Preface

Dear Colleagues,

Since the start of the Kompetenznetz “Akute und chronische Leukämien” five years ago in October 1999 great improvements have been achieved which was also affirmed by the international external advisory board at the second interim evaluation in June 2004.

Highlights were the establishment of the German AML Intergroup, the formation of the German MDS study group and the high number of patients treated within clinical trials.

Nevertheless funding will be significantly reduced for all networks in 2005 to about a quarter of the previous financial support. In consideration that the original funding period was restricted to five years by the BMBF, the prolongation of the project for three more years is in recognition of the successful work of the network. We therefore thank all partners for their cooperation during the last 5 years.

We would like to take the opportunity to invite you to the next Annual Symposium of the Competence Network “Acute and Chronic Leukemias” in Heidelberg from 1.-3. of February 2005.

I wish you a stimulating and interesting reading of the following circular.

Yours sincerely

Prof. Dr. R. Hehlmann
Network-Coordinator of the German Competence Network “Acute and chronic Leukemias” and the European LeukemiaNet
Protection of female fertility in patients with leukemia
E. Siebzehnrübl, Gyn. Endokrinologie und Reproduktionsmedizin, Dep. of Gynaecology and Obstetrics, University Frankfurt

Introduction
New, often very aggressive treatment schemes allow the successful healing of many young patients with cancer most of whom suffer from lymphatic diseases. But the price the young women have to pay is high: a high percentage of them loses ovarian function, and fertility. Oncologists develop a understanding that hormone replacement therapy is not enough for the patients only still.

While chemotherapy using antimetabolists induces ovarian failure only in a few percent of the patients, the risk after Doxorubicin®, Mitoxantron or Platin is between 30 and 60 percent. Cyclophosphamide or Busulphane induce an ovarian failure in 70% of the patients, and after a high dosage chemotherapy and radiation of the whole body about 92 percent of the patients are menopausal. The patient’s age is of major importance, because young women with mammarian cancer after chemotherapy seldom suffer from ovarian failure, the rate rises to nearly 100 percent for patients over forty.

Methods to preserve fertility
Since the nineteen nineties there are reports about good success in ovarian protection using gonadotrophin releasing hormone agonists (GnRHa) in the literature. It was proposed that these substances act by blocking the LH and FSH secretion of the hypophyse, and thereby block the proliferation of granulosa cells, and follicular development [1]. Unfortunately, there are no major randomised, prospective studies which show the effectiveness of this treatment.

An alternative is the cryopreservation of female gametes or ovarian tissue.

While the freezing of gametes is routinely used worldwide within the IVF / ICSI programs this is no option for most cancer patients. In most of the cases there is no time for stimulation, no partner is available, or the patient does not feel healthy enough to undergo the procedure. Moreover unfertilised oocytes are very difficult to handle during freezing. Although the method is used since 1984, only 60 children have been borne worldwide till now.

To avoid these problems some teams worldwide work on the cryopreservation of ovarian tissue which has up to several thousands follicles per cm². Till now, however, it was not possible to keep to thawed tissue living for an extended period of time, neither in vivo, nor in vitro.

State of the art
Even with low success rates, it was possible to produce living mouse pups after the transplantation of thawed ovaries to recipients. In sheep it was possible to get normal ovarian function after the transplantation of frozen / thawed ovaries.

Our own data show that most of the ovaries, but only forty percent of intact follicles survive freezing [2]. The xenotransplantation of parts of thawed human ovaries to SCID mice was successful, but it was evident that only a small part of the tissue was functional afterwards. Shaw et al. could show as early as 1996 that lymphoma can be transplanted also [3]. Therefore much work has to be done before a clinical study is possible.

Using in vitro culture after the thawing of cryopreserved human ovarian tissue was not able to grow follicles beyond the state of primordial follicles.

