FROM THE ANALYST'S COUCH

Landscape of cancer cell therapies: trends and real-world data

Ana Rosa Saez-Ibañez, Samik Upadhaya, Tanya Partridge, Monica Shah, Diego Correa and Jay Campbell

Credit: Tohid Hashemkhani/iStock/Getty Images Plus

Since tisagenlecleucel (Kymriah) was approved by the FDA in 2017, five more chimeric antigen receptor (CAR)-T cell therapies have gained approval, the last one of which, ciltacabtagene autoleucel (Carvykti), was approved in February 2022. The cell therapy field is still expanding and evolving beyond the early successes in haematological cancers. Novel technologies using other immune and stromal cell types are being investigated, and the list of targets in the global R&D pipeline keeps growing. Despite this pipeline expansion, the field also faces challenges — such as effective targeting of solid tumours, manufacturing complexities and barriers to clinical implementation — that affect the broad uptake of cell therapies into clinical practice. In this update, we provide an in-depth analysis of the current cell therapy landscape, including the development pipeline and clinical trials. We have also analysed real-world data to describe the current use of cell therapies in clinical practice and some of the challenges to their implementation.

Trends and top therapeutic modalities

As of 15 April 2022, there are 2,756 active cell therapy agents in the global immuno-oncology pipeline, compared to 2,031 active agents in our 2021 update. This represents a 36% increase and therefore a modest deceleration of R&D in oncologic cell therapy, compared to the 43% increase from 2020 to 2021, and the 61% increase from 2019 to 2020 (Supplementary Fig. 1). Of the various categories, CAR-T cells continue to lead the cell therapy pipeline and showed a 24% growth from last year, which is lower than the 38% increase from 2020 to 2021. Natural killer (NK) cell-based therapies also showed a blunted growth, with a 55% increase in the past year (compared to 65% in the previous year) (FIG. 1). By contrast, other cell therapies, including a variety of therapeutic agents different from T cells (such as dendritic cells, stem cells or myeloid cells, among others) grew by 129% this year, a rapid increase compared to the 37% growth between 2020 and 2021. Regardless of the specific modality, development of allogeneic therapies has increased more sharply (33%) than autologous modalities (23%) in the past year (Supplementary Fig. 2), with no major changes in the geographical distribution of these modalities (Supplementary Fig. 3), or in the academic versus industrial setting (Supplementary Fig. 4).

Top cell therapy targets

The overall blunted growth in the number of cell therapy agents is consistent with the slower increase in the number of targets being pursued: a 31% increase in the past year, compared to a 35% and 41% increase from 2019 to 2020 and 2020 to 2021, respectively.

As in 2021, in haematological malignancies, CD19, BCMA and CD22 continue to be the most frequently targeted proteins (FIG. 2a). Some new targets have showed a significant increase this year, such as GPRC5D (+200%), CLEC12A (+114%) and CD7 (+78%), although none of them appear in the top five of most-used targets (FIG. 2a). In solid tumours, unspecified tumour-associated antigens (TAAs), HER2 and mesothelin (MSLN) continue to be the most frequently targeted proteins (FIG. 2b). Some of the targets in this list, although still relatively infrequent, have showed a sharp increase with respect to 2021, including CLDN18 (+400%), CD276 (+160%) and KRAS (+125%). TAAs have showed an increase of 220%, making them the only target of the fast-growing category that appears in the top five of most-pursued targets (FIG. 2b). Top targets according to tumour type are depicted in Supplementary Fig. 5.

Cell therapy clinical trials landscape

According to data pulled from ClinicalTrials.gov, as of April 2022 there are nearly 1,800 active cell therapy trials, a 33% increase from last year, compared to a 43% increase from 2020 to 2021 and 24% increase from 2019 to 2020 (Supplementary Fig. 6). This slower growth is reflected across virtually all therapy modalities, including NK/NKT cell therapy, although this modality is slowly recovering from the drop observed in 2020. Trials using 'other cell therapies' also continue to increase. As in previous years, most cell therapy trials focus on addressing haematological cancers.

