european research initiative on CLL

COVID-19 severity and mortality in patients with CLL: an update of the international ERIC study

Thomas Chatzikonstantinou

Wednesday, 9th of June, 2021

COVID-19 and CLL

european research initiative on CLL

ERIC and CLL Campus study

- **190** patients
- The **mortality rate** was **32,5%**
- COVID-19 **severity** increases with **age**
- **Anti-leukemic treatment** (particularly **BTK inhibitors**) appears to exert a **protective effect**
- **Age and comorbidities** did not impact on mortality.

Scarfo L et al. COVID-19 severity and mortality in patients with chronic lymphocytic leukemia: a joint study by ERIC, the European Research Initiative on CLL, and CLL Campus. Leukemia 2020; 34(9): 2354-63

COVID-19 and CLL

european research initiative on CLL

Mato et al. study

- **198** patients
- The overall case-fatality rate was **33%**
- **No difference** between **treated and untreated** patients in case of **severity and mortality**
- **Advanced age** and **specific comorbidities** conferred a worse prognosis
- **BTKi didn't show a protective effect** (in most cases, BTKis were held during the infection)

Mato AR et al. Outcomes of COVID-19 in patients with CLL: a multicenter international experience. Blood 2020; 136(10): 1134-43

COVID-19 and CLL

european research initiative on CLL

Cohort 1: ERIC/ CLL CAMPUS cohort combined with patients from Grupo Español de Leucemia Linfática Crónica
Cohort 2: Patients from US (66%), UK (23%), EU (7%), other countries (4%)

	Cohort 1 (n = 281)		Cohort 2 (n = 130)	
Univariable analyses	HR, 95% CI	P value	HR (95% CI)	P value
Sex (male vs. female)	1.09 (0.69-1.73)	0.70	0.62 (0.34 – 1.13)	0.12
Age at COVID-19 diagnosis (continuous)	1.04 (1.01 – 1.06)	<0.001	1.04 (1.01 – 1.07)	0.004
CIRS (≥6 vs. <6)	2.02 (1.22 – 3.35)	0.006	2.05 (1.12 – 3.77)	0.02
Lymphopenia (ALC ≥ 1.0 x 10^9/L vs. ALC < 1.0 x 10^9/L)	1.55 (0.79 – 3.06)	0.21	0.69 (0.32 – 1.50)	0.35
Lymphocytosis (ALC ≥ 30.0 x 10^9/L vs. ALC < 30.0 x 10^9/L)	2.02 (1.10 – 3.69)	0.02	1.69 (0.86 – 3.33)	0.13
CLL Treatment History				
Ever treated vs. "watch and wait"	1.60 (1.03 – 2.50)	0.04	0.75 (0.41 – 1.36	0.34
Currently treated vs. observation	1.47 (0.93 – 2.31)	0.1	0.57 (0.31 – 1.05)	0.071
Current BTKi therapy	1.33 (0.79 – 2.24)	0.28	0.73 (0.38 – 1.39)	0.33
Multivariable analyses				
Age at COVID-19 diagnosis (continuous)	1.03 (1.01 – 1.06)	0.01	1.03 (1.004 – 1.07)	0.028
CIRS (≥6 vs. <6)	1.64 (0.97 – 2.77)	0.07	1.61 (0.85 – 3.07)	0.15

Roeker LE et al. Worldwide Examination of Patients with CLL Hospitalized for COVID-19. Blood 2020; 136(Supplement 1): 45-9

Study purpose and design

- Observational **retrospective international** multicenter study aimed to assess the effect of CLL patient characteristics on **COVID-19 outcome**
- Investigators with **confirmed patients** with **CLL** experiencing **COVID-19** filled out a template with relevant clinical information
- Only patients with a diagnosis of CLL/SLL or MBL and a positive RT-PCR test for SARS-CoV-2 were included.

Participating sites

Country	Number of sites providing clinical data (n=90)
Italy	27
Spain	13
The Netherlands	7
Israel	5
Greece	4
United Kingdom	4
Czech Republic	3
Poland	3
Denmark	3
Belgium	2
Romania	2
Russian Federation	2
Germany	2
Argentina	2
Serbia	2
Croatia	1
Egypt	1
Ireland	1
Qatar	1
Switzerland	1
India	1
Sweden	1
Armenia	1
Nepal	1
Portugal	1

