

BACKGROUND

Clinical Context

- Fixed-duration venetoclax-based regimens in chronic lymphocytic leukemia (CLL) introduce treatment-free intervals (TFI), thus making retreatment strategies increasingly relevant.
- The effects of TFI and cytogenetic/molecular risk factors on retreatment outcomes remain incompletely defined.

Objective

- Determine the independent predictive value of TFI and cytogenetic/molecular risk on weighted retreatment overall response rate (wORR2) and weighted retreatment 2-year progression-free survival (wPFS2).
- We performed a pooled study-level analysis of nine venetoclax-based retreatment cohorts (N=190). Patients were stratified by TFI (<24 vs ≥24 months) and cytogenetic/molecular risk status (*IGHV* mutation and del[17p]/*TP53* mutation).

Statistical Methods

- DerSimonian-Laird RE models
- Spearman correlation + WLS meta-regression
- Multivariate: TFI adjusted for del(17p)/TP53 and IGHV independently

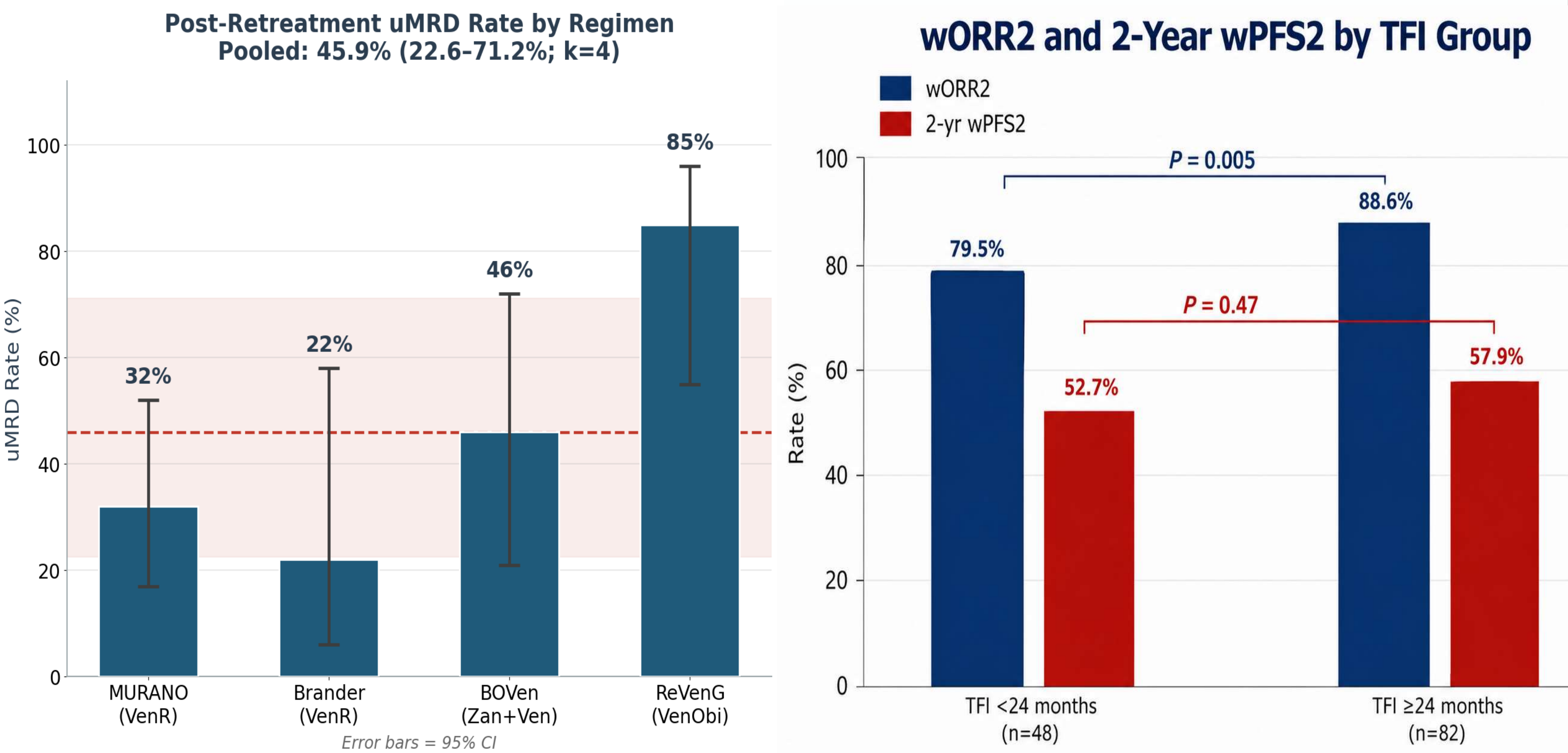
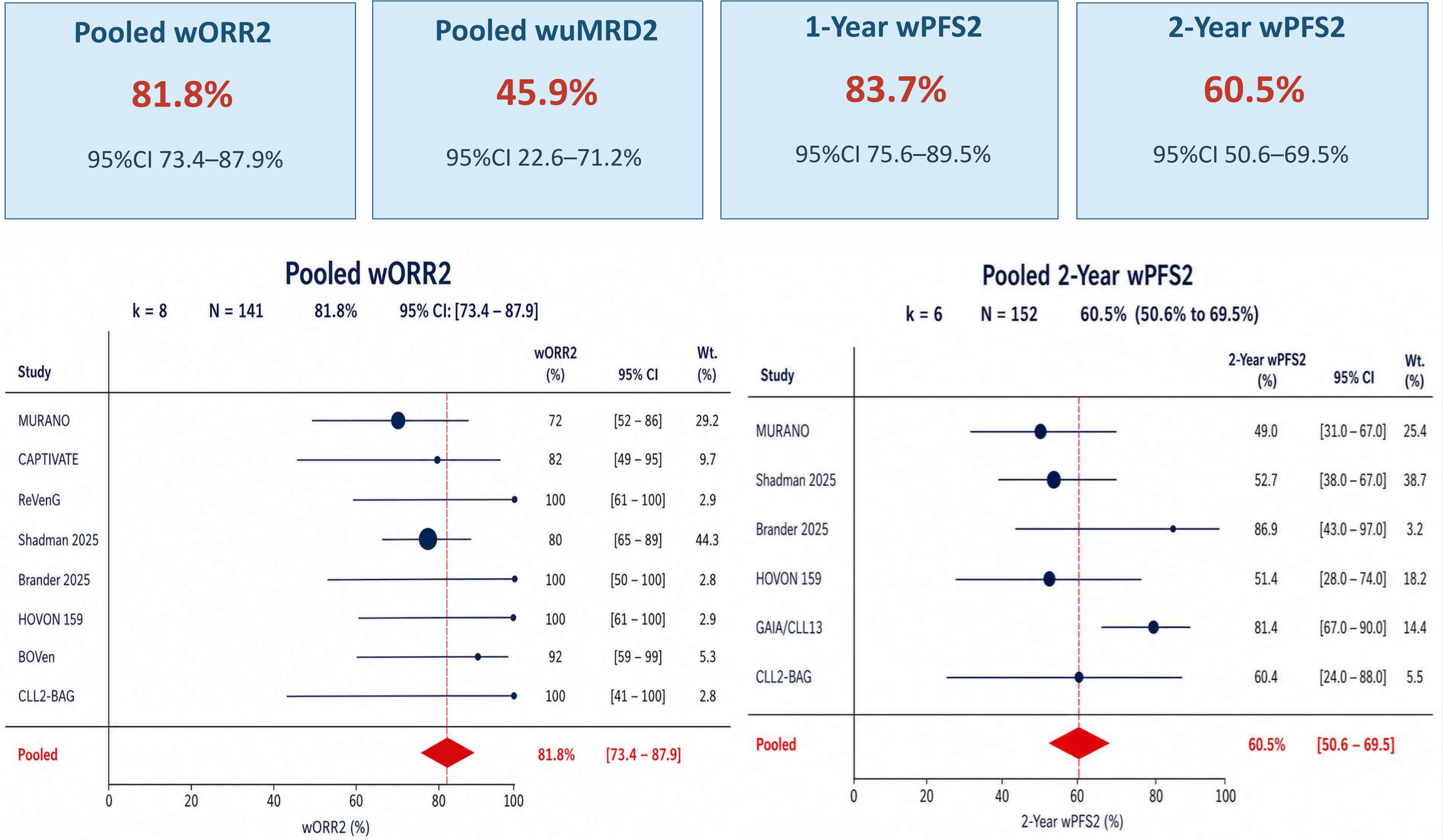
Study	n	Regimen	Median TFI	uMRD2	ORR2	2 year PFS2
MURANO	25	Ven+R	27.6 mo	32%	72%	49.0%
CAPTIVATE	11	Ven+Ibr	>24 mo	N/A	82%	N/A
ReVenG	15	Ven+Obi	53.3 mo	84.6%	100%	N/A
Shadman 2025	48	Ven-based*	21.2 mo	N/A	79.5%	52.7%
Brander 2025	9	Ven+R	38.4 mo	22%	100%	86.9%
HOVON 159	14	Ven+Acala	36.0 mo	N/A	100%	51.4%
BOVen	12	Ven+Zan**	29.0 mo	46%	92%	N/A
GAIA/CLL13	49	Ven-based*	N/A	N/A	N/A	81.4%
CLL2-BAG	7	Ven+Obi	68.0 mo	N/A	100%	60.4%

