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Overview of scientific reports and lectures at the XI Raisa Gorbacheva Meeting Hematopoietic Stem Cell Transplantation. Gene and Cellular Therapy (September 14-16, 2017, St. Petersburg, Russia)

Boris V. Afanasyev

R. M. Gorbacheva Memorial Institute of Children Hematology, Oncology and Transplantation, Chair of Hematology, Transfusiology and Transplantology, Pavlov First St. Petersburg State Medical University, L. Tolstoy St. 6-8, 197022, St. Petersburg, Russia.

Phone: +7(812) 338 6265
E-mail: bvafan@gmail.com

Summary

In September 2017, St.Petersburg hosted a regular meeting which was dedicated to the issues of hematopoietic stem cell transplantation and related problems. Special attention was drawn to application of novel targeted drugs in treatment of lymphoproliferative diseases, especially, Hodgkin's disease treated by means of brentuximab, and more recently, the lymphocyte apoptosis inhibitors (PD1 inhibitors). When treating acute myeloid leukemias with tyrosine kinase inhibitors (TKIs), a novel drug Sorafenib (an FLT3 inhibitor) is now introduced.

A strategy of chronic myeloid leukemia (CML) management and, an opportunity of their stoppage upon a long-term molecular remission were also discussed at the meeting. In chronic myeloproliferative disorders, drugs inhibiting oncogenic JAK kinase (e.g., ruxolitinib) are actively implemented. Upon treatment of acute lymphoblastic leukemia and other lymphoproliferative disorders, a number of monoclonal antibodies (e.g., rituximab or blinatumomab) are widely introduced, along with conventional cytostatic treatment protocols.

Some reports concerned new approaches to allogeneic HSCT, i.e., from a haploidentical donor, thus, together with optimal GHVD prophylaxis, results into clinical outcomes comparable to those achieved with unrelated HLA-compatible transplants. Several reports were dedicated to GVHD prophylaxis by means of cyclophosphamide post-transplant.

The issues of immune therapy in leukemias were discussed as a result of clinical implementation of specific recombinant cytotoxic antibodies and gene-modified T cells with chimeric antigens which are potentially able to destroy malignant cells in some oncohematological diseases.

A separate mini-symposium dedicated to gene therapy and outlooks for gene editing using some known enzyme systems (e.g., CRISP/Cas9 and TALEN), along with problems of legal regulation and cellular therapy. Moreover, a special session was performed for medical nurses who discussed urgent tasks and functions of nursing staff at the HSCT departments and intensive therapy.

Keywords

St. Petersburg, symposium, hematopoietic stem cell transplantation, target therapy, immune therapy, combined therapy, gene therapy.

Modern issues in lymphoproliferative diseases

A special educational session was arranged by the leading Russian clinicians performing studies of target drugs in oncohematology. I.e., Prof. Vadim V. **Baikov** (St. Petersburg) described the modern principles of diagnostics of different CD30+ lymphomas which are now successfully treated with Brentuximab vedotin targeted against CD30 antigen on the surface of malignant cells as well as a distinct role of Epstein-Barr virus for CD30+ expression.

Dr. Natalya B. **Mikhailova** (St. Petersburg) shared her clinical experience of PET-CT-guided treatment of refractory/resistant Hodgkin's lymphoma based on introduction of novel targeted drugs Brentuximab) into conventional treatment regimens (BEACOPP), or as monotherapy. Brentuximab may be also used as a second-line treatment, following auto-HSCT. Similar anticancer effects were obtained by Dr. I. **Belousova** upon treatment of CD30+ lymphomas manifesting with skin lesions.

Prof. Boris V. **Afanasyev** presented important data on application of anti-CD30 and PD-1 inhibitors in refractory/resistant Hodgkin's lymphoma patients. In this respect, brentuximab vedotin and Nivolumab proved to be effective as a «bridge» therapy before allo-HSCT and promising in combination with chemotherapy and allo-HSCT.

Dr. Maria O. **Ivanova** (St. Petersburg) reported clinical improvement in refractory/resistant chronic lymphocytic leukemia upon treatment with Ibrutinib, a specific inhibitor of the Bruton kinase.

