10.2 Required investigations

10.2.1 Required investigations at entry, during treatment and during follow up for phase I and II part

	Before registration[1]	During ramp-up (cycle 0) (every week)	During cycle 1 (every week)	At day 1 of cycle 2 to 6 and from cycle 7 to 26 at end of each cycle (day 22-29)	At end of cycle 9 (day 22-29)[2]	At end of cycle 15 (day 22-29)[2]	12 weeks after day 28 of cycle 26 (± 1 week)[2]	During follow up[3]	Progressive disease[2]
Informed consent, including biobank	X								
Medical history	X								X
Adverse events		X	X	X	X	X	X	X	X
Physical examination	X		X	X	X	X	X	X	X
Concomitant medications	X	X	X	X	X	X	X	X	X
CIRS and CCI	X								
Binet classification	X								
TLS risk category (appendix H)[4]	X	X[5]	X[6]						
Lab tests									
Hematology	X	X	X[6]	X	X	X	X	X	X
Blood chemistry	X	X	X	X	X	X	X	X	
Immunochemistry	X		X	X	X	X	X	X	X
Additional chemistry	X								
TLS lab (appendix H)	X	X	X[6]						
Serology	X[7]								
Pregnancy test (WOCBP)	X	**Only at day 1**	**Only at day 1**	X			X		
BM									
BM biopsy					X		X		X[8]
ECG	X								
High resolution contrast enhanced CT[12]	X				X	X	X		X
Response evaluation					X	X[11]	X		X
Quality of Life	X		X[9]		X		X	X[10]	

1) Within 42 days before registration. QoL should be completed after registration.

2) For BM and CT scan ± 7 days is allowed.

3) Every 3 months (± 14 days) during year 1, every 6 months (± 1 month) thereafter during years 2, 3 and 4 until 6 years after registration. After progression annually until 6 years after registration.

4) Always re-assess TLS risk after venetoclax dose interruption > 1 week during ramp-up or > 2 weeks at any time (**appendix H**).

5) To avoid hospital admission, patients can be restaged into a lower TLS risk category, on discretion of the physician, according to their absolute lymphocyte count or repetition of imaging (**appendix H**).

6 Weekly Hematology and TLS lab 1 hour before epcoritamab infusion.

7) Monthly HBV-DNA PCR for patients with positive anti-HBc and monthly HCV-DNA PCR for patients with positive HCV Ab until 12 months after last dose of study treatment.

8) Only in case necessary to define progression

9) Only at end of cycle 1

10) During follow up QoL annually until 6 years after registration or until progression, whichever comes first.

11) Response evaluation without BM biopsy, result of previous BM biopsy may be used to classify response if no signs of progressive disease.

12) German sites must refer to appendix N for instructions about CT scans

10.2.2 Collection for central lab and biobank.[1]

	After registration, before start of cycle 0 (C0D1)	At cycle 1 day 1	At cycle 1 day 8	At cycle 1 day 15 pre-dose and +6 hours (post-dose)	At cycle 1 day 16 and day 17[6]	At cycle 1 day 22	At cycle 2 day 1 and at cycle 3 day 1	At cycle 4 day 1	At cycle 6 day1	At end of cycle 9 (day 22-29)	At end of cycle 12, 15, 18, 21 and 24 (day 22-29)	12 weeks after day 28 of cycle 26 (± 1 week)	During follow up[2]	Progressive disease
For Phase I patients only (Central lab LabCorp)														
PK		X (pre-dose)	X (pre-dose)	X	X	X (pre-dose)	X (pre-dose)	X (pre-dose)	X (pre-dose)	X[7] (pre-dose)	X[7] (pre-dose)			
ADA		X (pre-dose)		X (only pre-dose)			X (pre-dose)	X (pre-dose)	X (pre-dose)	X[7] (pre-dose)	X[7] (pre-dose)	X[7] (pre-dose)		
For all patients in phase I and phase II (Central lab Amsterdam UMC, Netherlands)														
IGHV mutation status PB	X													
Flow cytometry baseline PB	X													
MRD:														
PB								X	X	X	X	X	X	X
BM aspirate										X		X		X[3]
FISH/SNP array/ NGS (TP53) PB	X													X (FISH)
Biobank and Side studies[5]														
PB (cells, serum, plasma, ctDNA)	X	X	X[4]	X (pre-dose)		X[4]	X	X	X	X	X	X	X	X
BM aspirate										X		X		X[3]

1) See lab manual for procedures of collection and shipment of samples.

2) Every 3 months (± 14 days) during year 1, every 6 months (± 1 month) thereafter during years 2, 3 and 4 until 6 years after registration or until progression, whichever comes first. After progression no central lab is required.

3) If BM aspirate is done please send for central lab MRD and side studies.

4) Serum only

5) Sides studies (see paragraph 10.7)

6) Day 17 only if feasible

7) PK/ADA samples should be done at indicated time points until cycle 6 for patients in arm A and until cycle 12 for patients in arm B (continuing epcoritamab until cycle 12). One ADA sample should be taken at 12 weeks after cycle 26 from patients in both arms.