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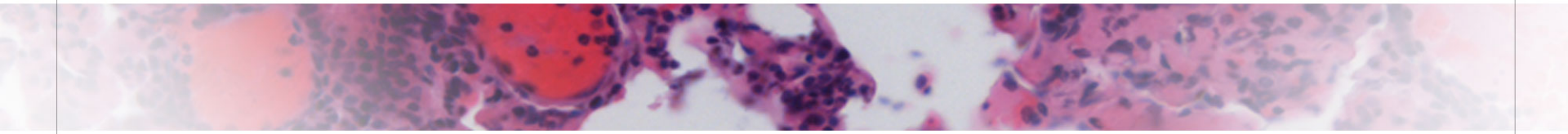

PHASE 1/2 STUDY OF CIRMTUZUMAB AND IBRUTINIB IN MANTLE CELL LYMPHOMA (MCL) OR CHRONIC LYMPHOCYTIC LEUKEMIA (CLL)

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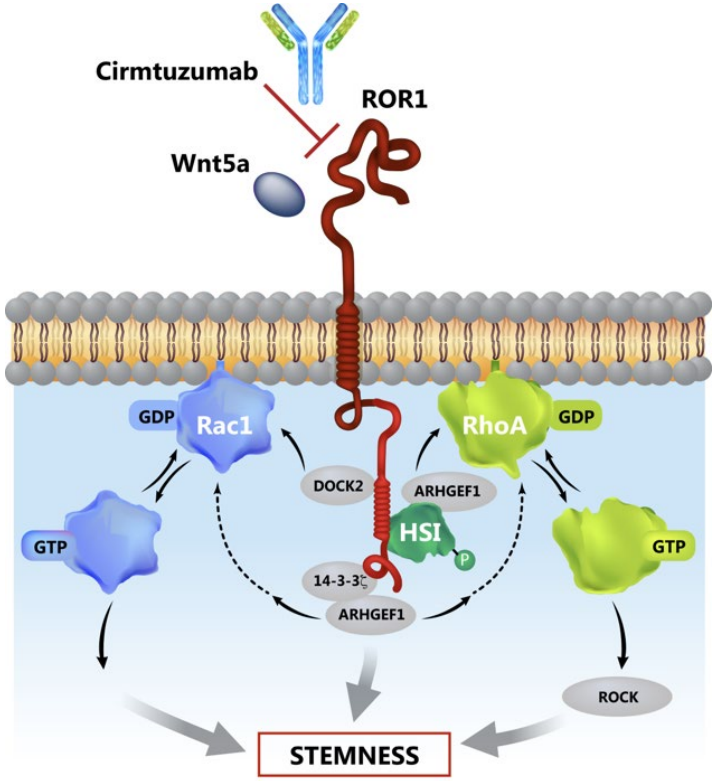
Background

Front-line use of multi-agent therapies are typically successful in suppressing chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL) and mantle cell lymphoma (MCL). However, these diseases are incurable, and patients require further therapy for disease control.

- ROR1 is an onco-embryonic tyrosine kinase receptor that is re-expressed at high levels on many solid and hematologic cancers including MCL and CLL, but not on normal adult tissues. ROR1 binds Wnt5a, resulting in increased tumor growth, survival, metastasis, cancer cell stemness and epithelial mesenchymal transition.
- Zilovertamab* (cirmtuzumab) is a humanized monoclonal antibody designed to inhibit the tumor promoting activity of ROR1.



*Formerly known as cirmtuzumab or UC-961

Phase 1/2 Study Design

Treatment naïve or Relapsed/Refractory (R/R) CLL/SLL or R/R MCL
Prior BTK-inhibitor is allowed for MCL

PART 1 (in MCL & CLL)	PART 2 (in MCL & CLL)	PART 3 (in CLL)	PART 4 (in MCL)
DOSE-FINDING COHORT • At 2, 4, 8 & 16 mg/kg and 300 & 600 mg doses evaluated • Ibrutinib added after one month (420 mg CLL, 560 mg MCL qd po)	**DOSE-EXPANSION COHORT** • Confirm Recommended Dosing Regimen (RDR) of zilovertamab* (600 mg) + ibrutinib at approved dose (420 mg CLL, 560 mg MCL)	**RANDOMIZED EFFICACY** • Zilovertamab + ibrutinib vs ibrutinib • Randomization ratio: zilovertamab + ibrutinib : ibrutinib = 2:1 • Primary endpoint: Complete Response rate	**EXPLORATORY** • Zilovertamab + ibrutinib (refractory to prior BTKi therapy or have achieved an inadequate response (SD, PR) to prior ibrutinib therapy)
Enrolled *CLL n = 18* *MCL n = 12*	***CLL enrolled 16*** *MCL Phase 2 enrolling* *n = 19*	***Enrolled*** *n = 31*	***Open for Enrollment***

