POST-ORLANDO 2025
Novità dal Meeting della Società Americana di Ematologia

Novità dal Meeting della Società Americana di Ematologia

Torino
Centro Congressi Lingotto
19-21 febbraio 2026

COORDINATORI
Angelo Michele Carella
Pier Luigi Zinzani

BOARD SCIENTIFICO
Paolo Corradini
Mauro Krampera
Fabrizio Pane
Adriano Venditti

Algoritmi terapeutici 2026: leucemia linfatica cronica

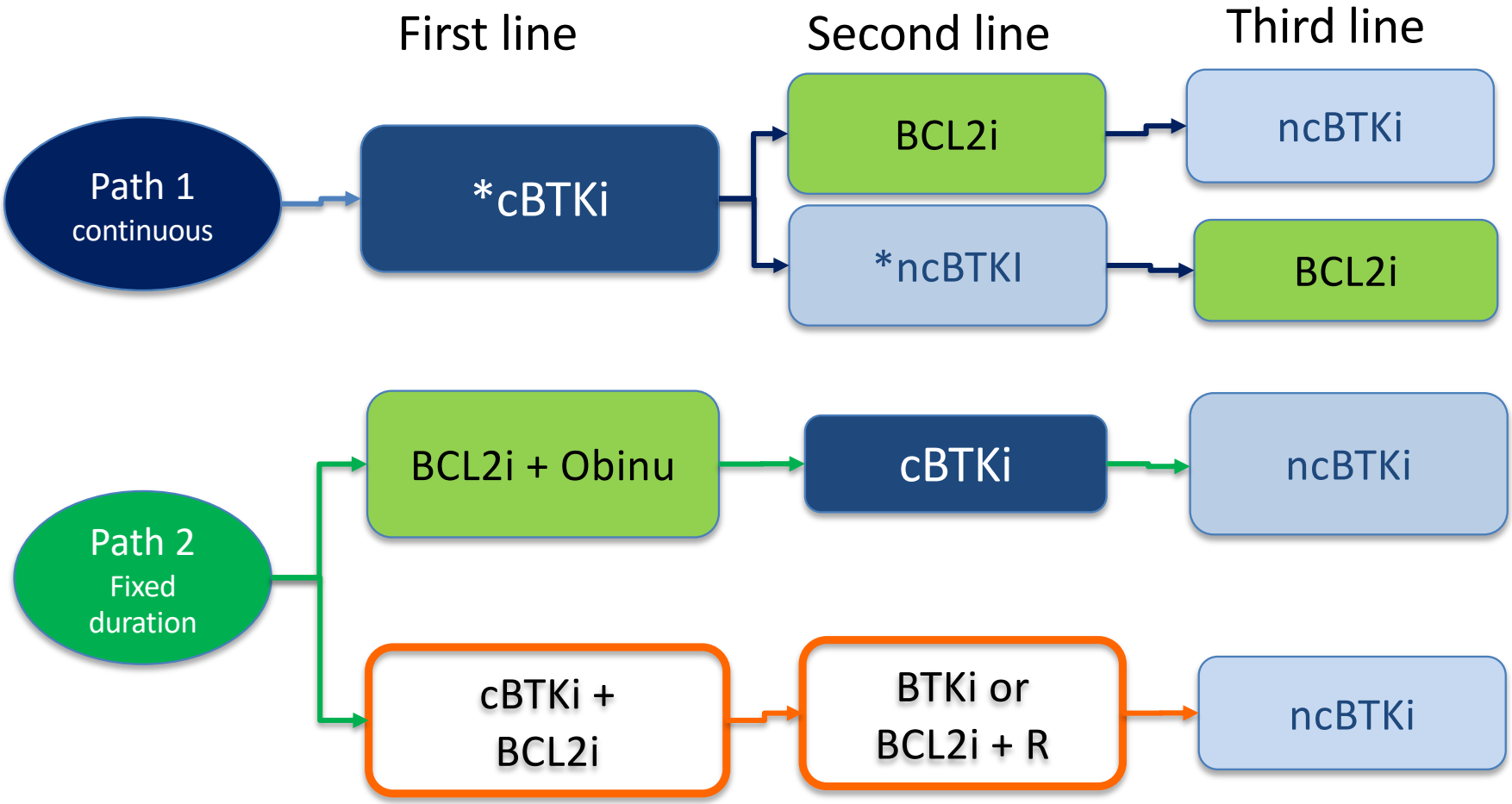
Prof. Antonio Cuneo, MD, PhD

Dipartimento di scienze mediche

DISCLOSURE Antonio Cuneo

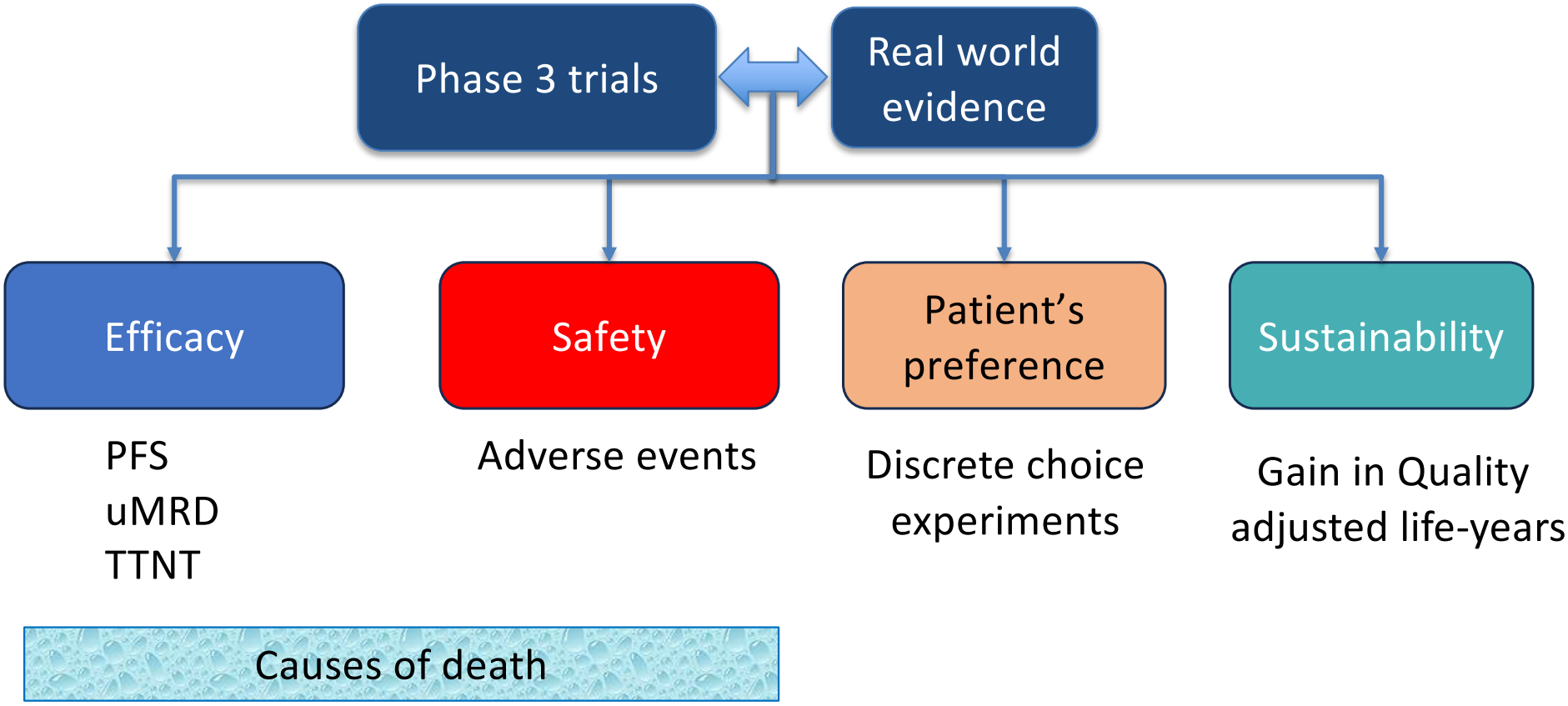
Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other
Abbvie					X	X	
Astra Zeneca					X	X	
Beigene					X	X	
Janssen					X	X	
Lilly					X	X	

