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Material and Method
A total of 4 children with a median age of 16 (range, 11-17) with refractory AML were enrolled in the study. Peripheral blood samples of 4 haploidentical donors (3 mothers and 1 father) with a median age of 42.5 years (range, 40.6–50.4) were the source of PBMCs for NK cells expansion. NK expansion was induced by co-culturing of donor PBMCs with feeder line K562-mbIL-21-41BBL obtained in our laboratory.
Course of immunotherapy consisted of a block of FLAG-based chemotherapy followed by NK cells infusions (from 1 to 3) during the period of cytopenia. NK cells were administered intravenously on day 0. Two patients received six dose of IL-2 ($1x10^6$ IU/m^2, Roncoleukin, LLC NPK BIOTECH, Russia) every second day starting on day -1, one patients received one dose of IL-2, another one was treated without IL-2.

Results
Totally 4 patients received 9 infusions of NK cells. The purity of NK cells was 95.5 % (77.3-98.3), median dose of infused NK cells was 4.1 (1.2-8.8)*10^7/ kg, CD3+ cells – 0.9 (0.8-11.5)*10^6 / kg. The majority of obtained NK cells had the phenotype of immature activated cells (NKG2A+, double bright CD56++CD16++, CD57-) expressing NKp30, NKp44, NKp46, NKG2D, CD69, HLA-DR and CD96.

Patient #1 received two courses of immunotherapy with one NK cells infusion per course. This patient achieved complete morphological remission (CRm) and received matched unrelated HSCT, is alive (+667 days).

Patient #2 received one course of immunotherapy with two NK cell infusions. After immunotherapy the level of blast cells in bone marrow decreased from 47.7 to 9.5%. However, the patient did not get the second course of immunotherapy because of infection status. The patient died from progression (+260 day).

Patient #3 received one course of immunotherapy with two NK cell infusions, achieved CRm and received matched related HSCT, is alive (+464 days).

Patient #4 received one course of immunotherapy with three NK cell infusions, achieved CRm. Further treatment was delayed because of infection complications. The patient is alive (+87 days).

Conclusions and Recommendations
Infusions of haploidentical ex vivo expanded NK cells were safe and well tolerated, provided clinical response in 3 out of 4 poor prognosis patients with refractory AML. Encouraging results stimulate us to continue the investigation of NK immunotherapy for patients with AML.

14. VRd Regimen for Treatment of Vertebral Plasmacytoma with Spinal Cord Compression

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Introduction and Aim
Patients with relapsed multiple myeloma (MM), who have received several lines of chemotherapy (CT), have limited specific treatment options and low probability to achieve a complete response. MM relapse increases the risk of secondary infiltration of the body's organs and systems due to soft tissue extramedullary tumors. Aimis to present the results of patient's management with relapsed MM, which clinically manifested by spinal cord compression on the background vertebral plasmacytoma development at the level of Th5-Th7, the effectiveness of combined CT with bortezomib, lenalidomide and dexamethasone was evaluated.

Case report
Our case report involves a patient born in 1971, with light Kappa chains Multiple myeloma stage III A (Durie, Salmon), with bone lesions of the skull, ribs, spine (wedge-shaped vertebrae deformation C6, Th3, 5, 7, 8, 9), pelvic bones, femurs, vertebral plasmacytoma at the level of Th5-Th7 with secondary acute spinal cord compression, ischemic myeloneuropathy and senestopathic syndrome.
In August 2020 she was hospitalized to the hematology department of PE "Poltava Regional Clinical Hospital n.a. M.V. Sklifosovsky PCR" with complaints of pronounce sensitivity decrease, paresthesia in the lower extremities, gait disorders, loss of pelvic functions control.

From the anamnesis it is known that patient was diagnosed with multiple myeloma in September 2012 based on changes in the myelogram: 44% of plasma cells. The patient had received 3 lines of chemotherapy (CT): 1) VAD

(vincristine, doxorubicin, dexamethasone) in 2012 with a partial response; 2) TCD (thalidomide, cyclophosphamide, dexamethasone) in 2015; 3) and a similar course of TCD in 2018 with further maintenance therapy with thalidomide until December 2019.

