643 **A FIRST IN HUMAN PHASE I/IIA TRIAL OF PERSONALIZED TUMOR-TRAINED LYMPHOCYTES, PTTL, DERIVED FROM REGIONAL LYMPH NODES FOR TREATMENT OF COLORECTAL CANCER**

[1,2]Sofia Berglund, [1,2]Anne-Laure Joly, [1,2]Erwan Le Maitre, [2]Kelly Day, [1,2]Luigi Notari, [2]Claudia Carvalho-Queiroz, [1,2]Ola Nilsson, [1,2]Andreas Kaiser, [3]Maximilian Kordes, [3]Jeffrey Yachnin, [1,4]Mattias Carlsten, [1,4]Stephan Mielke, [5]Abbas Chabok, [5]Maziar Nikberg, [5]Ahmed Salim Tarfy, [2]Andrea Salmén, [2]Samuel Svensson, [1,2]Hanjing Xie, [1,2]Guro Gafvelin*, [1,2]Hans Grönlund. *[1]Karolinska Institutet, Stockholm, Sweden; [2]Neogap Therapeutics AB, Stockholm, Sweden; [3]Karolinska University Hospital, Solna, Sweden; [4]Karolinska University Hospital, Huddinge, Sweden; [5]Centre for Clinical Research of Uppsala University, Västmanlands hospital Västerås, Västerås, Sweden*

Background The new generation of adoptive T cell therapy utilizing high-precision neoantigen targeting is gaining increasing interest, especially in solid tumors, where the unmet medical need is high. Personalized tumor trained lymphocytes (pTTL) is a novel autologous adoptive T cell therapy targeting patient-specific neoantigens. A phase I/IIa First in Human (FIH) clinical trial of pTTL in Stage IV colorectal cancer (CRC) patients has started 2023.

Methods pTTL is produced through *in vitro* expansion of T cells derived from tumor-adjacent regional lymph nodes (RLN). The T cells are stimulated with a patient-specific array of neoantigens utilizing the proprietary EpiTCer® technology. Tumor-specific mutations are identified from next generation sequencing data obtained from tumor and normal tissue samples, and personal neoantigen epitopes are selected and ranked using the in-house bioinformatic software PIOR®. Polypeptides containing the selected neoantigens are designed, produced and linked to paramagnetic micro-particles to form EpiTCer® beads, a tumor-selective T cell expansion stimulus used for pTTL manufacturing.

Results pTTL can be manufactured with a high rate of success despite the product's personalized nature. pTTL consists mainly of T cells, with small proportions of NK and B cells. The CD4/CD8 T cell ratio varies between products. pTTL contains a significant proportion of memory T cells expressing markers indicating functionality, with limited levels of late-stage T cells. TCR sequencing has demonstrated increased T cell clonality in pTTL compared to in the RLN starting material, indicating antigen-specific expansion.

Conclusions The ongoing FIH Phase I/II trial will include up to 16 patients with Stage IV CRC. pTTL is administered as a single-dose monotherapy after chemotherapy-based preconditioning with cyclophosphamide and fludarabine. A dose-escalation design is applied.

The trial is divided into three parts. Part I: Collection of materials for sequencing and pTTL production (tumour biopsy, surgical collection of RLNs), and manufacturing of EpiTCer® beads and pTTL. Part II: pre-conditioning, administration of pTTL and follow-up for 6 months. Part III: Long-term follow-up to 5 years after pTTL administration.

The primary endpoint is safety. Secondary outcomes include response, overall survival, and progression-free survival. Biomarkers for pTTL persistence, pTTL characteristics, and response will be evaluated.

Trial Registration Trial Registration EUDRA CT #2022–000394-96.

Clinicaltrials.gov Identifier #NCT05908643

Ethics Approval The trial is approved by the Swedish MPA (5.1–2022-89272) and the Swedish Ethical Review Authority (2022–01842-01). All patients must give their informed consent to participation before inclusion in the trial.

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