

Chronic lymphocytic leukemia and associated chronic lung diseases

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Appendix: List of variables

Age During Diag

Sex

Binet Stage

IGHV Mutation Status

Deletion 11q22

Trisomy 12

Deletion 13q14

Deletion p53

IPI Score

Chronic Respiratory Disease

Smoking Status

History of IBD

History of Solid Organs Transplant

History of Ulcerative Colitis

History of Kidney failure

History of Obesity

History of Ischemic heart disease

History of Overweight

History of HTN

History of DM

CLL Treatment

Albumin

Alkaline Phosphatase

ALT GPT

AST GOT

Basophils #

Basophils %

Beta.2 Microglobulin

C R P

Calcium

Cholesterol

CK

Coombs Direct

Creatinine

eGFR

Eosinophils #

Eosinophils %

Erythrocytes

Iron

Ferritin

FLC Ratio

GGT

Glucose

Haptoglobin

HbA1C

HDL.Cholesterol

Hemoglobin

Immunoglobulin A

Immunoglobulin G

Immunoglobulin M
K. Potassium
Kappa FLC
Lambda FLC
LDH.Lactic Dehydrogese
LDL.Cholesterol
Lymphocytes #
Lymphocytes %
Monoclonal Band quant
Monocytes #
Monocytes %
Sodium
Neutrophils #
Neutrophils %
Non.HDL Cholesterol
Phosphore
Platelets
Protein Total B
Triglycerides
Urea
WBC Leucocytes

IVIG
Covid Vac.
Influenza Vac.
PNEUVAX Vac.
PREVENAR Vac.

Pneumonia Last Year
Other Acute Resp. Disease Last Year
Pulmonologist Consultation Last Year
Hospitalization Total Days Last Year

AMINOGLYCOSIDE Last Year
ANTIBIOTICS Last Year
ANTIVIRALS UNSPECIFIED Last Year
CEPHALOSPORINES Last Year
MACROLIDES Last Year
OTHER ANTIBIOTICS Last Year
OTHER_BETA_LACTAMLastYear
PENICILLIN Last Year
QUINOLONES Last Year
SYSTEMIC ANTIFUNGAL Last Year
TETRACYCLINES Last Year
TRIMETHO.SULPHA Last Year

Supplement table 1: Characteristics of the patients at index date. Patients were assigned to the group according to their leading respiratory diagnosis. Patients diagnosed during the follow-up period were also included in their corresponding respiratory diagnosis group.

Variable	Asthma (N=446)	BRONCHIECTASIS (N=184)	COPD (N=242)	None (N=2791)	p value
IGHV					0.305
- M	3 (0.7%)	0 (0.0%)	0 (0.0%)	21 (0.8%)	
- U	4 (0.9%)	2 (1.1%)	0 (0.0%)	17 (0.6%)	
- Unknown	439 (98.4%)	182 (98.9%)	242 (100.0%)	2753 (98.6%)	
Deletion_11q22					0.024
- No	12 (2.7%)	4 (2.2%)	3 (1.2%)	85 (3.0%)	
- Unknown	433 (97.1%)	174 (94.6%)	233 (96.3%)	2674 (95.8%)	
- Yes	1 (0.2%)	6 (3.3%)	6 (2.5%)	32 (1.1%)	
Trisomy_12					0.909
- No	9 (2.0%)	7 (3.8%)	6 (2.5%)	82 (2.9%)	
- Unknown	433 (97.1%)	174 (94.6%)	233 (96.3%)	2674 (95.8%)	
- Yes	4 (0.9%)	3 (1.6%)	3 (1.2%)	35 (1.3%)	
Deletion_13q14					0.055
- No	10 (2.2%)	2 (1.1%)	4 (1.7%)	58 (2.1%)	
- Unknown	433 (97.1%)	174 (94.6%)	233 (96.3%)	2674 (95.8%)	
- Yes	3 (0.7%)	8 (4.3%)	5 (2.1%)	59 (2.1%)	
Deletion_p53					0.726
- No	11 (2.5%)	7 (3.8%)	6 (2.5%)	95 (3.4%)	
- Unknown	433 (97.1%)	174 (94.6%)	233 (96.3%)	2674 (95.8%)	
- Yes	2 (0.4%)	3 (1.6%)	3 (1.2%)	22 (0.8%)	
Baseline Blood Work					
WBC Leucocytes Very High (>50K)	8 (1.8%)	8 (4.3%)	14 (5.8%)	147 (5.3%)	0.017
Hemoglobin <LNL	196 (43.9%)	79 (42.9%)	73 (30.2%)	1232 (44.1%)	0.005
Lymphocytes # >UNL	323 (72.4%)	119 (64.7%)	173 (71.5%)	2021 (72.4%)	0.285
Monocytes #>UNL	48 (10.8%)	22 (12.0%)	46 (19.0%)	341 (12.2%)	< 0.001
Monocytes %>UNL	11 (2.5%)	5 (2.7%)	5 (2.1%)	66 (2.4%)	0.081
Neutrophils #					0.088
- High	14 (3.1%)	5 (2.7%)	17 (7.0%)	102 (3.7%)	
- Low	40 (9.0%)	24 (13.0%)	21 (8.7%)	289 (10.4%)	
Neutrophils %					0.823
- High	4 (0.9%)	3 (1.6%)	1 (0.4%)	16 (0.6%)	
- Low	293 (65.7%)	120 (65.2%)	168 (69.4%)	1941 (69.5%)	
Platelets <LNL	62 (13.9%)	38 (20.7%)	39 (16.1%)	449 (16.1%)	0.058
Protein Total <LNL	11 (2.5%)	7 (3.8%)	5 (2.1%)	59 (2.1%)	< 0.001
FLC Ratio					< 0.001
- High	32 (7.2%)	13 (7.1%)	13 (5.4%)	155 (5.6%)	

