Understanding the Efficacy and Safety of Stem Cell Therapy and CAR T-cell Therapy in Leukemia Patients – A Meta-Narrative Review

Johnny Duong*, Betelhem Negash*, Cong Nguyen*, Amita Panda*, Wendy Perla*, Kimberly Hoggatt Krumwiede, Mary Coolbaugh-Murphy, Denise M. Juroske Short

Undergraduate Program, School of Health Professions, UT MD Anderson Cancer Center *Authors contributed equally and are listed in alphabetical order

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Introduction

Leukemia	Leukemia is a type of cancer that is characterized by an abnormal increase in white blood cells. The proliferation of defective white blood cells can compromise the body's immune system. Treatments for leukemia include chemotherapy, radiation therapy, and immunotherapy.
Stem Cell Therapy	Stem Cell Therapy is a treatment that uses human pluripotent cells and mesenchymal stem cells to selectively target and treat various conditions. It is often used in conjunction with other treatments .
CAR T-cell Therapy	CAR T-cell therapy is a type of cancer treatment that utilizes T-cells that have been modified to include Chimeric Antigen Receptors (CARs). These artificially engineered T-cells trigger the immune system to targe and destroy cancer cells. However, this treatment can cause adverse effects such as neurotoxicity and cytokine release syndrome (CRS).

Significance of Research

The significance of this study includes evaluating current day therapies to understand how effective and safe they are in patients with leukemia. Specifically, the implications of this study allow patients to understand the benefits and disadvantages of both therapies. Additionally, comparing pros and cons of CAR T-cell therapy and Stem cell therapy increases knowledge on previous current day techniques, fostering development in this field of cancer treatment. Additionally, the foundational understanding of both therapies paves the way for future advancement.

Research Question/ Hypothesis

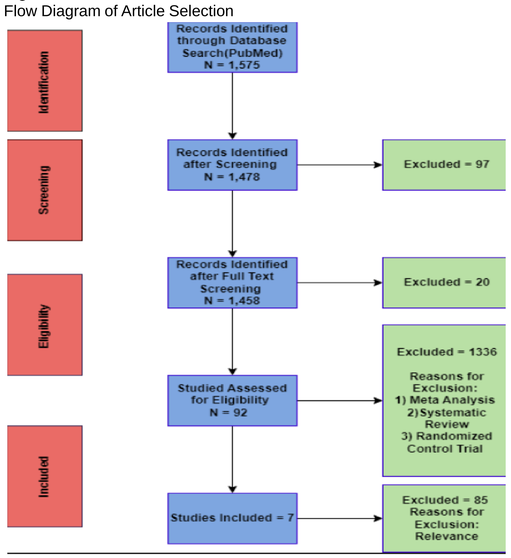
How effective and safe is CAR T cell therapy in Leukemia recurrence given that Stem Cell Therapy and CAR T Cell therapy are both effective treatments?

Methodology

A meta-narrative approach was selected for synthesis of relevant information. The database criteria expanded to include all types of leukemia in order to gain sufficient data and analysis.. Review of the articles specifically included comparing the efficacy and safety of CAR T-Cell therapy to Stem Cell therapy in patients with leukemia using meta narrative principles. Databases used included PubMed, Wiley Online Library, and Google Scholar. Search criteria was as follows: "CAR T Cell Therapy", "Stem Cell therapy", and "Leukemia". Original human clinical trials, publications within the past five years, primary sources, peer-reviewed research, and reputable medical journals were included in the selection process. All other publications were not included as criteria for selection. The articles were interpreted in February of 2023. The dates of articles spanned from 2020 to 2023. The data extracted from the articles included statistics, general information about CAR T-Cell Immunotherapy, the usage of chimeric antigen receptors, successful therapies in secondary acute myeloid leukemia, stem cell therapy, and T-cell lymphoblastic leukemia. The articles were compared based on efficacy, successfulness, and type of leukemia treated.

Source Selection

Figure 1
Flow Diagram of Article Selection



Note: The figure above depicts the selection process of articles used in the below table. Articles were chosen based on relevance and reputability. The database used was PubMed.