CLL 2026: therapeutic options



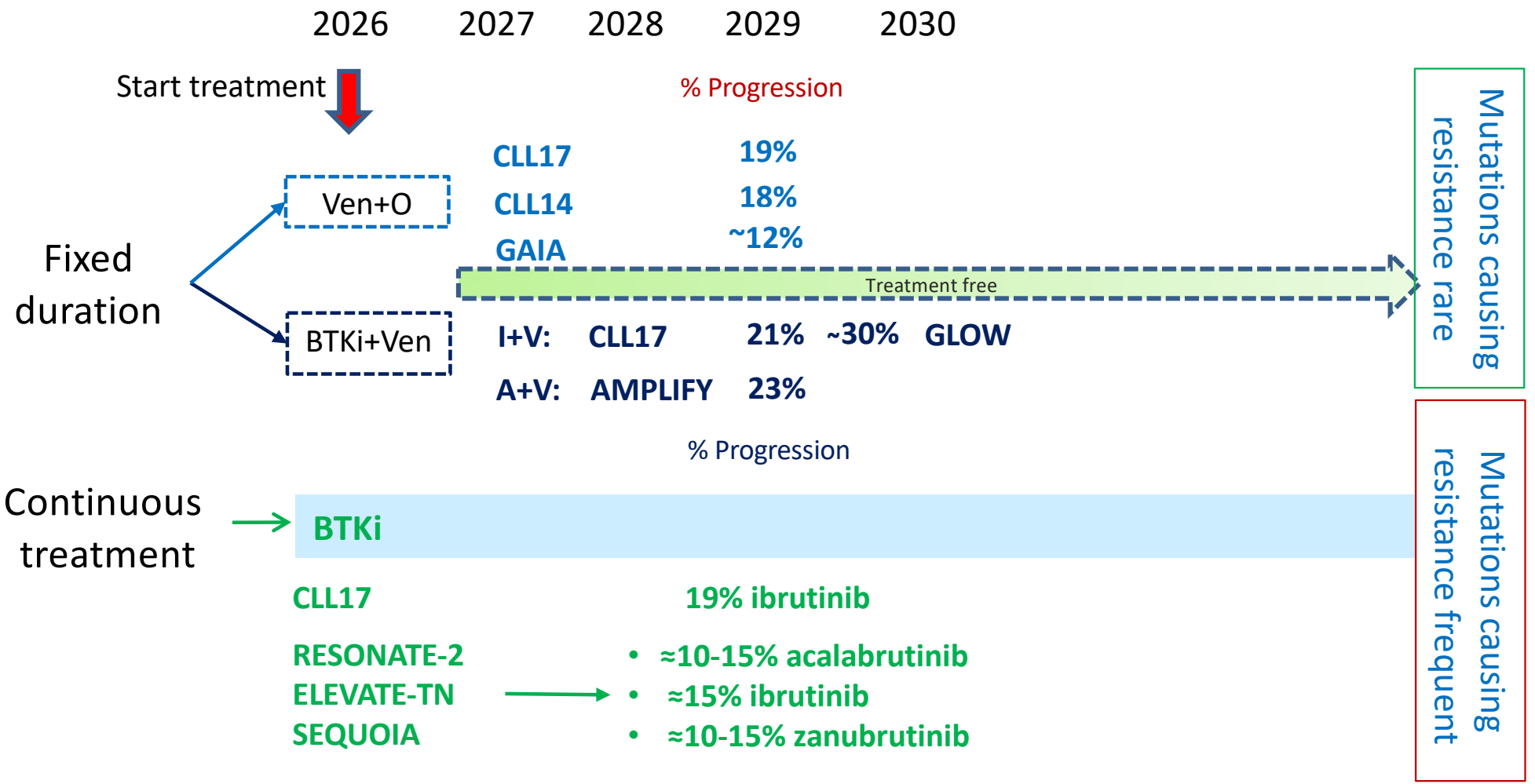
cBTKI: acalabrutinib, ibrutinib or zanibrutinib; ncBTKi: pirtobrutinib; BCL2i: venetoclax

Drivers of choice



Efficacy

Expected outcome at 3 yr in CLL treated with 1st line targeted therapy (phase 3 trials) – Cave: don't do cross-trial comparison



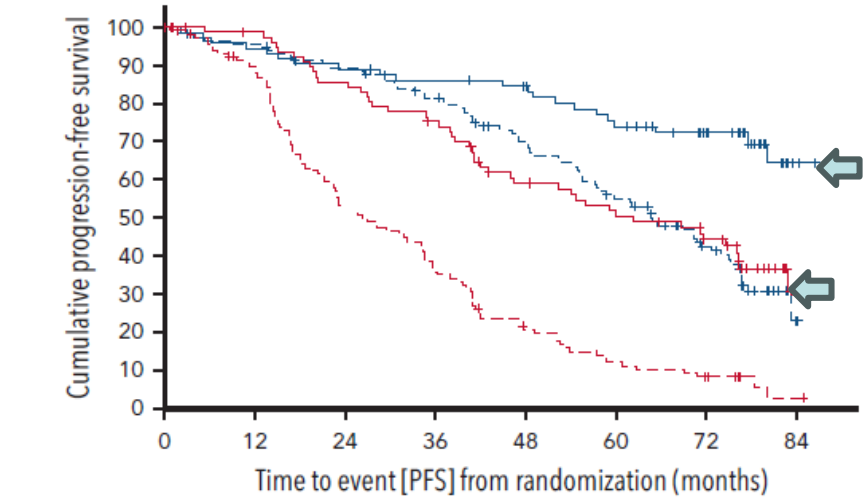
I-Sawaf O. Blood 2024; **Furstenau M, Lancet Oncol 2024;** Al Sawaf NEJM, 2025 **Niemann C**. Lancet Oncol 2023; **Ghia P ASH 2023; Brown J ASH 2024; [6]Sharman JP,** Leukemia 2022. **Woyach J Blood, 2024**; **Munir T** #639; EHA2023;