- Low	3 (0.7%)	3 (1.6%)	3 (1.2%)	10 (0.4%)	
GGT					< 0.001
- High	18 (4.0%)	8 (4.3%)	17 (7.0%)	152 (5.4%)	
Glucose					< 0.001
- High	233 (52.2%)	101 (54.9%)	153 (63.2%)	1378 (49.4%)	
- Low	2 (0.4%)	4 (2.2%)	0 (0.0%)	14 (0.5%)	
Haptoglobin					0.321
- High	9 (2.0%)	3 (1.6%)	3 (1.2%)	34 (1.2%)	
- Low	2 (0.4%)	5 (2.7%)	4 (1.7%)	30 (1.1%)	
HbA1C					< 0.001
- High	225 (50.4%)	101 (54.9%)	124 (51.2%)	1197 (42.9%)	
HDL Cholesterol					< 0.001
- Low	124 (27.8%)	66 (35.9%)	91 (37.6%)	813 (29.1%)	
Non HDL Cholesterol>NUL	89 (20.0%)	35 (19.0%)	52 (21.5%)	580 (20.8%)	0.002
K Potassium					< 0.001
- High	18 (4.0%)	6 (3.3%)	19 (7.9%)	122 (4.4%)	
- Low	6 (1.3%)	6 (3.3%)	4 (1.7%)	40 (1.4%)	
Kappa FLC					< 0.001
- High	53 (11.9%)	22 (12.0%)	16 (6.6%)	212 (7.6%)	
- Low	2 (0.4%)	2 (1.1%)	2 (0.8%)	4 (0.1%)	
Lambda FLC					< 0.001
- High	15 (3.4%)	11 (6.0%)	6 (2.5%)	64 (2.3%)	
- Low	5 (1.1%)	1 (0.5%)	1 (0.4%)	11 (0.4%)	
LDH Lactic Dehydrogenase					< 0.001
- Low	9 (2.0%)	6 (3.3%)	6 (2.5%)	94 (3.4%)	
- High	363 (81.4%)	152 (82.6%)	194 (80.2%)	2051 (73.5%)	
LDL Cholesterol					0.118
Protein Total					< 0.001
- Low	127 (28.5%)	45 (24.5%)	51 (21.1%)	575 (20.6%)	
Triglycerides					0.01
- High	142 (31.8%)	63 (34.2%)	81 (33.5%)	850 (30.5%)	
Urea					0.017
- High	46 (10.3%)	27 (14.7%)	32 (13.2%)	325 (11.6%)	
- Low	8 (1.8%)	3 (1.6%)	3 (1.2%)	43 (1.5%)	

Supplement table 2: Association of Confounding Variables with pneumonia, hospitalization, time to first treatment and overall survival. All variables other than sociodemographic variables were defined as time-dependent covariates. The table includes only variables that met the criteria for the proportional-hazards assumption on the basis of the results of Schoenfeld's global test. CLL treatment variables were excluded for time to first treatment event, as they are not relevant during the watch and wait period. CLL treatment was also excluded for overall survival, because their temporal nature for these events can be misleading (As patients get older they are increasingly likely to be treated for CLL. Thus, the administration of a certain CLL drug might just be a marker of already having survived longer.). A p-value lower than 5% are considered to be statistically significant. *Anti-CD 20 was considered still influential during 12 months following the last dose.

