International Symposium

ACUTE LEUKEMIAS XVI

Biology and Treatment Strategies

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Munich, Germany
Dr. med. Thomas Büchner, Professor Emeritus of the Westfalian Wilhelms-University in Muenster, Germany, died suddenly gardening in his home in Muenster on August 5, 2016. Until his last day Thomas was active as a scientist and teacher in Muenster’s University and in the international leukemia community.

Thomas was born on 22 September 1934 in Berlin. He moved with his family to Freiburg and grew up in this university town in the south-west of Germany. In 1955 Thomas began to study Medicine at the University of Freiburg and completed his exams and his MD degree in 1961. The title of his experimental MD thesis was: ‘Autoradiographic studies concerning cell kinetics in the mouse’. This was the basis of his life-long interest in experimental and clinical research in hematology. In 1962 Thomas Büchner moved to the University of Muenster and was active in the Faculty of Medicine until recently. He joined the Department of Medicine (DGHO) in 2008.

Thomas Büchner was elected Honorary Member of the German Society of Hematology and Oncology (DGHO) in 2008. The focus of Thomas Büchner’s clinical and scientific interest was acute myeloid leukemia (AML). When he started working in this field in the 1960s, the median survival of persons with AML was 0.5 months and the disease killed almost everyone. At that time hematologists had only few drugs in their hands such as thioguanine and cytarabine and took advantage of the so-called synchronisation effect of cytarabine.

In parallel, systematic supportive care was optimized by platelet transfusions, effective antibiotics and treatment in a protected environment. Under this regimen the AMLCG observed the first long-term survivors. Thomas was very serious, but he had also a deep sense for humor. In his first AML trial after few patients were accrued the survival curve dropped sharply and Thomas declared it as a ‘plateau destroyer we have to avoid in the future’! Study generations followed, in which the AMLCG concentrated on adding maintenance therapy for up to 3 years and on intensifying remission induction by introducing double induction and to a successful series of multicenter trials throughout Germany. In the first of this series of AMLCG trials under the charismatic leadership of Thomas, the TAD-9 protocol for remission induction was established consisting of cytarabine, daunorubicin and thioguanine. This concept was based on Thomas’ extensive preclinical research and took advantage of the so-called synchronisation effect of cytarabine.

The AMLCG 1999 randomized trial addressed several open questions for induction and postremission therapy in 43000 subjects. This trial showed the limits of further dose escalation of chemotherapy in induction and consolidation maintenance. It also showed the enormous prognostic impact of age. Whereas with the intensive treatment approach of double induction, consolidation plus maintenance and modern supportive care approximately half of the patients <60 years survived, progress in older patients was substantially worse with <30% long-term survivors. From the beginning the AMLCG trials were complemented by highly sophisticated central diagnostics allowing identification of biologic and prognostic subgroups, which paved the way for translational research projects.

However, as Thomas kept teaching us: we still are not able to really understand and explain the molecular basis of the ‘age factor’—as he named it. He hypothesized the ‘age factor’ as a result of accumulating genetic changes with increasing age. Besides novel anti-leukemia treatment strategies Thomas with his group improved systematic supportive care in cooperation with the Paul-Ehrlich Society within the AMLCG studies. This approach resulted in a close cooperation of hematologists and microbiologists and the establishment of a DGHO working group that developed national and international guidelines and protocols for patients with several cancers and Thomas Büchner took over the task of coordinating the German national AML trials. This led to the foundation of the German AML Cooperative Group (AMLCG) and to a successful series of multicenter trials throughout Germany. In the first of this series of AMLCG trials under the charismatic leadership of Thomas, the TAD-9 protocol for remission induction was established consisting of cytarabine, daunorubicin and thioguanine. This concept was based on Thomas’ extensive preclinical research and took advantage of the so-called synchronisation effect of cytarabine.

