23rd Ultmann Lymphoma Symposium

Dana-Farber Cancer Institute

Richter's Transformation: Current Considerations and Treatment

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Disclosure Information

I have the following relevant financial relationships to disclose:

Consulting: AbbVie, Ascentage Pharma, AstraZeneca, BeOne Medicines, BMS, Eli Lilly, Genentech, Genmab, Janssen, MSD, Nuvalent, Schrödinger

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THE AMERICAN JOURNAL OF PATHOLOGY

VOLUME IV JULY, 1928 NUMBER 4

GENERALIZED RETICULAR CELL SARCOMA OF LYMPH NODES ASSOCIATED WITH LYMPHATIC LEUKEMIA *

MAURICE N. RICHTER, M.D.

(From the Department of Pathology, Columbia University, and the Pathological Laboratories, Bellevue Hospital, New York, N. Y.)

Leukemia, or even a leukemoid blood picture, is an unusual occurrence in the course of tumors. When the cells in the blood are morphologically identical with those of the tumor, a genetic relationship between the blood picture and the organ changes is generally assumed. If (less frequently) the leukemic cells are of entirely different structure from those of the tumor, a relationship is less firmly established. In every instance the interpretation is difficult, and the diagnosis frequently in doubt.

The case which forms the basis of this communication is one in which lesions thought to be those of an unusual tumor of the lymphatic apparatus, are associated with those of lymphatic leukemia.

REPORT OF CASE

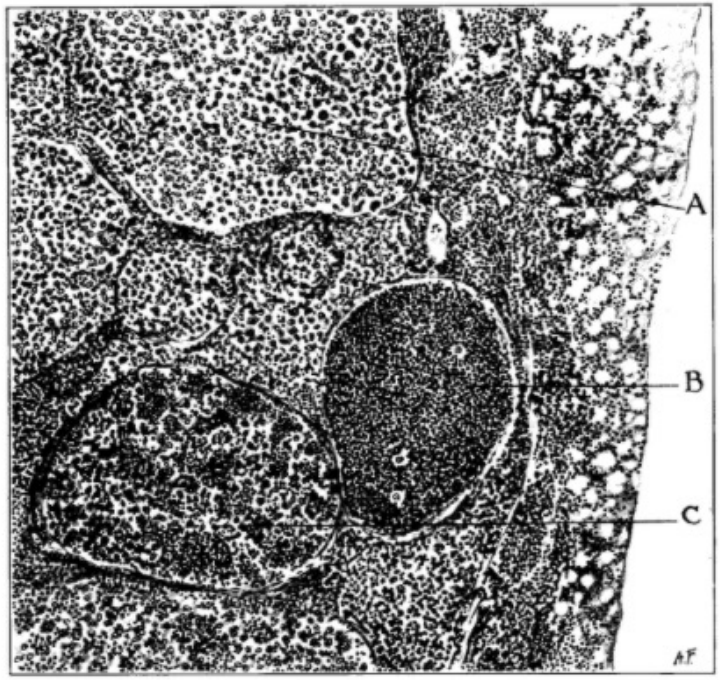
Clinical History: W. H., Shipping clerk, age 46 years. Entered Bellevue Hospital June 14, 1926, complaining of swelling on the left side of neck, duration seven weeks.

Family History and *Past Personal History:* Irrelevant.

Present Illness: Seven weeks ago the patient noticed a swelling on the left side of the neck which increased gradually in size. It was not painful. The patient had occasional pains in the epigastrium and suprapubic regions, of short duration, which had no relation to meals, defecation or exertion. He had lost a great deal of weight in the last two months.

Physical Examination: (Positive findings only.) Adult white male, appears chronically ill. Marked emaciation. Eyes: Petechial hemorrhages in palpebral conjunctivae. Neck: Masses of nodes in left cervical region, anterior and posterior chains. The individual nodes appear to be about 2 cm. in diameter. There are smaller ones in both supraclavicular regions. The nodes are firm and

* Received for publication March 20, 1928.



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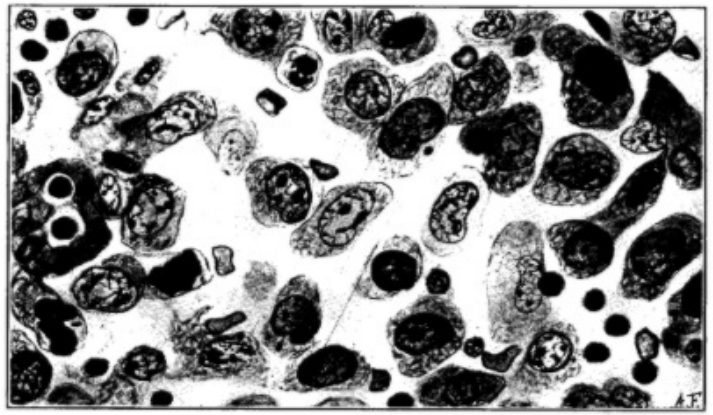

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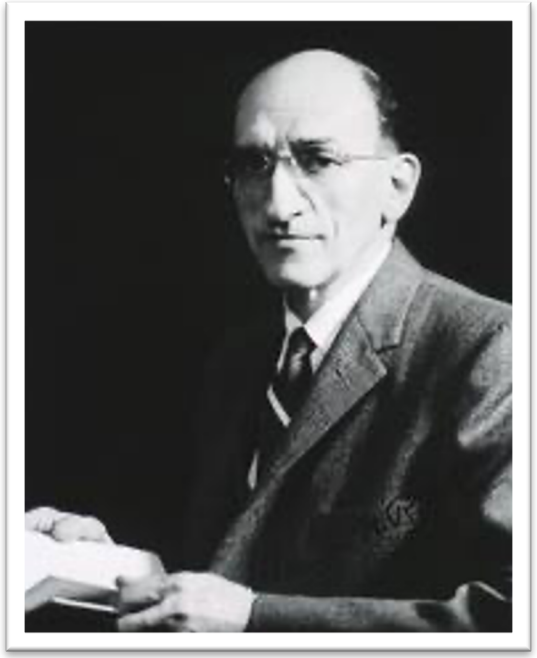
Richter Reticular Cell Sarcoma and Lymphatic Leukemia



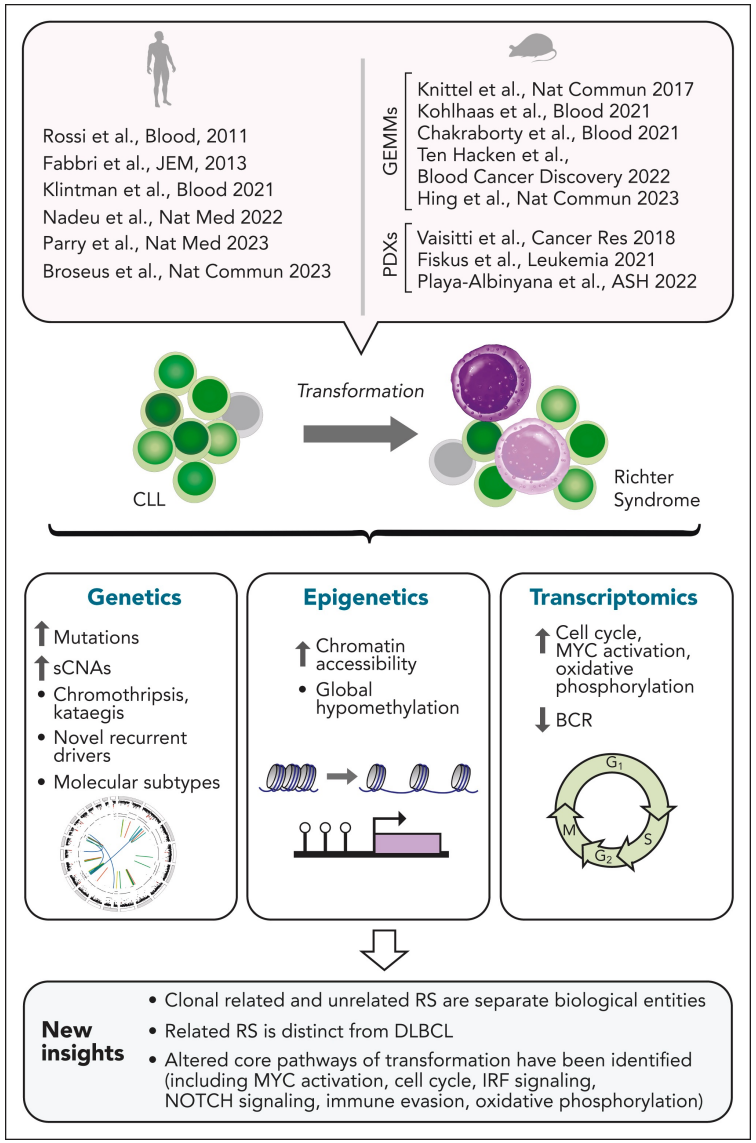
Maurice N. Richter (1959)

„Leucemie lympoide chronique secodairement associee a une reticulpathie maligne, **syndrome de Richter**“

Lortholary P, Boiron M, Ripault J, Levy JP, Manus A, Bernard J. *Nouv Rev Fr Hematol*. **1964**;78:621– 644

(slide adapted from O. Al-Sawaf)

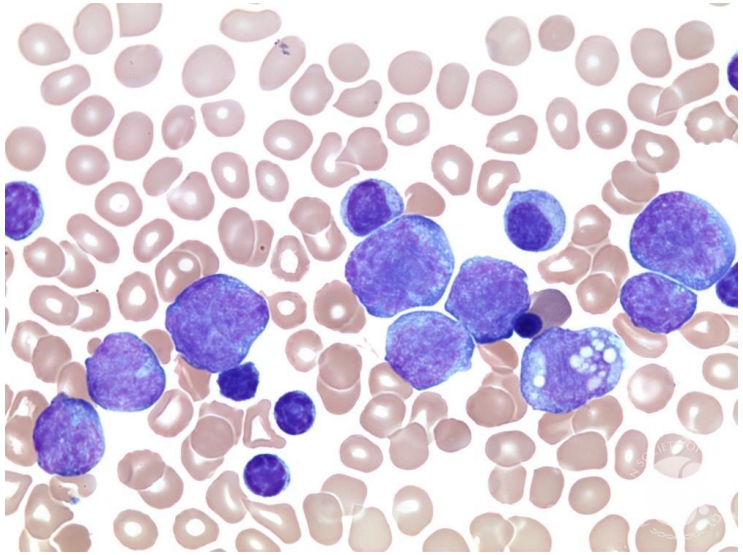
RT pathophysiology



Parry, ten Hacken, Wu, *Blood*, 2023

RT Diagnosis

- Suspect RT in CLL/SLL if patient shows physical deterioration, fever in the absence of infection, rapid and discordant growth of lymph nodes, and/or sudden and excessive rise in LDH levels
- Bone marrow biopsy, ^{18}FDG PET/CT of lesions, however:
- PET-FDG avidity provides insufficient sensitivity and specificity
- Histological diagnosis mandatory: PET-guided biopsy
- CLL FISH, *TP53*^{mut}, clonal relationship with CLL



Mato et al. *Haematologica*. 2019.

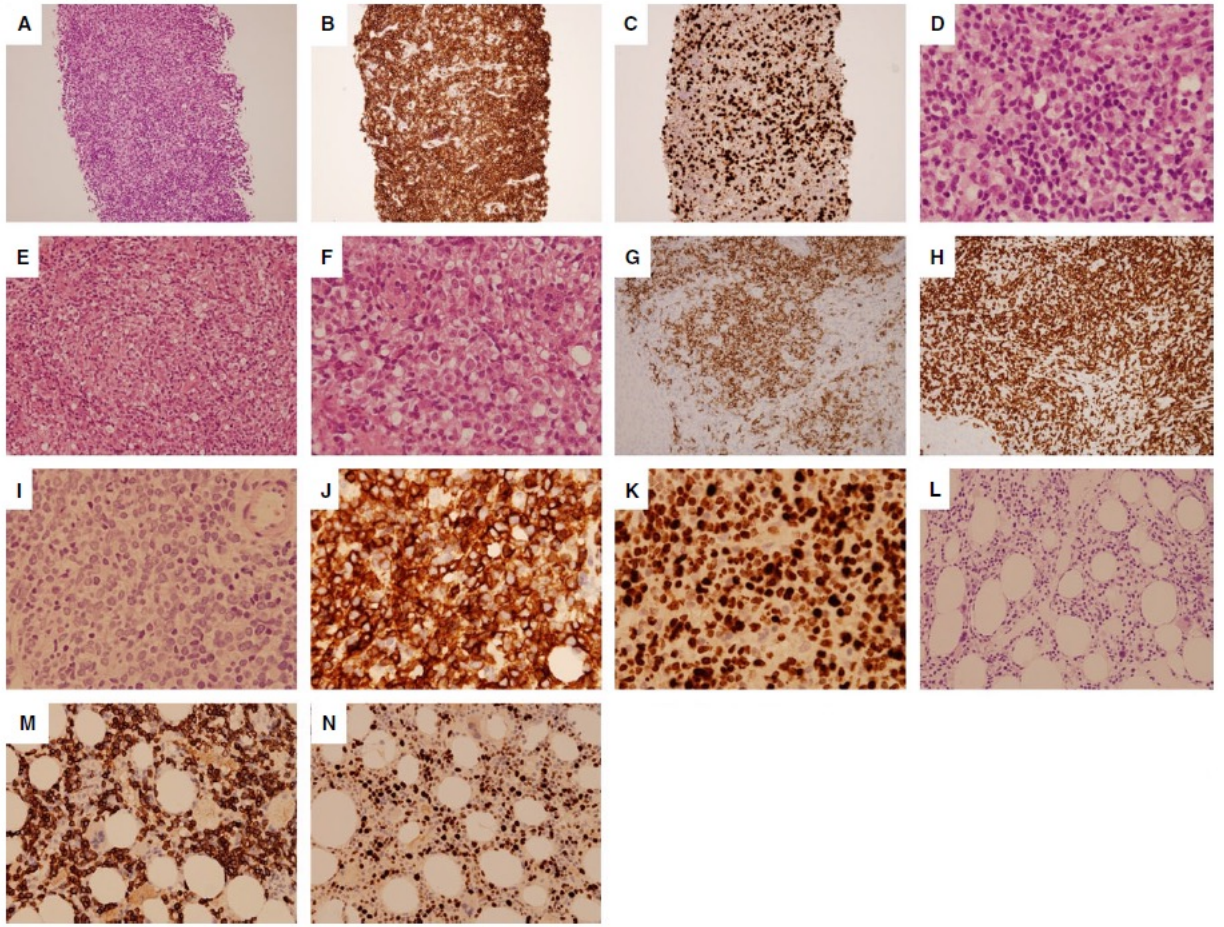
Diagnosis of RT can be challenging

Diagnostic dilemmas of high-grade transformation (Richter's syndrome) of chronic lymphocytic leukaemia: results of the phase II National Cancer Research Institute CHOP-OR clinical trial specialist haemato-pathology central review

Elizabeth J Soilleux [1], Andrew Wotherspoon [2], Toby A Eyre [3 4], Ruth Clifford [3], Maite Cabes [5], Anna H Schuh [3 5]