Multiple myeloma was discussed in several reports. E.g., Dr. J.-M. **Tangen** et al. (Oslo, Norway) presented a population study comparing survival of myeloma patients ≤65 years with multiple myeloma in South-Eastern Norway 2001-2010. Median survival terms within period proved to be 20 months longer that what was found in the previous Nordic study. It is assumed that this result reflects the impact of new drugs introduced over last 10-15 years.

Acute leukemias

Professor Arnon **Nagler** (Jerusalem) prepared a comprehensive review on modern AML diagnostics and treatment. Detailed DNA- and cytogenetic diagnostics allows to develop an AML classification based on genetic and other prognostic factors. Hence, the therapy in CR1 AML allows risk-adapted strategies based on dozens of gene mutations and minimal residual disease (MRD) levels during post-treatment period. Transplant decision in AML CR1 should take into account molecular prognostic risk factors. Allo-HSCT with myeloablative conditioning is recommended for unfavorable cases in 1st remission. A machine learning algorithm was tested to predict early posttransplant mortality. MRD is the most important for relapse risk and overall survival. Sorafenib and other FLT3 inhibitors are effective as maintenance therapy after allo-HSCT in CR1 in cases of FLT3-ITD AML. In favorable cases, in 1st remission, allo-HSCT may be avoided, auto-HSCT is possible in these cases at low MRD levels.

Professor Robert Peter **Gale** (London–LosAngeles) addressed the question of the factors which influence selection of AML patients for allo-HSCT in clinical trials. In his opinion, there are evident and latent variables which may influence the doctor's decision in HSCT, and their contribution changes with time after starting CML treatment. Among the latent variables there are: minimal residual disease, mutation landscape and leukemia stem cell profile. Hence, a big deal of uncertainty exists when a doctor is deciding on HSCT option.

Professor Dieter **Hoelzer** (Frankfurt a/M, Germany) concerned the current role of HSCT for high-risk or refractory/relapsed ALL treatment in modern era of targeted drugs. The conclusions are based on analysis of several trials. In summary, HSCT is recommended in the 1st complete remission. In MRD positive cases, immunotherapy may be beneficial. In Ph+ ALL, TKIs combined with immunotherapy (Inotuzomab, Blinatumomab, CAR-T cells) are also promising. In general, such immunotherapies increase clinical response rates and MRD results.

Professor Valery G. **Savchenko** (Moscow) presented the data concerning strategy of allo-HSCT for adults in 1st remission of Ph-negative ALL which should be done in high-risk patients. Different treatment protocols define different risk factors. The cases with t(4;11) aberration seem to be essentially transplanted. Allocation of allo-HSCT in adults with Ph-negative ALL in the 1st CR should be done according to indications related to a distinct protocol.

Chronic myeloproliferative diseases

A lecture concerning long-term survival in CML with imatinib *versus* HSCT as first-line treatment was presented by Prof. Rüdiger **Hehlmann** (Heidelberg). As based on the European CML studies, he postulated a decisive role of Imatinib and other TKIs for a longer survival and deeper molecular remission. Outcome of CML is currently more determined by disease biology, patients' demographics, e.g., smoking and micro-economic elements than by initial treatment selection. At the present time, Imatinib withdrawal is possible at long-range periods. However, 10-years deep molecular remission rates of 70-80% indicate that the majority of IM treated patients are candidates for treatment discontinuation.

Professor Axel **Zander** (Hamburg–Utah University) presented a big lecture on the place of stem cell transplantation for myeloproliferative diseases (MPD). Among broad spectrum of myeloproliferative diseases, he mainly addressed chronic myeloid leukemia (CML) that was previously treated with allo-HSCT. With advent of Imatinib, tyrosine kinase inhibitors (TKIs) became the frontline therapy for newly diagnosed CML. However, in advanced/relapsing CML, HSCT remains a rescuing option. In primary myelofibrosis, allo-HSCT is a common treatment, with results depending on the underlying molecular mutation. Ruxolitinib is effective during pre-transplant period. In chronic myelomonocytic leukemia, allo-HSCT sufficiently increases the chance for survival which is higher with hypomethylating drug treatment before transplant. In systemic mastocytosis, ASXL1 and/or CBL mutations are associated with low survival terms. In summary, general recommendations are given for allo-HSCT in different MPDs.

