Abstract

After a peak during the first 2 years of life, the incidence of acute myelogenous leukemia (AML) is low (five per million 5- to 9-year-olds per year in the United States) until after 9 years of age, when it slowly increases during adolescence and adulthood (to nine per million 15- to 19-year-olds per year in the United States). Biological features of pediatric and young adult AML appear to be similar, albeit future studies in genomics and proteomics are likely to disclose differences. Treatment results in AML have improved during the last 20 years for all age groups; however, outcome decreases with advancing age even when risk factors are considered. In contrast to data about children and adults, data on biological features and outcome are scarce in the adolescent age group. This is partly due to the low number of patients of this age group participating in clinical trials. Differences in outcome for adolescents participating in pediatric or adult trials seem to be significant when different protocols are used, but minor with similar or identical protocols. As the needs of adolescents are different from those of young children and those of adults and elderly patients, it is recommended to treat these patients in special units whenever possible.

Introduction

AML represents approximately 15–20% of all leukemias in children, about one-third in adolescents and about 50% in adults (Fig. 6.2). In general, the biological features of pediatric and adult AML appear to be
similar, but the differences have not been reviewed systematically. Treatment results in childhood AML have improved considerably over the last 20 years, with a 5-year survival in the range of 50–60% [1, 2]. In adults, outcome is less favorable, with overall cure rates of 30% or even less.

The number of adolescents and young adults included in clinical trials is relatively small, both in cooperative group studies of adults and in pediatric trials. Treatment protocols designed for children and adults often differ in various aspects from each other, and there are no data elucidating which kind of therapy could be particularly appropriate for young adults. It is our aim to describe the biological features, clinical symptoms and signs, treatment modalities, and outcome of this age cohort.

7.3 Epidemiology/Etiology

7.3.1 Incidence

Data herein were derived from United States SEER [3, 4] and the Automated Childhood Cancer Information System Europe (ACCIS 2003) [5] and the German Childhood Cancer Registry (GCCR 2003) [6]. The data are slightly different probably due to relatively low patient numbers or differences in race in different countries.

Based on these data, the acute leukemias represent 31–34% of all cancer cases in children younger than 15 years of age; they account for 6% of cancer in 15- to 29-year-olds. Age-adjusted annual incidence rates (per million) of AML are given in Table 7.1. Fig. 7.1 shows the variation of incidence of AML in children and adolescents in different age groups. AML rates are highest in the first years of life, but subsequently decrease with a nadir at approximately 9 years of age followed by slowly increasing rates during adolescence and adulthood [4]. Therefore, with advancing age the percentage of AML increases within the total leukemias, resulting in an inversion of the frequency of acute lymphoblastic leukemia (ALL) and AML in late adolescence.

The incidence of AML is similar for males and females during adolescence (Fig. 7.1) [3, 4]. Slightly more affected female young adults were seen in the European studies (AML-CG; Table 7.2), but United States population data shows a male predominance from age 20 to 35 years (Fig. 7.1) [3, 4]. The incidence of AML, unlike that of ALL, was similar for white and black children for all age groups [4].

The SEER report [3, 4], the German Children Cancer Registry [7] and the Nordic countries [8] have not reported an increase in incidence in AML in children under 15 years. However, the rate of AML among adolescents and young adults does show some evidence of increase. In England the rate in 15- to 24-year-olds has increased from 6.6 per million per year in 1979–1983 to 8.1 per million per year in 1993–1997 [9]. It likewise appears to have increased among adolescent/young adults aged 15–24 years in The Netherlands [10] and in the United States among 20- to 24-year-olds in the period 1975–1998 [4].

7.3.2 Etiology

There are only a few proven etiologic factors for childhood AML, for example in utero exposure to alcohol, exposure to benzene, ionizing radiation, or different drugs that may contribute to AML in young children. The risk of AML is increased in children with congenital syndromes such as Fanconi anemia, Shwachman syndrome, and Down syndrome. Somatic mutations of the GATA 1 gene are seen in virtually all cases of AML associated with Down syndrome and may be implicated in
the 500-fold increased risk of megakaryoblastic AML seen in these patients [12, 13]. Such mutations may also confer enhanced leukemic sensitivity to cytarabine via dysregulation of cytidine deaminase gene expression [14]. AML as a secondary malignancy after intensive chemotherapy is quite often seen in older children and adults (cumulative incidence of 0.6% for children treated for ALL or solid tumors by 10 years follow-up, and 3.3–10% for adults treated for different types of solid tumors) [15, 16].

