FROM THE ANALYST'S COUCH

The clinical pipeline for cancer cell therapies

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Earlier this year, idecabtagene vicleucel (Abecma), a chimeric antigen receptor (CAR)-T cell therapy targeting B cell maturation antigen (BCMA) was approved by the FDA for the treatment of multiple myeloma, becoming the first CAR-T cell therapy for a target other than CD19 to receive approval. There are currently five cell therapies approved by the FDA, all of which are CAR-T cell therapies. This analysis gives an updated view of the cancer cell therapy landscape, including the global R&D pipeline of agents, the status of clinical trials, and real-world data evidencing their current use in clinical practice.

Steady growth of the R&D pipeline

As of 16 April 2021, there were 2,073 active cell therapy agents in the global pipeline, 572 more than the previous update in 2020. This represents a 38% increase in the past year compared with a 48% increase from 2019 to 2020. Among the different types of cell therapy, CAR-T cells continue to dominate the landscape with 299 new agents added to the pipeline, a 35% increase from 2020 (FIG. 1). Most CAR-T cell agents (80%) are at the preclinical and phase I stage.

The T cell receptor (TCR) T cell therapy class added 80 new agents, followed by natural killer (NK)/NKT cells (67) and novel T cells (51). Most (835) cell therapies are of autologous origin, with twice as many autologous agents in development as allogeneic agents (Supplementary Fig. 1). There was a significant increase in the number of allogeneic agents in preclinical and early-clinical (phase I) development in the past year (48% and 42%, respectively), more modest than the increase observed the year before (80% and 95%, respectively). There was, however, a higher increase in allogeneic cell therapy agents in phase II development (48%) compared with last year (33%). For most cell therapy agents in phase II and beyond in regions outside the United States, such as China, it has not been disclosed whether they are autologous or allogeneic (Supplementary Fig. 2).

Top targets for cell therapy agents. We explored targets and pathways for cell therapy agents. CD19, BCMA and CD22 remain dominant targets for haematological indications (FIG. 2), but the rise in the number of agents pursuing these targets in the past year is modest (15%, 23% and 56%, respectively) compared with the significant increases observed in the previous year (51%, 83% and 80%, respectively). Reasons behind such a sharp year-on-year decline in the number of agents across these targets could include market saturation and the impact of COVID-19 on drug R&D. The top solid tumour targets explored remain largely the same, with undisclosed tumour-associated antigen (TAA) being at the top. Most of the agents for solid tumours use CAR-T cell modalities enhanced to overcome the challenges associated with recognition, trafficking and surviving in the tumour microenvironment. Of note, development of cell therapy agents targeting glypicans 2 and 3 (GPC2 and GPC3) continues its fast growth, nearly doubling each year since 2019 (Supplementary Fig. 3). Most of this activity is in liver cancer, as glypicans are highly expressed in hepatocellular carcinomas.

