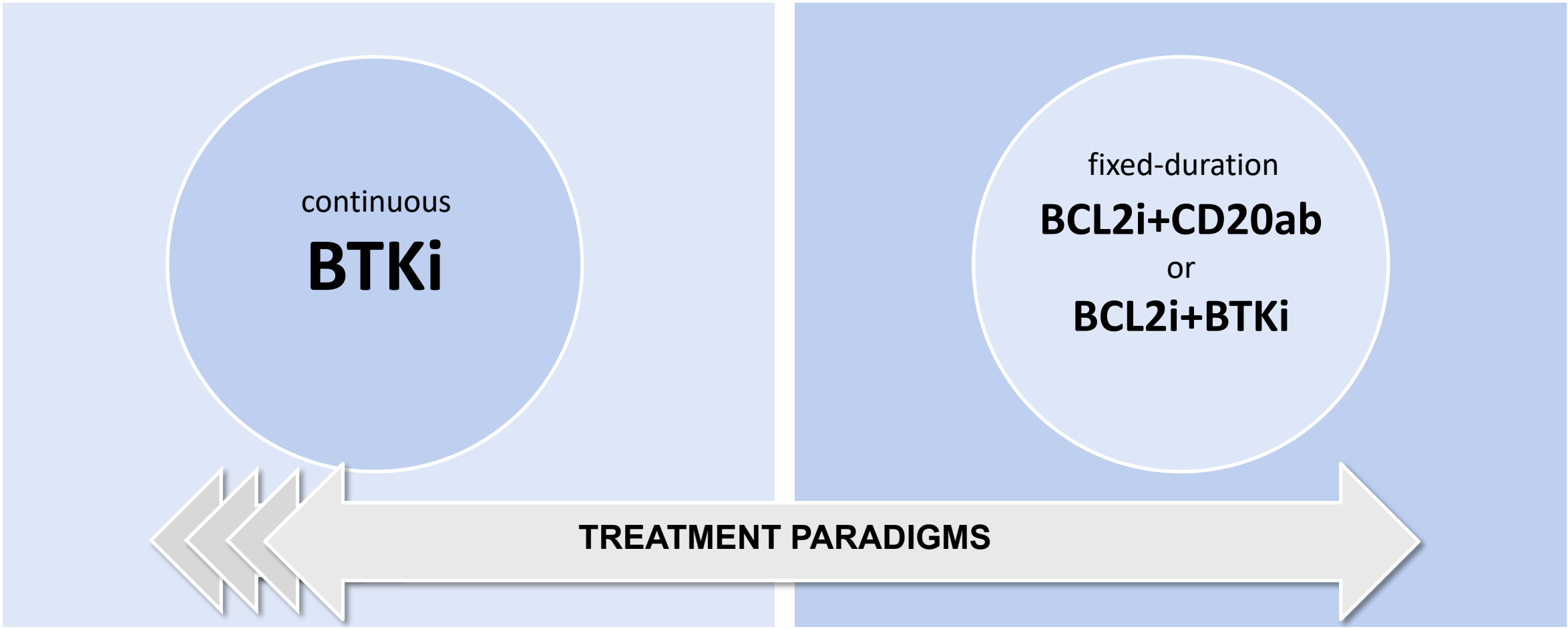
- **Pirtobrutinib + Venetoclax + Obinutuzumab for Richter Transformation**

# 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.**

Slide adapted from Al-Sawaf ASH 2025 Plenary Session

# 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)**

Slide adapted from Al-Sawaf ASH 2025 Plenary Session

# ADVERSE EVENTS (AE)

## Selected adverse events of interest, all CTC grades

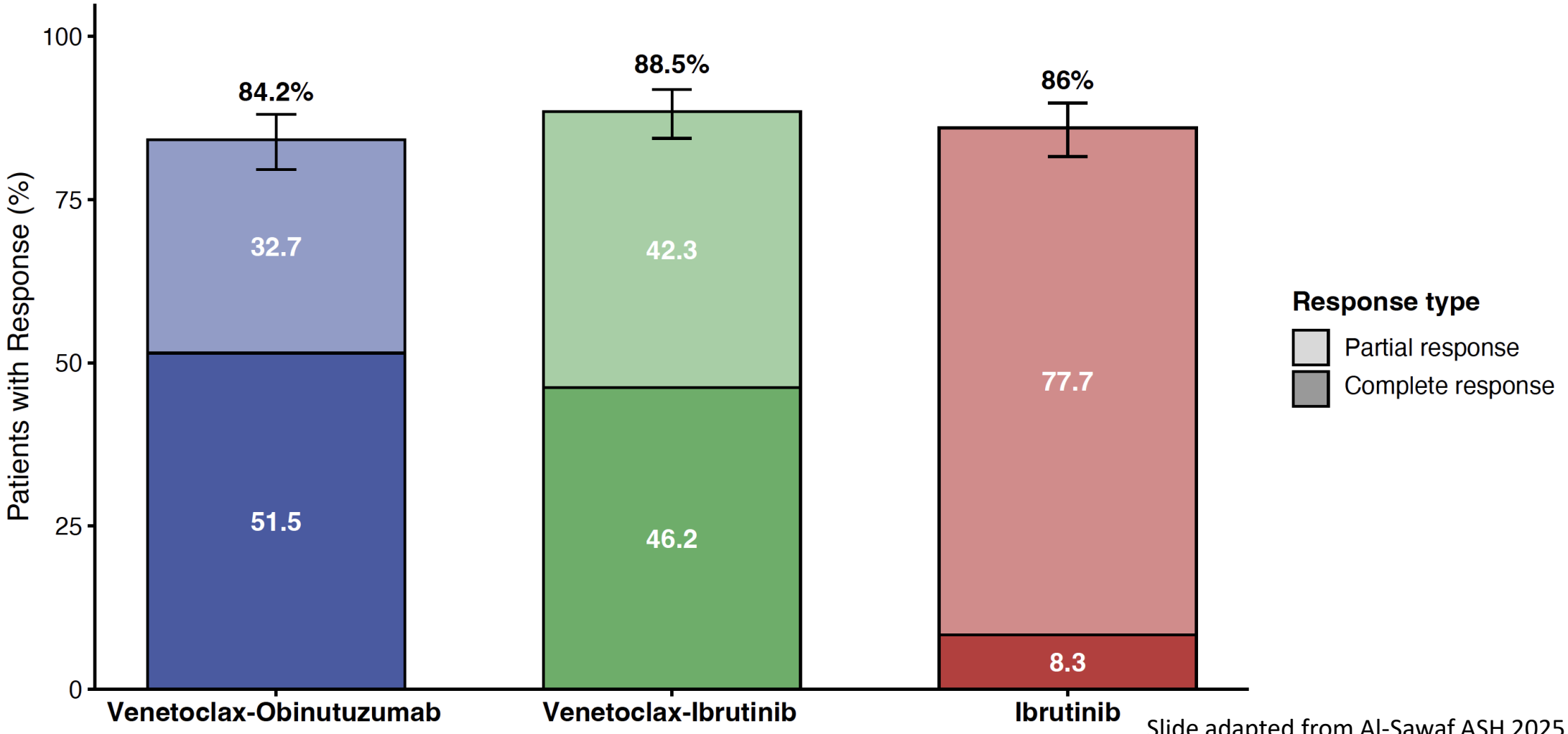
| | VO | VI | I |
|---|---|---|---|
| **Safety population** – No. (%) | **295** | **303** | **298** |
| **Blood and lymphatic system disorders** | 174 (59.0) | 130 (42.9) | 85 (28.5) |
| Febrile neutropenia | 14 (4.7) | 7 (2.3) | 0 (0) |
| Neutropenia (low neutrophil count) | 155 (52.5) | 110 (36.3) | 49 (16.4) |
| **Cardiac disorders** | 41 (13.9) | 72 (23.8) | 103 (34.6) |
| Atrial fibrillation | 11 (3.7) | 38 (12.5) | 50 (16.8) |
| **Gastrointestinal disorders** | 176 (59.7) | 225 (74.3) | 189 (63.4) |
| Diarrhea | 80 (27.1) | 143 (47.2) | 104 (34.9) |
| **Infections and infestations** | 225 (76.3) | 243 (80.2) | 238 (79.9) |
| COVID-19 | 113 (38.3) | 128 (42.2) | 117 (39.3) |
| Pneumonia | 41 (13.9) | 28 (9.2) | 40 (13.4) |
| **Metabolism and nutrition disorders** | 90 (30.5) | 75 (24.8) | 72 (24.2) |
| Tumor lysis syndrome | 12 (4.1) | 4 (1.3) | 1 (0.3) |
| **Neoplasms benign, malignant and unspecified** | 35 (11.9) | 35 (11.6) | 55 (18.5) |
| Richter Transformation | 4 (1.4) | 1 (0.3) | 4 (1.3) |
| **Vascular disorders** | 60 (20.3) | 102 (33.7) | 124 (41.6) |
| Hypertension | 34 (11.5) | 51 (16.8) | 72 (24.2) |



