EUROPEAN HEMATOLOGY ASSOCIATION

EHA2021 VIRTUAL

LB1903

SAFETY AND EFFICACY OF CD37-TARGETING NARATUXIMAB EMTANSINE PLUS RITUXIMAB IN DIFFUSE LARGE B-CELL LYMPHOMA AND OTHER NON-HODGKIN'S B-CELL LYMPHOMAS – A PHASE 2 STUDY

Topic: 19. Aggressive Non-Hodgkin lymphoma - Clinical

Keywords: DLBCL, Monoclonal antibody, Non-Hodgkin's lymphoma, Targeted therapy

Moshe Yair Levy[1], Zhanet Grudeva-Popova[2], Marek Trneny[3], Wojciech Jurczak[4], Halyna Pylypenko[5], Deepa Jagadeesh[6], Marc Andre[7], Sunita Nasta[8], Dalit Rechavi-Robinson[9], Sara Toffanin[9], Sandrine Micallef[9], Antoine Attinger[9], Elisabeth Rouits[9], Mariola Dymkowska[9], Heidi Nauwelaerts[9], Feng Jung Sherida Harriette Woei-A-Jin[10]

[1] Texas Oncology-Baylor Charles A. Sammons Cancer Center, Dallas, United States
[2] Medical University of Plovdiv, Plovdiv, Bulgaria
[3] General Hospital, Prague, Czech Republic
[4] Maria Sklodowska-Curie National Research Institute of Oncology, Krakow, Poland
[5] Cherkassy Regional Oncological Center, Cherkassy, Ukraine
[6] Cleveland Clinic, Cleveland, United States
[7] CHU Dinant-Godinne, UCL Namur, Yvoir, Belgium
[8] University of Pennsylvania, Philadelphia, United States
[9] Debiopharm International SA, Lausanne, Switzerland
[10] University Hospitals Leuven, Leuven, Belgium

Background: Naratuximab emtansine (nara, Debio 1562, formerly IMGN529) is an antibody-drug conjugate consisting of a humanized anti-CD37 antibody, K7153A, conjugated via a thioether-based linker to a cytotoxic maytansinoid, DM1. CD37, a lymphocyte surface marker, is highly expressed in B-cell non-Hodgkin lymphoma (B-NHL), including diffuse large B-cell lymphoma (DLBCL). In preclinical models of B-NHL, nara demonstrated strong antitumor activity, further enhanced by co-administration of rituximab (RTX). A Phase 1 monotherapy study of nara revealed a good safety profile and promising efficacy (22% overall response rate [ORR] in DLBCL at all doses).

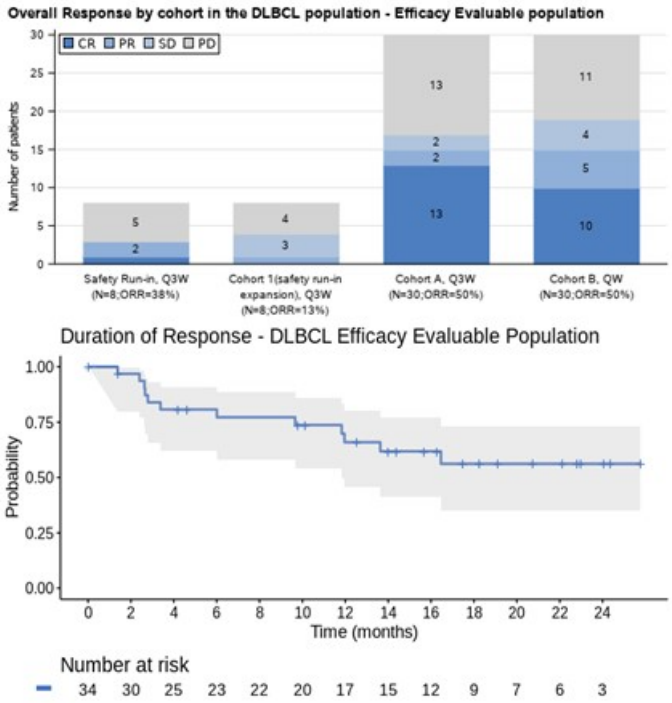
Aims: The aim of this open-label Phase 2 study was to evaluate the safety and efficacy of nara in combination with RTX in patients (pts) with relapsed and/or refractory (R/R) DLBCL and other forms of B-NHL.

Methods: R/R B-NHL pts who were not candidates for stem cell transplant, with 1-6 prior lines of treatment, were recruited to two study parts. In Part 1, which included a safety run-in followed by an expansion, pts received 0.7 mg/kg nara in combination with 375 mg/m^2 RTX every 3 weeks (Q3W). In Part 2, only R/R DLBCL pts were included. Pts were assigned to either the Q3W regimen (cohort A), or to a weekly regimen of 0.4, 0.2, and 0.2 mg/kg nara administered on days 1, 8 and 15, respectively (cohort B), combined with 375 mg/m^2 RTX on day 1. Six cycles of treatment were administered with possible extension. Primary endpoints were treatment emergent adverse events (TEAEs) and ORR. Safety is reported in all pts; efficacy in DLBCL pts only. Pharmacokinetics (PK) and pharmacodynamics evaluations included receptor occupancy to investigate CD37 target engagement. The follow-up period was up to 1 year after last pt first dose (NCT02564744).

Results: 100 pts were enrolled in the study: 80 DLBCL and 20 other B-NHL pts, of whom 81 (81%) experienced grade ≥3 TEAEs, the most common being neutropenia 54 (54%), leukopenia 19 (19%), lymphopenia 17 (17%) and thrombocytopenia 12 (12%). Eight (8%) pts discontinued nara due to a TEAE. Only very few grade ≥3 TEAEs, known to be associated with free DM1, were reported: 3 (3%) pts with liver events (1 toxic hepatitis, 1 GGT increased, 1 ALP increased) with no sequelae; and 2 (2%) pts with neuropathy (1 motor and 1 sensory). Of the 80 DLBCL pts, 10 (12.5%) were primary refractory, 24 (30%) were refractory to last line, 62 (78%) had Ann Arbor stage III/IV, and 35 (44%) had at least 2 prior systemic cancer therapies. Of the 80 DLBCL pts, 76 were efficacy evaluable, i.e. had one baseline and at least one post-baseline tumor assessment or an assessment of clinical progression. The ORR was 44.7%, with 24 (31.6%) complete responses (CR), 10 (13.2%) partial responses. In addition, 9 (11.8%) stable disease and 33 (43.4%) progressive disease were observed. 30 pts were efficacy evaluable in each of the two major cohorts (A and B).ORR was 50% in each cohort (CR rate: 43.3% in cohort A; 33.3% in cohort B). Median duration of response

in the 76 DLBCL pts was not reached, (lower 95% confidence interval 12 months). Median duration of follow-up in responders was 15 months. PK data showed acceptable systemic release of cytotoxic DM1 and catabolites. Treatment resulted in full peripheral target engagement and B-cell depletion.

Image:



Summary/Conclusion: The combination of nara + RTX resulted in good OR and CR rates, durable responses, a manageable safety profile, and full CD37 target engagement. Consequently, nara + RTX could be considered an attractive option for the treatment of R/R DLBCL.

Abstract Book Citations: Authors, Title, HemaSphere, 2021;5:(S2):pages. Abstract Book, DOI:
http://dx.doi.org/10.1097/HS9.0000000000000566