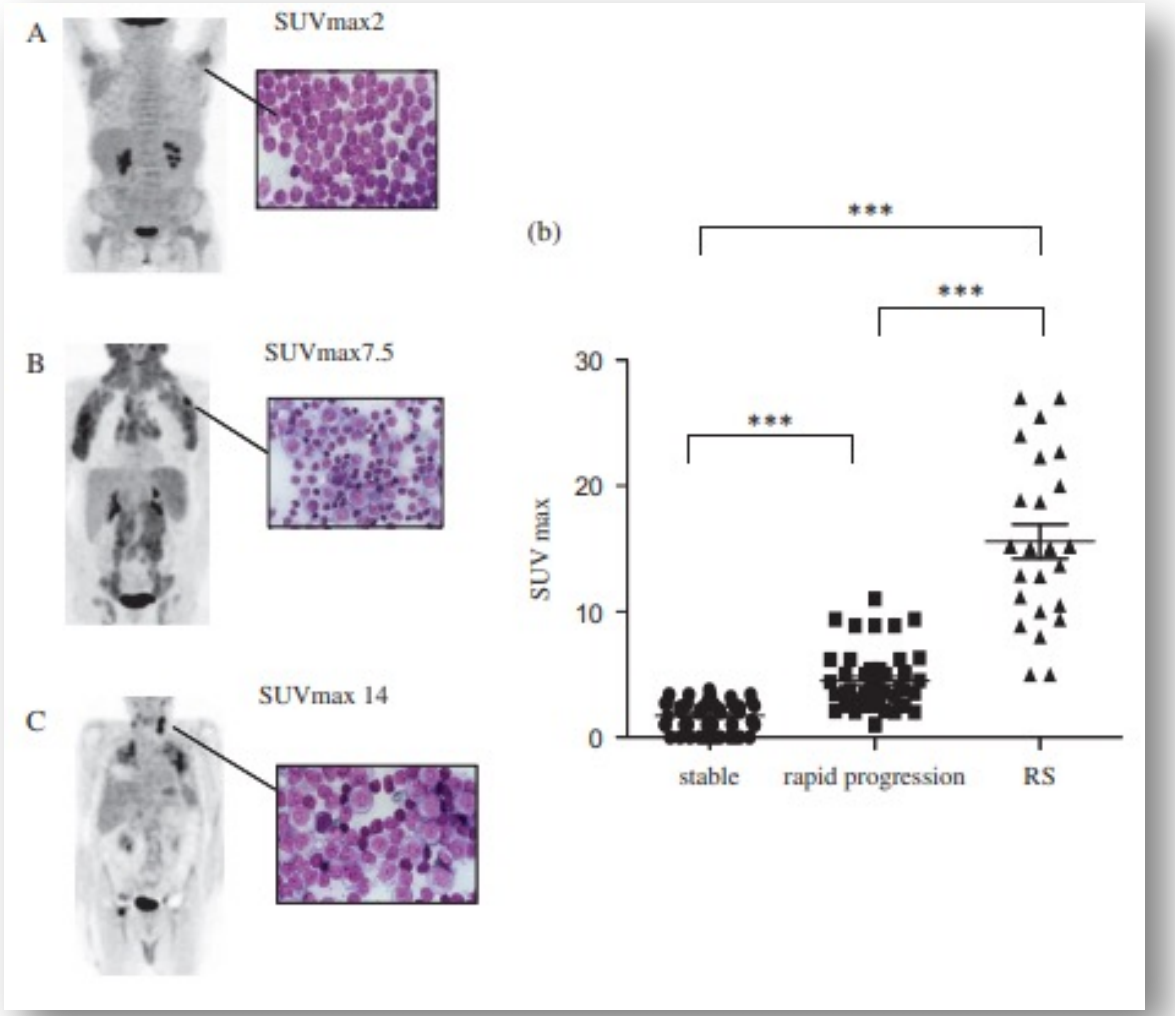
17.5% of alleged RT cases could not be confirmed

Central histopathologic review is helpful when possible



Soilleux et al. *Histopathology*. 2016

PET/CT is useful to predict risk of RT post CIT



SUVmax >10 predictive of RT (n=240 -> n=24 RT)

Michallet et al., *Leuk & Lymph*, 2016

Utility of PET/CT post-BCRi may be less

Ferrata Storti Foundation

Haematologica 2019
Volume 104(11):2258-2264

Utility of positron emission tomography-computed tomography in patients with chronic lymphocytic leukemia following B-cell receptor pathway inhibitor therapy

Anthony R. Mato,[1] William G. Wierda,[2] Matthew S. Davids,[3] Bruce D. Cheson,[4] Steven E. Coutre,[5] Michael Choi,[6] Richard R. Furman,[7] Leonard Heffner,[8] Paul M. Barr,[9] Herbert Eradat,[10] Sharanya M. Ford,[11] Lang Zhou,[11] Maria Verdugo,[11] Rod A. Humerickhouse,[11] Jalaja Potluri[11] and John C. Byrd[12]

[1]CLL Program, Leukemia Service, Division of Hematologic Oncology, Memorial Sloan Kettering Cancer Center, New York, NY; [2]University of Texas MD Anderson Cancer Center, Houston, TX; [3]Dana-Farber Cancer Institute, Boston, MA; [4]Georgetown University Hospital, Washington, DC;

Table 1. Positron emission tomography-computed tomography findings and baseline characteristics for screened patients.

	Screened patients N=167
PET-CT findings at screening	
Number of FDG-avid nodes,* median (range)	5 (1 – 12)
SUVmax, median (range)	5 (0 – 73)
SUVmax ≥10	25 (15)
Baseline patient characteristics	
Age, median (range), years	67 (28 – 85)
N. of prior therapies, median (range)	4 (1 – 15)
Ibrutinib, n (%)	104 (62)
Idelalisib, n (%)	55 (33)
Ibrutinib and idelalisib, n (%)	37 (22)
Purine analogs, n (%)	104 (62)
Rituximab/other monoclonal antibodies, n (%)	146 (87) / 56 (34)
Bendamustine/other alkylating agents, n (%)	75 (45) / 124 (74)
Bulky nodes ≥5 cm, n (%)	69 (41)
Bulky nodes ≥10 cm, n (%)	17 (10)
β-2 microglobulin,‡ median (range), mg/L	3.4 (0 – 59.6)
Lactate dehydrogenase above the upper limit of normal,† n/N (%)	111/164 (68)
Prognostic factors,‡ n/N (%)	
Unmutated IGHV	93/118 (79)
del(17p)	69/166 (42)
del(11q)	56/165 (34)
TP53 mutation	48/161 (30)
CD38 positive	70/155 (45)
ZAP-70 positive	45/125 (36)

PET-CT: positron emission tomography-computed tomography; FDG: 18-F-fluorodeoxyglucose, SUVmax: maximum standardized uptake value of FDG. *PET-avid defined as SUV >3 per nuclear medicine ranges provided by participating institutions. ‡Site reported data; presented for all patients with available data. N/n: number.

Table 3. Detection of biopsy-confirmed Richter's transformation (RT) *versus* chronic lymphocytic leukemia (CLL) progression based on positron emission tomography-computed tomography and clinical factors.

	Logistic regression analyses					
	Sensitivity	Specificity	PPV	NPV	ROC area	Odds ratio [95% CI], logistic *P*
PET-CT SUVmax <10/≥10	71%	50%	26%	88%	61%	2.5 [0.4–15], *P*=0.318
PET-CT SUVmax <5/≥5	71%	4%	16%	33%	63%	0.09 [0.01–1.2], *P*=0.071
PET-CT SUVmax <11/≥11	71%	61%	31%	89%	66%	3.8 [0.6–24], *P*=0.143
PET-CT SUVmax <12/≥12	57%	68%	31%	86%	63%	2.8 [0.5–15], *P*=0.231
Lactate dehydrogenase ≤/>ULN	83%	29%	20%	89%	56%	2 [0.2–20], *P*=0.554
SPD at baseline	67%	48%	24%	86%	59%	1 [1–1], *P*=0.244
TP53* mutated/unmutated	60%	63%	25%	88%	61%	2.5 [0.35–18], *P*=0.362
IGHV * mutated/unmutated	25%	86%	25%	86%	56%	2.1 [0.16–28], *P*=0.569
CD-38* positive/negative	25%	40%	6%	77%	68%	0.22 [0.02–2.5], *P*=0.220
ZAP-70* positive/negative	50%	23%	9%	75%	64%	0.3 [0.01–6.4], *P*=0.440
β2 microglobulin * </≥3 mg/L	75%	25%	20%	80%	50%	1 [0.08–13], *P*=1.0

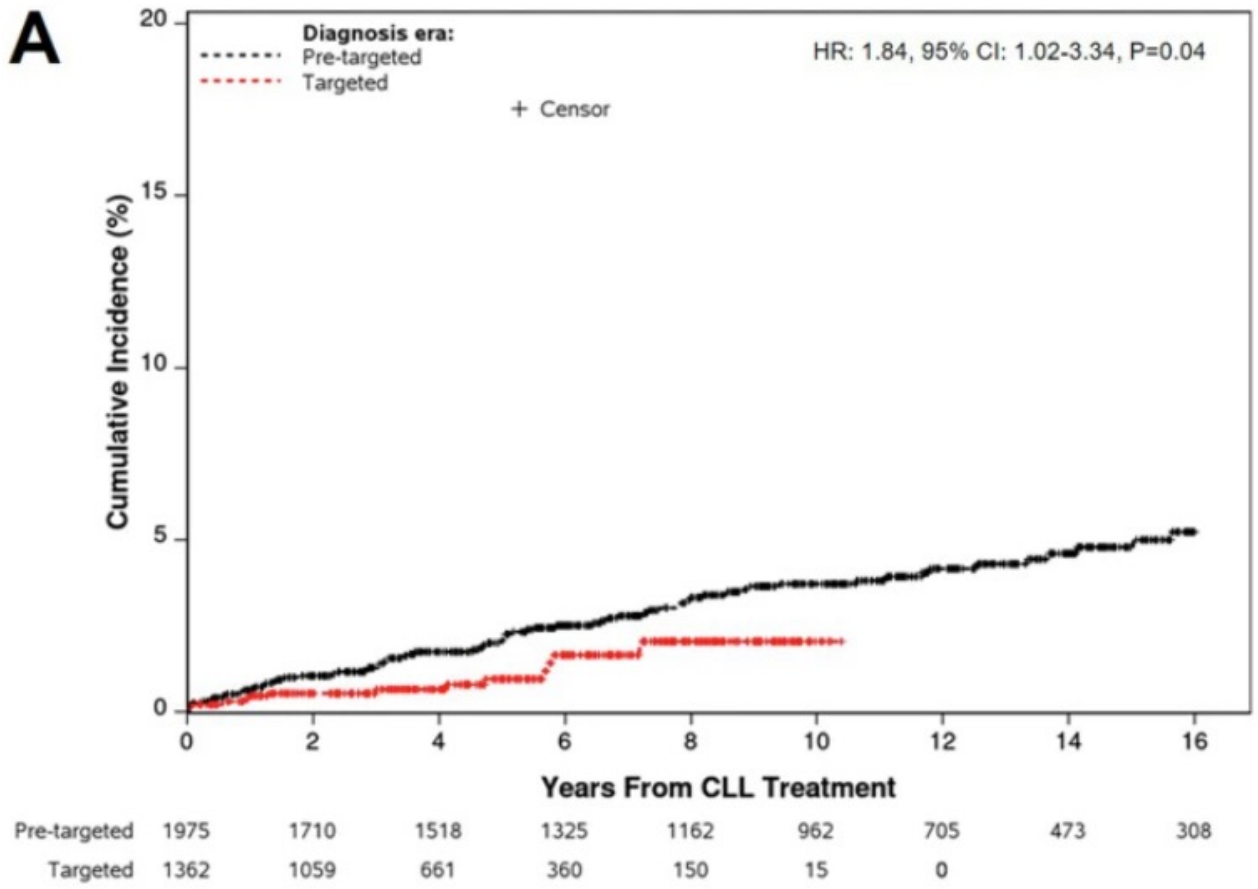
PPV: positive predictive value; NPV: negative predictive value; ROC: Receiver Operator Characteristic; PET-CT: positron emission tomography-computed tomography; SUVmax: maximum standardized uptake value of 18-F-fluorodeoxyglucose; ULN: upper limit of the normal range; SPD: sum products of the greatest transverse diameters (tumor size). *Site-reported data. The logistic regression analyses only included patients with available data.

N=167 -> n=8 RT

Mato et al., *Haematologica*, 2019

Incidence of RT may be less in the targeted therapy era

The incidence of RT from time of CLL diagnosis was significantly different between the 1975 patients diagnosed with CLL in the pre-targeted therapy era and the 1362 patients diagnosed with CLL in the targeted therapy era ([HR] 1.84, 95% CI: 1.02–3.34, P = 0.04)

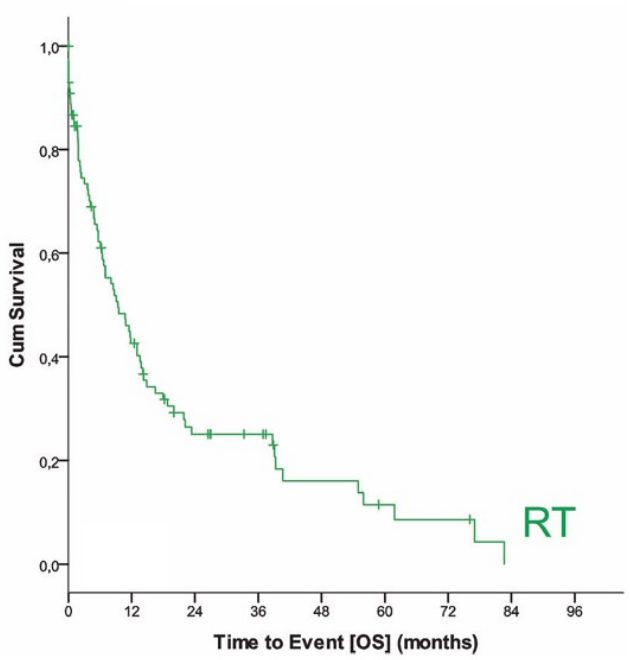


Both cohorts had prior CIT

Hampel et al, *Leukemia*, 2025

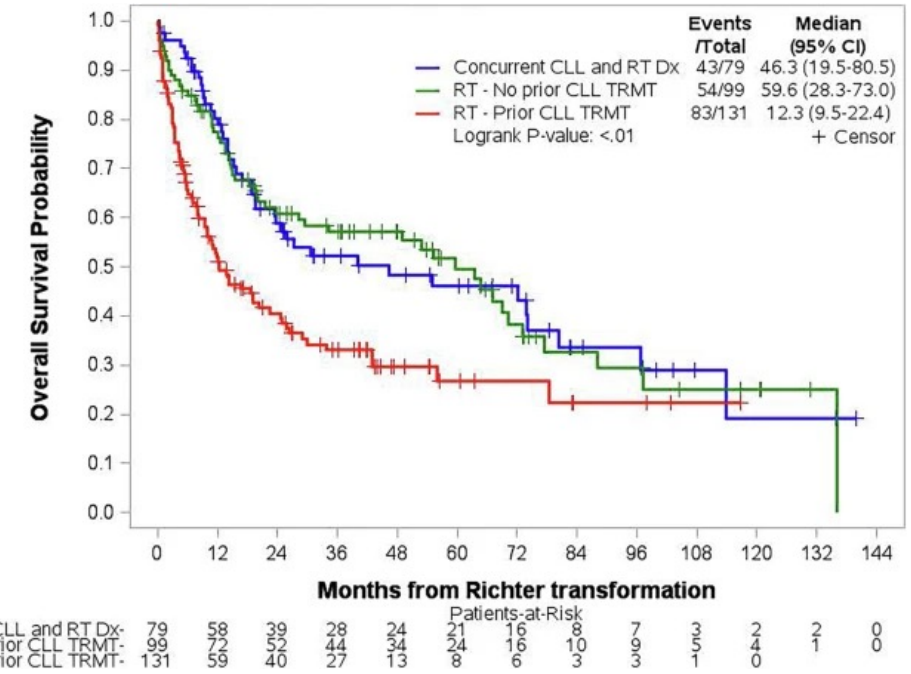
RT prognosis has been poor historically, and remains so today

