Diffuse Large B-Cell Lymphoma During The COVID-19 Pandemic in Two Tertiary Centers: The Israeli/Italian Study

O. Giladi[1,2], G. Bagnato[3,4], M. Gentilini[3,4], S. Shimony[1,2,5], O. Pasvolsky[1,2,6], T. Berger[1,2], G. Itchaki[1, 2], P. Raanani[1,2], A. Broccoli[3,4], V. Stefoni[3,4], G. Lolli[3,4], L. Argnani[3,4] PL. Zinzani [3,4], R.Gurion[1,2]

1 Institute of Hematology, Davidoff Cancer Centre, Rabin Medical Centre, Petach Tikva, Israel
2 Sackler School of Medicine, Tel Aviv University, Tel Aviv, Israel
3 IRCC, Azienda Ospedaliero-Universitaria di Bologna, Instituto di Ematologia "Seragnoli", Bologna, Italy
4 Dipartmento di Medicina Specialistica, Diagnotica e Sperimentale, Universita di Bologna, Bologna, Italy
5 Medical Oncology, Dana Farber Cancer Institute, MA, USA
6 Department of Stem Cell Transplantation and Cellular Therapy, University of Texas M.D. Anderson Cancer Center, Houston, TX, USA

Introduction

- The COVID-19 pandemic posed a major challenge in cancer care worldwide, which might have an impact on the management of life-threatening hematologic malignancies as aggressive lymphoma (1).
- Israel and Italy were affected differently by the COVID-19 outbreak, and changes in Diffuse Large B-Cell Lymphoma (DLBCL) characteristics, course, management and outcomes during the pandemic may vary.

Objective

To compare the characteristics. Management, and outcomes of DLBCL patients diagnosed during the first year of the COVID-19 pandemic compared to the previous year.

Methods

- **Retrospective cohort study** compared DLBCL patients diagnosed from 1/3/2020 to 28/2/2021 (the COVID-19 time) and those diagnosed between 1/3/2019 and 28/2/2020 (the pre-COVID-19 time) in two tertiary centers in Italy and Israel.
- Demographics, disease related, treatment and outcome data were extracted from EMR.
- The **primary outcomes** included 1-year-Progression-Free-Survival (PFS) and complete remission (CR) at the end-of-treatment-PET-CT
- **Secondary outcomes** included time from symptoms to diagnosis, time from diagnosis to treatment, dose density and intensity, febrile neutropenia, any hospitalization and COVID-19 infection.
- The median follow up periods during and before the pandemic were 15.2 months and 25.5 months, respectively.

Results

- 182 patients were diagnosed with DLBCL during the study period in both centers.
- The **Israeli** patients were **older** and had higher rates of **diabetes mellitus**, **hypertension**, **obesity** and poor performance status compared to the **Italian** patients.
- In the Italian cohort there was a trend towards older age at diagnosis during the pandemic compared to the year before.
- Five and four patients were diagnosed with COVID-19 during treatment in Italy and Israel, respectively.

Table 1 - Patients' characteristics and outcomes

	Italian Cohort		Israeli Cohort	
	Pre-Covid19 time (n=29)	Covid19 time (n=60)	Pre-Covid19 time (n=39)	Covid19 time (n=54)
Characteristics				
Age, years median (range)	61 (20-82)	67 (18-86)	70 (18-90)	71 (40-90)
Male sex, n (%)	15 (52)	38 (63)	26 (67) *	23 (43) *
ECOG 2-4, n (%)	2 (7)	5 (8)	16 (41)	15 (30)
Symptoms to diagnosis interval, days median (range)	41 (7-339)	64 (9-304)	73 (6-380)	81 (2-691)
Diagnosis to treatment interval, days median (range)	35 (1-229)	35 (3-83)	18 (0-55)	14 (0-92)
Elevated LDH, n (%)	16 (55)	29 (48)	25 (64)	34 (63)
Stage III-IV, n (%)	24 (83)	52 (87)	22 (56) *	55 (83) *
IPI 3-5, n (%)	15 (52)	29 (48)	21 (54)	31 (57)
Transformation, n (%)	5 (17)	7 (12)	5 (13) *	16 (25) *
Average interval between cycles, days median (range)	22.6 (21.0-29.8)	22.0 (18.6-42.0)	21.6 (20.0-34.4)	21.2 (20.5-29.6)
Treatment period, days median (range)	105 (49-108)	105 (42-250)	109 (100-172)	107 (103-148)
Dose reduction, n (%)	5 (17)	12 (20)	17 (44)	20 (37)
Hospitalizations, n (%)	7 (25)	21 (35)	20 (51)	17 (32)
Neutropenic fever, n (%)	3 (10)	6 (10)	12 (31)	10 (18)
Primary Outcomes				
E-PET-CT – CR, n (%)	25 (86)	43 (72)	29 (74)	38 (70)
1-year-PFS (%)	89.7	74.4	74.4	74.1

* - statistically significant (p<0.05)
Abbreviations: CR – complete remission; E-PET-CT – end of treatment positron emission computed tomography; ECOG – Eastern Cooperative Oncology Group performance status; IPI – international prognostic index; LDH – lactate dehydrogenase; PFS – progression free survival

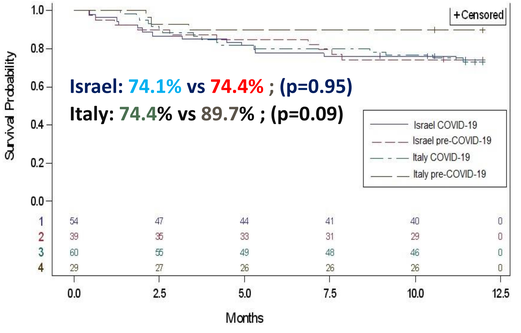


Figure 1: 1-year-PFS in the Israeli and Italian cohorts before and during COVID-19 time

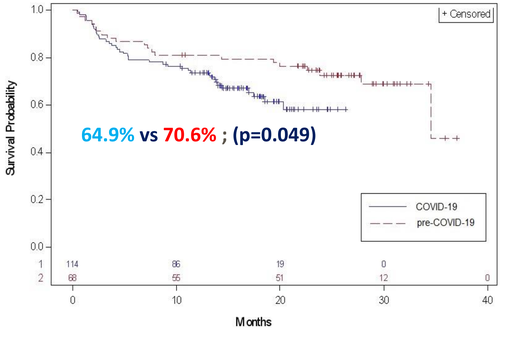


Figure 2: PFS before and during COVID-19 time

- In analysis for PFS of both cohorts (Italian and Israeli) together, PFS was shorter during the pandemic compared to the year before. See figure 2.
- In univariate analysis for PFS, diagnosis during the pandemic, older age, transformation from indolent lymphoma, advanced disease and gender were associated with in increased risk for progression.
- In multivariate analysis only age and transformation retained their prognostic significance for PFS. Diagnosis during the pandemic was not independently related to progression.

Conclusions

- In both cohorts, patients' characteristics were comparable between the periods.
- More patients were diagnosed with DLBCL during the pandemic, and the interval between symptoms to diagnosis was longer compared to the year before.
- Still, there was no difference in treatment in term of dose density and intensity.
- Diagnosis during the pandemic was not independently related to progression.

References

1. Shah V et al. *Br J Haematol.* 2020;190.