German AML Intergroup Study : Extension to patients of 60 years and over
Th. Büchner for the German AML-Intergroup

By the activation of their joined protocol in early 2002 the German AML Intergroup started its trial activity. This first step involved patients under 60 years of age. In the meantime, some 1000 patients have been centrally up- front randomised with 90% assigned to the protocol of the individual study group and 10% to the common standard treatment arm. After the trial network proved practicable and effective in the younger age group, the joined protocol has now been extended by a new amendment to the age group of 60 years and over.

The structural basis of the protocol for the younger age group has been maintained as far as possible for the older patients but also age adjusted where necessary. As in the younger group the standard arm contains 2 induction courses of araC 100mg/m² per day continuous i.v. infusion over 7 days, with daunorubicin 60mg/m² i.v. on days 3, 4 and 5. Differently form the younger group of 60 years and over.

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The German AML Intergroup trial network provides to the participating trial groups a therapeutic standard to validate their trial own therapy and to compare therapies across the individual trials (1,2).

An extension to patients 60 years of age or older is suggestive and highly warranted. For this age group the opinions about disease biology, resistance and therapy intensity diverge substantially. Only 1/3 of patients in large multicentre trials are over 60 although 2/3 of the entire AML patients belong to this age group (overview 3).

Summary
The cryopreservation of ovarian tissue before chemotherapy and / or radiation for cancer is a very interesting, but clinically not relevant option to preserve fertility of female cancer patients, today. The alternative, and at least published in a number of studies is the treatment with GnRH anaologa before and during the chemotherapy. But looking at the effect of highly aggressive treatments this is the only chance for the patients to preserve fertility. Many teams work on the solutions of the presents problems worldwide. Even if it is not possible to guarantee the success of the cryopreservation today this treatment offers a possibility to retain fertility to the patients, which has a great importance, and if only for psychological reasons.

Literature: www.kompetenznetz-leukaemie.de
In October 2003 the AML Study Group (AMLSG) held up its constituent assembly at the Reisenburg in Günzburg (Figure 1). The joint AMLSG arises from the study groups of the Süddeutsche Hämoblastose Gruppe directed from Hannover/Frankfurt as well as the former AML Study group of Heidelberg and since 2000 of Ulm the AMLSG ULM. Both study groups introduced 10 years ago risk-adapted treatment strategies in Germany resulting in several treatment trials in this period (AML 2-95, AML 1-99, AML HD93, AML HD 98A). With the initiation of the Kompetenznetz “Akute und chronische Leukämien” the two study groups intensified their cooperation. In 1998 we initiated the first joint analyses of cytogenetically defined subgroups in AML within the Kompetenznetz “Akute und chronische Leukämien” resulting in the original-data based meta-analysis of the German AML Intergroup on core binding factor acute myeloid leukemia (Schlenk et al. JCO 2004). One major finding of this analysis was that in the future a single study will not be able to answer clinically relevant questions in cytogenetically defined subgroups. Therefore, first discussions on new treatment strategies and new prospective treatment trials between the two study groups commenced in 2002. Initially, these discussions were restricted to transplantation strategies in high risk patients defined by primary refractory AML and/or by cytogenetics resulting in the integration of additional radioimmunotherapy into the strategies for high risk patients. Actually the active multicenter treatment trials of both groups have been closed (AMLD98A, AMHD98B, AML 1-99). During our first joint meeting of the whole study group in October 2003 at the Reisenburg we discussed our treatment-trial strategies. Based on this discussion we initiated three Multicenter treatment protocols which have been activated in August 2004:

- AMLSG 05-04 primary refractory AML, age 18–60 years, phase II
- AMLSG 06-04 newly diagnosed AML, age >60 years, phase III
- AMLSG 07-04 newly diagnosed AML, age 18–60 years. Phase II

The concepts of the studies are as follows:

**AMLSG 06-04**: The title of this study is “phase III study” on valproic acid in combination with all-trans-retinoic acid, standard induction and consolidation therapy in elderly patients with newly diagnosed acute myeloid leukemia”. The trial is summarized in figure 4. The standard-arm of this study is based on the results of the randomized AMLHD98B study (Schlenk et al. Leukemia 2004). In this study we were able to show that the addition of all-trans-retinoic acid to standard induction and consolidation therapy resulted in a significantly better remission-rate after induction therapy and a significantly better event-free and overall survival. Additionally, a second intensive consolidation therapy with idarubicine and etoposide was significantly better compared to a per oral maintenance therapy with the same drugs concerning the cumulative incidence of relapse and overall survival.

