Rethinking the feasibility and safety of venetoclax-obinutuzumab in chronic lymphocytic leukemia: non-traditional factors may play a role in clinical practice

Anna Maria Frustaci,[1*] Andrea Galitzia,[1,2*] Mariano Lucignano,[3] Lorena Appio,[4] Jacopo Olivieri,[5] Alessandro Sanna,[6] Claudia Baratè,[7] Fabrizio Pane,[8] Luana Schiattone,[9] Beatrice Casadei,[10] Isacco Ferrarini,[11] Amalia Figuera,[12] Paolo Sportoletti,[13] Giacomo Loseto,[14] Caterina Stelitano,[15] Andrea Visentin,[16] Melania Celli,[17] Francesca Romana Mauro,[18] Massimiliano Palombi,[19] Marta Coscia,[20] Vanessa Innao,[21] Riccardo Moia,[22] Marina Motta,[23] Filomena Russo,[24] Monica Tani,[25] Annalisa Arcari,[26] Elia Boccellato,[27] Chiara Borella,[28] Enrico Capochiani,[29] Angela Ferrari,[30] Massimo Gentile,[31,32] Roberta Giachetti,[33] Annamaria Giordano,[34] Martina Bullo,[35] Enrico Lista,[36] Luigi Malandruccolo,[37] Maurizio Musso,[38] Marzia Varettoni,[39] Federico Vozella,[40] Francesca Cibien,[41] Michele Merli,[42] Laura Nocilli,[43] Maria Cristina Pasquini,[44] Azzurra Anna Romeo,[45] Valentina Rossi,[46] Gloria Turri,[47] Anna Vanazzi,[48] Marina Cavaliere,[49] Alessandro Gozzetti,[50] Lara Crucitti,[51] Moira Lucesole,[52] Marina Deodato,[1] Annamaria Tomasso,[53] Arianna Zappaterra,[1,54] Roberta Murru,[55] Caterina Patti,[56] Luca Laurenti[53] and Alessandra Tedeschi[1]