Efficacy

Impact of IGHV mutational status

Fixed duration and continuous treatment

PFS is shorter in uIGHV CLL

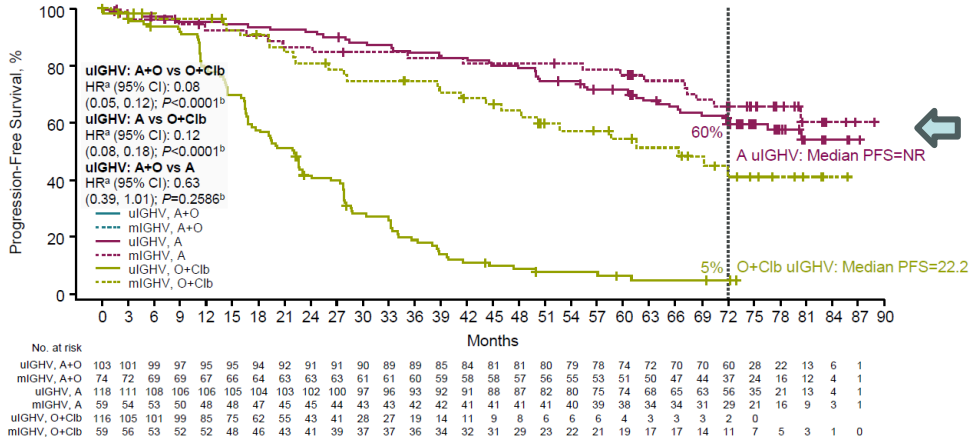


CLL14 trial

Al Sawaf O et al, Blood 2024: 144; 1924-35

PFS is similar in uIGHV and mIGHV CLL

IGHV status impacts PFS for patients treated with O+Clb, but not with acalabrutinib regimens



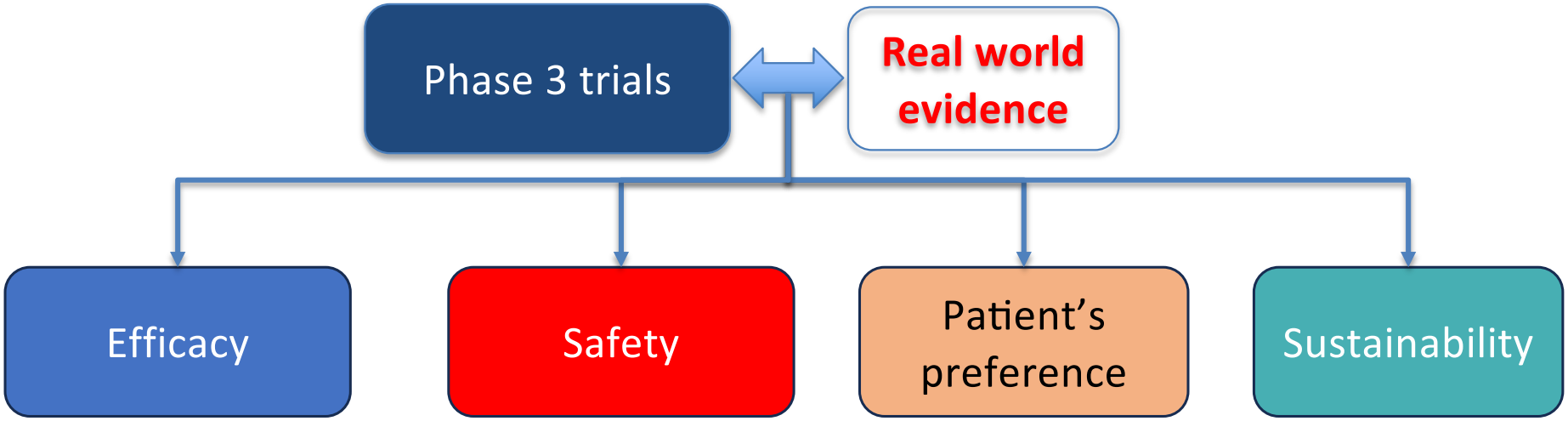
[a]Hazard ratio based on unstratified Cox proportional-hazards model.
[b]*P*-value based on unstratified log-rank test.

9

ELEVATE-TN 6 Year Update

Sharman J, Blood 2025; 146: 1276-85

Drivers of choice



Efficacy RWE

First Analysis:

Outcomes in patients with chronic lymphocytic leukemia and TP53 aberration who received **first-line ibrutinib**: a nationwide registry study from the Italian Medicines Agency

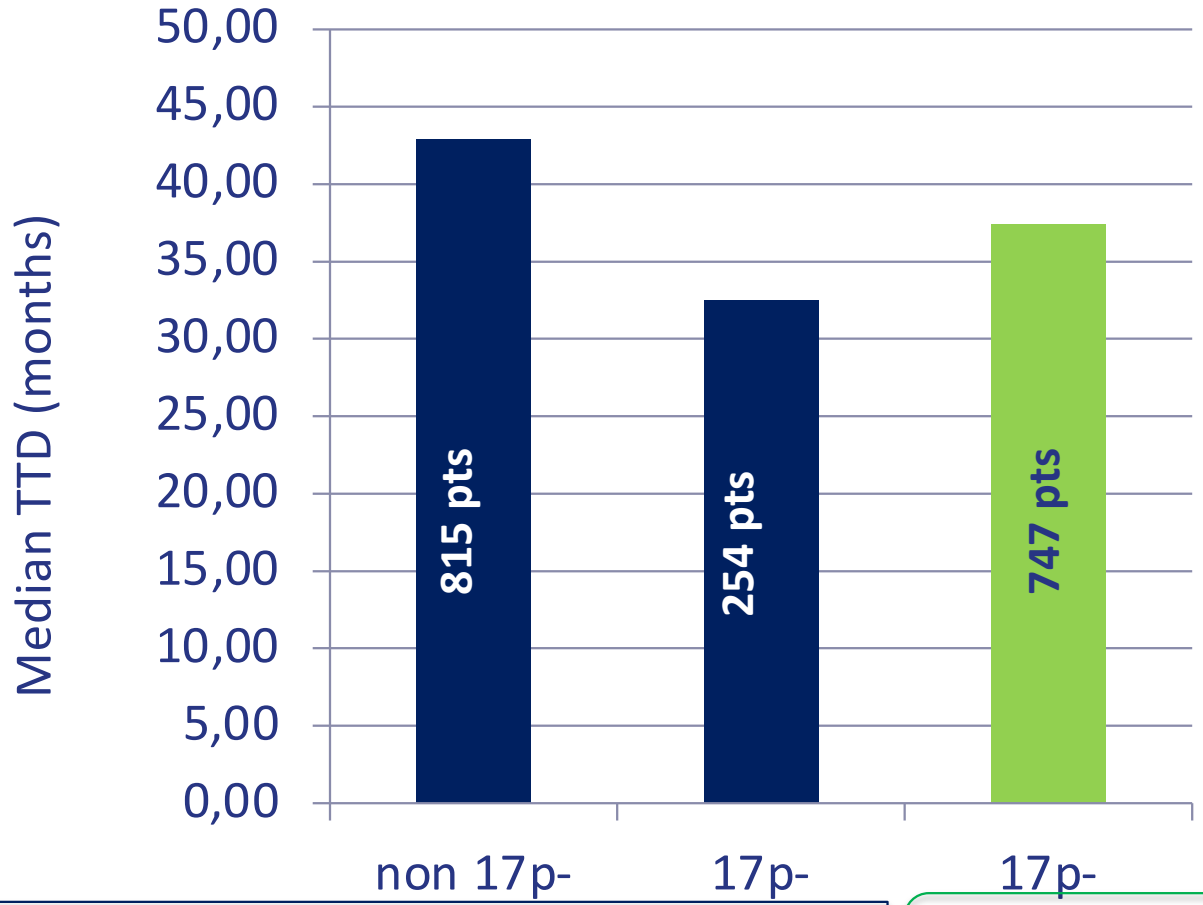
AIFA ibrutinib CLL monitoring Registries