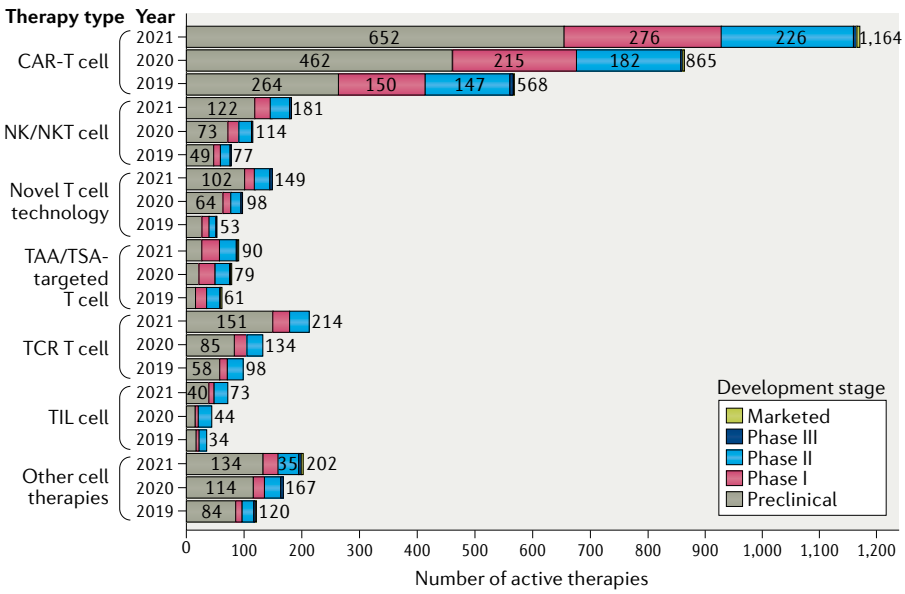

Fig. 1 | **Changes in the cancer cell therapy pipeline.** Comparison of cell therapy agent development pipeline across various therapy types from 2019 to 2021. NK, natural killer; TAA, tumour-associated antigen; TCR, T cell receptor; TIL, tumour-infiltrating lymphocyte; TSA, tumour-specific antigen.

Cell therapy trial landscape

According to data pulled from ClinicalTrials.gov, as of April 2021 there are 1,358 active cell therapy trials; this represents an increase of 43% from 2020 to 2021, compared with a 24% increase from 2019 to 2020 (Supplementary Fig. 4). Most of that growth has been due to CAR-T cell clinical trials (which have increased 83% since our 2019 update) along with more trials testing 'other cell therapies', TCR T cells, and tumour-infiltrating lymphocytes. The number of trials testing NK/NKT cells dropped off and has not fully recovered. Similar to previous years, most trials are focusing on haematological malignancies, and 40% of trials are for solid tumours (Supplementary Fig. 5), most of which are in early stages. This is probably a reflection of the inherent challenges of using cell therapies for solid tumours. Some examples from early-phase clinical readouts of recent data outputs are promising (Supplementary Table 1).

We also researched which sites are handling most of the trials. We found that all the top hospitals and universities conducting cell therapy trials are located in the United States (FIG. 3), indicating that, despite a global interest in cell therapies, the United States remains the leader in trial administration.

