MARKET ANALYSIS OF CAR-T CELL IMMUNOTHERAPY- 2021

Dissertation submitted to

The IIHMR University, Jaipur

For the partial fulfilment for the award of the degree of

Master's in Business Administration (MBA)

in

Hospital and Health Management

by

Pranchita Tiwari

Under of Supervision and Guidance of

Dr. S.D. Gupta

2021

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To whomsoever it may concern

DECLARATION BY STUDENT

I hereby declare that this dissertation titled "**Market Analysis of Car-T Cell Immunotherapy-2021"** is the bonafide record of my original research work. I declare that it has not been submitted to any other university or institution for the award of any degree or diploma. Information derived from the published or unpublished work of others has been duly acknowledged in the text.

Pranchita Tiwari
30.06.2021

CERTIFICATE

This is to certify that dissertation title "**Market Analysis of Car-T Cell Immunotherapy-2021"** is a record of the research work undertaken by Pranchita Tiwari in partial fulfillment of the requirements for the award of the degree of MBA (Hospital and Health Management) from the IIHMR University, Jaipur under my guidance and supervision and his/her approach to the research study has been sincere, scientific, and analytical.

Faculty Guide:
Dr. S.D Gupta
Chairman
IIHMR University, Jaipur
Date: 30.06.2021

School Dean:
Dr. Dhirendra Kumar
IIHMR University, Jaipur

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Abbreviations

CAR-T: **ALL:**	**Chimeric antigen receptor T**
ALL:	Acute Lymphoblastic Leukaemia
AML:	Acute Myeloid Leukaemia
DLBCL:	Diffuse Large B Cell Lymphoma
FL:	Follicular Lymphoma
CLL:	Chronic Lymphocytic Leukaemia
MM:	Multiple Myeloma
AI;	Artificial Intelligence
ML:	Machine Learning
R&D	Research and Development
PCNSL	Primary Central Nervous System Lymphoma
MCL	Mantle Cell Lymphoma
NHL	Non-Hodgkin Lymphoma
ACT:	Adoptive cell transfer therapy
TILs:	Tumor-infiltrating lymphocytes
TCR:	T cell Receptor
MHC:	Major histocompatibility complex
ITAM:	Immunoreceptor tyrosine-based activation motif
FDA:	Food and Drug Administration
TAA:	Tumor-associated antigen
B-ALL:	B cell acute lymphoblastic leukemia
CLL:	Chronic lymphocytic leukemia
B-NHL:	B cell non-Hodgkin's lymphoma
CRS:	Cytokine release syndrome
CRES:	CAR-T-related encephalopathy syndrome
TME:	Tumor microenvironment
scFv:	Single-chain antibody fragment.
Axi-cel	Axicabtagene Ciloleucel (Yescarta)
LY	Life years
QALY	Quality Adjusted Life Years.

MARKET ANALYSIS OF CAR-T CELL IMMUNOTHERAPY- 2021

1. Introduction

Comprehensive knowledge about the intricate association of the immune system and working of the tumor cells has delivered the enhanced development in the field of cancer treatment such as the reconstruction of host immunity, the application of immunity mediating cells against cancer-causing cells, eradicating immune cell debilitations against malignant antigens while leaving many supplemental turfs minimally uncovered. Over the years malignancies management has consolidated with surgery, radiotherapy, and chemotherapy but with the last few decades of focused therapies, the treatment field has accepted and surfaced the new targeted therapies as the standard regime for many cancers. Trastuzumab (Herceptin) and Imatinib (Gleevec) target specified drugs working against target cancer cells, primarily through molecular changes.[1] With the advancement in immunotherapy, an adjacent new regime in the sector of treatment of cancer expanded to the horizons of CAR-T immunotherapy.

Training immune cells against the tumor cells in in-vitro conditions with reinfusion in cancer patients or immunity mediated through self-antibodies as therapeutics has been an exceptional instance of immunotherapy against cancer.[234] Genetically engineered and reprogrammed immune cells are vital for easy recognition and destruction of natural, immunity surveillance escaping tumor cells. Various cell-based therapies are extensively researched by employing antibodies in immunotherapies,[3] exogenic stem cell replacement, and[5] immunotherapy with Chimeric Antigen Receptors (CARs)[6] Proteomics, genomics, transcriptomics, and cell-based assays better comprehension has stemmed in the exceptional expansion in the region of immunotherapy. However, further evaluation[7] is needed due to the apparent development of resistance in long tenure follow-ups.[89]

With the 21st century leveraging big data and modern technology, CAR-T is coming up as new advancement bound to change the field of cancer treatment, especially against

hematological malignancies. [10] T cells are immune cells which have a variety of functions in the fight against disease, including directly eliminating infected cells. CARs, or Chimeric Antigen Receptors, are in-vitro engineered and developed receptors that implant a monoclonal antibody's subjective specificity onto T cells, with retroviral carriers or vectors facilitating in sequence configuration transmission.[11] The receptors are called chimeric because they are constituted of sections from separate sources. 2017 landmarked with the first two "chimeric antigen receptor (CAR)T therapies" developed against CD19 antigens targeted approved by FDA.[12]

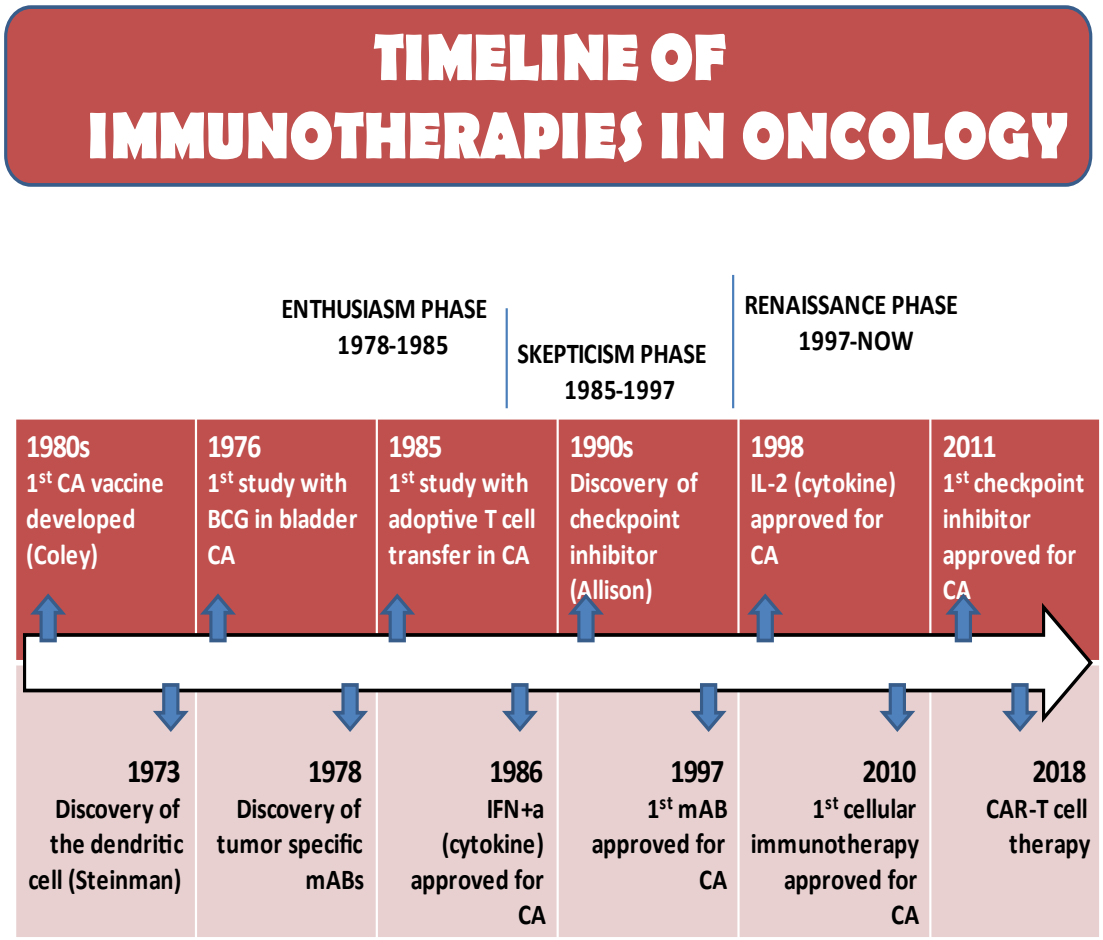
CAR-T cells are customized according to the T cells of the patient with a prolonged time of activity as well as some grave side effects. Kymriah (tisagenlecleucel) of Novartis is the first CAR-T immunotherapy to be approved by the FDA for non-Hodgkin lymphoma and relapsed/refractory ALL patients under the age of 25. Yescarta or axicabtagene ciloleucel by Kite Pharma/Gilead Sciences came second in the line of FDA approvals against indications like large B-cell lymphoma, (types like mediastinal and high-grade) and transmuted follicular lymphoma. Tescartus or brexycabtagene autoleucel was next indicated for patients of relapsed/refractory mantle cell lymphoma without any success in preceding treatments.[13] These treatments exhibited astonishing effectiveness in hematological malignancies and centered a standard replacement in cancer treatment therapy

The timeline in the below figure shows the concise innovation and development of immunotherapies from 1970s and aftermath. Chimeric antigen has seen a gradual yet steady growth over the decades with enthusiasm, scepticism and then renaissance of the immunotherapy. The next few decades could be equally significant and monumental in curing cancer.