ETL: First-line carrying TP53 aberrations

Cohort: 747 treated in the approved therapeutic indication between January 2016 and December 2020 in the framework of INHS reimbursement (**census**)

*Rigolin, G.M., Olimpieri, P.P., Summa, V. et al. Outcomes in patients with chronic lymphocytic leukemia and TP53 aberration who received first-line ibrutinib: a nationwide registry study from the Italian Medicines Agency. Blood Cancer J. **13**, 99 (2023). https://doi.org/10.1038/s41408-023-00865-z*

Median time to discontinuation in CLL with 17p-/TP53 mutation: real world data with first line ibrutinib



Median age 71 y
ECOG-PS 0-1: 93.2%

No difference in TTNT based on the experience of the centre
- n. of pts
- >/= 3 pts
- <3 pts

Mato A et al Haematologica 2022	815 pts mFU 20.1 mos	254 pts mFU 20.1 mos	747 pts mFU 26 mos	Rigolin et al Blood Cancer Journal 2023

Outcomes and prognostic factors in 3306 patients with relapsed/refractory CLL treated with ibrutinib outside of clinical trials: a nationwide study

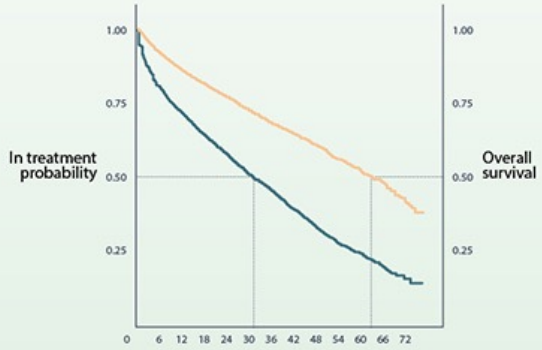
Start of ibrutinib

3306 RR/CLL
Nationwide study
100% capture

57.9% stilll receiving ibrutinib

42.1% discontinued

Discontinuation at 24 months



TTD and OS at a median f.u. of 42.2 months

- Median time from diagnosis: 75.65 m.
- Median age 72 years
- ECOG PS 0-1: 90.50%
- ≥2 previous lines of treatment: 42%

Prognostic factors for: early discontinuation and shorter survival

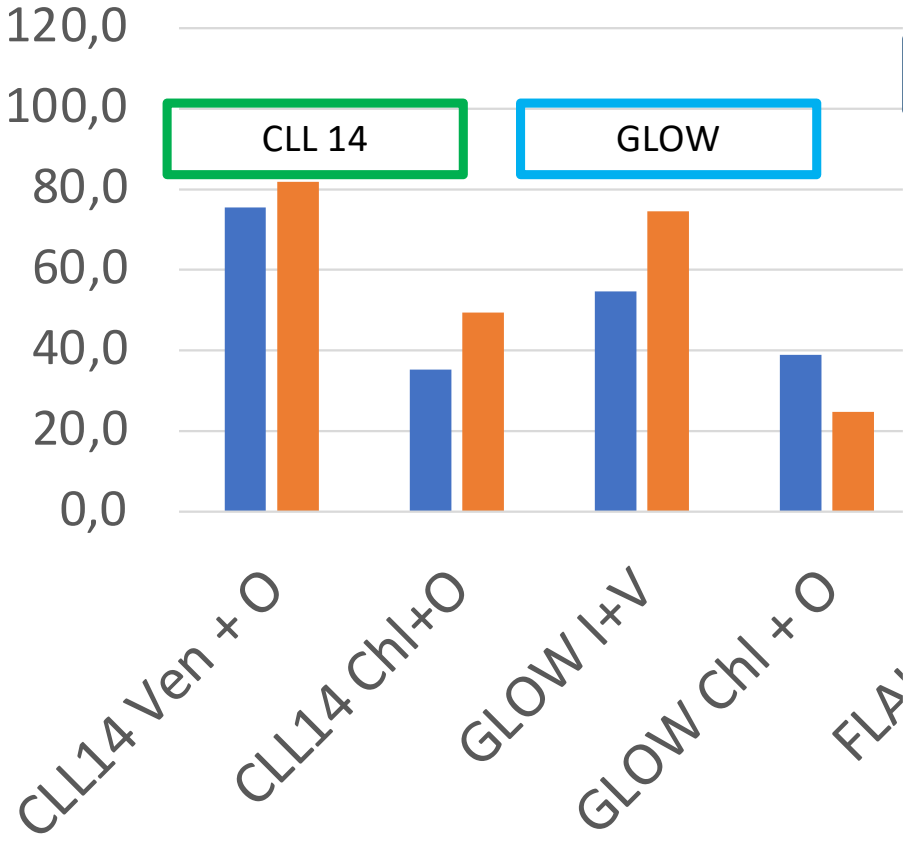
HR > 1 — Refractory disease — Double Hit *TP53* — Age — ECOG-PS — HR > 3

