

TERAPIA CAR-T DIRECIONADA AOS ANTÍGENOS CD19 E CD30 NO TRATAMENTO DE NEOPLASIAS HEMATOLÓGICAS

CD19- AND CD30-DIRECTED CAR-T CELL THERAPY IN THE TREATMENT OF HEMATOLOGICAL MALIGNANCIES

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RESUMO

Introdução: A terapia com células T portadoras de receptor quimérico de antígeno, conhecida como terapia CAR-T, utiliza linfócitos T modificados geneticamente para reconhecer antígenos presentes em células tumorais. **Objetivo:** Analisar a aplicação da terapia CAR-T direcionada aos antígenos CD19 e CD30 em neoplasias hematológicas e discutir seus principais resultados e limitações. **Método:** Foi realizado estudo documental, descritivo, a partir de dois estudos clínicos selecionados por avaliarem células CAR-T dirigidas ao CD19 e ao CD30 em pacientes com doenças hematológicas recidivadas ou refratárias. **Resultados:** No estudo de Maude et al., 27 de 30 pacientes com leucemia linfoblástica aguda alcançaram remissão completa após tratamento com células CAR-T anti-CD19. No estudo de Ramos et al., entre os pacientes com linfoma de Hodgkin ativo que receberam linfodepleção baseada em fludarabina, a resposta objetiva foi de 72%, com resposta completa em 59%. **Discussão:** Os resultados indicam que diferentes antígenos podem ser utilizados como alvos da terapia CAR-T, ampliando sua aplicação para além das neoplasias de células B. **Conclusão:** A terapia CAR-T apresenta atividade antitumoral relevante contra diferentes doenças hematológicas, embora ainda existam desafios relacionados à toxicidade, à produção celular e à seleção dos pacientes.

Palavras-chave: Terapia CAR-T. Imunoterapia. Neoplasias Hematológicas. Linfoma de Hodgkin. Linfócitos T.

ABSTRACT

Introduction: Chimeric antigen receptor T-cell therapy, known as CAR-T therapy, uses genetically modified T lymphocytes to recognize antigens expressed by tumor cells.

Objective: To analyze the application of CAR-T therapy directed against CD19 and CD30 in hematological malignancies and discuss its main results and limitations. **Method:** A descriptive documentary study was conducted based on two clinical studies evaluating CD19- and CD30-directed CAR-T cells in patients with relapsed or refractory hematological diseases. **Results:** In the study by Maude et al., 27 of 30 patients with acute lymphoblastic leukemia achieved complete remission after treatment with anti-CD19 CAR-T cells. In the

study by Ramos et al., among patients with active Hodgkin lymphoma who received fludarabine-based lymphodepletion, the objective response rate was 72%, with complete response in 59%. Discussion: The findings indicate that different antigens can be used as targets for CAR-T therapy, expanding its application beyond B-cell malignancies.

Conclusion: CAR-T therapy shows relevant antitumor activity in different hematological diseases, although challenges remain regarding toxicity, cell manufacturing, and patient selection.

Keywords: CAR-T Therapy. Immunotherapy. Hematologic Neoplasms. Hodgkin Lymphoma. T-Lymphocytes.

INTRODUCTION

Cancer treatment has changed considerably with the development of therapies that use the immune system as part of the antitumor response. Chimeric antigen receptor T-cell therapy, known as CAR-T therapy, is one of these approaches and involves modifying the patient's T lymphocytes to recognize specific targets expressed by malignant cells.

CD19 is one of the main targets used in B-cell malignancies, including acute lymphoblastic leukemia. Another target of interest is CD30, which is commonly expressed by Hodgkin lymphoma cells. In both approaches, T lymphocytes are collected, genetically modified in the laboratory, expanded, and reinfused into the patient.

In the study by Maude et al., 27 of 30 patients with relapsed or refractory acute lymphoblastic leukemia achieved complete remission after treatment with CD19-directed CAR-T cells.¹ Ramos et al. evaluated CD30-directed CAR-T cells in patients with relapsed or refractory Hodgkin lymphoma and reported an objective response rate of 72% and a complete response rate of 59% among patients with active disease who received fludarabine-based lymphodepletion.²

These findings are relevant because they show that CAR-T therapy can be directed against different antigens and applied to distinct hematological malignancies. However, important limitations remain, including cytokine release syndrome, hematologic toxicity, complex manufacturing, cost, and disease relapse. Therefore, this study aimed to analyze the clinical results of CD19- and CD30-directed CAR-T therapy in hematological malignancies and discuss its main benefits, limitations, and perspectives.