Variable	Pneumonia		Hospitalization due to pneumonia		Time To First Treatment		Overall Survival	
	Hazard	p-value	Hazard	p-value	Hazard	p-value	Hazard	p-value
Age>65	1.18 (0.99-1.4)	0.071	1.47 (1.15-1.89)	0.002**	0.71 (0.59-0.84)	<0.001***	1.95 (1.58-2.4)	<0.0001***
Sex is Male	1.33 (1.12-1.59)	0.001**	1.52 (1.2-1.91)	<0.0001**	0.86 (1.57-2.2)	0.126	1.68 (1.41-2)	<0.0001***
Binet Stage C	1.7 (1.42-2.02)	<0.0001***	2.18 (1.68-2.82)	<0.0001**	5.48 (4.46-6.74)	<0.0001***	3.57 (2.81-4.54)	<0.0001***
Medical History								
Asthma	1.29 (1.07-1.55)	0.008**	1.17 (0.9-1.51)	0.235	0.88 (0.72-1.08)	0.229	1 (0.8-1.25)	0.985
BRONCHIECTASIS	1.7 (1.35-2.15)	<0.0001***	2.13 (1.81-2.57)	0.008*	0.98 (0.76-1.28)	0.902	1.08 (0.81-1.42)	0.604
COPD	1.38 (1.09-1.76)	0.008**	1.41 (1.03-1.92)	0.03*	1.1 (0.86-1.41)	0.46	0.96 (0.74-1.25)	0.786
Socio-Economic Level	0.97 (0.94-1)	0.053	0.96 (0.92-1)	0.049*	0.99 (0.96-1.03)	0.67	0.97 (0.94-1.01)	0.101
Never smoked	1.08 (0.57-2.06)	0.807	0.86 (0.41-1.8)	0.688	0.61 (0.37-1.02)	0.058	0.53 (0.35-0.82)	0.004*
Quit smoking	1.21 (0.62-2.36)	0.58	1 (0.46-2.19)	0.992	0.65 (0.37-1.13)	0.123	1.59 (1.37-1.96)	0.032*
Currently smoking	1.34 (0.69-2.6)	0.382	1.14 (0.53-2.44)	0.735	0.64 (0.37-1.11)	0.114	1.57 (1.35-1.93)	0.024*

IBD	0.82 (0.1-6.89)	0.857	1.7 (0.25-11.57)	0.585	2.04 (0.42-9.78)	0.375	6.55 (0.93-46.26)	0.06.
Ulcerative Colitis	0.98 (0.38-2.53)	0.963	1.45 (0.41-5.2)	0.565	0.97 (0.36-2.63)	0.946	1.17 (0.42-3.31)	0.763
Kidney failure	1.23 (1.04-1.45)	0.014*	1.55 (1.25-1.93)	<0.001***	1.05 (0.88-1.24)	0.606	1.61 (1.33-1.95)	<0.0001***
Obesity	0.92 (0.73-1.16)	0.484	0.95 (0.7-1.28)	0.724	0.99 (0.78-1.26)	0.956	2.46 (2.03-2.99)	<0.0001***
Ischemic heart disease	1.12 (0.91-1.37)	0.291	1.25 (0.97-1.61)	0.08.	1.17 (0.95-1.44)	0.152	1.4 (1.16-1.68)	<0.0001***
Overweight	0.97 (0.78-1.19)	0.742	0.72 (0.53-0.98)	0.034*	1.02 (0.83-1.26)	0.841	0.97 (0.26-2.88)	0.313
HTN	0.95 (0.8-1.12)	0.534	1.06 (0.85-1.33)	0.594	0.84 (0.71-1.02)	0.061	1.35 (1.11-1.64)	0.003*
DM	0.93 (0.78-1.12)	0.463	0.9 (0.72-1.14)	0.383	0.96 (0.8-1.15)	0.686	1.2 (1.01-1.43)	0.042*
Treatment for CLL								
Anti CD20*	1.46 (1.13-1.9)	0.004531**	1.4 (1.01-1.94)	0.044369*	NA	NA	NA	NA
ACALABRUTINIB	1.78 (0.74-4.33)	0.2	2.91 (1.49-5.69)	0.001783**	NA	NA	NA	NA
BENDAMUSTINE +Anti CD20	1.23 (1.06-0.95)	0.042*	2.09 (0.84-5.2)	0.11	NA	NA	NA	NA
CHLORAMBUCIL +Anti CD20	1.38 (0.71-2.68)	0.338	1.73 (0.77-3.86)	0.182	NA	NA	NA	NA
FC	0.3 (0.04-2.12)	0.23	0.49 (0.06-4.18)	0.512	NA	NA	NA	NA
FCR	2.51 (1.7-3.71)	<0.0001***	1.96 (1.27-3.42)	0.017*	NA	NA	NA	NA
IBRUTINIB	1.29 (0.83-2)	0.255	1.18 (0.74-1.83)	0.489	NA	NA	NA	NA

