Schedule of Assessments (observation and treatment arms) Version 5.0 – 20 Feb 2023	**Pre-screening**[1]	**Screening**[2]	**C1D1**[4]	**C1D8**[3,4]	**C1D15**[3,4]	**C1D22**[3,4]	**C2D1**[4]	**C3D1**[4]	**12 weeks after C1D1** End of treatment	**24 weeks after C1D1**	**Every 3. months for two years**	**1 year after C1D1**	**2 years after C1D1**	**Progressive disease**
				Applies only for treatment arm (for management of TLS risk)										
Visit window			± 4 days	± 4 days	± 4 days	± 4 days	± 4 days	± 4 days	± 4 days	± 4 days	± 7 days	± 7 days	± 7 days	± 7 days
Informed consent	X	X												
CLL confirmation	X													
Medical history, vaccine usage, immunoglobulins	X[5]	X												
Adverse events			X	X	X	X	X	X	X	X	X	X	X	X
B-symptoms (NCI criteria)			X				X	X	X	X	X	X	X	X
Concomitant medication		X	X				X	X	X	X	X	X	X	X
New CLL treatment														X
Physical examination		X	X				X	X	X	X	X	X	X	X
CIRS/CCI		X												
ECOG Performance Status	X	X							X	X		X	X	
Binet stage	X	X												
TLS risk category		X												
Clinical Response Assessment (IWCLL 2018)							X	X	X	X	X	X	X	X
Quality of Life Questionnaire		X					X	X	X	X	X[6]	X	X	
Pregnancy test[7]		X	X[8]				X[9]	X[9]	X[9]					
HIV test		X												
Electrocardiogram (ECG)		X												
(PET)-CT scan		X								X				X
Lab tests (blood)														
Hematology*		X	X	X	X	X	X	X	X	X	X	X	X	X
Serum chemistry**		X	X	X	X	X	X	X	X	X	X	X	X	X
Additional chemistry***		X							X	X		X	X	X
Hep B and C testing		X												X
Central labs														
Biobank		X		X[3]	X[3]		X	X	X	X		X	X	X
TruCulture and DuraClone		X							X	X				X
IGHV, FISH, TP53 mutation	X[10]													X
Flow-MRD		X							X	X		X	X	X
Bone marrow														
Biopsy and aspirate local		X								X				X
Aspirate (biobank)		X								X				X[11]
Microbiome samples														
Feces, saliva, skin, buccal swabs[12] **(biobank)**		X							X	X				

***Hematology:** Complete blood count (CBC) with differential incl. hemoglobin, hematocrit, platelet count, absolute neutrophil count (ANC) and absolute lymphocyte count (ALC).

****Serum chemistry:** Alkaline phosphatase, alanine aminotransferase (ALT), bicarbonate, calcium (total or ionized), chloride, creatine, C-reactive protein (CRP), glucose, lactate dehydrogenase (LDH), magnesium, phosphate/phosphorus, potassium, sodium, total bilirubin, total protein and uric acid.

*****Additional chemistry:** IgA, IgG, IgM, albumin, beta 2 microglobulin (B2M, only at screening and week 24).

******TLS chemistry:** Creatinine, calcium, phosphate/phosphorus, uric acid, LDH, potassium, sodium.

[1] No laboratory testing except for standard of care based on the discretion of the local investigator and IGHV and FISH, this visit is for informed consent to assemble data for assessment by the CLL-TIM algorithm.
[2] Max 42 days from screening to randomization, however FISH and TP53 mutational results are accepted up to six months prior to randomization, max 14 days from randomization to cycle 1 day 1 (C1D1).
[3] Only for treatment arm.
[4] For patients in treatment arm: TLS chemistry**** the day before (24 h) before next dose increase of venetoclax, 6 h after ramping up dose of venetoclax and the day after. Minimum 7 days at each dose level.
[5] Medical history for pre-screening is including infections (requiring hospitalization) and blood cultures within the past 7 years and inflammation (from pathology report).
[6] Only every 6. months for two years.
[7] Only applies for women of childbearing potential.
[8] A negative pregnancy test is required for all women of childbearing potential within 7 days before start of study treatment.
[9] Only applies for the women of childbearing potential in the treatment arm.
[10] Only if not already analyzed. FISH and TP53 mutation is only a requirement for enrolled patients if not already analyzed. IGHV is a requirement for the pre-screening.
[11] Include biopsy from lymph node if available.
[12] Buccel swab only at screening.