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

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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 target and destroy cancer cells. However, this treatment can cause adverse reactions 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, facilitating progress 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, 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

Flow Diagram of Article Selection

Figure 1

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

Figure 2

Venn diagram comparing CAR T-cell therapy and Stem Cell Therapy

Figure 3

Source Characteristics

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Article Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liu et al.</td>
<td>2021</td>
<td>Understanding the effects of CD19 and CD20 CAR-T-cell therapy in patients who already received hematopoietic cell transplantation. The overall survival rate excluding patients that did not transfer to HSCT was 88.5% at 12 months and 87.5% at 18 months.</td>
</tr>
<tr>
<td>Leu et al.</td>
<td>2020</td>
<td>Licensed to understand the long-term effects of CD19– and CD20-directed T-cell lymphoblastic leukemia. 62% of patients were in complete remission. For patients who continued HSCT treatment with HSCT treatment as well. 85% of patients to 70% after treatment.</td>
</tr>
<tr>
<td>Zhang et al.</td>
<td>2020</td>
<td>To review articles about CAR T-cell therapy on Chronic Lymphocytic Leukemia. One dose of CAR T-cell therapy extended the survival of these patients. The CAR therapy was administered in higher response rates of leukemia.</td>
</tr>
<tr>
<td>Sauer et al.</td>
<td>2019</td>
<td>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 a down regulation of the target antigen. The study shows the efficacy results of a 2nd generation of CAR T-cell therapy manufactured for improved receptor binding. This increased the overall remission and safety of patient response.</td>
</tr>
<tr>
<td>Singh et al.</td>
<td>2020</td>
<td>To discuss an improvement of a syngeneic SB CD19 CAR-T-cell induction for safety and efficacy. CAR-T cell therapy is the best option for leukemia patients.</td>
</tr>
<tr>
<td>Maude et al.</td>
<td>2018</td>
<td>Understanding: Trisomyegenesis in Children and Young Adults with B- Cell Lymphoblastic Leukemia. Outcomes of Allogeneic Hematopoietic Cell Transplantation after Deluge Therapy in Children and Young Adults with Relapsed Acute Lymphoblastic Leukemia. The results support that allogeneic HSCT has a high rate of remission and improved overall survival rate.</td>
</tr>
<tr>
<td>Salhota et al.</td>
<td>2020</td>
<td>Understanding: Cooperative co-existence and co-evolution of therapies contribute to synergies in the treatment of AML and other hematologic malignancies. The results suggest that allogeneic HSCT has a high rate of remission and improved overall survival rate.</td>
</tr>
</tbody>
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Note: The above table includes the articles selected for inclusion of the meta-narrative.

Strengths and Limitations

One strength of the review is that multiple types of leukemias that were researched to process a generalization conclusion overall. The review 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.

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 supportive 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 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).

References


Maude et al. (2018). Targeted on Chimeric Antigens: Chimeric Antigen Receptors. Leukemia; Leukemia, 32(8), 1719–1725. doi:10.1038/leu.2018.188