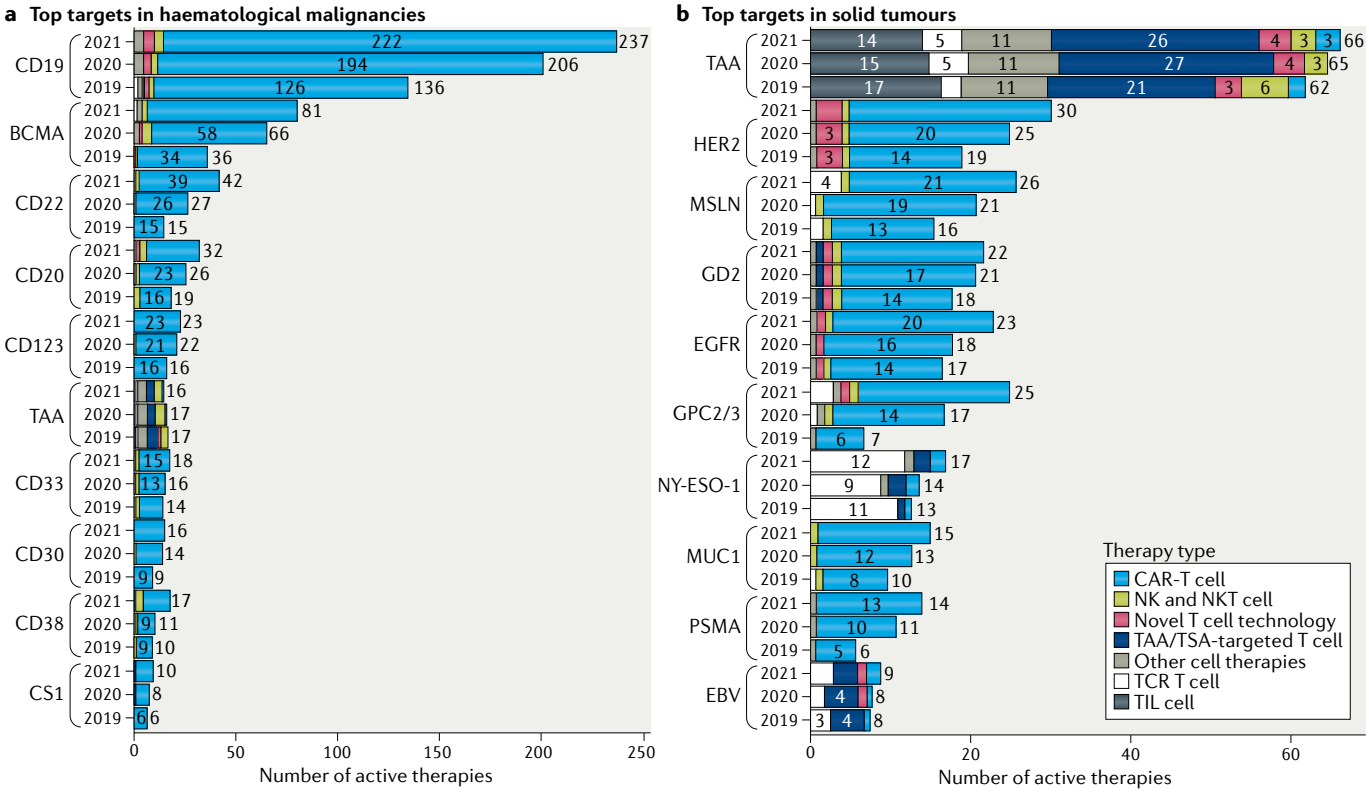

Fig. 2 | **Top targets of cell therapies for blood and solid tumours.** Targets in haematological malignancies (part **a**) and targets in solid tumours (part **b**). NK, natural killer; TAA, tumour-associated antigen; TCR, T cell receptor; TIL, tumour-infiltrating lymphocyte; TSA, tumour-specific antigen.

Global development pipeline

The United States and China continue to dominate the cell therapy development pipeline with a total of 791 and 695 agents in each region, respectively (Supplementary Fig. 6). The cumulative number of cell therapies in development increased by 31% in the United States and 40% in China versus an increase of 40% and 69%, respectively, from 2019 to 2020, consistent with an overall reduced spike in the number of agents (from 48% to 38% as previously mentioned). The distribution of cell therapy assets among academic institutions and industry in the United States and China remains largely the same to the previous year: most agents (83%) in the United States are being developed in industry, whereas in China the split is more even (60% industry and 40% academic).

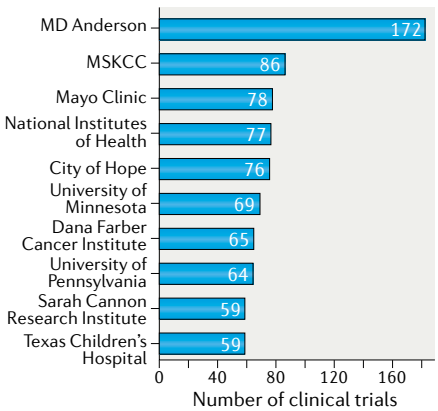

Fig. 3 | **Top 10 cell therapy development sites.** The United States remains the leader in trial administration. MSKCC, Memorial Sloan Kettering Cancer Centre.

CAR-T cell real-world data

We used a IQVIA proprietary database containing US medical and prescription claims to assess the number of patients receiving CAR-T cells in clinical practice based on CPT and ICD-10 codes (Supplementary Fig. 7). We noted a marked decline in the number of patients receiving CAR-T cells during the months of March and April 2020, which coincided with the first wave of the COVID-19 pandemic in the United States. This may have reflected instability in the health-care system during the initial wave of COVID-19, a decline in the use of more elective therapies, a decrease in availability of staff and resources to support CAR-T cell-related procedures, and an unwillingness of both patients and medical staff to expose patients with refractory disease to a potentially high-risk hospital environment.

Conclusions

Our current analyses indicate that the clinical development of cellular therapies continues, albeit at a slower pace compared to previous years. Whereas cell therapy clinical trials are accruing, real-world data show that there was a decrease in the number of patients in clinical practice receiving cell therapies, especially during the height of the pandemic in 2020. With stabilization of COVID-19 cases and the evolution of the clinical, social and economic landscape, we are seeing an upturn in the number of cell therapy trials being launched. Given continued improvements in managing COVID-19 and ongoing innovation in the field of oncology cell therapy, the promise of cell therapy remains.

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

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