Abstract 3594

EO2463 peptide immunotherapy combined with rituximab for first-line treatment of low-tumor burden follicular lymphoma (FL): a feasibility evaluation in study EONHL1-20/SIDNEY (NCT04669171)

2025 ASH Annual Meeting, Dec 6-9, Orlando, Florida, USA | Session 623. Mantle Cell, Follicular, Waldenstrom's, and Other Indolent B Cell Lymphomas: Clinical and Epidemiological: Poster II | Sunday, December 7, 2025; 6:00 PM - 8:00 PM; room OCCC – West Halls B3-B4

Authors: Stephen Smith[1], Francesc Bosch Albareda[2], Danielle Wallace[3], Jose Villasboas Bisneto[4], Carlos Grande[5], Jean-Pierre Marolleau[6], Reid Merryman[7], Luca Arcaini[8], Antonio Pinto[9], Norma Gutiérrez[10], Brian Till[1], Cristina García Herce[2], Maria Rocío Figueroa Mora[5], Pierre Morel[6], Sara Rattotti[8], Philippe Rinaudo[11], Jean-Marie Carpier[11], Jan Fagerberg[11], Pier Luigi Zinzani[12], Philippe Armand[7], Jonathan Friedberg[3], Stephen Ansell[4]

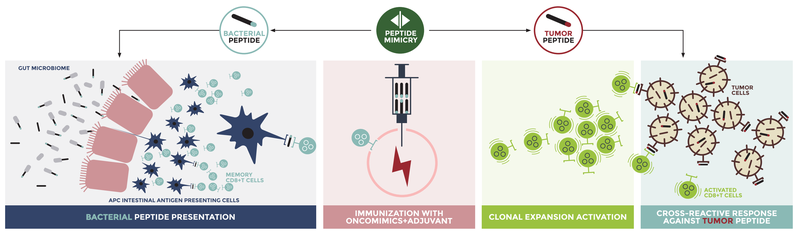
1 Fred Hutchinson Cancer Center, University of Washington, Seattle, WA; 2 University Hospital Vall d'Hebron, Barcelona, Spain; 3 University of Rochester, Rochester, NY; 4 Mayo Clinic, Rochester, MN; 5 Universidad de Navarra, Pamplona, Spain; 6 Centre Hospitalier Universitaire Amiens-Picardie, Amiens, France; 7 Dana-Farber Cancer Institute, Boston, MA; 8 Fondazione IRCCS Policlinico San Matteo and University of Pavia, Pavia, Italy; 9 Fondazione 'G. Pascale', IRCCS, Naples, Italy; 10 Hospital Universitario De Salamanca, IBSAL, Salamanca, Spain; 11 Enterome, Paris, France; 12 University of Bologna, Bologna, Italy

BACKGROUND

Single-agent rituximab is a common 1st-line therapy for patients with FL, especially those with low-tumor burden advanced stage disease or comorbidities.

EO2463 is a therapeutic vaccine generated from non-self protein sequences from gut bacteria, including 4 HLA-A2 CD8 T cell epitopes that mimic B cell-specific markers: CD20, CD22, CD37 and BAFF-receptor. EO2463 also contains a CD4 helper epitope UCP2.

EO2463 expands pre-existing memory CD8 T cells recognizing non-self-protein sequences from gut bacteria which can cross-react with B cell antigens on tumor cells. The aim adding EO2463 to rituximab is to safely increase the depth and duration of responses.



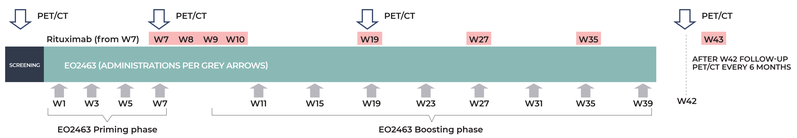
METHODS

Cohort 3 of trial EONHL1-20/SIDNEY includes patients with HLA-A2 and previously untreated low-tumor burden (GELF) FL grade 1-3A in need of treatment (per patient/treating physician).