**AMLSG 07-04**: The title of this study is "randomized phase II study on valproic acid, all-trans retinoic acid and their combination in addition to standard induction and consolidation therapy as well as Pegfilgrastim in the consolidation therapy of younger patients with newly diagnosed acute myeloid leukemia". The trial is summarized in figure 3. This phase II study integrated a risk stratification based on the initial response to induction therapy and on cytogenetics. Patients with primary refractory acute myeloid leukemia after first induction therapy are off-study concerning the AMLSG 07-04 protocol and were treated within a separate protocol AMLSG 05-04. Patients with a good response to induction therapy but unfavorable cytogenetics are intended to receive two induction cycles and are off-study thereafter. They are eligible for our dose intensified conditioning regimen protocols before allogeneic transplantation. All patients within the AMLSG 07-04 protocol are up-front randomized between the standard-arm and the experimental arms with either all-trans retinoic acid or valproic acid or their combination. This initial randomization is valid for induction and consolidation therapy. For consolidation the backbone therapy with high-dose cytarabine is identical to the consolidation therapy used in the common standard arm of the German AML-Intergroup. An allogeneic transplantation will be intended only in standard risk patients and not in patients with core binding factor AML if an HLA-identical family donor is available. This decision is based on the meta-analysis of the AMLSG on 792 patients with normal karyotype showing a significantly better relapse free survival after an allogeneic transplantation from an HLA-identical sibling donor in first complete remission. As in the AMLSG 06-04 study in the AMLSG 07-04 study we introduced valproic acid and all-trans retinoic acid into first line therapy of newly diagnosed AML in a randomized manner.
AMLSG 05-04: The title of this study is "phase II study on Gemtuzumab Ozogamicin in combination with all-trans retinoic acid, high-dose cytarabine and mitoxantrone in patients with primary refractory acute myeloid leukemia [60-A-HAM]". This study is open for patients with primary refractory acute myeloid leukemia aged 18 to 60 years and is integrated in the concept of the AMLSG 07-04 study (Figure 3). The study is summarized in Figure 2. The induction of a complete remission before allogeneic transplantation is a prerequisite for long-term survival. Therefore, this study is designed to increase the rate of patients achieving a complete remission after this salvage therapy.

Within our new treatment trials cytogenetics and morphology are performed centrally, and immunophenotyping will be reviewed centrally. The scientific program for the three studies includes gene-expression profiling, matrix-based comparative genomic hybridization and a target-monitoring concerning valproic acid and all-trans retinoic acid.

During the following two years the studies will recruit about 1000 patients. Therefore, the design of our next study generation will have to be initiated in 2005. The fusion of the two study groups allows us now to answer clinical and scientific questions within a limited time period. This will augment our international competitiveness.

Protocols:
www.kompetenznetz-leukaemie.de

The prognosis of patients with refractory or relapsed AML is limited. Despite complete remission rates of about 50%, the median duration of leukemia-free survival is only about 6 months in median. In our previous study with the triple combination mitoxantrone, topotecan and cytosine-arabinoside (MTC) a CR rate of 30-70% was achieved dependent on the first remission duration, with a second remission duration of about 6 months. If ever possible, however, patients received an allogeneic stem cell transplantation (SCT) in 2nd CR. As the clinical results are not satisfactory so far, new approaches to improve patients outcome including the induction of 2nd CR to perform allogeneic SCT is needed.

