SP 03

Risk scores and risk factors in CML, are they helpful?

Tomasz Sacha

There are multiple risk scores developed in the last decades to describe entry disease characteristics, enable risk stratification, and predict the clinical outcome of chronic myeloid leukemia (CML) therapy. The treatment-free remission is a new goal of CML therapy postulated and defined also by recent ELN recommendations. In this context, early predictors of good response and chance to reach this ambitious goal are of special interest. The importance of Sokal, EURO (Hasford), EUTOS, and ELTS scores will be discussed. The other risk factors such as additional chromosomal aberrations, additional genetic mutations, BCR/ABL1 transcript type, the dynamics of early BCR/ABL1 transcript decline, the presence of ABL1 KD mutations, and the quality of molecular response could have an important role in planning the optimal treatment. In the era of tyrosine kinase inhibitors and many possible choices, the analysis of risk factors could be considered as a key factor in the decision-making process. This will be discussed during the presentation.

SP 04

Minimal residual disease detection in multiple myeloma: methods and prognostic significance

Evangelos Terpos

The novel response criteria in antimyeloma therapy, published by the International Myeloma Working Group (IMWG), include minimal residual disease (MRD) assessment in multiple myeloma (MM), aiming to identify better definitions of complete response (CR) than those traditionally defined by conventional methods. IMWG has defined new response categories including (i) marrow MRD negativity with the use of next generation flow cytometry (NGFC) or next generation gene sequencing (NGS), with a cut-off value of 10^{-5}; (ii) imaging MRD negativity using PET/CT; and (iii) sustained MRD negativity (marrow and imaging MRD negativity that remains for 12 months).

The sensitivity of NGS seems to be similar than that of NGF and can be used for detection of rare residual myeloma BM cells at the level of 10^{-6}. However, an advantage of NGS is that it can be applied retrospectively on stored material including not only cryopreserved cells but also archival BM slides. On the other hand, the most commonly utilized NGS-based ClonoSEQ (Adaptive Biotechnologies) platform for MRD evaluation has high cost and requires specialized centers for sample preparation and data interpretation, which, in its current form, makes it challenging for daily clinical management. The major advantage of NGF is its high applicability in 99% of MM patients and the relatively simple manual set-up in diagnostic labs equipped with the appropriate 8-color cytometers, following the standardized EuroFlow guidelines. The cost of

the technique is significantly more affordable and the results may be available within a few hours upon BM aspiration. There is no need for a prior diagnostic sample evaluation due to the elegantly elaborated 8-color marker combinations that can efficiently discriminate between normal and aberrant plasma cells in the whole spectrum of intra-phenotypic heterogeneity. Furthermore, NGF methodology allows for an intra-quality control check for hemodiluted samples – the major pitfall for both NGF and NGS approaches- by identifying cellular components (i.e., mast cells, B cell precursors, erythroblasts) that are mainly present in the BM. This point is commonly underestimated, though it consists one of the major advantages of NGF; the multiparametric panels allow for the global characterization of BM cells.

There is no doubt that the achievement of MRD negativity confers a more favorable outcome for treated MM patients. The first meta-analysis by Landgren et al in 2016 and the one that followed by Munshi et al in 2017 have verified the prognostic impact of MRD negativity in the clinical outcome. The latter meta-analysis showed a 59% reduced risk of progression and 43% reduced risk of death for MRD negative patients with a median PFS of 54 months vs. 26 months and a median OS of 98 months vs. 82 months for MRD negative vs. MRD positive patients respectively.

When compared with other prognostic factors, MRD has been shown to be superior and the most relevant predictor of clinical outcome. In multivariate analyses, the achievement of MRD negativity is proven to be the strongest independent prognostic factor which surpasses other favorable prognostic parameters. Patients with high-risk baseline cytogenetics who achieved MRD negativity after treatment, had significantly improved outcomes when compared with MRD persistent counterpart, but most importantly, they experienced similar survival outcomes with standard-risk patients who also achieved MRD negativity. It is important to stress that the favorable prognostication of MRD negativity stands independent of the assigned treatment.

SP 05

Treatment of relapsed, refractory multiple myeloma: focus on new drugs

Angelo Maiolino

In recent years several new drugs were approved for multiple myeloma (MM) treatment. Three classes are included in almost all lines of MM treatment: proteasome inhibitors (bortezomib, carfilzomib, and ixazomib), immunomodulators (thalidomide, lenalidomide, and pomalidomide) and monoclonal antibodies (daratumumab and elotuzumab) in different combinations.[1] In a relapsed setting, the decision about the new line of treatment should consider patient's related factors and previous MM treatment. Age, frailty, cytogenetics risk, and performance status at relapse have to be analyzed combined with the relapse aggressiveness, exposition to prior therapies, and the history of disease's responses.[2] Patients previously unexposed or those not refractory to lenalidomide, have better outcomes with a triple combination of lenalidomide and