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Treatment options for T-cell lymphomas: a single-center study

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Summary

T-cell lymphomas (TCL) comprise a group of aggressive non-Hodgkin lymphomas, which do not have successful treatment standards. Almost 70% of patients undergoing first-line therapy develop a relapse or refractory (r/r) disease. A number of novel therapy approaches are aimed for improvement of outcomes in patients with r/r TCL. This report summarizes clinical experience of Pavlov Medical University in the treatment of T cell lymphomas. We analyzed data of 47 patients with TCL treated from 2005 to 2019. Of them, 44 had r/r TCL, and 3 patients were in complete response after first line therapy. The median age was 45 years (range 1-72 years). These were predominantly patients with peripheral T-cell lymphomas not otherwise specified (TCL-NOS, 41%). 26 patients (55% of total) had a primary chemoresistant disease, while the remaining 18 patients (38% of total) had a relapse after initial treatment.

Our center has implemented new treatment options for r/r TCL, i.e., anti CD30 monoclonal antibody brentuximab, ALK inhibitor crizotinib, immunotherapy with checkpoint inhibitors nivolumab, and hematopoietic stem cell transplantation (HSCT). A total of 24 patients underwent: high-dose chemotherapy with autologous HSCT (auto-HSCT) was performed in 16 cases, 13 patients were subjected to allogeneic HSCT (allo-HSCT), including 5 relapsed patients after auto-HSCT. At the time of analysis, 35 patients remained alive. The median follow-up of surviving patients was 35 months (6-122 mo). The median overall survival (OS) was not reached, 5-year survival rate was 81%, and 8-year survival rate was 78%. Complete remission (CR) at the last follow-up was diagnosed in 22 patients; partial response (PR), in 4 cases, and progression of the disease (PD) was revealed in 21 patients. Among factors significantly associated with adverse prognosis were lower ECOG performance status and B-symptoms at the time of diagnosis (p=0.06). The patients who underwent HSCT showed significantly better disease status at the moment of last follow up: 17/19 (89%) were in CR, *versus* 5/16 (31%) among the patients not subjected to HSCT. 5-year overall survival rates after auto-HSCT and allo-HSCT were 87% and 77%, respectively. The results show that implementation of novel therapeutic agents, as well as consolidation with high-dose chemotherapy and auto- or allo-HSCT in selected cases improve outcomes in patients with r/r TCL. Brentuximab vedotin and nivolumab-based regimens may be successfully used as a bridge therapy before HSCT.

Keywords

T-cell lymphoma, autologous hematopoietic stem cells transplantation, allogeneic hematopoietic stem cells transplantation, brentuximab vedotin, nivolumab.

TREATMENT OF RELAPSED AND REFRACTORY T-CELL LYMPHOMAS: FIRST PAVLOV STATE MEDICAL UNIVERSITY OF SAINT-PETERSBURG EXPERIENCE

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Elena Lepik

Contributions

ABSTRACT

Abstract

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Background

T-cell lymphomas represent rare and heterogeneous group of aggressive non Hodgkin lymphomas. There are currently no standards for the treatment of relapsed/refractory T-cell lymphomas (r/r PTCL). A number of novel therapy approaches are aimed for improvement of outcomes in patients with r/r PTCL.

Aims

This report summarizes the First Pavlov State medical University experience in the treatment of patients with T-cell lymphomas.

Methods

We analyzed data of 34 patients with r/r PTCL eligible for stem cells transplantation treated in First Saint-Petersburg state medical University from 2005 to 2018. Among them n8 with anaplastic large cell lymphoma (ALK+), n3 with anaplastic large cell lymphoma (ALK-), n4 with angioimmunoblastic T-cell lymphoma, n5 with hepatosplenic T-cell lymphoma, n1 with γδ T cell lymphoma and n13 with PTCL not otherwise specified (PTCL-NOS). The median age was 46 years (range 11 – 73 years).

