Required investigations at entry, during treatment and during follow up for all patients

	Before registration1[1]	After each cycle (day 21-29)	After lead-in (cycle 3 day 21-29)	During venetoclax ramp-up (every week)	At end of cycle 5 (day 21-29)	At end of cycle 8 (day 21-29)	At end of cycle 11 (day 21-29)	At end of cycle 15 (day 21-29)[2]	Registration 2 (day 1 of intensification or observation)	At end of cycle 19 and 22 (day 21-29) or after 12 and 24 weeks of observation)	9 months after registration 2 [2]	During follow up[3]	Progressive disease in follow up
Informed consent (incl biobank)	x												
Medical history	x												x
Adverse events		x	x	x	x	x	x	x		x[4]	x	x	x
Physical examination	x	x	x		x	x	x	x		x	x	x	x
CIRS and CCI	x												
Binet classification	x												
TLS risk category (appendix G)	x		x[5]	x[5]									
Lab tests													
Hematology	x	x	x	x	x	x	x	x		x	x	x	x
Blood chemistry	x	x	x	x	x	x	x	x		x	x	x	
TLS lab (appendix G)				x									
Serology	x												
Pregnancy test	x												
BM													
BM biopsy								x[6]			x[6]		
ECG	x												
^{18}F-FDG PET-CT scan (and uploaded/send in for review)	x					x		x			x		
High resolution contrast enhanced CT[7]	x		(x)[5]			x		x			x		x
Response evaluation						x		x[8]			x		x
Quality of Life	x		x			x		x		x[9]	x		

1) Within 42 day before registration 1.
2) If patient teminates protocol early for whatever reason a complete response evaluation should be done. Patients who are withdrawn before end of cycle 15 should have response evaluation immediately according to timepoint end of cycle 15. Patients who are withdrawn after cycle 15 but before 9 months after registration 2, should have response evaluation immediately according to timepoint 9 months after registration 2, unless evaluation end of cycle 15 was performed within 28 days before.
3) After 9 months after registration 2: Every 3 months until 2 years after registration 2 and every 6 months thereafter until 4 years after registration 2 or until progression (whatever comes first). After progression once a year until 4 years after registration 2.
4) Please note that (serious)adverse events must also be reported during observation and until 30 days after observation
5) To avoid hospital admission, patients can be restaged into a lower TLS risk catergory, on discretion of the physician, according to their absolute lymphocyte count or repetition of imaging (**appendix G**)
6) Biopsy only for confirmation of CR(i), aspirate for central lab (MRD) always at indicated time points
7) Measurement of lymph nodes on CT scan according to Cheson
8) Response must be confirmed before continuation to intensification or observation ((pre)-registation 2 , see section 15)
9) Only at end of cycle 19 or at 12 weeks after registration 2 and PRO-CTCAE only

Collection for central lab.[1]

	After registration 1 (Before start treatment)	After each cycle (day 21-28)	After lead-in (cycle 3 day 21-29)	During venetoclax ramp-up (cycle 4, day 8)[2]	At end of cycle 5 (day 21-29)	At end of cycle 8 (day 21-29)	At end of cycle 11 (day 21-29)	At end of cycle 15 (day 21-29)	Registration 2 (day 1 of intensification or day 1 of observation)	At end of cycle 19 and 22 (day 21-29) or after 12 and 24 weeks of observation	9 months after registration	During follow up[3]	Progressive disease in follow up
IGHV mutation status PB	x												
Flow cytometry PB	x												x
MRD													
PB	x		x		x	x	x	x		x	x	x	x
BM aspirate								x			x		x[4]
FISH/CGH array/TP53 PB	x												x
Side studies[5]													
PB (cells, plasma, cfDNA)	x		x	x	x	x	x	x		x	x	x	x
BM aspirate								x			x		
LN biopsy[6]	x												
LN FNA[6]						x							

1) See lab manual for procedures of collection and shipment of samples
2) Before venetoclax 50 mg is given
3) After 9 months after registration 2: Every 3 months until 2 years after registration 2 and every 6 months thereafter until 4 years after registration 2 or until progression (whatever comes first).
4) BM aspirate at progression is optional. If BM aspirate is done please send in.
5) Side studies see section 10.8 and lab manual for procedures for collecting and handling samples
6) Any LN that is > 1.5 cm and easy accessible (either cervical, axillary or inguinal)