[1]ASST Grande Ospedale Metropolitano Niguarda, Dipartimento di Ematologia, Niguarda Cancer Center, Milano; [2]Struttura Complessa di Ematologia, Ospedale San Francesco, ASL Nuoro, Nuoro; [3]Andrea Tortora Hospital ASL Salerno, Pagani; [4]ASST Valle Olona, Busto Arsizio; [5]Clinica Ematologica, Centro Trapianti e Terapie Cellulari "Carlo Melzi", Azienda Sanitaria Universitaria Integrata di Udine, Udine; [6]Hematology Unit, Department of Oncology, AOU Careggi, Florence; [7]Department of Oncology Section of Hematology University of Pisa, Pisa; [8]Hematology and Hematopoietic Stem Cell Transplant Center, Department of Medicine and Surgery, University of Naples Federico II, Naples; [9]Ematologia Clinica, Ospedale Civile S. Spirito Pescara, Pescara; [10]IRCSS Azienda Ospedaliero-Universitaria di Bologna, Bologna; [11]Department of Engineering for Innovation Medicine, Section of Innovation Biomedicine, Hematology Area, University of Verona, Verona; [12]Divisione di Ematologia, A.O.U. Policlinico G. Rodolico – S. Marco, Catania; [13]Department of Medicine and Surgery Institute of Hematology Centro di Ricerca Emato-Oncologica (CREO) University of Perugia, Perugia; [14]IRCCS Istituto Tumori "Giovanni Paolo II", Hematology and Cell Therapy Unit, Bari; [15]Department of Hematology Azienda Ospedaliera Bianchi Melacrinò Morelli, Reggio Calabria; [16]Hematology unit Department of Medicine University of Padova, Padova; [17]Hematology, Ospedale degli Infermi, Rimini; [18]Department of Translational and Precision Medicine Hematology Unit 'Sapienza' University, Roma; [19]Hematology Unit, Tor Vergata University, S. Eugenio Hospital, Roma; [20]Division of Hematology, ASST Sette Laghi - Ospedale di Circolo di Varese and Department of Medicine and Surgery, University of Insubria, Varese; Division of Hematology, A.O.U. Città della Salute e della Scienza di Torino and Department of Molecular Biotechnology and Health Sciences, University of Turin, Turin; [21]UOC di Ematologia, Azienda Ospedaliera di Rilievo Nazionale di Alta Specializzazione, ARNAS-G-Garibaldi di Catania, Catania; [22]Division of Hematology Department of Translational Medicine Università del Piemonte Orientale, Novara; [23]Hematology ASST Spedali Civili, Brescia; [24]Ematologia e CTMO Ospedale Maggiore di Parma, Parma; [25]Hematology Unit, Santa Maria delle Croci Hospital, Ravenna; [26]Hematology Unit, Ospedale Guglielmo da Saliceto, Piacenza; [27]Department of Hematology, Santa Croce e Carle Hospital, Cuneo; [28]Hematology Division, IRCCS San Gerardo dei Tintori Hospital, Monza; [29]Hematology Unit Center for Translational Medicine Azienda USL Toscana NordOvest, Livorno; [30]Azienda Unità Sanitaria Locale-IRCCS Arcispedale Santa Maria Nuova, Reggio Emilia; [31]Hematology Unit AO of Cosenza, Cosenza; [32]Department of Pharmacy, Health and Nutritional Sciences, University of Calabria, Rende; [33]SOS Oncoematologia Pistoia e Pescia, Azienda USL Toscana Centro, Pescia; [34]UOC Ematologia con Trapianto - Azienda Ospedaliero-Universitaria-Consorziale Policlinico di Bari, Bari; [35]University Division of Hematology and Cellular Therapy A.O. Ordine Mauriziano, Torino; [36]UO Ematologia, Ospedale Santa Chiara, APSS, Trento; [37]U.O.C. Ematologia, Trapianto di Cellule Staminali e Terapia Genica, Frosinone; [38]UOC di Oncoematologia e TMO "La Maddalena", Palermo; [39]Division of Hematology, Fondazione IRCCS Policlinico San Matteo, Pavia; [40]University Campus Bio-Medico and Fondazione Policlinico Universitario Campus Bio-Medico, Rome; [41]Hematology, Ospedale Ca' Foncello, Treviso; [42]Division of Hematology, Fondazione IRCCS Cà Granda Ospedale Maggiore Policlinico, Milan; [43]Hematology Azienda Ospedaliera Papardo, Messina; [44]Oncology Unit, ASST of Crema, Crema; [45]Hematology Unit Ospedale Santa Maria Goretti, Latina; [46]SC Ematologia, ASST Fatebenefratelli Sacco, Polo Universitario Luigi Sacco, Milano; [47]Hematology and Bone Marrow Transplant Center, Central Hospital Of Bolzano, Bolzano; [48]Onco-Hematology Division, IEO European Institute of Oncology IRCCS, Milan; [49]UO Internal Medicine-ASL 2, Savona; [50]Hematology, Department of Medical Science, Surgery and Neuroscience University of Siena, Siena; [51]UOSD Ematologia, Azienda Sanitaria Provinciale Trapani, Castelvetrano; [52]Internal Medicine, IRCCS INRCA, Osimo; [53]Section of Hematology

Correspondence: A.M. Frustaci
annamaria.frustaci@ospedaleniguarda.it

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Department of Radiological and Hematological Sciences Catholic University Fondazione Policlinico Universitario A. Gemelli, Roma; [54]Department of Medicine and Surgery, University of Milano-Bicocca, Monza; [55]Hematology and Stem Cell Transplantation Unit Ospedale Oncologico A. Businco ARNAS “G. Brotzu”, Cagliari and [56]Division of Hematology, Azienda Ospedali Riunita Villa Sofia-Cervello, Palermo, Italy

**AMF and AGa contributed equally as first authors.*

Supplementary material

Methods:

Supplementary Table 1: Baseline Characteristics and Definitions. This table defines the baseline characteristics collected and analyzed in this study, including patient demographics, comorbidities, concomitant medications, laboratory parameters, disease staging, and biological markers. Variables are reported as continuous or categorical, with clinically relevant cut-offs where applicable.