RT in the CIT Era



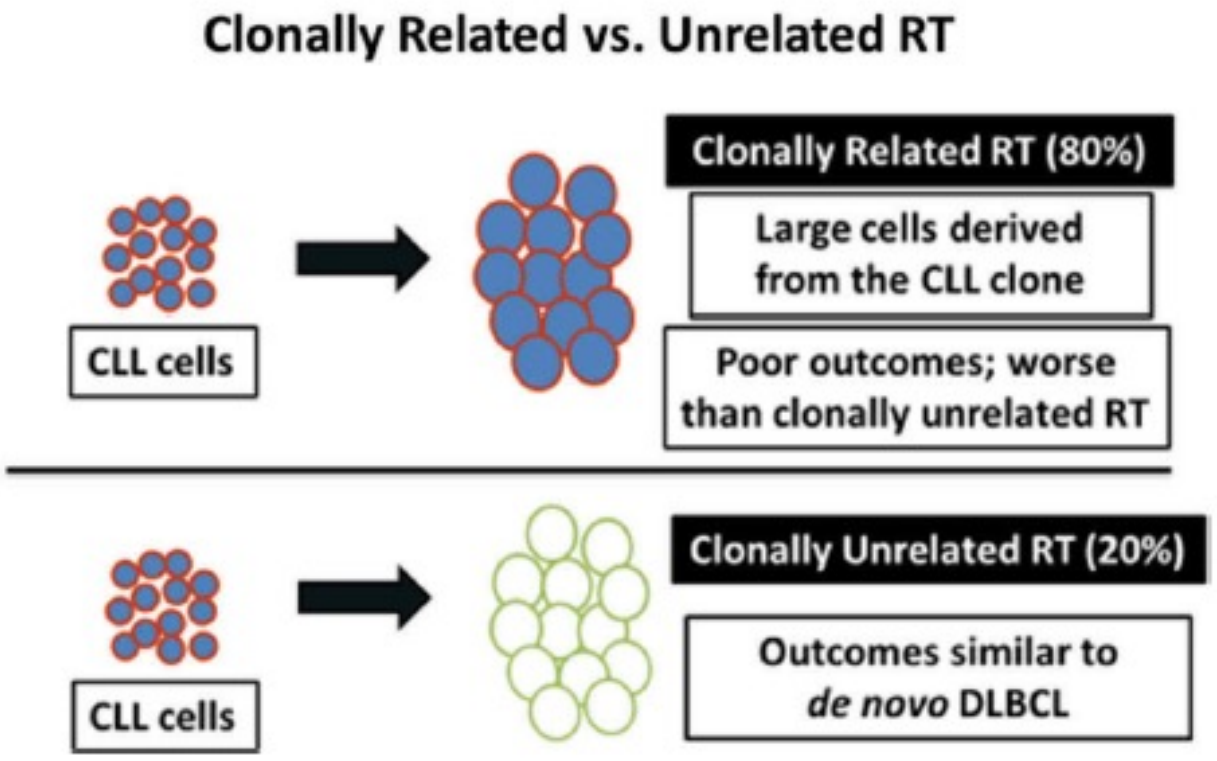
Al-Sawaf et al., *Leukemia,* 2021

RT in the Targeted Therapy Era

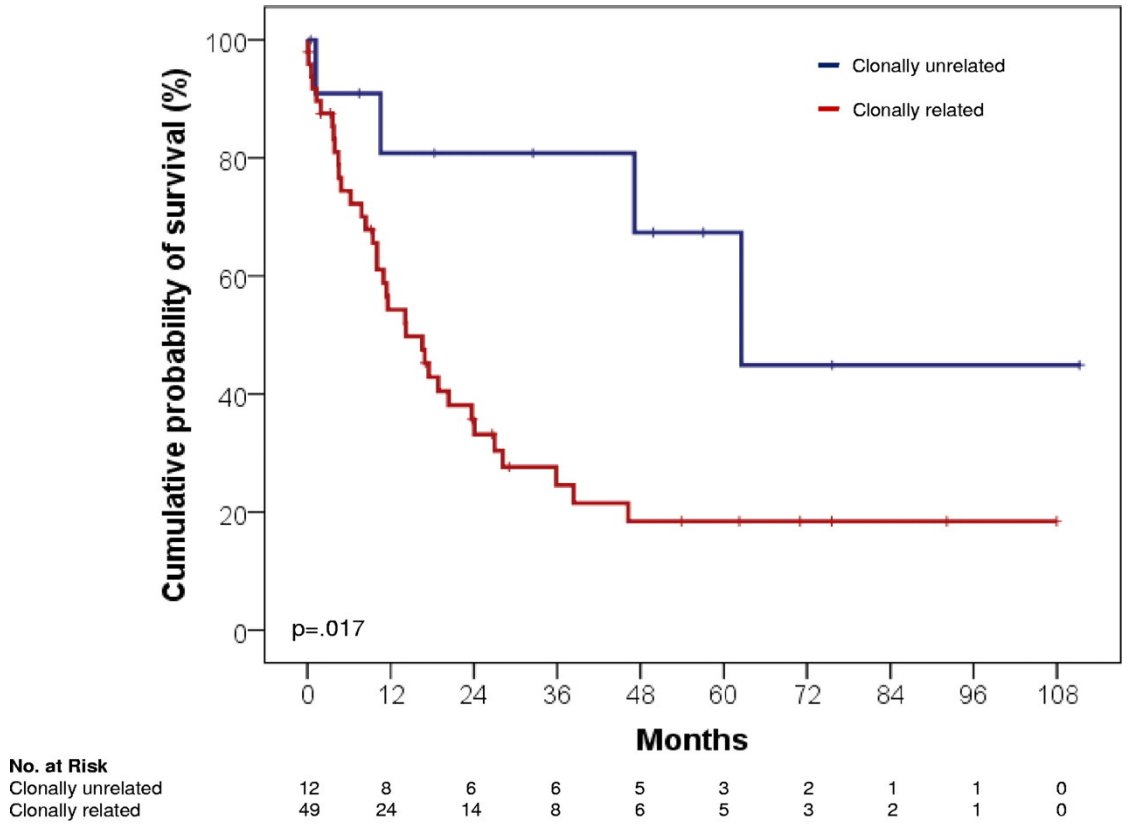


Kittai et al., *Blood Cancer J*, 2025

RT etiology affects prognosis



Jain et al. *Expert Rev Hematol*. 2016



Rossi et al. Blood 2011;117:3391-3401

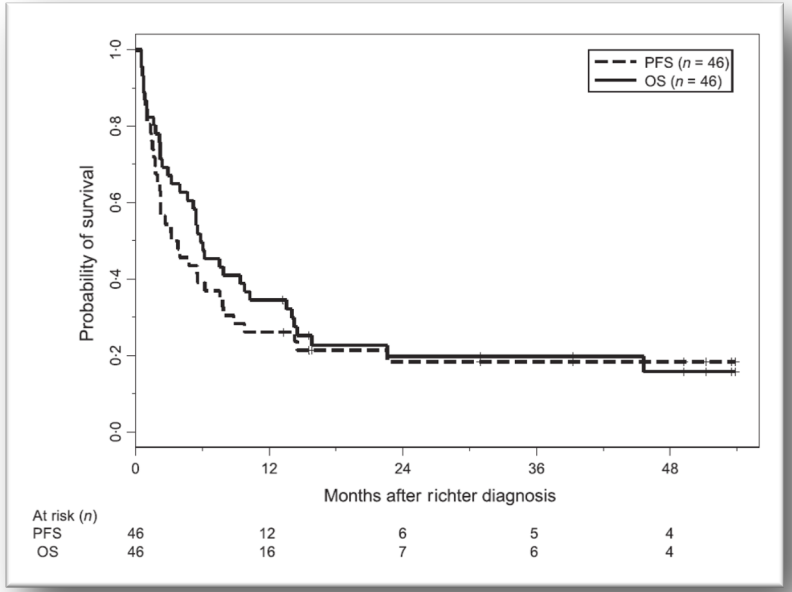
Treatment of Richter transformation: patient considerations

- **Age, fitness, medical co-morbidities**
  - Are they a candidate for anthracycline-chemoimmunotherapy?
- **Prior CLL therapies**
  - Previously untreated vs. prior treatments
- **CLL genetics**
  - *TP53* status, clonal relatedness (if known)
- **Availability of clinical trials**

Chemoimmunotherapy

- **Treatment for DLBCL RT has been based on treatment regimens for *de novo* DLBCL[1]**
- **For most patients with DLBCL RT, combination chemoimmunotherapy with anthracycline- or platinum-based regimens is recommended[1]:**
  - R-CHOP
  - R-DA-EPOCH
  - R-hyperCVAD
  - OFAR
- **CR with chemoimmunotherapy is rare and typically short-lived for RT, and a clinical trial is the preferred approach[1]**
  - ORR ~40% and CR rates ~5%-20%[2]

R-EPOCH for Richter's Syndrome

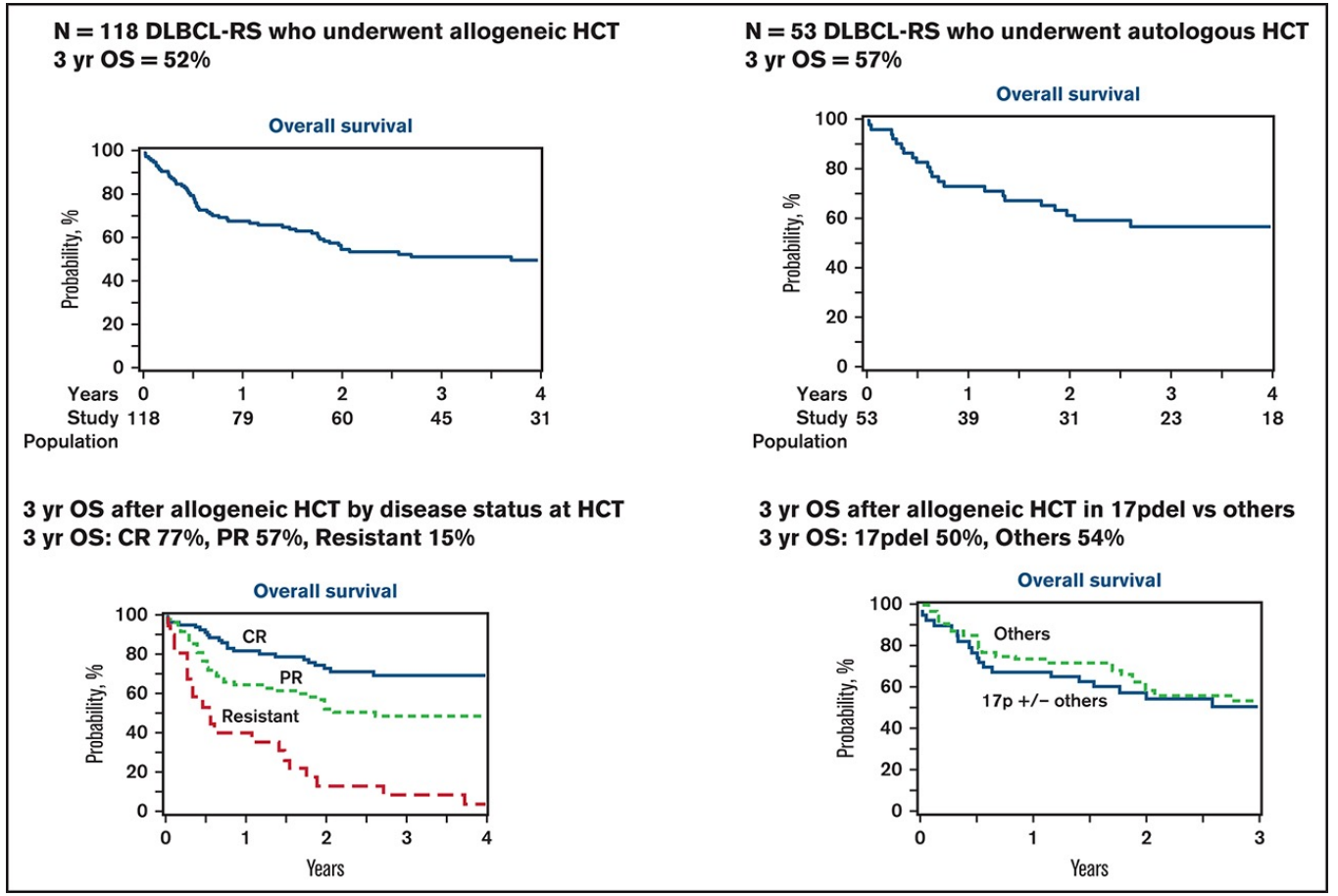


Rogers et al. *Br J Haematol*. 2017.

OFAR, oxaliplatin, fludarabine, cytarabine, and rituximab; R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone; R-DA-EPOCH, dose-adjusted etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin, and rituximab; R-hyper-CVAD, rituximab, hyperfractionated cyclophosphamide, vincristine, adriamycin, and dexamethasone.

1. NCCN. Clinical Practice Guidelines in Oncology. CLL/SLL. **2.** Allan JN, Furman RR. *Int J Hematol Oncol*. 2019;7(4):IJH09.

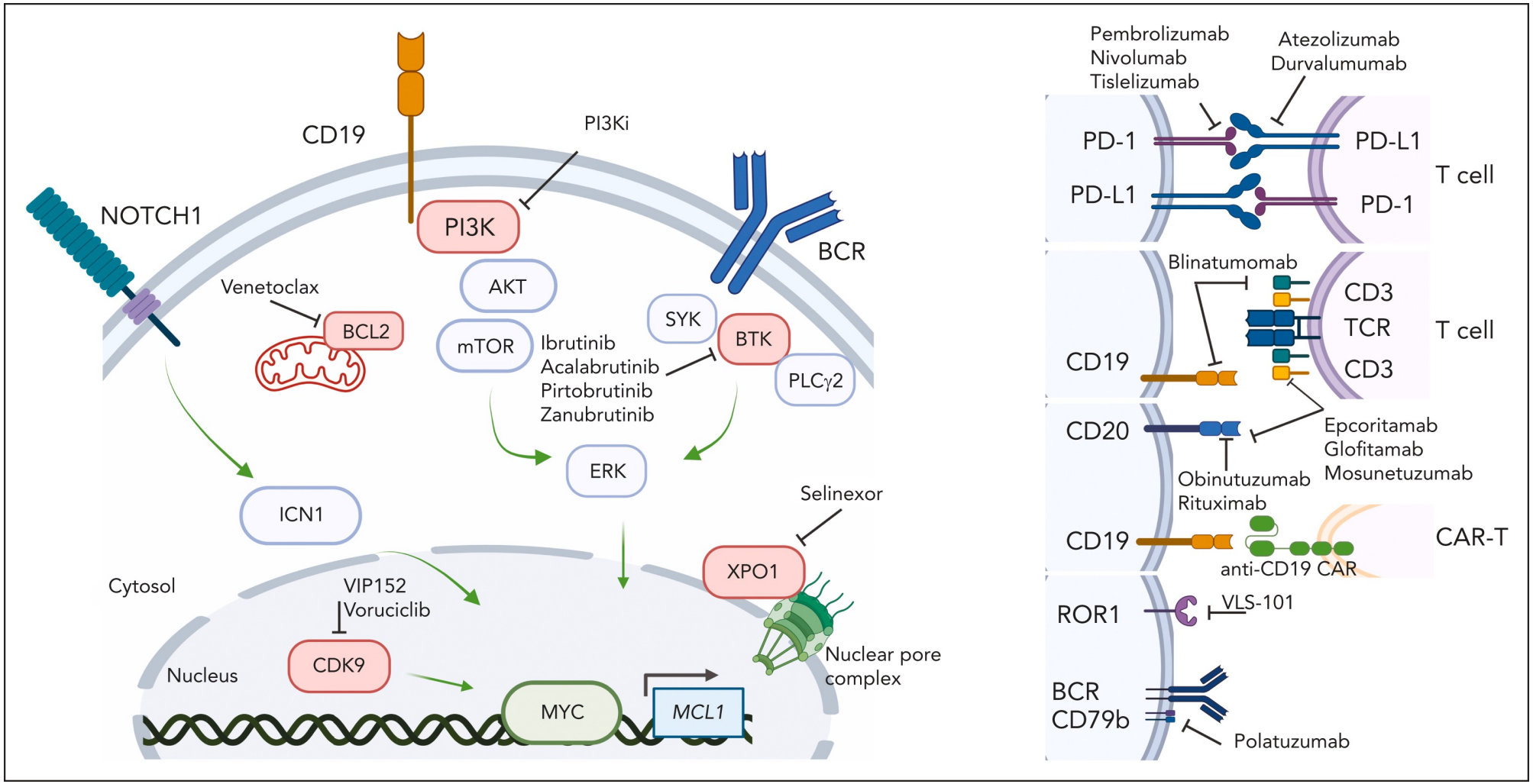
Transplantation for RT



- **Allo-HCT and auto-HCT produce durable remissions in patients with DLBCL-RT**
- **Outcomes after allo-HCT are associated with remission status at HCT but not with receipt of prior novel agents or 17p status**