HemaSphere

Rigolin G at al, Hemasphere. 2024 Oct 8;8(10):e70017. doi: 10.1002/hem3.70017

Efficacy

% uMRD 10-4 and PFS rate at 3 yrs* in phase 3 trials



* At 42 mo.s in GLOW

Safety

Adverse events of clinical interest by regimen

Ven-based regimens

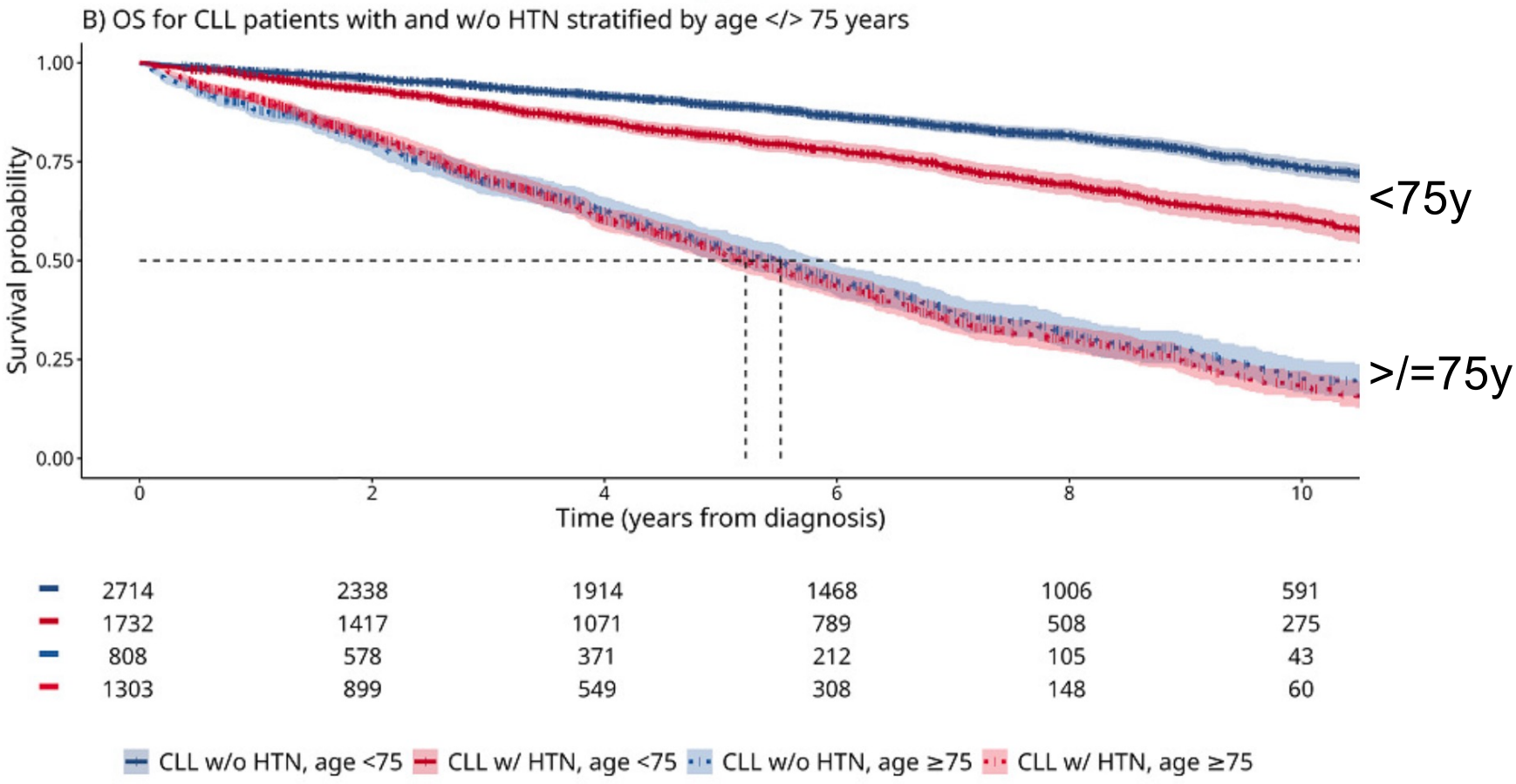
- TLS (laboratory, rarely clinically significant)
- Neutropenia
- Triplets (Ibru Ven Obinu or Acala Ven Obinu): infections

BTKi containing regimens

- Afib: Ibrutinib > vs Acalabutinib, Zanubrutinib and Pirtobrutinib
- Hemorrhage: Ibrutinib > vs Acalabrutinib
- Hypertension: Ibrutinib > vs Acalabrutinib and Pirtobrutinib

Ven+O CLL14 Al Sawaf O et al, Blood 2024: 144; 1924-35 -- Ven+O, Ven + Ibu + O GAIA. N Engl J Med. 2023 May 11;388:1739-1754 -- I+V FLAIR Munir T et al, NEJM 2025: 393: 2280 --- Acala ELEVATE-RR Byrd J Clin Oncol. 2021;39(31):3441–3452---- Zanu: ALPINE Brown J N Engl J Med. 2023;388:319-332-----Niemenn I+V GLOW Lancet Oncol. 2023 Dec;24(12):1423-1433.

Kaplan Meier curves presenting OS by age and hypertension from CLL for the Danish Lymphoid Cancer Research (DALY-CARE) ressource



Vainer N, et al, Blood Adv. 2026 Jan 28:bloodadvances.2025018771. .

Safety

Deaths by cause (%) in phase 3 trials with at least 5 yr follow-up

528 events in 2488 patients = 21.2%

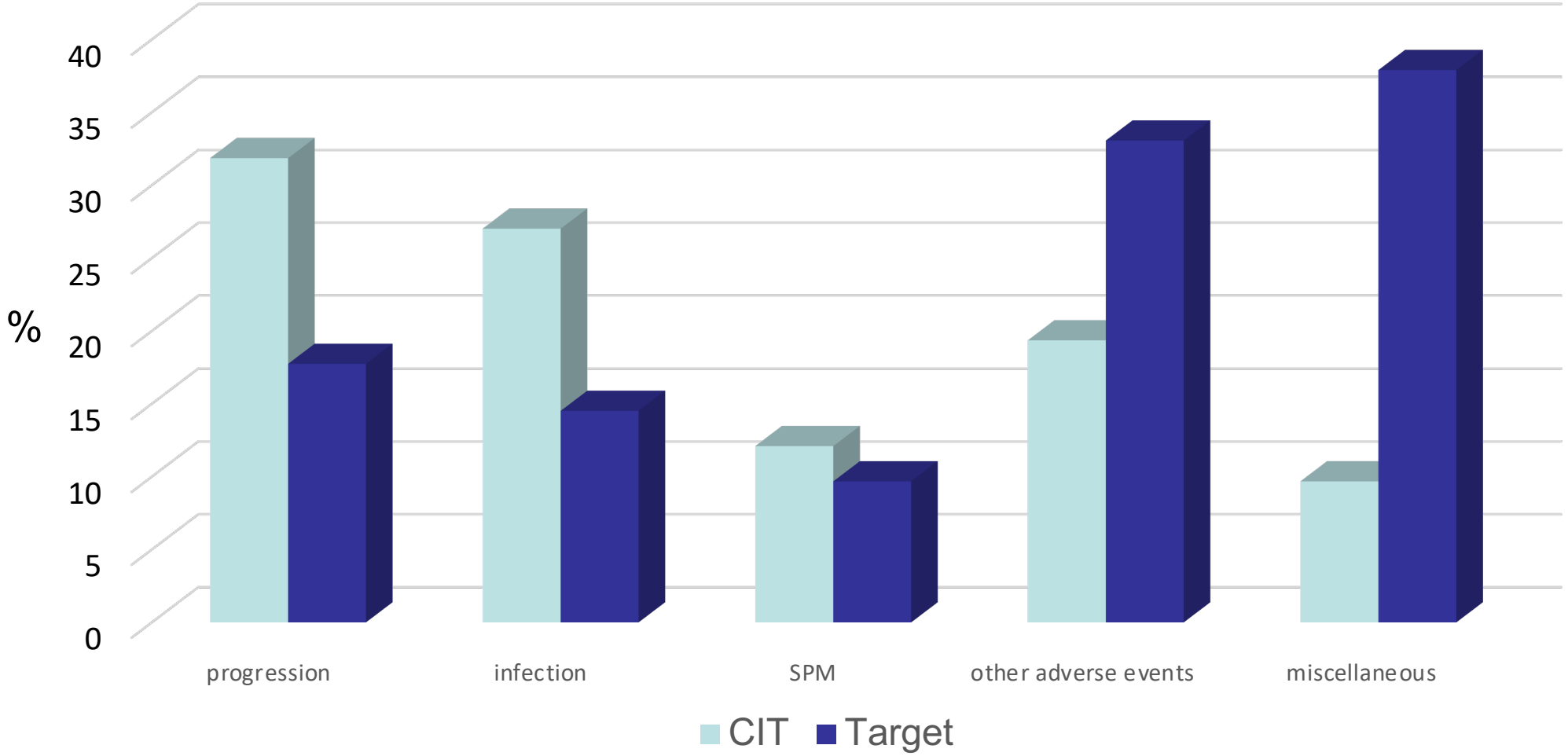
- Chemoimmuno: 248 events in 741 pts = 33,5%
  - Chlor+O CLL11 median f.u 62.5 m
  - FCR CLL8 median f.u. 59 m