Table 7.1 Age-adjusted annual incidence rates per million for specific leukemia by age groups, all races, both sexes, United States SEER 1990–1999, Automated Childhood Cancer Information System Europe (ACCIS) [5] 1993–1997 and acute myelogenous leukemia (AML) – Germany (AML intergroup trials) [11]. n.g. Not given

<table>
<thead>
<tr>
<th>Age (in years) at diagnosis</th>
<th>&lt;5</th>
<th>5–9</th>
<th>10–14</th>
<th>15–19</th>
<th>&lt;15a</th>
<th>Period</th>
</tr>
</thead>
<tbody>
<tr>
<td>(% of total leukemias)</td>
<td>10.3 (14%)</td>
<td>5.0 (13%)</td>
<td>6.2 (24%)</td>
<td>9.3 (36%)</td>
<td>7.0 (16%)</td>
<td></td>
</tr>
<tr>
<td>AML – Germany (n=439)</td>
<td>9.1</td>
<td>5.2</td>
<td>5.8</td>
<td>n.g.</td>
<td>6.6</td>
<td></td>
</tr>
<tr>
<td>AML – Germany (AML intergroup) [11]</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>6.2</td>
<td></td>
</tr>
<tr>
<td>AML – UK, England and Wales (n=190)</td>
<td>8.2</td>
<td>4.4</td>
<td>6.5</td>
<td>n.g.</td>
<td>6.5</td>
<td></td>
</tr>
<tr>
<td>AML – ACCISc (n=29–71)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>6.8–12.7</td>
</tr>
</tbody>
</table>

aRates are adjusted to the 1970 US standard population. Numbers in parentheses represent the percentage of the total cases for the specific age group.
bACCIS = Automated Childhood Cancer Information System Europe
cACCIS data from individual countries: Denmark, Ireland, The Netherlands, Slovakia and UK, and Scotland

Table 7.2 Initial clinical data according to age groups (Age: <2, 2–12, 13–21, 22–30 years). Data from the AML-Berlin-Frankfurt-Munster (BFM) Studies 93/98 and AML Cooperative Group (AMLCG)92 trial. WBC White blood cell count, CNS central nervous system

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>&lt;2</th>
<th>2–12</th>
<th>13–21</th>
<th>22–30</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender male:female (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.66</td>
</tr>
<tr>
<td>WBC median, range/µl</td>
<td>17900</td>
<td>17200</td>
<td>14000</td>
<td>19700</td>
<td>0.28</td>
</tr>
<tr>
<td>WBC &gt;100,000/µl (%)</td>
<td>22</td>
<td>15</td>
<td>21</td>
<td>13</td>
<td>0.029</td>
</tr>
<tr>
<td>Hepatomegaly &gt;5 cm (%)</td>
<td>24</td>
<td>25</td>
<td>27</td>
<td>35</td>
<td>0.36</td>
</tr>
<tr>
<td>Splenomegaly &gt;5 cm (%)</td>
<td>28</td>
<td>27</td>
<td>34</td>
<td>26</td>
<td>0.61</td>
</tr>
<tr>
<td>CNS involvement (%)</td>
<td>17</td>
<td>8</td>
<td>10</td>
<td>n.g.</td>
<td>0.008</td>
</tr>
<tr>
<td>Extramedullary organ involvement (%)</td>
<td>36</td>
<td>19</td>
<td>26</td>
<td>n.g.</td>
<td>0.00001</td>
</tr>
<tr>
<td>Total (n)</td>
<td>231</td>
<td>448</td>
<td>210</td>
<td>72</td>
<td></td>
</tr>
</tbody>
</table>
AML is most common and more likely to occur than ALL in the older age group (>65 years old), correlating to prolonged duration of exposure to environmental carcinogens proportional to age [17]. Only the incidence of acute promyelocytic leukemia (French-American-British, FAB, classification M3) appears approximately constant with respect to age after the first decade [18]. The FAB subtype M3 shows a high frequency (20–24%) in certain ethnic populations (e.g., Italian and Latin American) compared to other ethnic groups (5–8%), which may suggest a genetic predisposition for acute promyelocytic leukemia and/or specific environmental exposures [19].

