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EDITORIAL

Haploidentical HSCT–going from strength to strength

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Since our very first symposium in Eilat by the Red Sea, conceived together with Massimo Martelli two decades ago, we have organized together nine symposia dedicated to Haploidentical Hematopoietic Stem Cell Transplantation (HSCT). Clearly, each one was very special, thanks in great part to a remarkable international group of dedicated scientists and clinicians, in addition to the creative approaches described to meet each new set of challenges as the field has continued to evolve, and last but not least, the unique locations in Israel and in Italy. Notably, our symposia continue to go from strength to strength, as was evidenced by the lectures presented by the outstanding faculty who gathered last year. I am delighted that most of the speakers were able to contribute articles to our present supplement. Collectively, these articles reflect the significant progress associated with the current explosion of haploidentical HSCT, which has become a clinical reality for many patients around the world.

The structure of this supplement, in parallel to the symposium, starts with an update regarding T cell depleted megadose haplo-HSCT in pediatric (Lang, Bielorai) and adult (Aversa, Martelli) leukemia patients undergoing myeloablative conditioning, as well as treatment based on a novel non-myeloablative approach for attaining safer Haplo-HSCT, combining megadose T cell depleted HSCT with post-transplant cyclophosphamide (PTCY) (Reisner).

Next, we present a set of clinical updates, describing the current alternatives to T cell depletion, making use of T cell replete haplo-HSCT. These approaches include BM from G-CSF treated donors (Huang), or PTSC with non-depleted BM (Ciurea, Bachigalupo). Both of these approaches require intensive post-transplant immune suppression.

Subsequently, the results of haplo-HSCT when used for therapy of leukemia patients in Europe (Nagler), as well as the current controversies and remaining challenges (Gale) are critically reviewed. Finally, this part of the supplement ends with an update describing clinical results of haplo-HSCT in pediatric patients with Hemoglobinopathies (Sodani).

Following this first series of clinical updates, we continue with studies addressing potential approaches for improving haplo-HSCT outcomes with a special focus on novel means to enhance post-transplant immune reconstitution. These include the use of ex vivo generated human T lymphoid progenitors (Cavazana), augmentation of intestinal flora (Van-den-Brink), the use of bispecific antibodies (Einsele), virus-specific T cells (O'Reilly), Cytokine Induced Killer (CIK) cells (Lang), therapeutic vaccine strategies to induce tumor-specific T-cell responses (Eyrich), adoptive transfer of immune cells in conjunction with Tregs to avoid GVHD (Velradi), as well as application of CAR T (Turtle, Jacoby) or CAR NK (Rezvani) cells. The role of Tregs (Negrin, Luznik) and Mesenchymal Stem Cell-Derived Exosomes (Shpall) in immune tolerance are critically discussed, followed by pre-clinical and clinical updates regarding the potential use of hematopoietic chimerism induction as a platform for kidney transplantation (Strober, Sykes). Finally, we conclude with a study describing the merits of checkpoint inhibition in allogeneic HSCT (Soiffer).

Taken together, it is our hope that this supplement will describe the state of the art including achievements and challenges in Haplo-HSCT, and will further encourage young researchers to embark on this rapidly evolving field of clinical and basic investigation.

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