- Target agents: 280 events in 1747 pts = 16%
  - Ven+O CLL14 median f.u. = 76.4 m.
  - IR FLAIR median f.u. = 97 m.
  - I+V GLOW median f.u. =57.3 m
  - I+V FLAIR median f.u = 62.2
  - Acala ELEVATE-TN median f.u. =74.5 m
  - Zanu SEQUOIA median f.u. =61.2 m
  - I+/-R A041202 median f.u. = 55 m

Chlor+O CLL11 Goede V et al. Blood AdvBlood Adv. 2024;9: 2431-2435; FCR CLL8 Fischer K et al. Blood. 2016;127:208-215; Ven+O CLL14 Al Sawaf O et al, Blood 2024: 144; 1924-35; IR FLAIR Munir T et al, ASH 2025 abs#2128 ; I+V GLOW Follows G et al ASH 2023; I+V FLAIR Munir T et al, NEJM 2025: 393: 2280; Acala ELEVATE-TN Sharman J et al, Blood 2025; 143: 12761285; Zanu SEQUOIA Shadman M et al, JCO 2025; 43:780-787; I+/-R A041202 Woyach J et al Blood 2024; 143: 1617-27

Safety

Few deaths due to progression in CLL in the target agents era



Chlor+O CLL11 Goede V et al. Blood AdvBlood Adv. 2024;9: 2431-2435; FCR CLL8 Fischer K et al. Blood. 2016;127:208-215; Ven+O CLL14 Al Sawaf O et al, Blood 2024: 144; 1924-35; IR FLAIR Munir T et al, ASH 2025 abs#2128 ; I+V GLOW Follows G et al ASH 2023; I+V FLAIR Munir T et al, NEJM 2025: 393: 2280; Acala ELEVATE-TN Sharman J et al, Blood 2025; 143: 12761285; Zanu SEQUOIA Shadman M et al, JCO 2025; 43:780-787; I+/-R A041202 Woyach J et al Blood 2024; 143: 1617-27

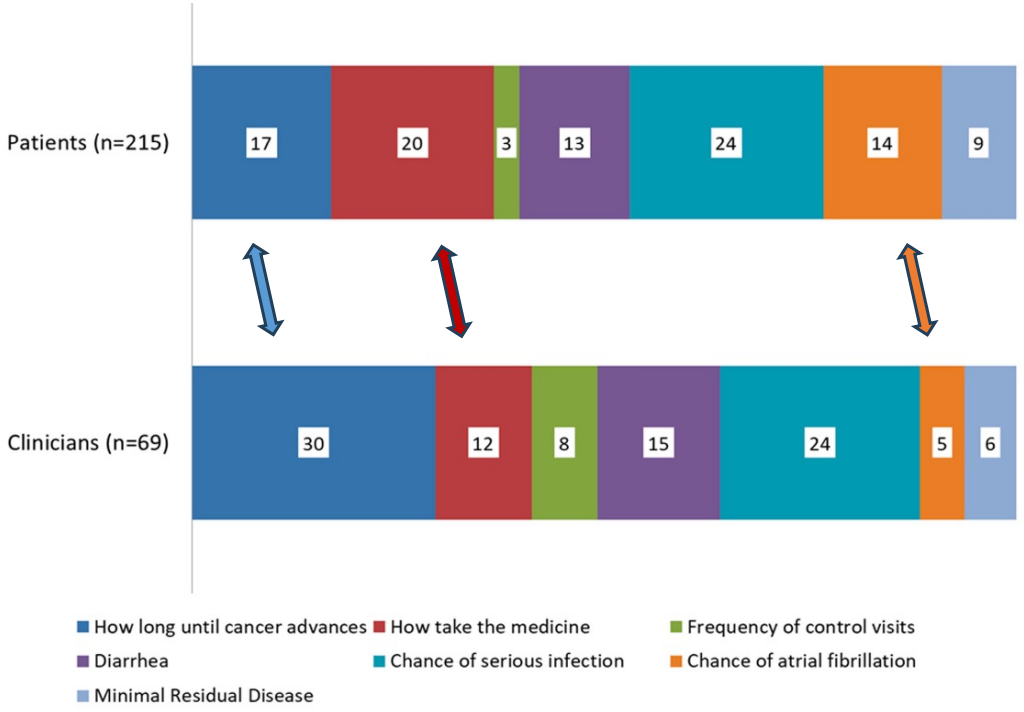
Pts preference

Relative importance of attributes for patients and clinicians

- The board of experts choose the attributes

- 384 patients accessed the online survey (invited by AIL*)
- 215 provided consent and completed the survey

- 183 doctors were the target population of clinicians
- 109 clinicians accessed the survey
- 69 completed the questionnaire



*AIL: associazione Italiana Leucemie –
Laurenti L et al. Hemasphere. 2022 Aug 31;6(9):e771.

