needs to be defined, and this technology is still not fully incorporated into the routine work-up of our patients.
In summary, molecular analyses have become technically feasible in virtually all patients with haematological neoplasms. They may help to define "molecular entities" as a starting point to find new more specific therapies. They often provide prognostic information which although easily publishable, has limited practical importance as such (a personal statement that will predictably yield some controversy from the audience). Predictive markers useful to select individualised treatment are welcome, but still not applicable in the majority of cases seen in our clinics. To refer to the title, molecular biologists are encouraged to continue to improve our understanding of the "gene pathology" of these cancers, but should seek links with clinicians, who in turn need to speak their language for an improved mutual understanding.

8
Acute myeloid leukemia

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The treatment of acute myeloid leukemia (AML) in spite of a steady progress is still associated with considerable failure rates. This applies to patients with AML of any age. The majority of patients with AML are 60 years of age or older, in whom treatment disease outcome has remained most unsatisfactory. When treated with chemotherapy, this age group has an estimated survival of approximately 10–20% at 5 years. There has been an intense interest in the introduction of new modalities and exploring new ways of using conventional approaches. In this respect particularly the use of high-dose daunorubicin chemotherapy in patients with AML has raised recent interest.
From a biologic and clinical viewpoint acute myeloid leukemia is an extraordinarily heterogeneous disease. The molecular heterogeneity of the leukemia is the key determinant of treatment failure. Today, cytogenetics are commonly used in clinical practice for the assessment of individual prognosis. The recently postulated monosomal karyotype appears to provide better predictability of adverse outcome than the classical complex karyotype. Modern high-throughput approaches provide powerful tools for the discovery genetic biomarkers and the evaluation of their clinical relevance. Numerous, widely diverse genetic abnormalities (gene mutations, expression abnormalities) have been discovered. Examples of clinically relevant gene aberrations involve CEBP-alpha, RAS, nucleophosmin-1, FLT-3, WT1, EVI-1, MN-1, ERG, TET-2, IDH1 but there are many more to come.
The remarkable genomic heterogeneity is a reflection of the underlying somatic genetic abnormalities in transformed hematopoietic stem cells that as successive events over years accumulate in the neoplastic clone of a patient's leukemia during the evolution of the disease. As these genetic changes perturb diverse cellular pathways and functions, they often confer a profound impact upon the clinical phenotype of the disease at presentation and treatment response. Knowledge about the somatic mutations and genetic alterations driving these phenotypic variations in the leukemia will establish novel defined diagnostic subtypes of AML with diverse prognosis (diagnosis). The identification of biomarkers with prognostic significance using genome-wide approaches and large numbers of well defined cohorts will construct an informative background for risk adapted treatment decisions according disease risk (prognosis and treatment choice). For instance, allogeneic hematopoietic stem cell transplantation (alloSCT) furnishes the most effective antileukemic postremission modality available today but the advantage in terms of antileukemic activity has to be cautiously balanced against the increased risk of death and morbidity that is typically connected with alloSCT. The increasing insight into the remarkably diverse genetics of AML provides a backgound for a decision algorithm of alloSCT in AML according the estimated individual relapse risks of patients with AML. Finally, these insights will most likely furnish leads to potential therapeutic targets for drug development (treatment). Thus therapeutic and diagnostic developments emerging at the interface of laboratory and clinical research create a perspective of personalized therapeutics in AML.

9
Chronic lymphocytic leukaemia

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Rapid progress has been achieved recently in the management of chronic lymphocytic leukemia (CLL). New insights into the molecular pathology of CLL have generated a plethora of biological markers that predict the prognosis and influence therapeutic decisions. Moreover, fludarabine, bendamustine, and two monoclonal antibodies, alemtuzumab and rituximab, have been approved by European and/or American regulatory agencies. Additional monoclonal antibodies targeting CD20, CD23, CD37, CD38 or CD40, as well as drugs designed to interfere with proteins regulating the cell cycle, the apoptotic machinery, or the leukemic microenvironment (e.g. flavopiridol, oblimersen, ABT-263, or lenalidomide) are currently tested in clinical trials. An increased experience with reduced-intensity allogeneic progenitor cell transplantation allows offering this option to physically fit patients. In my presentation, I will review and summarize the current use of these different modalities in CLL therapy.

10
Myeloproliferative neoplasms Ph- negative

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Polycythemia Vera (PV), Essential Thrombocythemia (ET) and Primary Myelofibrosis (PMF) are included in the group of classical Ph-negative Myeloproliferative Neoplasms (MPNs) Understanding of the pathophysiology of these disorders dramatically improved following the description, in the last five years, of recurrent molecular abnormalities represented by: (1) the V617F mutation in *JAK2* exon 14, that is the most frequent and involves >95% of PV and ~60–70% of ET patients; (2) a number of molecular alterations located in *JAK2* exon 12, that have been described in 50–80% of the *JAK2*-wild type PV patients; (3) mutations in *MPL*, mostly represented by the W515L or W515K allele, that are presented by ~7% of ET patients; (4) mutations of the TET2 (ten-eleven translocation (2) gene reported in 20% of MDS and MPN/MDS and 8–15% of MPNs. Genotyping for such molecular abnormalities has already become a standard tool in the diagnostic work-up of patients suspected to have a MPN and constitutes a major criterion for diagnosis, according to the new WHO classification of myeloid neoplasms. As a consequence of an early diagnosis, it is very likely that the frequency and clinical presentation of these disorders will change in the next future. Currently, there is no therapy able to eradicate the molecular hallmark leading to these malignant diseases. Thus, therapy is aimed at preventing the major clinical relevant complications such as thrombosis in PV and ET and to alleviate anemia and splenomegaly in PMF.
Polycythemia Vera and Essential Thrombocythemia Major causes of morbidity and mortality in polycythemia vera (PV) and essential thrombocythemia (ET) are represented by