Herrera et al., *Blood Adv*, 2021

Targeted Therapy for RT



Parry, ten Hacken, Wu, *Blood*, 2023

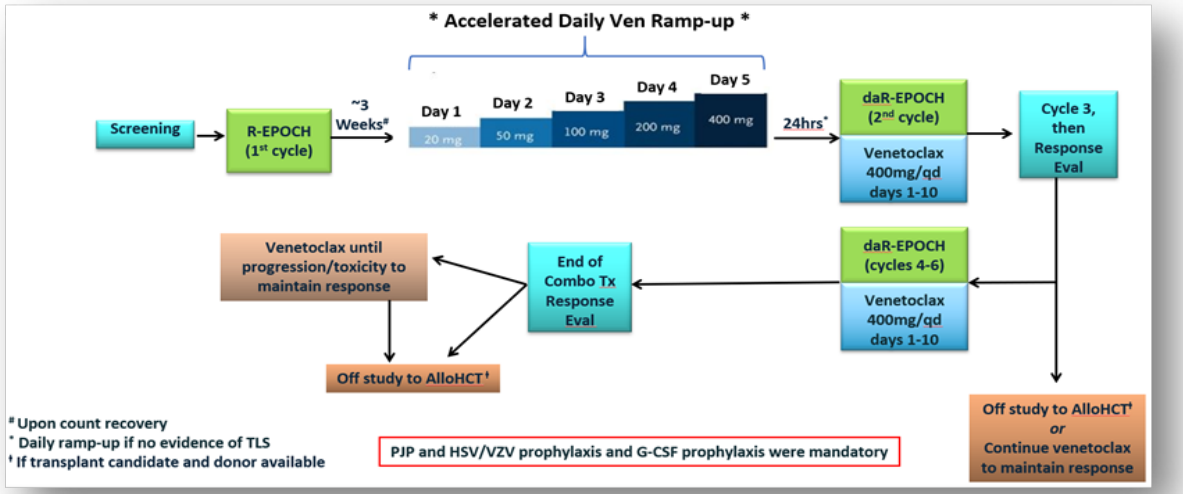
Venetoclax may enhance the efficacy of CIT in RT: VR-EPOCH

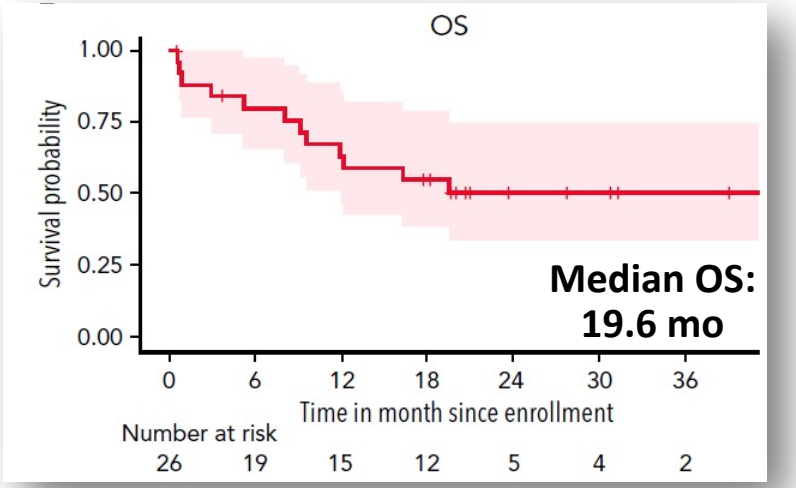
CLINICAL TRIALS AND OBSERVATIONS

Venetoclax plus dose-adjusted R-EPOCH (VR-EPOCH) for Richter syndrome

Matthew S. Davids,[1,*] Kerry A. Rogers,[2,*] Svitlana Tyekucheva,[3] Zixu Wang,[3] Samantha Pazienza,[1] Sarah K. Renner,[4] Josie Montegaard,[1] Udochukwu Ihuoma,[1] Timothy Z. Lehmberg,[1] Erin Parry,[1] Catherine J. Wu,[1,5] Caron A. Jacobson,[1] David C. Fisher,[1] Philip A. Thompson,[4,†] and Jennifer R. Brown[1,†]

[1]Department of Medical Oncology, Dana-Farber Cancer Institute, Boston, MA; [2]Division of Hematology, The Ohio State University, Columbus, OH; [3]Department of Data Science, Dana-Farber Cancer Institute, Boston, MA; [4]Department of Leukemia, The University of Texas MD Anderson Cancer Center, Houston, TX; and [5]Broad Institute of MIT and Harvard, Cambridge, MA





- **Efficacy summary**
  - CR at end of combination: (primary endpoint): 13/26 (50%)
  - Best response in evaluable patients: ORR: 16/26 (62%)
  - 11 patients with CR were BM-uMRD for CLL
- **Safety summary**
  - Rates of cytopenias, infections were typical for aggressive chemoimmunotherapy in this population
  - No TLS occurred with daily venetoclax ramp-up

Dana-Farber Cancer Institute

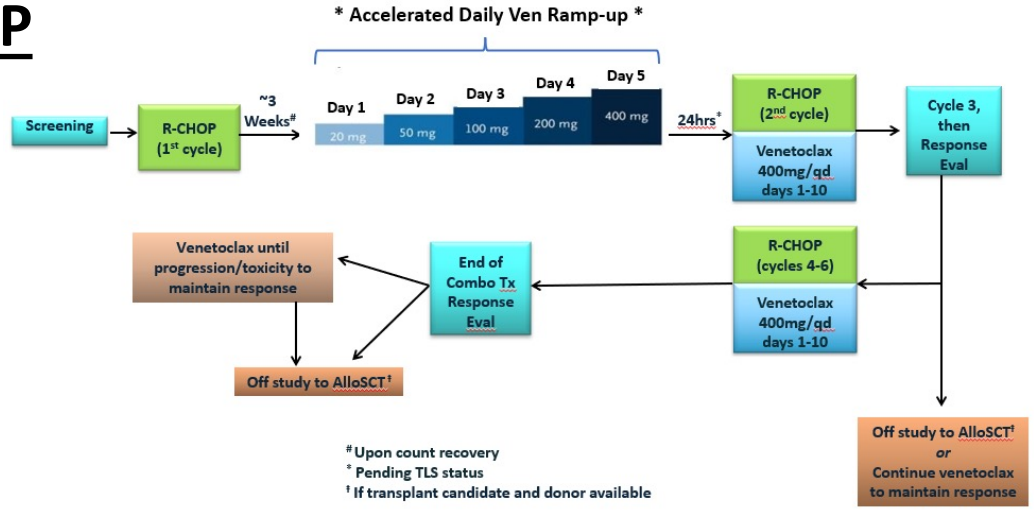
The James
The Ohio State University Comprehensive Cancer Center

The University of Texas MD Anderson Cancer Center

Davids et al. *Blood, 2022*

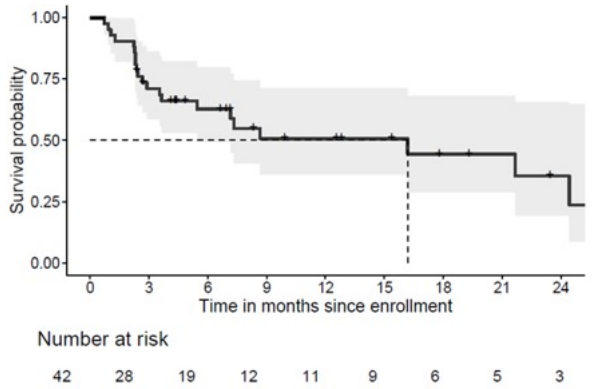
VR-CHOP may allow similar efficacy but less toxicity

VR-CHOP



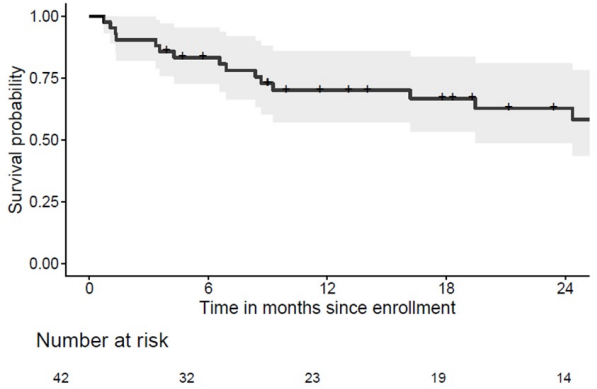
- The toxicity profile of VR-CHOP appears favorable relative to VR-EPOCH:
  - Gr 3/4 neutropenia (50% vs. 65%), febrile neutropenia (24% vs. 38%)
  - Gr 3/4 infection (19% vs. 42%)
- 57% of patients completed full course of combination therapy (27% with VR-EPOCH)
- TLS was not observed with daily venetoclax ramp-up (after 1 cycle of R-CHOP debulking)
- CR rate of 52% is favorable in light of historical rates with R-CHOP alone (20-30%)

PFS



Median PFS: 16.2 mo

OS



Median OS: not reached at median f/u of 15.1 mo.

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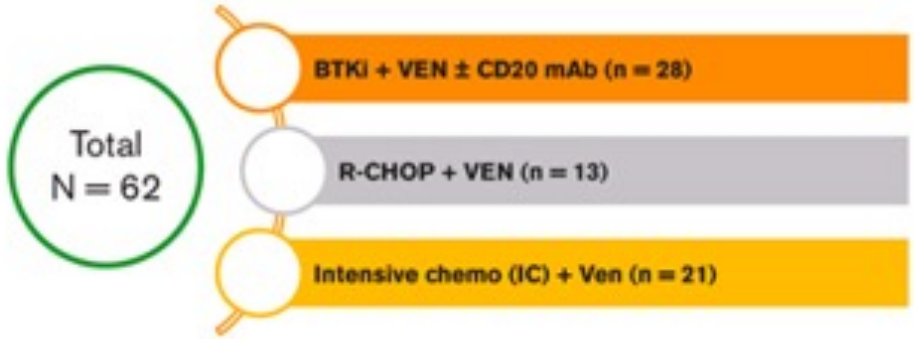
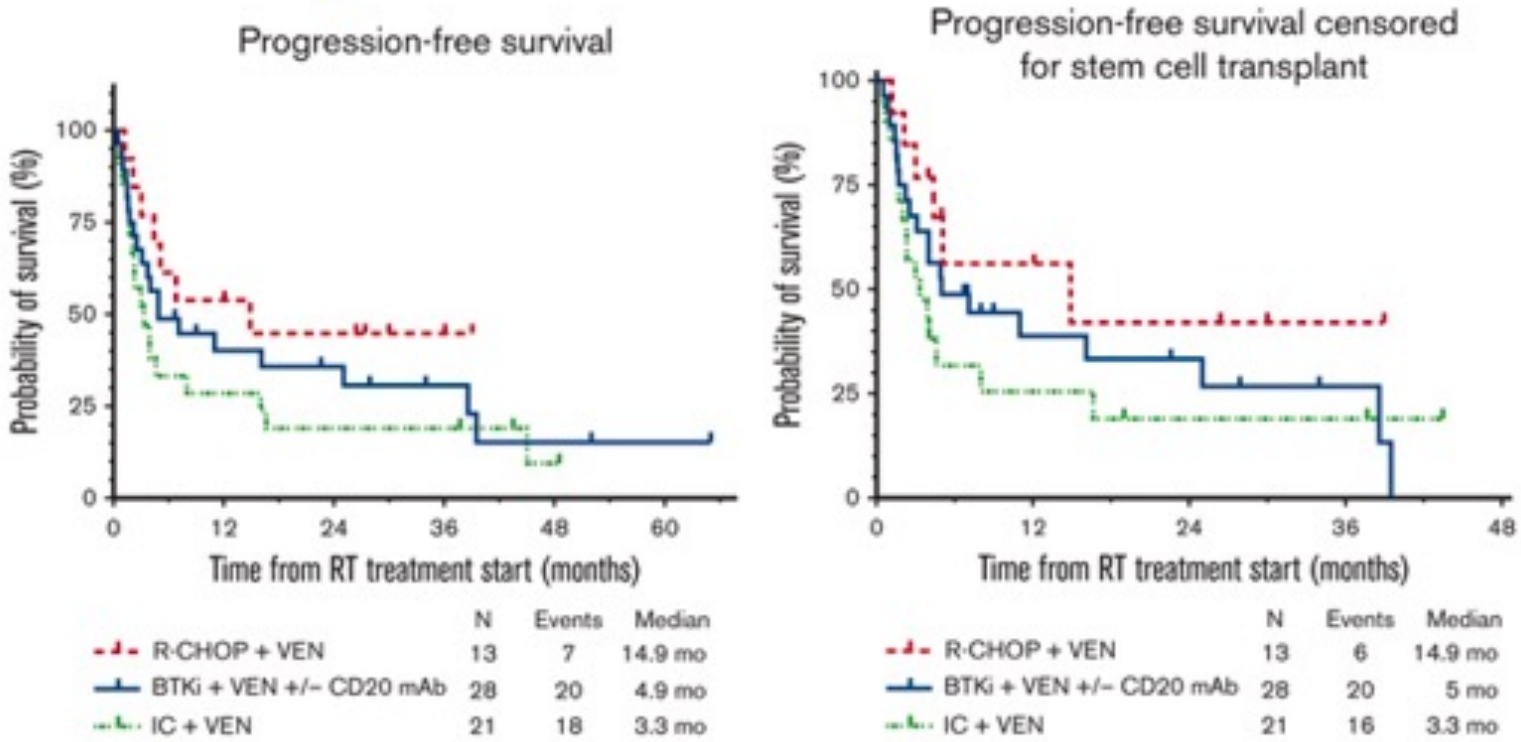
Davids et al. *ICML, 2025*

VR-CHOP is also effective in clinical practice





Hampel et al., *Blood Adv, 2024*

Novel treatment options: BTK inhibitor monotherapy

- In a single-institution, open-label study, 4 patients with DLBCL RT were treated with **ibrutinib**[1]
  - 3 of the 4 responded, including 1 CR
  - Among responders, DOR ranged from 2.8 to 10.8 months (median, 6.1 months)

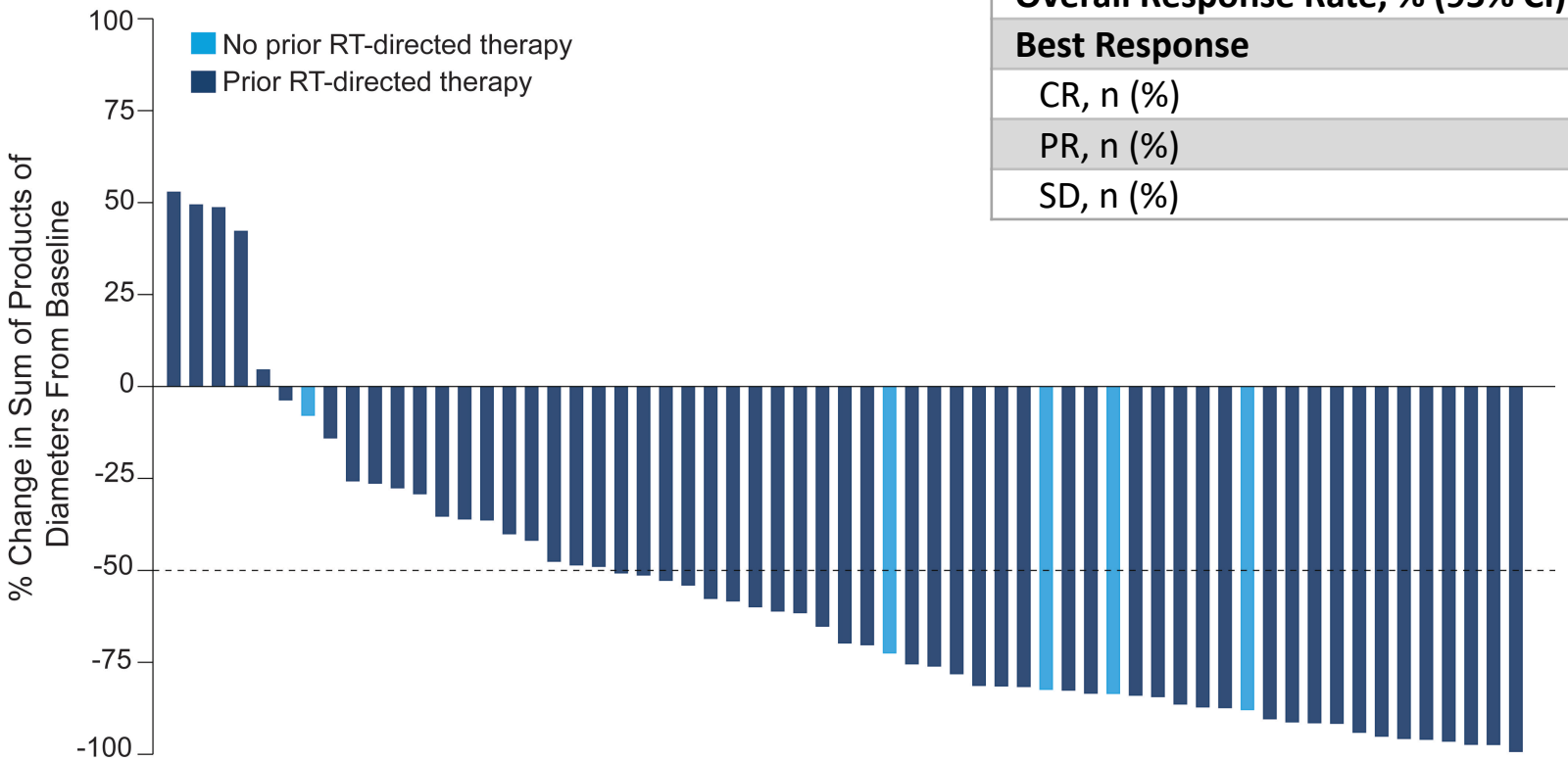
- In the RT arm of the phase ½ ACE-CL-001 clinical trial, **acalabrutinib** was evaluated in 29 patients with RT (efficacy population, n = 21)[2]
  - ORR: 38% (CR: 14%)
  - Among responders, median DOR was 5.7 months, and 2 patients went on to HSCT