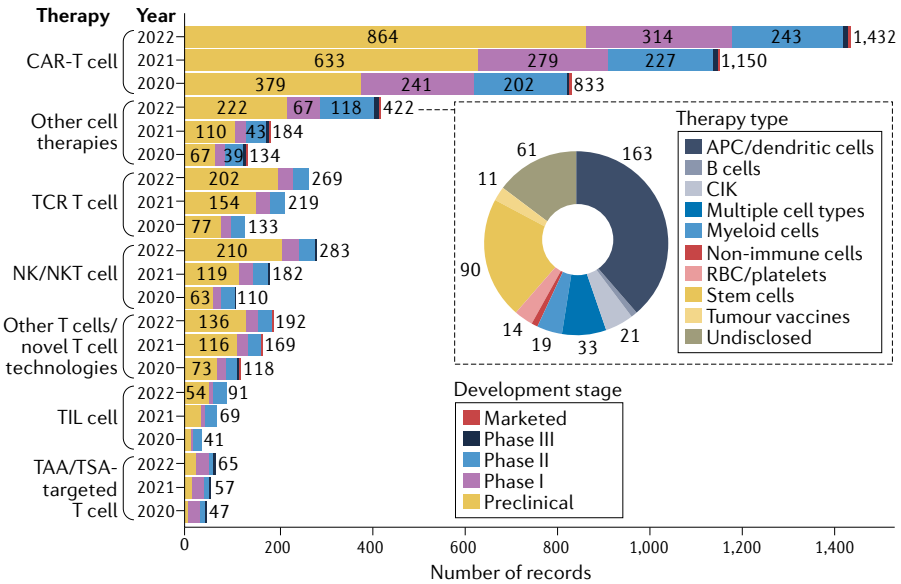


Fig. 1 | **Changes in the cancer cell therapy pipeline by therapy type and year.** Comparison of cell therapy agent development pipeline across various therapy types from 2020 to 2022. APC, antigen-presenting cell; CIK, cytokine-induced killer; NK, natural killer; RBC, red blood cell; TAA, tumour-associated antigen; TCR, T cell receptor; TIL, tumour-infiltrating lymphocyte; TSA, tumour-specific antigen. The pie chart shows the composition of the 'other cell therapies' category in 2022.

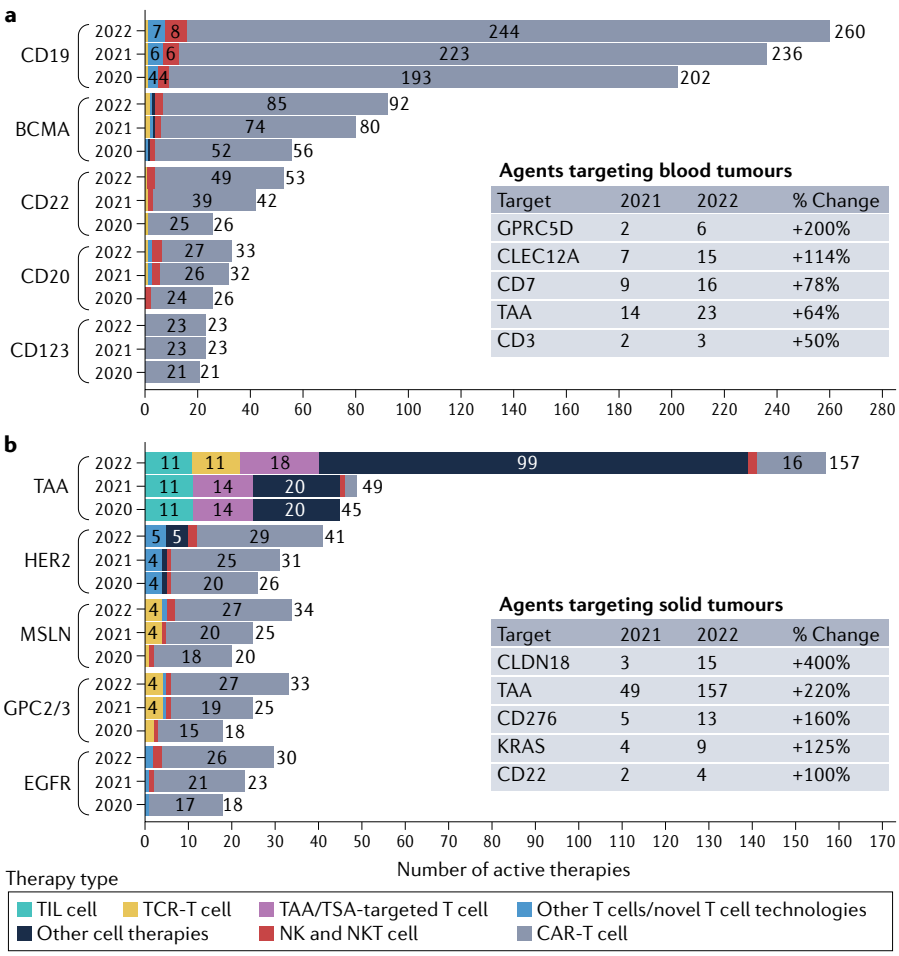
However, trials assessing cell therapies in solid tumours constitute 43% of all trials and have reached the highest year-over-year increase (44% from 2021 to 2022) (Supplementary Fig. 7).