Sustainability

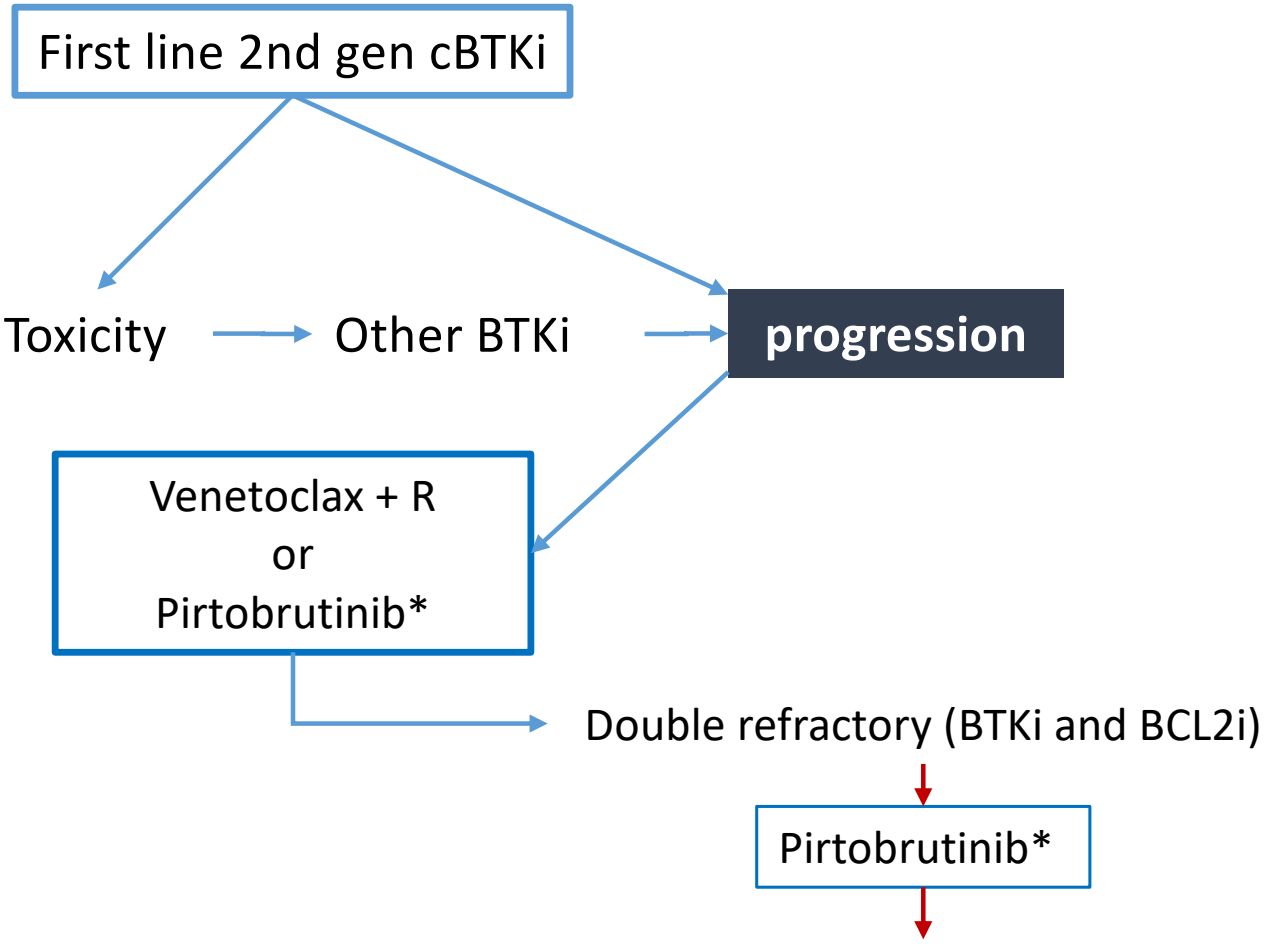
Cost-effectiveness analyses of target agents in first-line treatment of CLL

Source/Country/ Reference	WTP/QALY	Treatment	Comparator	Target Population	ICER	Comments	Cost-Effective
NICE/U.K./114	GBP 20,000 to 30,000	V + O	Ibrutinib	17p	GBP 549,699 saved per QALY lost *	V + O results in cost saving of GBP 199,622 and QALY loss of 0.363 *	YES ^
			Chlor + O	Unsuitable for FCR/BR	NR	Dominant effect V + O vs. Chlor + O ° (more effective and less costly)	YES ^
			FR/BR	Suitable for FCR/BR	GBP 47,494 vs. FCR GBP 67,445 vs. BR per QALY gained	ICERs varied widely if the upper and lower bounds of the PFS and OS HR-CI were applied	NO
NICE/U.K./119		Acalabrutinib	Chlor + O	CLL unsuitable for FRC/BR, including 17p	GBP < 30,000 per QALY gained	Considering confidential discounts	YES
NICE/U.K./120	GBP 20,000 to 30,000	Ibrutinib and venetoclax	FRC/BR	CLL suitable for FRC/BR, including 17p	GBP < 30,000 per QALY gained	Considering confidential discounts	YES
			Chlor + O and V + O	Unsuitable for FRC/BR, including 17p	GBP <30,000 per QALY gained	Dominant effect vs. Chlo + O °	YES
			Acalabrutinib and ibrutinib		NR	Cost saving and a small QALY loss compared with acalabrutinib and ibrutinib	YES