Here, new tumor targeting agents modifying or blocking signal transduction pathways or inducing apoptosis might be of interest especially in combination with chemotherapy. Such an new agents is the tyrosin-kinase inhibitor Imatinib (Glivec®). Imatinib has a high efficacy in chronic myloid leukemia (CML) and GIST via inhibiting the bcrl/abl and/or c-kit related tyrosinkinase. In AML patients responses were described, additionally, whereby the relevance of c-kit or PDF-GR expression is still undefined.

In the new study patients with relapsed AML will be treated with a combination of Imatinib and the chemotherapy schedule MTC. Primary endpoint is the CR rate of MTC-Glivec, secondary endpoints are tolerability, relapse-free survival (RFS) and overall survival (OS). Glivec will be sponsored for this study.

The start of this protocol will be September 2004. Protocol and further details can be asked for by the study coordinator (Prof. Dr. L. Bergmann, phone +49-69-6301-5121, Fax +49-69-6301-3876, email L.Bergmann@em.uni-frankfurt.de) or via the websites of the “Kompetenznetz Leukämie” www.kompetenznetz-leukaemie.de

Further details:
www.kompetenznetz-leukaemie.de

The Open-label Multicenter Trial of Glivec® (imatinib mesylate, formerly known as STI571) in Combination with Chemotherapy (MTC) in Patients with Refractory or Relapsed Acute Myeloid Leukemia (AML) - AMLSG-R1 (SHG-AML-R2)
The German MDS Study group performs a variety of different scientific as well as clinical studies. Since the Competence-Network "Acute and chronic Leukemias" was established, three different projects located in Düsseldorf, Duisburg and Hannover were funded.

The MDS registry in Düsseldorf served as a database for epidemiological studies, assessment of prognosis and risk stratification and was the basis for the German MDS registry.

We observed an increase in the number of registered patients. At the moment, 2520 MDS patients, including 135 secondary MDS are registered and followed-up.

Standardized diagnostics of blood and bone marrow slides by central morphology for all registered patients are performed in Duisburg and Düsseldorf. Our data demonstrated, that MDS belong to the most frequent hematologic malignancies with an incidence of about 5 patients /100000 inhabitants per year.

Assessment of prognosis aims a risk stratification leading to risk adapted studies.

Based on the registry a new working party was established (German-Austrian-MDS Prognosis working party), including Düsseldorf, Duisburg, Freiburg (Prof. Lübbert), Göttingen (PD Haase), Wien (Prof. Valent, PD Pfeilstöcker, Dr. Nösslinger), Linz (Dr. Krieger) and Innsbruck (Prof. Stauder).

To validate the prognostic impact of cytogenetic findings, a data set including more than 1500 MDS patients, in whom chromosomal findings were available, was established. The next meeting of this study group will take place in Düsseldorf, on September 15th.

The German MDS Study Group performed diverse clinical studies intended for the different MDS risk groups. The study for patients with 5q- anomaly with All-trans-Retinoic acid was closed after inclusion of 29 patients. About 20% of these patients show an increase in cell counts. In another study conducted by Prof. Aul and Dr. Giagounidis for Germany, patients with 5q- anomaly were treated with CC5013. Within a few weeks, 34 patients have been included. The majority of patients became transfusion independent. Some patients even achieved cytogenetic remission.

Two studies on Thalidomide were performed, organized and published by Prof. Gattermann, Dr. Strupp and Prof. Ganser in Düsseldorf and Hannover. Treatment with Thalidomide lead to haematologic improvement in about 30% of the patients. In a few patients a cytogenetic remission could be achieved. However there is a large number of patients who stopped thalidomide treatment due to side effects.

A phase II study comparing ATG to ALG was performed and published by Prof. Ganser and Dr. Stadler. Immunotherapy leads to an improvement in cell counts especially in patients with RA and normal karyotype. On the basis of these data, a phase III trial of the German MDS study group and the SAKK with ATG and CSA versus best supportive care, was initiated by Prof. Ganser for low risk MDS patients.

