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Lymphoma: anything new?

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In the recent years, the armamentarium for the treatment of hematological malignancies has been substantially enriched by the implementation of novel classes of drugs that target specific signaling or metabolic pathways and/or the microenvironment of the malignant cells. Proteasome inhibitors and immunomodulatory drugs have revolutionized the treatment of multiple myeloma patients; and this fascinating development is still ongoing as second generation novel drugs and monoclonal antibodies will soon find their way into the clinics, which are likely to further improve the survival of our patients. Small drugs have been also introduced in the treatment of myeloid malignancies and now, such drugs targeting essential pathways are also available for chronic lymphocytic leukemia, the most common leukemic disease in the western world.

In this issue of MEMO, Lukas Weiss and his colleagues [1] give a clinical update on inhibitors of B-cell receptor kinases in this disease. These new agents have potent activity in heavily pretreated patients as well as in patients whose disease is characterized by the chromosomal aberration del(17), a hallmark of a usually dismal prognosis. Despite substantial improvements in the treatment of B-CLL, especially for younger patients using modern immunochemotherapy regimens, the time is ripe for a revolution in the management of very high-risk patients and patients' refractory to currently established treatments.

The two further topics that are covered in this issue are characterized by occasionally occurring uncertainty in daily clinical practice. First, positron emission tomography (PET) in conjunction with CT scanning can add substantially to the staging techniques and response evaluation in various malignancies. Undoubtedly, PET scanning is useful in the staging of aggressive non-Hodgkin's lymphoma and Hodgkin's disease. However, against the background of conventional methods as CT scans, up- or down-staging of the disease can occur using these techniques, issues that merit special attention to avoid over- or undertreatment. During the follow-up of patients with a high curative potential, e.g., Hodgkin's disease, the radiation exposure, which can be approximately two-fold higher per single whole-body PET/CT than the average annual exposure from the environment, must be taken into account when considering repetitive PET/CT scans during follow-up.

Dr. Uprimny [2] summarizes the established indications of this technique in malignant lymphoma and gives valuable information for the use of PET/CT scanning in clinical practice.

The second topic that causes problems in the clinics, which is discussed by Dr. Fridrik [3], is the treatment of double-hit lymphomas. Simultaneous translocations of MYC and/or BCL2 and BCL-6, respectively (so called "double-hit" lymphomas) can be detected in a small proportion of patients with DLBCL. Usually, but not in every single patient, this represents a *signum mali ominis* regarding the prognosis, i.e., many of these patients are refractory to conventional treatment regimens like R-CHOP. Therefore, all patients with DLBCL should be assessed for MYC and BCL2/6 translocations at diagnosis.

As most of these patients have a dismal prognosis when treated with R-CHOP, alternative treatments whenever possible within controlled clinical trials, are the strategies of choice. Recent data suggest no benefit for these patients when treated with highly aggressive chemotherapeutic regimens as dose-adjusted EPOCH-R or autologous stem cell transplantation. Therefore, innovative strategies are urgently required for these patients.

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These three articles cover important points and can be a helping hand in optimizing the diagnostics and treatment of our patients with malignant lymphomas in a rational manner, even though much knowledge has to be gained in very high-risk lymphomas. The lessons that we have learned, e.g., from Hodgkin's disease and testicular cancer, nowadays curable in a very high proportion of patients, are teaching us that improvements can only be achieved via well-controlled clinical trials.

Conflict of interest
The author declares that there is no conflict of interest.

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