Median time from initial diagnosis to relapse or progression after primary therapy was 6.7 months (1,8-41). Among all patients n18 (53%) had a primary chemoresistant disease, while the rest n14 (47%) had a relapse after initial treatment. All patients received at least one line of salvage chemotherapy. The treatment was tailored according to biological factors presented in patients. In 7 patients with CD30+ PTCL the brentuximab vedotine was used. One patient with ALK+ anaplastic lymphoma received ALK inhibitor crizotinib. One patient with γδ TCL and PD-L1 hyperexpression was treatment with nivolumab. Responses were consolidated with hematopoietic stem cells transplantation. Overall 16 patients undergo SCT: high dose chemotherapy with autologous stem cells transplantation was performed in 10 patients, 11 patients underwent allogeneic hematopoietic stem cells transplantation (among them 5 patients with relapses after auto-SCT).

Results

At the time of analysis, 25 patients remain alive. The median follow up of alive patients was 29 months (1,5-101 mo). The median overall survival was not reached and 2-year survival rate was 82%. The disease status at the last follow up was CR in 15 patients, PR in 3 patients and PD in 16. Among factors significantly associated with adverse prognosis was lower ECOG performance status at the time of diagnosis (p=0,03). Patients that had underwent salvage SCT showed significantly better disease status at the moment of last follow up: 12/16 (75%) were in CR, versus 3/18 (17%) in patients who did not undergo SCT. No difference was found in OS between relapsed and primary refractory patients (p=0,73).

Conclusion

The results of analysis show that introduction of novel agents and consolidation with high dose chemotherapy and autologous stem cells transplantation or allogeneic stem cells transplantation in selected cases may improve outcomes in patients with relapsed and refractory peripheral T-cell lymphomas. Brentuximab vedotine based regimens may be successfully used as a bridge therapy before stem cells transplantation.

Session topic: 19. Aggressive Non-Hodgkin lymphoma - Clinical

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Abstract Submission

19. Aggressive Non-Hodgkin lymphoma - Clinical

EHA-3543

PLACE OF ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION IN PATIENTS WITH T-CELL LYMPHOMAS: PAVLOV UNIVERSITY RETROSPECTIVE STUDY

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Background: T-cell lymphomas (TCL) represent rare and heterogeneous group of aggressive non Hodgkin lymphomas. Unfortunately, 70% of patients undergoing first-line treatment, have relapsed or refractory (r/r) disease. Allogeneic hematopoietic stem cell transplantation (allo-HSCT), in turn, has the most solid evidence that it can significantly prolong survival or cure the disease. Patients with r/r T/NK-cell lymphomas who received HSCT (allogeneic and/or autologous) had a better outcome compared to the subset of non-transplanted patients (3-year survival rates of 48% and 18%, respectively [Bellei M., 2018]. This report summarizes our center experience in allo-HSCT of patients with r/r TCL.

Aims: To analyze the results of alloHSCT in patients with r/r TCL.

Methods: We analyzed data of 47 patients with TCL treated in Raisa Gorbacheva Memorial Research Institute of Pediatric Oncology, Hematology and Transplantation of Pavlov University from 2005 to 2019. 13 patients with r/r TCL underwent alloHSCT (among them 5 patients with relapses after autoHSCT). Among them 5 were with anaplastic large cell lymphoma (ALK+), 1 with angioimmunoblastic TCL, 1 with hepatosplenic TCL, 1 with γδ TCL, 5 with PTCL not otherwise specified. The median age at transplantation was 45 years (range 18 –57 years). The median number of lines of therapy before allo-HSCT was 4 (1-4). The median observation before allo-HSCT was 21 months (5-55 mo). 5 patients with CD30+ TCL had bridge therapy of brentuximab vedotin and 4 patients with PD-L1 hyperexpression had bridge therapy of nivolumab. The treatment was tailored according to biological factors presented in patients.