Patient Characteristics

Characteristic	Result
Number of patients	**941**
Median age, y (range, y)	69 (36-96)
Male/female	628/313
Median number of comorbidities (range)	2 (0-11)
Type of comorbidities	
• Other respiratory	61 (6.5%)
• COPD	61 (6.5%)
• Cardiac Failure	30 (3.2%)
• Arrythmias	87 (9.3%)
• Coronary artery disease	94 (10%)
• Other cardiovascular	83 (8.9%)
• Hypertension	440 (47%)
• Diabetes	173 (18.5%)
• Chronic renal disease	51 (5.4%)
• Other non-hematological malignancies	75 (8%)

Patient Characteristics

CLL treatment history	
▪ Previously untreated (%)	394 (41.9)
▪ **Received treatment (%)**	**547 (58.1)**
○ 1 line of treatment	275 (50.7)
○ 2 lines of treatment	149 (27.5)
○ 3 lines of treatment	60 (11.1)
○ 4 lines of treatment	33 (6.1)
○ >4 lines of treatment	25 (4.6)
On treatment at the time of COVID-19 (%)	**320 (34)**
▪ **BTK inhibitor (acalabrutinib, ibrutinib, zanubrutinib)**	**179 (56.3)**
▪ Venetoclax-based regimens	51 (16)
▪ Idelalisib	13 (4)
▪ Anti-CD20 only	8 (2.5)
▪ Chemotherapy	22 (6.9)
▪ Chemoimmunotherapy	29 (9.1)
▪ BTKi + Venetoclax	9 (2.8)
▪ Steroids only	7 (2.2)

Results

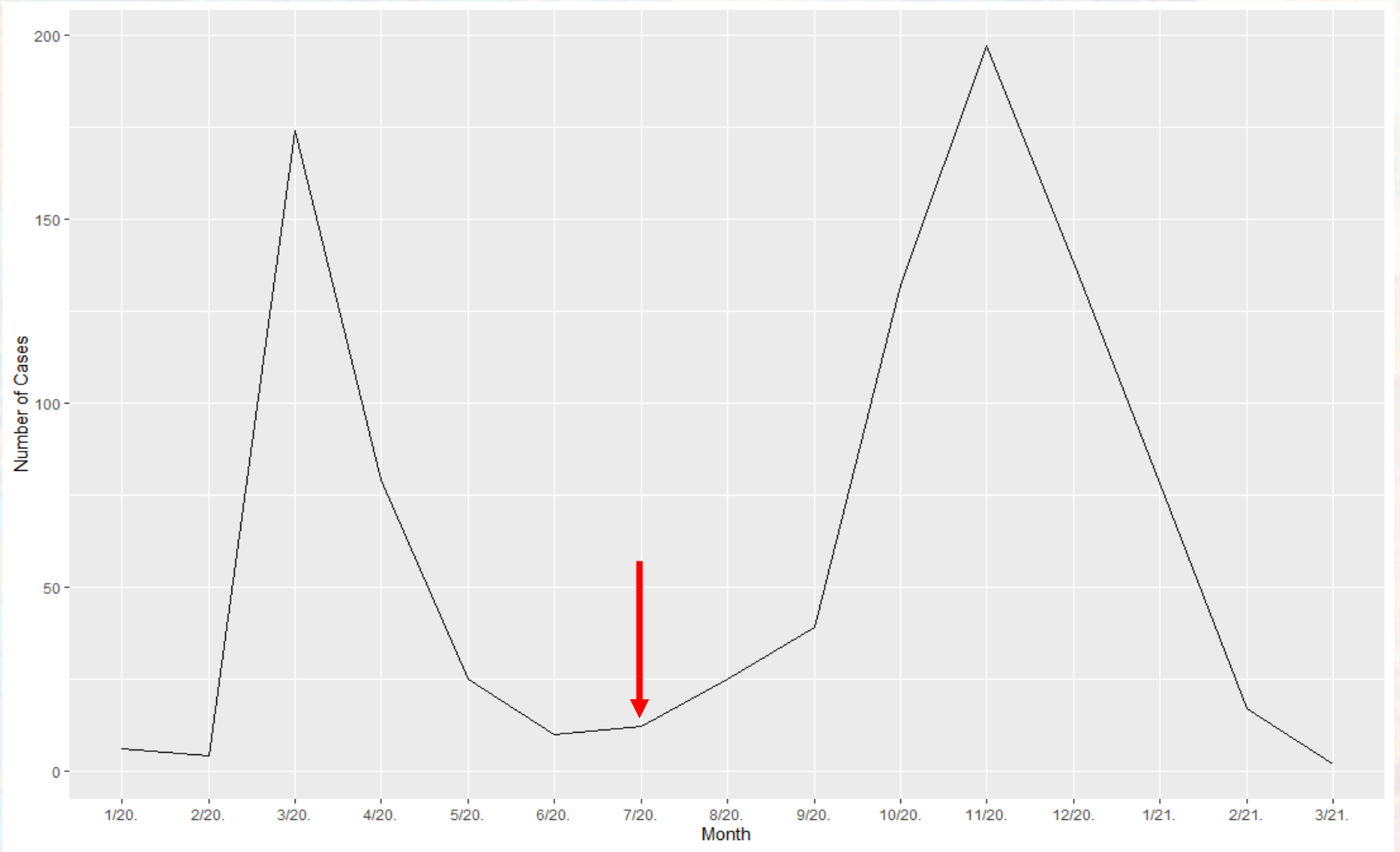
699 (74.7 %) patients were admitted to the hospital

