

Navigating Regenerative Medicine: Highlights from the CIRM-CURA

Roundtable Conversation

In January 2020, the California Institute for Regenerative Medicine and the CURA Foundation hosted a roundtable discussion titled *Navigating Regenerative Medicine*. Participants included thought-leaders attending the JP Morgan Health Care conference among others. The roundtable was organized as a series of panels comprised of patients and representatives from patient advocacy organizations, pharma, government agencies, academia and the broader health-care industry. CIRM and the CURA Foundation organized the roundtable to consider what infrastructure is needed to enable patients to make informed choices in the emerging regenerative medicine space.

The need for patient access to objective and reliable information is particularly acute in the regenerative medicine space in light of two contemporary developments. First, we are at a turning point in regenerative medicine where the initial wave of treatments has obtained FDA approval. Some patients ask: *are these treatments right for me?* There are also numerous regenerative medicine products in the development pipeline and in some cases multiple treatments for the same indication, e.g., gene therapy treatments for sickle cell disease. Patients may wonder if participating in a clinical trial is the best choice for them, and looking forward, they may need to consider what is the best approved treatment options for their disease.

The second development is the proliferation of “unproven stem cell treatments.” In the process of seeking information about promising new regenerative medicine treatments, patients are likely to encounter advertisements for fee-for-service “stem cell treatments.” Typically, such treatments cost thousands of dollars, lack evidence of clinical effectiveness and may have dangerous side effects. Ultimately, unproven treatments can put patients in medical and financial risk without alleviating their underlying condition.

Against the backdrop of promising regenerative and potentially curative treatments emerging alongside the proliferation of unproven treatments, the roundtable sought to address a fundamental question:

How does a patient navigate this environment and get trusted and reliable information to help sort through their options?

To address this question the roundtable participants were asked to consider three broad themes:

- 1) **Quality Information:** What systems are needed to enable patients, health care providers and payers to objectively evaluate regenerative medicine treatment options?
- 2) **Policy and Infrastructure:** How can we advance evidence-based treatments that demonstrate clinical benefit while curtailing the marketing of products that pose medical and financial risk?
- 3) **Regenerative Medicine and Society:** How can we empower patients and the public to be active participants in research and medical decision-making?

The roundtable was divided into three panel discussions where participants were asked to provide their perspective on the discussion theme. Discussion among all participants followed the panelists remarks. This report summarizes the panelists major themes and the ensuing roundtable discussion. The summary is organized by session and thematic area.

I. Opportunities to Enhance Patient-Centered Personalized Care

Theme 1: There is a Growing Gap Between Standard of Care and Optimal Care

There is a lag in the uptake in technologies that have the potential to optimize patient care. Genomics, imaging and other advanced diagnostics can serve to identify an optimal treatment plan. Previous research suggests that 45 percent of the time patients are not getting prescribed evidence-based medicine. More recently JAMA reported that for the most common cancer mutations about one-third of patients are not receiving the best treatment based on genomic testing. A number of barriers to optimal care were identified, including:

- Lack of information among health care providers
- Resistance to change or sticking with what feels safe
- Concerns over cost-containment especially if the new treatment is more expensive

These barriers actually have the potential to increase health care disparities if some patients have access to optimized care while others do not. The City of Hope described an initiative it has developed to partner with employers. Employers are considered “great partners” because “they care not just about affordability, but also the patient experience and health outcomes.” The partnership focuses on employees diagnosed with cancer and is designed to allow City of Hope to work directly with a patient’s treating physician (regardless of health plan). City of Hope analyzes the advanced diagnostic data and provides the treating physician with options of optimal care. Today numerous companies are using this suite of services to improve employee care.

Theme 2: The Value of a Relationship-based Care

Regenerative medicine is causing providers to reevaluate their systems for the delivery of care. These treatments tend to be complex so managing the delivery system is becoming more important. Effective delivery systems seek to align human and physical resources with the overall patient journey. Alignment is accomplished through:

- Redesigning facilities based on how patients move around them
- Continually interacting with patients and their families to understand how to improve the patient experience
- Including emotional support along the treatment continuum
- Maintaining patient portals that allow any question regarding the patient journey (from “where do I park” to “where are my medical records”?) to be addressed through a single point of contact

Theme 3: Patients Should be Active Participants in Therapy Development

In the rare disease space, Global Genes has been working with patients so they can become actively engaged in therapeutic discovery and development. A major focus is the “hows” and “whys” of data collection and management. One aim is to arm patients with “research-ready” data so they can become partners in research. The overall goal is to forge partnerships with patients to improve the speed, efficacy and efficiency of rare disease research.

Theme 4: Sickle Cell Disease (SCD) is an Opportunity to Build a Navigation Platform

There are a number of curative SCD treatments in the pipeline and the American Society of Hematology (ASH) has made a “full commitment” to create a collaborative research infrastructure. This infrastructure includes a data hub and clinical trial network representing 52,000 patients. Despite this success, barriers remain including:

- Finding qualified investigators to manage clinical trials within the network
- Locating the appropriate patient population for specific regenerative medicine treatments
- Educating patients early-on about their treatment opportunities
- Identifying ways of financing treatment

Discussion Points:

- We must be aware of the psychosocial needs of patients. Many patients have developed a community or identity related to their disease condition. It will be important to work with patients early on to understand how to provide psychosocial support.
- Related to the point above, it is critical to engage the patient community to ensure they are interested in new treatments. This point is particularly important for non-life-threatening conditions that patients may have adapted to.
- Patient navigation will be critical for conditions such as sickle cell disease where there are a number of regenerative medicine treatments. Patients will need support determining if there is a treatment that is right for them and also consider what is currently available versus those in the pipeline.

