AMERICAN ACADEMY™
OF OPHTHALMOLOGY

CLINICAL STATEMENT

Intraocular Stem Cell Therapy

Introduction

The potential of stem-cell based technologies hold promise for the repair, restoration and regeneration of dysfunctional cells in the eye, yet significant challenges remain. These treatments appear to offer hope to patients who may have limited options for recovery of vision, including patients with non-neovascular age-related macular degeneration (AMD), retinitis pigmentosa (RP), and Stargardt disease (STGD).[1]

Clinical Trials

Several Phase I/II clinical trials are underway to study different types of stem-cell treatments for retinal diseases such as STGD and nonneovascular AMD. Stem cells can be derived from several sources, including embryonic stem cells, fetal stem cells, hematopoietic stem cells, mesenchymal stem cells, adult stem cells and induced pluripotent stem cells.[2] Trials of stem cell therapy have taken several approaches. One approach is a subretinal or intravitreal injection of bone marrow derived or human embryonic tissue derived stem cells. Another approach is transplantation of retinal pigment epithelium cells derived from either human embryonic stem cells or from the patient's own induced pluripotent stem cells. Questions remain about optimal delivery methods, host immune responses, in vivo monitoring, long-term adhesion, function and survival of cells, and adverse effects.[3-6]

Treatment Outside of FDA-Approved Clinical Trials

Some clinics across the United States have been offering "stem-cell therapy" to patients outside of clinical trials even though the Food and Drug Administration (FDA) has not approved their treatments.[7] The majority of treatments at these clinics use adipose-derived stem cells, known as a stromal vascular fraction (SVF) product. A liposuction aspirate is collected from the patient, the stem cells are separated from the surrounding fat tissue and then reinjected into the patient's target tissue. This stem-cell product is not approved by the FDA, and the risks and efficacy are largely uncharacterized. These products have skirted FDA regulation in the past because they are claimed to be of low risk based on the fact that they are injected in the patient from whom they are derived, and are minimally manipulated. Patients are paying for these procedures out of pocket because insurers do not currently provide coverage.

The FDA regulates the use of stem cells to ensure safety and effectiveness. It is concerned that patients are vulnerable to the marketing of stem-cell treatments that are not supported by adequate study, illegal and may be harmful. The FDA cautions that patients should check to be sure that any stem-cell treatment is approved by the FDA or is under a clinical investigation that has been approved by the FDA.[8] The FDA's Office of Criminal Investigations has worked with federal agencies to prosecute those who have manufactured, sold and utilized stem-cell products without FDA approval. The FDA has issued warning letters to stem-cell clinics across the country that utilize the SVF product from donors for autologous use, citing violations such as the lack of a valid biologics license, deviations from current good manufacturing practice and current good tissue practice, such as procedures intended to prevent microbial contamination, process control measures, laboratory testing of drug batches, quality control processes, etc.

The FDA issued a draft guidance in October 2015 to more clearly delimit homologous use for products such as stem-cell products, defining such use as cells and tissues that are identical to the recipient cells or tissues and perform one or more of the same functions in the

recipient as the cells performed in the donor.[8] In contrast, adipose-derived stem cell products are not intended for the same function in the patient, and are usually targeted for a spectrum of diseases. The risk is that stem cells that are implanted in another environment and intended to perform a different function than their original function may multiply, may form tumors or incite inflammation and may migrate elsewhere other than the intended site. Additional draft guidance from the FDA specifically addressed adipose-derived stem-cell products that are intended for a variety of conditions, require cell separation from its tissue structure and other manipulation that is considered more than minimal, and are combined with other substances the FDA would then place these into the category of a drug or product that is subject to premarket approval and manufacturing regulations, if implemented.[9-11]

Conclusion

The Academy believes that, in the interests of public health and patient safety, the FDA should continue to investigate unlicensed clinics that offer unapproved stem-cell therapy and to take appropriate regulatory actions. These treatments require further scientific evaluation to assure their safety and effectiveness to the public in well-conducted clinical trials under the aegis of the FDA.

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