### 7.3.3 Trends in survival

Survival rates in children under 20 years with AML have improved over the last three decades. Population-based estimates of 5-year survival increased from 23% in the period 1975–1984 to 41% in the period 1985–1994 [4]. Current 5-year survival in children, adolescents, and young adults enrolled in clinical trials (which tend to be higher estimates because trials may exclude patients with unfavorable features or patients from small hospitals) is in the range of 45–60% [1, 20–22]. Results from the AML-BFM studies (patients <18 years old) showed an improvement of 5-year survival from 49% (study AML-BFM 87, period 1987–1992) to 60% (period 1993–1998) [1]. The improvement in prognosis over the last decades in all age groups was made possible by intensified chemotherapy and supportive care. With intensive induction chemotherapy, 80–90% of young patients achieve complete remission (CR).

Little data specifically analyze survival for adolescents and young adults. Population-based data from regions of England and Wales showed that 5-year survival improved significantly from 36% in the period 1984–1988 to 46% in the period 1989–1994 for AML patients between 15 and 29 years old. For patients of this age group treated in the MRC-trials AML 9 and AML 10, 5-year survival increased from 35% to 55% (p=0.012) from the first to the second period [2].

According to SEER data on 15-to 29-year-olds, 5-year survival increased from 15% (1975–1980) to 40–42% between 1987 and 1998 [4].

### 7.3.4 Prognostic factors

Outcome for females with AML was somewhat better than that for males. Outcome was similar for white and for black children younger than 20 years of age [4], but recent data suggest that improvements in survival have preferentially favored whites, probably on a genetic basis [23].

Increasing age is a known poor prognostic factor in adults with AML [24]. In population studies, 5-year survival rates drop with age: 44% for patients aged 0–15 years, 42% for those aged 15–29 years, and 32% for those aged 30–44 years for the recent time period 1993–98 [4]. However, prognosis in different age groups of children and older adolescents treated similarly have rarely been reported.

The Children’s Cancer Group (CCG) trials include children and adolescents less than 22 years old. Five-year survival in CCG trial 213 (1986–89) was 39% and therewith significantly higher than in the previous CCG 251 study (1979–83: 29%) [25]. In this study survival rates were not different in 2- to 10-year-old children and adolescents aged 10–21 years [26]. The same was seen in the recent CCG-2891 trial: in younger (0–16 years) and older (16–21 years) patients treated with intensive timing chemotherapy, survival at 5 years was 49% and 51%, respectively [27]. The British Medical Research Council (MRC) AML 10 trial (1988–1995) included AML patients up to age 35 years on the same treatment regimen. They achieved high CR rates for children under 15 years (91%) and young adults aged 15–34 years (85%). The induction death rate increased slightly, from 5% in children to 7% in young adults; a similar small increase in resistant disease was seen (5–7%). Survival at 5 years was 53% and 60% in children up to age 15 years (after daunorubicin-cytarabine-etoposide and daunorubicin-cytarabine-thioguanine induction, respectively) and 46–47% for the 15–24 year and 25–34 year age groups [20].

The same trend to decrease in survival with age was reported for the event-free survival (EFS) rates but not overall survival in more than 1,000 Japanese AML patients aged 1–29 years consecutively diagnosed in the period 1986–1999, who were treated in a variety of institutions and protocols. Seven-year probability of EFS (pEFS) for AML decreased from 34% in the age
groups 10–15 years to 32% for 15- to 19-year-old adolescents, and to 26% in the 20- to 29-year-old young adults [28].

Treatment schedules and dosing of the AML-BFM 93/98 studies for children and adolescents (n=869) and the AMLCG92 study for adults (n=832) were similar during induction and consolidation [29]. In the adult study, 92 patients were 16–30 years old. A common analysis of patients of both studies showed that the CR rate was highest in the age group 2–12 years (89%) and lower in infants and patients of older age (<2 years, 80%; 13–<21 years, 83%; 21–30+ years, 75%). Long-term treatment results were also most favorable among 2- to 12-year-old children (5-year pEFS ±SE, 54±3%), slightly inferior in adolescents (46±4%, p=0.03), and unfavorable in young adults (28±5%, p=0.0001). Excluding patients with low-risk cytogenetics [t(8;21), inv16 and t(15;17)], results were inferior in adolescents (pEFS 32±5%) and young adults (pEFS 26±7%) compared with children aged 2–12 years (pEFS 47±4%) [30].