II. Essential Policy and Infrastructure for Regenerative Medicine

As was discussed in Theme 1, there is a mismatch between the care patients are getting and optimal evidence-based care. Perhaps the most striking indicator is the fact healthcare technologies are better than ever but on a population basis, health outcomes are getting worse. The policy challenge becomes not only getting better treatments to market but also translating this innovation into better health in the population.

Theme 5: Manufacturing Challenges in Stem Cell Research Need to be Addressed

We are “now at an inflection point” where regenerative medicine treatments may provide optimal care for some patients. Current success stories include gene modified stem cells for blood diseases and immune therapies for cancers. The longer-term vision for the field is to have

allogenic treatments for a wider range of diseases. Because of “the degree of complexity of cell-based therapy,” we need to start a “collective think” about how to “bring variables under control.” To reach this point, a rational drug design paradigm is needed where manufacturing processes can be replicated to produce products that perform consistently from trial to trial. We “haven’t really gotten there yet.” As a field, there needs to be focus on the critical quality attributes in manufacturing and development of standardized tools (cell line, reagents, and processes) to support rational design.

Theme 6: Unproven Treatments are the Enemy of the Good

The good faith efforts of those committed to overcoming the challenges to advancing the field are being put at risk by people who “are just trying to make a buck.” People are paying tens of thousands of dollars out of pocket for a series of treatments for the “muck du jour.” Further, those profiting from unproven treatments are trying to frame the issue as a libertarian right to use your cells rather than an issue of efficacy – do these treatments work and is the product effective. At the policy level, right-to-try laws are examples where providers of unproven treatments are attempting to circumvent scientifically rigorous test in products.

Theme 7: Coverage and Pricing are Critical Policy Considerations

If we want to bring regenerative medicine to all, we must have products “that will be reimbursed by payers in the United States across the board.” Up until today there have been a relatively small number of regenerative medicine products for conditions that tend to be rare in the population. As a consequence, such treatments have not registered on the payer side, but that is changing. We have seen examples, internationally, of payers agreeing to reimbursement models that are tied to outcomes over time. Over the next five to ten years, we can anticipate new gene therapies. We must continue to consider different reimbursement models to help address current funding constraints. For example, sickle cell is one case where many could benefit from these treatments, but they are covered through state Medicaid programs where there is little or no budgetary “slack.”

Theme 8: Leverage Interoperability Standards and Evidence to Accelerate Treatments

The efficacy of regenerative medicine treatments will be determined by clinical evidence that definitively demonstrates “measurable effect sizes.” We have made great strides in setting interoperability standards for formatting and exchanging clinical data – Fast Healthcare Interoperability Resources (FIRE). Further, the 21 Century Cures Act provides a framework for enabling real-world-evidence to support product registration. Optimally we should develop an evidence engine that allows us to link clinical outcomes “in the post-market setting” to reimbursement decisions (Theme 7). There have been efforts, through federal legislation, to develop information systems to support regenerative medicine treatments. To be successful, these efforts will require partnerships between the public, private and non-profit sectors to continue to develop objective, standardized and reliable data.

Theme 9: Aim for International Data Harmonization (Regulatory)

Early regenerative medicine development programs faced challenges compiling data related to manufacturing, safety, efficacy and long-term outcomes. Requirements have varied between international jurisdictions (e.g. EMA vs. FDA). This regulatory variation may be expected in a new field, and ideally, variation would diminish over time as evidentiary standards harmonize. In addition, organizations like CIRM should focus academic programs to develop standardized data as early as possible. International harmonization for manufacturing standards (Theme 5) will also be important for ensuring safety and efficacy evaluation. One participant encapsulated this theme by stating, “until we treat cellular therapies like we would any other medical products, defined products, well-made, well-understood, well-studied, they are going to languish.”

III. Regenerative Medicine and Society

Theme 10: Patients Advocacy Groups are Spreading Awareness

Patient advocacy groups are effectively utilizing social-media and other advocacy tools “to spread that awareness and let the other (patients) know that what you are doing is legitimate.” These networks emerged both to fill information gaps and expand support options where patients-to-patient communication allows the sharing of clinical trial and treatment experiences. Advocates play a valuable role in directing new patients away from “quacks” or “muck” and toward scientifically rigorous clinical trials or treatments. Advocacy organizations fill the role of trusted intermediaries for patients considering clinical trials or approved treatments. Increasingly, patient networks are partnering with medical centers and other providers to support comprehensive patient navigation.

Theme 11: Patients / Researcher Partnerships Enhances Clinical Research

Patient organizations and support groups have approached disease research programs at medical research centers. The support groups have the ability to disseminate information to patients in the service area, particularly for more prevalent indications (e.g. Parkinson’s disease). This dissemination can be particularly valuable for supporting clinical trial recruitment. Fundamentally, you have networks of people that are “trusted and interact to become socially connected.” Organizations that have developed this connectivity are ideal partners for clinical researchers.

Theme 12: Trusted Intermediaries are Critical for Regenerative Medicine

Digital information providers (e.g. GoogleHealth) face a challenge of deciding where to go for trusted and reliable evidence. Obtaining unbiased information about medical products is a challenge. Content providers need to know who to trust so they can “prioritize intermediaries.” This can be particularly complicated in the United States because states regulate the practice of medicine while the FDA addresses products. Addressing these issues to serve patients and the public will require robust information systems (Theme 9) and trusted organizational systems (Theme 10). Public organizations and non-governmental organizations might consider partnerships to provide unbiased information.