Prof. Nicolaus **Kröger** (Hamburg) reported his opinion on the role of HSCT in myelodysplastic syndrome (MDS) treatment. It was demonstrated that MDS is a genetically heterogenous disease with multiple somatic mutations influencing the outcome. Survival rates differ substantially, depending on molecular and other risk factors which are encountered in elderly patients including age, comorbidities, transfusion dependency etc. Novel treatment approach using 5-azacytidine is not curative but prolongs survival. HSCT may eradicate the disease but treatment-related mortality is high. IPSS and other scoring systems are used to assess the risks of transplant.

Prof. Anna **Turkina** (Moscow) reported about the TARGET project based on data obtained by an Internet-based questionnaire for hematologists. The study covered various regions; 614 doctors worldwide participated in this study which aimed to get real data on diagnostics and management of CML patients in routine clinical practice. Sufficient data are provided on the drugs used at different clinics (mostly Imatinib generics), and relatively uniform diagnostics in various institutions.

Dr. António **Almeida** (Lisbon, Portugal) presented current state of 2nd-line treatment in CML. In view of thyrosine kinase inhibitors (TKIs) mostly used at initial stages, the main prognostic value is given to data on molecular remission (either bcr/abl or cytogenetic results) at 3-12 months of Imatinib therapy. Nilotinib and dasatinib could be regarded as effective options.

Dr. David **Ross** (Australia) presented modern classification and risk distribution in myeloproliferative neoplasias, as based on pathological findings and DNA mutation profiles in PV, ET. Clinical results of Ruxolitinib treatment trials (COMFORT-1 and -2 studies) were reported. Prof. Boris V. **Afanasyev** (St. Petersburg) held a lecture on risk-adapted therapy of myeloproliferative Ph-negative disorders including allo-HSCT and Ruxolitinib. The latter drug could be successfully used for GVHD prevention post-HSCT. Dr. Elena V. **Morosova** presented her data on Ruxolitinib therapy before allo-HSCT in primary myelofibrosis. Dr. Vasily **Shuvaev** (St. Petersburg) has also presented data from Moscow and St. Petersburg on treatment of myelofibrosis by means of Ruxolitinib (a total of 48 patients). The disease showed atypical course and multiple life-threatening complications. Ruxolitinib therapy resulted in quick clinical and hematological response.

Pediatric treatment protocols

Professor Olga **Aleinikova** (Minsk) presented a lecture on acute GVHD (aGVHD) after HSCT in pediatric acute leukemia based on treatment of their 142 patients. Main attention was given to severe steroid-resistant aGVHD which may be effectively treated by mesenchymal stem cells, and, more recently, with some novel therapeutic antibodies inhibiting different mediators of alloimmune response, or Ruxolitinib (a JAK inhibitor).

Professor Alexander I. **Karachunsky** (Moscow) presented updated results on refractory ALL treatment with applications of novel nucleoside analogues, e.g., Clofarabine, Nelarabine, recently combined with Blinatumomab, total body irradiation and haplo-HSCT.

Prof. Georgyi **Mentkevich** (Moscow) has reported about auto-HSCT in pediatric tumors (neuroblastoma, Ewing sarcoma, medulloblastoma etc.). Current results are better than 20 years ago and may be improved by using new chemotherapeutic agents, combined with local irradiation and immunotherapy after HSCT. Epigenetic therapy was performed in neuroblastoma.

Problems with treatment of high-risk relapsing neuroblastoma were discussed by Dr. Ilya V. **Kazantsev** (St. Petersburg) who reported a single-center experience. Existing chemotherapy alone or in combination with targeted therapy is not effective. Allo-HSCT is also followed by transitory effect. More effective immunotherapy should be developed for such conditions.

