

**Table I.** Summary of selected studies assessing subsequent therapies following venetoclax failure

Author	Study	Number of patients	ORR (with CR)	Median I (month)	Median OS (months)	Comments
Mato et al. [43]	Retrospective study	Anthracycline-based immunochemotherapy — 3	ORR 0.0% (CR 0.0%)	NA	NA	Short observation time with a median follow-up of 7 months
		Rituximab monotherapy — 3	ORR 66.7% (CR 0.0%)			
		Ibrutinib — 5	ORR 20.0% (CR 0.0%)			
		Idelalisib — 2	ORR 50.0% (CR 50.0%)			
		CAR-T — 2	No assessment			
		allo-HCT — 3	ORR 66.7% (CR 66.7%)			
Anderson et al. [41]	Retrospective study	Immunochemotherapy — 1	Unknown response	NA	NA	
		Ibrutinib — 6	ORR 83.3% (CR 0.0%)			
Harrup et al. [54]	Retrospective study	Immunochemotherapy — 15	Unknown response	NA	NA	Patients treated earlier within phase III MURANO trial
		BTKi — 18	ORR 100.0% (CR 7.1%)			
		Retreatment with venetoclax — 32	ORR 72.2% (CR 5.6%)			
Mato et al. [55]	Retrospective study	BTKi: ibrutinib, acalabrutinib (BTKi-naïve) — 44	ORR 83.9% (CR 9.0%)	32	NA	With a median follow-up of 7.7 months (1–48 months) for

		BTKi: ibrutinib, acalabrutinib, noncovalent BTKi (BTKi-exposed) — 30	ORR 53.4% CR 10.0%	12	NA	patients treated with BTKi post-venetoclax, estimated median PFS to post-venetoclax BTKi was 32 months in BTKi-naïve patients, not reached in BTKi-intolerant patients, but was only 4 months in patients who were known to be BTKi resistant
		PI3Ki — 17	ORR 46.9% (CR 5.9%)	5	NA	
		CAR-T — 18	ORR 66.6% (CR 33.3%)	9	NA	
		Anti-CD20 — 19	ORR 32.0% (CR 16.0%)	2	NA	
Brown et al. [58]	Retrospective study	Ibrutinib — 11	ORR 90.9% (CR 0.0%)	NA	NA	Time on ibrutinib therapy ranged from 0.5 to 30 months, with only three patients having discontinued
Brown et al. [60]	Retrospective study	Ibrutinib — 27	ORR 56.0% (CR 4.0%)	NA	NA	Ibrutinib-naïve patients progressing after venetoclax ORRs were 1/25 CR, 13/25 PR. Time to progression on ibrutinib ranged from 3.0 to 53.0 months (n = 10). Median duration of ibrutinib therapy was 18.3 (3.7–53.2) months, and 20.0 (4.9–44.3) months for those remaining on ibrutinib (8/27)
Lin et al. [59]	Retrospective study	BTKi: ibrutinib — 21, zanubrutinib — 2	ORR 90.0% (CR 13.0%)	34	42	
Mato et al. [67]	Phase 1/2 study	LOXO-305 — 121	ORR 62.0% (CR 0.0%)	NA	NA	

allo-HCT — allogeneic hematopoietic cell transplantation; BTKi — Bruton’s tyrosine kinase inhibitor; CAR-T — chimeric antigen receptor t-cell; CR — complete remission; NA — not reached; ORR — overall response rate; PFS — progression-free survival; PI3Ki — phosphoinositide

3-kinase inhibitor; PR — partial remission