Slide adapted from Al-Sawaf ASH 2025 Plenary Session

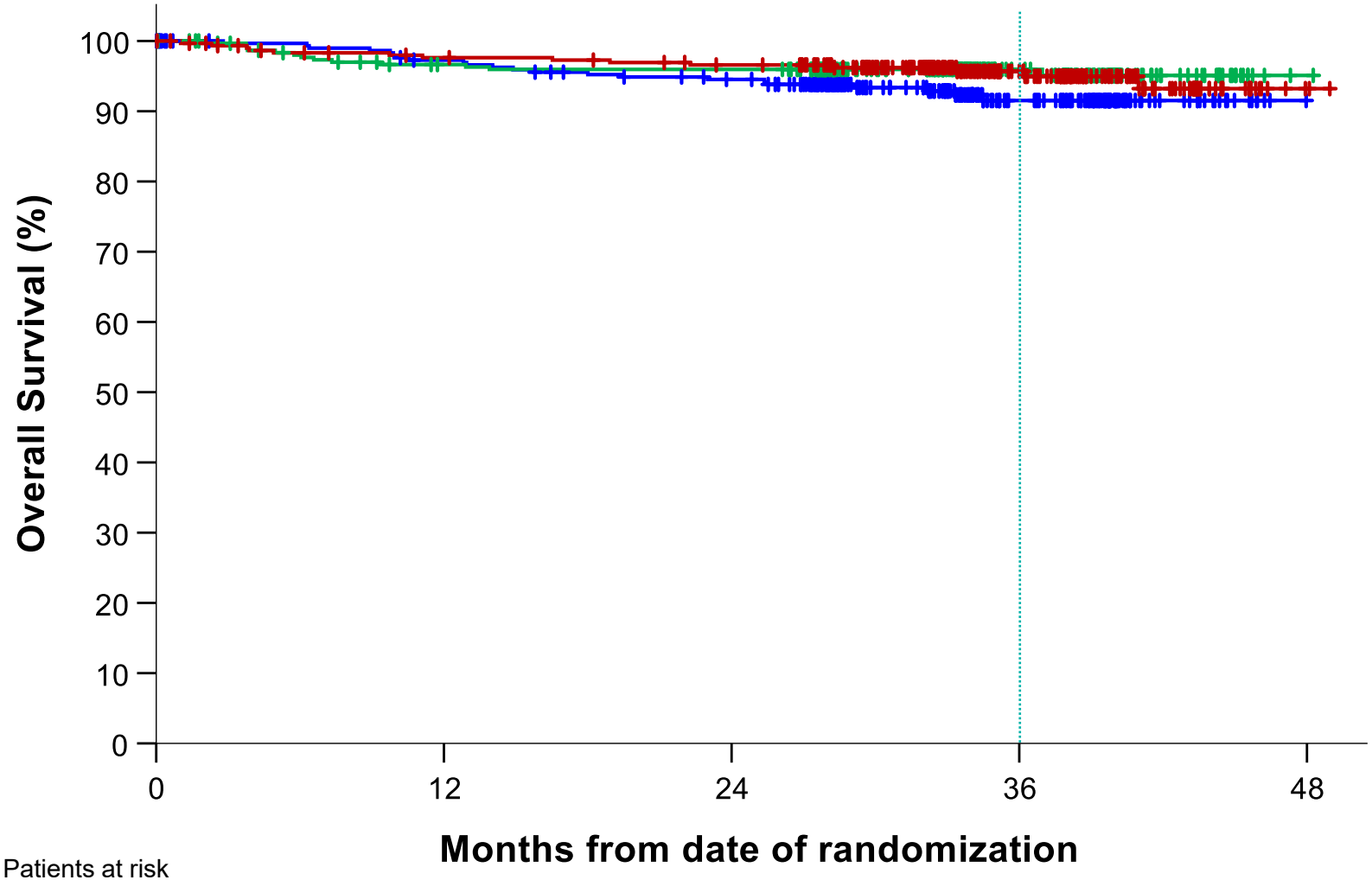
# RESPONSE TO TREATMENT

## iwCLL response at final restaging (C18D1)




Slide adapted from Al-Sawaf ASH 2025 Plenary Session

# OVERALL SURVIVAL (OS)




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

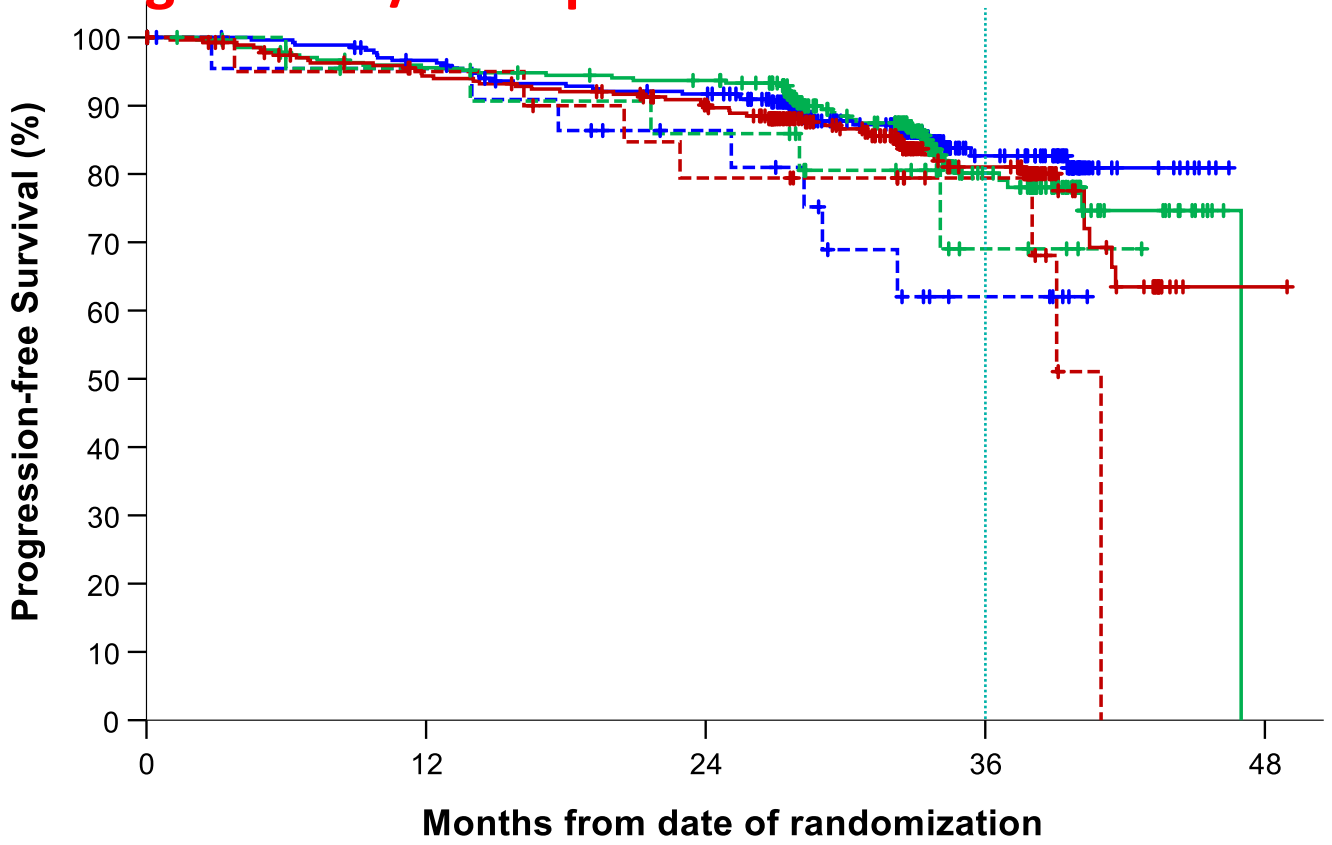
**3-year-OS**

| | |
|---|---|
| I | 95.7% |
| VI | 96.0% |
| VO | 91.5% |

Slide adapted from Al-Sawaf ASH 2025 Plenary Session

# PROGRESSION-FREE SURVIVAL (PFS)

## According to *TP53*/del17p status




| Patients at risk | | | | | |
|---|---|---|---|---|---|
| VO, del/mut | 23 | 21 | 16 | 5 | 0 |
| VO, WT | 280 | 257 | 240 | 72 | 0 |
| VI, del/mut | 25 | 20 | 18 | 4 | 0 |
| VI, WT | 279 | 257 | 248 | 78 | 0 |
| I, del/mut | 21 | 19 | 15 | 7 | 0 |
| I, WT | 279 | 247 | 227 | 87 | 1 |

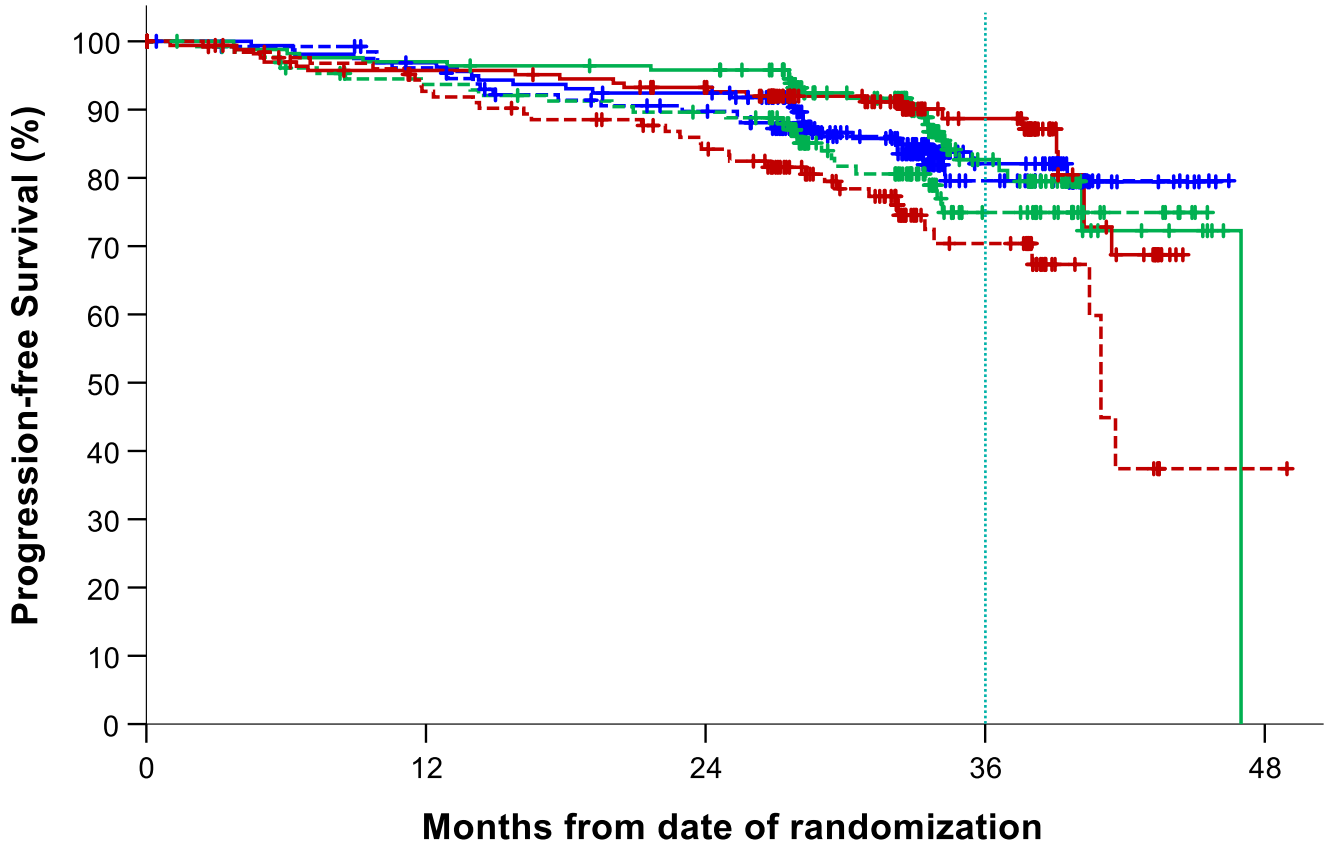
**3-year-PFS**

| | | |
|---|---|---|
| ----- | I, *TP53*del/mut | 79.4% |
| —— | I, *TP53*-WT | 81.0% |
| ----- | VI, *TP53*del/mut | 69.0% |
| —— | VI, *TP53*-WT | 80.1% |
| ----- | VO, *TP53*del/mut | 62.0% |
| —— | VO, *TP53*-WT | 82.7% |

Slide adapted from Al-Sawaf ASH 2025 Plenary Session