Antifungal therapy

A comprehensive lecture on this subject was presented by Prof. Malcolm **Richardson** (Manchester, UK) concerning pharmacodynamics and clinical effects of liposomal Amphotericin B (AmbiSome) which was more effective in aspergillosis and, seemingly, less toxic than its non-encapsulated form. Professor Nikolai N. **Klimko** (St. Petersburg) reported about current guidelines on diagnostics and clinical efficiency of fungal invasions in oncohematological patients. Liposomal Amphotericin B has shown high efficiency in aspergillosis and mucormycosis, as compared to Voriconazole and related antifungals.

Conditioning treatment in HSCT

Prof. Tapani **Ruutu** (Helsinki) presented interesting data about busulfan-based conditioning regimens and pharmacokinetics of intravenous busulfan compared to oral formulation. Nevertheless, a considerable heterogeneity in regimens of busulfan conditioning, especially in children and obese subjects requiring appropriate guidelines is to be developed.

Dr. Michael A. **Maschan** (Moscow) provided interesting data on application of ThioTEPA in pediatric HSCT. This potent drug may easily pass through the blood/brain barrier and could be introduced as a component of conditioning regimens, both in auto- and allo-HSCT pediatric settings.

Haploidentical transplantation

Professor Andrea **Bacigalupo** (Rome) spoke about haploidentical HSCT which becomes rather common now, due to high availability of family donors, economic reasons and good clinical results. To prevent immune conflict, T cell depletion may be performed either *ex vivo*, or *in vivo* (e.g., cyclophosphamide post-HSCT). However, the issues of better conditioning regimen, and clinical benefits of haplo-HSCT *versus* grafting from unrelated compatible donor remain to be studied in future.

Dr. Dmitry **Motorin** (St. Petersburg) made a report on haplo-HSCT at the local Almazov Center which was performed in 60 adult patients, mostly with acute leukemias. The HSCT was followed by posttransplant cyclophasphamide GVHD prophylaxis. In summary, haplo-HSCT proved to be a clinically low cost treatment option for AML and advanced CML showing a comparable efficiency to matched sibling donors

Immune therapy

A key lecture was presented by Prof. H.-J. **Kolb** (Munich) who discussed current opportunities for enhancing antitumor response after allogeneic HSCT and DLI in solid and hematological malignancies, i.e., enhancing T-cell specific response against tumor cells, selection of virus and tumor-specific immune cells, effects of allo-HSCT in solid carcinomas. Allogeneic response seems to be more important than tumor antigen-directed cytotoxicity.

Dr. Olesya V. **Paina** (St. Petersburg) reported about a variety of recipient- and donor-dependent factors modifying the recovery rates of immune system after HSCT. Some novel pharmacological tools (e.g., Privigen, Sunitinib, anti-CD25 antibodies etc.) are aimed to replace or alleviate the posttransplant immune deficiency.

Prof. Alexei A. **Maschan** (Moscow) presented his view on novel immunotherapies in pediatric ALL. Blinatumomab (anti-CD19 Mab) and allo-HSCT (GvL effect) have shown a promising effect in refractory/relapsed ALL cases, being more safe and more effective than chemotherapy, in terms of molecular remission and survival rates.

Dr. Michael Yu. **Drokov** (Moscow) reported his data on immune reconstitution after HSCT followed by the cyclophosphamide immune suppression (PTCy). As compared to conventional schedules, the PT/Cy prophylaxis was associated with affected reconstitution of CD4, NK cells and monocyte recovery only in BM recipients, as well as with altered T-reg cells reconstitution.

Dr. Ivan S. **Moiseev** (St. Petersburg) presented a single-center randomized trial of post-transplant GVHD prophylaxis (PTCy) versus Thymoglobulin in unrelated SCT recipients with MPNs and MDS. The study has shown a decreased graft failure incidence, higher overall survival and decreased non-relapse mortality in PTCy arm compared to antithymocyte globulin prophylaxis.

A more special topic was discussed by Dr. Magne **Børset** (Trondheim, Norway) who shared numerous data about potential usage of CAR T cells (cells with chimeric antigen receptors) and specific monoclonal antibodies in treatment of multiple myeloma (MM) whereas checkpoint inhibitor drugs were not effective so far. Adenosine may be an active cytostatic agent in MM.