7.3.5 Treatment Differences

Adolescents and young adults, however, are not always treated on pediatric trials. Recently, adolescents of 16–21 years treated on CCG 2891 with intensive timing (1989–1995) were compared with patients of the same age group treated at the University of Texas MD Anderson Cancer Center on relatively less aggressive adult protocols (1980–2000). Patient characteristics were similar; however, 5-year survival for patients treated on the CCG-trials was 51% compared to 32% in the adult trial. Based on these results, the MD Anderson Cancer Center will now examine the role of intensive timing induction therapy in young adults with de novo AML [31].

7.4 Biology/Pathology

Biologic parameters across the entire age spectrum are reported rarely in the literature. Jeha et al. [29] reported on the influence of vascular endothelial growth factor (VEGF) in pediatric and adult patients. Unlike in adults, VEGF and VEGF-R2 levels in pediatric AML patients did not correlate with survival. Also contrary to the case in adults, expression of the multidrug resistance gene (MRD1) failed to define a poor prognostic group in childhood AML [32]. The frequency of cytogenetic subgroups of AML are age specific, certainly in adults, with an increase in the poor prognosis unbalanced aberrations with age [33].

We have analyzed the initial clinical, morphological, and cytogenetic data of children, adolescents, and young adults treated in the pediatric trials AML-BFM 93/98 (n=869) and of 92 young adults (<30 years) of the AMLCG92 study. Age classifications were infants (≤2 years), children between 2 and 12 years of age (because there were significant differences in biologic parameters in these age groups) [34], adolescents between 13 and 21 years of age, and young adults between 21 and 30 years. Results show (Fig. 7.2) that French-American-British (FAB) distribution was quite different in young children <2 years, 68% (147/213), who presented with FAB subtypes M5 or M7, compared to 18% (133/730) in the older age groups (χ² p<0.0001). However, apart from a trend toward increasing M1 and decreasing M7, there was no difference in FAB types for children (2–12 years) and patients 13–30 years old. The favorable karyotypes t(8;21), t(15;17), and inv16 were rarely seen in children
<2 years (8/163=5%) compared to the 2- to ≤21-year-olds (141/580=24%; Fisher p=0.01; Table 7.3). With the limitation of the low patient number, it is of interest, that t(8;21) was seen less frequently in young adults compared to the 2- to 21-year-old group.

Our data do not show significant differences in biological parameters between the age groups of 2- to 12-year-old children, adolescents, and young adults, albeit there was a lower incidence of 11q23 and t(8,21) above age 12 years than below this age. Only patients younger than 2 years of age present with significant differences in comparison to older patients. Genomic and proteomic studies currently underway are likely to disclose other age differences, such has already been demonstrated for acute lymphoblastic leukemia.

One exception is the occurrence of the subtype M3, which has a high prevalence in Latinos [19]. In a single institute in Mexico, 20% of all AML patients and 30% of adolescents (11–21 years old) presented with FAB M3 [35]. A report from Japan ascertained a gradual increase of M3 in adolescence: 1–4 years (~5%); 5–9 years, 8%; 10–14 years, 12%; 15–19 years, 19%; 20–24 years, 22%; 25–29 years, 21% [28].

### Table 7.3 Karyotypes in the different age groups. Data from the AML-BFM studies 93/98 and AMLCG92

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>&lt;2</th>
<th>2–12</th>
<th>13–21</th>
<th>21–30</th>
<th>p (χ²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>t(8;21) (%)</td>
<td>1</td>
<td>18</td>
<td>10</td>
<td>5</td>
<td>0.0001</td>
</tr>
<tr>
<td>t(15;17) (%)</td>
<td>2</td>
<td>6</td>
<td>8</td>
<td>10</td>
<td>0.02</td>
</tr>
<tr>
<td>inv16 (%)</td>
<td>2</td>
<td>8</td>
<td>6</td>
<td>9</td>
<td>0.07</td>
</tr>
<tr>
<td>11q23 (%)</td>
<td>27</td>
<td>11</td>
<td>7</td>
<td>n.g.</td>
<td>0.0001</td>
</tr>
<tr>
<td>Total (n)</td>
<td>164</td>
<td>320</td>
<td>150</td>
<td>43</td>
<td></td>
</tr>
</tbody>
</table>