# PROGRESSION-FREE SURVIVAL

## According to fitness (cumulative illness rating scale >6 and/or GFR <70 ml/min)




Patients at risk

| | | | | | |
|---|---|---|---|---|---|
| VO, unfit | 134 | 123 | 109 | 30 | 0 |
| VO, fit | 167 | 153 | 145 | 47 | 0 |
| VI, unfit | 136 | 116 | 109 | 29 | 0 |
| VI, fit | 169 | 162 | 158 | 53 | 0 |
| I, unfit | 130 | 112 | 97 | 33 | 1 |
| I, fit | 171 | 155 | 146 | 61 | 0 |

**3-year-PFS**

| | |
|---|---|
| ----- I, unfit | 70.4% |
| —— I, fit | 88.7% |
| ----- VI, unfit | 74.9% |
| —— VI, fit | 82.7% |
| ----- VO, unfit | 79.6% |
| —— VO, fit | 82.1% |

Slide adapted from Al-Sawaf ASH 2025 Plenary Session

# CONCLUSION

- **Fixed-duration targeted therapy**
  - Venetoclax-Obinutuzumab and Venetoclax-Ibrutinib achieved **non-inferiority in progression-free survival** compared with continuous ibrutinib.
  - Ongoing follow-up will help clarify differences across clinical and biologic subgroups.

- **Safety considerations**
  - Risk of Infections remains relevant in CLL with all therapies, and particularly with CD20 antibodies.
  - Safety profiles consistent with known adverse event profiles of these agents.