VENETOC LAX + Anti-CD20	1.25 (0.43- 2.96)	0.81	1.84 (0.86- 3.99)	0.12	NA	NA	NA	NA
Recent history of Pneumonia, vaccination and treatment								
Pneumonia Last Year	1.25 (1.13- 1.49)	<0.00 01 ***	1.66 (1.48-1.9)	0.00 9**	1.12 (0.96- 1.3)	0.157	1.63 (1.45- 1.82)	<0.000 1***
Other Acute Resp. Diseases Last Year	1.13 (0.91- 1.41)	0.273	0.86 (0.62- 1.19)	0.35 5	1.25 (1.02- 1.53)	0.033*	1.09 (0.87- 1.36)	0.476
IVIG	0.74 (0.43- 1.29)	0.289	0.69 (0.46- 0.92)	0.02 6*	1.11 (0.69- 1.77)	0.666	0.01 (0- 0.07)	<0.000 1***
Covid- Vaccine Coverage	0.88 (0.69- 1.12)	0.303	0.53 (0.18-2)	0.2	1.24 (0.97- 1.53)	0.069	0.87 (0.5- 1.34)	0.624
Influenza Vaccine Coverage	0.99 (0.84- 1.16)	0.889	0.85 (0.69- 1.05)	0.13 9	1.1 (0.94- 1.3)	0.24	0.62 (0.53- 0.73)	<0.000 1***
Pneumovax Coverage	0.84 (0.61- 1.15)	0.273	0.75 (0.47- 1.18)	0.21 4	1.29 (0.51- 1.65)	0.47	0.7 (0.46- 1.09)	0.116
Prevnar Coverage	0.87 (0.54- 1.4)	0.564	0.87 (0.17- 0.98)	0.00 9**	1.68 (0.23- 2.3)	0.102	0.62 (0.32- 1.19)	0.15
Pulmonolog ist Consultatio n Last Year	1.06 (0.94- 1.18)	0.337	1.06 (0.92- 1.22)	0.41 8	1.09 (0.98- 1.21)	0.097.	0.94 (0.84- 1.04)	0.24
Days in Hospital Last Year	1 (1-1)	0.471	1 (1-1)	0.72 8	1 (1- 1.01)	0.091.	1.01 (1.01- 1.01)	<0.000 1***
AMINOGL YCOSIDE	0.49 (0.14- 1.71)	0.26	0.99 (0.55- 1.76)	0.96 2	0.55 (0.1- 2.9)	0.48	0.59 (0.25- 1.37)	0.218
ANTIVIRA LS UNSPECIF IED	1.08 (1.01- 1.16)	0.024 *	1.06 (0.97- 1.16)	0.18 5	0.97 (0.9- 1.05)	0.399	1.03 (0.95- 1.12)	0.437
CEPHALO SPORINES	1.07 (0.94- 1.21)	0.315	1.11 (0.96- 1.28)	0.15 7	1.08 (0.97- 1.2)	0.154	1.1 (0.98- 1.23)	0.092.
MACROLI DES	0.95 (0.86- 1.06)	0.386	1.09 (0.95- 1.26)	0.23 6	1.15 (1.04- 1.27)	0.006* *	1.06 (0.98- 1.14)	0.179
OTHER ANTIBIOT ICS	1.07 (0.94- 1.21)	0.332	0.99 (0.84- 1.17)9	0.88 1	1.04 (0.91- 1.2)	0.551	1.14 (1.01- 1.29)	0.035*

