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Navigating CAR T Delivery In Autoimmune Indications: Impact & Opportunity

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The cell and gene therapy landscape has grown tremendously in the past few years, partly driven by the expansion of CAR T-cell therapy development across indications. The first CAR T approval, Yescarta (axicabtagene ciloleucel), took place in 2017 to treat relapsed or refractory large B-cell lymphoma.[1] Since then, the FDA has approved six CAR T products, with an estimated 1000 CAR T-cell therapies currently in development at various pipeline stages worldwide.[2]

Advancements in the CAR T space over the past 20 years have been particularly focused in the oncology sector for indications such as relapsed or refractory B-cell acute lymphoblastic leukemia, relapsed or refractory diffuse large B cell lymphoma, primary mediastinal large B-cell lymphoma, and mantle cell lymphoma. However, the rise of next-generation CAR T technologies have brought new mechanisms of action into play that can reduce unwanted side effects and treatment burden on patients in therapeutic areas within as well as beyond oncology.

Recently, there has been rising interest in using CAR T-cell therapies to treat autoimmune diseases. This opportunity brings excitement and challenges for the industry, making it imperative for sponsors to understand how new challenges could impact the future success of CAR T in treating these complex autoimmune indications, says Emily Merrell, global head of cell & gene therapy, drug development solutions at ICON.

Meeting An Unmet Need

Autoimmune diseases have a high unmet need in the life science industry. Due to the complexity of the disease, patients who suffer from these often-lifelong conditions do not have many treatment options available to them. This phenomenon, in turn, opens the door for CAR T-cell therapy to make an impact.

“Treatment options largely focus on the control of symptoms rather than tackling the root cause or the underlying etiology of the disease,” explains Merrell, “which can often be quite complex and unclear and therefore often give rise to ephemeral results, in addition to the risk of serious repercussions of lifelong immunosuppression. A considerable number of patients don’t respond to those lifelong treatments with immunosuppressive or immunomodulatory drugs as well.”

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The shift has also been amplified by the promising data from a study led by Professor Georg Schett at the University of Langan in Germany. This study, published in 2023, enrolled 15 patients with various autoimmune diseases in Germany, measuring response over a minimum of 15 months. The results showed that CAR T-cell therapy could cure all patients or put them into remission with no occurrence of relapse.[3]

There are still more safety and efficacy trials to be conducted in this new field of research, though reaching positive clinical outcomes at an early stage is an encouraging sign of CAR T treatment potential for this patient population.

"The common characteristic of this group of diseases is that there's a pathogenesis which is driven by an uncontrollable response of the immune system. This opens the possibility of cell therapy, such as CAR T, to play an important role in its treatment. That early data that we've seen from Schett and others that's starting to come through in the public domain has indicated that CAR T may have that potential to offer a long-term solution for these patients," Merrell adds.

Impact On Clinical Trial Stakeholders

While CAR T has a well-understood mechanism of action, efficacy and safety profile within a number of oncology indications, it is unclear how effective it will be in managing the underlying pathology of these autoimmune diseases in the long term and how the safety profile may look, says Merrell. As the industry prepares to respond to upcoming challenges in this space, it is crucial to understand how each stakeholder involved in CAR T-cell therapy development will be affected.

Site Perspective

CAR T-cell therapies are notoriously complex for sites to deliver, even more so in their autologous form. Despite growing site capabilities and infrastructure that has aided in expanding access beyond a small group of specialists, these therapies have almost exclusively evolved within the oncology setting. Therefore, sponsors should consider the unique expertise needed to successfully deliver CAR T-cell therapies to patients with autoimmune diseases.

Historically, CAR T expertise has grown within cell therapy teams in stem cell transplant centers. "In this scenario, it's vitally important to ensure the involvement of both the cell therapy team, where most likely the cell therapy experience exists and the responsibility of treatment delivery will lie, in collaboration with the referring and/or primary care specialist," Merrell notes. "For example, with lupus, that would be the rheumatologist, and they will remain responsible for the onward care of the patient following treatment."

Communication and relationship-building between clinical teams across sites are of utmost importance for these CAR T-cell therapies, in addition to implementing an effective strategy to support the establishment of working models. "This is an additional complexity that we're faced with [as an industry] in this new landscape that requires new ways of working to reduce the risk of fragmenting patient management and decreasing the patient's safety," she emphasizes.

Lastly, it is essential to identify sites with experience in delivering cell therapy and expertise specific to a target indication. Overcoming the challenge of identifying a suitable site that meets both criteria will require "access to deep insight, experience, and data-driven site intelligence," Merrell says.

Patient Perspective

From the patient's perspective, this new treatment offers a different kind of hope that does not currently exist within standard of care. CAR T holds the promise of long-term remission by resetting the immune system, but how will patients perceive this new possibility, balanced against the potential for serious side effects which comes along with this innovative technology?

Currently approved CAR T-cell therapies are targeted towards cancer patients who are in later stages of their disease management where there are arguably limited options left available to them. These therapies offer a lifeline that is otherwise not there. For autoimmune patients, whilst standard of care may not offer the possibility of a "cure", there are options that will enable many to live with their condition, albeit with a variable degree of quality of life. So, the risk-benefit may be perceived as somewhat different when these therapies are transposed into this new setting.

Another challenge worth noting is the ongoing difficulties associated with manufacturing scalability, which need to be considered as CAR T development potentially extends into larger patient populations.

"Industries are working assiduously to overcome these manufacturing challenges, which many would argue are some of the biggest hurdles for CAR T developers to overcome if there's to be success in serving larger, more diffuse patient populations beyond the clinical trial setting," says Merrell. "There's mounting pressure to make manufacturing more scalable, both in terms of more convenient delivery at sites and to drive down costs."

Keys To Success

Industry partnerships with trial sites are key to ensuring that these sites will be ready to participate in CAR T trials for autoimmune diseases and, most importantly, as Merrell stresses, to adopt these types of therapies once approved clinically.

"It's important that we think now about what additional support is required by less experienced sites to enable them to be ready to deliver and for us to drive expansion of existing site networks beyond those largest and most experienced sites. This is crucial to enable scalability, greater patient access, accelerating enrollment into clinical trials, and encouraging greater diversity and inclusion – all of which will be important for us to be able to close that gap that we know exists between regulatory approval and patient access," she explains.

It is evident that CAR T within autoimmune indications, such as Lupus, has become a hugely competitive landscape, making it even more important for sponsors to think very carefully about their study design. To anticipate development challenges, planning trials that are less complex and burdensome for sites and patients will accelerate the start-up process and make it easier to recruit patients. In addition, sponsors' openness to expanding their geographic footprint for clinical trials and devoting more resources to patient education and awareness, including working with community-based organizations, will be paramount.

"As the industry learns more about what successful development entails in autoimmune indications, there are high hopes that CAR T-cell therapies will transform the treatment paradigm for this area of high unmet need."

"It will be vital that sponsors work with community-based organizations that can help provide input into trial design," says Merrell. "[This may include] careful consideration of endpoints that are meaningful to patient populations and raising awareness of this new and innovative treatment modality, deepening that recruitment potential through access to patient networks."

As the industry learns more about what successful development entails in autoimmune indications, there are high hopes that CAR T-cell therapies will transform the treatment paradigm for this area of high unmet need. Merrell and the rest of ICON are excited to continue partnering with organizations involved in this ongoing transformation to heighten scientific innovation and increase patient access to life-saving treatments.

References

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