ORIGINAL ARTICLE, MEDICINE

Treatment of Childhood Acute Myeloid Leukemia in Bulgaria

Hasan A. Burnusuzov¹, Maya N. Yordanova², Boryana E. Avramova², Nadezhda N. Yurukova², Konstantin N. Bachvarov², Albena B. Muchinova², Irena H. Vlahova², Angelina A. Stoyanova¹, Ivan N. Mumdzhiyev¹, Liliya R. Ivanova¹, Neofit Y. Spasov¹, Elina Ts. Peteva³, Milena I. Belcheva³, Hristina Hristozova³, Mariya I. Spasova¹, Valeriya I. Kaleva³, Dragan Bobev², Dobrin N. Konstantinov²

¹ Department of Pediatrics and Medical Genetics, Medical University of Plovdiv, Plovdiv, Bulgaria

² Clinic of Children's Oncohematology and Transplantation, Queen Johanna University Hospital - ISUL, Sofia, Bulgaria

³ Department of Pediatrics and Medical Genetics, Medical University, Varna, Bulgaria

Correspondence:

Hasan A Burnusuzov, Department of Pediatrics and Medical Genetics, St George University Hospital, Medical University of Plovdiv, 15A Vassil Aprilov Blvd, 4000 Plovdiv
E-mail: hassan_md@abv.bg
Tel: +359 892 979 279

Received: 10 May 2017

Accepted: 24 Aug 2017

Published Online: 27 Sept 2017

Published: 30 June 2018

Key words: acute myeloid leukemia, children, relapse

Citation: Burnusuzov HA, Yordanova MN, Avramova BE, Yurukova NN, Bachvarov KN, Muchinova AB, Vlahova IH, Stoyanova AA, Mumdzhiyev IN, Ivanova LR, Spasov NY, Peteva ETs, Belcheva MI, Hristozova H, Spasova MI, Kaleva VI, Bobev D, Konstantinov DN. Treatment of childhood acute myeloid leukemia in Bulgaria. *Folia Med (Plovdiv)* 2018;60(2):234-40.

doi: 10.1515/folmed-2017-0090

Background: During the last four decades the prognosis of childhood acute myeloid leukemia (AML) has been substantially improved due to an increase in complete remission (CR) rates, event-free survival (EFS) and reduced early mortality. The relapsed AML still remains a therapeutic challenge.

Aim: To report the AML treatment results of the Bulgarian pediatric oncohematological centers.

Materials and methods: Retrospective analysis of the treatment results of children and adolescents (age from 0 to 20 years) with primary AML. Unified AML BFM- backbone type treatment protocol is used.

Results: This study included 97 newly diagnosed patients (44 girls and 53 boys) with AML in Bulgaria between 2003 and 2016. The median age at diagnosis was 10.2 years. The most frequent FAB-morphologic subtype was M2 followed by M4. First complete remission (CR1) was achieved in 83 patients (85.6%). The 13-year EFS was 49%, while the overall survival (OS) was 54.6%. Twenty seven (27.8%) patients relapsed, with only 5 of them being still alive towards the end of the study period.

Conclusion: The EFS and OS for the children with AML in Bulgaria are comparable with those reported by other European groups. The prognosis of relapsed AML remains still unfavorable for the past 13 years.

BACKGROUND

Acute myeloid leukemia (AML) comprises a heterogeneous group of closely related clonal disorders of the hematopoietic cells and constitutes nearly 5% of all malignancies and approximately 18% of the childhood acute leukemia cases.^{1,2} Recent advances in the diagnosis and treatment of AML have led to a significant improvement of the prognosis worldwide.³⁻⁷ With modern chemotherapeutic protocols a complete clinical and hematological remission (CR) can be induced in about 80% - 90% of the children with newly diagnosed AML, and in nearly

30% to 70% of the cases the remission is sustained. However, severe bleeding, leukostasis, infectious complications or a refractory disease are major causes of remission-induction failure and early death in about 10% to 20% of patients. Moreover, 30% to 40% of the children will experience a relapse, even if CR is achieved. That is why the prognosis of patients with primary-refractory or relapsed AML still remains poor, with a 5-year overall survival (OS) rates of only about 25-35%, which turns their treatment into a challenge.⁸⁻¹⁰

AIM

Since 2003, a Berlin-Frankfurt-Muenster (BFM) – type protocol has been approved for the treatment of children and adolescents with primary AML in all the 3 pediatric oncohematological centers in Bulgaria, with the aim of improving the prognosis in these patients. This article reports the results of such an approach for the period 2003-2016.

