nature reviews drug discovery

https://doi.org/10.1038/d41573-025-00085-z

Supplementary information

The race to reset autoimmune diseases

In the format provided by the authors and unedited

Database assembly and analysis

We compiled a comprehensive database of 380 unique clinical trials across only clinical development (phase I, II, III and IV), excluding all research, preclinical and marketed assets, that have the potential to reset the immune response, as of March 2025.

Core source. The comprehensive list of clinical trials in the database was compiled across various sources. The initial set of clinical trials across all modalities was compiled by using a list of relevant assets from PharmaProjects. The PharmaProjects database was filtered based on several keywords, such as "CD19", "CD20", "CD22" and "CD38" for the target, and "autologous", "bispecific" and "trispecific" for the modality (not exhaustive). The different filtered lists of PharmaProjects assets were compiled and a comprehensive list of unique assets was created. This list was then manually checked to see if any of the assets have ongoing/future clinical trials for autoimmune indications. To ensure the PharmaProjects scan was exhaustive, the analysis was supplemented with detailed press searches and literature reviews, searching for autologous and allogeneic assets that have the potential to reset the immune response as well as those that target CD19/CD20/CD22/CD38. The final list of assets was de-duplicated across the various sources to ensure a comprehensive, unique list. Once both cell therapy and antibody assets were determined, unique clinical trials for autoimmune indications were manually pulled from ClinicalTrials.gov. Only assets that are considered to be "Active, not recruiting", "Recruiting", or "Not yet recruiting" were included.

It should also be noted that within this clinical landscape, there are several clinical trials that originate from basket trials. For the purpose of this analysis, each basket trial was considered as an individual trial in this analysis – one for each unique autoimmune indication. For example, BMS's CC-97540, an auto CAR T asset, has a phase I clinical trial (NCT05869955) for 3 autoimmune indications: SLE, IIM, and SSc. In our database, each of these indications represent a unique trial, so the same NCT05869955 is considered 3 times.

Validation. The resulting database was manually cross-checked against company websites and press searches. 98% of clinical trials presented in this database have a ClinicalTrials.gov ID associated with it. There are 8 (~2% of the database) clinical trials that can be found on company websites but not found on ClinicalTrials.gov. To ensure a comprehensive database, these trials were still included, especially since they are phase I onwards and not yet discontinued, according to company websites. In order to verify that the current list is up to date, only trials that were last updated since 2020 were included. For trials found on ClinicalTrials.gov, this is indicated by their "Last Update" date being 2020+. For trials found on company websites, their last update is based on any information presented on the website, and if not, assumed to be within the past 5 years, assuming that the websites are up to date with active/recent clinical trials. While these clinical trials were last updated in March 2025, coverage of trials from this database may not be representative of the current landscape (for example, current trials could become completed, terminated, withdrawn, etc.) upon manuscript publication.

Modality. The clinical trials presented in this landscape are categorized into 10 different modality categories. The CAR T clinical trials can be split up into: Allo CAR T and Auto CAR T. Within Allogeneic, there are 3 categories: "Allo CAR NK", "Allo CAR T", and "Other allo". Within Autologous, there are also 3 categories: "Auto CAR T", "Auto CAR Treg", and "Other auto". These categories were determined by volume of trials (please note the database has a larger number of modalities that were categorized in 'other' (e.g., allo Treg). Within antibody clinical trials, the three categories are"

mAbs", "Bispecific", and "Trispecific". Any other clinical trials that do not fit within these categories are placed into the "Other non-cell" category.

