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## Treatment strategy of patients with relapsed and refractory aggressive B-cell non-Hodgkin lymphoma

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## Background

Up to 40-50% of patients with aggressive B-cell non-Hodgkin lymphoma (B-NHL) remain refractory to treatment, or develop relapse (r/r) after 1-2 lines of therapy. The prognosis of this patient's group remains unfavorable. However, the emergence of new methods of targeted drug and immunotherapy (polatuzumab vedotin, Pola; glofitamab) may improve both progression-free survival (PFS) and overall survival (OS) rates in the patients with r/r B-NHL. The aim of our study was to suggest the treatment strategy for this population of patients, as well as to determine place for allogeneic hematopoietic stem cell transplantation (allo-HSCT).

## Patients and methods

The study included 28 patients (pts) with r/r B-NHL treated with a bispecific drug (anti-CD20/anti-CD3) glofitamab (G) within Russian Early Access Program. G was administered at escalated schedule, i.e., 2.5 mg D8C1, 10 mg D15C1, 30 mg D1C2-12. Anti-CD20 antibody was administered 1 week before the G therapy was started. Overall response rates (ORR), progression-free survival (PFS), overall survival (OS) were estimated in the course of G therapy, with regard of prior treatment strategy. Treatment efficacy was assessed by PET-CT (Lugano criteria). Adverse events (AEs) were assessed by the NCI CTCAE 5.0.

## Results

Median age at G initiation was 50 years (21-83); male/female ratio, 11/17 (39/61%). Median number of previous lines of therapy before G therapy was 3 (2-8). Autologous SCT was conducted in 7 pts (25%), polatuzumab vedotin (Pola) in 7 (25%) pts. ECOG status >1 before G initiation was registered in 7 cases (25%); B symptoms, in 6 pts (21%), and bulky disease was documented in 8 (29%) pts. Median follow-up was 6 (1-15.9) months. ORR was 67% in the total group: complete response (CR), in 15 (56%) pts; partial response (PR),

in 3 cases (11%); stable disease (SD), in one patient (4%); disease progression (PD), in 8 cases (30%). Eight patients died during G therapy including 5 pts (18%) who deceased due to disease progression. Eight patients died at the time of analysis, including PD in 5 cases (18%). Median OS was not reached, 6-month OS was 75.1% (95% CI, 52.0-88.2); median PFS was 10.7 months (95% CI, 5.4-NA); 6-month PFS comprised 58.8% (95% CI, 35.9-75.9). Other factors, e.g., number of previous lines of therapy, r/r clinical course, auto-HSCT, Pola therapy did not influence both OS and PFS, and development of response to G. In the course of analysis, 22 (79%) pts discontinued therapy due to PD (n=10, 36%); 5 pts (18%) had severe COVID-19 infection; 5 pts (18%) completed the scheduled therapy, and 2 pts (7%) cancelled their treatment by other reasons. The median number of G cycles was 6 (2-12). COVID-19 of any grade was revealed in 9 (32%) pts. Three pts (11%) died due to severe COVID-19. The group of patients who received Pola-BR (n = 7) before G therapy was also monitored: CR was achieved in 3 pts; PR, in 2 cases, and 2 pts developed PD. Among the patients who achieved CR during Pola-BR therapy (n=3), 2 pts had relapses during the therapy, and one patient, 11 months after Pola-BR completion. The achievement of response to Pola-BR did not influence clinical response to the G therapy.

## Conclusion

New targeted and immunotherapeutic agents significantly improve clinical prognosis in the patients with r/r B-NHL. However, curative potential of such therapy has not yet been determined, thus requiring long-term observation, as well as selection of the patients who will benefit from allo-HSCT.

## Keywords

Non-Hodgkin lymphoma, immunotherapy, targeted therapy, glofitamab, polatuzumab vedotin, adverse events.

## Стратегия лечения пациентов с рефрактерными/рецидивирующими агрессивными В-клеточными неходжкинскими лимфомами

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## Введение

До 40-50% пациентов с агрессивными В-клеточными неходжкинскими лимфомами (В-НХЛ) остаются рефрактерными или рецидивируют (р/р) после 1-2 линии терапии. Прогноз этой группы пациентов остается не-

благоприятным. Тем не менее, появление новых методов таргетной и иммунотерапии (полатузумаб ведотин, глофитамаб) в настоящее время позволяют улучшить как беспрогрессивную (БПВ), так и общую выживаемость (ОВ) пациентов с р/р В-НХЛ. Целью нашего исследования была оценка стратегии лечения этой популяции