INTRODUCTION

The management of elderly patients over 80 years with diffuse large B-cell lymphoma (DLBCL) remains challenging, and evidence-based data for optimal treatment of these patients with decreased fitness and frequent comorbidities are lacking.

In the real world, the anthracycline-based chemotherapy regimens are often subject to attenuation or the patients are provided with less intense chemotherapy.

OBJECTIVES

The aim of this observational population-based multicentric study was to evaluate clinical features, treatment and outcomes of patients over 80 years of age with DLBCL prospectively and to determine the most effective treatment strategy.

This study was a part of prospective project NIHIL, registered in GovTrial (NCT03199066).

METHODS

From the total of 4473 patients diagnosed with de novo DLBCL during a 16-year period 1999-2014 in the Czech Republic (median age 64 years), 415 patients (9%) 80 years of age or older were registered.

372 patients with complete medical records and follow-up entered the final analysis:

- 53 patients (14%) didn’t receive any chemotherapy;
- 319 patients (86%) received chemotherapy:
  - 152 patients (41%) received first-line anthracycline-based regimens (CHT-A), from which 115 patients (31%) received CHT-A with rituximab (R-CHT-A), and 37 patients (9.9%) obtained CHT-A without rituximab;
  - 167 patients (45%) received other than CHT-A regimens with (n=97; 26.1%); R-CHT or without rituximab (n=70; 19%; CHT).

Important clinical parameters including performance status according to Eastern Cooperative Oncology Group (PS ECOG), clinical stage according to Ann Arbor staging system, International prognostic index (IPi), and age adjusted IPi (AA-IPi) were confirmed.

Responses to treatment were classified as overall response rate (ORR), complete remission (CR), partial remission (PR), stable disease, and progressive disease according to the criteria of Cheson 1999.

Primary endpoint of the study was the overall survival (OS), secondary endpoints included the progression-free survival (PFS), and the response rate to the therapy.

RESULTS

Patients population: The studied 372 elderly patients (median age 82 years; range 80-94 years) were diagnosed with:

- advanced clinical stage (III-IV) in 45%, worse PS ECOG (2-4) in 48%, higher IPi (3-5) in 52%;
- R-CHT-A group was significantly younger (age median 81 vs. 82 years, p=0.001), and had initial better PS ECOG compared to other patients (PS ≤ 35% vs. 50%; p=0.035).

The application of rituximab was more frequent in CHT-A (76%) than in CHT regimens (58%), with continuously increasing proportion in time, reaching 95% in CHT-A vs. 74% in non-CHT-A regimens during the last 4 years of observation. Median follow-up of the whole cohort was 42 months.

Outcome: Patients treated with rituximab reached more frequently CR (52%) in comparison to other treatment modalities (34%; p=0.031).

The addition of rituximab improved both OS, and PFS:

- in whole cohort (2-year OS 55% vs. 35%, HR 0.68, p=0.001; 2-year PFS 49% vs. 28%, HR 0.55, p=0.001);
- R-CHT-A vs. CHT-A (2-year OS 60% vs. 46%, HR 0.68, p=0.06; 2-year PFS 56% vs. 41%, HR 0.66, p=0.037);
- R-CHT vs. CHT (2-year OS 50% vs. 29%, HR 0.59, p=0.002; 2-year PFS 41% vs. 23%, HR 0.55, p=0.001).

Significantly improved ORR was observed in the group of patients treated by R-CHT-A regimens vs. other treatment modalities (76% vs. 52%; p=0.034).

Superior OS and PFS in the R-CHT-A group were also observed:

- R-CHT-A vs. other (2-year OS 60% vs. 42%, HR 0.59, p=0.001; 2-year PFS 56% vs. 34%, HR 0.57, p=0.001);
- R-CHT-A vs. with PS ECOG 2-4 (2-year OS 48% vs. 28%, HR 0.51, p=0.001; 2-year PFS 43% vs. 20%, HR 0.5, p=0.001).

CONCLUSIONS

- Anthracycline-based chemotherapy is used in approximately 40% of DLBCL patients ≥80 years old in the real-world settings.
- Rituximab reduces risk of death by 20% (whole cohort), and the benefit is hold even in chemotherapy without anthracyclines (risk reduction by 21%).
- The combination of rituximab and anthracycline-based chemotherapy leads to a superior outcome, but the patients have to be carefully selected.
- Rituximab should be used even if the patients are eligible only for chemotherapy without anthracyclines.

ACKNOWLEDGEMENTS

We are grateful to Jitka Dlouha and Marie Tmíkova from the Data Centre of the Czech Lymphoma Study Group for their contribution on data collection and analysis.

REFERENCES


CONTACT INFORMATION

Emails: tmery@cesnet.cz, prokop.vodicka@vfn.cz