Characteristic	CLL/SLL (prior BTKi), n=276[23]	MCL (prior BTKi), n=90[24]	RT, n=82 [25]	WM n=78[26]
Median age, y (range)	69 (36-88)	70 (46-87)	67 (26-95)	69 (42-84)
Median # prior therapies	3 (1-11)	3 (1-11)	2(RT)/4(CLL+RT)* (0-13)	3 (1-11)
Reason prior BTKi discontinued				
Progression	75	82	NR	66
Toxicity	25	18	NR	34
Prior therapies				
BTKi	100	100	34	78
CD20 mAb	88	96	78	92
Cytotoxic chemotherapy	80	88	76	83
BCL2 inhibitor	44	16	38	6
PI3K inhibitor	24	3	10	5
CAR-T	6	4	11	NR
Stem cell transplant	2	21	6	6
Immunomodulator	NR	21	4	10

Supplementary table 1. Pre-treatment patient characteristics from publicly reported data in key populations of patients. Abbreviations: CLL chronic lymphocytic leukemia; MCL, mantle cell lymphoma;

Supplementary Table 2.

Disease	Phase/sponsor/Trial number	Comparator	Pirtobrutinib regimen	Primary endpoint and study aim
First line CLL/SLL	III. LOXO/Lilly/NCTNCT04023980	Bendamustine and rituximab	Pirtobrutinib monotherapy	PFS – superiority. Establish pirtobrutinib as a 1L standard of care.
R/R CLL/SLL	III. LOXO/Lilly/ NCT04666038	Investigator's choice of idelalisib + R or BR	Pirtobrutinib monotherapy	PFS – superiority. Broad R/R registration strategy. Similar design to ASCEND, which led to acalabrutinib registration[31]
R/R CLL/SLL, 80% with prior BTKi	III. LOXO/Lilly NCTNCT04965493	Venetoclax + rituximab as per MURANO (Seymour NEJM 2018)	Pirtobrutinib (2 years, fixed duration) + standard VR.	PFS – superiority. Establish superiority of PVR to VR, especially in previously BTKi-treated patients
CLL/SLL, 1L and R/R	III. LOXO/Lilly NCT05254743	Ibrutinib	Pirtobrutinib monotherapy	Overall response rate. Establish to covalent BTK inhibitor.
Mantle cell lymphoma R/R NCT04662255	III. LOXO/Lilly NCT	Investigator's choice of approved BTKi	Pirtobrutinib monotherapy	PFS – superiority. Establish pirtobrutinib as agent of choice in 2L treatment of MCL
CLL – 1L and R/R (NCT05317936)	II M.D. Anderson	N/A	Pirtobrutinib added to venetoclax for MRD eradication. MRD adapted – 2 years of combination then up to 3 years of pirtobrutinib monotherapy in MRD+ patients	U-MRD4 in blood by NGS. Evaluate whether pirtobrutinib added to venetoclax will achieve U-MRD4 in patients who remain MRD+ after 12 months of venetoclax.
CLL – 1L and RT (NCT05536349)	II – MD Anderson	N/A	Pirtobrutinib + venetoclax + obinutuzumab. Time limited – 6 cycles of obinutuzumab. 6-12 cycles of venetoclax + pirtobrutinib according to MRD response	CLL – U-MRD. RT – ORR.
CLL – 1L (NCT05677919)	II – Mayo Clinic	N/A	Pirtobrutinib + venetoclax – 15 cycles, fixed duration	U-MRD6 by Clonoseq.
MCL – R/R (NCT05529069	II – M.D. Anderson	N/A	Pirtobrutinib + venetoclax	ORR @1y

Select ongoing studies evaluating pirtobrutinib in CLL and MCL. Abbreviations: BR, bendamustine and rituximab; CLL, chronic lymphocytic leukemia; MCL, mantle cell lymphoma; ORR, overall response rate; PFS, progression-free survival; RT, Richter transformation; U-MRD4 (undetectable measurable residual disease with 10^{-4} sensitivity); U-MRD6, undetectable measurable residual disease with 10^{-6} sensitivity;