Variable	Definition / Notes
Patient Characteristics	
Age	Measured in years (continuous); categorized as ≥65, and ≥75 years
Need for a Caregiver	Indicates whether the patient requires a caregiver (recorded as Yes/No)
ECOG – PS	Assessed on a 0–5 scale to evaluate functional status; a score ≥2 is considered impaired performance
Comorbidities	Presence of comorbid conditions based on organ/system involvement (e.g., cardiac, renal, endocrine, respiratory, cancer history).
Cumulative Illness Rating Scale (CIRS)	Measured as a continuous score; high comorbidity burden defined as >6. Severe single organ impairment is defined as any organ with a CIRS score ≥3 (CIRS3+).
Charlson Comorbidity Index (CCI)	Measured as a continuous score; high burden defined as >2.
CLL Comorbidity Index (CLL-CI)	Measured as a continuous score; high burden defined as ≥2 (*high risk* cathegory).
Concomitant Medications	Total number of medications taken (excluding CLL-directed therapy or prophylaxis), collected as a continuous variable; polypharmacy is defined as the use of >3 concomitant drugs.
Venetoclax-drug interaction	Evaluated for interactions with strong/moderate CYP3A4/P-glycoprotein inhibitors.
HBV Status	Classified as Negative, Occult (OBI), or replicative (active HBV infection).
Creatinine Clearance	Calculated via the Cockcroft-Gault formula (mL/min); cut-off at ≥70 mL/min.
Liver Function	Assessed using standard liver function tests (normal vs compromised).
Disease Characteristics – Clinical	
Rai Stage	Clinical staging for CLL according to the Rai system (recorded as a categorical variable).
Complete Blood Count (CBC)	Includes: Hemoglobin (Hb): measured in g/dL; anemia defined as <10 g/dL. Absolute Neutrophil Count (ANC): measured in $\times 10^9$/L; neutropenia defined as <1.5×10^9/L. Platelet Count (PLT): measured in $\times 10^9$/L; thrombocytopenia defined as <100×10^9/L. Absolute lymphocite count (ALC): measured in $\times 10^9$/L, recorded as a continuous variable; cut-off ALC >25×10^9/L.
Largest Nodal Diameter	Measured in centimeters; recorded as a continuous variable and may also be categorized (e.g., >5 cm and >10 cm).
Spleen Size	Measured in centimeters; bulky spleen is defined as >6 cm below the left costal margin.
IgG Levels	Measured in mg/dL; hypogammaglobulinemia is defined as IgG <500 mg/dL.
Disease Characteristics – Biological	
IGHV Mutational Status	Classified as mutated or unmutated (categorical).
FISH According to Döhner	Classified based on Döhner's criteria (categorical).
TP53 Mutational Status	Classified as mutated or unmutated (categorical).
Karyotype	Determined by cytogenetic analysis; a complex karyotype is defined as the presence of ≥3 chromosomal abnormalities.

Results:

Supplementary table 2. Comorbidities details.

Comorbidity	**n (%)**
Hypertension	107 (39.5)
Cardiac comorbidities	61 (22.5)
- History of arrhythmia	31 (11.4)
- Acute coronary syndrome	26 (9.6)
- Structural cardiomyopathy or chronic heart failure	23 (8.5)
Vascular disease	53 (19.6)
Endocrine comorbidities	47 (17.3)
- Metabolic disorders (e.g., diabetes, dyslipidemia, or obesity)	27 (10)
- Thyroid disease	18 (6.6)
Upper gastrointestinal comorbidities	25 (9.2)
History of other malignancies	22 (8.1)
Chronic pulmonary disease (CPD)	21 (7.7)
Chronic kidney disease (CKD)	15 (5.5)

Supplementary Table 3. Univariable logistic regression analysis for baseline factors associated with selected adverse events. This table presents the univariable logistic regression results for baseline factors associatedwith selected adverse events including tumor lysis syndrome (TLS), any grade infusion-related reactions (IRR), any adverse event of grade ≥3 (Any AE ≥3), grade ≥3 hematologic toxicity (Hem Tox), and grade ≥3 infections. For each baseline variable, the odds ratio (OR) with 95% confidence interval (CI) and the corresponding p-value are provided.