MATERIALS AND METHODS

Patients between 0 and 20 years old, diagnosed with AML according to the French-American-British (FAB) or WHO classification were included. Cases with Down syndrome or AML as secondary malignancy, or MDS with <20% blasts, were excluded. Risk group (high risk – HR and standard risk – SR) assignment is according to the treatment protocol used.

STATISTICAL ANALYSIS

In this clinico-epidemiologic, retrospective descriptive analysis the quantitative variables were indicated in absolute values, percentage or as an arithmetic mean. For OS, deaths from any cause were considered an event. Event free survival (EFS) was calculated from the date of diagnosis to the last follow-up or first event (failure to achieve remission, resistant leukemia, relapse or death of any cause). Survival probabilities were calculated using the Kaplan-Meier method, with the level of significance set at $p < 0.05$. Graphical analysis was applied for descriptive purposes.

RESULTS

For the thirteen-year period, a total of 106 AML cases from all the three institutional databases were collected. Of these, 97 (44 girls and 53 boys) were included in this analysis. Median age at diagnosis was 10.2 years (0.2 – 20 yrs). The diagnosis was based on the examination of bone marrow smears by the local hematologists and cytogenetic and flow cytometry analyses - at the local and/or referent pathology departments. Morphological FAB phenotype was documented in 74.2% of the cases, with M2 being the most common (23.7%), and molecular - or cytogenetic results were found in 34%. In 66% of all cases there was no data from either molecular or cytogenetic studies and in 25.8% - the FAB subtype was missing, most of these children being diagnosed and treated before 2008. Detailed demographic and disease characteristics of the patients are given in **Table 1**.

First-line therapy in all the three centers was carried out utilizing the Berlin-Frankfurt-Muenster (BFM) AML treatment backbone (AML BFM-98 and subsequently AML BFM-2004 protocols, described in detail in Creutzig et al., JCO 2006). Forty-four children (45.4%) were classified as high risk (HR), 43 (44.3%) – as standard risk (SR) patients and for 10 (10.3%) – no risk assignment was found. Death within the first 42 days of therapy was documented in 14 (14.4%) patients: 5 from severe bleeding, 2 from systemic infection, another 2 from leukostasis and respiratory distress syndrome, and 5 from resistant disease. Complete remission (CR1) was achieved in 83 children (85.6%). Five patients died in CR1 (bleeding - 1, RDS - 1, infection - 3 children). Hematopoietic stem cell transplantation (HCST) was used in CR1 in 4 HR patients: 1

Figure 1. Follow-up of the whole group for the 13-year period – the overall survival is 54.6%. Kaplan-Meier method was used.

Figure 2. Event-free survival of the group for the 13-year period is 49%. Kaplan-Meier method was used.

Table 1. Patient characteristics

Characteristics				CR 1		Recurrences	Transplant	Status
				Yes	No	Yes	Yes	Dead
Sex	n	%	% within group	% within group		n	N	
Female	44	45.4	84.1	15.9		15	4	22
Male	53	54.6	86.8	13.2		12	9	19
Age, yrs								
<1	13	13.4	61.5	38.5		2	1	7
1 – 9	34	35.1	94.1	5.9		10	4	14
>10	50	51.5	86.0	14		15	8	20
FAB type								
M1	3	3.1	100	0		1	1	1
M2	23	23.7	91.3	8.7		4	2	5
M3	5	5.2	80.0	20.0		0	0	1
M4	20	20.6	80.0	20.0		9	2	9
M5	16	16.5	75.0	25.0		4	3	10
M6	3	3.1	100	0		1	2	1
M7	2	2.1	100	0		1	0	1
Unknown	25	25.8	88.0	12.0		7	3	13
Molecular or cytogenetic testing								
t(8;21) or AML1-ETO	5	5.2	100	0		2	0	2
t(15;17) or PML-RARa	3	3.1	100	0		0	0	0
FLT3-IDA	11	11.3	90.9	9.1		5	1	6
inv16	5	5.2	80.0	20.0		3	2	1
complex karyotype	5	5.2	100	0		0	1	0
Del13	1	1.0	0	100		0	1	1
EVI1	1	1.0	100	0		0	0	0
t(5;11)	1	1.0	100	0		0	0	0
t(6;11)	1	1.0	100	0		1	0	1
Unknown	64	66.0	82.8	17.2		16	8	30
Risk group								
HR	44	45.4	72.7	27.3		17	8	27
SR	43	44.3	100	0		8	4	9
Unknown	10	10.3	80.0	20.0		2	1	5