- **Meaning for patients**
  - For most patients with previously untreated CLL, fixed-duration treatment is a primary option.

Slide adapted from Al-Sawaf ASH 2025 Plenary Session

# BRUIN CLL-314 – Pirtobrutinib vs. Ibrutinib in Replapsed/Refractory (R/R) and Treatment Naïve (TN) CLL

No prior BTKi

Primary Endpoint – overall response rate (ORR), with progression free survival (PFS) as a key secondary endpoint

N = 662

| | ITT, No. (%) | | R/R, No. (%) | | TN, No. (%) | |
|---|---|---|---|---|---|---|
| BOR[a] | Pirtobrutinib (n = 331) | Ibrutinib (n = 331) | Pirtobrutinib (n = 219) | Ibrutinib (n = 218) | Pirtobrutinib (n = 112) | Ibrutinib (n = 113) |
| ORR (PR or better) ratio | 1.1080 | | 1.1233 | | 1.0797 | |
| 95% CI | 1.034 to 1.187 | | 1.020 to 1.237 | | 0.989 to 1.179 | |
| *P* value for NI[b] | <.0001 | | <.0001 | | — | |
| ORR (PR or better) | 288 (87.0) | 260 (78.5) | 184 (84.0) | 163 (74.8) | 104 (92.9) | 97 (85.8) |

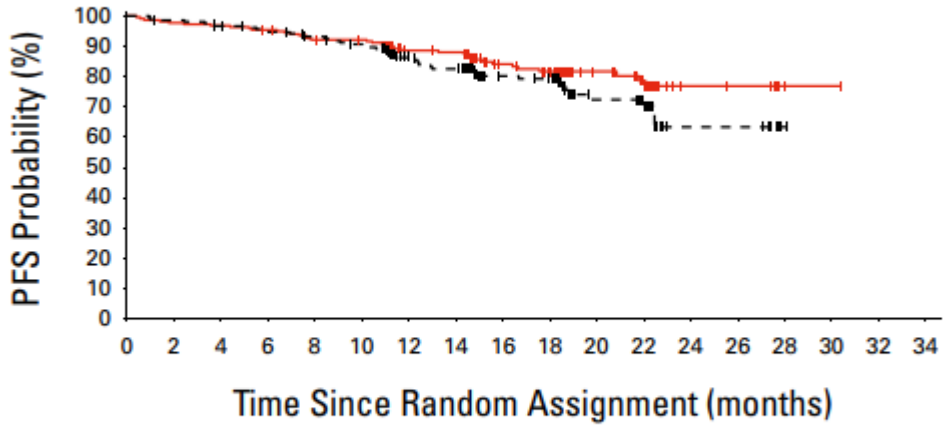
Woyach et al JCO 2025

# PROGRESSION-FREE SURVIVAL

## Relapsed/Refractory

B

| | No. of Patients | No. of Events | 18-Month PFS Rates (95% CI) | HR (95% CI) | P* |
|---|---|---|---|---|---|
| Pirtobrutinib | 219 | 37 | 81.7 (75.1 to 86.7) | 0.729 (0.471 to 1.128) | .1563 |
| Ibrutinib | 218 | 45 | 79.2 (72.3 to 84.6) | | |



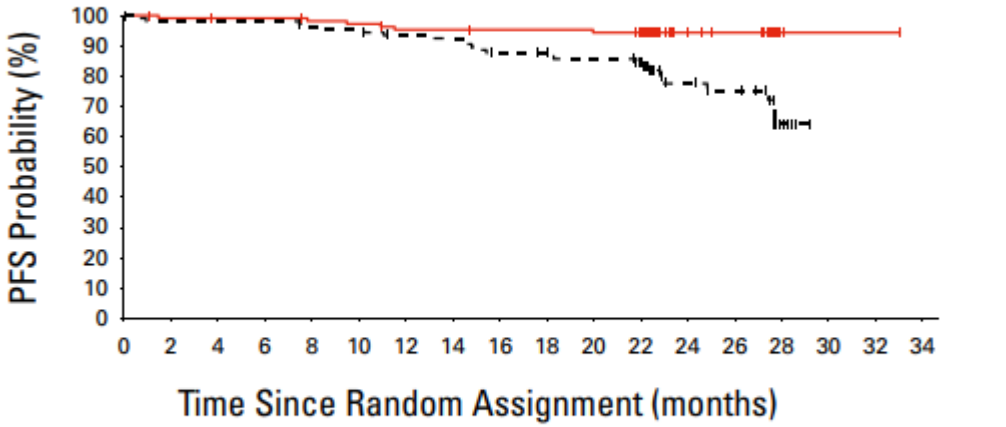

Number at risk
(number censored)

| | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Pirtobrutinib | 219 (0) | 212 (2) | 209 (3) | 205 (4) | 197 (5) | 195 (7) | 157 (38) | 155 (39) | 106 (82) | 99 (86) | 56 (129) | 46 (137) | 13 (169) | 12 (170) | 3 (179) | 2 (180) | 0 (182) | 0 (182) |
| Ibrutinib | 218 (0) | 205 (10) | 198 (13) | 192 (15) | 186 (18) | 179 (20) | 138 (53) | 131 (54) | 87 (95) | 84 (97) | 43 (133) | 37 (139) | 12 (161) | 12 (161) | 1 (172) | 0 (173) | 0 (173) | 0 (173) |

## Treatment Naïve

C

| | No. of Patients | No. of Events | 18-Month PFS Rates (95% CI) | HR (95% CI) | P* |
|---|---|---|---|---|---|
| Pirtobrutinib | 112 | 6 | 95.3 (89.1 to 98.0) | 0.239 (0.098 to 0.586) | .0007 |
| Ibrutinib | 113 | 24 | 87.6 (79.7 to 92.6) | | |




Number at risk
(number censored)

| | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Pirtobrutinib | 112 (0) | 107 (4) | 106 (5) | 106 (5) | 104 (6) | 103 (6) | 100 (7) | 100 (7) | 99 (8) | 99 (8) | 98 (8) | 94 (12) | 35 (71) | 33 (73) | 4 (102) | 1 (105) | 1 (105) | 0 (106) |
| Ibrutinib | 113 (0) | 105 (6) | 105 (6) | 105 (6) | 102 (7) | 101 (7) | 97 (9) | 96 (9) | 90 (10) | 89 (11) | 86 (12) | 81 (16) | 32 (61) | 29 (63) | 5 (84) | 0 (89) | 0 (89) | 0 (89) |

Woyach et al JCO 2025

# SAFETY

| | Pirtobrutinib (n = 330), No. (%) | | Ibrutinib (n = 325), No. (%) | |
|---|---|---|---|---|
| AE | Any Grade | Grade ≥3 | Any Grade | Grade ≥3 |
| Any TEAE | 320 (97.0) | 181 (54.8) | 318 (97.8) | 174 (53.5) |
| AE of interest | | | | |
| Anemia[c] | 51 (15.5) | 20 (6.1) | 51 (15.7) | 12 (3.7) |
| Atrial fibrillation and atrial flutter[d] | 8 (2.4) | 3 (0.9) | 44 (13.5) | 13 (4.0) |
| Bleeding | 115 (34.8) | 11 (3.3) | 118 (36.3) | 9 (2.8) |
| Bruising[e] | 45 (13.6) | 0 | 39 (12.0) | 0 |
| Petechiae and purpura | 17 (5.2) | 0 | 25 (7.7) | 0 |
| Hemorrhage[f] | 78 (23.6) | 11 (3.3) | 81 (24.9) | 9 (2.8) |
| Hypertension | 35 (10.6) | 11 (3.3) | 49 (15.1) | 16 (4.9) |
| Infections[g] | 226 (68.5) | 56 (17.0) | 241 (74.2) | 54 (16.6) |
| Infection without COVID-19 | 214 (64.8) | 53 (16.1) | 234 (72.0) | 49 (15.1) |
| Neutropenia[h] | 103 (31.2) | 83 (25.3) | 76 (23.4) | 57 (17.5) |
| Thrombocytopenia[i] | 39 (11.8) | 12 (3.6) | 57 (17.5) | 13 (4.0) |