Baseline Condition	TLS	IRR	Any AE ≥ 3	Hem Tox	Infections
Sex Male	1.58 (0.53 - 5.78, p=0.439)	1.07 (0.64 - 1.81, p=0.801)	0.55 (0.33 - 0.92, p=0.025)	0.75 (0.45 - 1.27, p=0.282)	0.90 (0.44 - 1.91, p=0.769)
Age>65	1.22 (0.44 - 3.50, p=0.705)	0.58 (0.35 - 0.95, p=0.030)	1.20 (0.75 - 1.94, p=0.451)	1.02 (0.62 - 1.68, p=0.932)	1.20 (0.59 - 2.45, p=0.616)
Need for a caregiver	1.26 (0.19 - 4.84, p=0.769)	0.79 (0.33 - 1.78, p=0.582)	1.64 (0.74 - 3.84, p=0.231)	1.12 (0.49 - 2.47, p=0.782)	3.79 (1.50 - 9.05, p=0.003)
ECOG-PS	0.69 (0.21 - 1.60, p=0.465)	1.53 (1.04 - 2.29, p=0.033)	1.29 (0.88 - 1.94, p=0.206)	0.95 (0.63 - 1.41, p=0.816)	2.03 (1.26 - 3.28, p=0.003)
ECOG ≥2	0.00 (NE - NE, p=0.992)	2.02 (0.75 - 5.54, p=0.164)	1.64 (0.61 - 4.89, p=0.343)	0.70 (0.22 - 1.94, p=0.511)	4.07 (1.32 - 11.5, p=0.010)
CIRS	0.99 (0.84 - 1.15, p=0.914)	1.01 (0.93 - 1.09, p=0.870)	1.08 (1.00 - 1.16, p=0.055)	1.06 (0.98 - 1.14, p=0.162)	1.13 (1.01 - 1.25, p=0.024)
CIRS>6	0.53 (0.08 - 1.98, p=0.413)	1.37 (0.75 - 2.49, p=0.301)	2.13 (1.16 - 4.04, p=0.017)	1.65 (0.91 - 3.00, p=0.099)	3.38 (1.59 - 7.09, p=0.001)
CIRS3+	0.65 (0.10 - 2.43, p=0.576)	2.14 (1.14 - 4.05, p=0.018)	1.57 (0.83 - 3.02, p=0.170)	1.03 (0.53 - 1.95, p=0.924)	3.23 (1.47 - 6.91, p=0.003)
Upper GI	2.44 (0.53 - 8.31, p=0.188)	1.66 (0.72 - 3.81, p=0.231)	3.02 (1.23 - 8.51, p=0.023)	3.43 (1.48 - 8.41, p=0.005)	1.73 (0.55 - 4.65, p=0.304)
Endocrine	1.64 (0.44 - 4.98, p=0.409)	0.77 (0.38 - 1.48, p=0.437)	2.10 (1.09 - 4.18, p=0.030)	2.03 (1.08 - 3.85, p=0.029)	1.73 (0.72 - 3.85, p=0.197)
Cancer	1.68 (0.25 - 6.59, p=0.513)	1.80 (0.74 - 4.36, p=0.189)	3.21 (1.2 - 10, p=0.026)	1.47 (0.60 - 3.55, p=0.388)	2.74 (0.92 - 7.24, p=0.051)
CLL-CI	1.83 (0.98 - 3.30, p=0.047)	1.00 (0.70 - 1.41, p=0.982)	1.55 (1.09 - 2.24, p=0.016)	1.69 (1.19 - 2.41, p=0.003)	1.30 (0.80 - 2.03, p=0.268)
CLL-CI Risk high	3.76 (1.08 - 11.8, p=0.027)	1.01 (0.44 - 2.22, p=0.987)	3.29 (1.4 - 8.64, p=0.009)	3.57 (1.62 - 8.24, p=0.002)	1.58 (0.49 - 4.33, p=0.401)
N°of Conc medications	1.08 (0.88 - 1.29, p=0.398)	1.00 (0.90 - 1.11, p=0.993)	1.12 (1.01 - 1.25, p=0.030)	1.08 (0.98 - 1.20, p=0.120)	1.09 (0.95 - 1.24, p=0.207)
Polipharmacy	1.58 (0.55 - 4.39, p=0.378)	0.83 (0.49 - 1.40, p=0.492)	1.88 (1.12 - 3.18, p=0.017)	1.80 (1.07 - 3.03, p=0.026)	1.31 (0.62 - 2.67, p=0.470)