CAR-T cell immunotherapy changes an individual's own T cell for easy recognition and direct attack on the cancer cells. T cells are extracted from the patient's blood and then the T cell is grafted with a specific gene to bind to the specific protein on the cancer cells of the patient. The position of cancers as incurable is likely to alter in the future as a result of CAR-T immunotherapy. CAR-T immunotherapy was first introduced in 1992 with primary T-cell engineering, followed by CD cell-based first and second-generation CARs in 1993 and 2002, respectively. After FDA approval of CD19 CAR treatment for paediatric ALL and NHL, CAR-T became more widely known. Yescarta and Kymriah are such technology that medically operates only when the patient has had at two unsuccessful attempts of different cancer therapies. The FDA has approved Yescarta for

relapsed or refractory large BCLand Kymriah for paediatric or young patients with B-cell acute lymphoblastic leukaemia.

Figure 1.1 Flowchart for Timeline of Immunotherapies in Oncology

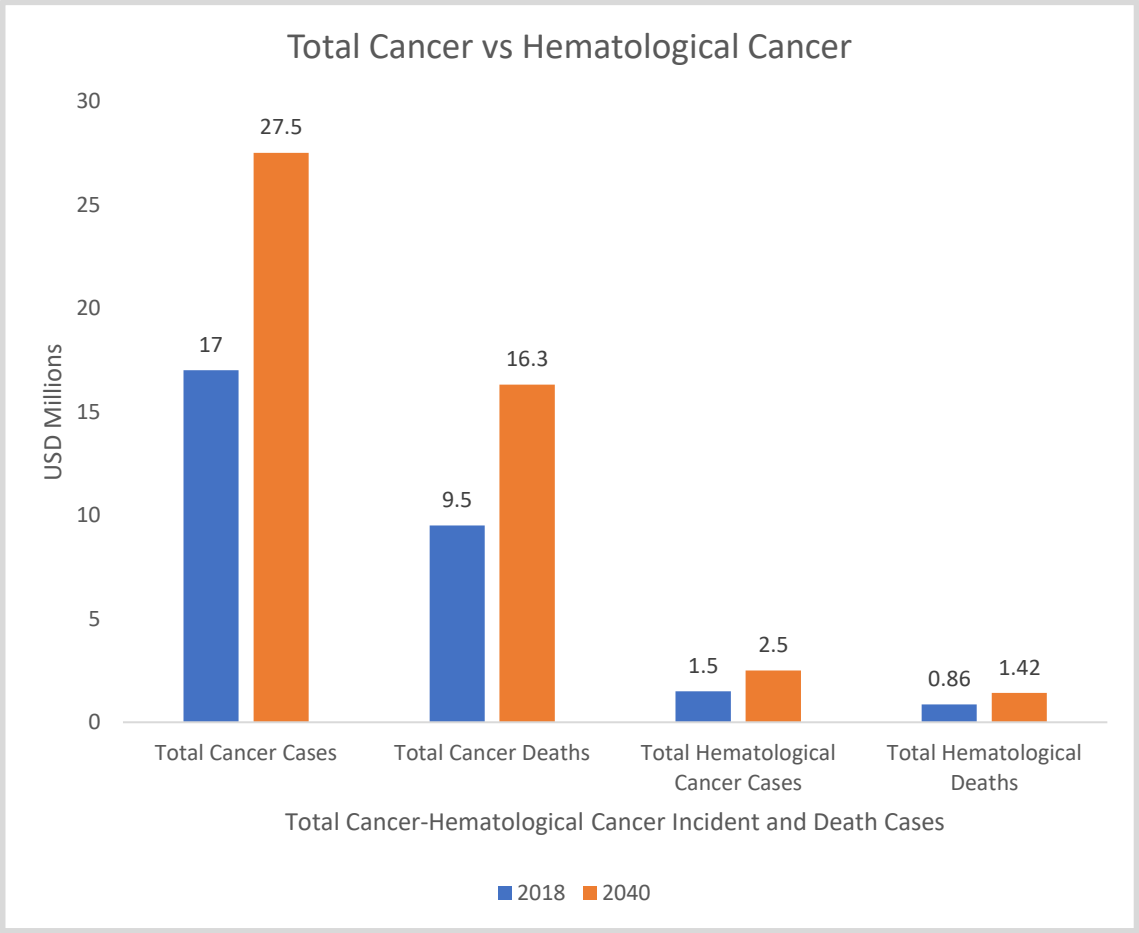


Better affordability would give more potential to CAR-T immunotherapy to reduce a significant amount of cancer disease burden. Other elements that could improve the therapy's accessibility and affordability comprise training and development of a skilled workforce, well-established infrastructure, and reduced manufacturing costs based on the unmet need. In 2018, there were 17 million cancer cases and 9.5 million cancer-related deaths globally, according to the "International Agency for Research on Cancer (IARC)."Hematologic malignancies account for 9% of all cancer incident cases, with 1.5 million novel cases detected each year.[14] The global cancer burden is expected to rise

to 27.5 million novel cases and 16.3 million cancer mortality by 2040. [15] Hence, the hematological malignancies would grow to rise 2.5 million approximately by the same period. Leukemia is projected to have a global incidence of 300,000 new cases per year, accounting for around 2.8% of the entire cancer cases. In 2017, the total number of cases was 64,2000. As a result, there is a substantial unmet demand for cost-effective medicines to meet the needs of the world's ageing and growing population, particularly in developing nations. The following chart elaborates the epidemiology of cancer and hematological malignancies.

With such innovations, CAR-T cell monoclonal immunotherapy also faces obstacles in the identification of exclusive antigens on the exterior facade of solid tumours. Mechanisms of the microenvironment that encompasses the solid tumours collude to dampen the immune response.

Figure 1.2 Global demographics of total and hematological cancer in 2018 and 2040



2. Rationale of the study

CAR-T immunotherapy is costly, with prices ranging from $30 million to $40 million. There will undoubtedly be pressure to save money on prescription expensive

pharmaceuticals due to the rising cost of ancillary care, which is up 11% equated to general drug price growth of 1.5 percent. CAR-T that is sourced domestically or indigenously can attempt to fill this deficit in healthcare services. With indigenous innovation and expert training, it is envisaged that costs would decline, enabling the potential to expand. The following topics are covered in this report:

- Current status of CAR-T innumotherapy-2021.
- Competitive landscape of CAR-T market across US.
- Regulatory changes in the CAR-T immunotherapy approval pathways and policies.
- Factors driving the growth of the market

3. Research Question

What are the key market trends for CAR-T immunotherapy in the second quarter of 2021, and how will the competition environment shift?

4. Research Objectives

- To analyze the current market scenario through reports in the second quarter of 2021 of CAR-T immunotherapy global market.
- To understand the competitive landscape associated with CAR-T immunotherapy.
- To comprehend the developments in CAR-T immunotherapy regulatory regimes.
- To learn about the market's drivers and obstacles.

5. Literature review

Research was conducted to study various clinical trials, secondary research, journal publication to describe the study, design of the research and salient features extracted from the research.

Table 1.1 Review of Literature

Author (year)	Study	Research Design	Salient features
Li, D., Li, X., Zhou, W., Huang, Y., Liang, X., Jiang, L., Yang, X., Sun, **(2019)**	Genetically engineered T cells for cancer immunotherapy	Descriptive study	It encapsulates the advancement of genetically engineered T cells, summarize the most current studies examining genetically engineered T cells for the treatment through cancer immunotherapy, and discuss strategies for improving the performance of these T cells in fighting cancers.
Philipp Vormittag, Rebecca Gunn, Sara Ghorashian, Farlan S Veraitch **(2018)**	A guide to manufacturing CAR T cell therapies	Descriptive study	The movement in CAR T cell engineering is towards mechanization. Customized off-the-shelf apparatus for CAR T cell production is essential.
Challice L Bonifant, Hollie J Jackson, Renier J Brentjens, Kevin J Curran **(2016)**	Toxicity and management in CAR T-cell therapy	Descriptive study	The utility of CAR T cells as ACT for the treatment of malignancy will depend both on the ability to easily manufacture the cellular product as well as the feasibility of safe administration
Sophia Stock, Michael	Optimizing Manufacturing	Descriptive study	Costs may be reduced through more efficient

Schmitt, Leopold Sellner (2019)	Protocols of Chimeric Antigen Receptor T Cells for Improved Anticancer Immunotherapy		production protocols. The potential of anticancer immunotherapy improvement by optimizing the ex vivo expansion conditions during the CART cell manufacturing process has not yet been fully exploited. Therefore, further efforts are mandatory for standardizing and optimizing CART cell production protocols.
Z. Ou (2019)	Pcn198 global regulatory challenges of car t-cell therapies: approval, pricing, and access	Descriptive study	CAR T generates an exceptional challenge for judgment makers. Additional novel regulatory structures are required to simplify transforming its principles to patients.
Miguel-AngelPerales Partow Kebriaei Leslie S.Kean, MichelSadelain (2018)	Building a Safer and Faster CAR: Seatbelts, Airbags, and CRISPR	Descriptive study	Cellular therapy has remarkable efficacy, even in highly chemotherapy-resistant tumors, with response rates up to 90% for patients with relapsed B cell ALL and greater than 60% for patients with relapsed NHL.