BETA LACTAM	2.23 (0.73-6.78)	0.158	2.52 (0.65-9.83)	0.182	1.07 (0.82-1.52)	0.413	2.97 (1.37-6.41)	0.006* *
PENICILLIN	1.13 (1.05-1.22)	0.001**	1.2 (1.09-1.31)	<0.0001**	1.12 (1.04-1.2)	0.004* *	1.01 (0.92-1.12)	0.789
QUINOLO NES	1.08 (0.96-1.21)	0.215	1.02 (0.87-1.18)	0.837	0.96 (0.85-1.08)	0.464	1.18 (1.09-1.29)	<0.0001***
SYSTEMIC ANTIFUNGAL	0.92 (0.76-1.11)	0.383	0.86 (0.61-1.2)	0.372	0.95 (0.75-1.2)	0.678	1.03 (0.93-1.14)	0.585
TETRACYCLINES	1.05 (0.87-1.25)	0.629	1.08 (0.89-1.32)	0.427	0.85 (0.64-1.14)	0.277	1.01 (0.75-1.36)	0.942
TRIMETHO-SULPHA	1.05 (0.96-1.15)	0.31	1 (0.9-1.11)	0.996	0.98 (0.88-1.08)	0.638	1.23 (1.13-1.34)	<0.0001***
Blood test								
Albumin__B_High	0.02 (0.01-0.04)	<0.0001***	0.1 (0.04-0.24)	<0.0001**	0 (0-0)	<0.0001***	1.26 (0.57-2.8)	0.573
Albumin__B_Low	1.34 (0.94-1.92)	0.106	1.48 (0.97-2.26)	0.067	1.41 (0.92-2.15)	0.114	2.64 (2.11-3.3)	<0.0001***
ALKP.Alkaline_PhosphataseHigh	1.1 (0.87-1.39)	0.411	1.16 (0.87-1.54)	0.327	1.38 (1.08-1.77)	0.011* *	1.21 (0.99-1.47)	0.069.
ALKP.Alkaline_PhosphataseLow	1.36 (0.54-3.47)	0.514	1.82 (0.55-6.05)	0.329	2.84 (1.04-7.74)	0.041* *	1.02 (0.47-2.2)	0.962
ALT__GPT_High	1.03 (0.74-1.44)	0.847	0.87 (0.53-1.44)	0.587	0.69 (0.46-1.01)	0.058.	0.97 (0.72-1.3)	0.833
AST__GOT_High	0.96 (0.64-1.44)	0.848	1.1 (0.64-1.88)	0.741	1.38 (0.96-1.98)	0.086.	1.53 (1.12-2.09)	0.008* *
AST__GOT_Low	1.06 (0.56-2.03)	0.856	0.63 (0.26-1.51)	0.302	0.49 (0.21-1.18)	0.113	0.98 (0.66-1.45)	0.913
Basophils_numHigh	0.01 (0.01-0.02)	<0.0001***	0.03 (0.01-0.05)	<0.0001**	1.24 (0.35-4.35)	0.739	0.69 (0.22-2.18)	0.522
Beta.2_Microglobulin__B_High	0.94 (0.71-1.24)	0.657	1.22 (0.85-1.74)	0.278	1.07 (0.77-1.49)	0.675	1.23 (0.9-1.68)	0.189
Beta.2_Microglobulin__B_Low	0.04 (0.01-0.09)	<0.0001***	0.1 (0.03-0.28)	<0.0001**	0 (0-0)	<0.0001	0.56 (0.28-1.12)	0.103