** Ven+ Zan cohort was pretreated with zanu + obi + ven
*Ven-based included ven+obi, ven+R, ven+BTKi

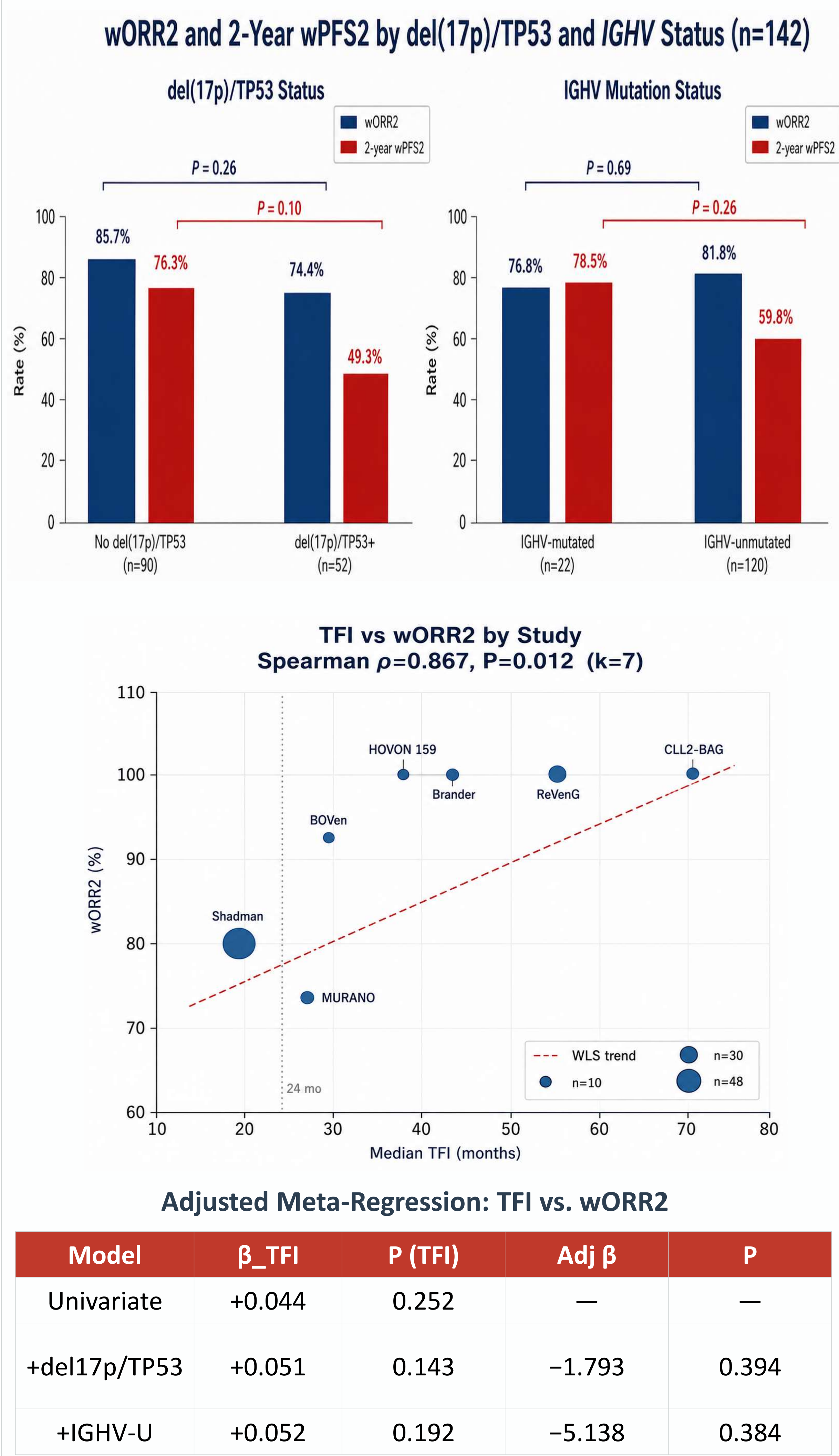
CONCLUSIONS

- Venetoclax-based combination retreatment demonstrates consistent clinical activity with pooled wORR2 of 81.8%, 2-year wPFS2 of 60.5% and uMRD2 of 45.9% in this pooled study-level analysis.
- TFI ≥24 months is independently associated with higher wORR2 (Spearman ρ=0.87, P=0.012) after multivariate adjustment for del(17p)/TP53 and IGHV status.
- TFI does not significantly affect 2-year wPFS2 (P=0.47). Del(17p)/TP53 mutation is the more dominant determinant of PFS2 depth (76.3% vs 49.3%).
- TFI should be incorporated as a stratification variable in prospective relapsed/refractory CLL retreatment trials.

RESULTS — EFFICACY & uMRD



RESULTS — SUBGROUP ANALYSIS



REFERENCES

- Kater AP, et al. The MURANO study: final analysis and retreatment/crossover substudy results of VenR for patients with relapsed/refractory CLL. *Blood*. 2025;145(23):2733-2745. doi:10.1182/blood.2024025525.
- Ghia P, et al. Final analysis of fixed-duration ibrutinib plus venetoclax for chronic lymphocytic leukemia/small lymphocytic lymphoma in the phase 2 CAPTIVATE study. *J Clin Oncol*. 2025;43(16 Suppl):7036. doi:10.1200/JCO.2025.43.16_suppl.7036.
- Davids MS, et al. Preliminary results of the ongoing multicenter, phase 2 study of retreatment with venetoclax plus obinutuzumab (ReVenG) in patients with recurrent chronic lymphocytic leukemia. EHA Congress 2025. Abstract PF575.
