Emergence of gene therapy: a ten year analysis of chimeric antigen receptor (CAR) T-cell publications

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Background

• Chimeric Antigen Receptor (CAR) T-cell therapy has emerged as an innovative treatment in the hematology/oncology space.
• CAR-T therapy involves genetically engineering a patient's own T-cells to target certain malignancies.
• Over the past ten years, there have been advancements in understanding the safety, efficacy, and feasibility in engineering these CAR T-cells to recognize and destroy multiple cancers.
• These advancements have led to the first CAR-T approval in August 2017 with tisagenlecleucel for refractory B-cell precursor acute lymphoblastic leukemia.

Objectives

• Identify the trend of CAR-T articles being published over the past ten years.
• Discover the number of phase I, II, and III CAR-T studies that have been published.
• Understand the types of malignancies being treated in clinical trials.
• Determine the types of CAR T-cell therapies being engineered.

Methods

• The investigators conducted a primary literature search utilizing PubMed and EMBASE.
• Search terms included “CAR-T”, “chimeric antigen receptor”, and “T-cell”.
• Medical subject Heading (MeSH) terms utilized included: “Receptors, Chimeric Antigen” and “T lymphocytes”.
• Articles were limited to clinical trials (Phase I, II, and III) between the dates of January 1st 2009 to 2019.
• Articles involving manufacturing, in-vitro analysis, translational studies, case reports, or preclinical data were excluded.
• The investigators analyzed each article by identifying the following criteria:
  • The year when the article was published.
  • What phase was the clinical trial in at publication.
  • Primary endpoint of the study.
  • Specific malignancy/malignancies being studied.
  • Type of CAR T-cell therapy.
• The investigators standardized the clinical trial phase, primary endpoint, and malignancies being studied to maintain consistency.
• If the above criteria was not explicitly stated in the article, the investigators would collectively decide the appropriate answer.

Results

• Sixty publications were utilized in the primary analysis:
  • 70% (n=42) Phase I, 22% (n=13) Phase I/II, 8% (n=5) Phase II.
  • No Phase III studies were found in the search of literature.
  • Response rate was utilized in all of the phase II trials (n=13).

• Only published articles were recorded in this analysis and ongoing clinical CAR-T trials that have not published were not captured.
• Only clinical studies were analyzed, other types of studies such as real world evidence-based studies were not included.

Conclusions

• There has been an exponential increase in CAR-T publications within the last 10 years since the inception of CAR-T therapy.
• The majority of CAR-T publications investigate various B-cell malignancies.
• 70 percent of published clinical trial data were from Phase I studies evaluating safety.
• 100 percent of Phase II studies used response rate as the primary endpoint in the evaluation of efficacy.
• No Phase III studies were found in the search of literature.

Table 1. Disease States in CAR-T Studies

<table>
<thead>
<tr>
<th>Disease(s)</th>
<th>Number of Studies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute Lymphoblastic Leukemia</td>
<td>14</td>
</tr>
<tr>
<td>B-Cell Malignancies</td>
<td>10</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>9</td>
</tr>
<tr>
<td>Acute Myeloid Leukemia</td>
<td>1</td>
</tr>
<tr>
<td>Chronic Lymphoblastic Leukemia</td>
<td>2</td>
</tr>
<tr>
<td>Glioblastoma, Liver Cancer, Pancreatic Cancer, Pluripotent Mesenchymal Stem Cells, Sarcoma</td>
<td>17</td>
</tr>
<tr>
<td>CEACAM5+ Tumors, Head and Neck Squamous Cell Carcinoma, Neuroendocrine, Ovary Cancer, Prostate Cancer, Renal Cell Carcinoma</td>
<td>4</td>
</tr>
</tbody>
</table>

Figure 1. CAR-T Publications by Trial Phase

Figure 2. CAR-T Publications by Year

Figure 3. Specific CAR-T Targets

DISCLOSURE

Author(s) of this presentation have nothing to disclose.

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