Steroids (any other reason)	0.00 (NE – NE, p=0.989)	0.95 (0.28 - 2.83, p=0.925)	1.60 (0.54 - 5.33, p=0.410)	1.30 (0.42 - 3.85, p=0.636)	4.05 (1.18 - 12.5, p=0.018)
Anticoagulant	3.53 (0.93 - 11.1, p=0.042)	0.90 (0.37 - 2.05, p=0.800)	1.02 (0.45 - 2.32, p=0.971)	1.29 (0.55 - 2.90, p=0.549)	2.15 (0.74 - 5.52, p=0.129)
Hb g/dl	1.01 (0.79 - 1.30, p=0.926)	0.97 (0.86 - 1.09, p=0.595)	0.80 (0.70 - 0.90, p=0.000)	0.82 (0.72 - 0.92, p=0.002)	0.81 (0.68 - 0.97, p=0.024)
ANC x10^9/l	1.02 (0.87-1.17, p=0.752)	1.00 (0.93-1.08, p=0.980)	0.92 (0.85-0.99, p=0.027)	0.84 (0.76-0.92, p<0.001)	1.04 (0.93-1.14, p=0.462)
Baseline neutropenia	0.00 (NE - NE, p=0.992)	0.93 (0.31 - 2.52, p=0.887)	3.00 (1.03 - 10.9, p=0.060)	4.53 (1.62 - 14.6, p=0.006)	2.13 (0.57 - 6.47, p=0.208)
ALC>25	0.60 (0.22 - 1.73, p=0.325)	1.03 (0.61 - 1.76, p=0.899)	1.41 (0.85 - 2.35, p=0.187)	1.20 (0.71 - 2.05, p=0.507)	2.68 (1.14 - 7.37, p=0.035)
PLT x 10^{10}/l	0.91 (0.83-0.98, p=0.028)	0.97 (0.94-1.00, p=0.091)	0.98 (0.95-1.00, p=0.103)	0.96 (0.93-0.99, p=0.025)	1.02 (0.98-1.06, p=0.330)
PLT<100	2.92 (1.04 - 8.25, p=0.039)	1.28 (0.73 - 2.21, p=0.385)	1.35 (0.79 - 2.34, p=0.280)	1.49 (0.86 - 2.58, p=0.152)	0.89 (0.38 - 1.93, p=0.779)
IgG<500	1.45 (0.44 - 4.14, p=0.510)	0.81 (0.45 - 1.45, p=0.490)	1.89 (1.07 - 3.40, p=0.030)	1.61 (0.91 - 2.83, p=0.099)	1.23 (0.54 - 2.64, p=0.608)
LN>10 cm	7.82 (2.22 - 24.9, p=0.001)	0.43 (0.12 - 1.23, p=0.148)	1.21 (0.47 - 3.22, p=0.691)	0.78 (0.27 - 2.03, p=0.619)	0.34 (0.02 - 1.75, p=0.307)
Spleen size (cm)	1.13 (1.00 - 1.28, p=0.055)	1.07 (1.00 - 1.14, p=0.041)	1.02 (0.96 - 1.09, p=0.482)	1.04 (0.97 - 1.10, p=0.253)	0.98 (0.89 - 1.07, p=0.597)
Splenic bulky	2.83 (0.97 - 7.93, p=0.048)	1.32 (0.73 - 2.34, p=0.350)	1.27 (0.72 - 2.27, p=0.413)	1.32 (0.73 - 2.34, p=0.350)	0.96 (0.39 - 2.14, p=0.920)
Steroid dose premedication (mg/kg)	1.64 (0.53 - 4.62, p=0.366)	0.38 (0.20 - 0.70, p=0.003)	2.11 (1.17 - 3.94, p=0.016)	1.37 (0.78 - 2.44, p=0.273)	1.47 (0.67 - 3.15, p=0.321)
N° of days of steroids	0.99 (0.90 - 1.02, p=0.648)	0.99 (0.96 - 1.00, p=0.269)	1.05 (1.01 - 1.10, p=0.038)	1.02 (1.00 - 1.05, p=0.047)	1.02 (1.01 - 1.04, p=0.008)
Steroid days>6	0.43 (0.07 - 1.58, p=0.268)	0.97 (0.54 - 1.72, p=0.917)	1.73 (0.99 - 3.10, p=0.059)	1.48 (0.84 - 2.60, p=0.174)	2.24 (1.05 - 4.65, p=0.032)
Rasburicase	0.72 (0.22 - 2.03, p=0.547)	0.45 (0.26 - 0.76, p=0.004)	0.75 (0.46 - 1.22, p=0.245)	0.65 (0.38 - 1.08, p=0.100)	1.17 (0.57 - 2.38, p=0.663)