*Formerly known as cirmtuzumab or UC-961

Demography and Disease Characteristics

Population: High-risk disease and heavily pre-treated

	MCL (N=31)	CLL (Parts 1 & 2) (N=34)
Median Age, years (min, max)	64 (45, 85)	68 (37, 86)
Male, n (%)	26 (83.9%)	26 (76.5%)
ECOG 0-1, n (%)	28 (90.3%)	34 (100.0%)
Median time from diagnosis to study start, years (range)	1.96 (0.04, 9.15)	6 (0.03, 31.33)
Ki-67 ≥ 30%, n (%)	16 (51.6%)	NA
sMIPI Intermediate/High, n (%)	14 (45.1%)	NA
Bulky disease ≥ 5cm, n (%)	7 (22.6%)	NA
RAI staging, ≥2, n (%)	NA	24 (70.6%)
LDH >250 U/L, n (%)	NA	15 (44.1%)
Received prior systemic regimens, n (%)	31 (100.0%)	22 (64.7%)
Median number of prior systemic regimens, n (range)	1 (1,4)	2.0 (1, 15)ˣ
Prior BTK inhibitor, n (%)	5 (16.1%)Ŧ	0
Prior Transplant/Cell Therapy, n (%)	8 (25.8%)*	1 (2.9%)‡

Data cut: 01OCT2021; Lymphocytosis at baseline- ALC > 4 x 10/L; NA- not applicable; sMIPI - Simplified Mantle Cell Lymphoma International Prognostic Index; LDH- lactate dehydrogenase; Ŧprior BTK inhibitor = ibrutinib; ˣMedian number of prior systemic regimens among previously treated patients (n=22). *Autologous stem cell transplant (n=8), Allogeneic stem cell transplant (n=1); CAR-T (n=1) patients could have received more than one; ‡Autologous stem cell transplant (n=1).

Safety MCL: Treatment Emergent AEs ≥20%

Zilovertamab + ibrutinib generally well tolerated with AEs similar to ibrutinib alone. Most TEAEs Grades 1-2, hematologic adverse events infrequent.

MCL N=31	Overall	Grade 1-2	Grade ≥3
Fatigue	15 (48.4%)	11 (35.5%)	4 (12.9%)
Diarrhea	12 (38.7%)	11 (35.5%)	1 (3.2%)
Contusion	10 (32.3%)	10 (32.3%)	0
Cough	9 (29.0%)	9 (29.0%)	0
Dizziness	8 (25.8%)	8 (25.8%)	0
Myalgia	8 (25.8%)	7 (22.6%)	1 (3.2%)
Nausea	8 (25.8%)	8 (25.8%)	0
Stomatitis	8 (25.8%)	5 (16.1%)	3 (9.7%)
Treatment Emergent Hematological Laboratory Abnormalities			
Hemoglobin decrease	21 (67.7%)	18 (58.1%)	3 (9.7%)
Platelets decrease	20 (64.5%)	17 (54.8%)	3 (9.7%)
Neutrophils decrease	8 (25.8%)	5 (16.1%)	3 (9.7%)

Data cut: 01OCT2021; MCL patients include Part 1 &2; Patients are counted only once at the maximum grade observed after first dose of study medication.