CR1 - first complete remission; HR - high risk group; SR - standard risk group.

from sibling donor and 4 from matched unrelated donor (MUD). One child with refractory AML was MUD-transplanted with no CR1 achieved. For the whole group, the overall survival for the 13-year period was 54.6% (**Fig. 1**). The EFS was 49% and varied significantly for the different risk groups (**Fig. 2 and Table 2**).

Relapse occurred in 27 patients (27.8%), 12 of them (44.4%) being within the first 12 months of

the initial diagnosis, and the latest – in their 6th year. Distributed by location, the majority – 23 were bone marrow (BM), and 4 – combined (BM/breast-1; BM/skin-2; BM/CNS/orbit). Relapse rates, within the risk groups, were as follows: 63% in the HR group, 7% in the SR and 30% in the group with no risk assignment. Eight of the relapsed patients were transplanted with hematopoietic stem cells after achieving a second remission (CR2) induced by

Table 2. Distribution of the patients according to the risk groups, EFS and number of events within the risk groups. HR- high risk group; SR- standard risk group; U/A- no information for risk group assignment. The differences between the groups are statistically significant (Breslow (generalized Wilcoxon) Chi-square 17.314, $p < 0.001$)

Risk Group	Patients n	EFS	Events within the group n	%
U/A	10	46.7%	5	50.0%
HR	44	25.3%	31	70.5%
SR	43	74.7%	10	23.3%
Overall	97	49%	46	47.4%

FLAG (Fludarabin, Cytarabin, Granulocyte-colony stimulating factor) or Idarubicin-FLAG chemotherapeutic regimens. Two of them were autologous peripheral blood stem cells (PBSC) transplantations, one of these two being retransplanted with MUD PBSC after a second relapse. The rest of the HSCT in CR2 were allogeneic: 4 MUD PBSC, 1 MUD BM, and 1 cord blood stem cells). Towards 2016, 5 of the relapsed patients were alive: 3 after salvage chemotherapy alone (Ida-FLAG) and 2 after allogeneic PBSC transplantation.

DISCUSSION

Pediatric AML is a rare disease, the average incidence rate for our country of about 7.5 patients / year for the period. This rate is comparable to the standardized incidence of AML in children in most European countries, ranging from 5.1 to 8/1000000¹¹, given the average children population in Bulgaria for the period 2003 – 2016 of 1440733¹². The

Table 3. Comparison of the event free survival (EFS) and the overall survival (OS) of 97 children with primary AML, diagnosed and treated in Bulgaria between 2003 and 2016 with the results of leading international clinical trials. BFM- Berlin-Frankfurt-Muenster; NOPHO- Nordic Society of Pediatric Hematology and Oncology¹⁴⁻¹⁶

	Follow-up	EFS	OS
AML BFM 93	5 yrs	50%	58%
AML BFM 98	5 yrs	49%	62%
NOPHO-AML93	7 yrs	49%	64%
Our group	13 yrs	49%	54.6%

thirteen-year EFS and OS achieved, are currently comparable to those of leading European centers (Table 3). These results are based on data from the three institutional record offices. Yet, a certain

amount of information was missing, mainly in the old files, for example the FAB-subtype in 25%, or risk group assignment for nearly 10% of the cases was not known. Basic diagnostic criteria, like cyto- or molecular-genetic tests are locally used ever since 1990s, and are routinely performed since 2008 in a central laboratory, yet the results for nearly 65% of the patients are missing. Although every centre has its own archive, the lack of universal specialized and regularly updated childhood cancer register in Bulgaria is an obstacle that we faced during data collection and we realize that more efforts should be made in establishing and maintaining such a database.

