FROM THE ANALYST'S COUCH

The global pipeline of cell therapies for cancer

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The recent FDA approvals of pioneering cell therapies to treat CD19-positive haematological cancers have encouraged substantial R&D efforts with cell therapies in oncology. Indeed, cell therapies now represent the largest number of active agents in development in the immuno-oncology field overall (*Nat. Rev. Drug Discov.* **17**, 783–784; 2018). In this article, we describe the latest development pipeline of cell therapies for cancer and the number of clinical trials for such agents, and we also compare the current landscape survey conducted in March 2019 with our previous one performed in March 2018 (*Nat. Rev. Drug Discov.* **17**, 465–466; 2018).

Trends in the cell therapy landscape

Cancer cell therapy platforms and targets. The global cell therapy pipeline includes 1,011 active agents, 258 more than a year ago. Among the different cell therapy types, the number of chimeric antigen receptor (CAR)-T cell therapies has grown substantially more than the others

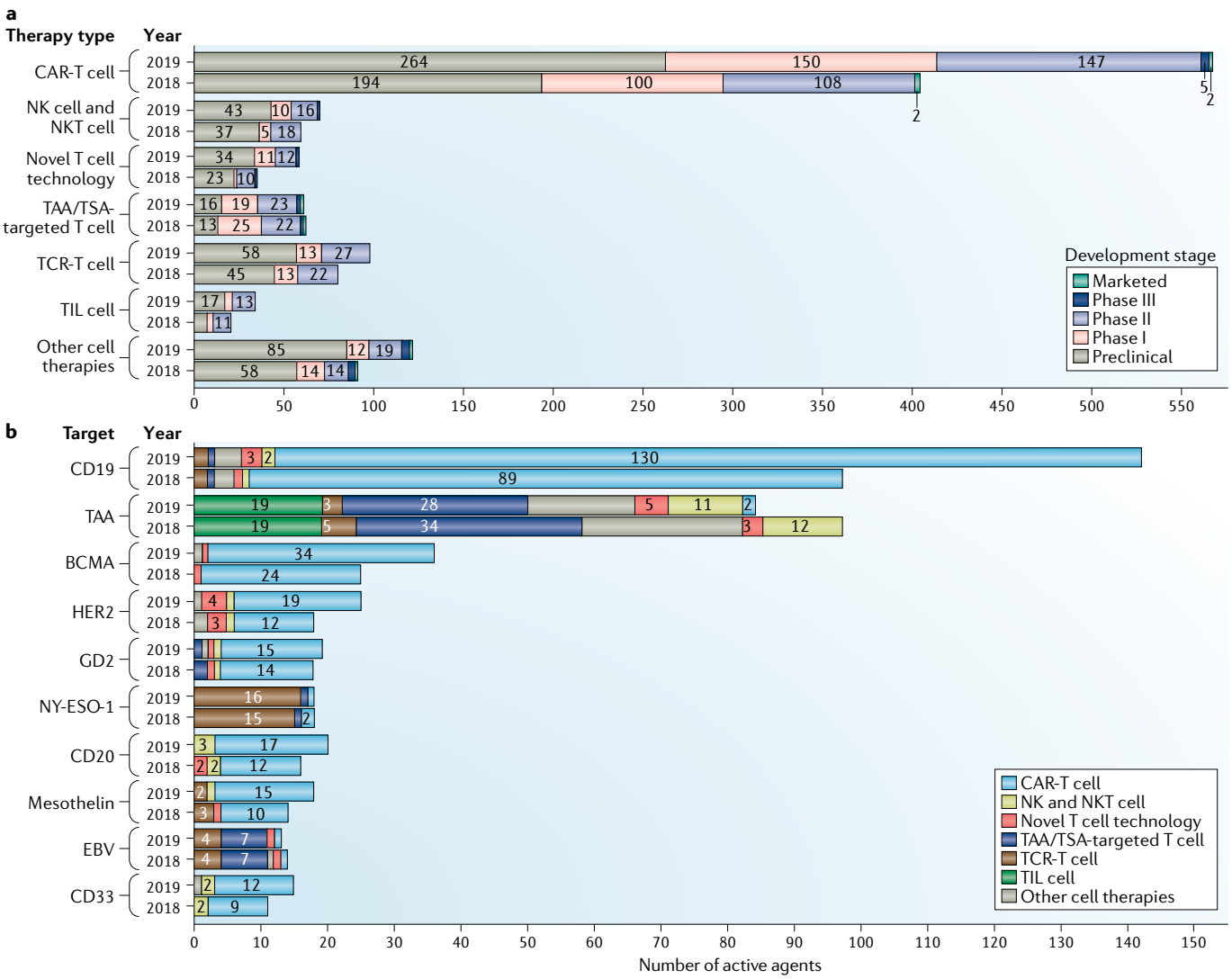

Fig. 1 | **Trends in the cancer cell therapy pipeline.** The figure compares the characteristics of the pipeline of 1,011 active agents in March 2019 with that of 753 agents in March 2018, categorized by the type of platform (part **a**) and the top 10 targets (part **b**). In 2019, a total of 134 targets are being pursued, 20 more than in 2018. TAA, tumour-associated antigen; TSA, tumour-specific antigen. For details, see Supplementary Information and the dashboard in Related links. Sources: Cancer Research Institute IO analytics, ClinicalTrials.gov and GlobalData.