METHOD

A descriptive documentary study was conducted through the analysis of two clinical studies addressing CAR-T therapy in hematological malignancies. The studies were selected

because they directly evaluated CD19- and CD30-directed CAR-T cells in patients with relapsed or refractory disease.

The first study, published by Maude et al. in the New England Journal of Medicine, evaluated autologous CD19-directed CAR-T cells in patients with relapsed or refractory acute lymphoblastic leukemia.¹ The second study, published by Ramos et al. in the Journal of Clinical Oncology, evaluated CD30-directed CAR-T cells in patients with relapsed or refractory Hodgkin lymphoma.²

The variables considered were patient population, target antigen, treatment characteristics, response rate, and relevant adverse events. No primary data were collected and no participants were recruited. The analysis was based exclusively on previously published clinical data.

RESULTS

In the study by Maude et al., 30 children and adults with relapsed or refractory acute lymphoblastic leukemia received autologous T cells modified to express a CD19-directed chimeric antigen receptor. Complete remission was achieved in 27 patients, corresponding to 90% of the sample. The modified cells were also detected in blood, bone marrow, and cerebrospinal fluid among responding patients.¹

Cytokine release syndrome was observed in all patients in the study by Maude et al. Severe cases occurred in 27% of patients and were associated with a higher disease burden before infusion. Severe cytokine release syndrome was effectively treated with tocilizumab.¹

In the study by Ramos et al., 41 patients with relapsed or refractory Hodgkin lymphoma received CD30-directed CAR-T cells. Among the 32 patients with active disease who received fludarabine-based lymphodepletion, the objective response rate was 72%, including complete response in 19 patients, corresponding to 59%. Cytokine release syndrome occurred in 10 patients and was grade 1 in all cases; no neurologic toxicity was observed.²

Together, these findings show that CAR-T therapy can be directed against different antigens and used in distinct hematological malignancies. The responses observed with CD19- and CD30-directed products were relevant in heavily pretreated patients, although the studies involved different diseases and treatment protocols.

DISCUSSION

The results demonstrate that the choice of antigen is an important part of CAR-T therapy. CD19 is mainly used in B-cell malignancies, while CD30 provides a target for

diseases such as Hodgkin lymphoma. This difference allows the same general cellular therapy concept to be applied to tumors with distinct biological characteristics.

The 90% complete remission rate reported by Maude et al. is particularly relevant because the patients had relapsed or refractory acute lymphoblastic leukemia. The response occurred in a population with limited treatment options, supporting the antitumor potential of CD19-directed CAR-T cells.¹

The results obtained with CD30-directed CAR-T cells are also relevant. Ramos et al. reported a 72% objective response rate and 59% complete response among patients with active Hodgkin lymphoma who received fludarabine-based lymphodepletion.² These findings suggest that targeting CD30 may be useful for patients who have already received several lines of treatment.

The safety profile differed between the studies. Cytokine release syndrome was a relevant adverse event in both approaches, but its severity was not the same. In the CD30 study, all reported cases were grade 1 and no neurologic toxicity was observed.² In the CD19 study, severe cytokine release syndrome occurred in a subset of patients and was associated with higher disease burden.¹

Despite the promising results, CAR-T therapy cannot be considered a definitive solution for all patients. Relapse, persistence of the modified cells, tumor antigen expression, manufacturing complexity, and treatment cost remain important challenges. The two studies also evaluated different diseases and CAR-T products, which limits direct comparison of their response rates.

A limitation of this study is the use of only two clinical studies as its documentary basis. Even so, they provide a useful comparison between two important CAR-T targets and illustrate how this therapy has expanded beyond CD19-directed treatment.

CONCLUSION

The analyzed studies demonstrate that CAR-T therapy can produce substantial clinical responses in different hematological malignancies when the target antigen is appropriately selected. CD19-directed therapy showed a high complete remission rate in relapsed or refractory acute lymphoblastic leukemia, while CD30-directed therapy demonstrated relevant responses in heavily pretreated patients with Hodgkin lymphoma.^{1 2}

Despite its potential, CAR-T therapy remains associated with toxicity, relapse, complex production, and high cost. Further clinical studies are needed to define the best patient selection and treatment strategies and to improve the durability and safety of CAR-T therapy.

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