Gene therapy and genome editing

A special mini-symposium was dedicated to current prospectives of gene correction and gene therapy using hematopoietic stem cell transplantation techniques. Professor Boris **Fehse** (Hamburg) provided a two-part presentation on gene editing. It is a real revolution in basic and applied sciences in different areas of biotechnology and biomedicine. Due to ease of use and flexibility, CRISPR/Cas (and similar systems with RNA-based targeting) is preferable for any research. With regard to clinical application genome editing faces similar challenges as "classical" gene therapy, particularly for *in-vivo* applications. The "classical" gene therapy deals with diseases caused by *errors* in the genetic information, and appropriate therapy is based on *correction* of genetic information. Several problems still should be resolved, i.e., delivery, immunogenicity of a foreign genetic material; its efficiency (correction rate) as well as precision (error rate). *Ex-vivo* manipulations with, e.g., hematopoietic stem cells are technically less demanding and can be readily controlled with regard to efficiency and safety. It seems to be no real therapeutic rationale for germline editing.

A prominent expert in clinical gene therapy, Prof. Gerard **Wagemaker** (Rotterdam), dedicated his lecture to practical aspects of transduction and preparation of gene-modified hematopoietic cells for subsequent autologous transplantation to the patients. As a result, at least, partial restoration of the deficient enzyme activity is achieved, as shown by experimental treatment of a mitochondrial disease (MNGIE) occurring due to a defect of thymidine phosphorylase. Another lecture by Prof. Wagemaker dealt with hematopoietic stem cells (HSC) as a most suitable object for gene therapy. HSCs are unique in providing a perpetual factory of blood cells and also unique in providing both immune tolerance and monocytic descendants crossing the blood brain barrier. Hematopoietic stem cells have wide applications in gene therapy of inherited and acquired immune deficiencies. Some technical aspects of optimized HSC culture conditions and their in vitro cellular properties were also discussed.

Dr. Waseem **Qasim** (London, UK) reported on their experience with treatment of pediatric ALL with chimeric antigenic receptors (CAR) in T cells specific for CD19, aiming for targeted anti-leukaemia effect. A commercial preparation of CART19 cells was presented; molecular tools for gene editing (TALEN, CRISP/Cas9) are discussed. Results of the 1st -phase CAR T cell therapy in resistant ALL before HSCT were presented.

Dr. Michael **Maschan** (Moscow) reported the experience of a pediatric HSCT center with TCR alpha/beta depletion of hematopoietic cells transplants, especially recommended for haploidentical HSCT. CD45RA depletion, especially, in donor lymphocyte infusions, is also subject to a trial, aiming to decrease allogeneic response posttransplant.

Dr. Ian **Johnston** presented an original automatic closed system for cell cultures providing some examples for automation of such complex processes, i.e., manufacturing of geneticall-modified immune cells (CAR T cells) products. The cells obtained from a patient are then processed by a CliniMACS® Prodigy – closed system including the following steps: cells sample preparation; washing/density gradient separation; MACS cell separation; cell activation; genetic modification followed by cell propagation in culture. The system is highly flexible: different types of cell product can be manufactured on a single platform.

Dr. Andrey **Gorchakov** (Novosibirsk) shared their considerations concerning optimized design of the CAR T cells. Moreover, the authors proposed an ECAR NK cell platform targeted for different cancer cell antigens. Specifically, a genetically modified YT cell line was designed and proved to serve as a promising platform for developing allogeneic CAR NK cells. E.g., bispecific BiFn-CARs have been successfully constructed and functionally characterized *in vitro*.

Dr. Alena I. **Shakirova (St. Petersburg)** presented some experimental data on the CCR5 gene editing in hematopoietic stem cells using CCR5-Uco-TALEN system. The aim was to optimize the CCR5 knockout protocol for the CD34+ cells. Gene editing efficacy of the CCR5 gene in hematopoietic stem cells reached 46±7%. Frequency of the off-target events was directly associated with the mRNA concentration [0%-10%].

