auto-HSCT. The conditioning regimens had acceptable toxicity. Complications grade 3-4 were observed in 36% of cases after the first HDCT and in 24% cases after the second HDCT. The main complications were severe mucositis, infections and hepatotoxicity. Two-year overall survival (OS) in all patient's group was 70% and disease free survival (DFS) was 59%. DFS rate of patients who had received tandem HDCT was 65%, while all patients who had received only the first auto-HSCT died (8 – due to disease progression, 1 – after acute neurological complication). Patients in CR at the moment of HDCT had better DFS rate than patients in PR: 75% and 51% (p=0,043), respectively. **Conclusions:** tandem HDCT with auto-HSCT in pediatric patients with high-risk CNS tumors may be a feasible option for patients in CR or PR after induction chemotherapy. It has an acceptable toxicity.

RES-086

Distribution Chemotherapy Response Modulating Genetic Polymorphisms in Armenian Population

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Primary chemotherapy drug resistance is a one of the major issues of medical hematology-oncology affecting about 20% of all patients. In Armenia, clinical data suggest that the rate of primary resistance depends on the disease and treatment type and varies in the range of 10-30%. One of the mechanisms of resistance is a drug inactivation mediated by metabolizing enzymes and it has been known that the variability of those genes contributes to the response to drugs and treatment efficacy. In Armenia a number of drugs are used for treatment acute and chronic hematology-oncological diseases, such as doxorubicin and vincristine (leukemia or lymphoma), rituximab (lymphoma), cladribine (hairy cell leukemia), interferon alfa-2a (chronic myeloid leukemia) and asparaginase (acute lymphoblastic leukemia). However, the distribution of genetic polymorphisms that modulate response to the above mentioned drugs in unknown in Armenians. In this study we were aimed at performing pilot characterization of distribution of single nucleotide polymorphisms affecting chemotherapy treatment response in Armenian population.

We used genome wide genotyping data of 168 healthy Armenians from three freely available datasets used in population genetics studies. 112 single nucleotide polymorphisms (SNPs) interfering the mentioned treatment agents were obtained from PharmgKB database. The distribution of allele frequencies in Armenians was compared to the allelic rates in European population available in 1000 Genomes and HapMap project (retrieved using LDLink software).

Minor allele frequency (MAF) associated with altered response to drugs (Table 1) varied in the range of M±SD: 0.25±0.14, minimum-maximum: 0.00-0.49. The minor allele frequency of 18 SNPs was significantly higher in Armenians compared with European population. Another 18 SNPs were significantly underrepresented in Armenians. Six SNPs (MAF min-max: 0.22-0.48) were associated with the altered response to 5 and more drugs.

Table 1 Number of Chemotherapy Response Associated SNPs and Their MAF Distribution

Drug/Treatment	N, SNPs	MAF min-max
Doxorubicin and Vincristine	28	0.05-0.49
Rituximab	14	0.05-0.44
Cladribine	2	0.10-0.28
Interferon alfa-2a	13	0.28-0.46
Asparaginase	2	0.24-0.46

Our preliminary results demonstrate the overall enrichment of genetic factors connected to the risk of failure and toxicity of chemotherapy in Armenian population and necessitate the further research on their cumulative impact on the chemotherapy response in patients with blood cancers.

RES-092

Investigating the Mechanisms of Methotrexate Neurotoxicity in Patients With Childhood Leukemia and Long-Term Survivors

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Background/Objectives: Adverse neurological events are common (4-20%) during treatment for pediatric acute lymphoblastic leukaemia (ALL) and include seizures, stroke like syndrome and leukoencephalopathy. In addition, chronic neurotoxicity is emerging as a worrying late effect of treatment with long-term survivors experiencing decreased executive function, processing speed and memory function. Survivors are also at increased risk of experiencing learning difficulties, social withdrawal issues and inattention hyperactivity disorders. Methotrexate, an anti-folate chemotherapy agent, is a mainstay of pediatric leukemia treatment regimens globally and is widely implicated as a cause of these neurological side effects. We hypothesise that methotrexate disrupts DNA methylation via effects on S-adenosyl methionine, a key metabolic component that has previously been described to regulate genes involved in myelination. **Design/Methods:** Using both the oligodendrocytic-like cell line MO3.13 and glial cells derived from induced pluripotent stem cells (iPSC) treated with methotrexate, we assayed for changes in DNA methylation and effects on gene expression using whole-genome methylation arrays and RNAseq, respectively. Genes with corresponding methylation and expression