Safety CLL Part 1 & 2: Treatment Emergent AEs ≥20%

Zilovertamab + ibrutinib well tolerated with AEs similar to ibrutinib alone

CLL N=34	Overall	Grade 1-2	Grade ≥3
Contusion	19 (55.9%)	19 (55.9%)	0
Hypertension	16 (47.1%)	9 (26.5%)	7 (20.6%)
Diarrhea	15 (44.1%)	13 (38.2%)	2 (5.9%)
Upper respiratory tract infection	15 (44.1%)	15 (44.1%)	0
Fatigue	14 (41.2%)	14 (41.2%)	0
Arthralgia	12 (35.3%)	11 (32.4%)	1 (2.9%)
Dyspnea	10 (29.4%)	9 (26.5%)	1 (2.9%)
Muscle Spasms	10 (29.4%)	10 (29.4%)	0
Hypophosphatemia	9 (26.5%)	8 (23.5%)	1 (2.9%)
Onycholclasis	9 (26.5%)	9 (26.5%)	0
Rash	9 (26.5%)	9 (26.5%)	0
Cough	8 (23.5%)	8 (23.5%)	0
Dizziness	8 (23.5%)	8 (23.5%)	0
Gastroesophageal reflux disease	8 (23.5%)	8 (23.5%)	0
Haematuria	8 (23.5%)	8 (23.5%)	0
Headache	7 (20.6%)	7 (20.6%)	0
Hypercreatinaemia	7 (20.6%)	6 (17.6%)	1 (2.9%)
Palpitations	7 (20.6%)	7 (20.6%)	0
Thrombocytopenia	7 (20.6%)	6 (17.6%)	1 (2.9%)
Treatment Emergent Hematological Laboratory Abnormalities			
Hemoglobin decrease	25 (73.5%)	25 (73.5%)	0 (0.0%)
Platelets decrease	25 (73.5%)	24 (70.6%)	1 (2.9%)
Neutrophils decrease	16 (47.1%)	10 (29.4%)	6 (17.6%)

Data cut: 01OCT2021; CLL/SLL patients include Part 1 &2; Patients are counted only once at the maximum grade observed after first dose of study medication.

Efficacy: Clinical Response

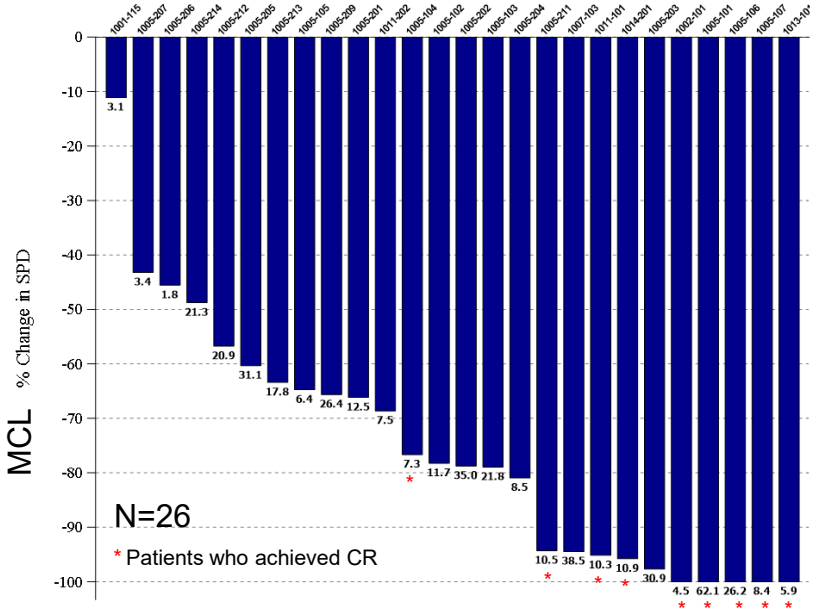
High response rates and durable responses observed in both MCL and CLL