The progression of MM was recorded in August 2020. Clinically, MM relapse manifested by progressive neurological symptoms, pelvic dysfunction. The level of free Kappa light chains in the serum was 344.0 mg/l (norm up to 19.4 mg/l). MRI with contrast of the thoracic and lumbar spine diagnosed an intradural extramedullary plasmacytoma of the vertebral canal at the level of Th5-Th7 with spinal cord compression.

In order to treat the third MM relapse, the patient was offered the 4 line of CT: VRd regimen (bortezomib 1.3 mg/m^2 1, 4, 8, 11 days, lenalidomide 25 mg per day 1-21 days, dexamethasone 20 mg per day 1, 2, 4, 5, 8, 9, 11, 12 days). After the third course of CT, the general condition of our patient significantly improved, sensitivity in the lower extremities and control of pelvic organ functions were restored.

After 8 courses of VRd regimen, a very good partial response was achieved according to the criteria of the International Myeloma Working Group (IMWG): free Kappa light chains in the blood serum decreased to 33.8 mg/l by 90.2% lower. According to MRI of the thoracic and lumbar spine, the extramedular neoplasm on the Th6 vertebrae level significantly reduced, there are myelopathic changes in the spinal cord at this, which occurred after the spinal cord compression by plasmacytoma. After completing the VRd in April 2021, the patient was followed by lenalidomide maintenance. To date, no progression of MM was recorded during the 12-month period.

Discussion and Conclusions
Combined chemotherapy with bortezomib, lenalidomide, and dexamethasone may be the treatment of choice for relapsed patients with soft tissue extramedullary plasmacytomas.

15. *CALR* 52 bp Mutation Impairs Oxidative Stress Response and Increases Oxidative Stress-Induced Apoptosis Level in UT-7 Cell Line

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Background and Objectives
BCR-ABL1-negative classic myeloproliferative neoplasms (MPN) include primary myelofibrosis, polycythemia vera, and essential thrombocythemia. Calreticulin (*CALR*) 52 bp deletion and 5 bp insertion were discovered to be involved in MPN pathogenesis, particularly in *JAK2* and *MPL* unmutated essential thrombocythemia and primary myelofibrosis. Calreticulin, a Ca^{2+}-binding chaperone, is implicated in Ca^{2+} homeostasis, protein folding, and response to oxidative stress. It is well known that oxidative stress induces the accumulation of reactive oxygen species (ROS) that damage membrane lipids, proteins, and DNA. Moreover, several studies demonstrated that MPN patients show high serum levels of intracellular ROS, which can lead to chronic inflammation and genomic instability. However, there is not much data on how mutated calreticulin affects oxidative stress response and oxidative stress-induced apoptosis. Therefore, we aimed to investigate the response to oxidative stress and apoptosis induction in UT-7 cells expressing either *CALR* WT or *CALR* 52 bp deletion.

Material and Method
The UT-7 cell line was used in our study. CRISPR/Cas9 system was chosen for *CALR* 52 bp deletion initiation in cells. After the selection of potential DNA targets in gDNA, corresponding tabs were cloned into a vector (pSpCas9(BB)-2A-Puro (PX459) V2.0) that is optimized for Cas9 and RNA-guided expression in eukaryotic cells. Transfection of plasmid construct and HDR template into UT-7 cells was performed by electroporation. The following electrotransfection parameters were applied: 1 HV pulse of 1600 V/cm with 500 μs pulse duration and the electroporation system BTX T820 was used. The transfected cells were selected in puromycin (1 μg/ml). Further, UT-7 cells expressing WT and *CALR* 52 bp deletion were treated with H_2O_2 for 24 hours. The intracellular oxidative stress and apoptosis induced by H_2O_2 were measured by means of Muse® Oxidative Stress Kit and Annexin V & Dead Cell Kit, respectively. Cells were examined using the Muse® Cell Analyzer and at least 5000 events were detected for each sample.

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