6. Study Design and Methodology

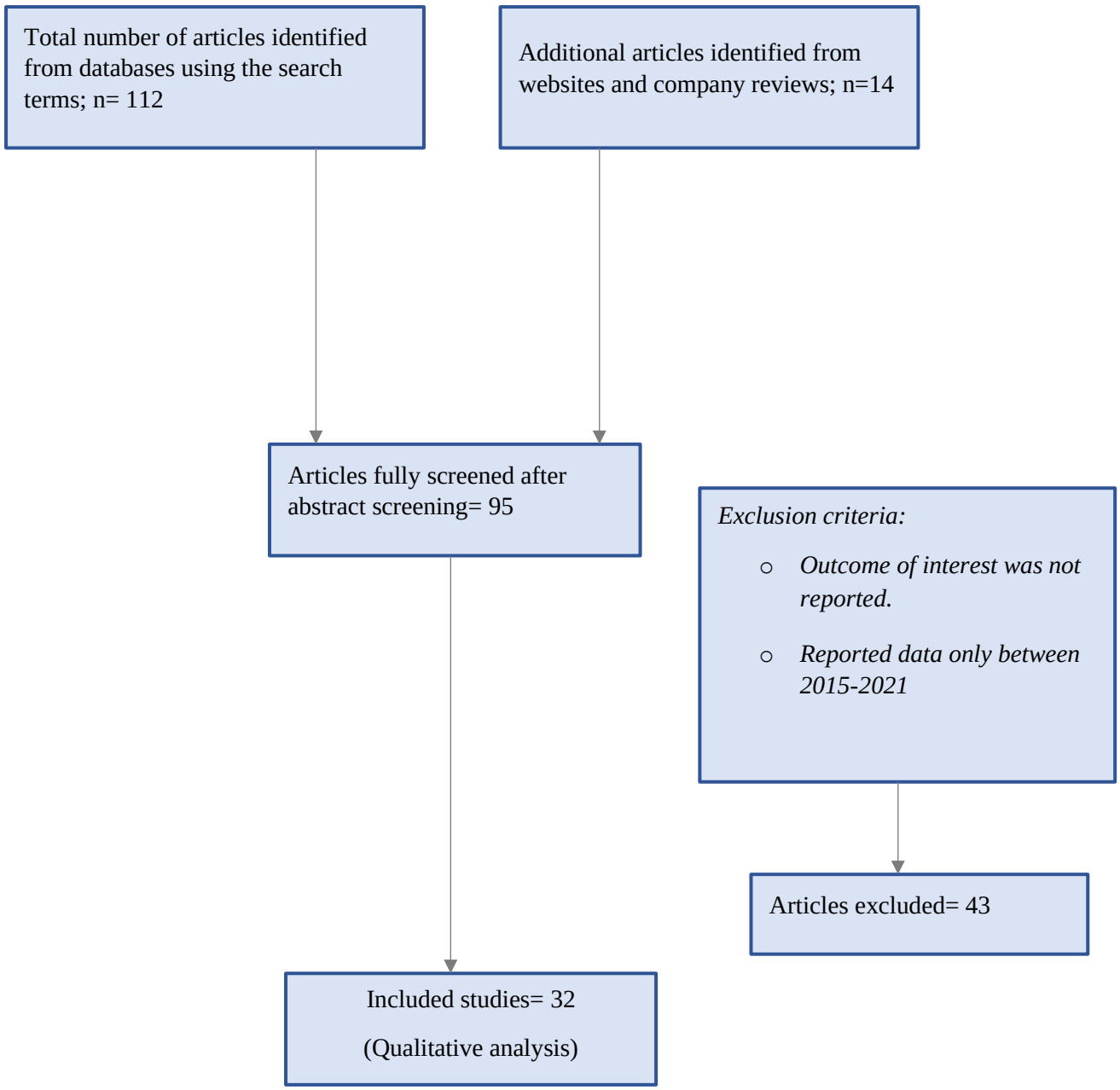
To critically evaluate the economic landscape concerning CAR-T immunotherapy, a review of research methods using numerous techniques, as well as prominent mainstream media pieces, was accomplished. A desk/secondary research will be conducted out, with the proposed technique being used to locate publications that are related to the research topics. On March 15th, 2021, the preliminary exploration began. On June 15th, 2020, the investigation came to a halt. The author used the following search terms and database-appropriate syntax to review the literature on the overview and market of CAR-T immunotherapy: “Google Scholar, PubMed/MEDLINE, were searched using the following search terms and database-appropriate syntax to review the literature on the overview and market of CAR-T immunotherapy”:

- ("CAR-T"[All Fields] OR "Chimeric Antigen Receptor therapy"[All Fields] OR " Recent hematological malignancies treatment recent "[Supplementary Concept] OR " CAR-T immunotherapy "[All Fields] OR "CAR-T"[All Fields] OR "India"[All Fields] OR "CAR-T"[All Fields] AND (“Market Analysis” [Title/Abstract]) AND CAR-T [Title/Abstract] OR market [Title/Abstract]) [Supplementary Concept])
- Market research study as a research design (Descriptive study)
- Surveys, analyst reports, and company websites are all good sources of secondary data.
- MS Excel is a good tool for data analysis.

CAR-T immunotherapy as an inclusion criterion
Criteria for exclusion: Other immunotherapies

The author pursued to explain with a non-systematic random, virtual, digital study for the estimated and evaluated market landscape CAR-T therapy. Market analysis was also accomplished with evaluating the opportunities and obstacles in Market of CAR-T immunotherapy.

Figure 5.1 Flowchart for literature search process



- **Data Collection Methods and Tools**

Secondary research resources comprised journals, product brochures, company websites, documents, corporate biographies, twelve-monthly reports, as well as widespread internet searches. This was carried out to discover numerous topics of proficiency and publications that could take the lead to market evaluations and estimates. Secondary

research and databases offered online were used to assemble information regarding significant clinical trials, mergers, deals, procurements, and innovative CAR-T drugs introduces that will have an influence on the industry.

7. Results

7.1 CAR-T Immunotherapy Overview

Specific cell-mediated immune response with persistent periods of cancer remission has been the distinctive tool used by CAR-T immunotherapy for the management of malignancies. The growing cancer burden with more than 19 million cases registered globally in 2020 easily portrayed the high unmet need for a better treatment regime.

The global incidence is estimated to further increase with a rate of 70% till 2040. Conventional treatment option accredited for 50% mortality and a failure rate of approximately 90%. All these factors further amplified the need and ascribed with the various contributory influences necessary for the research and development of CAR-T immunotherapy.

CAR-T immunotherapy is highly specific, customized, and aggressive technology targeted to distinguish and attack tumour cells. With abridged hazard of treatment refusal and graft versus host the indication would bring an updated safety profile to the cancer treatment regime. Programmed cells create and augment the immune memory against tumour cells strengthening the potential long-term interests. Despite the fact that immunotherapies are still in the research phase, numerous clinical trials and studies have confirmed the therapeutic efficacy, superiority, and tolerability of CAR-T technology that has the potential.

Globally more than 750 candidates are in clinical trials for drugs that are in either clinical development or preclinical stages. 62% cover the clinical phases of the development while preclinical stages have 38% of the total candidates. The pharmaceutical industry saw more than 220 deals in the time period of 2011-2020 pertaining to upliftment the research field of CAR-T immunotherapy. The market's robust expansion across several territories was exhibited by a CAGR of more than 28 percent. All of these concepts, which have demonstrated likely outcomes in clinical and preclinical trials. It is estimated to account for a considerable fraction of the multibillion-dollar cancer management and

therapy market. This is further consolidated with the greater volume of allied chatter on Twitter and corroborated by distinguished representatives from research groups, eminent companies, and industry stakeholders proclaiming the confidence adjoining CAR-T immunotherapies market. After the approval of Yescarta and Kymriah, there was a more than 200% surge in the number of global tweets on Twitter in the time-period of 2016 and 2017.[16]

7.2 Mechanism of CAR-T immunotherapy

CAR-T therapy is represented by the collection of T-lymhocytes cells from the patient. The process used here is leukapheresis. Followed by laboratory processing with T cell stimulation. Later, before patient impregnation, transduction using a CAR-comprising viral vector and expansion of CAR-stating T cells were performed. As a result, Chimeric Antigen Receptors are made up of an antibody stemmed section that recognises tumour antigens combined with costimulatory particles that help T cells expand and stay in the body longer.