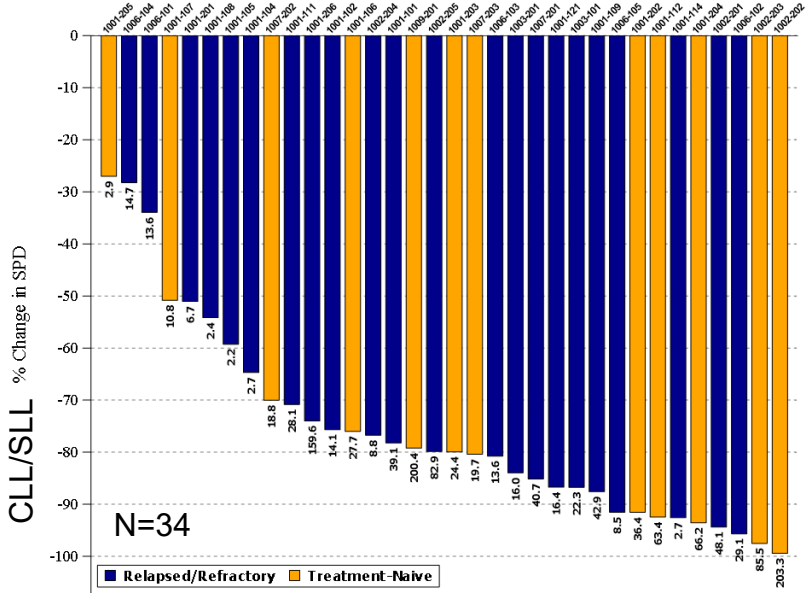
	MCL (N=26)	CLL (Parts 1 & 2) (N=34)
Overall Response Rate (ORR), n (%)	21 (80.8%)	31 (91.2%)
CR, n (%)	9 (34.6%)	2 (5.9%)
PR, n (%)	12 (46.2%)	29 (85.3%)*
SD, n (%)	3 (11.5%)	3 (8.8%)
PD, n (%)	2 (7.7%)	0
Median Duration of response, months (95% CI)	34.13 (13.67, 34.13)	33.5 (0.0, 33.5)**
Median Duration of follow-up, months (95% CI)	14.4 (11.38, 19.31)	29.0 (27.64, 31.61)

Data cut: 01OCT2021; Seven patients received prior stem cell transplant ± CAR-T therapy prior to enrolling in the study and achieved responses of 5 CRs, 2 PRs. Meanwhile, 2 CRs, 2 PRs, 1 SD were observed in the 5 patients that received prior ibrutinib treatment.
* Include PR-Lymphocytosis; ** min, max.

Efficacy: Waterfall Plot of Best % Tumor Reduction from Baseline

Marked reductions in tumor size were observed in both MCL and CLL



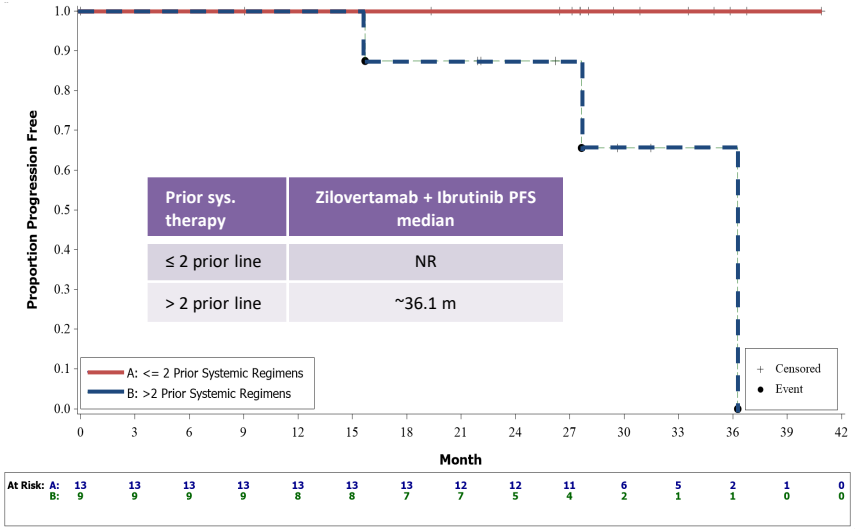


SPD = Sum of the Products of the Diameters
Number under bars represent baseline SPD.
Data cut: 01OCT2021

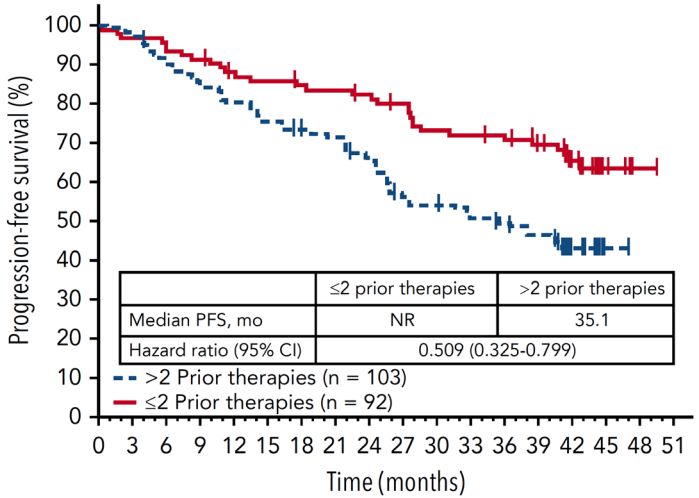
Relapsed/Refractory = subjects ≥ 1 prior treatments for CLL/SLL only.
Treatment Naïve = subjects with no prior systemic treatment for CLL/SLL.