Supplementary Table 4. Univariable and Multivariable logistic regression models for treatment modifications during the debulking phase. The table presents adjusted odds ratios (ORs) with 95% confidence intervals (CI) and p-values for treatment modifications occurring during the debulking phase period

	Univariable			Multivariable		
Baseline condition	**Debulking phase feasibility**	**Debulking phase prolonged**	**Debulking phase discontinuation**	**Debulking phase feasibility**	**Debulking phase prolonged**	**Debulking phase discontinuation**
CIRS	1.07 (0.99-1.16, p=0.104)	1.01 (0.91-1.12, p=0.820)	1.34 (1.14-1.60, p=0.001)	-	-	-
CIRS>6	1.61 (0.84-3.01, p=0.142)	0.85 (0.35-1.89, p=0.712)	5.97 (1.83-20.93, p=0.003)	-	-	-
Endocrine	1.41 (0.69-2.75, p=0.328)	1.22 (0.49-2.76, p=0.643)	5.29 (1.58-17.71, p=0.006)	-	-	6.95 (1.69-31.80, p=0.008)
Cancer	1.35 (0.50-3.35, p=0.533)	0.28 (0.02-1.43, p=0.223)	10.13 (2.75-35.26, p<0.001)	-	-	20.40 (4.06-127.2, p<0.001)
Concomitant Medications	2.15 (1.16-4.18, p=0.019)	1.90 (0.92-4.25, p=0.096)	2.50 (0.64-16.50, p=0.244)	-	-	-
Anticoagulant	4.60 (2.01-10.83, p<0.001)	4.27 (1.78-10.06, p=0.001)	0.85 (0.05-4.64, p=0.876)	4.40 (1.89-10.57, p=0.001)	4.33 (1.78-10.37, p=0.001)	-
Baseline neutropenia	3.48 (1.28-9.66, p=0.014)	2.30 (0.69-6.69, p=0.142)	1.37 (0.07-7.77, p=0.767)	-	-	-
PLT<100	1.88 (1.04-3.36, p=0.034)	2.21 (1.12-4.29, p=0.020)	0.23 (0.01-1.24, p=0.169)	2.04 (1.10-3.77, p=0.022)	2.24 (1.12-4.45, p=0.022)	-
Splenic bulky	1.33 (0.70-2.47, p=0.366)	2.00 (0.99-3.97, p=0.049)	0.00 (NA-NA, p=0.990)	-	-	-
N° steroid days before obinutuzumab	1.01 (1.00-1.03, p=0.082)	1.01 (0.99-1.02, p=0.418)	1.02 (1.01-1.04, p=0.003)	-	-	-
Steroid days>6	1.92 (1.05-3.48, p=0.032)	1.56 (0.74-3.17, p=0.229)	18.04 (4.59-119.5, p<0.001)	1.98 (1.05-3.72, p=0.033)	-	33.39 (6.54-311.21, p<0.001

Supplementary Table 5. Multivariable logistic regression models for treatment modifications during the overall treatment period The table presents adjusted odds ratios (ORs) with 95% confidence intervals (CI) and p-values for various treatment modifications throughout the overall treatment period.