- **177 in ICU**
- **440 needed oxygen supplementation**
- **78 were hospitalized without the need of oxygen**

The **case mortality rate** was **27,4%** for all patients, and **38,4% for patients** with severe COVID-19.

No difference between the two waves

european research initiative on CLL



Univariate analysis

european research initiative on CLL

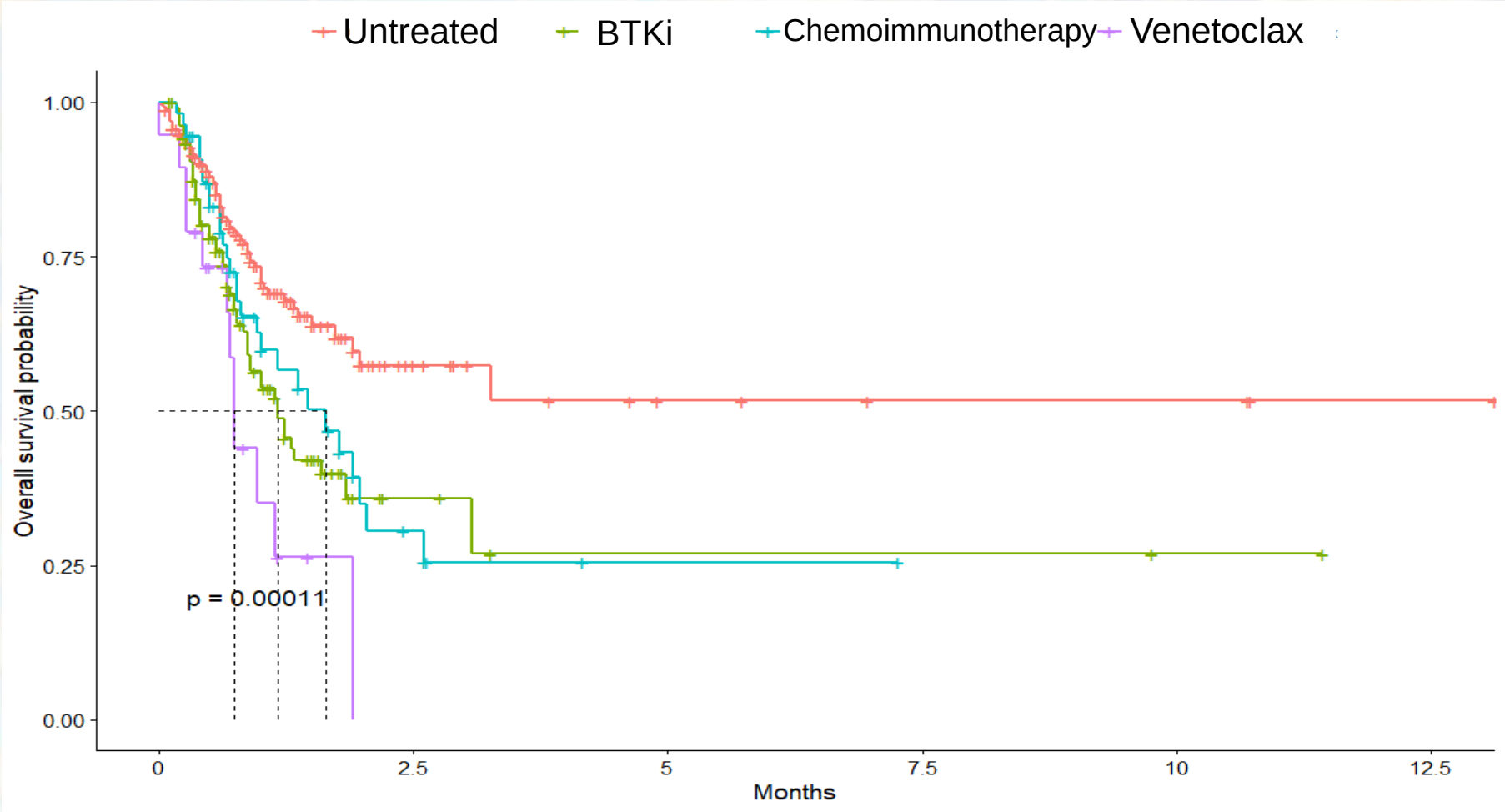
Risk factor	p-value
Age (≥ 65 vs < 65)	**0.011**
Age (≥ 75 vs < 75)	**<0.001**
Gender (Male vs Female)	0.560
IGHV gene status (Unmutated vs Mutated)	0.013
CIRS score (> 6 vs ≤ 6)	**<0.001**
Other respiratory (YES vs NO)	0.820
COPD (YES vs NO)	0.120
Cardiac Failure (YES vs NO)	**<0.001**
Coronary artery disease (YES vs NO)	0.056
Other cardiovascular (YES vs NO)	0.160
Hypertension (YES vs NO)	0.097
Diabetes (YES vs NO)	0.520
Chronic renal disease (YES vs NO)	0.020
Other non-hematological malignancies (YES vs NO)	0.870
Obesity (YES vs NO)	0.980
Smoking	0.800
Hypogammaglobulinemia (Present vs absent)	0.083
CLL treatment status (Untreated vs Treated)	**<0.001**
CLL treatment during COVID-19 (Treated vs Untreated)	**<0.001**
Treated in last 12 months/6 months (Treated vs Untreated)	**0.01 /0.001**