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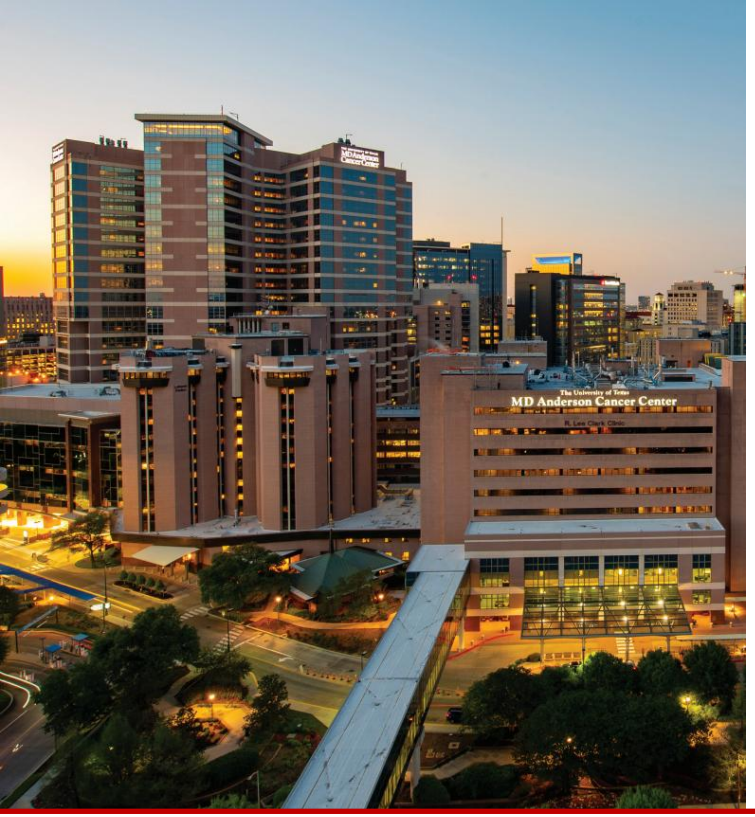
# CONCLUSIONS

Pirtobrutinib versus Ibrutinib in CLL:

- Pirtobrutinib demonstrated non-inferiority of ORR vs ibrutinib in the intention to treat and R/R patients.
- PFS trended in favor of pirtobrutinib
- Better safety profile with pirtobrutinib:
  - Fewer cases of atrial fibrillation.
  - Fewer treatment discontinuations due to adverse events.




# Pirtobrutinib, Venetoclax, and Obinutuzumab for Patients with Richter Transformation (RT): A Phase 2 trial

Nitin Jain, Niranjan Khaire, Mahesh Swaminathan, Alessandra Ferrajoli, Jan Burger, Vishruth Shah, Kelly Chien, Gautam Borthakur, Koichi Takahashi, Naveen Pemmaraju, Prithviraj Bose, Jo Ishizawa, Beenu Thakral, Naveen Garg, Hyunsoo Hwang, Wei Qiao, Cameron Garcia, Anna Evangelio, Ana Ayala, Guillermo Garcia-Manero, Deepa Sampath, Varsha Gandhi, Michael Keating, Hagop Kantarjian, William Wierda

# BACKGROUND

- Richter transformation (RT) represents transformation of CLL to an aggressive lymphoma histology, most commonly DLBCL

- Chemoimmunotherapy regimens like R-CHOP or R-EPOCH are commonly used frontline therapies with median survival of 6-12 months

- Clinical trials reported efficacy of targeted therapies including BTK, BCL2, and PD-1 inhibitors

  - R-EPOCH + Ven (n=26, 92% frontline RT) — 62% ORR, median PFS 10.1 mos
  - Tislelizumab + Zanubrutinib (n=48, 79% frontline RT) — 58% ORR, median PFS 10 mos
  - Atezolizumab + Ven + Obin (n=28, all frontline RT) — 68% ORR, median PFS ≈10 mos

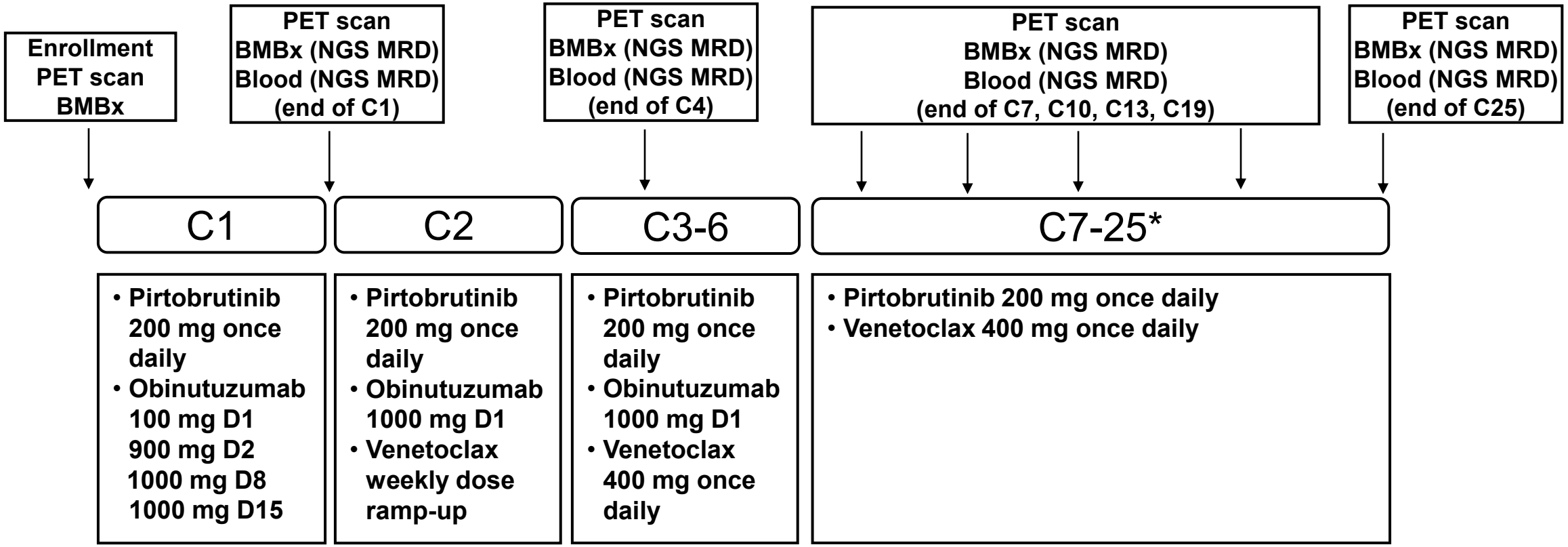
- Pirtobrutinib is a non-covalent BTKi approved for patients with R/R CLL with activity reported in RT
  - Pirtobrutinib (n=82, 74/82 relapsed RT): 50% ORR, median PFS 3.7 mos

- We report results of a phase II trial of pirtobrutinib, venetoclax and obinutuzumab for patients with RT

Rossi et al. Blood 2018; Davids et al. Blood 2022; Al-Sawaf et al. Nature Medicne 2024; Tedeschi et al. Lancet Onc 2024; Wierda et al. Lancet Haem 2024; Ding et al. Blood 2017; Youines et al. Lancet Haem 2019; Jain et al. Blood Adv 2023

Jain, PVO in RT, ASH 2025, Abs 89

# PVO IN RT: TREATMENT SCHEMA

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# PVO IN RT: PRIOR TREATMENTS (N=15)