Patients within the high-risk group (IPSS >2.5) can be treated with AML-like protocols. A study of the German MDS study group together with the AMLCG (Prof. Aul) compares Idarubicin- versus Fludarabin based induction followed by HAM and auto or allogeneic transplantation.

Some other clinical studies have been performed within the German MDS study group (Amifostin (PD Haase), Trisenox (Prof. Gattermann and Prof. Ganser), Iron chelation with CT1670 (Prof. Gattermann and Prof. Ganser) and Farnesyltransferase-Inhibitor Zarnestra (Prof. Ganser, Prof. Aul, PD Germing)). Other studies are in preparation.

Central morphology and prospective patient registration as well as numerous clinical trials in all MDS risk groups result from a close collaboration of all participating centres. Based on this scientific projects like gene expression profiling, proteomics, methylation studies, karyotype evolution etc.) are ongoing. Figure 1 shows the clinical trials of the German MDS study group that are open for inclusion.

The MDS Study group opened a phase III study in Co-operation with the EORTC (Prof. Lübbert), which compares Decitabine with supportive care. Another study compares 5-Azacytidine to best supportive care or chemotherapy (Prof. Gattermann).

A new approach is the histone-deacetylase inhibitor Valproic acid. A series of 23 patients was published and showed haematologic improvement in 8 patients. The German MDS study group initiated a study, conducted by Prof. Gattermann and Dr. Kündgen to further evaluate the therapeutic benefit.

Two studies with hypomethylating agents are ongoing. 5-Azacytidine and 5-Aza-2-deoxycytidine lead to inhibition of DNA-Methyltransferase. Response rates of 50-60% including partial remission and haematologic improvement, even in patients with complex karyotype, are reported from earlier trials.
A primary objective of our project is the optimization of quality of cytogenetic diagnostics in leukemias. Hence, we established an external karyotype review procedure and inter-laboratory examinations of chromosomal banding analyses.

The central karyotype review covers the external evaluation of chromosomal findings including the review of the respective karyotypes, and has been installed in two domains:

1. Random review of the quality of the results raised in the context or outside of studies for different leukemia entities among voluntarily participating laboratories. This review is performed by a committee which is organized by the investigators which participate in the karyotype review.

2. Review of all chromosome findings of the patients recruited in the combined standard arm of the AML studies of the competence net leukemia. This review is performed by a standing committee which was authorized by the study coordinators.

A coordination center for the central karyotype review was established in Marburg and a preliminary procedure for the external karyotype review was defined. The chromosomal findings including a minimum of 3 karyotypes per aberrant clone were made anonymous and digitized, and then sent by email to the coordination center. After acquisition and formal checks, the findings were emailed to three independent experts. Possible outcomes of the review were accepted, questionable, or rejected. If chromosomal findings were not accepted or no consensus between the experts was reached, the coordination center invited to an online conference (via ipath-server: http://telepath.patho.unibas.ch/tpdb/). After completion of the external reviews, experts and cytogenetic laboratories were informed about the results. The coordination center stored the data collected during the procedure in a database for later analyses.

For a random karyotype review, we asked laboratories to provide us with their first case with CML of the second quarter of 2003. Seventeen cytogenetic laboratories submitted chromosomal findings of CML at the time of diagnosis or, if not available, during progression. Generally, quality of graphical data was high, but loss of quality was experienced after scanning printed karyotypes. A total of seven independent experts were involved in the external review and most of them completed the review within 5 days. Fourteen out of seventeen chromosomal findings were accepted (82%), and the results were questioned in 3 cases (18%). In the latter cases, an online conference was initiated. Based on this successful implementation of an external karyotype review, we plan further surveys for other leukemia entities.