T cells are harvested with from the patient and genetically modified with newly introduced antigen receptors. Consequently, a Chimeric T cell is formulated with combined antibody specificity. ((Placeholder2). CAR-T therapies target haematological malignancies with the potential development in solid tumours. Dendritic cells mediated immunity in solid tumours are further supplemented by CAR-T cells with the expression of focussed antigen being CD40 ligand and claudin 6. Another potential target antigen CSPG4 can bring relief against melanoma, glioblastoma, and breast cancer. Other prospective lymphocytes that need more research would be CIK cells, NK, NKT, and γδ T cells. Research also portrays possible effectiveness against viral infections like HBV.[17]

The anti-tumour effectiveness of indigenous T cells and modified CAR-T cells is further impeded by the inhibitory regulation of particular intracellular proteins and extracellular receptors, that has an inhibitory immune response. High levels of Reactive Oxygen Species accelerators in the microenvironment of the tumours are responsible for the sensitization of tumour cells to CAR-T cell therapy. Apparently in-vitro laboratory settings showed successful results against leukaemia and lymphoma with potentials in patient settings.[18]

In vitro settings showcased results with novel targets marking ovarian cancer cells.[19] The engineering of optimized CAR-T cells and their expansion in the patient plays a vital role

in the therapeutic success of the technology.[20] Strategies revising ecto and endo spheres of CARs with multi-level targeting is the way forward for improving the efficacy of the therapy.[21] Nanobody technology regime is another advancement that aids the clinical treatment against malignancies.[22]

7.3 Therapies in detail

In August 2017, the FDA authorised Kymriah for the treatment of relapsed or refractory (R/R) B cell ALL in patients under the age of 25. Within three months of being impregnated with CAR-T immunotherapy, 83 percent of clinical patients showed complete remission or incomplete blood count recovery. The FDA is now reviewing Kymriah for adults in the treatment of R/R DLBL. It is also being evaluated in Europe for all of the above indications. FL (follicular lymphoma), multiple myeloma (MM), CLL (chronic lymphocytic leukaemia), and second-line DLBCL are among the additional indications being investigated.

Yescarta was approved by the Food and Drug Administration in October 2017 for adult R/R BCL, which includes DLBL and other severe non-Hodgkin lymphomas (NHL). It is still being debated in Europe. Yescarta exhibited a CR rate of 58 percent with an overall response rate (ORR) of 82 percent in clinical studies.

The FDA approved both drugs as part of a limited programme that included a risk assessment abatement technique to address major side effects like neurotoxicity and cytokine release syndrome (CRS) CAR-T still requires more clinical trials and research in order to establish long-term safety and the danger of subsequent cancers.

- **Approved drugs**

An initial start of five drugs approved by FDA enlists breakthrough technology indicated for multiple diseases. Abecma, also known as idecabtagene vicleucel, has been certified for MM patients who have had “more than or equal to four prior lines of therapy, including an immune regulatory prescription, a proteasome inhibitor, and a monoclonal antibody called anti d CD38. BREYANZI (lisocabtagene maraleucel), an FDA-certified CAR T-cell immunetherapy for adult patients with relapsed or refractory large B-cell lymphoma after two or more lines of systemic therapy, comprising:

- Diffuse large B cell lymphoma (DLBCL) not otherwise specified (including DLBCL arising from indolent lymphoma)

- High-grade B-cell lymphoma
- Primary mediastinal large B-cell lymphoma
- Follicular lymphoma grade 3B

For patients with relapsed or refractory mantle cell lymphoma, TECARTUS (brexucabtagene autoleucel) is an FDA-certified CAR T-cell treatment. KYMRIAH (tisagenlecleucel), an FDA-approved CAR T-cell therapy for: Adults with relapsed or refractory diffuse large B-cell lymphoma (DLBCL). Patients of age 25 or less with relapsed or refractory acute lymphoblastic leukemia (ALL)

YESCARTA was the first CAR T-cell immunotherapy passed by the FDA for people with a variety of characteristics of BCL. The US Food and Drug Administration has approved this therapy for patients who have one or more of the following requirements but have not progressed to or relapsed after more than two systemic treatments:

- FL
- DLBCL
- DLBCL that results from follicular lymphoma.
- High grade BCL
- Primary mediastinal B-cell lymphoma

Clinical patients will experience a widespread assessment to establish their suitability for this exceedingly focused treatment. With a paradigm shift in the therapeutic regime against cancer, the pipeline for CAR-T is rapidly expanding for better safety, novel target antigens and lesser risk. JCAR017 of Juno Therapeutics has a favorable efficacy with CR of 68% and ORR of 74% and manageable safety of 1% CRS and 14% neurotoxicity. Therefore, it can be a potential competitor for Kymriah and Yescarta, specific to the same indications. Off the shelf forms of CAR-T from Celletics/Pfizer (UCART19).

7.4 Pipeline Drugs

CAR-T therapy for solid tumours has numerous obstacles, including an essentially impermeable stroma, an immunosuppressive tumour microenvironment, and antigen heterogeneity. Although there is limited evidence to support CAR-T in solid tumours, more research is needed.

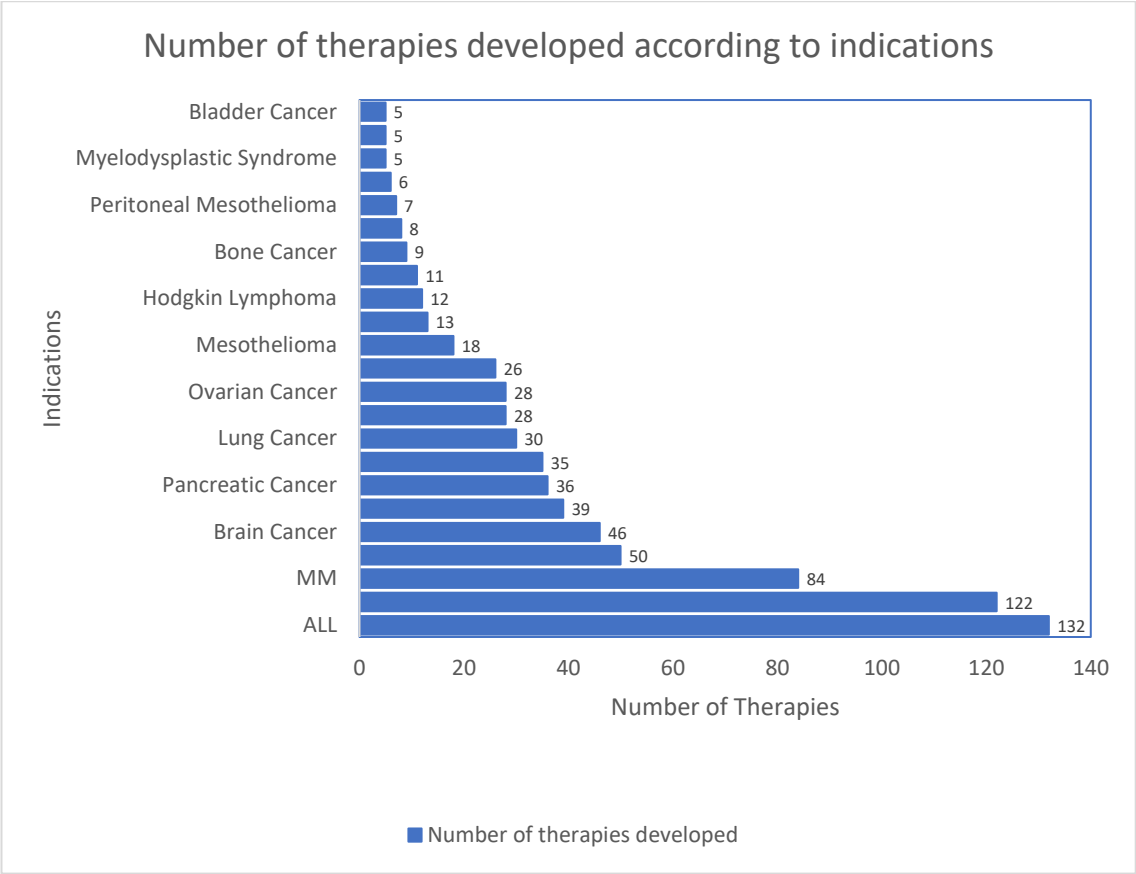
The pipeline has multiple projects developing in various indications and the distribution can be displayed in the following table:

Table 7.4.2 Summary of the number of therapies in different disease

Disease Indication	Disease	Number of therapies developed
Hematological Cancers	ALL	132
Hematological Cancers	NHL	122
Hematological Cancers	MM	84
Hematological Cancers	AML	50
Solid Tumour	Brain Cancer	46
Hematological Cancers	CLL	39
Solid Tumour	Pancreatic Cancer	36
Solid Tumour	Liver Cancer	35
Solid Tumour	Lung Cancer	30
Solid Tumour	Stomach Cancer	28
Solid Tumour	Ovarian Cancer	28
Solid Tumour	Breast Cancer	26
Hematological Cancers	Mesothelioma	18
Solid Tumour	Colon Cancer	13
Hematological Cancers	Hodgkin Lymphoma	12
Hematological Cancers	Sarcoma	11
Solid Tumour	Bone Cancer	9
Hematological Cancers	Melanoma	8
Hematological Cancers	Peritoneal Mesothelioma	7
Hematological Cancers	Esophageal Cancer	6
Hematological Cancers	Myelodysplastic Syndrome	5
Solid Tumour	Head and neck Cancer	5
Solid Tumour	Bladder Cancer	5

Source: Biomedtracker as accessed on 10th June 2021

Figure 7.4.3 Number of therapies developed according to indications.