The medications used in the treatment of AML have not changed significantly since the 1980s, suggesting that on a global scale current improvement is largely due to: (a) optimization in treatment strategies; (b) establishment of specific risk factors and better stratification of patients; (c) meticulous supportive care; (d) use of allogeneic HSCT in HR patients.¹⁰ However some of the most important chemotherapeutics used in the AML-BFM backbone today are still not licensed for the treatment of children and adolescents in Europe and are currently being used on an off-label basis.¹³ The OS and EFS rates of children with AML we report are largely due to the use of a unified treatment strategy, using a single treatment protocol. In all of the 3 Bulgarian pediatric oncohematology centers standardized risk group assignment is applied, with timely HLA-typing and referral for transplantation for the HR patients. However, we still do not have unobstructed access to such medications as liposomal daunorubicin, proven to cause less treatment-related toxicity and to be more active against certain types of AML^{17,18}, because of their legal registration regimen and pricing policy.

The prognosis of children with relapsed or primary refractory AML is still unfavorable. The

duration of CR1 has been found to be the most important prognostic factor in these patients, with little add-on from the other risk factors (cytogenetic, site of relapse, etc.). About 50% of the relapses are early (within 1 year of initial diagnosis) and the prognosis for these patients is poor.^{8,19} Unfortunately, about half of the relapses of our patients fall into this particular group.

The exact reasons for relapse are not fully established. Available data suggests that the persistence of minimal residual disease (MRD) might have prognostic significance.²⁰ For MRD monitoring, highly sensitive techniques are recommended, such as multiparameter flow cytometry (FCM) and real time quantitative polymerase chain reaction (RQ PCR). Importantly, the kinetics of relapse differs between genetic subtypes with a median time from molecular to clinical relapse between 2 to 8 months²¹, but more clinical studies are needed in order to determine the exact role of these methods in the monitoring and treatment of children with AML²²⁻²⁴. Currently routine MRD monitoring in children with AML in Bulgaria is available by RQ PCR and FCM, and these studies are becoming increasingly incorporated in the risk stratification of our patients. Unfortunately none of our treatment centers has participated in a large international pediatric AML clinical trial so far.

Second remission could be induced in approximately half of the children with relapsed AML and 20% to 40% of them could be long-term survivors with chemotherapy and HSCT.^{8,25} Cytostatic regimens include FLAG, IDA-FLAG or DNX-FLAG. The latter includes liposomal daunorubicin (DNX) to reduce cardio toxicity, while maintaining high antileukemic efficiency.^{8,17,18} In our cases FLAG and IDA-FLAG are used as a second-line treatment. Stable remission after 2x FLAG, without HSCT is achieved in only 3 cases, and 8 of the others are transplanted in CR2. Unfortunately, there is scarce data in the subsequent medical records regarding CR2 and its duration for most of rest of the relapsed children. This recalls the questions about the national pediatric cancer register.

HSCT has long been used to achieve stable remission in children with relapsed AML. However, the role of allogeneic HSCT in CR1 has recently been revised and today it is reserved only for children with HR AML.²⁶⁻³² For relapsed patients, HSCT in CR2 is the standard, and autologous HSCT is generally not recommended.^{33,34} In our group autologous HSCT was performed in two

children at an early period (before 2005) when data about auto-HSCT were controversial, and both of them relapsed. Allogeneic HSCT is utilized in less than one third of all relapsed children. Possible explanations for the low HSCT rates in the period include failure to achieve CR2 and lack of compatible family donors (small families), necessitating the search of MUD, often abroad. This is a time-consuming process involving great human and financial resources and not always successful in short term in a country with limited resources like Bulgaria. Although the first Bulgarian pediatric transplantation center operates since 1997 and is well experienced, no national donor registry has existed until recently, and it has just started to develop. Many reasons contribute: legal, ethical, moral, last but not the least - financial. Transplantation is a proven reserve for improving the survival rates, quality of life and a definitive cure for children with relapsed AML. Therefore the question of donation as a prerequisite for a greater share of HSCT in children with hematological malignancies in Bulgaria, remains open.