7.6. Treatment/Management

Treatment regimens for AML are often but not always similar in children, adolescents, and adults, generally starting with intensive induction courses with cytarabine and anthracyclines of an adequate dosage to achieve remission. Induction therapy is followed by postremission phases to destroy residual blasts in the bone marrow or at other sites. The duration and the optimal type of postremission therapy remain to be established. In general, intensive chemotherapy cycles (referred to as consolidation and/or intensification courses) should include one or more courses of high-dose cytarabine. They are administered together with some kind of CNS prophylaxis and may be followed by a less intensive maintenance chemotherapy. Allogeneic

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7.5. Diagnosis: Symptoms and Clinical Signs

The clinical presentation in children, adolescents, and young adults is mostly similar (Table 7.2). It reflects the degree to which the bone marrow has been infiltrated with leukemic blasts and the extent of extramedullary involvement, and can be both a reflection of tumor biology and health services factors (host- and provider-related delays in diagnosis). The most common symptoms and physical findings result from anemia, thrombocytopenia, and neutropenia, and include pallor and fatigue, anorexia, petechiae, purpura, bleeding, and infection. Occurrence of initial hyperleukocytosis (white blood cell count>100,000/µl) did not vary significantly in the different age groups. Initial involvement of the central nervous system (CNS) is seen less often in adolescents (~10%) and in children aged 2–13 years (~8%) than in infants (~17%) with AML (data not available for young adults, who rarely get diagnostic lumbar puncture). Infiltration of the skin, especially in monocytic leukemias, is also most frequent (~20%) in young children (<2 years) and rarely seen in older children and adolescents. Likewise, leukemic infiltrations of the periosteum and bone occur more often in young children than in adolescents.
or autologous stem-cell transplantation may be included as another form of intensification, and indications and rates vary between countries, study groups, and between pediatric and adult providers.

For some specific subgroups, special treatment is available. The most successful special treatment was the introduction of the differentiating agent all-trans-retinoic acid (ATRA) for patients with AML-M3, inducing cell differentiation and maturation instead of cell destruction [36, 37]. A trial using this therapy for AML-M3 patients of all ages was the first biologically based clinical trial cooperation between adult and pediatric clinical trial groups in the United States.

Acute management and supportive care are required during all treatment phases, especially during the first few days and weeks of intensive induction therapy. With recent improvements in AML treatment results, the balance between treatment intensity and toxicity has become more important than in the past, requiring trials to perform risk-adapted therapy.

Generally speaking, the acute and chronic toxicity of chemotherapeutic agents has a similar impact on children, adolescents, and young adults. In adolescents, a higher degree of anticipatory vomiting is seen and, in our experience, a somewhat less rapid recovery from myeloablative treatment. Although the compliance during intensive treatment phases in the adolescent age group is not different from that in children and older patients, as most if not all chemotherapy is given in the hospital, in our experience it may be lower during maintenance therapy, just as adherence to oral chemotherapy has been shown to be lower in adolescents with ALL.

Most difficult in the management of adolescents is the indispensable psychosocial care. The needs of adolescents are different from those of young children and are accompanied by the conventional problems that are associated with this age group (e.g., need of autonomy and independence, social development, sexual maturation, education, and employment) [39]. These problems are the same as for adolescents and young adults suffering from other types of cancer.

### 7.7 Participation in Clinical Trials

More than 90% of children less than 15 years of age with AML are treated within clinical trials in the Nordic countries [39], 67% in the United Kingdom [40], and more than 60% in the United States. However, for all cancer patients aged >15 years, the percent enrolled in clinical trials is much lower [41, 42]. This was true for AML patients aged 15–29 years in the United Kingdom from 1989 to 1994, where only 39% of patients aged >15 years were entered on clinical trials [2]. New data from the five German AML intergroup trials included in the Competence Network “Acute and Chronic Leukaemias” indicate that young adults are now generally included in clinical trials [11]. Benja-
min et al. [40] reported on the percentages of patients with acute leukemia entered in the MRC trials from 1991 to 1995. Questionnaires were sent to 121 hospitals, and data from the 96 that responded showed that 82% of pediatric AML patients (61% aged between 15 and 19 years and 52% between 20 and 29 years) were entered “always” or “whenever possible” into MRC trials [40]. This low percentage is also a reason for the lack of data in clinical trials regarding the adolescent age group and a possible bias of results including comparisons in age groups.