15 patients enrolled

Median follow-up 16.5 months

| Prior lines of therapies | | n (%) or median [range] |
|---|---|---|
| Prior Rx for CLL | | 1 [0-4] |
| Prior Rx for RT | | 1 [0-4] |
| Total prior lines of Rx (CLL+RT) | | 2 [1-4] |
| Prior CLL and RT Rx | Chemotherapy | 11 (73) |
| | Anti-CD20 mAb | 13 (87) |
| | BTKi | 8 (53) |
| | BCL2i | 9 (60) |
| | PD-1/PD-L1i | 4 (27) |
| | Allo-SCT | 1 (7) |
| | CD19 CAR T | 1 (7) |

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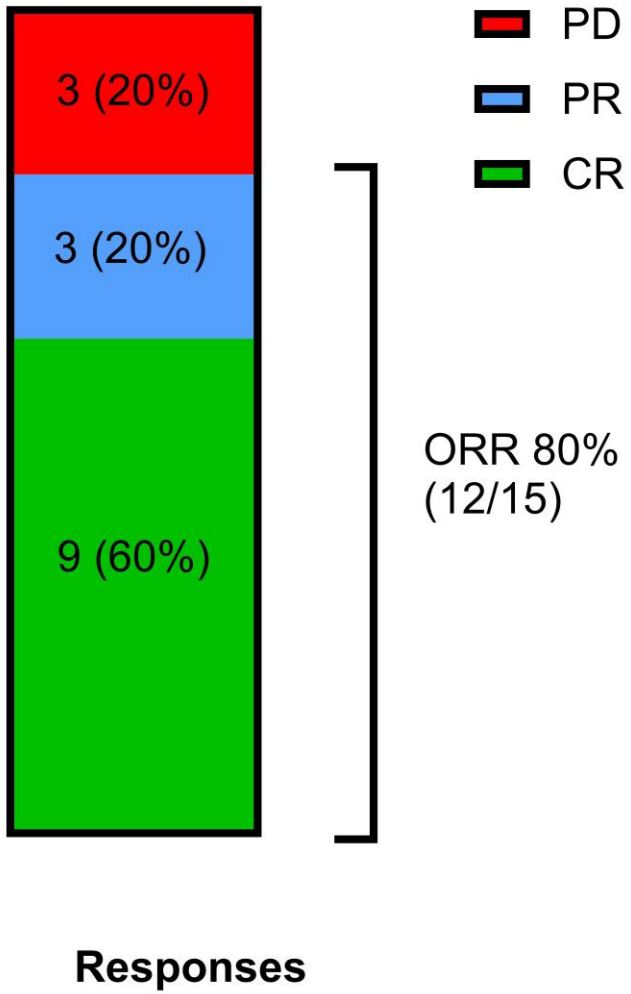
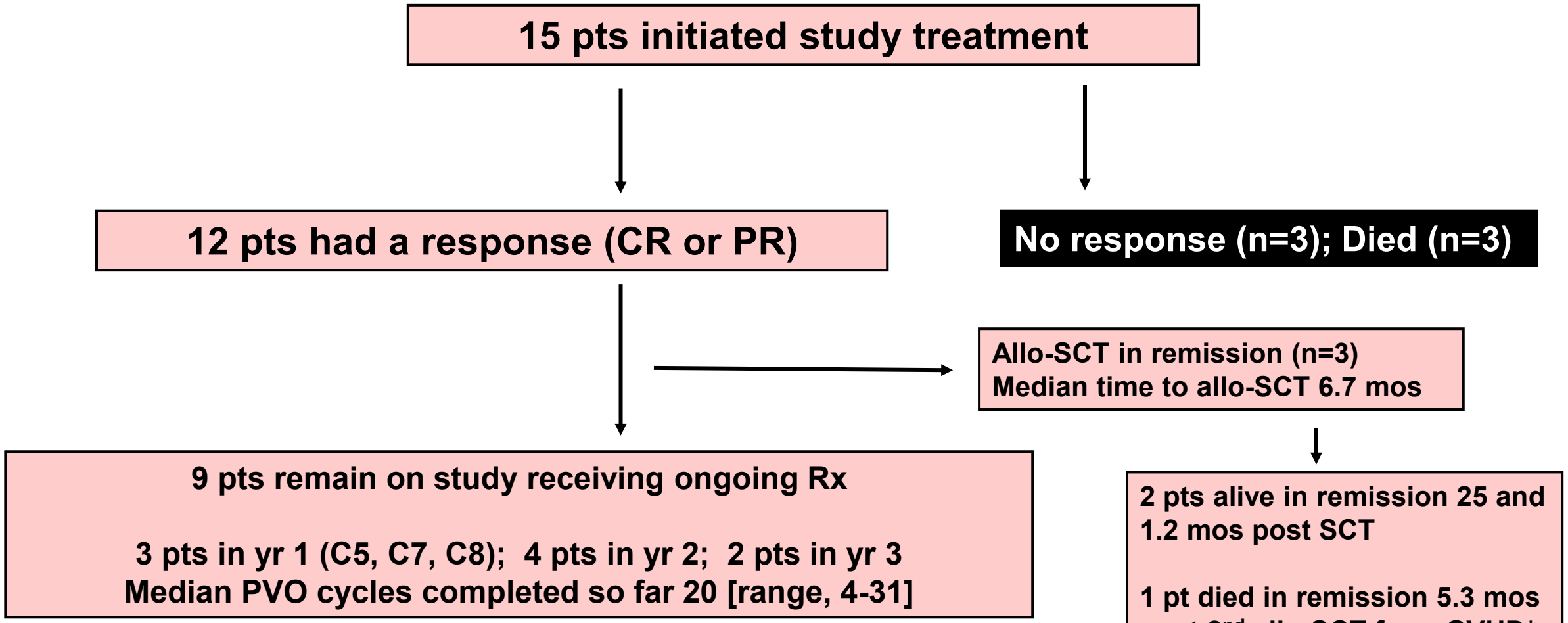
# PVO IN RT: BEST RESPONSE




- Best Overall response rate 80% (12/15)
  Lugano criteria (PET scan)
- No. of cycles to response
  median 1 [range, 1-7]