CONCLUSIONS

Children with newly diagnosed AML in Bulgaria can achieve EFS and OS rates, comparable with those reported by other European groups. Nevertheless, to further increase our OS, a decline in the rates of early death and death in CR1 is needed. Subgroup-directed therapy can be optimized by a precise dynamic risk stratification, utilizing centralized diagnosis reviewing and contemporary minimal residual disease follow-up, by immunophenotyping, karyotyping, FISH and PCR techniques. Essentially, there is a clear need for more successful attempts to cure our children with relapsed AML, because their prognosis is still unfavorable. Administrative limitations in the legal application of second and 3rd line drugs, and the insufficient local participation in clinical studies with experimental medications (as a less-privileged country) contribute to that and should be judiciously addressed. Additionally, there are clear indications for upfront allogeneic transplantation of PBSC in refractory or relapsed AML, and the early HLA-typing with timely referral to the transplantation centre is of utmost importance.

REFERENCES

1. Kaatsch P. Epidemiology of Childhood Cancer. *Cancer Treat Rev* 2010;36:277-85.
2. Horner MJ, Ries LAG, Krapcho M, et al. SEER

- Cancer Statistics Review 1975-2006. Available at http://seer.cancer.gov/archive/csr/1975_2006.
3. Cheson BD, Bennett JM, Kopecky KJ, et al. Revised recommendations of the International Working Group for Diagnosis, Standardization of Response Criteria, Treatment Outcomes, and Reporting Standards for Therapeutic Trials in Acute Myeloid Leukemia. *J Clin Oncol* 2003;21(24):4642-9.
 4. Cheson BD, Cassileth PA, Head DR, et al. Report of the National Cancer Institute-sponsored workshop on definitions of diagnosis and response in acute myeloid leukemia. *J Clin Oncol*. 1999;8(5):813-9.
 5. Gatta G, Botta L, Rossi S, et al. Childhood cancer survival in Europe 1999–2007: results of EURO-CARE-5 - a population-based study. *Lancet Oncol* 2014;15:35-47.
 6. Kaspers GJ, Creutzig U. Pediatric acute myeloid leukemia: international progress and future directions. *Leukemia* 2005;19:2025-9.
 7. Kaspers GJ, Zwaan CM. Pediatric acute myeloid leukemia: Towards high-quality cure of all patients. *Haematologica* 2007;92:1519-32.
 8. Sander A, Zimmermann M, Dworzak MN, et al. Consequent and intensified relapse therapy improved survival in pediatric AML: results of relapse treatment in 379 patients of three consecutive AML-BFM trials. *Leukemia* 2010;24:1422-8.
 9. Creutzig U, Tallen G. Treatment results for children and adolescents with acute myeloid leukemia in middle and eastern European countries. *Memo* 2013;6:5-8.
 10. Pession A, Masetti R, Rizzari C, et al. Results of the AIEOP AML 2002/01 multicenter prospective trial for the treatment of children with acute myeloid leukemia. *Blood* 2013;122:170-8.
 11. Kwan ML, Buffler PA, Abrams B, et al. Breastfeeding and the risk of childhood leukemia: a meta analysis. *Public Health Rep* 2004;119:521-35.
 12. National Statistic Institute of Bulgaria. Available at https://infostat.nsi.bg/infostat/pages/reports/result.jsf?x_2=1168. Accessed on 13 Nov 2016.
 13. Dworzak MN. Cure and care for children and adolescents with acute myeloid leukemia in Middle and Eastern European countries: part II. *Magazine of European Medical Oncology* 2014;7(1):3-5.
 14. Lie SO, Abrahamsson J, Clausen N, et al. Treatment stratification based on initial in vivo response in acute myeloid leukaemia in children without Down syndrome: results of NOPHO-AML trials. *Br J Hematol* 2003;122:217-25.
 15. Creutzig U, Zimmermann M, Lehnbecher T, et al. Less toxicity by optimizing chemotherapy, but not by addition of granulocyte colony-stimulating factor in children and adolescents with acute myeloid leukemia: results of AML-BFM 98. *J Clin Oncol* 2006;24:4499-4506.
 16. Creutzig U, Ritter J, Zimmermann M, et al. Idarubicin improves blast cell clearance during induction therapy in children with AML: results of study AML-BFM 93. *AML-BFM Study Group. Leukemia* 2001;15(3):348-54.
 17. Creutzig U, Zimmermann M, Bourquin JP, et al. Randomized trial comparing liposomal daunorubicin with idarubicin as induction for pediatric acute myeloid leukemia: results from Study AML-BFM 2004. *Blood* 2013;122(1):37-43.
 18. Kaspers GJ, Zimmermann M, Reinhardt D, et al. Improved outcome in pediatric relapsed acute myeloid leukemia: results of a randomized trial on liposomal daunorubicin by the International BFM Study Group. *J Clin Oncol* 2013;31(5):599-607.
 19. Stahnke K, Boos J, Bender-Gotze C, et al. Duration of first remission predicts remission rates and long-term survival in children with relapsed acute myelogenous leukemia. *Leukemia* 1998;12(10):1534-8.
 20. Rubnitz JE, Inaba H, Dahl G, et al. Minimal residual disease-directed therapy for childhood acute myeloid leukaemia: Results of the AML02 multicentre trial. *Lancet Oncol* 2010;11:543-52.
 21. Omenn HB, Schnittger S, Jovanovic JV, et al. Strikingly different molecular relapse kinetics in NPM1c, PML-RARA, RUNX1-RUNX1T1, and CBFB-MYH11 acute myeloid leukemia. *Blood* 2010;115(2):198-205.
 22. Kern W, Haferlach C, Haferlach T, et al. Monitoring of minimal residual disease in acute myeloid leukemia. *Cancer* 2008;112:4-16.
 23. Krauter J, Gorlich K, Ottmann O, et al. Prognostic value of minimal residual disease quantification by real-time reverse transcriptase polymerase chain reaction in patients with core binding factor leukemias. *J Clin Oncol* 2003;21:4413-22.
 24. Steinbach D, Bader P, Willasch A, et al. Prospective validation of a new method of monitoring minimal residual disease in childhood acute myelogenous leukemia. *Clin Cancer Res* 2014;21(6):1-7.
 25. Abrahamsson J, Clausen N, Gustafsson G, et al. Improved outcome after relapse in children with acute myeloid leukaemia. *Br J Hematol* 2007;136:229-36.
 26. Niewerth D, Creutzig U, Bierings MB, et al. A review on allogeneic stem cell transplantation for newly diagnosed pediatric acute myeloid leukemia. *Blood* 2010;116:2205-14.
 27. Woods WG, Neudorf S, Gold S, et al. A comparison of allogeneic bone marrow transplantation, autologous bone marrow transplantation, and aggressive chemotherapy in children with acute myeloid leukaemia in remission: A report from the Children's Cancer Group. *Blood* 2001;97:56-62.

