Stem Cells for the Treatment of Heart Failure: What is Still Missing for a Prime Time Use?

Philippe Menasché, MD, PhD

Department of Cardiovascular Surgery, University Paris Descartes & INSERM U-970, Hôpital Européen Georges Pompidou 20, rue Leblanc 75015 Paris, France

Despite encouraging experimental results, clinical trials of stem cells in heart failure patients have still only yielded marginal benefits. These outcomes unlikely reflect the intrinsic inefficacy of stem cells which have been tested so far but rather their suboptimal utilization. It seems that to make this therapy a prime time option, at least three conditions still need to be met. First, it is critical to get a more precise mechanistic insight, i.e., determine whether the grafted cells generate a neo-myocardial tissue or act by harnessing endogenous repair pathways; this understanding can impact the choice of the cells although there is increasing evidence that regardless of the mechanism of action, cells intrinsically committed to a cardiac lineage or engineered to acquire it seem to be the most functionally effective. Second, it is critical to optimize cell transfer to ensure that the cells will reside long enough in the target tissue to exert their effects, whichever they are; depending on whether cells are delivered percutaneously by a catheter or surgically, the strategies to enhance early retention may include enhancement of biologic homing signals, development of new catheters and combination of cells with biomaterials; importantly, early retention should be distinguished from long-term survival which may be less critical than initially thought if the host-associated repair mechanisms, once activated by the grafted cells, can remain operational by their own in a sustained fashion. The third requirement pertains to clinical translatability. This requires that the above mentioned processes be developed in light of manufacturing, quality control and release criteria settings that may comply with the stringent regulations surrounding the so-called ATMP (Advanced Therapy Medicinal Products). Furthermore, this development plan should also fit an economically viable business model. If these different measures can be successfully implemented, then stem cells could be moved to a prime time setting through their integration in the clinical armamentarium of therapies offered to heart failure patients who have exhausted conventional treatments.