IMiDs, the Past and the Future

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Background. Multiple Myeloma is the second most frequent hematology malignancy, characterized with a median survival of 5 to 7 years, with almost all the patients that will relapse, eventually become refractory to all existing therapeutic agents for myeloma, and ultimately be exposed to certain death related to myeloma or related comorbids conditions. However, in recent years, there has been tremendous progress made in the understanding of the biology of myeloma, and several new generations of agents from classes already developed in myeloma, along with new classes in development have come to birth.

Methods. Review of the literature including most recent appearance in international meetings of the IMiDs class.

Results. The "oldest" most recent novel agent approved in Myeloma was Lenalidomide, the first in class IMiDs, a class of anti myeloma agents characterized with direct antimyeloma effect and indirect effect through action on the BM microenvironment. Importantly, a third mechanism was outlined although with quite few data gathered in the past 10 years to support this mechanism that is the Immunomodulatory effect. The most recent agent of the class, the Pomalidomide, has shown impressive activity in line with the expected effect of the class, and in parallel an encouraging safety profile. This agent is moving towards early relapse from end stage where he was initially developed and demonstrated its initial impressive results in MM.

Nonetheless, these developments are already part of the past, having been produced less than 5 years ago, a great signal of the tremendous progress made in MM. Still, certainly, the greatest most recent progress comes from the first 2 class of therapeutic monoclonal antibodies (MoAbs) developed in Myeloma, with various mechanisms of action, that preclude the start of a new era in myeloma. The anti-CD38 and the anti-SLAMF7 have certainly demonstrated impressive benefits and become the first monoclonal antibodies to be developed in Myeloma after long years of tries and failures with all kinds of immunology oncology drugs, from MoAbs to vaccines. Interestingly, and almost naturally, the studies have combined these MoAbs to IMiDs and validated the Immunomodulatory effect. This data has open the "Pandora box" in a way as most of the new agents that will be developed in the near future in MM will certainly be MoAbs-based, such as vectorized MoAbs and check point inhibitors, and will be rapidly if not immediately combined to IMiDs as a proof of concept, if needed, of their Immunomodulatory effect.

Conclusion. The need is great in Myeloma, as still, 100% of patients will see disease refractory to any agent known so far, and certainly this will lead to death from myeloma or any related complications.

In recent years there have been impressive developments in myeloma, and the hope to push survival beyond 10 years is close, not talking about the promise to cure 10-20% of patients with myeloma in the very near future.