Abstract

NI-1801, a mesothelin x CD47 bispecific antibody: Safety and activity as single agent and in combination with pembrolizumab, in heavily pretreated (≥ 4 prior lines) mesothelin expressing platinum resistant epithelial ovarian cancer patients

Thibault De La Motte Rouge MD PhD1, Emanuela Romano MD PhD8, Matteo Simonelli MD3,10, Andrea Zivi MD7, Jacques Medioni MD PhD4, Giuseppe Curigliano MD PhD5,6, Heloise Bourien MD1, Kristi Beshiri MD2, Etienne Bastien MD8, Francesca Zacchi MD7, Alice Rossi MD7, Audrey Bellesoeur MD8, Agnese Losurdo MD3,10, Beatrice Taurelli Salimbeni MD5, Anja Seckinger MD9, Walter Ferlin PhD9, Nicolas Fischer PhD9, Santiago M. Martin-Pastor MD9, Jose Saro MD9, and Kaissa Ouali MD2

(1) Centre Eugene Marquis, Rennes, Brittany, France, (2) Gustave Roussy, Villejuif, Ile de France, France, (3) IRCCS Humanitas Research Hospital, Rozzano (Milan), Italy, (4) Hospital Europeen Georges Pompidou, Paris, France, (5) European Institute of Oncology, IRCCS, Milano, Italy, (6) University of Milano, Milano, Italy, (7) AOUI di Verona, CRC di Verona, Verona, Italy (8) Institut Curie, Paris, Ile de France, France, (9) Light Chain Bioscience – Novimmune SA, Plan Les Ouates, Switzerland, (10) Humanitas University, Pieve Emanuele (Milan), Italy

Background: Chemotherapies (ChT) and antibody drug conjugates offer limited efficacy (PFS ≤ 3.9 months) and significant toxicity in patients (pts) with high grade serous or endometrioid platinum resistant epithelial ovarian cancer (PROC) who received ≥ 4 prior ChT. NI-1801 is a human mesothelin (MSLN) x CD47 bispecific antibody developed to selectively engage CD47 on MSLN+ tumor cells and designed to enhance tumor cell phagocytosis blocking CD47-SIRPa interactions. This abstract presents safety data from all study pts and efficacy data from 38 MSLN+ PROC pts, 4 recent pts not included.

Methods: 30 pts treated with NI-1801 as monotherapy (SA) at doses ranging from 15 mg to 2000 mg and 26 pts treated with NI-1801 at doses from 300 mg to 900 mg in combination (CO) with pembrolizumab. In both cohorts, a modified accelerated titration design was applied. Activity evaluated by RECIST 1.1 criteria. Data cutoff 12.05.25.

Results: At 600 mg and 900 mg in SA, 21 PROC pts treated. 1 pt with an ongoing partial response (PR) beyond 77 weeks (w), 7 pts had stable disease (SD) ranging 9 – 51 w, immature

PFS rate at 16 w is 28% with 3 pts ongoing. In the CO at 600 mg and 900 mg, 21 PROC pts have been treated; 5 pts (28%) experienced PR with a duration of response ranging from 24 w to 55+ w, 4 PR ongoing. Immature PFS rates at 24, 32 and 40 w are 39%, 33% and 28% respectively, 3 pts had SD, with 8 pts ongoing (3 before w 8 CT scan). NI-1801 as SA and in CO with pembrolizumab was safe and well tolerated. In SA, most adverse events (AEs) were mild (≤ grade 2). At 900 mg 3 transient related G3 AEs, 2 thrombocytopenia and 1 lymphopenia. In CO safety consistent with NI-1801 and pembrolizumab safety profiles. ORR and PFS data will be mature in October 2025.

Conclusions:

NI-1801 SA demonstrated encouraging signs of activity in fragile, heavily pretreated pts with mesothelin expressing PROC. The combination with pembrolizumab showed enhanced efficacy, with a promising response rate of 28%, durable responses and a clinical benefit rate (ORR + SD) of 44%. Notably, this clinical benefit was achieved with a chemotherapy free regimen, which was well tolerated and had a favorable safety profile.

Clinical trial information: NCT05403554