Leukemia Myeloma Spotlights Reprint Collection (2009), R1–R2

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EDITORIAL

Spotlight review series on multiple myeloma

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In the last decade, we have witnessed unprecedented progress in the diagnosis and treatment of multiple myeloma.[1,2] These advances, although helped by a few serendipitous observations, are associated with a major improvement in our understanding of myeloma cytogenetics and biology, and a greater realization of the role played by the bone marrow microenvironment in disease pathogenesis and progression.[3–6]

Myeloma evolves from an asymptomatic premalignant stage termed monoclonal gammopathy of undetermined significance (MGUS), which is prevalent in over 3% of the population above the age of 50 years.[7] MGUS seems to originate as an aberrant response to antigenic stimulation mediated by aberrant Toll-like receptor (TLR) expression.[8–10] Approximately 50% of MGUS is associated with primary translocations in the clonal plasma cells involving the immunoglobulin heavy chain (IgH) locus on chromosome 14q32 and various partner chromosome loci, such as 11q13 (CCND1 (cyclin D1 gene)), 4p16.3 (FGFR-3 and MMSET), 6p21 (CCND3 (cyclin D3 gene)), 16q23 (c-maf), and 20q11 (mafB).[11] Most of the remaining cases of MGUS are associated with hyperdiploidy (IgH nontranslocated MGUS).[12]

MGUS progresses to myeloma or related malignancy at the rate of 1% per year.[13] The progression of MGUS to myeloma is accompanied by additional cytogenetic changes such as secondary translocations and p53 mutations, as well as alterations in the bone marrow microenvironment, including induction of angiogenesis, suppression of cell-mediated immunity, increased dickkopf 1 (DKK1) expression, increase in receptor activator of nuclear factor κB ligand (RANKL) expression and a reduction in the level of its decoy receptor, osteoprotegerin (OPG).[14]

The evolution of MGUS to myeloma is marked by familiar signs of end-organ damage, including osteolytic bone lesions, anemia, hypercalcemia and renal failure. Myeloma remains incurable, but new treatment options such as thalidomide,[15] bortezomib[16–18] and lenalidomide[19,20] have dramatically altered the treatment of the disease, and significantly prolonged the survival of myeloma patients.[21] Additional agents such as carfilzomib and pomalidomide are on the horizon. These new agents produce high rates of response, which was hitherto possible only in the context of stem cell transplantation.

Today, many investigators consider myeloma to be a heterogenous mix of cytogenetically distinct entities sharing a similar phenotype. The prognosis and response to therapy of myeloma vary greatly based on baseline cytogenetic abnormalities.[22–28] In fact, it is likely that in the future treatments will be delivered in a more individualized manner based on underlying chromosomal and gene-expression characteristics.[29] To highlight and critically evaluate recent advances in the biology and treatment of myeloma, we published a special spotlight series of 14 comprehensive review articles in *Leukemia*. The reviews in this spotlight series cover the most important advances in the clinical and laboratory aspects of the disease in recent years and lay the directions for future myeloma research. Each review was authored by investigators who played a leading role in the advances described. The rapid pace of changes in the myeloma field has resulted in the need for revising existing diagnostic, prognostic and response criteria, as well as treatment recommendations.[23,30] In this regard, the spotlight series[31–44] includes consensus statements on controversial and evolving areas such as molecular classification and new laboratory tests. We are confident that the myeloma spotlight series will be a resource for all investigators in the field, as well as clinical practitioners treating myeloma, laboratory scientists in related fields and other hematologists.

Conflict of interest

The authors declare no conflict of interest.

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