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international guidelines for to manage infections in hematology and oncology. For the statistical design of the AMLCG 1999 trial Thomas introduced the principle of ‘up-front’ randomization into different treatment algorithms, a principle widely discussed in the leukemia community. Some felt it not so helpful in guiding care in distinct situations where specified randomization might give a more precise answer. However, in the Intergroup trial of the German Network for Leukemia Thomas and many others used the powerful instrument of up-front randomization to compare the different therapies specifically designed by the five multicenter trial groups for AML, which evolved in Germany in the meantime—and found no significant differences in outcome. Thomas always explained this to us—with his typical deep but subtle sense of humor—and by this gave further impulse to many of us to seek completely new ways of AML treatment.

Science needs communication and also in this field Thomas Büchner was a driving force. Together with the pediatrician Gunther Schelling from Muenster, who was one of the pioneers of the BFM group for studies on children’s leukemia and lymphoma, Thomas Büchner and others founded the BFM group for studies on children’s leukemia research has lost a pioneer, a wonderful person, a good friend, a mentor, an eminent colleague and first of all an intellectual human who will smile forever with friendly humor about what we do and what we try. Thomas Büchner’s favored song was ‘Imagine’ by John Lennon; there is nothing to add.

We go back to 1971, 46 years ago. We met over our passion for leukemias and the new field of impulscytophotometrie = Flow Cytometry. I invited Thomas to Heidelberg where I organized, in my first year of residency, the First German Flow Cytometry meeting. We measured DNA in single cells at a rate of 1,000 per second!!! It had taken me 3 years to measure DNA and RNA in 900 cells as specified in my thesis. It was always renting typical American muscle cars as special. Thomas, the quiet German professor, had this very cool, understated sense of humor, which I relished. He and “Kiepenkerl”, the pig was paraded through the dining room in complete darkness, with sparklers blazing away. Thomas had this very cool, understated sense of humor, which I relished. He and „Kiepenkerl“, the Muenster original, could tell the best stories.

We had many meetings in the US, first on flow cytometry, later on leukemias. Asilomar stood out that they symbolized. We both recognized immediately the paradigm-changing power of this technique. And we had the tumor cells that we could get by simply drawing blood, while the solid tumor folks had to liberate them from tumor biopsies.

This professional bond developed into a true friendship. Thomas was incredibly supportive, kind and inspirational. I was just at the beginning of my career and he was already „Herr Professor“, the scion of a family famous for its medicine professors.

We had an early meeting in Munich where we all bonded over „fluidics“ of another sort. Later, Thomas sent me his best young doctor to Sloan Kettering where I had landed, Wolfgang Hiddemann, and a second life-long friendship developed. In the meantime and over more than 25 years, Thomas invited me to each of the wonderful Muenster meetings on Acute Leukemias, which later moved to Muenchen under the tutelage of Wolfgang. I remember one Muenster meeting where a suckling pig was paraded through the dining room in complete darkness, with sparklers blazing away. Thomas had this very cool, understated sense of humor, which I relished. He and „Kiepenkerl“, the Muenster original, could tell the best stories.

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Thomas was, to the end, the most driven hematologist I met: quiet but persistent over a life time, driven by the urge to cure more, if not all of his patients. He presented highly innovative protocols,
Thomas Büchner was the central figure of two international conferences: the International Symposium on Acute Leukemias in Munich, now Munich, which he chaired and co-chaired for almost 30 years, and the Raisa Gorbacheva Symposium in St. Petersburg organized by Boris Arafatiev which he introduced since its inception in 2007 with the Memorial Lecture named after his most prominent patient Raisa Gorbacheva. I remember well a steering committee session of the Kompetenzzentrum Leukämen at Frankfurt Airport in 1999 which he left unexpectedly early to reach a plane to Moscow. I only learned later that he left to see Raisa Gorbacheva.

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Since Thomas died only a few weeks before he was supposed to give the Raja Gorbacheva Memorial Lecture 2016, I had to step in on request of Boris Arafatiev and also give his obituary.