Beta.2_Mic roglobulin_ _B_Very High	1.14 (0.86- 1.51)	0.354	1.08 (0.75- 1.54)	0.68 8	0.96 (0.69- 1.33)	0.796	1.17 (0.87- 1.58)	0.295
C_R_PHigh	1.18 (0.91- 1.54)	0.214	0.96 (0.67- 1.38)	0.83 5	0.98 (0.69- 1.41)	0.932	1.11 (0.84- 1.47)	0.456
C_R_PVery High	1.12 (0.87- 1.45)	0.367	1.11 (0.82- 1.51)	0.49 3	1.31 (0.99- 1.72)	0.056.	1.42 (1.14- 1.78)	0.002* *
Ca.Calcium __B_High	1.31 (0.66- 2.62)	0.44	1.05 (0.37- 2.98)	0.92 2	2.1 (0.89- 4.95)	0.089.	1.83 (0.99- 3.38)	0.053.
Ca.Calcium __B_Low	0.96 (0.76- 1.21)	0.706	1.04 (0.78- 1.38)	0.80 5	0.82 (0.63- 1.07)	0.142	1.15 (0.95- 1.38)	0.149
Cholesterol High	0.91 (0.58- 1.43)	0.672	0.54 (0.33- 0.89)	0.01 6*	0.79 (0.46- 1.37)	0.407	0.83 (0.55- 1.25)	0.38
CKHigh	1.2 (0.86- 1.68)	0.274	1.17 (0.72- 1.91)	0.52 4	1.01 (0.63- 1.63)	0.958	0.83 (0.56- 1.23)	0.353
Creatinine_ _B_High	1.04 (0.79- 1.36)	0.791	0.93 (0.67- 1.29)	0.64 3	1.19 (0.86- 1.65)	0.299	1.18 (0.94- 1.47)	0.152
Creatinine_ _B_Low	0.83 (0.66- 1.05)	0.129	1.07 (0.78- 1.46)	0.67 3	0.73 (0.57- 0.95)	0.02*	1.2 (0.96- 1.51)	0.11
eGFRLow	1.12 (0.85- 1.47)	0.417	1.1 (0.8- 1.51)	0.55 6	0.97 (0.7- 1.33)	0.829	0.82 (0.64- 1.03)	0.091.
eGFRVery Low	1.3 (1.06- 1.59)	0.013 *	0.79 (0.6- 1.04)	0.09 6.	0.91 (0.71- 1.17)	0.479	0.87 (0.71- 1.06)	0.174
Eosinophils _numHigh	1.41 (0.98- 2.03)	0.066 .	1.6 (0.97- 2.64)	0.06 4.	0.82 (0.5- 1.36)	0.449	1 (0.64- 1.56)	0.984
Fe._IronHi gh	0.84 (0.42- 1.69)	0.632	1.32 (0.62- 2.81)	0.47 6	1.49 (0.77- 2.91)	0.239	1.49 (0.84- 2.65)	0.172
Fe._IronL ow	0.89 (0.74- 1.07)	0.214	1.2 (0.95- 1.52)	0.13 1	0.99 (0.79- 1.23)	0.912	1.1 (0.92- 1.3)	0.302
FerritinHig h	1.03 (0.74- 1.43)	0.881	1.17 (0.82- 1.66)	0.39 6	1 (0.7- 1.43)	0.998	1.42 (1.14- 1.76)	0.002* *
FerritinLow	1.02 (0.48- 2.16)	0.961	0.47 (0.12- 1.83)	0.27 9	0.4 (0.13- 1.2)	0.101	1.01 (0.49- 2.1)	0.979

GGTHigh	1.05 (0.79-1.39)	0.74	1.03 (0.72-1.49)	0.859	1.01 (0.7-1.46)	0.961	1.06 (0.84-1.34)	0.62
Glucose__B_High	1.1 (0.94-1.29)	0.244	1.06 (0.85-1.32)	0.612	1.1 (0.91-1.34)	0.333	1.08 (0.92-1.27)	0.367
Glucose__B_Low	0.42 (0.11-1.67)	0.219	0.72 (0.18-2.87)	0.636	0.36 (0.14-0.94)	0.038*	1.09 (0.65-1.81)	0.751
Haptoglobi nHigh	1.03 (0.58-1.84)	0.913	0.88 (0.44-1.76)	0.72	0.85 (0.45-1.63)	0.625	0.94 (0.58-1.54)	0.811
Haptoglobi nLow	1.34 (0.86-2.09)	0.201	1.45 (0.84-2.48)	0.181	1.1 (0.63-1.92)	0.734	1.45 (0.93-2.25)	0.104
HbA1CHig h	1.06 (0.87-1.29)	0.57	0.96 (0.75-1.23)	0.721	1.17 (0.92-1.48)	0.201	0.89 (0.74-1.06)	0.195
HbA1CLow	2.39 (1.11-5.18)	0.027*	2.31 (0.95-5.66)	0.066.	1.14 (0.43-3.07)	0.791	1.28 (0.55-3)	0.566
HbA1CVer y High	0.98 (0.41-2.34)	0.961	0.93 (0.35-2.48)	0.886	1.05 (0.39-2.79)	0.926	1.09 (0.53-2.25)	0.814
HbA1CVer y Low	1.39 (0.28-6.84)	0.686	1.39 (0.19-10.16)	0.745	0 (0-0)	<0.0001***	0.3 (0.11-0.85)	0.023*
HDL.Chole sterolLow	1.17 (1-1.38)	0.054.	1.16 (0.93-1.45)	0.176	1.32 (1.07-1.61)	0.008* *	1.17 (0.99-1.38)	0.066.
Hemoglobi nLow	0.86 (0.67-1.12)	0.266	0.84 (0.59-1.21)	0.357	0.85 (0.63-1.14)	0.28	1.27 (1.09-1.47)	0.002* *
Hemoglobi n High	0.02 (0.01-0.04)	<0.0001***	0.08 (0.05-0.15)	<0.0001**	0 (0-0)	<0.0001***	1.12 (0.73-1.72)	0.592
Hemoglobi nVery Low	0.93 (0.65-1.35)	0.713	1.01 (0.64-1.61)	0.958	1.16 (0.8-1.69)	0.434	2.82 (2.25-3.55)	<0.0001***
Immunoglo bulin_AHig h	0.95 (0.59-1.53)	0.828	1.05 (0.59-1.88)	0.857	0.66 (0.32-1.37)	0.262	1.27 (0.81-1.98)	0.292
Immunoglo bulin_ALo w	1.05 (0.78-1.4)	0.767	1.05 (0.75-1.47)	0.79	1.02 (0.73-1.42)	0.917	0.92 (0.69-1.23)	0.566
Immunoglo bulin_GLo w	1.01 (0.81-1.25)	0.947	1.12 (0.85-1.47)	0.423	1.2 (0.94-1.54)	0.14	1.14 (0.92-1.41)	0.233