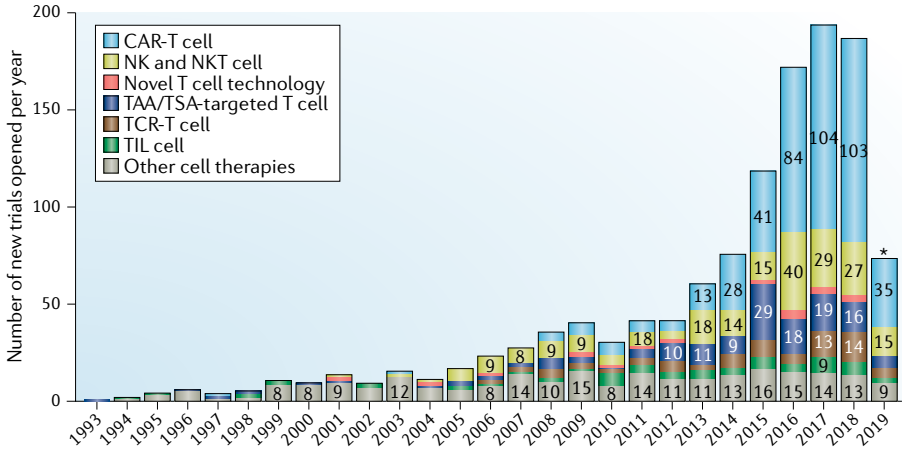

Fig. 2 | **The evolution of cell therapy trials for cancer since 1993.** Both currently active and inactive trials are included for this analysis, which is based on data extracted from ClinicalTrials.gov in March 2019, and so the data for this year is incomplete, indicated by an asterisk.

to a total of 568 agents, an increase of 164 agents (FIG. 1a).

CD19 continues to be the most popular target, with 142 active agents, including 130 CAR-T cell therapies. B cell maturation agent — the second most popular defined target, with 36 active agents — has gained 11 new agents (FIG. 1b), indicating increasing interest that has probably been driven by the promising clinical results released by multiple organizations recently.

Geographic distribution of the pipeline. As in our previous report, the United States and China hold the leading positions in the global cancer cell therapy pipeline, contributing 439 and 305 agents respectively, together constituting 74% of all agents (Supplementary Fig. 1).

The majority of agents being developed in the United States are at the preclinical stage (63%; 277 agents), whereas the majority of agents being developed in China are in clinical stages (77%; 236 agents) (Supplementary Fig. 2). Of the 26 novel targets for preclinical cell therapies added to the global pipeline in the past year, 15 new targets are for agents being developed in the United States compared with 3 from China.

Interestingly, 47% of cell therapies being developed in China are owned by companies, compared with 38% a year ago, indicating growth of the cell therapy industry in China in the past year (Supplementary Fig. 3).

Clinical trial landscape for cancer cell therapies. Using the ClinicalTrials.gov database, we identified 1,216 clinical trials that have so far been initiated to test cancer cell therapies from 1993 to March 2019. These data show that there has been a substantial growth of new trials each year in the past decade, largely owing to the explosion of trials for CAR-T therapies (FIG. 2).

The past year (March 2018–March 2019) saw an increase of 96 active trials to give a total of 762 active studies, with studies evaluating CAR-T cell therapies continuing to dominate, with 364 studies ongoing in March 2019 (Supplementary Fig. 4). The data also show that 188 new trials were opened in the past year, while 92 trials became inactive, indicating how dynamic this area is. Among the targets being evaluated in the clinical trials analysed, CD19 is the most popular (Supplementary Fig. 5), as in the pipeline overall (FIG. 1b).

Cell therapies for solid tumours. Although ~90% of cancer incidences globally are caused by solid tumours, only around half of all cell therapy trials that have been initiated since 1993 (596 out of 1,203 trials) have targeted solid tumours (Supplementary Fig. 6). In addition, the majority of cell therapy trials for solid tumours focus on a handful of tumour types —such as melanoma (79 trials), cancer of the brain and central nervous system (75 trials) and liver cancer (57 trials) — and many solid tumour types do not have any dedicated cell therapy trials ongoing (Supplementary Table 1).

These trends underline the greater challenges for cell therapy to tackle such malignancies compared with haematological cancers. Addressing these extra difficulties, which include high antigen heterogeneity, a strong immunosuppressive microenvironment and a dense extracellular matrix, may require the combination of cell therapy with other immuno-oncology agents or cancer drugs such as checkpoint inhibitors, which are being pursued in many ongoing trials. Different types of cell therapy beyond CAR-T cells may also offer opportunities to address some challenges. Indeed, although trials for CAR-T therapies account for more than half of all trials for haematological malignancies, cell therapy trials for solid tumours have fairly equal distribution among CAR-T and other platforms such as NK cells (Supplementary Fig. 6).

Finally, among the active preclinical cell therapies, 242 are designed specifically for solid tumours, compared with 172 for haematological cancers, suggesting booming interest in solid tumours within the cell therapy community (Supplementary Fig. 7).

Conclusion

The cell therapy class now has the largest number of active agents and the second largest number of active trials (after checkpoint inhibitors) in the immuno-oncology space. The progress in the past year suggests that the enthusiasm continues, exemplified by more therapies in the pipeline, more targets being explored, more trials opened and more patients being enrolled in trials. These efforts set the foundation for clinical breakthrough to benefit patients with cancer in the near future.

However, duplication has been on the rise, such as the increase in CD19-targeted CAR-T cell therapies and trials testing certain arguably redundant therapies. Consequently, channelling more efforts to targets other than CD19, to cell therapies beyond CAR-T therapies, and to the integration of new technologies such as CRISPR-edited cell therapies and induced pluripotent stem cells into next-generation cell therapies, may lead to greater progress. In addition, agents for targeting solid tumours have been under-represented in clinical trials compared with those targeting haematological cancers, despite the overwhelming burden of solid tumours on cancer patients. It is hoped that treating solid tumours with combinations of innovative cell therapies and other cancer drugs such as checkpoint inhibitors may offer a solution to the greatest challenge in cancer care.

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Competing interests
The authors declare no competing interests.

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