Dr. Kirill V. **Lepik** reported experimental data on the newly developed (PARG/DEXS) 3 and SiO 2 –coated multilayer microcapsules able to capture and efficiently bind the mRNA and pDNA. They also provide efficient intracellular delivery of CRISPR/Cas9 components in form of pDNA. The carrier shows high rate of internalization in HEK293 cell line with low *in vitro* toxicity.

Mikhail Yu. **Samsonov** (Moscow), an expert in drug regulation policy, spoke about regulatory and clinical development strategy in genome editing which was sufficiently changed over last year. He concerned some technical issues including ongoing and planned clinical trials of the edited gene and cell products, as well as potential off-target effects of the gene-editing tools limiting their chances for clinical approval. Special attention was drawn to current regulations for CAR-T cells as the most advanced product in the field.

HSCT in other chronic disorders

Monoclonal antibody-based drugs in paroxismal nocturnal hemoglobinuria (PNH) were featured in a report by Maria **Vinogradova** (Moscow) and Alexander D. **Kulagin** (St. Petersburg) who shared their common clinical experience in targeted treatment of hemolytic crisis occurring in PNH. A new drug, Eculizumab (an anti-C5 monoclonal antibody) was successfully used in order to cure and prevent hemolytic/thrombotic complications in the patients and as a preparative regimen for HSCT being based on comparative studies and therapy in dozens of PNH patients.

Autologous HSCT in multiple sclerosis (MS) was addressed in the lecture by Belinda **Pinto Simões** (Brazil). She described satisfactory clinical efficiency of auto-HSCT in cases selected for clinical and radiological features of active inflammatory process, rapid progression of disability after first or more lines of therapy.

Prof. D. **Fedorenko** (Moscow) reported experience in MS treatment based on a intensive immunosuppression followed by auto-HSCT and, in aggressive cases, with later supportive mitoxantrone therapy. Neurological outcomes as assessed by MRI and EDSS values at long-term period showed disability prevention in >90% of the patients subjected to early HSCT.

Dr. Kirill **Kirgizov** (Moscow) reported results of auto-HSCT for pediatric patients with autoimmune disorders of central nervous system, e.g., in MS. For neuromyelitis optica, only primary results of allo-HSCT being provided. A large group of patients with Hurler disease was treated by allo-HSCT, the early and late survival rates were presented.

Biological markers of the disease

Dr. David **Ross** (Adelaide, Australia) presented materials on probability of treatment-free remission in CML patients when stopping a long term treatment with tyrosine kinase inhibitors (TKI), mostly, with Imatinib. Criteria for molecular minimal residual disease (MRD) are given. Several large studies (STIM, EuroSKI etc.) with long-term molecular remission have shown that the TFR (MR4.5) was achieved after withdrawal of Imatinib in up to a half of CML patients with long-term follow-up.

Chromosome aberrations as a clinical risk index were discussed in a report by Prof. Nikolay N. **Mamaev** (St.Petersburg) who pointed to important role of complex cytogenetic disturbances and some specific gene mutations for clinical outcome risk determination in acute myeloid leukemia patients. A significance of secondary chromosome aberrations after intensive chemotherapy should be also taken into account when planning further treatment.

Molecular composition and potential clinical significance of plasma microvesicles (MV) and exosomes were considered in the report presented by Claudia **Lange** (Hamburg). It concerned various protein and lipid components of the MVs, and, especially, different cellular and viral RNA species. Some challenges are discussed including small amounts and reproducibility of MVs as a tool for intercellular transport and signaling.

Rehabilitation

A report by Dr. Alisa G. **Volkova** (St. Petersburg) concerned numerous rehabilitation approaches to the post-transplant pediatric patients. Numerous measures are aimed for improvement of general physical and mental activity, resolving specific problems of individual muscle groups, joints and nerves, development of self-confidence, treatment of chronic fatigue, and, thus, finally, improving quality of their life.

Dr. A. E. **Khain** (Moscow) considered emotional distress and coping problems over the entire period of hematopoietic transplantation. These disturbances could be effectively diagnosed by means of several distress evaluation scales allowing to arrange additional psychological support in the course of treatment.