Results: At the time of analysis, 10 patients remain alive. The median follow up of alive patients was 17 months (2-59 mo). The median overall survival was not reached and 5-year survival rate was 77%. 5-year progression-free survival for patients with TCL after allo-HSCT was 61%. The disease status at the last follow up was CR in 9 patients and PD in 1. Patients that had undergo allo-HSCT showed significantly better disease status at the moment of last follow up: 9/10 (99%) were in CR, versus 5/16 (31%) in patients who did not undergo allo-HSCT.

Summary/Conclusion: The results show that introduction of novel agents and allo-HSCT in selected cases improve outcomes in patients with r/r TCL. Brentuximab vedotin and nivolumab based regimens may be successfully used as a bridge therapy before allo-HSCT.

Keywords: Allogeneic hematopoietic stem cell transplant, Immune therapy, Monoclonal antibody, T cell lymphoma

Abstract Submission

17. Hodgkin lymphoma - Clinical

EHA-3873

BRENTUXIMAB VEDOTIN THERAPY IN PATIENTS WITH RELAPSED OR REFRACTORY CLASSICAL HODGKIN LYMPHOMA AFTER ALLOGENEIC STEM CELLS TRANSPLANTATION: SINGLE CENTER EXPERIENCE

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Background: Allogeneic hematopoietic stem cell transplantation (alloHSCT) has the curative potential in patients with classical Hodgkin lymphoma (cHL). However, relapse rate after allo-HSCT remains high, ranging from 31% to 81%. Over the past decade, significant changes have occurred in the treatment of patients with refractory or relapsed cHL (r/rHL), such as the introduction of anti-CD30 immunoconjugate brentuximab vedotin (BV). BV harbours a potential for achieving disease control in the setting of cHL relapse after alloHSCT with minimal toxicity toxicity.

Aims: This report includes the analysis of our center experience of BV treatment in patients with relapse or progression cHL after allo-HSCT.

Methods: This report included 17 patients (pts) with cHL who underwent allo-HSCT at the R.M. Gorbacheva Memorial Institute of Children Oncology, Hematology and Transplantation (CIC 725). All patients had a relapse or progression of the disease after allo-HSCT and were treated by BV-containing regimens in our center. A total of 10 pts received BV therapy as a bridge therapy, and 4 of them had a BV treatment failure; one of 17 pts received nivolumab therapy before the transplantation. At the moment of allo-HSCT 7 pts (41,2%) had complete remission (CR); 4 pts (23,5%) had partial remission (PR); 5pts (29,4%) had stable disease (SD) and one (5,9%) had progression of disease (PD). Three patients (17,6%) undergone maintenance BV-therapy after allo-HSCT. At the relapse/progression 14 out of 17 pts had extranodal lesions. Median time from allo-HSCT to relapse or progression of cHL was 4 months (1,3-35,2 mo). Median time from cHL relapse or progression to BV-therapy after allo-HSCT was 1,2 months (0-40 mo). Thirteen (76,4%) patients received BV monotherapy (13/17pts), 2/17 pts (11,8%) received BV+bendamustine combination, 2/17 (11,8%) -A+AVD. Patients received from 1 to 9 (median 3) courses. Nine pts received DLI during BV therapy. Response was assessed after median of 3 courses of therapy (1-6). At the moment of analysis, the median follow-up from the start of BV treatment was 47 months (0,3-69,5 mo).