Progression Free Survival for R/R CLL

Zilovertamab + ibrutinib demonstrates encouraging PFS based on number of prior lines of therapy compared to historical ibrutinib treatment alone.



Zilovertamab + Ibrutinib



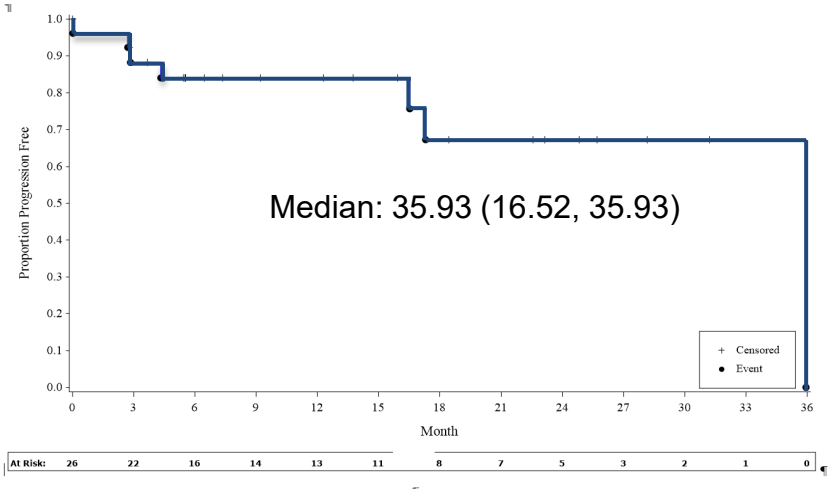
*PFS by prior therapies from single-agent ibrutinib treatment in high-risk, relapsed patients with CLL

Data cut: 01OCT2021; PFS is defined as the time from the first dose to the time of objective disease progression or death from any cause, whichever occurs first; NR- not reached. NE – not evaluable

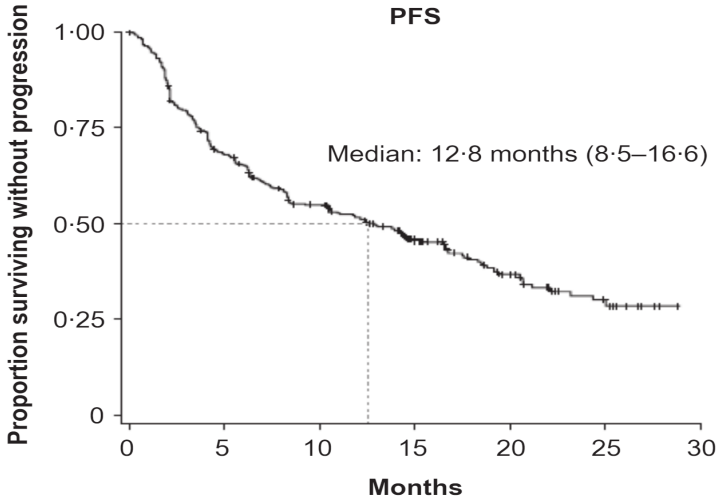
*Byrd, Blood 2019

MCL Efficacy: Progression Free Survival

Zilovertamab + ibrutinib combination provides favorable PFS benefit compared to historical ibrutinib treatment alone.



Zilovertamab + Ibrutinib



*Patient-level data from three single-agent ibrutinib studies, N = 370

Data cut: 01OCT2021; PFS is defined as the time from the first dose to the time of objective disease progression or death from any cause, whichever occurs first; NR- not reached. NE – not evaluable