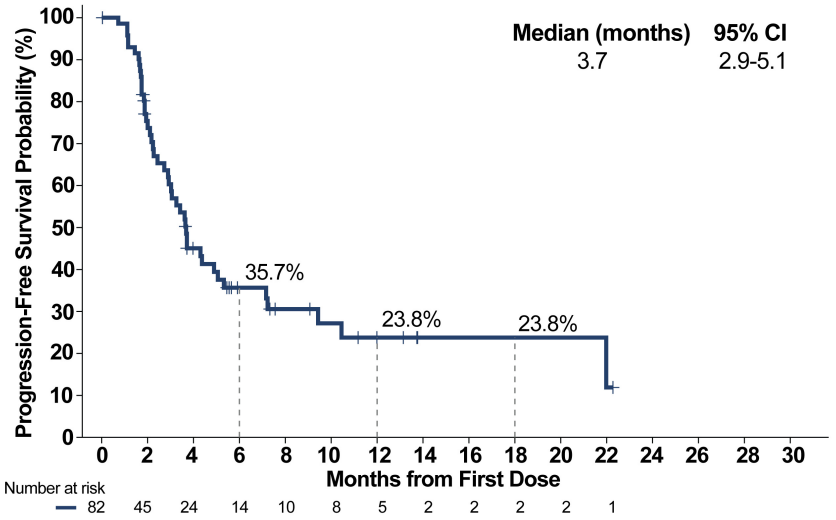
- Non-covalent BTKi: **Nemtabrutinib** (ARQ-531/MK-1026) led to response in 3 of 6 RT patients[3]

1. Tsang M et al. *Blood*. 2015;125(10):1676-1678. **2.** Hillmen P et al. *Blood*. 2016;128(22):60. **3.** Woyach J et al. *Blood*. 2019;134(Supplement_1):4298.

Novel treatment options: Pirtobrutinib

Response Evaluable RT Patients[a]	All n=75	Prior RT Therapy n=68
Overall Response Rate, % (95% CI)	**52.0 (40.2-63.7)**	**50.0 (37.6-62.4)**
Best Response		
CR, n (%)	10 (13.3)	9 (13.2)
PR, n (%)	29 (38.7)	25 (36.8)
SD, n (%)	10 (13.3)	10 (14.7)





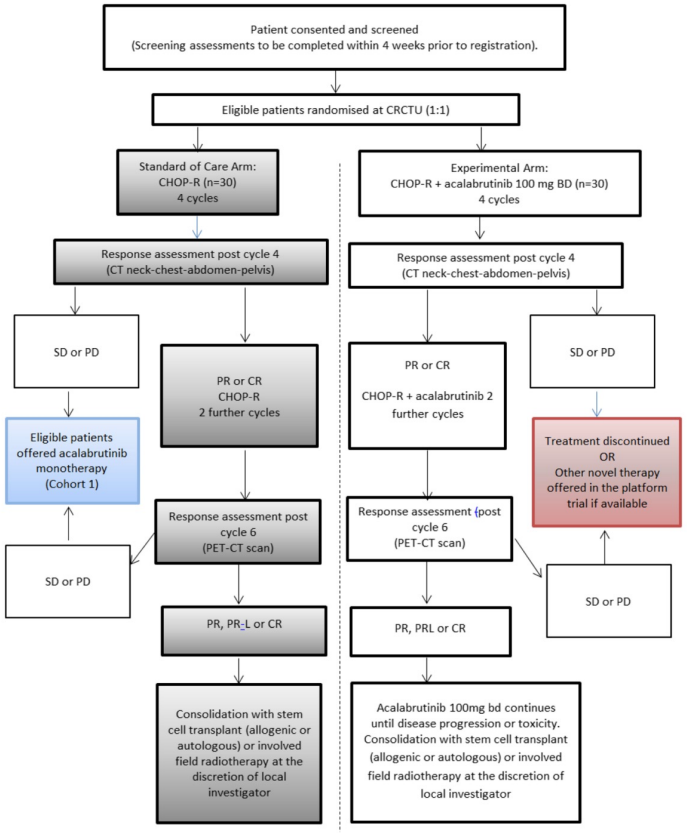
- Among 75 response-evaluable patients, the median time-to-response was 1.8 months (range, 0.9-9.2), median time on study was 6.7 months (range, 0.7-29.1), and median time on treatment was 3.4 months (range, 0.2-26.7)

Data cutoff date of 29 July 2022. Data for 14 patients are not shown in the waterfall plot due to no baseline or post-baseline assessment. [a]Response evaluable patients are those who had at least 1 post-baseline response assessment or had discontinued treatment prior to first post-baseline response assessment. Response as assessed by investigator based on Lugano criteria.

Wierda et al. *ASH Annual Meeting,* 2022 / *Lancet Haematol*, 2024

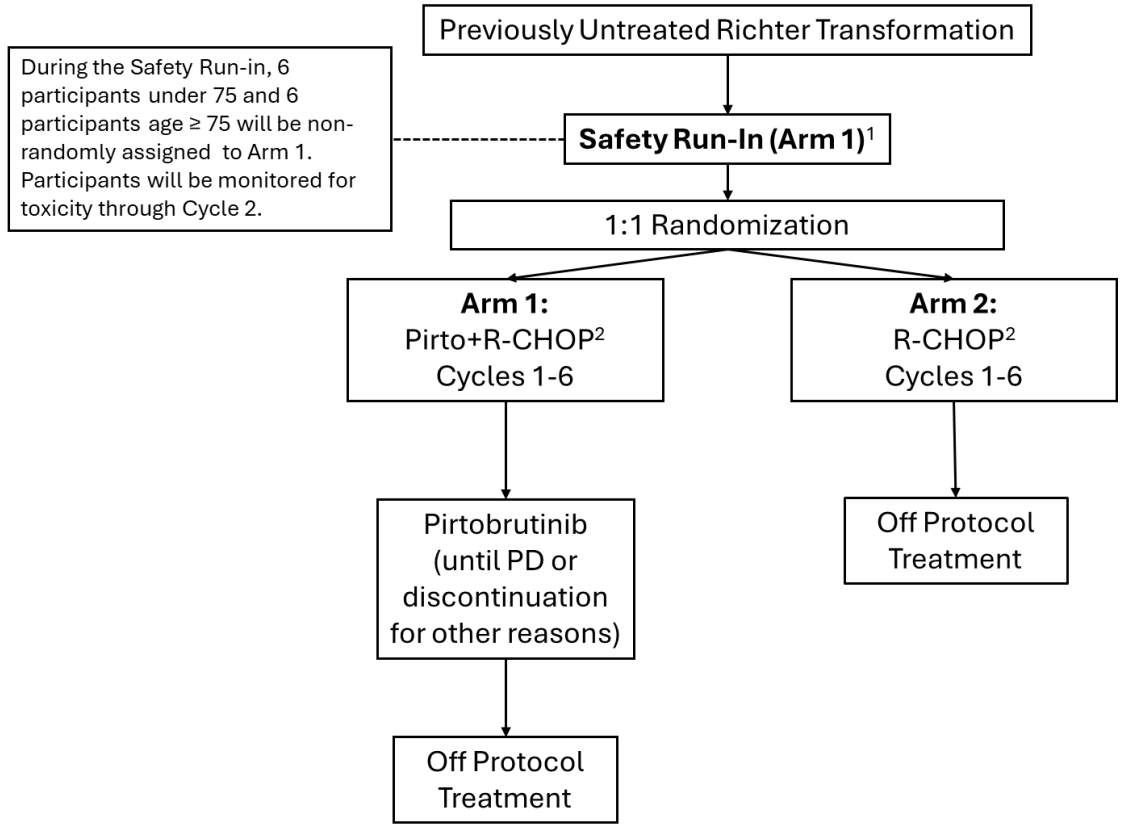
Randomized data for RT are on the horizon

UK Stellar study:
R-CHOP vs. R-CHOP plus Acalabrutinib



Appleby et al, BMC Cancer 2019

US SWOG S2504:
R-CHOP vs. R-CHOP plus pirtobrutinib

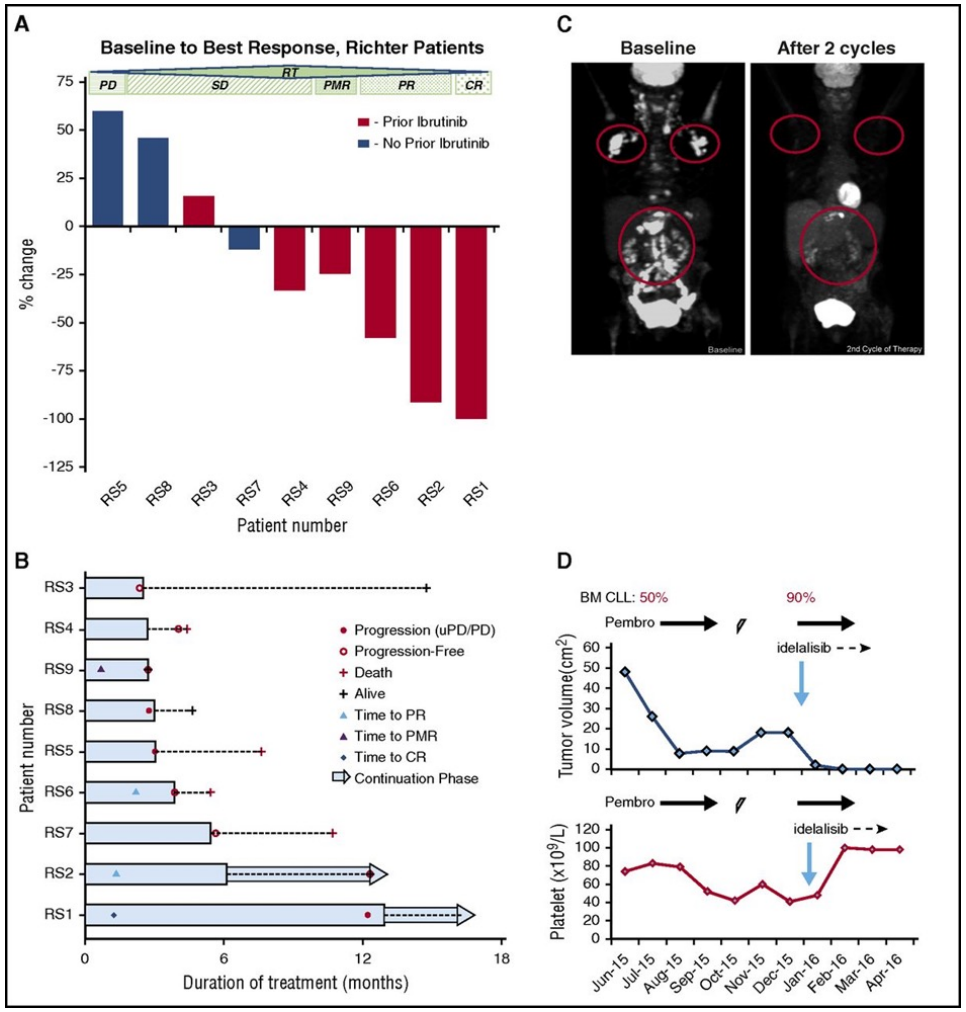


Courtesy of Alexey Danilov

Novel treatment options: PD-1 blockade monotherapy

- Initial promising data for **pembrolizumab** monotherapy, with 4/9 (44%) responses (though only 1 CR)[1]
  - Median OS 11 months

- Subsequent larger study was disappointing,[2] with 3/23 (13%) responses and only 1 (4.3%) CR
  - Median PFS/OS 1.6/3.8 months



1. Deng et al. *Blood.* 2017. **2.** Armand et al. *Br J Haematol.* 2020.

Novel treatment options: PD-1/BTK blockade

Nivolumab Ibrutinib combination in DLBCL-RT

- Patients≥ 18 years age
- ECOG PS ≤2
- Normal liver and renal function

DLBCL-RT R/R or N/D with underlying del 17p CLL

R/R CLL or N/D CLL with del17p*

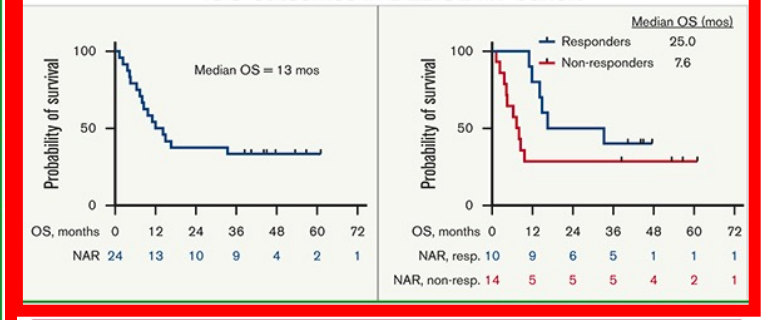
Nivolumab 3 mg/kg every 2 weeks from C1

Ibrutinib 420 mg/day from C2D1 or continued through C1 for patients already on ibrutinib before trial entry

- Safety
- Efficacy
  - Lugano 2014 PET criteria for DLBCL-RT
  - iWCLL 2008 criteria for CLL

DLBCL-RT (N = 24)		
Characteristics		N (%), median [range]
Baseline parameters	Age (years) Gender (male)	64.5 [47–88] 14 (58)
Disease parameters	IGHV unmutated Del17p	13/18 (72) 9 (45)
Prior therapy	Prior therapy for CLL Prior therapy for RT Prior exposure to BTK inhibitor Prior Allo-SCT Completely treatment naive	20 (83) 10 (42) 13 (54) 3 (13) 1 (4)
Study combination efficacy	**ORR** - CMR - PMR Post-trial therapy allo-SCT **Median OS (months)** - Whole cohort - Responders	**10 (42)** 8 (33) 2 (8) 4 (17) 13 25
Adverse events	Grade 3-4 immunological toxicity	4 (17) 4 (17)

OS outcomes in DLBCL-RT cohort



CLL (N = 10)		
Characteristics		N (%), median [range]
Baseline parameters	Age (years) Gender (male)	57 [42-70] 8 (80)
Disease parameters	IGHV unmutated Del17p	4 (40) 4 (40)
Prior therapy	Median lines of therapy	1 (1-3)
Efficacy	CR	3 (30)
Adverse events	Immunological toxicity	1 910)