Results: Eleven patients (64,7%) achieved an objective response: 7pts (41,2%) achieved CR and 4pts (23,5%) -PR. The median time from start of BV-therapy to objective response was 1,7months (0,9-3,7 mo). Nine pts with objective response had progression of disease; the duration of response for these pts was 6,4 months (2,5-27,2mo). At the time of analysis 12 pts remain alive. The median overall survival (OS) was not reached and 3-year OS was 70,6%. The median progression free survival (PFS) was 6 months (5,6-6,3 mo). Six month PFS was 47,1%. The disease status at the last follow up was CR in 6 pts, PR in 2 pts; 5 pts are continuing posttransplant therapy: 4pts with nivolumab-containing regimens (including: 1 pt with CR and 1pt with active cHL are nivolumab monotherapy, 1 pt with PR is nivolumab+lenalidomide, one with active cHL is nivolumab+gemcitabine), 1pt is continuing BV-therapy and 1pt does not receive treatment because of pregnancy. Among factors significantly associated with favorable prognosis were the following: regarding the OS the combination of BV- containing courses with donor lymphocyte infusion (BV+DLI) 88,9% vs 50% (p=0,025); regarding PFS the combined regimens of BV+bendamustine or A-AVD vs mono BV (100% vs 30,8% respectively (p=0,025).

Summary/Conclusion: Brentuximab vedotin shows efficiency in patients with relapse or progression of cHL after allo-HSCT. However, response was not durable, therefore the search for novel therapeutic regimens in this heavy pretreated patient group is needed.

Keywords: Bone marrow transplant, Hodgkin's lymphoma, Relapse, Treatment

Interim analysis of effectiveness and safety of Nivolumab 40 mg in relapsed/refractory Hodgkin lymphoma

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Introduction

Aim of the study was to determine effectiveness and safety of therapy with Nivolumab 40 mg in patients with relapsed/refractory Hodgkin lymphoma.

Materials and methods

Intermediate analysis included 14 patients with relapsed/refractory Hodgkin lymphoma who were treated with nivolumab 40 mg once per 14 days until disease progression/unacceptable toxicity. Response was assessed by PET/CT using LYRIC criteria every 3 month (6 cycles). The safety was estimated by registration adverse effects according to NCI CTCAE 4.03.

Results

Median follow-up time was 10 months. Median number of treatment cycles with nivolumab was 17 (12-22). Median dose of drug was 0,56 mg/kg (0.4-0.91 mg/kg). 9 patients (64.3%) achieved an objective response, 5 (35.7%) a complete response (CR), and 4 patients (28.6%) a partial response. 4 patients (28.6%) had intermediate response as their best response. Two (14.3%) patients had progressive disease (at the moment of 12th and 18th cycles). Ten (71.4%) patients had adverse effects (AE). Grade ¾ AE were reported in 3 (21%) patients and included an anemia, arthritis and hepatitis. In general, the treatment was well tolerated and the toxicity profile was similar to the previously published data.

Conclusion

According to the intermediate analysis, the structure of the response to therapy in patients treated with nivolumab 40 mg was comparable to patients treated with nivolumab in standard dose (3 mg/kg). The distribution of frequency, time of occurence and structure of adverse events was also similar to the standard therapy group. In conclusion, our data indicates that nivolumab 40 mg can be an effective and safety treatment option for R/R HL patients, but it's nessesary to continue the study to obtain the final results.

Keywords

Hodgkin lymphoma, nivolumab, immunotherapy, PD1 inhibitors, relapsed lymphoma, refractory lymphoma.

Промежуточный анализ эффективности и безопасности терапии ниволумабом в дозе 40 мг в лечении рецидивирующей и рефрактерной лимфомы Ходжкина

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Введение

Целью работы была оценка эффективности и безопасности терапии ниволумабом в дозе 40 мг у пациентов с рецидивирующей/рефрактерной лимфомой Ходжкина.

Материалы и методы

В промежуточный анализ были включены 14 пациентов с рецидивирующей/рефрактерной лимфомой Ходжкина. Ниволумаб в дозе 40 мг вводился 1 раз в 2 недели до прогрессирования заболевания или развития тяжелых нежелательных явлений. Каждые 3 месяца (6 введений) производилась оценка ответа на терапию при использовании критериев LYRIC по данным ПЭТ/КТ, а также оценка наличия нежелательных явлений на терапию в соответствии с критериями NCI CTCAE 4.03.