Up to now, the chromosomal findings have been reviewed in 66 of 74 patients randomized in the combined standard arm of the AML studies. Fifty-four findings (82%) were accepted in the external review and the diagnostic laboratories were informed about the results. In 12 cases (18%), chromosomal findings were questioned or no consensus was reached, and an online conference was initiated. A final decision is still pending.

To check the complete process of the chromosomal banding analysis including the pre-analytical, analytical and post-analytical phases, an inter-laboratory test procedure was developed with samples resembling leukemic peripheral blood. Nineteen laboratories participated in a pilot test procedure. All participants received a sample of a defined mix of chromosomally normal and aberrant cells. Twelve laboratories (63%) succeeded with identifying all karyotypes contained in the sample. Deviations from the correct karyotype were encountered including an incomplete registration of the chromosome alterations presented in subclones and the identification of unspecific alterations which were not detected in the original sample.

All together, the results of the procedures employed in our studies of quality control in leukemia cytogenetics demonstrate that an external review of chromosome findings and inter-laboratory tests are indispensable in our efforts to assure reliability and validity of the chromosome analysis in leukemias. Scrutiny of the cultivation and preparation methods applied by the distinct laboratories must be a top priority.

Standardized methods have to be developed, if reproducible results between laboratories are to be achieved. As a step towards it, minimum standards for the cultivation of samples of acute and chronic leukemia were established (http://knm1.ibe.med.uni-muenchen.de/tumorzytogenetik/index.html/ZytogenetischeTechniken). For the external karyotype review, a final set of criteria for the evaluation of the quality of chromosome preparations and of written chromosomal reports have to be developed.

**New studies of the GMALL study group**

<table>
<thead>
<tr>
<th>Short title</th>
<th>Type of study</th>
<th>Target group</th>
<th>Therapy</th>
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<tbody>
<tr>
<td>GMALL 07/2003 with Rituximab in B-precuror ALL</td>
<td>Multicenter TOP</td>
<td>B-precuror ALL Standard risk 15-55 yrs</td>
<td>According to GMALL 07/2003 + 6 doses Rituximab</td>
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<tr>
<td>GMALL 07/2003 in T- lymphoblastic lymphoma</td>
<td>Multicenter TOP</td>
<td>T-lymphoblastic lymphoma 15-65 yrs</td>
<td>According to GMALL 07/2003 for 1 year + mediastinal irradiation</td>
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<tr>
<td>DepoCyt® in CNS relapse</td>
<td>Multicenter Phase II</td>
<td>CNS relapse of ALL Burkitt, B-LGL &gt;=18 yrs</td>
<td>2-6 doses in 2-weekly intervals</td>
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*TOP=therapy optimisation protocol*
Ongoing studies within the competence network

Acute Lymphoblastic Leukemia

De novo ALL (<55-65 years):
- GMALL-Study 07/2003
- GMALL Study + Rituximab
- GMALL T-LBL 1/2004
- GMALL B-ALL/NHL 2002
- STi in Ph/BCR-ABL positive ALL with MRD

De novo ALL (> 55-65 years):
- GMALL Elderly 01/2003
- GMALL-STI571-Elderly-0102
- GMALL B-ALL/NHL 2002

Relapsed:
- GMALL DepoCyte
- GMALL-STI571-Flag-lida
- GMALL-STI571-IFN
- Compound 506U78 in T-ALL
- MahCampath in T-ALL
- ALL-Relapse Study - Rostock (coming soon)
- Aplidin in ALL

Supportive Care:
- Fasturtec vs. Allopurinol in ALL, B-ALL/NHL

Acute Myeloid Leukemia

De novo AML, sec. AML, AML post MDS (<60 years):
- AMLCG-2000
- AML-SHG
- DLI 2003
- AML 2002 OS0
- AML Intergroup
- AML Intergroup: intensified vs. reduced conditioning
- AMLSG 07-04