With rewarding financial assistance and a noteworthy increase in alliances, the CAR-T cell therapies are throbbing with pursuit. Recent development in the pharmaceutical industry saw a range of partnerships that further esteem the trend of growth of the therapy. R&D agreements account for 21% of the recent advancement while technology licensing account for 20% as well. 11% showed development and commercialization partnerships with 7% manufacturing agreements rising in the queue. Acquisitions, product licensing, and clinical trial collaboration with product development also account for 26% of the total share. Joint venture and supply chain management of the product account for 15% of the total market share.

7.5 Approaches in CAR-T immunotherapy

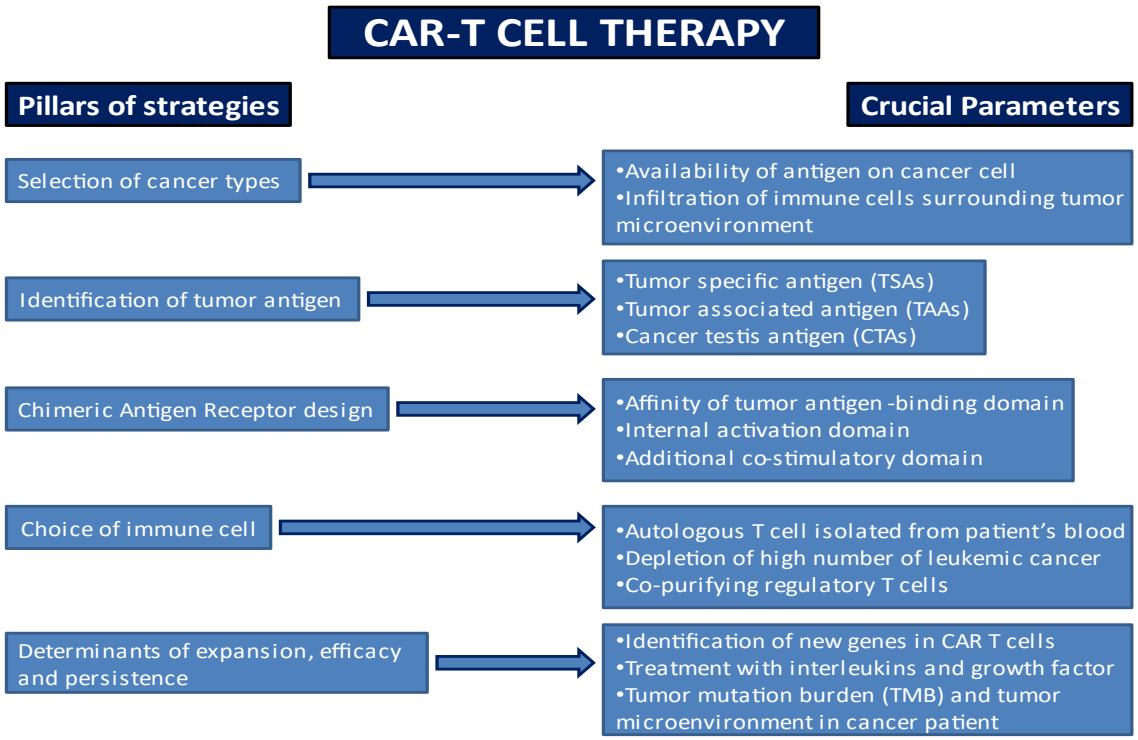
Approaches in CAR-T cell therapy has been curated with prudent considerations of the essential factors such as the assortment of cancers for its optimal action, detection of suitable tumour antigen, selective picking up of gene paradigms to enterprise chimeric receptors, recognition and programming of the immune cells with receptors against tumor antigen, determination of factors of impacting the affinity of chimeric receptors for antigens, determination of growth developers and toxicities associated with CAR-T cells.

Crucial factors to be exploited include actual time cellular assay and subsequent generation sequencing thus improving the behavior of the immunotherapy. Oppressive or pervasive is the two-mode of action for the engineered cells. With more success against hematological malignancies, solid tumours are yet to be explored as an indication for CAR-T therapy.[8] The tumour microenvironment causing immune suppression and physical barriers are few factors that prevent the anti-CAR-T cells from penetrating the solid tumours.[8] CD19 is the not a specific but most effective tumour-associated antigen (TAAs) in solid tumours[23]. Others being CD20, CD22 or CD19 and CD22, CD 30" are sculpting opportunities for the betterment of the treatment regime.[24]

With an increase, the cost-effectiveness , UniCAR (Universal CAR) and UniT-Cell (Univeral T-cell) surfaced as a resolution.[25] This technique abolishes the steps involving the patient but extracting T cells from healthy donors.[26] The allogeneic transplant also eradicates immunologic response by genetic disruption of the TCR gene.T cells seemed most apt due to the intrinsic property of proliferation, memory, persistence, efficacy, and cytotoxicity of the cells.[27]

These factors have been equally important for other T cell subtypes used in the same therapy[28]. As summarised in the figure, different approaches are enlisted.

Figure 7.5.4 Pillar of CAR-T immunotherapy and crucial parameters



7.5 Market Analysis

7.5.1 Current market analysis of CAR-T cell immunotherapies in the second quarter of 2021

In 2019, CAR-T immunotherapy reached a global market value of $734.0 million with an estimated growth rate of 32.3% and would reach $2250 million in 2023. The increasing number of prevalent cancer cases and awareness about the therapy would further skyrocket the market to $3150 million and $6100 million in 2025 and 2030, individually[29]. . An increase in the incidence rate of haematological malignancies, an increase in government healthcare spending, a competitive pipeline of drugs, and a growing focus on CAR-T immunotherapy are expected to accelerate the market and its cost.

Large amounts of therapy, repayment disputes, unfavourable events, intricate fabrication, and supply chain with COVID-19 affecting clinical trials and a decline in unrestricted global business are the most important considerations that could legitimise the expansion of the forecasted CAR-T immunotherapy market. Coronavirus pandemic is certain to have chief influence with disruption in the sales of the market with the target population being exceedingly susceptible to viral infections, bed ridden and immunity repressed. Delays in clinical trials due to global lockdown halted manufacturing and supply chain with further restrictions can be a barrier in the growth rate. COVID-19 has led CAR-T therapy medication clinical trials to be delayed. Manufacture is also being disrupted due to the reason that intercontinental lockdown, which is generating supply chain concerns.

The historic surge can also be associated with greater expenditure on healthcare, pharmaceuticals, and research and development, as well as scientific advancements in drug discovery and development. Factors affected like low-cost drug approvals challenges regulatory modifications and a restricted number of therapies centres have an impact on the growth. The market segment includes various products, company developers, with targets and indications as indicated in the table below: The ones still in research and development are growing in number and efficacy as well.