Jain, PVO in RT, ASH 2025, Abs 89

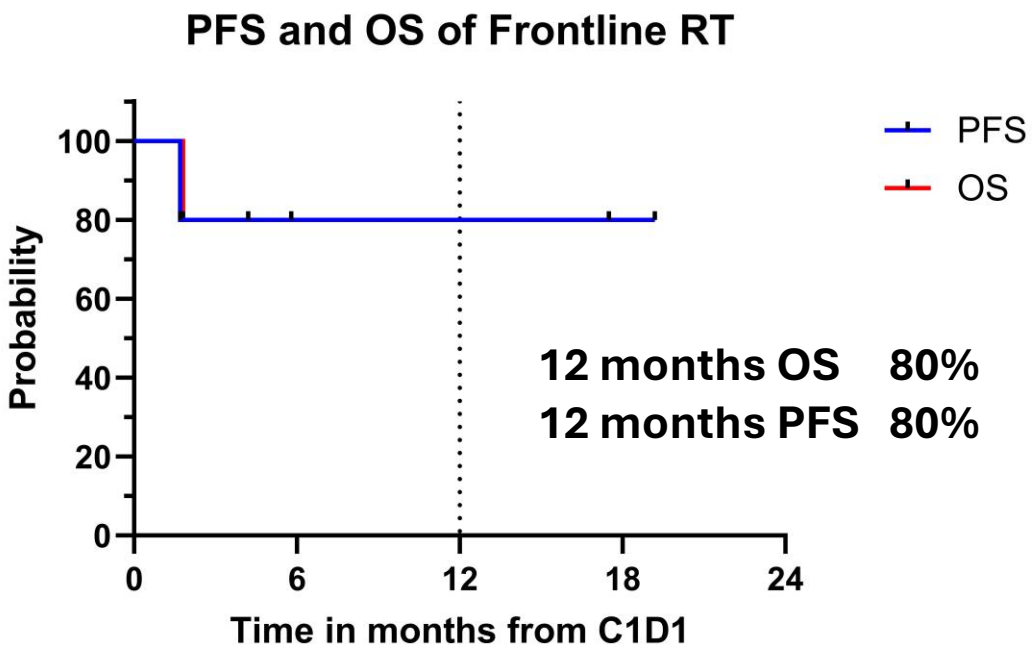
# PVO IN RT: PATIENT DISPOSITION

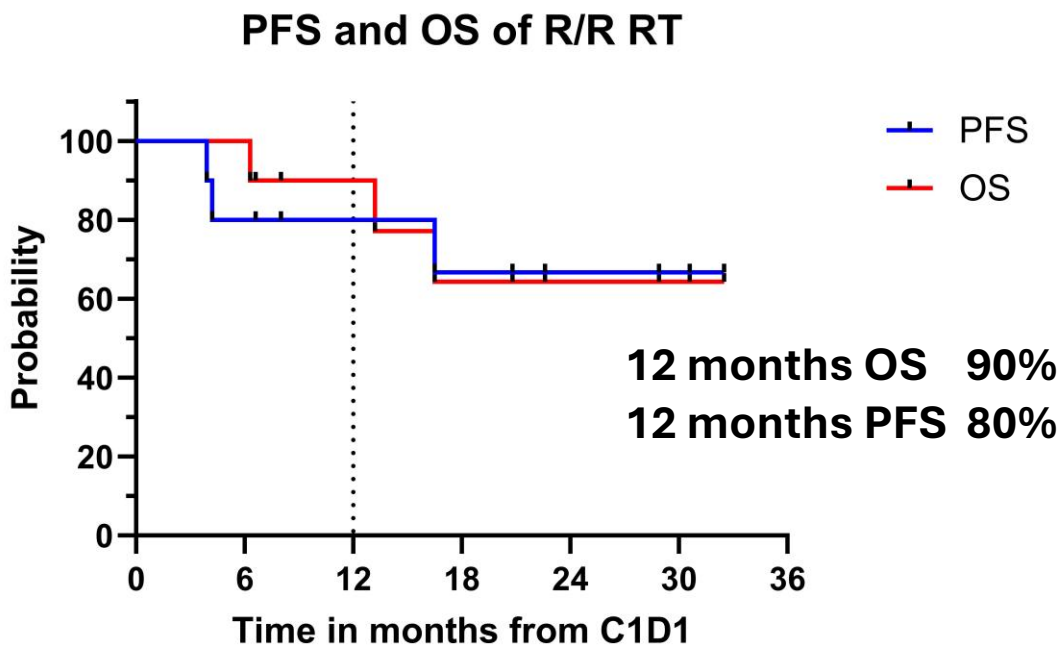



*61-yr-old with del(17p), *TP53* mutated and IGHV-unmutated CLL. Prior Rx included R-CHOP/VEN for RT followed by allo-SCT

Jain, PVO in RT, ASH 2025, Abs 89

# PVO IN RT: PFS AND OS FOR ALL PATIENTS (N=15)




| Number of Risk | | | | | | No of events |
|---|---|---|---|---|---|---|
| PFS | 5 | 2 | 2 | 1 | 0 | 1 |
| OS | 5 | 2 | 2 | 1 | 0 | 1 |

| Number of Risk | | | | | | | | No of events |
|---|---|---|---|---|---|---|---|---|
| PFS | 10 | 8 | 6 | 5 | 3 | 2 | 0 | 3 |
| OS | 10 | 10 | 7 | 5 | 3 | 2 | 0 | 3 |

Jain, PVO in RT, ASH 2025, Abs 89

# CONCLUSIONS

- We observed an ORR rate of 80% (12/15) with combined pirtobrutinib, venetoclax, and obinutuzumab in patients with Richter transformation
- 12-mo PFS and OS rates were 80% and 85.6%, respectively
  - Among 10 pts with R/R RT, 12-mo PFS and OS rates of 80% and 90%, respectively
- Among the responders (n=12), 12-mo duration of response is 100%
- Toxicity profile was similar to triplet combination regimens in CLL

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# ASH 2025 COMES TO YOU!

**Dr. Brian Koffman**
**Co-Founder and Chief Medical Officer, Emeritus**
**CLL Society, Inc.**

# 5 PROMISING AND IMPORTANT ABSTRACTS

1. Surprisingly strong real-world results for liso-cel CAR-T
2. Bexobrutideg: a BTK degrader in relapsed/refractory (R/R) CLL
3. BGB-16673: a BTK degrader in relapsed/refractory (R/R) CLL
4. Rocbrutinib: a novel dual binding BTKi in double exposed CLL
5. Impact of genetic testing on CLL outcomes (CLL Society research)

# SUPERIOR REAL-WORLD OUTCOMES OF LISOCABTAGENE MARALEUCEL IN CLL

- Lisocabtagene maraleucel (liso-cel) is a type of CAR T-cell therapy approved in March 2024 for people with CLL whose disease returned after multiple treatments
- This study looked at 30 USA real-world patients, not those in a clinical trial.
- Patients:
  - Were older (average age 67)
  - Had high-risk disease features with 67% with either del17p and/or mutated TP53
  - Had received many prior treatments (average 6) including BTKIs and venetoclax
  - Many received pirtobrutinib shortly before CAR T-cell

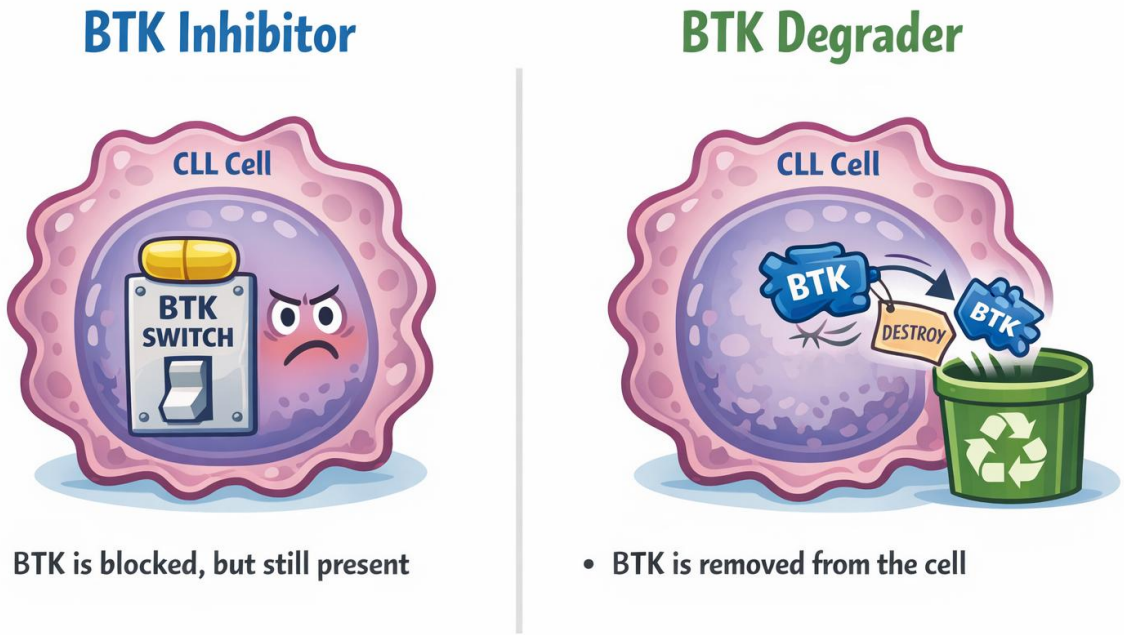
This was a difficult group of patients to treat