*Rule, British Journal of Haematology, 2017

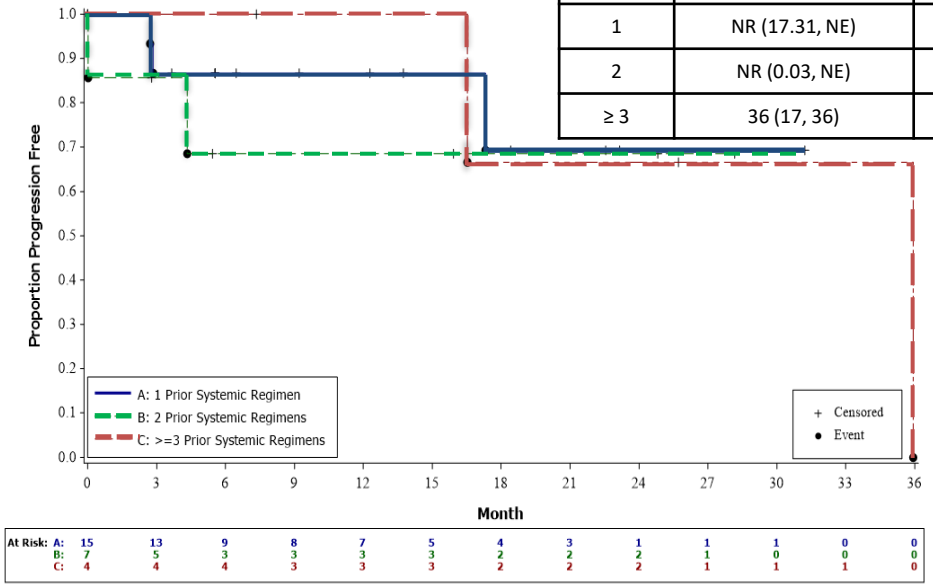
Summary

- Zilovertamab is a humanized monoclonal antibody designed to inhibit the tumor promoting activity of ROR1.
- Zilovertamab + ibrutinib generally well tolerated, safety profile similar to ibrutinib alone
  - Grade 3/4 neutrophil decrease was only 9.7% with zilovertamab plus ibrutinib in MCL, compared to 29% for ibrutinib alone from its registration study
- Encouraging response rates, particularly in patients with R/R disease
  - CLL ORR 91.2% (31/34), CR 5.9% (2/34), PR 85.3% (29/34)
  - MCL ORR 80.8% (21/26), CR 34.6% (9/26), PR 46.2% (12/26)
- Progression free survival favorable compared to historical ibrutinib alone
  - MCL median PFS 36 months, CLL median NR
- Encouraging efficacy in R/R MCL subsets traditionally difficult to treat with ibrutinib
  - Landmark PFS of ~70% at 24 months regardless of number of prior therapies
  - 80% ORR (2 CR, 2 PR) for patients who received prior ibrutinib (n=5)
- Study ongoing, investigating MCL BTKi resistance and consolidation.

MCL: PFS by Subtypes – Prior Systemic Therapy

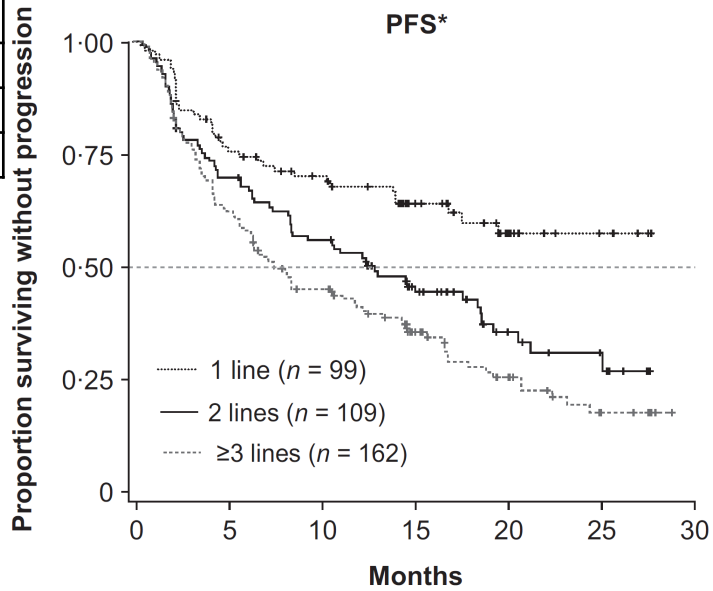
Encouraging PFS observed based on prior line of therapy compared to historical ibrutinib alone

Prior sys. therapy	Zilovertamab + Ibrutinib PFS , median (95% CI)	Ibrutinib PFS median*
1	NR (17.31, NE)	NR
2	NR (0.03, NE)	~12 m
≥ 3	36 (17, 36)	~8 m



Zilovertamab + Ibrutinib

Data cut: 01OCT2021



*Patient-level data from three single-agent ibrutinib studies, N=370

*Rule, British Journal of Haematology, 2017