Several authors state that the prognosis for adolescent leukemia sufferers may be improved by introducing pediatric trials that take into account the prognostic biological features [28]. Another point is the prognostic influence of referring these patients to centers with experience in the management of leukemia, or to centers that participate in clinical trials for children or adults. According to the data available, differences in outcome for patients treated in pediatric or adult trials were more pronounced for adolescent ALL than for AML patients [28, 43].

### 7.8 Expected Outcome, Including Late Effects

Late effects among survivors of AML during childhood and adolescence may have a significant impact on their quality of life. Long-term sequelae of treatments can include impaired intellectual and psychomotor functioning, neuroendocrine abnormalities, impaired reproductive capacity, and second malignancies [44]. However, most of these late effects, especially side effects after CNS irradiation (neurocognitive deficits, growth hormone deficiency, and secondary CNS tumor) given in the AML-BFM studies for all age groups, but not in other AML trials, affect the younger age group. Anthracycline cardiotoxicity is also seen at lower cumulative doses (<300 mg/m²) in patients younger than 18 years but rather at 550 mg/m² in those over 18 years [45].

The risk of endocrine dysfunction is relatively low in AML patients who are treated with standard chemotherapy only (without alkylating agents), however after stem-cell transplantation there is an increased risk of endocrine dysfunction [44]. Impairment of growth rates after busulfan/cyclophosphamide or cyclophosphamide/total body irradiation (TBI) conditioning regimens is a problem in children treated before or during their growth period. Gonadal toxicity is seen in all age groups, mainly as gonadal dysfunction; however, it is relatively low with modern conventional therapy [44]. Gonadal toxicity may cause disorder of pubertal development, infertility, sexual dysfunction, and the need for long-lasting hormone substitution. In adult women, high doses of alkylating agents and TBI increase the risk of ovarian failure and the probability of restoring the ovarian function decreases by a factor of 0.8 per year of age [46]. The addition of busulfan to cyclophosphamide causes permanent ovarian failure in nearly all female patients. In males the effects of both cytotoxic chemotherapy and TBI will damage the germinal epithelium of the testis, and for the majority of males in all age groups, permanent infertility is likely after TBI schedules [46].

Therefore, in the future, prior to stem-cell transplantation germ cells or gonadal tissue should be collected and stored with the aim of enabling patients to become parents later on [46].

Second malignant neoplasms have been described mainly in ALL patients, with a cumulative incidence of approximately 2–3% at 15 years of age [12, 44]. Data regarding second malignancies following treatment for AML are scarce, probably because the number of long-term survivors is much lower. Within the AML-BFM studies, only 12 second malignancies have been observed among 928 children, who were alive at least 3 years after treatment. Most of these patients had received chemotherapy only. After stem-cell transplantation, the risk of second malignancies is higher for any disease (standard incidence ratio from 6.7 to 11.6 in different studies compared to patients given chemotherapy only) [47]. AML and myelodysplastic syndrome are often reported as second malignancies after chemotherapy with alkylating agents or topoisomerase inhibitors, therefore it might be difficult to distinguish between relapse or second malignancy in primary AML patients.

In all age groups with leukemia and lymphoma, more depression and somatic distress were reported in comparison with sibling controls [44].
7.9 Summary

AML incidence increases with age, such that the frequency in adolescents lies in between that of children and adults. Biological factors vary by age, but the biology of AML in adolescents and young adults appear most similar to that of children. Outcome has improved for all age groups during the last 15–20 years, with the advent of better chemotherapy and supportive care. However, there continues to be a trend toward better survival in children than in young adults, which may be partly related to the intensity of treatment or to treatment in pediatric trials. Further research should be directed toward biologically based, not age-specific trials.

Acknowledgement

Thanks to Professor Thomas Büchner for generously providing data on young adults from the AMLCG Study

References


28. Büchner T, Hiddemann W, Berdel WE, et al (2003) 6-Thioguanine, cytarabine, and daunorubicin (TAD) and high-dose cytarabine and mitoxantrone (HAM) for induction, TAD for consolidation, and either prolonged maintenance by reduced monthly TAD or TAD-HAM-TAD and one course of intensive consolidation by sequential HAM in adult patients at all ages with de novo acute myeloid leukaemia (AML): a randomized trial of the German AML Cooperative Group. J Clin Oncol 21:4496–4504