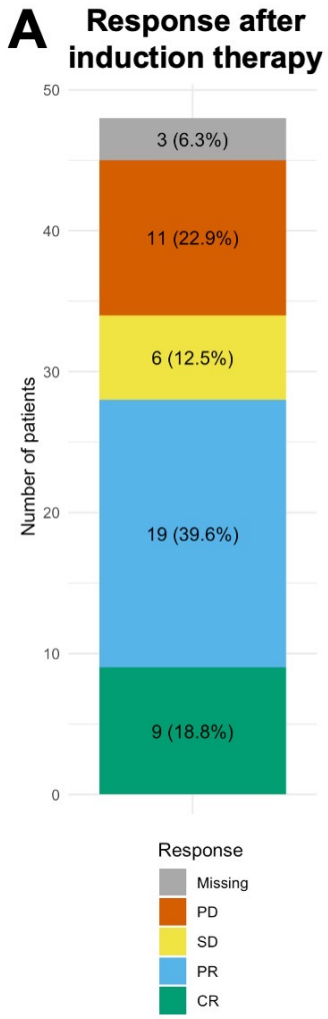
*CLL cohort stopped early due to poor recruitment
DLBCL-RT diffise large B-cell lymphoma Richter transformation, R/R- relapsed refractory, N/D- newly diagnosed
ORR- overall response rate, CMR- complete metabolic response, PMR- partial metabolic response, CR- complete remission

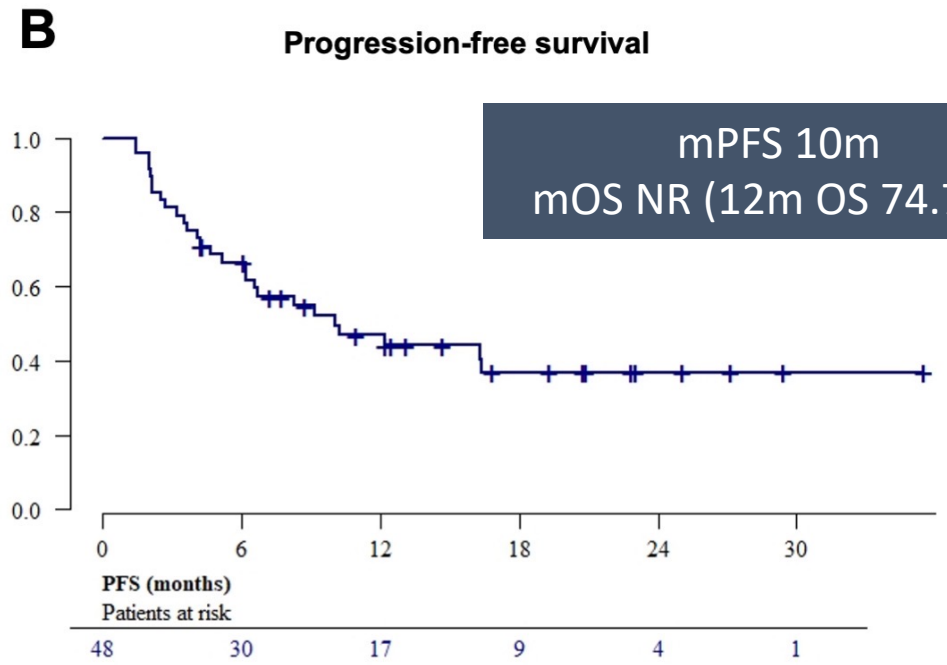
Jain N et al. *Blood Adv*. 2022

RT1 trial: Tislelizumab Plus Zanubrutinib Efficacy in RT Patients

N=59 enrolled
N=48 efficacy population
75% prior CLL Rx
27% prior RT Rx

ORR 58%
CR 19% in N=48





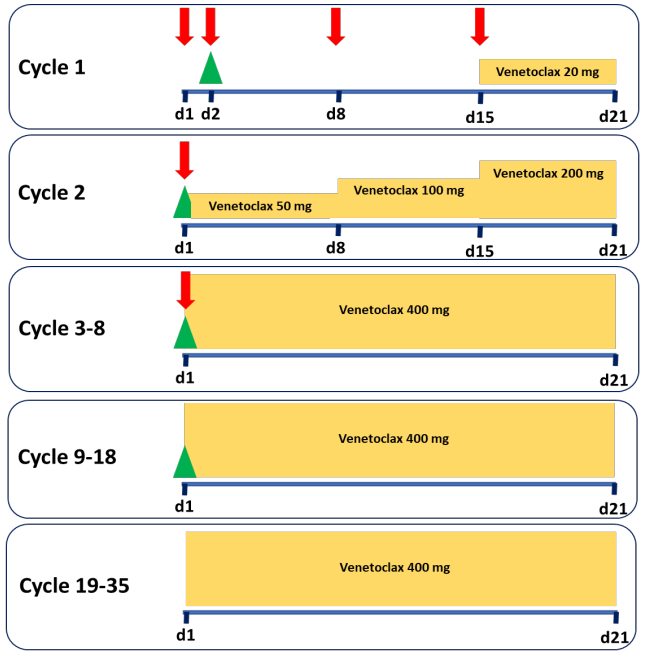
mPFS 10m
mOS NR (12m OS 74.7%).

AE ≥G3 28.5%
SAE 21.3%
3 d/c due to toxicity
Most common AEs infection 17.7%

Ongoing study extension with the addition of sonrotoclax (BGB-11417): n = 26

Al Sawaf et al, ASH 2023 and *Nat Med* 2023

MOLTO trial: Venetoclax-Obinutuzumab-Atezolizumab



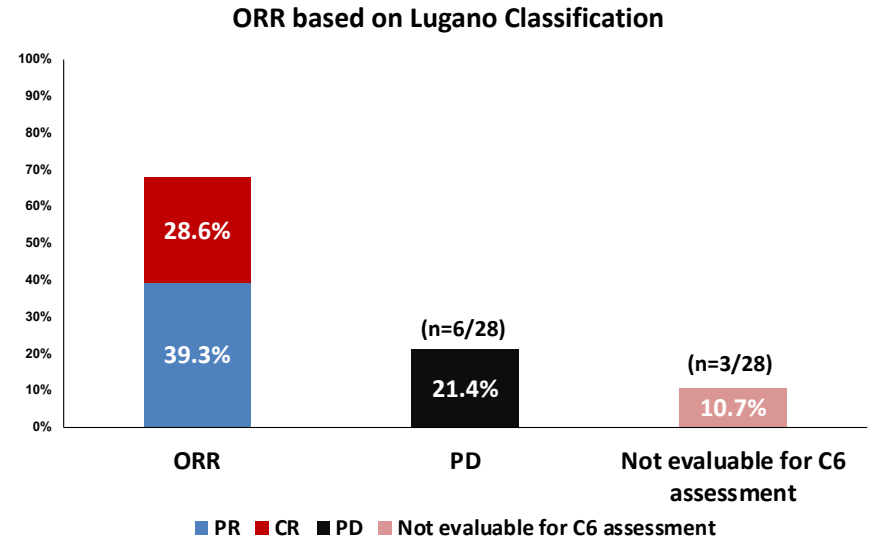
Obinutuzumab:
100 mg C1D1;
900 mg C1D2;
1000 mg C1D8, 15 and C2-8 D1