Real-world access to CAR-T cell therapy

To assess whether trends in the growth of the cell therapy pipeline correlate with clinical use of cell therapies, we analysed IQVIA proprietary medical and prescription claims data from 2019 to 2021 and evaluated the number of patients receiving CAR-T cell therapy in clinical practice based on CPT, HCPCS and ICD-10 codes. Overall, use of CAR-T cell therapies in 2021 was similar to that in the second half of 2020 (Supplementary Fig. 8). However, unlike 2020, when variations in CAR-T cell use associated with the COVID-19 pandemic were observed, use of CAR-T cell therapy throughout 2021 was consistent. Importantly, these data demonstrate that the use of CAR-T cell therapies in clinical practice has lagged behind the number of regulatory approvals, suggesting that there may be practical barriers to their use.

To understand these barriers, we leveraged data collected from IQVIA's CAR T-Cell Monitor survey, which included responses from community oncologists ($n = 100$) and oncologists at CAR-T cell-specialized centres ($n = 50$) about treatment, referral decisions and their perceptions about cell therapies (including accessibility, efficacy and logistics of treatment administration). Among community oncologists, the top three reasons cited for not referring a patient to cell therapy centres included the patient's health status (44%), costs to patients (37%) and geographic distance for the patient to travel for treatment (32%) (Supplementary Fig. 9).

Our analysis of US facilities equipped to perform cell therapy treatments shows great heterogeneity in site density, with most facilities concentrating in the East and West Coast (Supplementary Fig. 10). This lack of equal distribution contributes to geographic distance being a key barrier for referral for cell therapies. According to the oncologists at specialized centres that took part in the survey, cost was the main barrier to refer oncology patients to cell therapy treatments (65%), followed by patient eligibility and/or fitness (63%), and disease progression (54%) (Supplementary Fig. 11). Additionally, up to 35% of oncologists at specialized treatment centres noted waiting lists for treatment with approved CAR-T cell therapies, which may also be a reason for their slower implementation in clinical practice.



Agents targeting blood tumours

Target	2021	2022	% Change
GPRC5D	2	6	+200%
CLEC12A	7	15	+114%
CD7	9	16	+78%
TAA	14	23	+64%
CD3	2	3	+50%

Agents targeting solid tumours

Target	2021	2022	% Change
CLDN18	3	15	+400%
TAA	49	157	+220%
CD276	5	13	+160%
KRAS	4	9	+125%
CD22	2	4	+100%

Fig. 2 | **Top targets of cell therapies for blood and solid tumours.** We calculated percentage growth for the 40 most numerous agents present in the 2021 and 2022 pipeline, from which the top 5 targets in haematological malignancies (part **a**) and solid tumours (part **b**) are depicted in the bar chart. Tables show targets by percentage growth from 2021 to 2022. MSLN, mesothelin; NK, natural killer; TAA, tumour-associated antigen; TCR, T cell receptor; TIL, tumour-infiltrating lymphocyte; TSA, tumour-specific antigen.

Conclusions

The clinical pipeline for cell therapy R&D continues to grow, albeit at a slower pace than in previous years. Cell therapy modalities that do not rely on T cells have solidified their growth in the past year. Potential reasons for this rise could be independence from specific targets, better safety profiles, complementary mechanisms of action to that of T cell-based therapies or their feasibility for 'rapid' off-the-shelf manufacturing, among others. The clinical trials landscape also shows a modest growth compared to previous years, although trials focusing on solid tumours continue to increase. Our findings indicate that implementation of CAR-T cell therapies in clinical practice has not kept pace with the robust growth of its R&D pipeline. Some key limiting factors could be an incomplete understanding of patient eligibility, cost of treatment, and travel requirements and associated patient burden. Moving forward, academia, government and industry must continue to collaborate and place a greater emphasis on education, implementation, reimbursement and commercialization strategies for cell therapies. These critical aspects of clinical development should be carried out in parallel with clinical trials so that we not only invest efforts in growing the pipeline, but also on optimizing access to these effective therapies to patients around the world.

Ana Rosa Saez-Ibañez[1], Samik Upadhaya[1]✉, Tanya Partridge[2], Monica Shah[2], Diego Correa[2] and Jay Campbell[1]

[1]Anna-Maria Kellen Clinical Accelerator, Cancer Research Institute, New York, NY, USA.

[2]IQVIA, Durham, NC, USA.

✉*e-mail: supadhaya@cancerresearch.org*

https://doi.org/10.1038/d41573-022-00095-1

Competing interests

T.P., M.S., and D.C. are full-time employees of IQVIA. The other authors declare no competing interests.

Supplementary information

The online version contains supplementary material available at https://doi.org/10.1038/d41573-022-00095-1.