Table 7.5.3 Summary of the number of therapies with targets and indications

Product	Developer (collaborator)	Target(s)	Indication(s)
Kymriah	Novartis AG	CD19	ALL DLBCL MM, CLL, FL, SLL MCL PCNSL
Tescartus	Kite/Gilead	CD19	MCL
CD19 CAR-T	Sheba International	BCMA	MM
UCD19 CAR-T	University of Colorado	CD19	AML
Breyanzi/Lisocabtagene Maraleucel/ JCAR017	Juno Therapeutics/Celgene	CD19	B cell NHL (DLBCL)
UCART19	Cellectis/Pfizer	CD19	B cell ALL
bb2121	Bluebird bio	BCMA	MM
LCAR-B38M	Nanjing Legend Biotech	BCMA	MM
KITE-585	Kite Pharma/Gilead Sciences	BCMA	MM
+AUTO2	Autolus	BCMA and TACI	MM
MB-102	Mustang Bio	CD123	AML and BPDCN
UCART123	Cellectis	CD123	AML and BPDCN
CD33-targeted CAR	Ziopharm Oncology (Intrexon)	CD33	AML
BPX601	Bellicum Pharmaceuticals	PSCA	Pancreatic cancer
JCAR020	Juno Therapeutics	MUC16	Ovarian cancer
CAR-EGFR/EGFRvIII T	CARsgen Therapeutics	EGFRvIII	Glioblastoma

MB-101	Mustang Bio	IL-13Rα2	Glioblastoma
JCAR023	Juno Therapeutics	L1CAM	Neuroblastoma
CAR CLD18 T cells	CARsgen Therapeutics	Claudin-18.1	Gastric/pancreatic adenocarcinoma
AU105	Aurora Biopharma	HER2 and CMV	Glioblastoma

Source: 13. [Internet]. Rootsanalysis.com. 2021 [cited 22 June 2021]. Available from: https://www.rootsanalysis.com/dashboard/uploads/create_links/CAR-T-Therapies-Market-Development-Pipeline.PNG

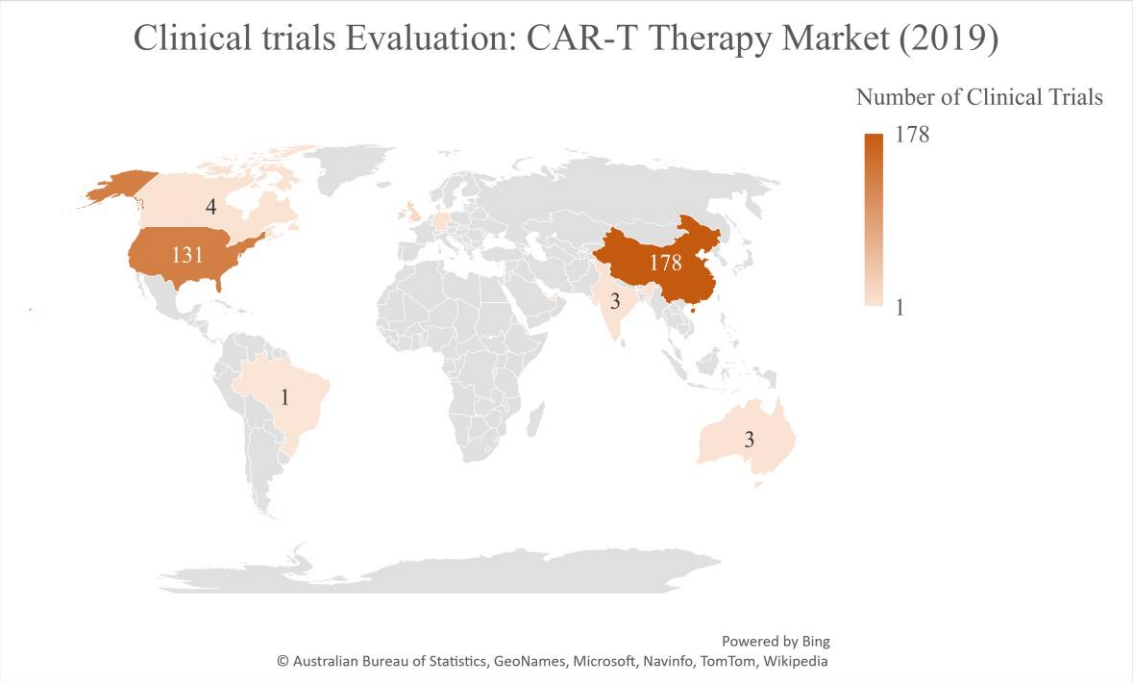
Analysis of the years 2019 and 2023 presented a promising market segmentation. Market segmentation on the basis of target antigen is dominated by CD19 with a 100% market share with a growing rate of 25.3%.[30] The chief prospects showing a global annual sale of profit of $1077.3 million USDA by 2023. Market segmentation based on indication included ALL, DLBCL, FL, CLL, ML with many others. DLBCL dominating with the largest market share of 56.1% in 2019. The other indications are directed to grow with a CAGR of 29.3%, also portraying a global annual sale of profit of $728.5 million USDA by 2023. The diffuse large BCL category, which will acquire $738.5 million in global twelve-month sales by 2023, would present the best potential in the CAR-T treatment market split by application.

Geographically, North America accounts for the largest market share of 60.9% in 2019 increasing to $744.9 million in 2023. Quicker drug discovery and approvals in Western Europe, Asia followed by others with CAGRs of 32.4% and 85.1% respectively in 2019. Clinical trials are carried out at a global level with an ever-snowballing number. In 2019, the evaluation showed a total 329 clinical trials practiced worldwide. East Asia had the maximum number with 178 clinical trials, followed by 131 in U.S. Europe also steadily followed with 20 clinical trials in 2019.[30]

CAR-T immunotherapy has major market players like Novartis and Gilead Pharmaceuticals dictating the segment. Market-trend-based approaches would include capitalising the R&D fore reprogramming CAR-T therapy, diminishing the neurotoxicity, generating allogenous CAR-T therapy for severe malignancies management, engineering, improving, next-generation CAR T cells, incorporating in AI and ML optimizing the technology, advancing innovation, the rise of mergers and acquisitions, collaborating with strategic partners can further enlarge the market. Competitive prices with larger salesforce, authorized distributors, using social media for purchasing and selling,

aggressive marketing, and physician and location specific targets can help in amplifying extent and incomes.

Figure 7.5 Clinical Trials Evaluation of CAR-T Therapy



Source: Persistence market research

Market Drivers

Elevated prevalence of global malignancies rate where CAR-T cell immunotherapy is leading treatment is guiding the expansion of the market.

Tactical partnership between the companies to make CAR-T readily available functioning as a catalyst for the market.

Ongoing clinical trials are being performed by numerous pharmaceuticals businesses are forcing the market growth.

Application of most recent skills and knowledge in the health care industry can also act as impetus to a market.

Market Restraints

Large cost implicated in study, research and development for CAR-T cell immunotherapy is hampering the development for the market.

Scientific and foremost technological challenges for fabrication of disease specific new CAR-T cell immunotherapy will impede the market growth.

Lack of proficiency and insufficient understanding about CAR-T cell immunotherapy in some economically growing countries

7.6 CAR-T and global regulations

More than 400 continuing clinical trials worldwide and the recent approval of axicabtagene ciloleucel and tisagenlecleucel, the global CAR T-cell market is projected to expand to over $3 billion in the upcoming decade. The United States, Europe, the United Kingdom, Australia, Canada, and Japan are the countries with the most CAR T trials currently underway, followed by the United States, Europe, the United Kingdom, Australia, Canada, and Japan. Because of the country's expanding investment in cutting-edge biotechnology and less severe regulation, the China CAR T business is rapidly growing The intricacy of quality management along the convoluted manufacturing technique, as well as the lack of long-term safety, efficacy, and quality-of-life data, exacerbate the authorisation difficulty. The FDA, EMA, CADTH, and MSAC are arguing over whether the therapy should be classified as an oncology drug, a medical device, or a hybrid. Its skyrocketing price also makes repatriation difficult. [31]

The marked price of Yescarta and Kymriah listed at $373,000 and $475,000, respectively, have raised the total cost of therapy for cancer. With an indication specific market to ALL, DLBCL, CAR-T immunotherapy is sure to dominate the market with approximately $1.1billion by the year 2026.[32] The estimation of the hematologic malignancies market is to exceed $20 billion at the same time-period, with CAR-T capturing the majority of market share in terms of paediatric and young adult patients. Increased uptake of JCAR017 is expected due to superior efficiency and safety results. CAR-T immunotherapy is expected to see the greatest uptake in the target population of pre-treated patients, limiting to small suitable populations. CAR-T immunotherapy is in its infancy of development and needs more certain exploration in solid tumour-targeted and off-the-shelf therapies.

FDA has approved four products and various other trials are under assessment for the treatment of numerous disease indications. The pipeline is perpetual mounting. According to the therapeutic area, 57% of products in the pipeline work on haematological cancer while 33% cater to solid tumours. 8% are being developed for other oncological disorders while only 2 % are being developed in non-oncological indications.[31]

Only 2% of drugs are either approved or are in Phase III drug stage development. Phase II/III and II have 5% drugs in development. With a majority of 56% in Phase I/II and I, the pipeline has booming prospects. 38% accounted for the preclinical stage.

CAR-T needs a detailed outlook on the CAR paradigm, disease markers, kind of cytokine, state of the patients, and their history before the treatment with consideration to the cardiovascular and renal functioning. Biomarkers-guided immunotherapies are the way forward in the treatment of malignancies.

7.7 Key Drivers and Challenges

The following are key drivers of CAR-T immunotherapy:

- Patients cannot finance and do not have access to advanced therapies.
- The disease profile is transitioning away from infectious disease to chronic diseases, which can be treated more effectively with substantial immunotherapies.
- The government is currently promoting the growth of the pharmaceutical industry.
- Physicians are the primary influencers and decision-makers in patient treatment, and they frequently recommend CAR-T immunotherapy concept of perceived financial ability to pay.