Robert Peter Gale

I first met Thomas in 1977 shortly after Prof. Martin J. Cline and I published a typescript in the Lancet reporting a high rate of complete remissions in adults with acute myeloid leukaemia (AML) treated with TAD (6-thioguanine, cytara-bine and daunorubicin). Thomas, ever curious, was impressed by our report and invited me to visit Munster. On arriving I noticed a rather formal professorial delegation awaiting the arrival of a small plane from Frankfurt with only 8 or 10 passengers and presumably bringing Prof. Gale. I was 32, a very junior academic and had flown overnight from Los Angeles in economy class. Thomas and his distinguished colleagues, in 3-piece suits waited anxiously outside the baggage claim area. I was the last person out. They seemed incredulous but somehow resigned. Perhaps they hoped Prof. Gale had missed his connection (easily done at FRK). I greeted Thomas saying: Regrettably, I am probably the person you are here to greet. Anyone who knows Thomas well will appreciate his extraordinary good manners and formality. He welcomed me warmly, made a kind comment on my UCLA sweatshirt and thus began a lovely and productive visit.

Thomas’ made many important contributions to AML therapy. In his later career he became interested in the role of age in AML which he termed the age factor. After adjusting for other prognostic variables such as cytogenetics, mutations, prior myelodysplastic syndrome (MDS) etc, age per se remained strongly correlated with AML outcomes in the AMLCG trials. Also, because he and his colleagues had thousands of subjects in their trials they could compare therapy outcomes in subjects 57-60 years receiving intensive therapy and these 61-63 years receiving less intensive therapy. Again they found similar outcomes suggesting we are not going to make much progress treating older subjects with increasingly intensive therapy. A last curious bond between Thomas and me was his fondness for red Hermes ties, often with an animal motif. These were always selected by Edith. I now have one of his to wear on special occasions recalling our deep friendship.

Rüdiger Hehlmann

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Thomas was highly dedicated to his fight against AML. He once told me that he would give a couple of years of his life if he could beat this disease. Until his very last moments Thomas continued his efforts and concentrated in his later years on the so called "age factor" in AML which describes the still unresolved problem of poor outcome in patients beyond 60 years of age.

Over the many years that I had the privilege to work with Thomas our personal relation changed and after having been a mentor in the beginning Thomas became a colleagues and finally close friend. Thomas' strong believe in his ideas and his dedicated efforts to understand the biology of AML and to improve the prognosis of patients suffering from this disease made him an internationally recognized leader in this field. With his charming personality and his special sense of humor Thomas has not only gained scientific recognition but will furthermore and maybe more importantly remain in our memories and hearts.
Jörg Ritter

I met Thomas Buechner for the first time in the late 1970s when he arrived at the Clinic for Paediatric Haematology/Oncology in Münster, then headed by Günther Schellong, from the Department of Paediatrics, Braunschweig Community Hospital. On his arrival we discussed the clinical significance of the DNA content, as measured by flow cytometry, of leukaemic blasts in children and adolescents with acute leukaemias. This discussion engendered fruitful cooperation also including Wolfgang Hiddemann and Bernhard Wörmann.

At that time we launched the paediatric AML-BFM (Berlin-Frankfurt-Münster) multi-center study together with Schellong and Ursula Creutzig of the Department of Paediatric Haematology/Oncology Muenster. It was a stroke of luck that at the same time Thomas initiated the AML Cooperative Group (AMLCG) for adults at Muenster University Hospital. This allowed us paediatricians to learn a lot about AML, which we then thought to be an ugly form of ALL, from Thomas’ group. We found out about the importance of early intensive polychemotherapy, especially in the form of “double induction”, and learned that the combination of high dose ARA-C with Mitoxantrone (HAM) is especially effective. We introduced HAM first in children and adolescents with relapsed AML and then in all children with AML. Furthermore we learned from the adult studies that severe opportunistic infections, especially invasive fungal ones, are a major obstacle against the cure of AML. We also gained a lot of knowledge about risk factors in AML, the most important being response of the individual patient to the treatment administered.