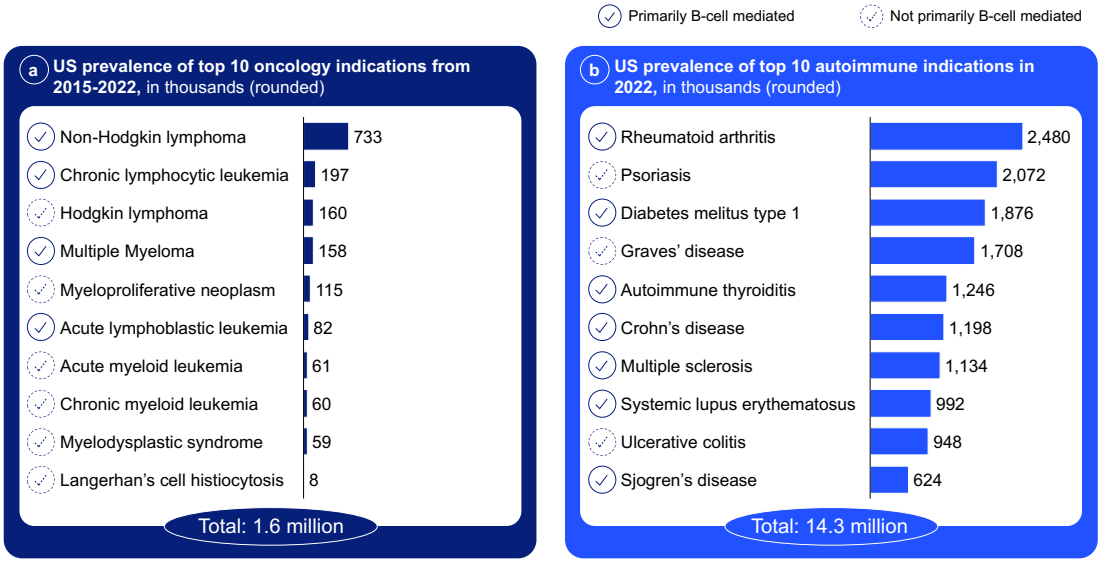
Stage of development. Only clinical assets are included in this landscape. These clinical assets have been categorized into three groups: Early development, Late development, and phase IV. "Early development" includes phase I and phase I/II trials. "Late development" includes phase II, phase II, and phase II/III trials. Research, preclinical and observational trials were not included in this database.

Indication. All clinical assets included in this database have one or more clinical trials associated with an autoimmune indication. Assets with clinical trials for autoimmune and another indication were still counted; however, it should be clearly noted that only the autoimmune indications were included in the database, each as unique trials. For trials on ClinicalTrials.gov, indications were taken from what was listed under "Conditions". For trials pulled from company websites (and not ClinicalTrials.gov), indications on the company website were considered. Some indications, such as multiple sclerosis, include all different forms (for example, relapsing/remitting, primary progressive). Any autoimmune indication that was classified as general or unspecified was labeled as "Undisclosed autoimmune disease".

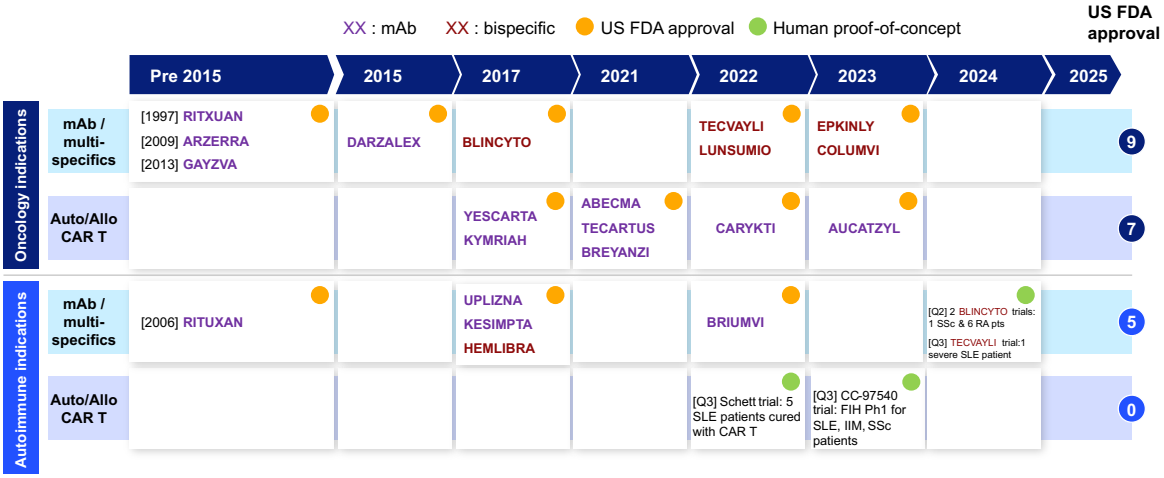
Target. For all clinical assets, the target was manually determined and confirmed based on inspection of "Mechanism of Action" or "Target" fields found on ClincalTrials.gov, company websites, and/or press releases. The Top 5 most common targets were presented in the main text (CD20, CD19, CD38, CD19/BCMA, CD19/CD20). All other targets were considered individually in the database and were put into the "Other" category as part of the final Figure 1.