changes were selected for further studies of expression by real-time qPCR and assessment of protein levels. **Results:** We identified DNA methylation and corresponding expression changes in genes involved in neurodevelopmental pathways and neurological disorders. Of particular interest was dose-dependent demethylation and increased gene expression of *IRS1*, a vital component of insulin signalling pathways that is highly expressed in neural tissue and implicated in regulating cognitive performance. We also detected altered DNA methylation within the *PLP1* gene, which encodes the most prevalent protein component of myelin. We found that methotrexate treatment in iPSC-derived oligodendrocytes resulted in increased *PLP1* methylation associated with a reduction in *PLP1* transcript levels as well as PLP1 protein levels. **Conclusions:** Our work provides insight as to the biological mechanisms behind methotrexate-induced neurological side effects for the first time and implicates altered insulin signalling and myelination pathways as a potential causative factor in neurotoxicity. Further work including the use of animal models is warranted for advancing these results towards informing clinical practice.

The authors would like to thank the JGW Paterson Foundation, the European Association for Cancer Research and Worldwide Cancer Research for supporting this project.

RES-095

Outcome of Neutropenic Fever in Hospitalized Cancer Patients During a One-Year Follow-up: A Single Center Experience

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Context: Febrile neutropenia is a relatively frequent event among cancer patients treated with chemotherapy. Since these patients lack the appropriate immunologic response, early recognition and empiric treatment is crucial. **Objective:** This study was conducted in order to determine the outcome and mortality rate of febrile neutropenia in patients admitted to a university hospital during one year, and to evaluate the accuracy of management. **Methods:** An epidemiologic, prospective study was conducted at the hematology-oncology unit at Notre Dame de Secours University hospital from September 2015 until December 2016. All adult patients admitted to the hospital with the diagnosis of febrile neutropenia were included. A statistical analysis was conducted to identify factors related to poor outcome and overall mortality rate. **Results:** Median age at the onset of febrile neutropenia was 61 years with a female predominance (64.7%). At diagnosis, 23 patients were already hospitalized (45.09%) and 28 were outpatients (54.9%). Patients were divided according to the MASCC score into three categories 47.1% mild, 31.4% moderate and 21.6% severe neutropenia. 50.98% of patients were found to have solid tumors while 49.01% had hematologic malignancies.

In 66.7% of the cases the causative germ was not identified; cultures grew Staph epi in 13.8%, followed by E.coli in 9.9% of the cases.

6 patients passed away (11.8%), 4 of them died from a septic choc, and one patient died of candidemia. All 6 patients were classified as severe by the MASCC score and they were well treated. **Conclusion:** Our study demonstrated that the overall mortality rate in our institution is comparable to international centers. In most cases, no germ is identified in cultures which justify the usage of broad spectrum antibiotics. The initial choice of antibiotics in our institution meets the international recommendations.

RES-096

Development of a Prognostic System to Predict the Response to Treatment of Neutropenic Fever in Patients With Hematological Malignancies

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Context: Predicting the response to treatment for NF is critical in patients with hematological malignancy. **Objective:** To evaluate different risk factors affecting treatment outcome. **Design:** A prospective observational study includes patients with haematological malignancies who presented to NEMROCK. Study conducted between 1st of June 2014 till the end of October 2015. **Setting:** This study demonstrated new risk factors to be considered in hematological malignant patients. **Patients or other participants:** All adult patients with hematological malignancies presented to NEMROCK with a NF attacks were included in the study. A total 142 patients suffered from 270 NF episodes. **Interventions:** According to the MASCC score, high risk patients were treated inpatients. All admitted patients were subjected to blood culture

Table 1 Multivariate Analysis

Variable	Odds ratio	95% CI		P value	WPS
Previous NF episode	1.47	0.307	7.023	0.63	–
Moribund	3.677	1.2	11.265	**0.023**	**2**
Hypotension	5.609	1.711	18.392	**0.004**	**3**
Previous fungal infection	1.905	0.407	8.91	0.413	–
Uncontrolled disease	4.222	1.019	17.493	**0.047**	**2.5**

The prognostic score ranged from 0 (best prognosis) to 7.5 (worst prognosis). Cut-off value of 4.5 was determined and it divides patients into two groups, ≤4.5 vs. >4.5