28. Horan JT, Alonzo TA, Lyman GH, et al. Impact of disease risk on efficacy of matched related bone marrow transplantation for pediatric acute myeloid leukemia: the Children's Oncology Group. *J Clin Oncol* 2008;26(35):5797-801.
29. Klingebiel T, Reinhardt D, Bader P. Place of HSCT in treatment of childhood AML. *Bone Marrow Transplant* 2008;42, Suppl 2:S7-9.
30. Appelbaum FR. Hematopoietic cell transplantation from unrelated donors for treatment of patients with acute myeloid leukemia in first complete remission. *Best Pract Res Clin Haematol* 2007;20(1):67-75.
31. Walter RB, Gooley TA, Wood BL, et al. Impact of pretransplantation minimal residual disease, as detected by multiparametric flow cytometry, on outcome of myeloablative hematopoietic cell transplantation for acute myeloid leukemia. *J Clin Oncol* 2011;29(9):1190-7.
32. Bonanomi S, Connor P, Webb D, et al. Successful outcome of allo-SCT in high-risk pediatric AML using chemotherapy-only conditioning and post transplant immunotherapy. *Bone Marrow Transplant* 2008;42(4):253-7.
33. Ljungman P, Urbano-Ispizua A, Cavazzana-Calvo M, et al. Allogeneic and autologous transplantation for haematological diseases, solid tumours and immune disorders: Definitions and current practice in Europe. *Bone Marrow Transplant* 2006;37:439-49.
34. Creutzig U, van den Heuvel-Eibrink MM, Gibson B, et al; AML Committee of the International BFM Study Group. Diagnosis and management of acute myeloid leukemia in children and adolescents: recommendations from an international expert panel. *Blood* 2012;120(16):3187-3205.