Patients receive EO2463 (300µg/peptide) SC with adjuvant Montanide, q2 weeks (w) x 4, then q4w for a total of 12 doses, combined with rituximab starting at w7 (375 mg/m² IV q1w x4, then q8w x4).

The primary objective is to assess safety; secondary objectives include EO2463 immunogenicity and preliminary efficacy.

At data extract (2025-10-10 safety DB; 2025-10-18 efficacy DB), all planned 6 patients had started EO2463; 5 completed planned treatment, and 1 patient had ongoing treatment.



BASELINE CHARACTERISTICS

Baseline Characteristics EONHL1-20/SIDNEY, Cohort 3		n = 6 patients
Age (years)	Median (range)	66 (46-73)
Gender [n (%)]	Male / Female	4 (67%) / 2 (33%)
Ethnicity [n (%)]	Not Hispanic or Latino	6 (100%)
	White / Asian	5 (83%) / 1 (17%)
ECOG Performance status [n (%)]	0 / 1	6 (100%) / 0 (0%)
Primary diagnosis [n (%)]	Follicular lymphoma	6 (100%)
Time since primary diagnosis [months]; [time intervals, n (%)]	Median (range)	12.5 (1.1-83.0)
	≤ 6 months	3 (50%)
	>6 to ≤ 12 months	0 (0%)
	>12 to ≤ 24 months	1 (17%)
	>24 months	2 (33%)
Ann Arbor stage [n (%)]	III / IV	1 (17%) / 5 (83%)
Number of nodal sites	Median (range)	3 (0*-6)
FLIPI [n (%)]	Low / intermediate / high risk	2 (33%) / 2 (33%) / 2 (33%)
FLIPI-2 [n (%)]	Low / intermediate / high risk	2 (33%) / 4 (67%) / 0 (0%)
GELF [n (%)]	Negative / positive	6 (100%) / 0 (0%)

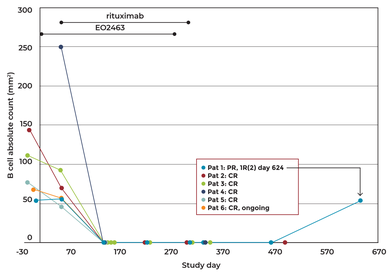
* One patient multiple bone lesions and BM involvement.

SAFETY

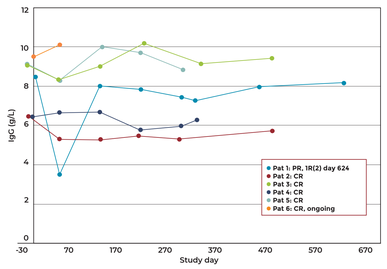
EONHL1-20/SIDNEY, Cohort 3, Safety (DB 2025-10-10)			n = 6 patients
	Irrespective of relationship	**Related to EO2463 + rituximab**	**Other safety information**
Any grade treatment emergent adverse events (TEAEs):	**Any grade ≥20%; or corresponding to related**	**All related**	**Adverse events Grade 4:** • none **Adverse events leading to death:** • none **Serious adverse events:** • none **Adverse event leading to interruption of EO2463:** • 1 non-related Grade 2 COVID-19 **Adverse event leading to early stop of EO2463:** • 1 related Grade 3 LASR **Local administration site reactions (LASRs):** • combined term including injection site reactions UNS, induration, erythema, pain • By event 83% **Grade 1**, 8% **Grade 2**, 8% **Grade 3** [2 events in the same patient] **MedDRA SOC Infections/infestations:** • 3 (50%) patients having in total 3 events, of which 1 event was assessed as related to rituximab (Grade 2 Enterocolitis infectious) • Two COVID-19 events, non-related, Grade 1 and 2 **Rituximab infusion interruptions:** • 5 patients with rituximab infusion interruptions – 4 infusion related reaction Grade 2 – 1 urticaria Grade 2 – all appearing at the 1st rituximab infusion • In addition, one patient repeat infusion related reaction Grade 2 at 2nd infusion (rest of planned infusions without events)
Local administration site reaction (LASR)	1 (17%)	1 (17%)	
Infusion related reaction (rituximab)	4 (67%)	4 (67%)	
Fatigue	3 (50%)	2 (33%)	
COVID-19	2 (33%)	0 (0%)	
Urticaria	1 (17%)	1 (17%)	
Diarrhea	1 (17%)	1 (17%)	
Anemia	1 (17%)	1 (17%)	
Lymph node pain	1 (17%)	1 (17%)	
Headache	1 (17%)	1 (17%)	
Dizziness	1 (17%)	1 (17%)	
Enterocolitis infectious	1 (17%)	1 (17%)	
Urinary retention	1 (17%)	1 (17%)	
Flushing	1 (17%)	1 (17%)	
Grade 3 TEAEs	**All Grade 3 events**	**All Grade 3 events**	
Local administration site reaction (LASR)	1 (17%)	1 (17%)	

