Can Regenerative Medicine Help Close the Gap Between the Medicine Pipeline and Public Health Burden of Cardiovascular and Musculoskeletal Diseases?

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ABSTRACT

Purpose: This commentary discusses the therapeutic and economic potentials of regenerative medicine (RM) by addressing how the reprioritization of resources in drug development may alleviate unmet medical need across many diseases, but especially cardiovascular diseases (CVDs) and musculoskeletal diseases (MSDs), the leading causes of mortality and morbidity, respectively, in the United States.

Methods: Data and perspectives represented in this commentary were obtained through an online literature search, public press releases from federal agencies and companies, online opinion pieces, published journal articles, and consulting agency reports; however, there were limitations to the available data because of the breadth and novelty of the therapeutic modalities involved.

Findings: Currently, the misallocation of resources within the therapeutic areas of CVDs and MSDs are possibly contributing to low approval rates, high cost of drug treatments, and consequently, disease burden. With a 2025 global market estimate of US $50.5 billion, RM is expected to become a major player in the pharmaceutical industry, with a potential to change the treatment paradigm and lessen disease burden across multiple disease areas, most notably in CVDs and MSDs.

Implications: While the public sector appears to be doing its fair share by funding basic research and revamping regulatory regimes to address the vagaries of RM as a rapidly emerging novel technology, the support framework necessary for transforming the field from a promising concept to available therapy requires levels of resource allocation and marketing support that only the private sector can provide. (*Clin Ther*. 2018;40:1066–1075)

Key words: cardiovascular, funding, musculoskeletal, regenerative medicine, resource misallocation, unmet medical need.

INTRODUCTION

The ability to effectively heal tissues, repair ligaments, and generate replacement cells continues to be one of the most anticipated medical advancements of the 21st century. The field of regenerative medicine (RM) has become multifaceted, encompassing cell therapy, gene therapy, and tissue engineering. Global attention to the field is expanding at a rapid pace. Dr. Shinya Yamanaka, who received the Nobel Prize in Medicine in 2012 for his discovery in converting a human skin cell to a stem cell, is a prime example of this recognition. This rapidly growing discipline is expected to become a breakthrough solution through its potential impact across many therapeutic areas, as the global market is estimated to reach $50.5 billion by 2025,[1] but in 2 therapeutic areas in particular, its effect could be transformative.

Cardiovascular diseases (CVDs) are the leading cause of death in the United States. The Centers for Disease Control and Prevention has established that 1 in 4 deaths can be attributed to heart disease.[2] Such a debilitating condition requires life-changing treatments. Patients with CVDs often experience long-term

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medical disability. The cost pressures associated with such conditions are high, as the total expenditures on CVDs in the United States reached $555 billion in 2016.[3] An example of a promising therapy in the CVD space, ixmyelocel-T, targets ischemic heart failure. This therapy utilizes selective cell-expansion techniques through the isolation of a patient's own bone marrow cells. Phase IIb results have indicated that intramyocardial delivery of these cells would improve overall health.[4]

Musculoskeletal diseases (MSDs) encompass >100 diseases characterized by injuries to joints and soft tissue,[5] and arguably constitute the leading cause of morbidity in the United States, where 46 million individuals have arthritis alone.[6] Other common ailments include carpal tunnel syndrome, trigger finger, and tendonitis. An investigative product that exemplifies the potential of RM in the treatment of MSDs is AST-OPC1 for spinal cord injury. This therapy uses oligodendrocyte progenitors derived from human embryonic stem cells to help repair demyelination disorders.[7]

In December 2016, the US Congress passed the 21st Century Cures Act with the intent of further incentivizing pharmaceutical and medical device companies to pursue advancements in technology that aid patients who are in dire need of care. The Act was intended to create a comprehensive policy framework for RM that allowed the US Food and Drug Administration (FDA) to more efficiently expedite its development and approval processes by building on already established approaches, including fast-track, breakthrough therapy designation; accelerated approval; and priority review.[8] In response, the FDA established a new framework called RM Advanced Therapy (RMAT) designation in November 2017.[9] Consideration for RMAT designation starts with meeting 3 requirements. First, the drug must qualify as an RM therapy. These areas include cell therapy, therapeutic tissue engineering, and human cell and tissue products. Second, the treatment must be intended to treat, modify, reverse, or cure a life-threatening condition. Last, there needs to be substantial preliminary clinical evidence that the drug has the potential to address unmet needs in the targeted indication. Successful designation allows for early FDA staff interactions and the potential to receive priority review and accelerated approval.[10] The importance of the RMAT program was summed up by FDA Commissioner Scott Gottlieb, MD, in a November 2017 press release: "To realize the full potential of regenerative medicine … we must advance a modern, efficient and least burdensome framework that recognizes the breakneck speed of advancement in the products we're being asked to evaluate, while ensuring patient tolerability".[11] Investigative products that have received RMAT designation within the past year, including the 2 examples of potential RM therapies just described, are listed in the **Table**.

This commentary discusses the therapeutic and economic potential of RM by addressing how the reprioritization of resources in drug development may alleviate unmet medical need across many diseases, but especially CVDs and MSDs, the leading causes of mortality and morbidity, respectively, in the United States.

MATERIALS AND METHODS

Data and perspectives represented in this commentary were obtained through online literature search, public press releases from federal agencies and companies, online opinion pieces, published journal articles, and consulting agency reports; however, there were limitations to the available data because of the breadth and novelty of the therapeutic modalities involved.

RESULTS

A total number of 60 articles were identified from the database searches. After the exclusion of 25 articles that were similar in conclusions or inadequately provided material on the therapeutic areas of interest, data from 35 articles (N = 148 patients) were included in the present review.

RM Potential Versus Therapeutic Area Needs

RM is defined by capabilities in rejuvenation (resident cell activation), regeneration (stem cell engraftment), and replacement (tissue transplantation).[12] This R^3 *paradigm* caters to the well-established goal of restoring structural and functional capacity following tissue displacement or injury. This goal encompasses long-term options for both chronic and degenerative diseases, which characterize the growing public health crisis that accompanies an aging population. The article by Jessop et al[13] highlights how various cell/tissue therapies capable of meeting this demand are spread across multiple medical specialties, including cardiology, neurology, respiratory, and rheumatology.