Baseline condition	Ven temp reduction	Ven Permanent reduction	Ven temp interruption	Treatment discontinuation	Obinutuzumab Omission	Global Feasibility
Need for a caregiver	0.91 (0.29-2.34, p=0.852)	0.51 (0.08-1.84, p=0.378)	3.05 (1.37-6.82, p=0.006)	3.35 (1.21-8.48, p=0.014)	1.31 (0.46-3.24, p=0.587)	1.59 (0.70-3.50, p=0.255)
Age	1.04 (1.01-1.08, p=0.013)	1.03 (1.00-1.07, p=0.081)	1.03 (1.00-1.06, p=0.033)	1.02 (0.98-1.06, p=0.325)	1.01 (0.98-1.05, p=0.391)	1.04 (1.02-1.07, p=0.002)
Age>65	1.85 (0.99-3.55, p=0.057)	1.77 (0.85-3.85, p=0.135)	2.11 (1.22-3.70, p=0.008)	1.37 (0.63-3.06, p=0.429)	1.25 (0.67-2.37, p=0.484)	1.77 (1.06-2.99, p=0.029)
ECOG-PS	1.14 (0.70-1.78, p=0.586)	0.96 (0.51-1.64, p=0.886)	1.78 (1.19-2.70, p=0.006)	1.45 (0.83-2.42, p=0.164)	1.53 (0.97-2.39, p=0.058)	1.53 (1.03-2.28, p=0.036)
CIRS	1.01 (0.91-1.10, p=0.916)	1.03 (0.92-1.15, p=0.592)	1.14 (1.05-1.24, p=0.002)	1.16 (1.04-1.30, p=0.010)	1.11 (1.01-1.22, p=0.030)	1.09 (1.01-1.18, p=0.023)
CIRS>6	0.58 (0.23-1.31, p=0.222)	0.88 (0.31-2.13, p=0.792)	3.02 (1.63-5.59, p<0.001)	2.24 (0.95-5.06, p=0.057)	2.29 (1.13-4.53, p=0.019)	1.69 (0.92-3.09, p=0.087)
CIRS3+	0.72 (0.28-1.63, p=0.455)	1.27 (0.48-2.99, p=0.603)	2.78 (1.45-5.32, p=0.002)	1.56 (0.58-3.74, p=0.341)	0.91 (0.37-2.02, p=0.834)	1.13 (0.58-2.15, p=0.721)
CCI	1.08 (0.94-1.23, p=0.265)	1.11 (0.95-1.29, p=0.181)	1.21 (1.08-1.38, p=0.002)	1.12 (0.94-1.31, p=0.189)	1.03 (0.89-1.18, p=0.671)	1.15 (1.02-1.29, p=0.019)
CCI>2	2.84 (1.23-7.72, p=0.024)	2.65 (0.99-9.18, p=0.078)	1.50 (0.79-2.99, p=0.233)	1.58 (0.62-4.86, p=0.372)	1.72 (0.79-4.15, p=0.195)	2.13 (1.13-4.23, p=0.024)
CLL CI>0	1.45 (0.77-2.70, p=0.245)	1.25 (0.58-2.61, p=0.551)	1.84 (1.06-3.19, p=0.030)	2.25 (1.03-4.95, p=0.040)	2.01 (1.06-3.79, p=0.031)	1.56 (0.92-2.63, p=0.098)
Endocrine	0.87 (0.35-1.91, p=0.736)	0.45 (0.10-1.33, p=0.199)	1.48 (0.74-2.87, p=0.256)	3.50 (1.49-7.94, p=0.003)	1.79 (0.82-3.71, p=0.126)	1.17 (0.60-2.24, p=0.636)
Cardio Comorbidities	1.07 (0.50-2.15, p=0.853)	0.89 (0.34-2.05, p=0.792)	2.08 (1.13-3.79, p=0.018)	1.64 (0.68-3.73, p=0.248)	1.35 (0.65-2.71, p=0.404)	1.29 (0.71-2.33, p=0.398)
Cancer	1.22 (0.33-3.59, p=0.734)	3.13 (0.94-9.13, p=0.044)	2.95 (1.21-7.22, p=0.016)	4.82 (1.69-12.78, p=0.002)	2.37 (0.86-5.99, p=0.078)	3.98 (1.64-10.35, p=0.003)