* 15 patients enrolled and starting treatment before protocol v3.0 when "CELF negative" not specified in eligibility

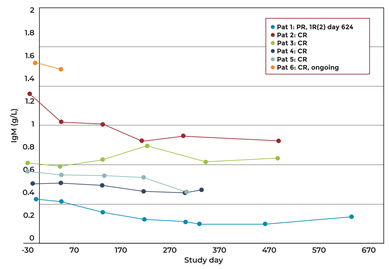
Absolute B cell count (cells/mm³)



IgG levels (g/L)

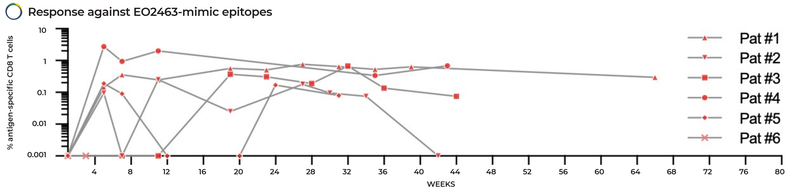


IgM levels (g/L)

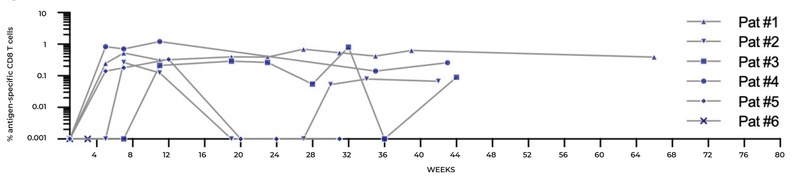


IMMUNE RESPONSE

Response against EO2463-mimic epitopes



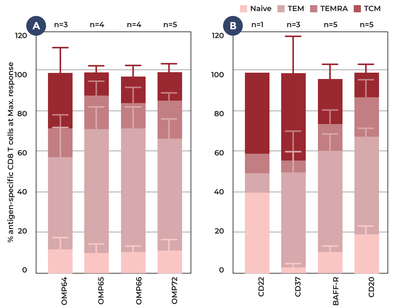
Response against B cell targets



Immune response to EO2463

CD8 T cells from PBMCs were stained ex vivo with tetramers at the indicated weeks to assess specific responses against EO2463-mimic (top) or B cell target (bottom) peptides. Zero values were set to 0.001 for logarithmic representation.

- 5 (83%) of 6 tested patients had expansion of CD8 T cells specific for EO2463-mimic and B cell target peptides during treatment. Note, the none-positive patient #6 has thus far only been tested at week 3 (after 1 administration of EO2463).



Phenotype of EO2463 induced immune response

CD8 T cells specific for EO2463-mimic (A; OMP64, OMP65, OMP66, OMP72) and B cell target peptides (B; epitopes on CD22, CD37, BAFF-R, CD20) were quantified using tetramers/flow cytometry on patient PBMCs ex vivo (time of maximal response). Memory phenotype was determined using CCR7 and CD45RA analysis within tetramer-positive populations. TEMRA: terminally differentiated effector memory T cells; TCM T central memory; TEM T effector memory.