# SUPERIOR REAL-WORLD OUTCOMES OF LISOCABTAGENE MARALEUCEL IN CLL

- 83% responded to treatment
- 60% had no detectable active disease (uMRD)
- 72% of those whose last prior treatment was pirtobrutinib responded compared to only 28% of those who did not receive it just before
- Most responses were ongoing at early follow-up (average 3 months)
- Adverse events (AE) or side effects included fever (CRS) and temporary confusion (neurotoxicity)
- Results are early but promising and much better than clinical trial data

# BEXOBRUTIDEG (NX-5948) A NOVEL BTK DEGRADER IN R/R CLL

- BTK is a protein that helps CLL cells survive
- BTK inhibitors (BTKi) block BTK activity
- Over time, CLL can work around BTKi by developing mutations that block binding
- BTK degraders remove BTK from the cell entirely
- This may help when BTK inhibitors stop working



# BEXOBRUTIDEG (NX-5948) A NOVEL BTK DEGRADER IN R/R CLL

**NX-5948-301 Phase 1, first-in-human trial of bexobrutideg in R/R B-cell malignancies (CLL/SLL focus)**

**Patients (n=97, CLL/SLL)**

- **Median age: 68 years; median prior therapies: 4 (range 1–12)**

**Prior exposure:**

- **cBTKi: 97.9%**
- **ncBTKi: 32%**
- **BCL2i: 74.2%**
- **BTKi + BCL2i: 73.2%**
- **Chemo/immunotherapy: 77.3%**
- **CAR-T: 6.2%**

**High-Risk Features**

- **BTK mutations: 42.4% (C481S/R, T474, L528, V416)**
- **PLCG2 mutations: 10.6%**
- **TP53 mutations: 42.4%**

**This was a difficult group of patients to treat**

# BEXOBRUTIDEG (NX-5948) A NOVEL BTK DEGRADER IN R/R CLL

- Time to first response: ~2 months; responses deepened over time
- Duration of response: median not reached; some patients on treatment >18 months
- Side effects: fatigue, diarrhea, bruising, low blood counts; serious side effects were rare
- Well tolerated even in high-risk patients with BTK mutations

Conclusion:

- Early results are promising with rapid and durable responses in heavily treated CLL
- Overall response rate (ORR): 78.6%

# BGB-16673, AN ORAL BTK PROTEIN DEGRADER, IN R/R CLL/SLL

**Study Design**

- Open-label Phase 1/2 R/R CLL/SLL patients ≥2 prior therapies

**Patients (n=67)**

- Median age: 70 years
- Median prior therapies: 4 (range 2–10)
- Prior exposure:
  - cBTKi: 94%
  - BCL2i: 82%
  - ncBTKi: 21%

**High-Risk Features**

- del(17p)/TP53: 66%
- Unmutated IGHV: 78%
- BTK mutations: 38%
- PLCG2 mutations: 16%

**This was a difficult group of patients to treat**

# BGB-16673, AN ORAL BTK PROTEIN DEGRADER, IN R/R CLL/SLL

**Safety:**

- Any-grade AEs: 95.5%
- Common AEs: fatigue, bruising, diarrhea, neutropenia (low neutrophil count)
- Grade ≥3 TEAEs: 62.7%
  - Neutropenia: 23.9%
  - Pneumonia: 10.4%
- AE-related discontinuation: 17.9%
- No treatment-related deaths

**Efficacy:**

- ORR: 86.4%
- CR/CRi: 4.5%
- ORR at 200 mg: 93.8%
- Responses deepened over time
- Consistent activity across:
  - Prior BTKi exposure
  - BTK-mutant disease
  - del(17p)/TP53

**Conclusion:**
Robust, durable responses in heavily pretreated patients

# ROCBRUTINIB (LP-168),A DUAL BINDING BTKi: PATIENTS IN THE TRIAL

**Patients with R/R or hard-to-treat CLL**

**Patients (n = 42)**

- **Median age: 66 years (range 45–81)**
- **83% male**
- **Median prior therapies: 4 (range 2–9)**

**Prior Treatments**

- **45% received >1 covalent BTK inhibitor**
- **21% received both non-covalent and covalent BTK inhibitors**
- **40% received venetoclax**

**High-Risk Features**

- **12 pts (30.8%) – Complex karyotype**
- **24 pts (58.5%) – del(17p) and/or TP53 mutation**
- **17 pts (40.5%) – del(11q)**
- **26 pts (65.0%) – C481S BTK mutation**
- **7 pts (17.5%) – other C481 BTK mutations**
- **12 pts (30.8%) – Gatekeeper T474 BTK mutation**
- **2 pts (5.1%) – L528W BTK mutation**
- **1 pt (2.6%) – A428D BTK mutation**
- **1 pt (2.6%) – V416L BTK mutation**
- **4 pts (10.3%) – PLCγ2 resistance mut.**

**This was a difficult group of patients to treat**

# ROCBRUTINIB (LP-168),A DUAL BINDING BTKi: SIDE EFFECTS (AEs)

**Most side effects were mild**

**Most common issues:**

- **Diarrhea**
- **Cough**
- **Headache**
- **Joint pain**
- **Fatigue**
- **Nausea**
- **Constipation**

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**More serious side effects were rare**

- **Low white blood cells**
- **Infections**

**Heart rhythm problems were rare**

**Bottom line:**

**The treatment was generally well tolerated by patients**

# ROCBRUTINIB (LP-168),A DUAL BINDING BTKi: MOA AND RESULTS

**Dual Mechanism of Action:**
**Rocbrutinib blocks BTK in two ways:**

- **Irreversibly (covalently) blocks normal BTK**
- **Reversibly (noncovalently) blocks mutated BTK (C481 mutations)**
- **This dual activity helps overcome resistance from prior BTK medicines.**

- **Overall response rate: 78%**
  - **16 partial responses**
  - **2 partial responses**
- **In patients also treated with venetoclax: 80% response rate**
- **Median PFS: 28 months**
- **45% of patients remained on therapy at last follow-up**

# IMPACT OF GENETIC TESTING ON CLL OUTCOMES (CLL SOCIETY)

## Impact of testing for genetic markers on treatment selection and clinical outcomes among patients with chronic lymphocytic leukemia (Dr. Brian Koffman)

**Who was studied?**

- **Over 5,400 people with CLL starting their first treatment**
- **Looked at whether patients had recommended genetic tests *before* treatment**

**Tests checked for:**

- **del17p**
- **TP53 mutation**
- **IGHV status**

**These markers help doctors:**

- **Choose the best treatment**
- **Avoid treatments that won't work well**
- **Predict how the disease may behave**

# IMPACT OF GENETIC TESTING ON CLL OUTCOMES (CLL SOCIETY)

**Patients who were tested:**

- Stayed on their first treatment ~12 months longer
- Had a lower risk of progression
- Were more likely to receive modern, guideline recommended therapies

**Patients who were NOT tested:**

- Started treatment without full information
- More likely to get older chemo
- **Shorter time before needing next treatment (TTNT)**

**Most important takeaway**

**Genetic testing is:**

- Simple
- Widely available
- Strongly linked to a better outcome

**Bottom Line:**

**Just getting appropriate genetic testing before treatment is a sign of excellent care, regardless of the results**

**Smart Patients Get Smart Care**

# AUDIENCE Q&A

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your feedback is important to us**

**If your question was not answered,
please feel free to email: asktheexpert@cllsociety.org**

**Join us for our next virtual event,**

## ASK ME ANYTHING – FEATURING DR. RYAN JACOBS AND DOREEN ZETTERLUND

**MARCH 6**

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