Acute promyelocytic leukemia (APL):
- AMLCG-M3
- AML AIDA 2000

De novo AML sec. AML, AML post MDS (>60 years):
- AMLCG-2000
- AML Elderly
- AML-Intergroup Elderly
- AML 97 OS0 (038, 045)
- AMLSG 06-04
- AML 2004 OS0

Relapsed:
- MTC-Glivec - AMLSG-R1 (SHG-AML-R2)
- AMLCG-Relapse
- LAO316
- SHG AML-REZ
- ATRA / Valproat
- PKC412
- AMLSG 05-04

Chronic Myeloid Leukemia

Chronic Phase:
- CML-IV
- Glivec/Pegasys Combination Study (Phase II)
- Imatinib in elderly Pat. >1 Y. after Diagnosis
- Therapy optimization after insufficient response to Imatinib:
  - Imatinib 800mg
  - Imatinib + RAD001
  - Imatinib + lonafarnib

Blast Crisis:
- SHG-AML-REZ
- GMALL-STI571-IFN

Myelodysplastic Syndromes

- AZA s.c. vs. conventional treatment
- ATGCSA
- Thalidomid in MDS
- Thalidomid in MDS or OMF
- ATRA / Valproat
- Decitabine

New studies for adult acute lymphoblastic leukemia

N. Gökbuget, D. Hoelzer, University Frankfurt for subproject 9 (ALL)

The advanced biological characterisation of acute lymphoblastic leukemia (ALL) showed that it is no uniform disease, but has subgroups with specific clinical, biological and prognostic characteristics. Accordingly there is a trend to subgroup specific and targeted therapies, which are represented foremost through the German all study group (GMALL). This results in an increasing number of newly activated studies for specific subgroups and stages of disease. Apart from the use of Imatinib in the treatment the Ph/BCR ABL + ALL this concerns particularly the use of monoclonal anti-bodies.

The CD20-antibody Rituximab was first used in the therapy of mature B-ALL, Burkitt lymphomas and other high-malignant B-NHL. After promising intermediate results with survival-rates of >90% evaluated after one year (1), Rituximab was introduced in the therapy of older ALL patients as well (GMALL Elderly 1/2003).

A further study with Rituximab for patients with B-precursor ALL and standard risk was now activated. Main objectives are the increase of molecular remissions, which are determined by measurement of the minimum residual disease (MRD). On basis of the current study GMALL 07/2003, Rituximab will be used also for high risk patients with B-precursor ALL in the future (Amendment 1 of the study 07/2003).

A study with the CD52-antibody MabCampath for relapsed or MRD-positive T-ALL was already activated some time ago.

Furthermore, a study for T-lymphoblastic lymphomas (T-LBL) was initiated by the GMALL study group. In this entity very good results were obtained with treatment according to the GMALL-protocols (2). The study was based on the GMALL study 07/2003, but considers biological characteristics of T-LBL in particular the therapy of mediastinal-tumors.

Finally a study with a new liposomal Cytarabine (DepoCyte®) for intrathecal (i.th.) therapy of CNS relapses is activated. Due to the longer half-life, one dose of DepoCyte® replaces the 2-3 weekly applications of conventional i.th. cytarabine for approximately 10 days, which is an improvement of quality of life for patients.

All studies are summarized in the table and are available for download on the website: www.kompetenznetz-leukaemie.de

Supportive Care

- AmBisome loading
- Antifungal secondary prophylaxis
- Broncho-alveolar lavage
- Ceftazidim vs. Piperacillin-Tazobactam
- Granulocyte transfusion study Tübingen
- Infektionen in CLL
- Itraconazol drug levels in i.w. treatment
- Oral empiric antifungal therapy
- Pharmacokinetics in severe infections
- Posaconzol prophylaxis
- Posaconzol therapy
- Thoracic computer tomography