Concomitant Medications	2.29 (1.12-5.06, p=0.030)	1.43 (0.66-3.37, p=0.391)	1.42 (0.80-2.61, p=0.242)	1.58 (0.68-4.14, p=0.314)	1.77 (0.88-3.83, p=0.123)	1.93 (1.10-3.49, p=0.025)
N° of concomitant medications	1.05 (0.93-1.18, p=0.406)	1.00 (0.86-1.15, p=0.966)	1.14 (1.03-1.27, p=0.015)	1.05 (0.90-1.21, p=0.489)	1.04 (0.91-1.17, p=0.556)	1.06 (0.96-1.17, p=0.264)
Polypharmacy	1.37 (0.72-2.55, p=0.334)	1.11 (0.51-2.32, p=0.795)	2.09 (1.20-3.63, p=0.009)	1.71 (0.77-3.72, p=0.178)	1.23 (0.64-2.34, p=0.526)	1.42 (0.83-2.41, p=0.193)
Venetoclax-drug interaction	3.17 (1.40-7.01, p=0.005)	2.77 (1.07-6.64, p=0.027)	3.90 (1.81-8.52, p=0.001)	1.73 (0.55-4.62, p=0.304)	1.42 (0.53-3.36, p=0.452)	2.39 (1.12-5.14, p=0.024)
Steroids (any other reason)	0.69 (0.11-2.64, p=0.635)	1.14 (0.17-4.42, p=0.872)	2.08 (0.66-6.21, p=0.188)	2.42 (0.52-8.37, p=0.195)	2.76 (0.82-8.42, p=0.081)	2.10 (0.70-6.31, p=0.179)
Anticoagulant	2.04 (0.79-4.86, p=0.120)	1.72 (0.54-4.60, p=0.313)	3.60 (1.58-8.33, p=0.002)	2.19 (0.68-5.97, p=0.148)	1.45 (0.51-3.64, p=0.453)	1.84 (0.80-4.16, p=0.145)
Hb g/dl	0.93 (0.80-1.08, p=0.319)	1.01 (0.85-1.20, p=0.910)	0.85 (0.74-0.97, p=0.020)	0.82 (0.67-1.00, p=0.051)	0.98 (0.84-1.14, p=0.751)	0.91 (0.80-1.03, p=0.149)
ALC>25	0.87 (0.46-1.67, p=0.661)	0.89 (0.42-1.94, p=0.756)	0.92 (0.53-1.64, p=0.778)	4.69 (1.59-20.08, p=0.013)	0.95 (0.50-1.89, p=0.888)	1.10 (0.64-1.91, p=0.736)
PLT<100	3.09 (1.63-5.86, p=0.001)	1.33 (0.59-2.83, p=0.477)	1.58 (0.88-2.82, p=0.121)	1.50 (0.64-3.33, p=0.335)	1.83 (0.94-3.52, p=0.072)	2.04 (1.17-3.56, p=0.012)
Splenic bulky	1.32 (0.64-2.59, p=0.437)	1.00 (0.40-2.26, p=0.995)	0.91 (0.46-1.70, p=0.763)	0.51 (0.15-1.37, p=0.225)	0.34 (0.11-0.82, p=0.029)	0.78 (0.41-1.43, p=0.427)
IgG<500	1.55 (0.78-3.00, p=0.202)	0.93 (0.38-2.10, p=0.874)	2.33 (1.29-4.19, p=0.005)	2.08 (0.90-4.61, p=0.076)	2.19 (1.11-4.23, p=0.021)	1.56 (0.87-2.76, p=0.128)
N° steroid days before obinutuzumab	1.00 (0.96-1.01, p=0.744)	1.00 (0.96-1.02, p=0.875)	1.00 (0.98-1.01, p=0.902)	1.00 (1.00-1.01, p=0.025)	1.02 (1.01-1.04, p=0.014)	1.01 (1.00-1.03, p=0.095)
Steroid days>6	1.68 (0.84-3.26, p=0.132)	1.77 (0.78-3.80, p=0.155)	1.00 (0.53-1.84, p=0.994)	3.41 (1.54-7.55, p=0.002)	3.08 (1.59-5.94, p=0.001)	2.39 (1.35-4.23, p=0.003)
Rasburicase	0.37 (0.17-0.73, p=0.006)	0.38 (0.15-0.85, p=0.028)	0.54 (0.30-0.96, p=0.039)	1.35 (0.61-2.93, p=0.451)	1.18 (0.62-2.22, p=0.606)	0.72 (0.42-1.22, p=0.229)