- Shadman M, et al. Venetoclax retreatment of real-world patients with chronic lymphocytic leukemia previously treated with venetoclax-based regimens. *Blood*. 2025;146(Suppl 1):2108. doi:10.1182/blood-2025-2108.
- Brander DM, et al. Retreatment with venetoclax and rituximab following disease progression while off therapy in patients with chronic lymphocytic leukemia. *Hemasphere*. 2025;9(12):e70284. doi:10.1002/hem3.70284.
- Kersting S, et al. Venetoclax-acalabrutinib for CLL patients relapsing after venetoclax-antiCD20 treatment: interim analysis of HOVON 159/REVEAL phase 2 trial. EHA Congress 2025. Abstract PS1563.
- Soumerai JD, et al. Multicenter phase II trial of zanubrutinib, obinutuzumab, and venetoclax (BOVen) in treatment-naïve chronic lymphocytic leukemia: 5-year follow-up, retreatment outcomes, and impact of MRD kinetics. *Blood*. 2024;144(Suppl 1):1867.
- Niemann CU, et al. Efficacy of 2nd-line treatment in CLL after venetoclax-based 1st-line treatment: results from the GAIA/CLL13 trial. *Blood*. 2025;146(Suppl 1):795. doi:10.1182/blood-2025-795.
- Mazot L, et al. Re-treatment with venetoclax-obinutuzumab after time-limited, MRD-guided venetoclax-obinutuzumab: final analysis of 7 patients with CLL treated in the CLL2-BAG trial of the GCLLSG. XXI International Workshop on CLL (iwCLL); 2025. Poster 1515.

CONTACT & ACKNOWLEDGEMENTS

Corresponding Author
Jun Chih Wang, MD
Memorial Cancer Institute
Memorial Healthcare System
Pembroke Pines, FL, USA
juwang@mhs.net

Acknowledgements
The authors thank investigators and patients of all contributing retreatment studies.

Disclosures
Pool analysis of published data. No pharmaceutical funding. Authors declare no conflicts of interest.