Manufacturers or pioneer pharmaceuticals frequently employ techniques to increase market positioning with a better product while maintaining pricing strategy. Depending on the diagnosis and management of patients, clinically differentiated goods combined with existing players' market access expertise may be more successful in obtaining market share.

Oncology has the majority of medications with mild to adverse drug reactions, CAR-T also has similar impacts on the immunity and comorbidity of the patient[33]. Few relapses were also seen in a year after the treatment.[3435] Complete remission was also seen in the rare case where an untimely mutation appeared in tumour suppressor genes, while the relapsed case was also encountered in B-cell ALL (Acute Lymphoblastic Leukemia).[3637]

A better comprehension of the immune responses and tumour microenvironment in the host is the major obstruction in the progression of immunotherapy.[38] Another challenge is the availability of the therapy for various cancers which needs research and development of CAR-T immunotherapy with verification of novel antigens and optimization of the therapies. Affordability with high pricing has cost-prohibitive measures and impacting the global accessibility of the therapy.[39] An improved tenacity and enhanced cytotoxic outline of CAR T cell immunotherapy are functional regions of research demanding long-term clinical trial follow-up. Adverse reactions due to drugs included neurotoxicity, B cell aplasia, tumour lysis syndrome, cytokine release syndrome, and anaphylactic shocks.[40] The following table further tells us about the limitations and their strategies.

Strengths

Responses in diseases that has been severely pre-treated or is resistant to treatment. CAR-T cells have a huge amount of potential in diseases that have been extensively pre-treated and are resistant to treatment. The approval of paediatric BCP-ALL and DLBCL, two very aggressive cancers, is a significant step forward.

Response that is long-lasting and has the potential to be cured. Long-term response and survival data are scarce. In aggressive lymphoma, low-grade lymphoma, and CLL patients treated with anti-CD19 CAR-T cells, ongoing CRs range from 43 to 113 months, suggesting hope for a cure.

Flexibility. CAR synthesis with two receptors can refine specificity with “OR”, “AND” and “NOT” Boolean logic gates. Additionally, disabling endogenous TCR expression allows for allogeneic CAR donors by preventing GVHD, rendering HLA matching unnecessary.

Quick time intermediation and single time treatment and surveillance are the noteworthy improvement of CAR-T over other therapies. Follow-up care would only need 2-3 weeks of observation.[41] The breakthrough technology has a long-term efficacy and persistent capacity to fight against tumour cells in relapsed patients[42] CAR-T proclaimed impressive results against relapsed patients of transplantation, substituting them.[43] CAR T cell therapy wholly eradicated the tumour relapsed subsequent numerous trans-plants disease. CAR-T immunotherapy is referred to as a “living drug” as the patient can profit from the corrective treatment.[44]

Table 7.7.4 Limitations and potential strategies

Limitations of CAR-T cell therapy	Potential strategies
Antigen escape	Targeting multiple antigens (dual or tandem CARs) ·Preliminary clinical trial results of CD19/CD22 targeted CARs for treatment of ALL/DLBCL and CD19/BCMA targeted for multiple myeloma have demonstrated promising efficacy[48,49,50,51]. ·Solid tumor: HER2 /IL13Ra2 (glioblastoma) and HER2/MUC1 (breast cancer) CARs produce superior antitumor responses compared to single target therapy
On-target off-tumor effects	Targeting tumor-restricted post-translational modifications ·Four major CAR-T cell targets have been investigated: TAG72[28], B7-H3[55,56], MUC1[16], and MUC16[57,58].
CAR-T cell trafficking and tumor infiltration	Local administration vs systemic delivery ·Superior therapeutic efficacy of intrapleural[63] and intraventricular[61,62] injection of CAR-T cells in mesothelioma and glioblastoma/brain cancer patients, respectively. Expressing chemokine receptors on CAR-T cells that match and respond to tumor-derived chemokines ·Integrin αvβ6-CAR-T cells modified to express CXCR2 or CAR-T cells overexpressing CXCR1/CXCR2 enhance trafficking and significantly improve antitumor efficacy[64,65,66]. Engineering CAR-T cells to enhance penetration through physical barriers (tumor stroma) ·CAR-T cells that express heparanase or fibroblast activation protein targeted CAR-T cells have shown enhanced infiltration and antitumor activity[68,69].

Immunosuppressive microenvironment	Combination immunotherapy with CAR-T cells and checkpoint blockade ·In hematological malignancy, combination PD-1 blockade and CD19 CAR-T cell therapy in B-ALL patients improved outcomes and improved CAR-T cell persistence[73]. ·In solid tumors, many studies are currently evaluating combination therapy[71,74]. Engineering CAR-T cells to provide immunostimulatory signals in the form of cytokines or CARs resistant to immunosuppressive factors. ·Engineering CARs to provide immunostimulatory signals have relied on IL-12 secretion[78], IL-15 expression[79], and redirecting immunosuppressive cytokines (e.g., IL-4) resulting in increased survival, proliferation, and antitumor activity[80]. ·CARs resistant to immunosuppressive factors in the hostile tumor microenvironment such as TGF β-mediated inhibitory signals have been developed[76].
CAR-T cell-associated toxicities	Altering CAR structure to ameliorate toxicity ·Decreasing CAR antigen-binding domain affinity to micromolar affinity[9]. ·Cytokine secretion can be modulated by modifying the CAR hinge and transmembrane regions[93]. ·Tailoring the costimulatory domain based on tumor type, tumor burden, antigen density, target antigen–antigen binding domain pair, and concerns of toxicity[94]. ·CAR immunogenicity can be decreased by utilizing human/humanized antibody fragments instead of murine-derived CARs[25,95,96]. Modifying CAR transduced T cells and neurotoxicity ·Inhibition of macrophage activating and monocyte activating cytokine GM-CSF with lenzilumab decreases CRS and neurotoxicity and increases CAR-T cell activity[87,98,99]. ·IL-1 receptor antagonists reduce a form of neuroinflammation in leukemia/lymphoma mouse models[102]. CAR “off-switches”.

	·CAR constructs engineered to express CD20 facilitate depletion of CAR-T cells via rituximab treatment104. ·Dasatinib treatment has exciting potential as it provides temporary inhibition of CAR-T cell function and could allow for rescue therapy after toxicities have subsided107

Source: "Sterner, R. C., & Sterner, R. M. (2021). CAR-T cell therapy: current limitations and potential strategies. *Blood cancer journal*, *11*(4), 69. https://doi.org/10.1038/s41408-021-00459-7"

Opportunities for engineered T-cell therapies

Other immune cells. Natural killer (NK) cells display GvT immunity without GVHD. Yet, tumour immune escape may emerge from cancer cell proteolytic shedding of immune-signalling ligands. Genetic deletion of immune checkpoints maintains NK activity, eliminating cancer more effectively than normal NKs. In phase I and II study, CD19 NK CARs achieved 75% ORR in relapse/refractory NHL and chronic lymphocytic leukaemia (CLL) without major toxicities.

New antigen targets. Target antigens are being evaluated in haematological and solid malignancies. The orphan G protein-coupled receptor, class C group 5 member D (GPRC5D) antigen offers comparable in vivo efficacy and toxicity in BCMA. GPRC5D is also expressed on CD138+ MM cells. Targeting CD22, expressed in B-ALL cancers, is a promising prospect currently under investigation in a phase I trial.

Improving efficacy. CARs revive exhausted T-cells and modulate inhospitable tumour microenvironment (TME). New 'armoured' CAR-T-cells stimulate IL-12 production, overcoming Treg- and myeloid cell-mediated immunosuppression, promoting CD8+ T-cell activity, and increasing myeloid cell recruitment and antigen presentation. In ovarian cancer models, IL-12-expressing-CARs against mucin 16 extracellular domain (MUC16ecto) were efficacious. A phase I trial in ovarian, fallopian or primary peritoneal cancer is ongoing. Chimeric cytokine receptor co-expression to stimulate IL-4-dependent cell proliferation enhances efficacy since IL-4 is abundant in the TME. This approach is effective across tumour-associated antigens (TAAs). Trials are ongoing for head and neck cancer. Transcription factor JUN overexpression confers resistance to CAR-T-cell exhaustion, offering therapeutic potential.

Reducing toxicity. IL-1 blockade is a novel intervention against CRS. Low-affinity CD19-specific CAR-T-cells reduced toxicity and enhanced efficacy. CAR-T-cell engineering with multiple receptor specificities further reduces toxicity. Transient receptor expression through mRNA-based methods and clonal deletion of infused cells by inclusion of a suicide cassette that is activated by exogenous agents, reduces cellular toxicity half-life.

CAR-T-cell combination therapy with other immunotherapies. Combining CAR-T-cells with immunotherapies overcomes cancer-mediated immunosuppression. Anti-PD-1 agents enhance CAR-T efficacy, prolonging OS. In one case report of relapsed DLBCL following sole CAR-T-cell therapy in a patient with high PD-L1 expression, combination of CD19 CAR-T-cells with pembrolizumab achieved rapid remission, increased CAR-T-cell numbers, and decreased PD-1 expression. Oncolytic viruses may enhance CAR entry and mobilization through chemokines.

