



RESEARCH TOPIC CLI25

Use of Loncastuximab Tesirine in patients with Relapsed/Refractory Diffuse Large B-Cell Lymphoma (DLBCL) or High-Grade B-Cell Lymphoma (HGBCL) who have progressive disease after CAR T-cell treatment

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Abstract

The unmet medical need - Chimeric antigen receptor (CAR) therapy targeting CD19 is a promising treatment for patients with relapsed or refractory (r/r) large B-cell lymphoma (LBCL). Three autologous CD19-directed CAR T-cell therapies are approved for r/r LBCL. However, approximately 60% of patients do not respond to CAR T-cell therapy.

Loncastuximab tesirine is an antibody-drug conjugate (ADC) comprising a CD19-targeting antibody and a cytotoxin. Phase 2 data have reported an overall response rate (ORR) of 48.3% with loncastuximab monotherapy in r/rDLBCL patients. In a small number of patients, Loncastuximab showed an ORR of 46% when administered after CAR T-cell failure.

Hypothesis - Loncastuximab has the potential to induce remission in patients who have failed CAR T-cells.

Study design - The present project is aimed at designing a phase II single arm, prospective, multicentric study to evaluate the feasibility and efficacy of loncastuximab after failure of CAR T-cells.

Scientific references

Spina V., Brusca A., Cuccaro A., Martini M., Di Trani M., Forestieri G., Manzoni M., Condoluci A., Arribas A., Terzi-Di-Bergamo L., Locatelli S.L., Cupelli E., Ceriani L., Moccia A.A., Stathis A., Nassi L., Deambrogi C., Diop F., Guidetti F., Cocomazzi A., Annunziata S., Rufini V., Giordano A., Neri A., Boldorini R., Gerber B., Bertoni F., Ghielmini M., Stüssi G., Santoro A., Cavalli F., Zucca E., Larocca L.M., Gaidano G., Hohaus S., Carlo-Stella C.*, Rossi D: Circulating tumor DNA reveals genetics, clonal evolution and residual disease in classical Hodgkin lymphoma. *Blood* 131:2413-2415, 2018 *Co-senior author

Hutchings M., Morschhauser F., Iacoboni G., Carlo-Stella C., Offner F.C., Sureda A., Salles G., Martínez-Lopez J., Crump M., Thomas D.N., Morcos P.N., Ferlini C., Bröske A.E., Belousov A., Bacac M., Dimier N., Carlile D.J., Lundberg L., Perez-Callejo D., Umaña P., Moore T., Weisser M., Dickinson M.J. Glofitamab, a Novel, Bivalent CD20-Targeting T-Cell-Engaging Bispecific Antibody, Induces Durable Complete Remissions in Relapsed or Refractory B-Cell Lymphoma: A Phase I Trial. *J Clin Oncol* 39:1959-1970, 2021

Caimi P.F., Ai W., Alderuccio J.P., Ardeshtna K.M., Hamadani M., Hess B., Kahl B.S., Radford J., Solh M., Stathis A., Zinzani P.L., Havenith K., Feingold J., He S., Qin Y., Ungar D., Zhang X., Carlo-Stella C. Loncastuximab tesirine in relapsed or refractory diffuse large B-cell lymphoma (LOTIS-2): a multicentre, open-label, single-arm, phase 2 trial. *Lancet Oncol* 22:790-800, 2021

Dodero A., Guidetti A., Marino F., Tucci A., Barretta F., Re A., Balzarotti M., Carniti C., Monfrini C., Chiappella A., Cabras A., Facchetti F., Pennisi M., Rahal D., Monti V., Devizzi L., Miceli R., Cocito F., Farina L., Ricci F., Rossi G., Carlo-Stella C., Corradini P.: Dose-Adjusted Epoch and Rituximab for the treatment of Double Expressor and Double Hit Diffuse Large B-Cell Lymphoma: impact of TP53 mutations on clinical outcome. *Haematologica* 107:1153-1162, 2022

Calabretta E., Hamadani M., Zinzani P.L, Caimi P., Carlo-Stella C.: The antibody-drug conjugate Loncastuximab Tesirine for the treatment of Diffuse Large B-Cell Lymphoma. *Blood* 140:303-308, 2022

Dickinson M.J., Carlo-Stella C., Morschhauser F., Bachy E., Corradini P., Iacoboni G., Khan C., Wróbel T., Offner F., Trněný M., Wu S.J., Cartron G., Hertzberg M., Sureda A., Perez-Callejo D., Lundberg L., Relf J., Dixon M., Clark E., Humphrey K., Hutchings M.: Glofitamab for Relapsed or Refractory Diffuse Large B-Cell Lymphoma. *N Engl J Med* 387:2220-2231, 2022

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