SCT / Cellular Immunotherapy

- AlloSCT with reduced conditioning in AML
- AlloPBET and subsequent immunotherapy in AML/AML
- Chemo-Immunotherapy with alloSCT in CLL
- DLI post alloSCT in CML
- DLI and GM-CSF
- Dendritic Cells in elderly Pat. with relapsed/refractory AML
- Dendritic Cells in BCR ABL-positive CML
- Gen-modified T-Cells
- MMF + CsA + MTX for GvHD-prophylaxis
- Modified conditioning in CML
- Prophylactic donor lymphocyte transfusion
- Radioimmuno conjugates in ALL, AML and CML
- AML Intergroup: intensified vs. reduced conditioning

Chronic Myeloproliferative Diseases

- Imatinib in Hyperesinophilic Syndromes
- Imatinib in Polycythemia vera
- Pegltnron in Polycythemia vera
- Thalidomide in MDS or OMF
A marathon for the "Stiftung Leukämie"  

N. Sittner, U. Berger for the Network Center

Nine employees of the III. Medizinische Universitätsklinik Mannheim placed emphasis on the struggle against leukemia and participated in the Mannheim Marathon. Two teams of four runners mastered the distance of 42,195 kilometers together, one of them ran the whole distance alone. They campaigned in public for the "Stiftung Leukämie". About 80,000 spectators saw this unique marathon, which started in the late afternoon of a sunny spring day at the town's landmark the „Wasserturm“.  

With combined power 126,585 kilometers for the "Stiftung Leukämie", Michele Giehl, Dr. Ute Berger, Gabriele Lalla, Dr. Alice Fabarius, Dr. Michael Schatz, PD Dr. Andreas Reiter, Dr. Armin Leitner und Dr. Paul La Rosée.

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**Symposia / meetings / education and training**

- **German AML study group (AMLSG)**
  - Prof. Dr. H. Döhner, Prof. Dr. A. Ganser
  - September 9 – 10, 2004, Reisensburg

- **German MDS study group**
  - Prof. Dr. C. Aul / Prof. Dr. A. Ganser
  - September 15, 2004, Düsseldorf

- **East-German study group for hematology/oncology (AML OSHO)**
  - Prof. Dr. D. Niederwieser
  - November 5 – 6, 2004, Magdeburg
  - April 29 – 30, 2005, Wörlich

- **German CML study group**
  - Prof. Dr. R. Hehlmann
  - Meeting of the SHG
  - November 5, 2004, Mannheim

- **German ALL study group (GMALL)**
  - Prof. Dr. D. Hoelzer
  - November 12, 2004, Frankfurt
  - February 4 – 6, 2005, Reisensburg
  - July 8, 2005, Frankfurt
  - November 11, 2005, Frankfurt

- **6th Annual Symposium of the German Competence Network „Acute and chronic Leukemias“ and 2nd Annual Symposium of the European LeukemiaNet**
  - Coordinator of the network: Prof. R. Hehlmann
  - February 1 – 3, 2005, Heidelberg

- **German CML study group, 14th International Workshop and XXII. Symposium of the IACRLRD**
  - Prof. Dr. R. Hehlmann
  - July 1 – 6, 2005, Heidelberg, DKFZ

**Congress**

- **Common conference of the German, Austrian and Swiss societies for Hematology and Oncology**
  - October 2 – 6, 2004, Innsbruck

- **Symposium of the German Competence Network "Acute and chronic Leukemias"**
  - October 6, 2004, 8.30 – 10.00 a.m.
  - Room „Brüssel“

- **Workshop: Haematological Cytology**
  - Prof. Dr. R. Fuchs, Eschweiler
  - November 5 – 7, 2004, München

- **111. Conference of the German Society for Internal Medicine**
  - April 2 – 6, 2005, Wiesbaden

- **10. Congress of the European Hematology Association (EHA)**
  - June 2 – 5, 2005, Stockholm

- **XXII. Symposium of the IACRLRD**
  - Prof. Dr. R. Hehlmann
  - July 2 – 6, 2005, Heidelberg, DKFZ