In 1986 we started a symposia series on Acute Leukemias in Muenster, the first chairmen were Büchner from Medical Oncology and Schellong from Paediatric Haematology/Oncology. These symposia were then worldwide the only ones dealing with all forms of acute leukaemias in both adults and children.

Thomas became a good friend of the paediatric AML studies, and we paediatricians were glad that he accepted our invitation to become a member of the paediatric AML – BFM study committee.
Charles Schiffer

A benefit of the privilege of participating in large scale clinical research is the opportunity to meet and work with colleagues from all over the world, who often become great friends, despite the fact that you see them infrequently. I first met Thomas Büchner at what some have called “Leukemia in the Woods” in the hut in Wilsede, when I was young and he was already renowned.

We were somewhat different in nature – he was a quiet, formal and serious gentleman (albeit with the potential for a twinkle in his eyes), always impeccably dressed, and addicted to double induction and maintenance therapy for AML, whereas I was from New York and somewhat irreverent. However, we shared a passion for moving beyond treatment-induced cell kinetics of acute myeloid leukemia using flow cytometry.

At the last Munich meeting, Thomas and I were chairing a session together (that’s what old men get asked to do), and I told him of my plans to introduce him with this story. He, of course, said “no”, but I could tell that he didn’t really mean it (and it wouldn’t have mattered anyway). The audience loved it, gaining some new insights about what lurked beneath his reserved demeanor. It was clear that Thomas was quite touched, in part because you see them infrequently. So, I choose this as my defining memory of Edith who had died recently. However, part of the laboratory equipment in- cluding the microscope was situated in Thomas Büchner’s fully cramped, but spatial office. Thus occurred in 1977, when I looked for a mentor for my doctorial thesis. He had his office on the top floor of the historic department of Internal Medicine in Münster, even with a terrace. In our first conversation, he checked the seriousness of my intentions and my readiness to work hard. Being satisfied, he directed me to Wolfgang Hiddemann, my doctorial thesis. He had his office on the top floor of the historic department of Internal Medicine, even with a terrace. In our first conversation, he checked the seriousness of my intentions and my readiness to work hard. Being satisfied, he directed me to Wolfgang Hiddemann, who was on an outpost at the department of nephrology, but had some exciting ideas for a subject on treatment-induced cell kinetics of acute myeloid leukemia using flow cytometry.

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Some anecdotes:

- I am sitting at the flow cytometer, and the phone on Thomas Büchner’s desk doesn’t stop ringing. Finally I lift the receiver. Thomas Büchner is on the phone. He had travelled to Southern Germany for a presentation on acute myeloid leukemia, but had left the invitation with description of the location on his desk.
- Thomas Büchner needed a new car. He started a phone call with a car dealer, and at some time-point he leaned towards me: “Herr Wörmann, this is not for your ears.”
- When he was invited for a major ASH presentation on elderly patients with AML, he meticulously rehearsed every word. He started as slowly as always: “Our first patient was 86 years old.” Pau- se. (I already got nervous,) He continued: “And this patient is now – pause (I almost went crazy) – 88! Big laughter in the audience. The rest of the presentation went smoothly.

In the following years, I got more clinically involved, also in the design of the largely successful AMLCG studies. We started to include not only patients with de novo AML, but also with sAML and iAML. Besides the clinical work, I learned hematologic cytology from Thomas Büchner. For long evening hours, he was sitting at the teaching microscope, slide after slide, focussing on single cells, discussing with me on granularity, nuclear shape, blast vs non-blast, etc.

When I decided in 1992 to leave Münster for Göttingen, moving further to Braunschweig and finally to Berlin, Thomas Büchner was disappoin- ted. We continued the professional exchange within the study group.

Bernhard Wörmann

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