Лечение острого миелоидного лейкоза у детей в Болгарии

Хасан А. Бурнусузов¹, Мая Н. Йорданова², Боряна Е. Аврамова², Надежда Н. Юркова², Константин Н. Бачваров², Албена Б. Мучинова², Ирена Х. Влахова², Ангелина А. Стоянова¹, Иван Н. Мумджиев¹, Лилия Р. Иванова¹, Неофит Я. Спасов¹, Елина Ц. Петева³, Милена И. Белчева³, Христина Христозова³, Мария И. Спасова¹, Валерия И. Калева³, Драган Бобев², Добрин Н. Константинов²

¹ Кафедра педиатрии и медицинской генетики, Медицинский университет - Пловдив, Пловдив, Болгария

² Клиника детской онкогематологии и трансплантации, УМБАЛ „Царица Йоанна“ - ИСУЛ, София, Болгария

³ Кафедра педиатрии и медицинской генетики, Медицинский университет - Варна, Болгария

Адрес для корреспонденции:

Хасан А. Бурнусузов, Кафедра педиатрии и медицинской генетики, УМБАЛ „Св. Георги“, Медицинский университет - Пловдив, бул. „Васил Априлов“ № 15А, 4000, Пловдив, Болгария
E-mail: hassan_md@abv.bg
Tel: +359 892 979 279

Дата получения: 10 мая 2017

Дата приемки: 24 августа 2017

Дата онлайн публикации: 27 сентября 2017

Дата публикации: 30 июня 2018

Ключевые слова: острый миелоидный лейкоз, дети, рецидив

Образец цитирования:

Burnusuzov HA, Yordanova MN, Avramova BE, Yurukova NN, Bachvarov KN, Muchinova AB, Vlahova IH, Stoyanova AA, Mumdzhiyev IN, Ivanova LR, Spasov NY, Peteva ETs, Belcheva MI, Hristozova H, Spasova MI, Kaleva VI, Bobev D, Konstantinov DN. Treatment of childhood acute myeloid leukemia in Bulgaria. *Folia Med (Plovdiv)* 2018;60(2):234-40.
doi: 10.1515/folmed-2017-0090

Введение: За последние четыре десятилетия прогноз детского острого миелоидного лейкоза (ОМЛ) значительно улучшился из-за увеличения частоты полной ремиссии (ПР), безрецидивной выживаемости (БРВ) и снижения ранней смертности. Рецидивирующий ОМЛ всё ещё остается не реализованной до конца терапевтической задачей.

Цель: Сообщить о результатах лечения ОМЛ в болгарских детских онкогематологических центрах.

Материалы и методы: Ретроспективный анализ результатов лечения детей и подростков (в возрасте от 0 до 20 лет) с первичным ОМЛ. Был использован унифицированный ОМЛ БНФ основной протокол (AML BFM backbone protocol) лечения.

Результаты: В число девяноста семи пациентов с первоначально диагностированным ОМЛ в Болгарии за период 2003-2016 годов включены 44 девочки и 53 мальчика. Средний возраст при диагностировании составляет 10,2 года. Наиболее частым ФАБ-морфологическим подтипом является М2, за ним следует М4. Первая полная ремиссия (CR1) была достигнута у 83 пациентов (85,6%). 13-летняя БРВ составляет 49%, а ОВ (общая выживаемость) - 54,6%. У двадцати семи (27,8%) пациентов установлен рецидив, из числа которых только 5 всё ещё живы к концу периода.

Заключение: БРВ и ОВ среди детей с ОМЛ в Болгарии сопоставимы с данными, представленными другими европейскими группами. Прогноз рецидивирующего ОМЛ по-прежнему остается неблагоприятным в течение последних 13 лет.