



Outcomes in patients with lymphoproliferative diseases and COVID-19: results of a subgroup analysis of the CHRONOS19 registry

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Background

Patients (pts) with lymphoproliferative diseases (LPD) are at high risk of COVID-19 severe and lethal course. Intensive chemotherapy, anti-CD20 directed therapy and immunosuppression in these patients are the possible causes of high mortality. Emerging data on risk factors and outcomes in this vulnerable patient population is aimed to support strategies of their medical care.

Objective

To evaluate treatment outcomes and risk factors in pts with LPD and COVID-19 in a real-world setting.

Materials & Methods

CHRONOS19 is an ongoing nationwide observational cohort study of adult (≥ 18 y) pts with hematologic disease (both malignant and non-malignant) and lab-confirmed or suspected (based on clinical and/or CT findings) COVID-19. We performed a subgroup analysis of pts with LPD and COVID-19. Primary objective was to evaluate treatment outcomes and identify risk factors associated with a higher mortality in this group of pts. Primary endpoint was 30-day all-cause mortality. Long-term follow-up was performed at 90 and 180 days. Data from 15 centers was collected on a web-based platform and managed in a deidentified manner.

Summary

As of data cutoff on April 14, 2021, 626 pts were included in the registry, 170 of them with LPD were eligible for primary endpoint assessment n(%): CLL – 64(38%), Hodgkin lymphoma – 18(10%), aggressive B-cell lymphomas – 49(29%), indolent B-cell lymphomas – 19(11%), another – 20(12%); M/F 96(56%)/74(44%), median age 56 [19-90] years, induction phase/ relapsed or refractory disease /treatment in remission **62(36%)/68(40%)/40(24%)**, myelotoxic agranulocytosis in 27(16%) pts, 41(24%) pts were transfusion dependent, comorbidities were recorded in 86(51%) pts. Complications developed in 126(74%) pts, including: pneumonia (72%), sepsis (7%), CRS (13%), ARDS (13%). One-third of pts had severe COVID-19, 25% were admitted to ICU, 20% required mechanical ventilation. We performed comparative analysis of basic characteristics between the groups of pts with LPD and all other hematologic diseases (acute leukemia, chronic myeloid leukemia, multiple myeloma, and other malignant and non-malignant diseases) which didn’t reveal any significant clinical differences.

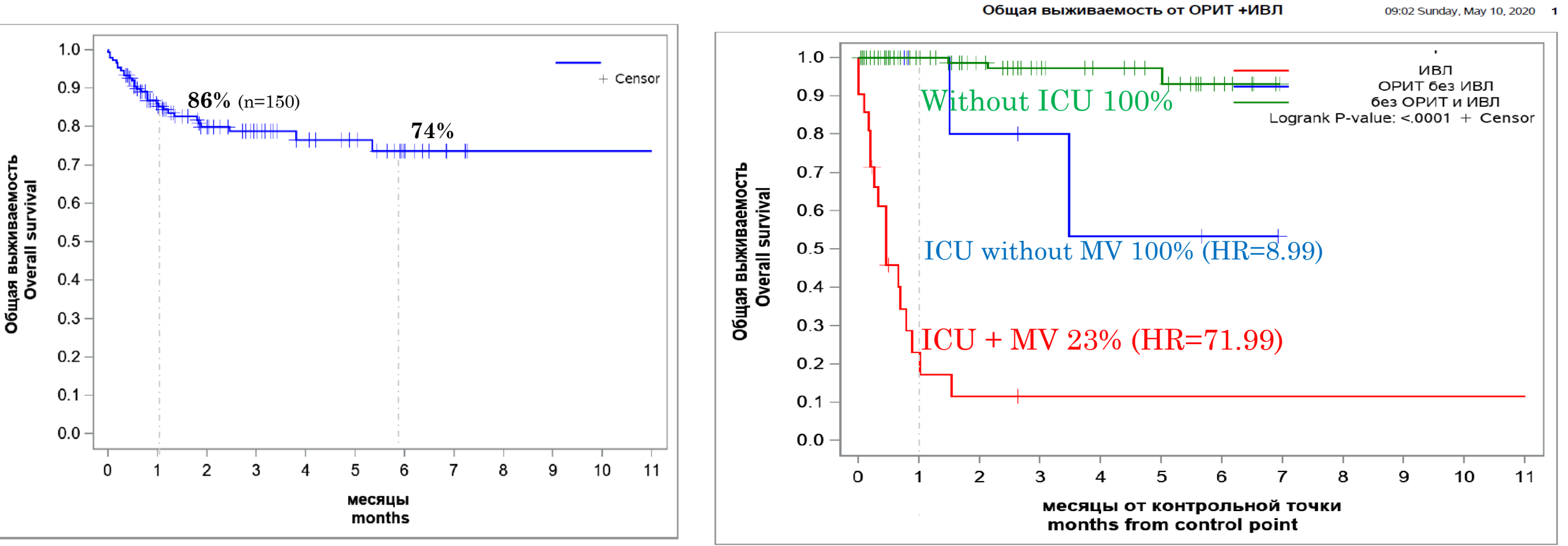
All-cause mortality at 30 days was 14% in pts with LPD vs. 15% in pts with other hematologic diseases (p=0,87); 86% of deaths were due to COVID-19 complications. At 90 days, 8 additional death due to COVID-19 occurred. At 180 days, 5 more deaths due to LPD progression were registered. Risk factors that were significantly associated with overall survival (OS) are listed in Table 1. In multivariate analysis, ICU + mechanical ventilation, HR, 71.99 (19.5-271.0) and age >60 years HR, 5.360 (1.08-11.8) were the most significant risk factors of death. COVID-19 affected treatment of LPD in 55% of pts, 52% experienced a treatment delay for a median of 4 [1-10] weeks. In 5 of 170 (2,9%) pts with LPD early relapse/refractory disease was detected, but the association of relapses with impaired treatment is unknown. COVID-19 re-infection was described in 1 patient. Data on IgG after SARS-CoV-2 infection is available for 65 patients with LPD: we detected antibodies to SARS-CoV-2 only in 44(66%) of them, and only in 60% of pts with CD20-positive LPD vs 100% of pts with T-cell and Hodgkin lymphomas (p=0,004).

Discussion

Thirty-day all-cause mortality in SARS-CoV-2-infected pts with LPD was comparable with the mortality in pts with other hematological diseases and higher than in general population of pts with COVID-19. CD20-positive patients had IgG to SaRS-CoV-2 significantly less often compared with other LPD which is probably due to anti-CD20 therapy.

Table 1. Univariate analysis of factors associated with lower OS

Risk Factor	HR (95CI)	p
ICU + mechanical ventilation	71.990 (19.5-271.0)	<0.0001
ECOG 4 vs. ≤ 3	6.83 (3.28-14.21)	<0.00013
Admission to ICU	5.41 (1.46-20.10)	<0.0001
COVID-19 severity	6.83 (3.28-14.21)	<0.0001
COVID-19 complications	2.99 (1.16-7.68)	0.0162
Transfusion dependence	4.31 (1.96-9.50)	0.0004
R/R disease	2.18 (0.97-4.86)	0.151
Age ≥ 60 vs. <60 y	5.36 (1.08-11.80)	<0.0001
MTA	1.62 (0.85-3.09)	0.0389
Male vs. female	1.48 (0.78-2.80)	0.2224
Comorbidities	1.63 (0.85-3.12)	0.1235



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