Результаты

Медиана наблюдения составила 10 месяцев. Медиана введений ниволумаба 17 (12-22). Медиана дозы препарата составила 0,56 мг/кг (0,4-0,91 мг/кг). Объективный ответ был получен у 9 (64,3%) пациентов, полный ответ у 5 (35,7%) и частичный ответ у 4 (28,6%) пациентов. Неопределенный ответ установлен у 4 (28,6%) пациентов. За время наблюдения у 2 (14,3%) пациентов было зафиксировано прогрессирование заболевания (после

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Impact of renal impairment on bortezomib-based treatment outcome in patients with plasma cell disorders

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Introduction

About 50% of newly diagnosed multiple myeloma (MM) patients have renal impairment (RI), 20% have acute kidney injury (AKI), and ~1–5% need hemodialysis at diagnosis. We evaluated the RI prevalence and its impact upon survival of patients with plasma cell disorders (PCD) treated at our center.

Patients and methods

We analyzed 258 consecutive patients with PCD treated in the I. Pavlov First St. Petersburg State Medical University since 2008 to 2017. 97 patients with systemic AL-amyloidosis were excluded. 71 patients with renal impairment were identified (RI-group): 62 (87.3%) with MM and 9 (12.7%) with monoclonal gammopathy of renal significance. All patients received bortezomib-based chemotherapy, but the response data was available only for 51 (81.7%) of the RI-group patients. Myeloma response and progression were accessed using International Myeloma Working Group definitions. The Kidney Disease Improving Global Outcomes (KDIGO) guideline was used to asses RI and AKI. Complete renal response (CRR) was defined by proteinuria levels of 0.5 g/24 h or less, with albuminemia levels of 30 g/L and no more than 10% decrease in glomerular filtration rate (eGFR, estimated by MDRD formula) from baseline value. Partial RR (PRR) was defined by posttreatment proteinuria between 0.5 and 2.5 g/24 h, or by 50% or more reduction from baseline value, with albuminemia levels of 25 g/L or more and no more than a 10% decrease in eGFR from baseline value. 40 patients (56.3%) underwent renal biopsy.

Results

Median follow-up was 621 day (93-3124). Median eGFR in RI-group at initial diagnosis was 23.03 (0.03-77.9) mL/min/1.73 m^2, median proteinuria was 6 g/day (0.15 – 33.95). In RI-group 23 patients (32.3%) had AKI greater than stage 1, 51 patients (57.7%) had severe RI (eGFR <30 ml/min/1.73 m^2), 14 (19.7%) patients needed of dialysis. Renal lesions included cast nephropathy (n=9, 22.5%), light chain deposition disease (n=9, 22.5%), C3 – glomerulopathy (n=3, 7.5%), light chain amyloidosis (n=13, 32.5%), tubulointerstitial nephritis (n=3, 7.5%), membranoproliferative glomerulonephritis (n=1, 2.5%). One patient presented with focal segmental glomerulosclerosis. After first-line therapy, 33% achieved complete hematological response, 20.5%, very good partial response, 35.9%, partial response. Median time to RR was 87 days (10 to 570). Complete RR, partial RR and no RR were estimated in 26.6%, 46.6%, 26.8% of RI-group patients, respectively. Median eGFR in RI-group after the first-line therapy significantly increased to 36 (11.28 – 88.9) mL/min/1.73 m^2 (p=0.001), median proteinuria significantly decreased to 0.64 (0-26.4) g/day (p=0.00007).

In presence of AKI, including dialysis-dependent conditions, RR did not influence overall survival (OS) and progression-free survival (PFS) in RI group (p>0.05).

Moreover, there were no statistically differences in overall survival and progression-free survival between RI-group and RI-free patients (n=90; p>0.05).

Conclusion

In our study, patients with plasma cells disorders frequently had detectable renal impairment, but it did not significantly influence overall and progression-free survival.

Keywords

Plasma cell disorders, chemotherapy, bortezomib, renal function, survival.