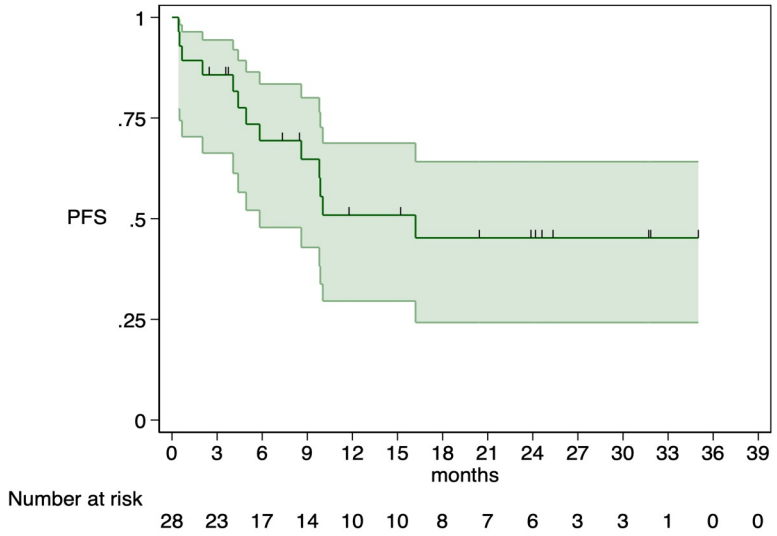
Atezolizumab:
1200 mg C1D2 and C2-18 D1

Venetoclax:
5 w ramp-up from C1D15,
then 400 mg C3D1-C35D21

1 cycle = 21 days

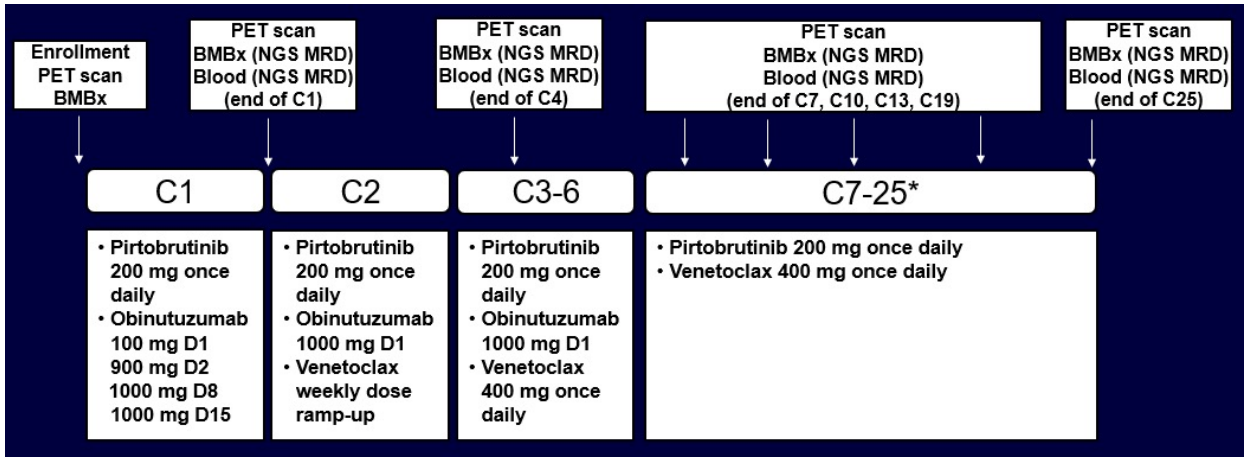
ORR 68%, CRR 29%
1-year-PFS 51%

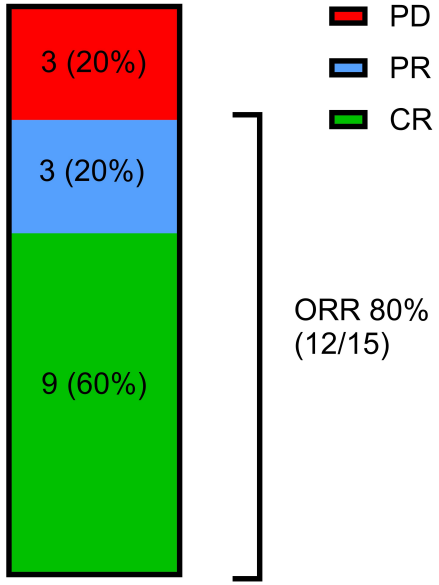


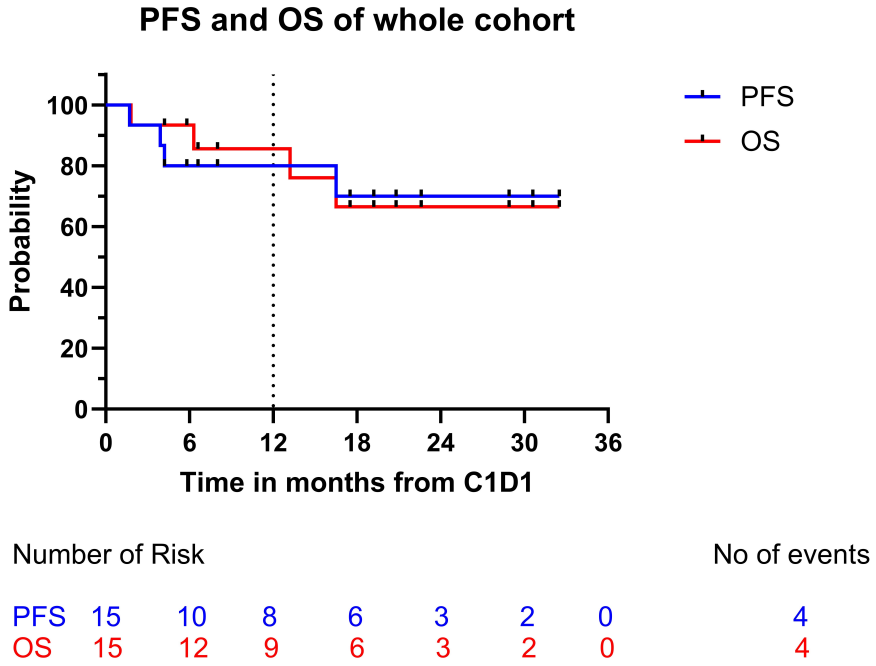


Tedeschi et al, Lancet Oncol, 2024

PVO: Pirtobrutinib-Venetoclax-Obinutuzumab in RT

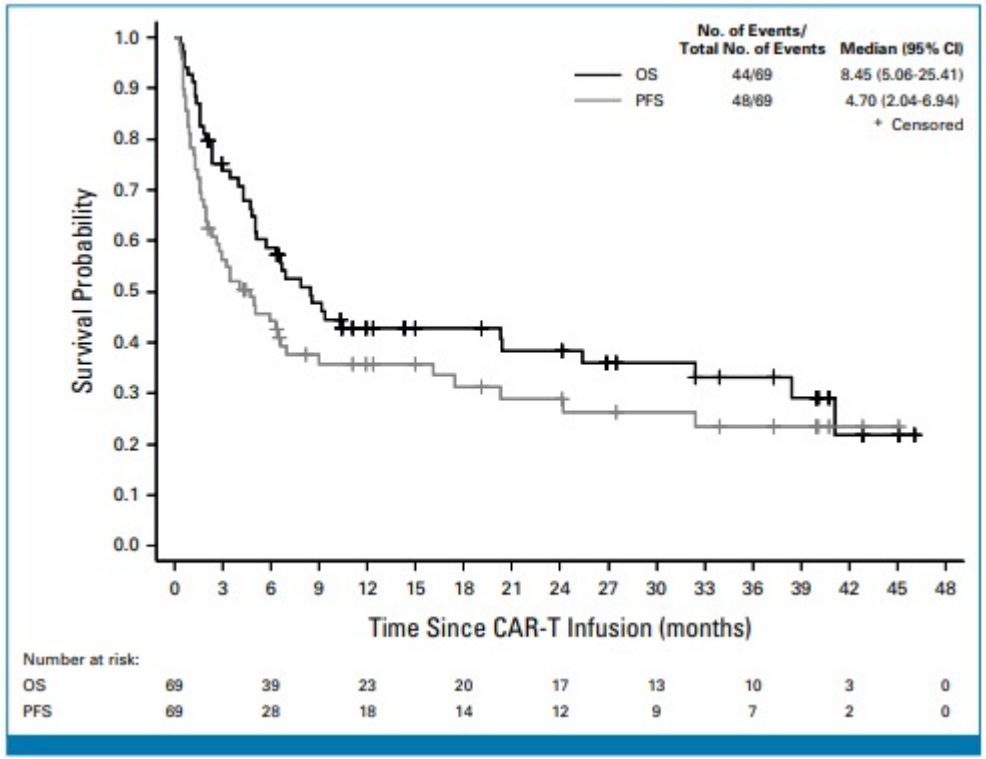


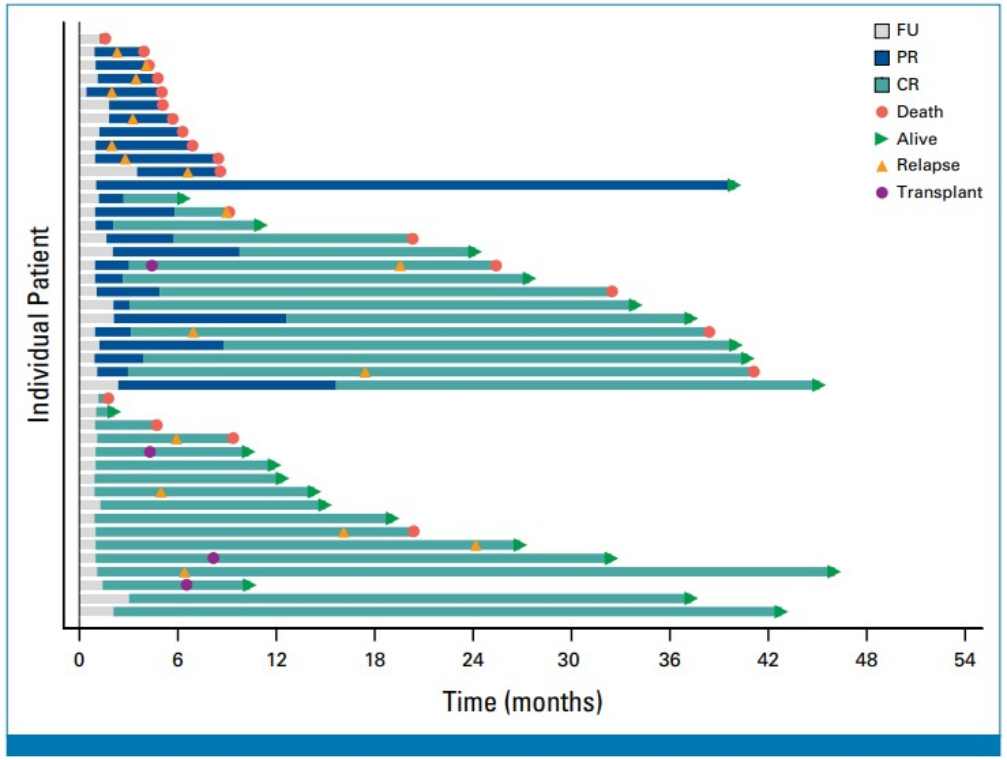




Jain N., et al., ASH, 2025

CD19 CAR-T in RT: retrospective data suggest limited benefit



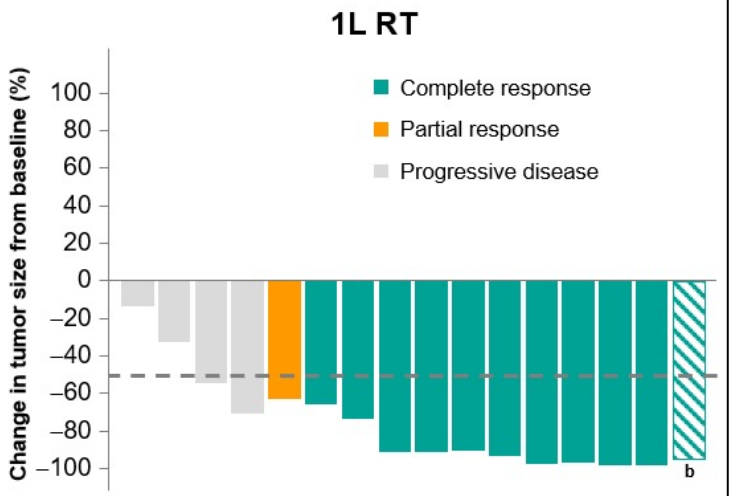


- 69 patients with median 4 prior lines of therapy
- ORR 63%, CR 46%, median PFS 4.7 mo., median DOR 27.6 mo
- Grade 3+ CRS and ICANS in 16% and 37%, respectively

Kittai et al., *J Clin Oncol*, 2024

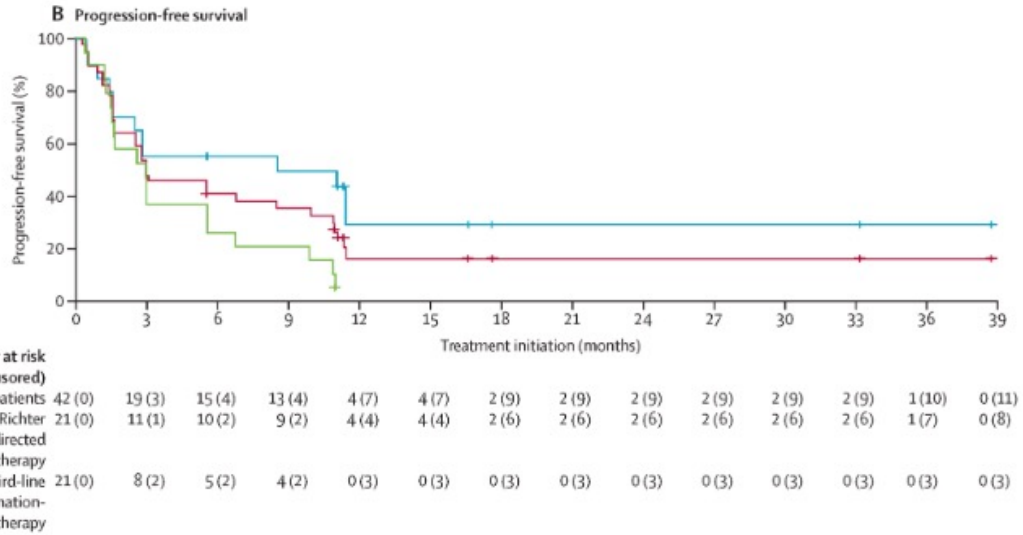
Bispecific Antibodies: Epcoritamab

Response, n (%)	1L RT (n=21)
Overall response rate [95% CI]	12 (57) [34.0–78.2]
Complete response	11 (52)
Partial response	1 (5)
Stable disease	0
Progressive disease	5 (24)
No assessment[a]	4 (19)



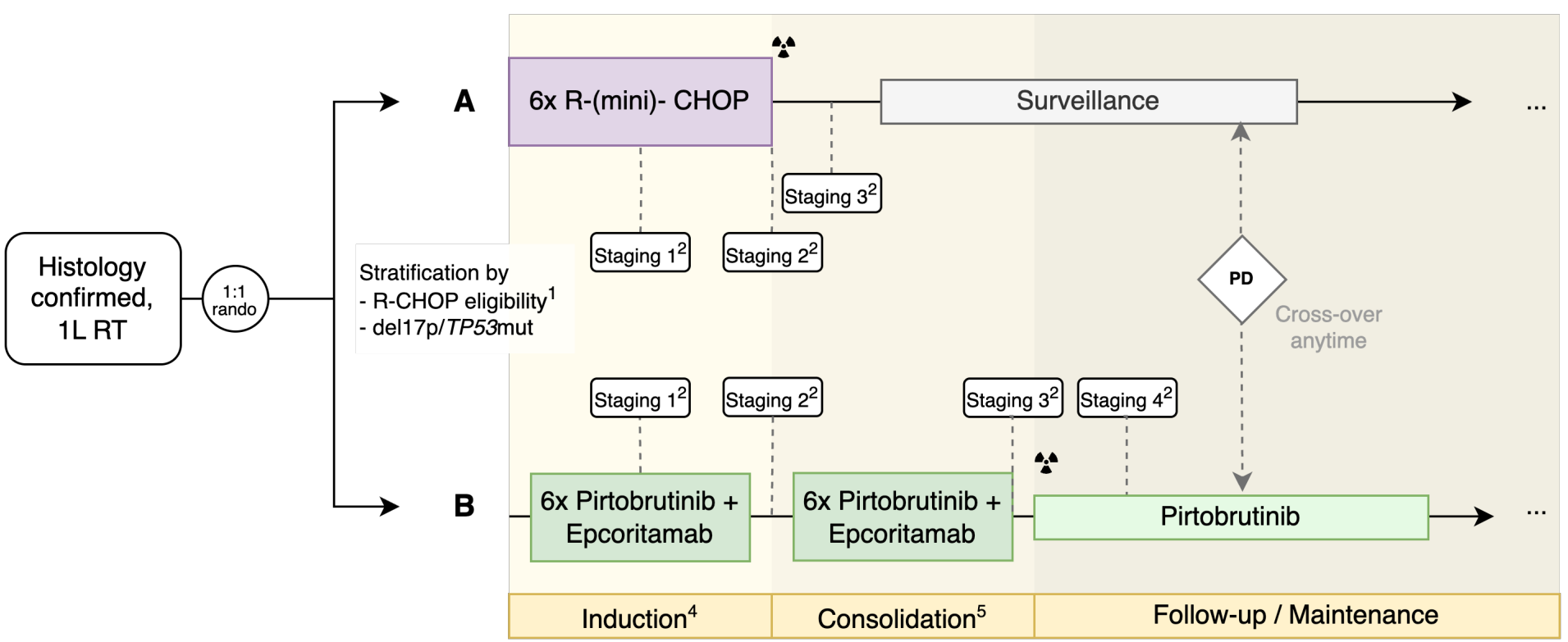
	1L RT (n=21)
PFS events, n	13
Median PFS, (95% CI)	8.5 (1.5–NR)

- CRS in 86% (7% Gr3),
- ICANS in 12% (all Gr1/2)



Kater et al., *iwCLL*, 2025 / *Lancet Haem*, 2026

RT2 Randomized Trial: Epco + Pirto vs. R-CHOP



Primary endpoint:
PFS[3]

Median PFS assumptions:
Arm A: 4 months
Arm B: 7 months

HR 0.571

Sample size
58 pts per arm (116 total)

Accrual time
33 months (3.5/mo)

[1] fit pts receive R-CHOP, unfit pts R-mini-CHOP
[2] if PD: Cross-over
[3] PFS event: PD, death
[4] 1 cycle à 21 days
[5] 1 cycle à 28 days

Radiation at end of (combination) treatment if residual PET-positive lesions

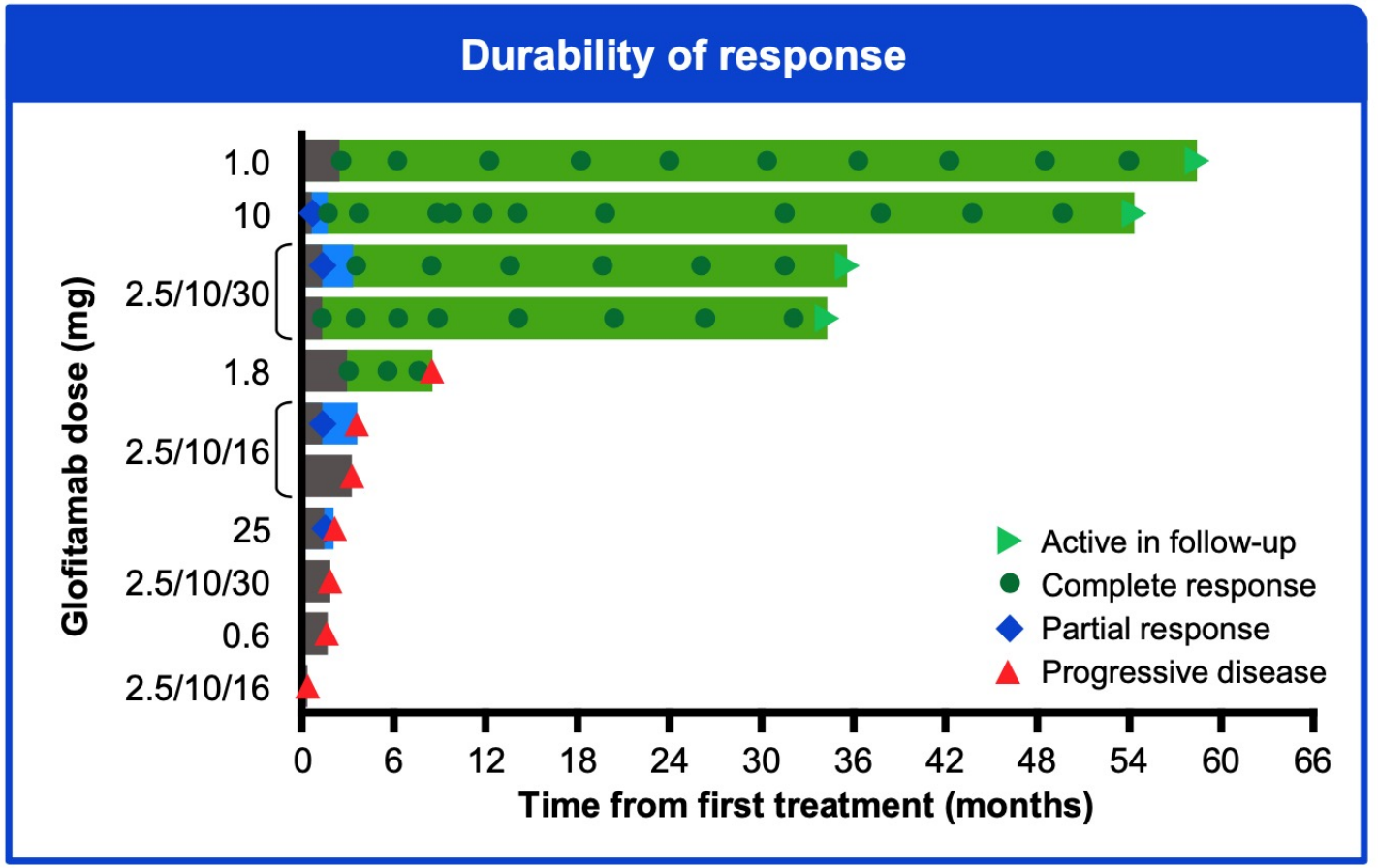
(courtesy of O. Al-Sawaf)

Bispecific Antibodies: Glofitamab

11 patients with RT treated with Glofitamab Monotherapy[2]

In RT:

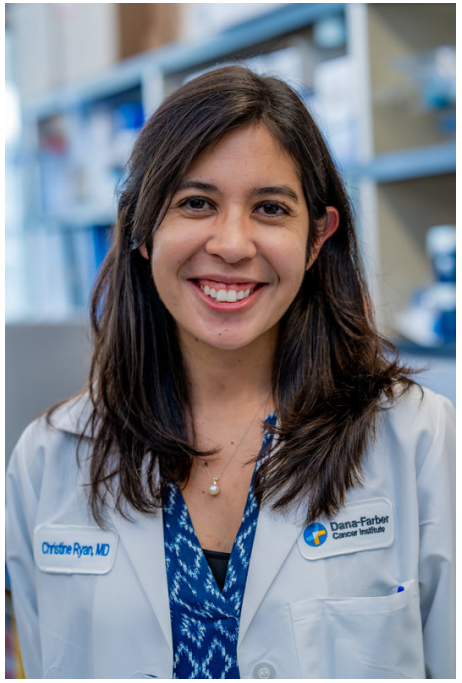
- ORR: 64% (7/11)
- **CR rate: 46%** (5/11)
- 4 of 5 patients who achieved CR with ongoing response > 33 months
- Median time to CR: 2.5 months
- CRS: 73% (n=1 each Gr3, Gr4)