CONCLUSIONS

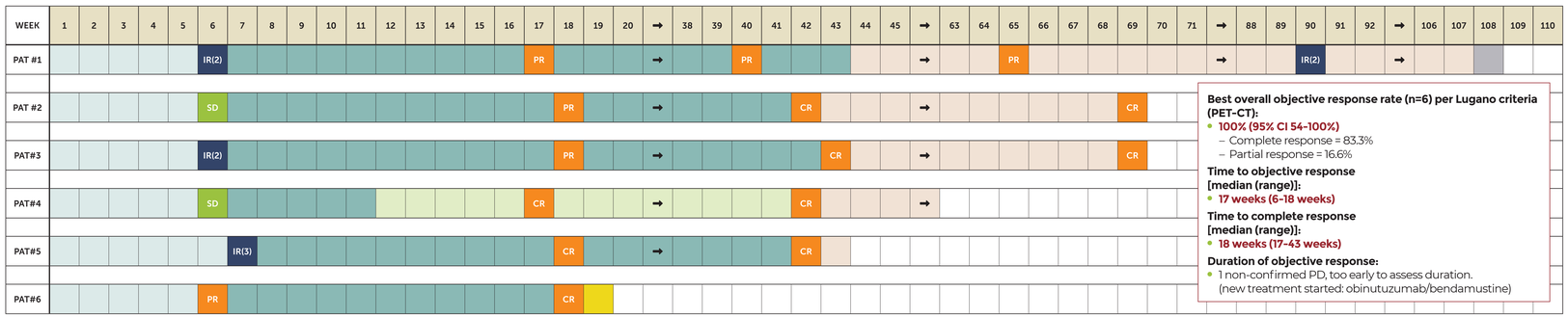
- The combination of EO2463 and rituximab has a predictable and benign safety profile, with EO2463 only adding local administration site reactions to the well-known rituximab safety profile.
- EO2463 elicits a rapid and strong sustained expansion of CD8 T cells specific for EO2463-mimic and B cell target peptides.
- EO2463-expanded specific CD8 T cells have a memory phenotype dominated by effector memory cells (EM).
- In this feasibility cohort including patients with previously untreated low-tumor burden follicular lymphoma, 5 of 6 patients had a Lugano criteria complete response and 1 of 6 had a partial response; an objective response rate of 100%.
- Acknowledging the very limited number of patients, the CR-rate is encouraging as compared with the expected CR-rate on rituximab monotherapy.
- Study EONHL1-20/SIDNEY also includes cohorts, not covered in this presentation, exploring EO2463 monotherapy in the "watch-and-wait" setting, and EO2463 plus lenalidomide / rituximab in relapsed FL/MZL.
- The combination of EO2463 and rituximab given as first-line treatment in patients with low-tumor burden follicular lymphoma is feasible and should be evaluated in further studies.

OBJECTIVE RESPONSE AND FOLLOW-UP

= EO2463 = EO2463 + rituximab = rituximab = treatment ongoing = follow up = complete / partial response = stable disease = non-confirmed PD = new anti-lymphoma treatment

IR(2) = appearance of new lesions or growth of one or more existing lesion(s) ≥ 50% at any time during treatment; in context of lack of overall progression (≤50%) or overall tumor burden

IR(3) = increase in FDG uptake of 1 or more lesion(s) without a concomitant increase in lesion size or number that meets PD criteria



Best overall objective response rate (n=6) per Lugano criteria (PET-CT):

- **100% (95% CI 54-100%)**
  - Complete response = 83.3%
  - Partial response = 16.6%

Time to objective response [median (range)]:

- **17 weeks (6-18 weeks)**

Time to complete response [median (range)]:

- **18 weeks (17-43 weeks)**

Duration of objective response:

- 1 non-confirmed PD, too early to assess duration. (new treatment started: obinutuzumab/bendamustine)

Contact info: medicalmonitoring-hem@enterome.com / ssmith50@fredhutch.org