Multivariate analysis

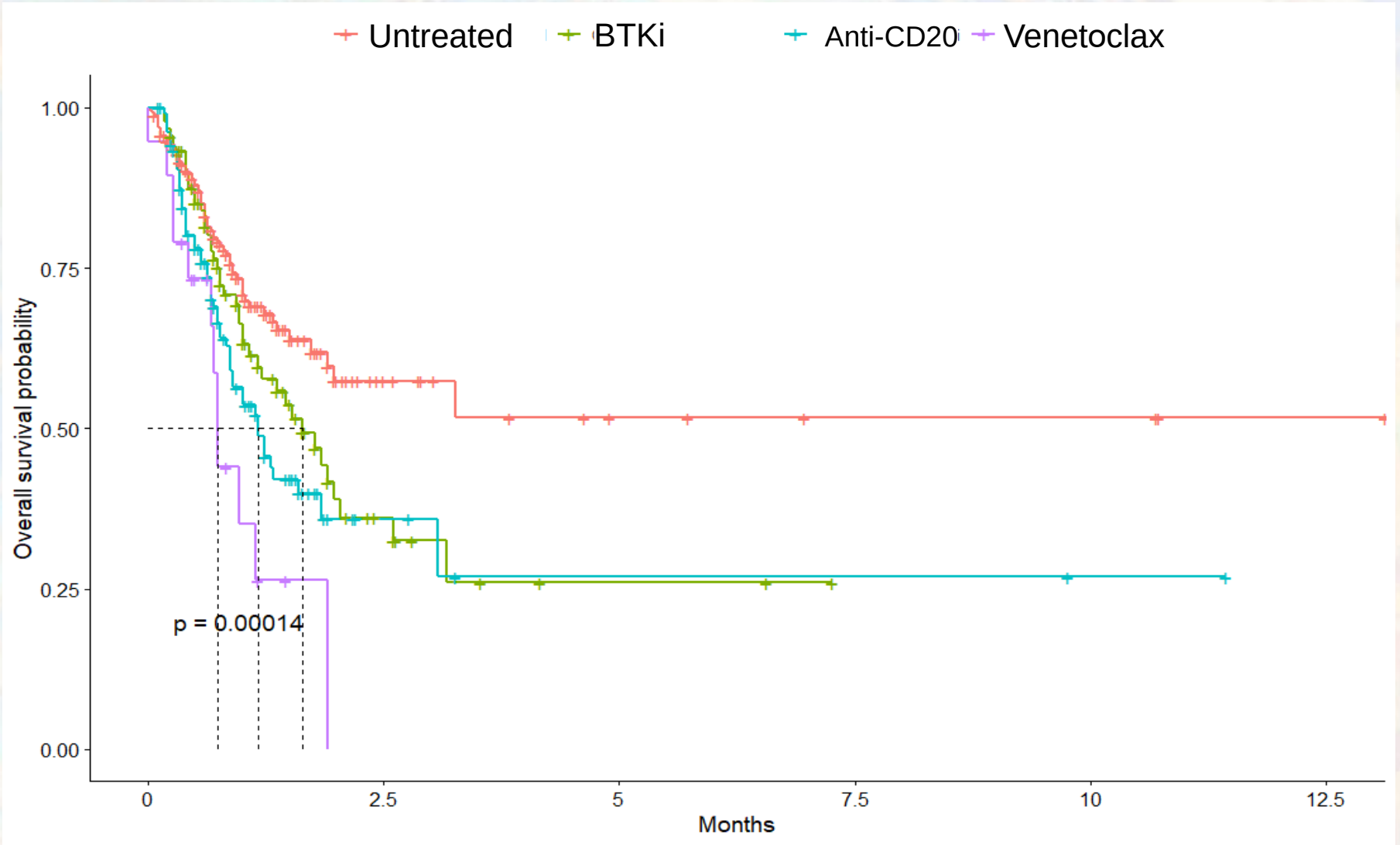
Risk factor	HR	95% CI	p value
Age	1.03	1.02 – 1.04	**<0.001**
Cardiac Failure (YES vs NO)	1.79	1.04 – 3.07	**0.035**
CLL treatment status (Untreated vs Treated)	0.54	0.41 – 0.72	**<0.001**