Immunoglobulin_GVery High	1.12 (0.7-1.8)	0.636	1 (0.54-1.82)	0.988	1.09 (0.63-1.9)	0.758	1.19 (0.76-1.86)	0.443
Immunoglobulin_GVery Low	1.18 (0.76-1.82)	0.47	1.11 (0.69-1.79)	0.662	1.53 (0.91-2.57)	0.106	0.95 (0.63-1.42)	0.787
Immunoglobulin_MHigh	1.18 (0.73-1.89)	0.5	1.26 (0.68-2.32)	0.458	1.27 (0.77-2.1)	0.347	0.92 (0.56-1.51)	0.733
Immunoglobulin_MLow	1.12 (0.92-1.36)	0.246	1.13 (0.88-1.46)	0.343	0.81 (0.64-1.03)	0.082.	1.04 (0.86-1.26)	0.702
K_Potassium_B_High	0.72 (0.51-1.03)	0.075	0.57 (0.36-0.92)	0.022*	1.05 (0.7-1.56)	0.829	1.01 (0.74-1.37)	0.971
K_Potassium_B_Low	0.73 (0.43-1.26)	0.258	0.78 (0.41-1.48)	0.441	1.35 (0.77-2.36)	0.291	1.23 (0.9-1.67)	0.191
Kappa_FLC__B_High	0.98 (0.62-1.56)	0.935	0.65 (0.4-1.07)	0.093.	1.96 (1.1-3.48)	0.022*	1.31 (0.85-2)	0.221
Kappa_FLC__B_Low	0.65 (0.11-3.82)	0.63	0.72 (0.08-6.83)	0.777	2.59 (0.66-10.11)	0.172	0.26 (0.11-0.61)	0.002*
Lambda_FL_C__B_High	0.85 (0.48-1.52)	0.584	0.96 (0.51-1.8)	0.89	0.93 (0.53-1.61)	0.784	1.35 (0.88-2.06)	0.17
Lambda_FL_C__B_Low	0.77 (0.29-2.08)	0.611	0.19 (0.05-0.81)	0.024*	0.89 (0.35-2.29)	0.811	1.57 (0.62-3.97)	0.339
LDH.Lactic_DehydrogenaseHigh	1.65 (1.07-2.53)	0.023*	1.28 (0.78-2.1)	0.328	1.25 (0.78-2.03)	0.357	1.57 (1.1-2.24)	0.012*
LDH.Lactic_DehydrogenaseLow	1.3 (0.72-2.34)	0.388	1.27 (0.64-2.52)	0.489	1.33 (0.63-2.81)	0.454	1.69 (1.08-2.62)	0.02*
LDL.CholesterolHigh	1.37 (0.6-1.99)	0.45	1.07 (0.74-1.55)	0.714	1.06 (0.78-1.45)	0.697	0.99 (0.76-1.29)	0.934
LDL.CholesterolVery High	0.93 (0.58-1.49)	0.761	1.48 (0.82-2.68)	0.194	1.21 (0.7-2.11)	0.493	0.94 (0.57-1.55)	0.819
Lymphocytes_num_Very High	0.66 (0.43-1.01)	0.055	0.75 (0.43-1.32)	0.321	0.53 (0.35-0.8)	0.003*	0.8 (0.52-1.23)	0.3
Lymphocytes_numLow	0.83 (0.64-1.06)	0.129	1.05 (0.73-1.5)	0.792	0.76 (0.54-1.07)	0.117	0.97 (0.73-1.28)	0.808