Dr. M. N. **Maltseva** (St. Petersburg) formulated a concept of a patient-oriented care when planning oncorehabilitation programs. Strategies of interaction with pediatric patients and their relatives are proposed in order to provide psychological support for the patient and his family.

Nursery in transplantation clinics

A special session was dedicated to the aspects of patients care by medical nurses. N. S. **Nekrasova** reported own data from Gorbacheva Institute concerning thraumas and measures to prevent them at the hematological clinics and ICU.

Role of nursing in epidemiological control at the BMT clinics were presented by A. A. **Apostolova**. Keeping aseptic and antiseptic measures, instructions for the patient's relatives, optimal selection of antiseptic agents are essential for the cytopenic patients.

Loss of weight and cachexia in immunocompromised patients was discussed by **Leshchuk** (Moscow). This rather common condition should be managed by nutritive support and nutritive therapy.

A report from the D. Rogachev Research Center of Children Hematology, Oncology and Immunology (Moscow) concerned psychological aspects of the posttransplant patients. R. B. **Miroshkin** et al. required an interdisciplinary cooperation when arranging medical and psychological correction of their behavioral and emotional problems.

Краткий обзор докладов на XI международном симпозиуме «Трансплантация гемопоэтических стволовых кроветворных клеток. Генная и клеточная терапия» (14–16 сентября 2017 г., Санкт-Петербург, Россия)

Борис В. Афанасьев

Главный редактор журнала «Клеточная Терапия и Трансплантация»
НИИ Детской Гематологии, Онкологии и Трансплантологии им. Р. М. Горбачевой, кафедра гематологии, трансфузиологии и трансплантологии, Первый Санкт-Петербургский государственный медицинский университет им. акад. И. П. Павлова

Резюме

В сентябре 2017 г. в Санкт-Петербурге состоялся очередной симпозиум, посвященный проблемам трансплантации гемопоэтических клеток и смежным вопросам. Особое внимание было уделено применению новых таргетных препаратов при лечении лимфопролиферативных заболеваний, в частности – лимфогранулематоза, где используют брентуксимаб и, в последнее время – ингибиторы апоптоза лимфоцитов (PD1-ингибиторы). При лечении острых миелобластных лейкозов стал применяться Сорафениб – ингибитор FLT3.

На симпозиуме обсуждался вопрос о тактике лечения хронического миелоидного лейкоза с помощью ингибиторов тирозинкиназ и возможности их отмены по достижении глубокой молекулярной ремиссии. При хронических миелопролиферативных заболеваниях активно внедряются препараты, ингибирующие онкогенную JAK-киназу (руксолитиниб).

В лечении острого лимфобластного лейкоза и других лимфопролиферативных заболеваний, наряду с обычным цитостатическим лечением по стандартным протоколам, широко применяются препараты моноклональных антител (например, ритуксимаб или блинатумомаб). Отдельные доклады были посвящены новым подходам к аллогенной трансплантации – например от гаплоидентичного донора, что, в сочетании с оптимальной профилактикой РТПХ, приводит к результатам, сопоставимым с применением трансплантата от неродственного полностью совместимого донора. Несколько сообщений были посвящены профилактике РТПХ посредством циклофосфамида после трансплантации.

Вопросы иммунотерапии при лейкозах затрагивались в связи с внедрением в клиническую практику специфических рекомбинантных цитотоксических антител и генно-модифицированных Т-клеток с химерными антигенами, потенциально способными уничтожать злокачественные клетки при некоторых онкогематологических заболеваниях. Отдельно был проведен мини-симпозиум, посвященный генной терапии и перпективам генного редактирования с помощью известных систем CRISP/Cas9 и TALEN, там обсуждали также вопросы правового регулирования генной и клеточной терапии. Кроме того, на симпозиуме была проведена специальная сессия для медицинских сестер, где обсуждались задачи и функции среднего медицинского персонала в работе отделений ТГСК и интенсивной терапии.

Ключевые слова

Санкт-Петербург, симпозиум, трансплантация гемопоэтических клеток, таргетная терапия, иммунотерапия, комбинированное лечение, генная терапия.