CAR-T-cell combination therapy with non-immuno-therapeutic modalities. Preclinical and clinical data support combinatorial chemotherapy with CAR-T-cells. Chemotherapy improves CAR-T-cell efficacy reducing tumour burden and immunomodulation. Chemotherapy sensitises tumours to immunotherapy, improves TAA presentation, inhibits immunosuppression, and inhibits autoimmunity prolonging CAR-T persistence in vivo.

Radiotherapy improves CAR-T-cell efficacy, stimulating tumour-specific immunity to enhance tumour control locally and distantly. Local irradiation sensitises tumours to cytotoxic lymphocytes through TAA and MHCI expression. Radiotherapy stimulates cytokines, including IFN-γ, facilitating CAR-T-cell trafficking and TME infiltration, and improving TAA presentation.

There is limited evidence for chemo-radiotherapy (CRT) combination. CRT may increase CAR-T-cell efficacy by increasing T-cell density and T-cell stimulation. Further research should investigate CAR-T-cell combinations with non-immunotherapeutic treatments.

Threats to engineered T-cell therapies

Although ATC therapies are at the forefront, ongoing breakthroughs may produce superior agents with improved on-target off-tumour toxicity, efficacy, response, and off-the-self availability. Examples of such agents include NK CARs.

7.8 CAR-T and India

As of June 4, 2021,India was no stranger to CAR-T immunotherapy anymore with successful testing conduction at the "Bone Marrow Transplant unit" at the "Advanced Centre for Treatment, Research and Education in Cancer (ACTREC)", "Tata Memorial Hospital" in Mumbai in association with "IIT Bombay". With a massive budget of Rs 19.15 Crore was assigned to the first in-human of phase-I/II of CAR-T, the "Department of Biotechnology (DBT)", part of the "Ministry of Science and Technology" conducted the testing. Despite the demonstrated global therapeutic perspective, therapy was still unavailable in India. The list price of therapy accounts for Rs. 3-4 crore per patient, thus posing a challenge to be both, scalar development, and easier affordability. Regionalized development can cater to the challenge of high list price.[45] The national team is acting on lowering this expense down to ₹20 lakh. A sizeable part of the manufacturing price goes to trained labour.[46]

In May 2021, China-based Pregene and India-based Dr. Reddy Laboratories announced an agreement for exclusive licensing, where the former qualified to obtain a product royalty, up to $150 million. Pregene focus area of therapy involved anti-BCMA CAR-T immunotherapy injection. The exclusive license would favour the clinical development and commercialization of PRG180 by Dr. Reddy Laboratory. This development would embolden the treatment of R/R Multiple Myeloma. China already has significant results got the same drug. This agreement would inflate Dr. Reddy's capability in the sphere of treatment of malignancies.[47]

A potential rollout of the CAR-T technology in India, Immuneel was founded in 2018 to histrionically enhance access to transformative cell-based therapies for tumour patients. The aim is to aims to lessen the expense of a course of action of CAR T-cell therapy to approximately $50 000, like the expenditure of a more accessible and affordable bone

marrow transplantation. The reduction would include channelizing manufacturing, skilled labour, transfusion, and follow-up care. Cardiac surgery can be seen as an affordable quality befitting example of treatment.[48]

CAR T Cell Immunotherapy - A Flicker of Optimism

CAR T cell therapy is a revolutionary treatment approach that is bringing new hope to multiple myeloma patients.[49] A brief comparison of results of two separate economic evaluation comparing CAR-T cell therapy from the ZUMA-1 single arm phase I/II trial1 with chemotherapy from the SCHOLAR-1 retrospective pooled analysis7, both in individuals with relapsed or refractory aggressive non-Hodgkin lymphoma.

Table7.8.5: Comparative economic analysis of CAR-T and Chemotherapy

Base Case	**Institute for Clinical and Economic Review analysis**	**Roth/Kite analysis**	**Difference**
Cost(lifetime)			
Axi-cel	625,500	552,921	72,077
Chemotherapy	105,000	172,737	67,737
Benefits (years)			
Axi-cel LY gained	7.57	9.49	1.92
Axi-cel QALY gained	6.06	7.67	1.61
Chemotherapy LY gained	6.06	2.60	0.63
Chemotherapy QALY gained	3.23	1.13	1.35
Axi-cel cost per LY gained ($)	2.48	55,128	64,872
Axi-cel cost per QALY gained ($)		58,146	87,012

Source: 7. Hay A, Cheung M. CAR T-cells: costs, comparisons, and commentary. Journal of Medical Economics. 2019;22(7):613-615.

Patient perspective

CAR-T immunotherapy is a method that ought to account for the requirements and viewpoints of patients, healthcare workers and curing physicians. Each of these stakeholders' cope with their own exclusive concerns and disputes, for example, with verdict reaching, registering, organizing, post-infusion managing and long-term follow-up. Additional tasks to overcome and guaranteeing trial permanence, pre-treatment supervision and patient protection against the infectious COVID-19 era as it narrates to regionalized and dispersed clinical trial resolutions, such as home nursing, home healthcare, telemedicine, and eConsent, that minimalize hazards in these multifaceted trials and aid sustenance to patients in their journey.[50]

It is significant to advise patients that roughly an account of 10% of them will not obtain therapy after leukapheresis, due of advancing disease, illnesses, or out of specification circumstances.[51] In most cases, a patient's general health, and function are more crucial than age in establishing suitability for CAR T-cell therapy.

Patient-physician interaction and communication is particularly valuable in older patients who are contemplating CAR-T immunotherapy. Clinical trials for may regulate partaking centered on age, irrespective of function done with patient safety in mind.[52`]

8. Discussion:

The CAR-T therapy market faced emerging competition every year with new products being pumped into the pipeline and gradually to approval. The China market offers challenges and opportunities, but the US. Market is emerging at a faster rate. The prospects of intensified competition could produce a downward price pressure. In such a dynamic landscape there can be various themes set to shape up the industry over the coming years-

Manufacturers can focus on high potential European market and fast paced U.S. market with the estimated compound annual growth. Cost of therapy with its value proposition make the market more decisive and performance friendly. Challenges will rise due to the legal limitation and global acceptance of the therapy. Lower development expenses and innovation can ensure a long-term future.

CAR-T immunotherapy id growing in Europe as well with multiple clinical trials being conducted and newer patents being filed for more efficient, safe, and specific therapies. CAR-T generates an exceptional task for judgment makers. Additional novel supervisory

structures with better technology are required to simplify transforming its principles to patients. In different diseases, development of technology would need methods alignment with specific diseases as in B cell ALL, patients would redeem an immune response to the tumour by improving preliminary efficacy, and CAR-T cell tenacity. In multiple myeloma with solid tumours, boosted infiltration abilities and enhanced endurance to the tumour microenvironment, would have better influence on the therapy. On the other hand, hematological malignancies would need updated combined methods of treatments and diseases. Upcoming years of technological advancements and overall development of the CAR-T cell therapy would further decline the cost of therapy. With the approval of recent CAR-T therapies by FDA, the idea of their inclusion in the cancer treatment will improve the lifespan and curing capacity of this scientific advancement. Although being an expensive treatment substitute, the faster research and development, patient acceptance and government recognition is sure to decrease the cost of therapy.

9. Conclusion

Well structured regulatory pathways with emerging market products could further accelerate the market expansion. CART-immunotherapy is expected to grow in popularity in market that are developed like China, the United States, Europe in the upcoming future. Companies would be aided by governments providing clear regulatory authorization guidelines. The payers will also encourage uptake to lower health-care costs. Due to these traits, as well as a gap in the access of physical and financial status to the expensive therapy, CAR-T immunotherapy manufacturers are anticipated to benefit the most in the future.

While the growth potential of CAR-T immunotherapy appears optimistic, the expansion of the market would not be a simple undertaking. Companies willing to develop or expand into developing economies should establish an approach that identifies the unique characteristics or brand identification they face while also integrating lessons learnt from countries having developed economies. A unique proposition to value would may be needed to tap the huge population in growing markets for those who find it difficult to access expensive therapy.

The businesses shall build solid access to market plans that talks about important “where to play” also “how to win” decisions, the willingness to make expenditures so as to encourage adoption, also convert their business models to volume rather than profits. The

beforehand investments would mostly require an elaborated emphasis on education of patients and physicians to talk about the accessibility, reduced consumption and investments in supply chain so that it enables greater availability of therapy. Salesforce, government, and physician support and awareness of methods and goods may all contribute to this education.

Lastly, manufacturers shall not ignore the chance to work with the localities to understand the navigation of the environment. Comprehensive understanding of local market modulation and lean, lower-cost manufacturing, connected with the popular brands internationally and recognition of the manufacturer would thrust the growth of CAR-T immunotherapy in markets that are emerging.

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