WTP/QALY: Willingness to pay threshold per QALY gain

Urso A et al. Cancers 2023

Proposed treatment sequencing in CLL in 2025

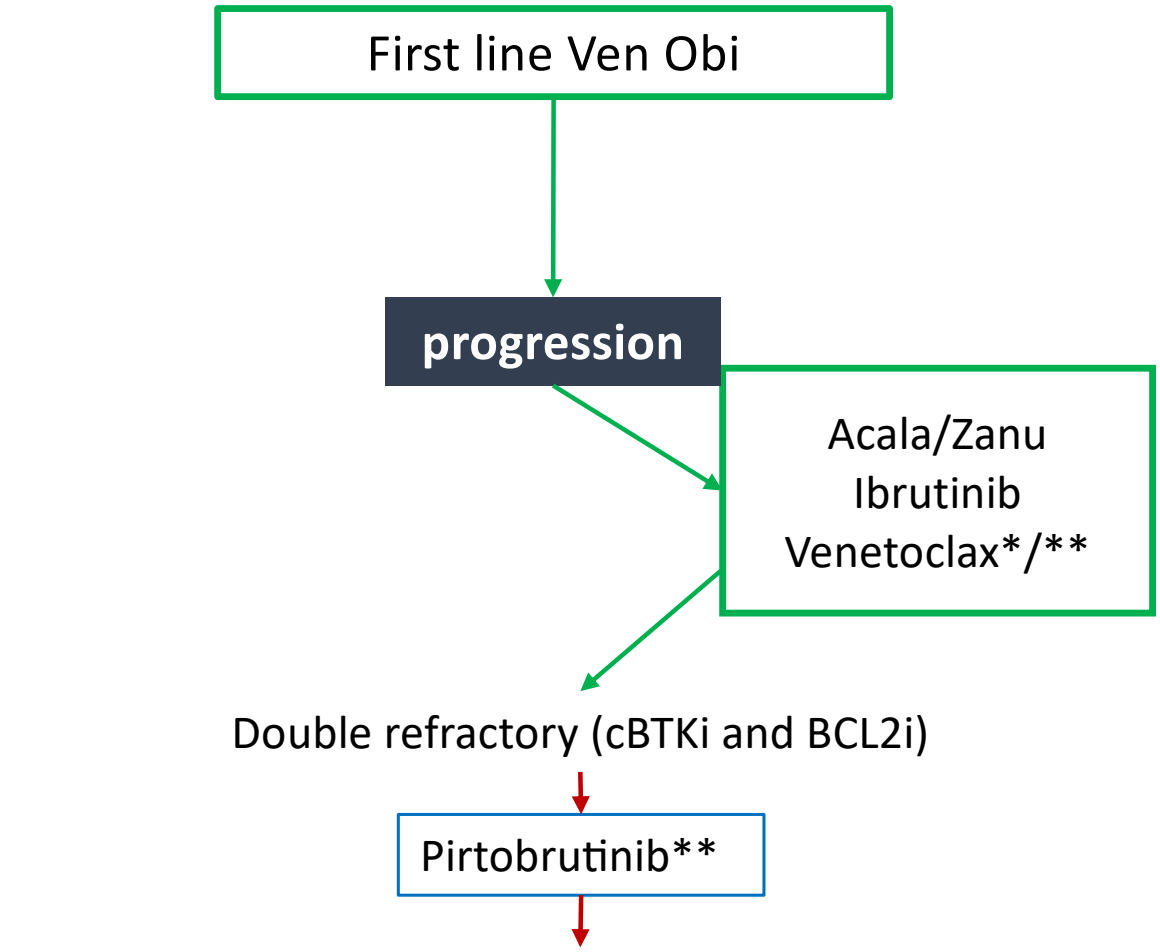


* FDA/EMA approved

Allo BMT (young) - **BTK degraders**/*bispecific MoABs*/*CAR-T*

A. Cuneo february 2026 - Personal opinion

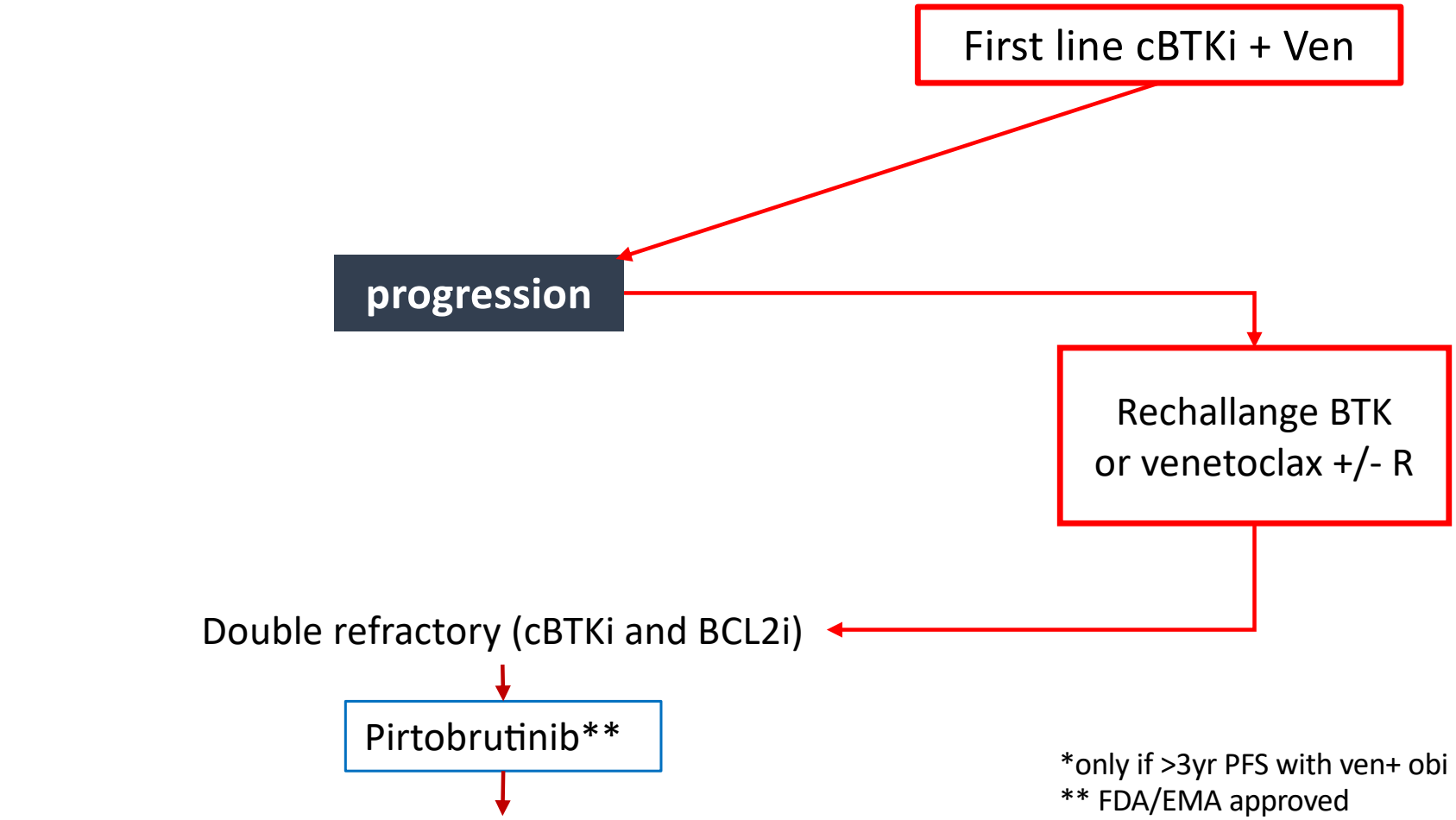
Proposed treatment sequencing in CLL in 2025



*only if >3yr PFS with ven+ obi
** FDA/EMA approved

A. Cuneo february 2026 - Personal opinion

Proposed treatment sequencing in CLL in 2025



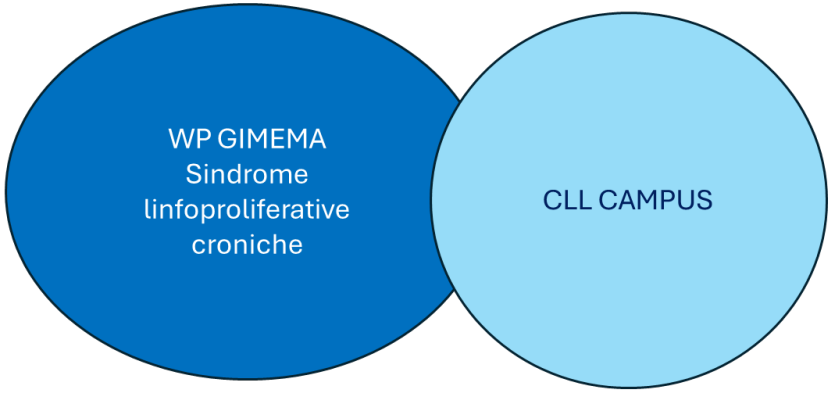
*only if >3yr PFS with ven+ obi
** FDA/EMA approved

A. Cuneo february 2026 - Personal opinion

Unmet needs

CLL CONNECT CLL CAMPUS

Obiettivi del progetto



Generare idee

- studi osservazionali
- studi interventistici
- studi biologici di area traslazionale
- spazio per le sindromi linfoproliferative croniche

Progetto
Pirtobrutinib real-life in Italia
Confronto tra Sequenze Terapeutiche (PFS2)
Utilizzo di anticoagulanti orali e gestione degli eventi emorragici
TP53 single hit vs double hit: significato biologico e rapporto con CK
(IV) e (VO) Valutare l'impatto di fattori centro-specifici e biologici sulla scelta del clinico tra VO e IV
Attività di acalabrutinib nelle citopenie immuni