ADVANCED THERAPIES

CONGRESS & EXPO 2021

The virtual Advanced Therapies Congress and Expo 2021 was held in May

Bringing together the advanced therapies community during this critical time, the main objective of this event was to reflect on how challenges have been overcome, collaborations have been strengthened and lessons have been learned to help patients access advanced therapies in the past tumultuous year. It also aimed to highlight key advances being made in the industry.

Across three days, the congress covered the latest themes in cell therapy, gene therapy and market access, offered by experts in a highly engaging discussion.

This document summarises the key messages gathered throughout the congress sessions and discussions.

CAR-T cell immunotherapy is expanding to broaden patient access and include new indications

CAR-T cell immunotherapy was one of the key themes discussed throughout the congress. Current major developments for this promising technology include application in haematological malignancies with a high unmet need, such as multiple myeloma. In particular, BCMA-targeted immunotherapy is one key strategy being developed globally within a very competitive space.

Advancing from haematological malignancies to solid tumour indications is presently seen as another fundamental step in the sector. The latest approaches leverage on recently characterised CAR macrophages (CAR-Ms) or adoptive CAR-T combination immunotherapy, including MSLN CAR-T cells and PD-1 checkpoint blockade antibody; CAR-T combination immunotherapy resulted in consistent mesothelioma regression in presented unpublished clinical data.

Allogeneic CAR-T cell therapy, although not yet a reality, is awaited to help expand current autologous strategies and improve patient access to these innovative cell therapy treatments.

Next steps in gene therapy will address technical limitations and will need to improve information sharing

Current major challenges in gene therapy mainly relate to technical limitations, such as manufacturing and targeted vector delivery. Novel strategies are being explored to help address the targeted delivery of AAVs, including innovative directed evolution technology that would potentially allow delivery to any cell type. AAV capsid engineering, achieved through selected amino acid modifications, would provide a valuable tool to prevent immune response to dominant antibodies, ultimately allowing treatment redosing. In addition to overcoming these technical limitations, a new set of delivery systems is being evaluated, including lipid nanoparticles and exosomes, although these carry inherent CMC challenges. Meanwhile, next-generation CRISPR technologies are proceeding towards improved genome editing specificity to help establish robust platforms and reduce rates of chromosomal translocation.

Most importantly, by realising the complexity of these technologies within the context of clinical application, the crucial need for information sharing and continued education for the benefit of patients, carers and their treating physicians was extensively highlighted.

Clinical development for rare inherited diseases may benefit from novel clinical trial design

Several speakers acknowledged a sense of pride in the industry for overcoming the relevant barriers in clinical development posed by the pandemic through intense global collaboration, timely rolling reviews and increasing patient access through the introduction of new tools such as virtual onboarding.

Focusing on clinical advancement in rare diseases, 'Shared molecular aetiology, or SaME, Therapeutics' is a novel pilot strategy that was proposed by the Office of Rare Diseases Research at NCATS, NIH (USA), which leverages the observation that although thousands of rare diseases exist, underlying genetic aetiologies are far fewer (e.g. premature stop codon mutations, missense or splice site mutations, or gain-of-function mutations).

Rather than grouping patients based on the traditional clinical manifestation (phenotype), this pilot proposes to design basket trials based on shared disease molecular aetiology – moving beyond the traditional concept of 'one disease at a time'. It is based on the hypothesis that designing a clinical trial for multiple rare diseases at the same time and using the same therapeutic platform (for example, the same AAV-based vector, route of administration and manufacturing procedure) but with a different therapeutic gene construct will increase trial efficiency and reduce clinical trial start-up time. The pilot 'Paving the Way for Rare Disease Gene Therapies' (PaVe-GT) programme is currently testing this novel approach, and key learnings will be made publicly available.

Human-centred design and innovation are key to improving patient access to advanced therapies

Recognising that significant opportunities exist to improve patient experience and information sharing within advanced therapies, the Mayo Clinic shared practical insights on how to develop an ideal CAR-T cell therapy experience by leveraging actual human-centred design.

The case study demonstrated that both patient and staff experience were markedly improved, in addition to improving overall service efficiency and teamwork. Built on patient interviews, the programme aims to better prepare patients and caregivers for each step in a complex service line by setting expectations prior to arrival at the treatment centre; it provides a venue where they can connect with others who have gone through similar experiences, improving the scheduling process and providing honest, patient-relevant information on procedures and possible side effects.

Throughout this process, patients and caregivers are prepared emotionally as well as logistically, and feel cared for owing to improved interactions with their care team.

ABBREVIATIONS:
AAV, adeno-associated virus; BCMA, B-cell maturation antigen; CAR, chimeric antigen receptor; CMC, chemistry, manufacturing and control; MSLN, mesothelin; NCATS, national center for advancing translational sciences; NIH, national institutes of health; PD-1, programmed cell death protein 1.

FURTHER READING:
Grosser R, *et al. Cancer Cell.* 2019; 11;36(5):471–482; Klichinsky M, *et al. Nat Biotechnol.* 2020; 38(8):947–953; Bulaklak K and Gersbach CA. *Nat Commun.* 2020;11(1):5820; Arnold FH. *Angew Chem Int Ed Engl.* 2018;57(16):4143–4148; NIH NCATS Paving the Way for Rare Disease Gene Therapies (PaVe-GT). Available at: **https://pave-gt.ncats.nih.gov** (Accessed: May 2021); Mayo Clinic CAR-T cell therapy program. Available at: **https://www.mayoclinic.org/departments-centers/car-t-cell-therapy-program/home/orc-20404317** (Accessed: May 2021).

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