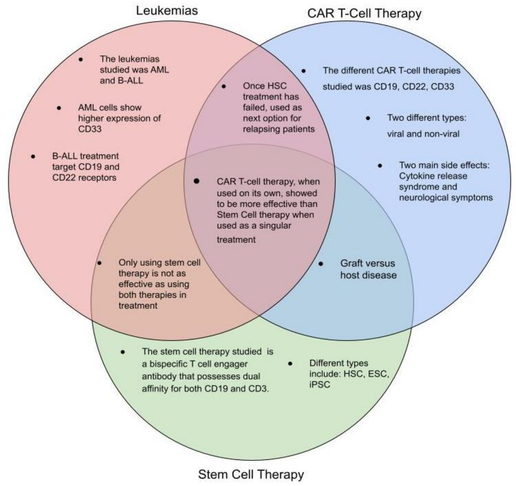
Source Characteristics

Table 1
Article Characteristics

Author	Year	Aim	Summary
Liu *et al.* Article 1	2021	Understanding the effects of CD19 and CD22 CAR T-cell therapy in patients who already received hematopoietic stem cell transportation.	The overall survival rate, excluding patient's that did not undergo the second-round of therapy, was 88.5% at 12 months and 67.5% at 18 months.
Lee *et al.* Article 2	2020	Looked to understand the long-term effects of CD19 – CAR T-cell therapy in children and adults with B-cell acute lymphoblastic leukemia.	62% of patient's were in complete remission. For patients who continued to have allo HSCT treatment as well, 95% of patient's lived up to 70 months after treatment.
Zhang *et al.* Article 3	2020	To review articles about CAR T-cell therapy on Secondary Myeloid Leukemia patients.	One dose of CAR-T cell therapy extended the remission of cancer for over a 10-month for AML patients. The CAR therapy produced higher relapse rates of leukemia.
Sauer *et al.* Article 4	2019	To discuss challenges of CAR T-cell therapy of acute myeloid leukemia.	The target antigen for CARs must be expressed on all cancerous cells but expressed at much lower levels on non-cancerous cells or not expressed at all. Tumor cells can also resist elimination by CAR-T cells through loss or down regulation of the target antigen
Singh *et al.* Article 5	2022	To discuss an improvement of a previous SB CD19 CAR T-cell infusion for safety and efficacy	This study shows the efficacy results of a 2nd generation of CAR T-cell therapy manufactured tor improved receptor binding. This increased the overall remission and safety of patient response.
Maude *et al.* Article 6	2018	Understanding Tisagenlecleucel in Children and Young Adults with B-Cell Lymphoblastic Leukemia	The study found that tisagenlecleucel had a high rate of remission and improved overall survival rate.
Salhotra *et al.* Article 7	2020	Outcomes of Allogeneic Hematopoietic Cell Transplantation after Salvage Therapy with Blinatumomab in Patients with Relapsed Acute Lymphoblastic Leukemia	The results suggest that salvage therapy with blinatumomab can improve the outcomes of allogeneic HCT in these patients, including overall survival and disease-free survival.

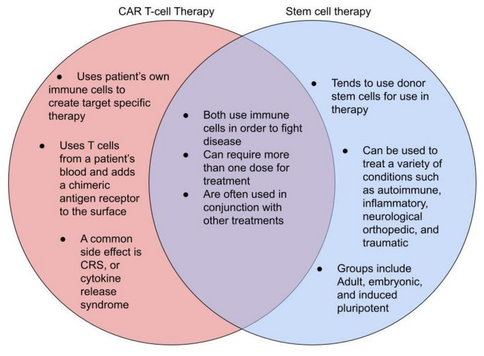
Note: The table above includes the articles selected for inclusion of the meta narrative.

Figure 2
Venn Diagram comparing Leukemias, CAR T-cell Therapy, and Stem Cell Therapy



Note: The figure includes synthesized generalizations made from research analyzed.

Figure 3
Venn diagram comparing CAR T-cell therapy and Stem Cell therapy



Note: The figure above compared and contrasted Stem Cell therapy and CAR T-cell therapy.

Strengths and Limitations

One strength of the review is that multiple types of leukemias that were researched to process a generalized conclusion overall. The research articles selected came from reputable primary sources within the past five years. Lastly, the review includes a broad range of ages, pediatric and adult, that were affected by different types of leukemias. The selection of the articles was applicable to leukemias studied and included information about CAR T-cell and Stem cell research.

Limitations of this review included: participants ranging from 1 - 50 participants. Due to the low number of affected individuals studied, the results may not be a complete representation of the entire population of those afflicted with leukemia. Another limitation is that many researchers worked off campus and remotely, adding to the limited interactions between the group members. Furthermore, the selection for articles to be analyzed included the judgment and ability of the researchers' individually. Lastly, the researchers' experience with meta narratives is limited as most participants are new to meta narratives.

Conclusions/Implications

- Most patients show a marked improvement overall with Stem Cell therapy and CAR-T cell therapy being used in conjunction with one another.
- Most of the patients were able to gain complete remission after exposure to both therapies, specifically CAR-T cell therapy following a previous allogeneic stem cell therapy.
- Side effects of CAR T-cell therapy included cytokine release syndrome, neurotoxicity, graft-vs-host disease, and other secondary infections.
- CAR T-cell therapy proved to be safer when compared to Stem Cell therapy; potential side effects were often mitigated early by secondary treatment.
- Graft-versus-host disease was more apparent with patients using Stem cell therapy as a primary treatment for leukemia.
- When compared to one another, CAR T-Cell therapy proved to be a more effective form of treatment when compared to Stem cell therapy.
- Thus, when both therapies are compared to one another, CAR T-cell proved to be more effective and safer when used as an only treatment; for refractory and relapsing leukemia patients, the CAR T-cell became more effective in remission overall.
- While the long-term effects of CAR T-cell therapy are still being studied, the safety of the treatment needs further improvement to reduce the typical patient response to Cytokine Release Syndrome, neurotoxicity, and Graft-vs-Host disease.
- In this review, the SB (novel Sleeping Beauty) CD19 CAR T-cell treatment showed to be the safest by using a non-viral vector produced by fish instead of the typical viral vector in other CAR T-cells (Singh, 2022).

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