european research initiative on CLL

Impact of treatment



Impact of treatment



Impact of treatment

Treatment	Infection Outcome		p-value
	Resolution	Death	
BTKi	55 (51.4%)	52 (48.6%)	<0.001
Untreated	190(73.9%)	67 (26.1%)	

Category	Infection outcome		p-value
	Resolution	Death	
Untreated	190 (73.9%)	67 (26.1%)	<0.001
Continued BTKi	20 (66.7%)	10 (33.3%)	
Stopped BTKi	36 (46.2%)	42 (53.8%)	

*No statistically significant difference between Continued and Stopped (p = 0.08)

Conclusions | CLL and COVID-19

- **Advanced age** and **cardiac failure** conferred a worse prognosis
- **Untreated** patients had a **better chance of survival** than those on **treatment or recently treated**

Thank you all

Kostas Stamatopoulos, Paolo Ghia

Lydia Scarfò, Argiris Kapetanakis, George Karakatsioulis

Olga Kalashnikova, Giulia Quaresmini, Marina Motta, Candida Vitale, Michael Doubek, Jose Antonio Garcia-Marc, José Ángel Hernández-Rivas, Fatima Mirás, Mónica Baile, Mattias Mattsson, Juan Marquet, Carsten U. Niemann, Gianluigi Reda, Talha Munir, Eva Gimeno, Monia Marchetti, Francesca Maria Quaglia, Marzia Varettoni, Julio Delgado, Sunil Iyengar, Ann Janssens, Roberto Marasca, Angela Ferrari, Carolina Cuéllar-García, Gilad Itchaki, Martin Špaček, Lorenzo De Paoli, Luca Laurenti, Mark-David Levin, Marta Morawska, Enrico Lista, Francesca R. Mauro, Martin Šimkovič, Ellen Van Der Spek, Elisabeth Vandenberghe, Livio Trentin, Ewa Wasik-Szczepanek, Rosa Ruchlemer, Dominique Bron, Maria Rosaria De Paolis, Giovanni Del Poeta, Lucia Farina, Myriam Foglietta, Massimo Gentile, Yair Herishanu, Tobias Herold, Ozren Jaksic, Arnon P. Kater, Sabina Kersting, Lara Malerba, Lorella Orsucci, Viola Maria Popov, Paolo Sportoletti, Mohamed Yassin, Barbara Pocali, Gabor Barna, Annalisa Chiarenza, Gimena dos Santos, Eugene Nikitin, Martin Andres, Maria Dimou, Alicia Enrico, Yervand Hakobyan,, Macarena Ortiz Pareja, Maria Papaioannou, Kristian Qvist, Martin Andres, Jorge Labrador Gomez, Nimish Shah, Amit Shrestha, Oana Stanca, Niki Stavroyianni, Gerassimos Pangalis, Rosa Collado, Roberta Murru, David Allsup, Mark Catherwood, Deepesh Lad, Maya Koren-Michowitz, Shaimaa El-Ashwah, Tomasz Wrobel,Elżbieta Kalicińska, Maria Gomes Da Silva, Michel van Gelder, Raul Cordoba, Lopez Garcia, Darko Antic, Jacopo Olivieri, Carlota Mayor Bastida, Tamar Tadmor, Inga Piskunova, Roel van Kampen, Lucrecia Yáñez San Segundo, Ivana Milosevic, Miguel Arturo Pavlovsky, Amit Shrestha, Marta Coscia, Giuseppe Rossi, Alessandro Rambaldi, Emili' Montserrat, Gian Matteo Rigolin, Robin Foà, Antonio Cuneo