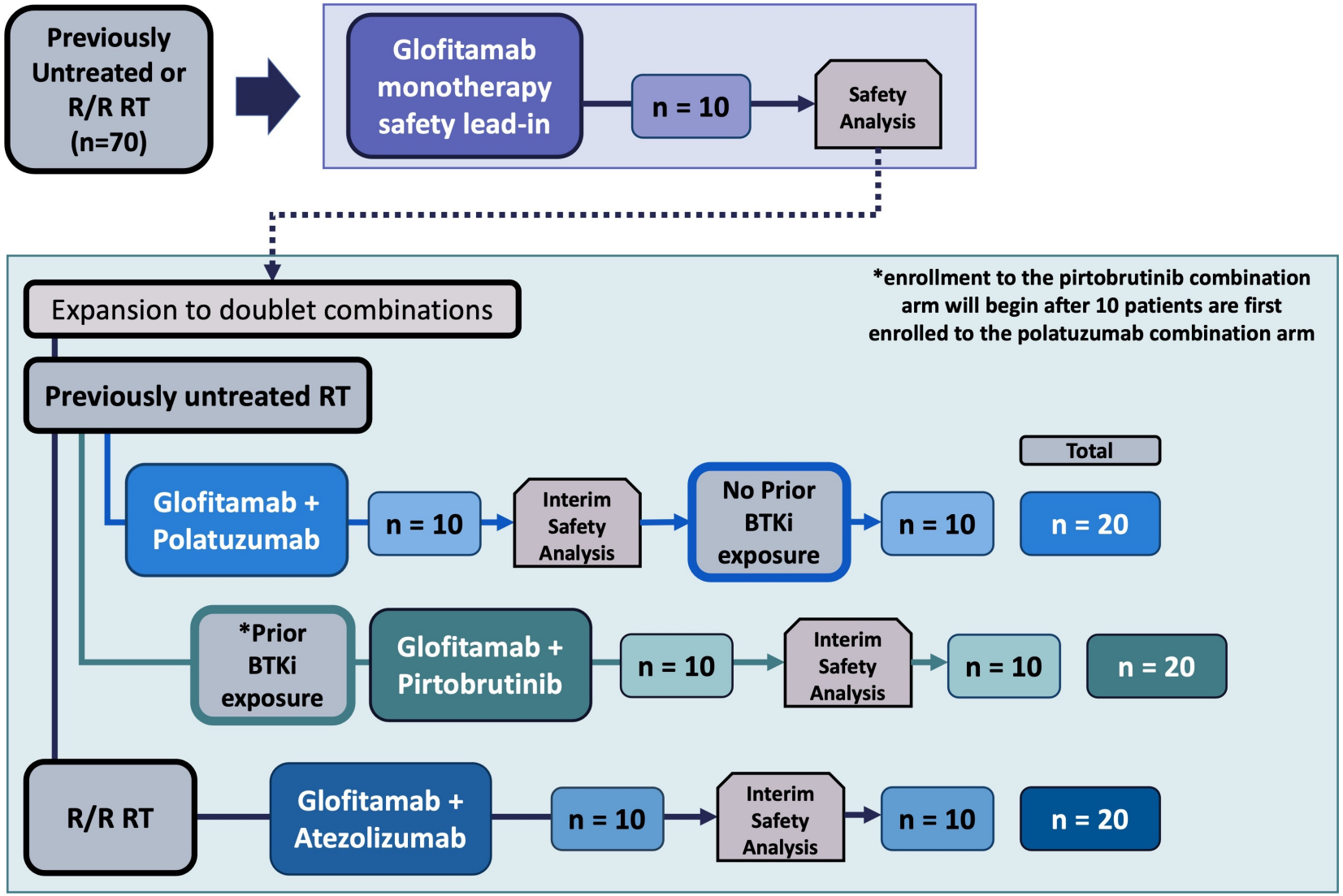
Carlo-Stella et al., ICML 2023

Bispecific Antibodies: Glofitamab

Ph2, Multicenter IIT: Glofitamab in RT



PI: Christine Ryan, MD
DFCI

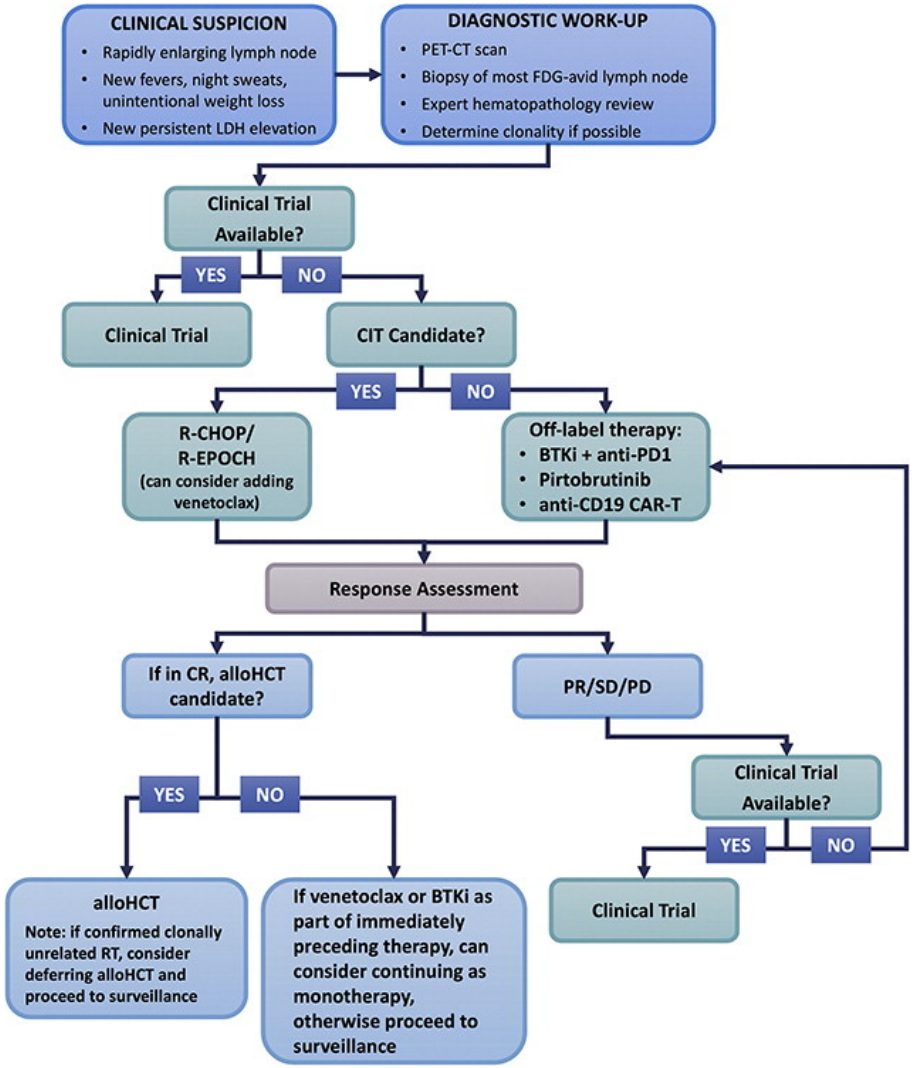


Selected ongoing clinical trials for Richter transformation

Combination Regimen	CIT		Mono-clonal Ab	Small-Molecule Inhibitors							Immunotherapy				ADC
				BTKi				BCL2i	PI3Ki		Immune Checkpoint Blockade			CAR-T	
	R-EPOCH	R-CHOP	OBIN	IBR	ACALA	ZANU	PIRTO	VEN	DUV	COPA	*Anti-* PD-1	*Anti-* PD-L1	*Anti-* CTLA-4	*Anti-* CD19	POLA
IBR + NIVO *NCT02329847, NCT02420912*				■							■				
IBR + NIVO + IPI *NCT04781855*				▨							▨		▨		
IBR + NIVO + Liso-Cel *NCT05672173*				▨							▨			▨	
ACALA + R-CHOP *NCT03899337*		▨			▨										
ACALA + VEN + DURVA *NCT05388006*					▨			▨				▨			
ZANU + TISLE *NCT04271956*						■					■				
PIRTO + VEN + OBIN *NCT05536349*			▨				▨	▨							
VEN + R-EPOCH/ VEN + R-CHOP *NCT03054896*	■	▨						■							
VEN + OBIN + ATEZO *NCT02846623, NCT04082897*			■					■				■			
VEN + DUV *NCT03534323*								■	■						
COPA + NIVO *NCT03884998*										■	■				
POLA + R-EPOCH *NCT04679012*	▨														▨

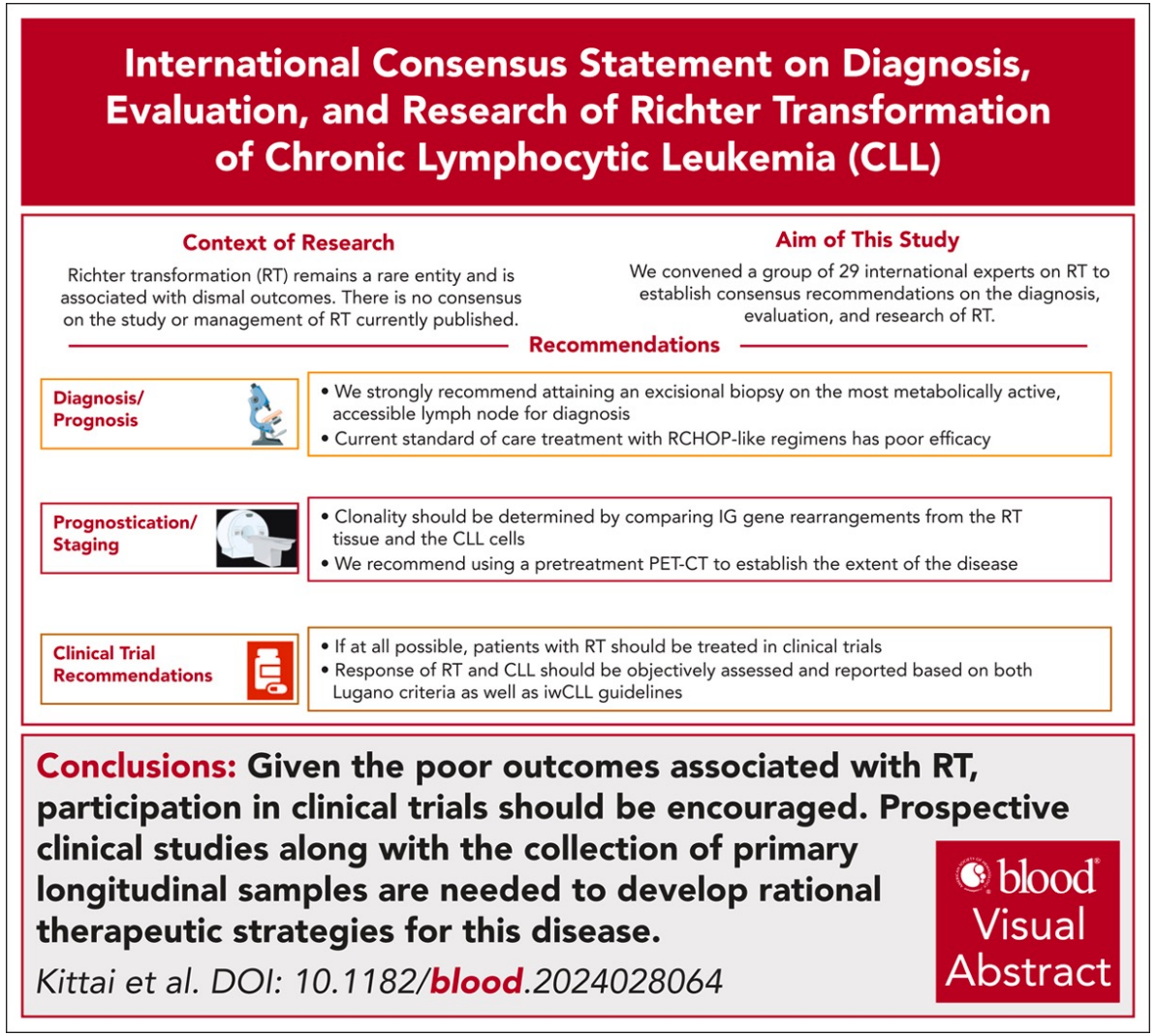
Ryan CE and Davids MS, *ASCO Ed Book*, 2023

Summary of algorithm for RT treatment in 2026



Ryan CE and Davids MS, *ASCO Ed Book*, 2023

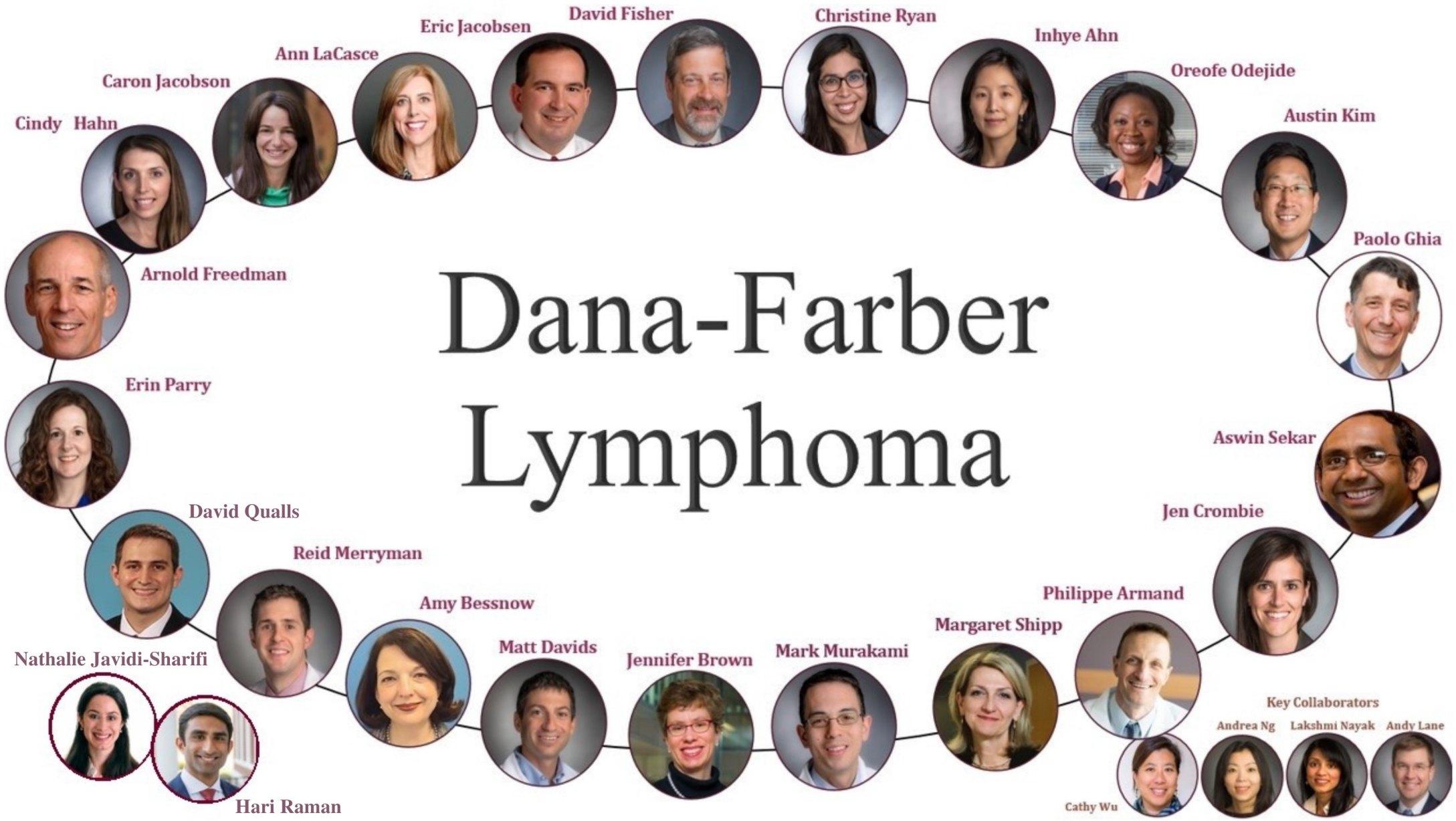
Toward a Consensus on Richter Transformation



Kittai et al., *Blood*, 2025

Conclusions

- **RT is rare, but carries a poor prognosis**
- **PET is not diagnostic, and specialized path confirmation critical**
- **Clonal relationship informs risk stratification**
- **Chemo has poorer outcomes than DLBCL, but allo HCT may confer long term survival**
- **Promising new treatment options are under investigation, including:**
  - Chemosensitization with ven
  - PD-1 blockade in combination with BTKi
  - Non-covalent BTKi combinations
  - CAR-T, bispecific antibody combinations
- **Active participation in clinical trials remains crucial**


Dana-Farber
Lymphoma
Eric Jacobsen
David Fisher
Christine Ryan
Ann LaCasce
Inhye Ahn
Caron Jacobson
Oreofe Odejide
Cindy Hahn
Austin Kim
Paolo Ghia
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David Qualls
Jen Crombie
Reid Merryman
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Amy Bessnow
Margaret Shipp
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