Sponsor type. Each clinical trial included in this database has a sponsor, which is affiliated with a company from industry or an AMC. Sponsor information can be found on ClinicalTrials.gov, under "Sponsor". For those trials with no direct ClinicalTrials.gov link, the company the asset is affiliated with is assumed to be the sponsor. Each sponsor is manually categorized into one of the three categories: Pharma, Biotech, or AMC. For industry sponsors, whether a company is "Pharma" or "Biotech" was determined by manually checking company websites and cross-checking with press searches. Sponsors are categorized as "AMC" if the sponsor is an independent researcher and/or is affiliated with a university/teaching hospital.

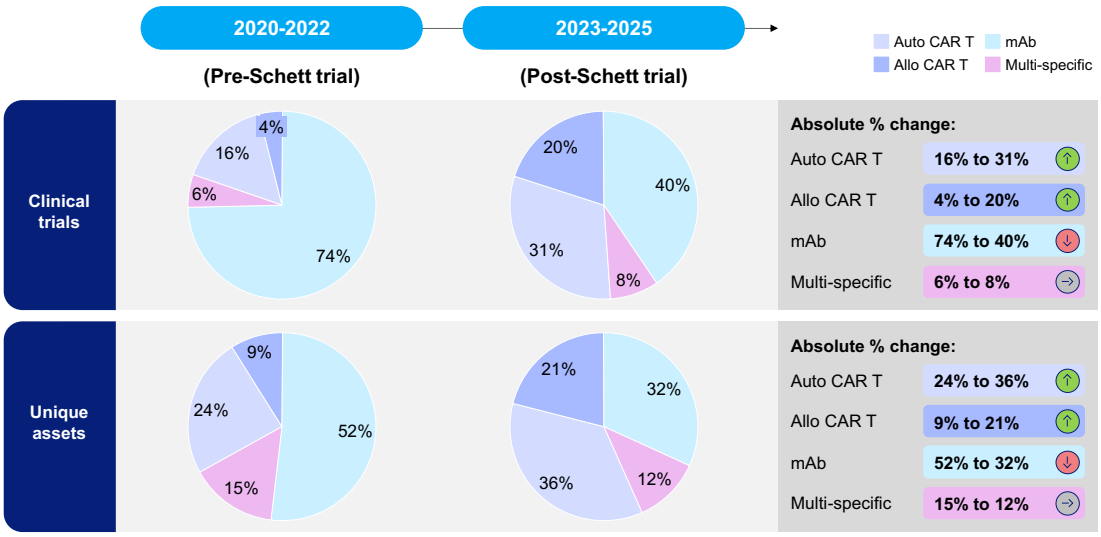
Sponsor geography. After obtaining the sponsor information, sponsor geography was determined for each trial. For industry sponsors, the location of company headquarters was manually determined. For AMC sponsors, sponsor geography was determined by the location of their affiliated AMC. These locations were grouped into a total of 4 categories: "US", "China", "EU/UK", and "RoW". Any company headquarters not located in US, China or EU/UK were put into the "RoW" category.



Supplementary Figure 1 | **Comparison of the prevalence of autoimmune diseases and cancer in the US in 2022**. We assume that US prevalence estimates are valid measures that can be extrapolated to represent global prevalence.



Supplementary Figure 2 | **Timeline for modality development for oncology and autoimmune diseases.** mAb, monoclonal antibody.



Supplementary Figure 3 | **Modality split before and after the Schett et al. trial of CAR-T cell therapy for SLE in 2022.** There are a total of 342 trials and 84 unique assets from 2020–2025. The number of assets may not match 1:1 to the number of clinical trials, because some clinical trials are basket trials for the same asset, where each indication is considered as a unique trial. The asset count is unique across each modality for each timeframe, but not across modalities and timeframe.

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