Monocytes_numHigh	1.08 (0.87-1.34)	0.49	1.09 (0.83-1.44)	0.527	1.65 (1.31-2.07)	0***	1.2 (0.95-1.5)	0.119
Na._Sodium__B_Low	0.9 (0.37-2.16)	0.808	0.91 (0.27-3.08)	0.882	0.42 (0.16-1.13)	0.086.	0.91 (0.52-1.57)	0.724
Neutrophils_numHigh	0.84 (0.11-6.52)	0.866	1.26 (0.07-24.39)	0.879	3.05 (0.24-38.07)	0.386	7.82 (0.99-61.58)	0.051.
Neutrophils_numLow	117.6 (34.48-401.1)	0 ***	64.34 (13.4-308.9)	0***	8520 (1805 - 40210)	<0.0001***	1.54 (0.32-7.42)	0.588
Non.HDL_Cholesterol_High	1.06 (0.79-1.44)	0.685	0.92 (0.59-1.42)	0.703	0.86 (0.59-1.23)	0.403	0.92 (0.68-1.26)	0.618
Non.HDL_Cholesterol_Very High	0.99 (0.61-1.62)	0.972	1.05 (0.54-2.03)	0.883	0.98 (0.52-1.88)	0.96	1.02 (0.63-1.64)	0.945
Phosphore__B__PO4_High	1.2 (0.3-4.88)	0.796	1.13 (0.42-3.02)	0.804	1.85 (0.36-9.51)	0.463	1.85 (0.92-3.72)	0.086.
Phosphore__B__PO4_Low	0.89 (0.4-1.95)	0.765	1.54 (0.71-3.3)	0.272	1 (0.4-2.53)	0.996	0.95 (0.59-1.54)	0.84
PlateletsHigh	0.96 (0.38-2.42)	0.923	1.48 (0.48-4.52)	0.496	0.75 (0.22-2.57)	0.653	1.14 (0.6-2.17)	0.682
PlateletsLow	1.1 (0.92-1.32)	0.284	1.3 (1.04-1.64)	0.024*	1.06 (0.87-1.3)	0.545	1.06 (0.87-1.27)	0.572
PlateletsVery Low	1.07 (0.84-1.38)	0.573	1.4 (1.05-1.86)	0.024*	0.79 (0.6-1.04)	0.091.	1.67 (1.36-2.05)	0***
Protein_Total__B_High	2.2 (1.24-3.89)	0.007**	2.51 (1.13-5.58)	0.023*	1.37 (0.66-2.86)	0.396	0.78 (0.36-1.67)	0.52
Protein_Total__B_Low	1.22 (1.03-1.44)	0.021*	1.34 (1.07-1.68)	0.01*	0.97 (0.79-1.19)	0.744	1.6 (1.36-1.88)	0***
TriglyceridesHigh	0.94 (0.79-1.11)	0.436	1.21 (0.98-1.49)	0.078.	0.91 (0.74-1.13)	0.398	1.23 (1.04-1.46)	0.016*
Urea__B_High	1.17 (0.94-1.44)	0.154	1.14 (0.89-1.46)	0.297	0.95 (0.74-1.23)	0.708	1.51 (1.26-1.81)	0***

Urea__B_Low	1.21 (0.65-2.25)	0.54	0.58 (0.19-1.77)	0.343	0.89 (0.47-1.68)	0.723	0.85 (0.46-1.57)	0.605
WBC.LeucocytesHigh	0.98 (0.82-1.17)	0.835	1 (0.78-1.28)	0.996	1.04 (0.81-1.34)	0.749	1.04 (0.87-1.25)	0.65
WBC.LeucocytesLow	1.03 (0.73-1.43)	0.887	0.95 (0.61-1.46)	0.805	0.92 (0.63-1.35)	0.67	0.91 (0.68-1.23)	0.557
WBC.LeucocytesVery High	1.37 (1.04-1.82)	0.027*	1.79 (1.26-2.54)	0.001**	3.6 (2.75-4.72)	<0.0001***	1.49 (1.14-1.93)	0.003*

Supplement table 3: Exposure to treatment for CLL and hospitalization due to pneumonia

TREATMENT NAME	# PATIENTS	MONTHS OF EXPOSURE	# EVENTS OF HOSPITALIZATION DUE TO PNEUMONIA
ACALABRUTINIB	130	1319	21
BENDAMUSTINE+RITUXIMAB	195	1146	10
CHLORAMBUCIL+ANTI-CD20	26	242	1
FCR	601	3724	27
IBRUTINIB	323	9984	66
VENETOCLAX+ANTI-CD20	151	1747	22