

Multiple myeloma: serious hopes of recovery thanks to new therapies

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At the time of the recent national meetings of the French Association of Multiple Myeloma Patients, it is appropriate, under this optimistic if not provocative title, given that this hemopathy was long considered incurable, to mention the major advances in its diagnosis, follow-up and treatment. The French-speaking Myeloma Intergroup, which brings together French and Belgian specialists, has played its full role in this progress for almost 30 years.

Multiple myeloma is a malignant hemopathy characterized by the clonal proliferation of plasma cells responsible for an invasion of the hematopoietic bone marrow and the secretion of a monoclonal immunoglobulin in the majority of cases. It represents 1 to 2% of cancers and 10 to 12% of hematological malignancies, with approximately 5400 new cases a year in France. The median age at diagnosis is close to 70, with one third of patients over 75 and one fifth over 80 years.

Recent years have seen an improvement of diagnostic and prognostic criteria and, in particular, medical imaging techniques for diagnosis and follow-up (magnetic resonance imaging and PET scan), and prognostic assessments by cytogenetics or genomics (determination of immunoglobulin free light chains in serum and assessment of so-called Minimal Residual Disease (MRD) in bone marrow by genomic analysis or flow cytometry.¹⁻⁴

This assessment of MRD, made relevant by therapeutic progress, leads more and more patients to a low-level or even undetectable disease (so-called MRD-negative patients). Above all, treatment has been progressing continuously and steadily for about 20 years. The word "cure" is no longer taboo and some patients of advanced age can benefit, even without definitive eradication of their disease, from its prolonged control while maintaining a decent quality of life, thanks to drugs with an improved tolerance profile, life expectancy with myeloma then joining that of people without myeloma.

In addition to the historical drugs such as alkylating agents, immunomodulators and proteasome inhibitors were added in the 2000s. These drug families were responsible for the first significant improvement in prognosis and are still well represented in current treatment plans. From 2010 onwards, an important milestone was reached with the development of anti-CD38 monoclonal antibodies⁵. Regardless of the type of treatment considered, the addition of an anti-CD38¹antibody has always improved the results of the therapy^{6,7}.

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As one advance follows another, the 2020s have seen the emergence of innovative immunotherapies using so-called bispecific antibodies⁸ or toxin-coupled antibodies, and cell therapies such as chimeric antigen receptor T-cell therapy (CAR-T), in which the patient's own lymphocytes are collected and genetically modified to destroy tumor cells^{9,10}. These promising therapies offer prospects for target diversification of tumor cells and numerous combinations or therapeutic sequencing modalities.

Underlining the dynamic therapeutic research in this field, several drugs for the treatment of myeloma are approved each year by the European Medicines Agency.

The French National Academy of Medicine wishes to draw attention to the progress made in the medical care of patients with multiple myeloma. In particular, it underlines that:

- immunotherapy will see further developments, and the need to support high quality academic research in this field (particularly with regard to CAR-T strategies) is necessary.

- continuous vigilance is required on the access to these expensive new treatments; access to date is generally satisfactory in our country, but with persistent questions about speed of access and the setting of a fair price, issues on the agenda of the Academy's working group on expensive cancer drugs.

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