Authors: C. Le Tourneau[1], JP Delord[2], A. Lalanne[1], C. Jamet[1], C. Spring-Giusti[3], A. Tavernaro[3], B. Bastien[3], M. Brandely[3], E. Quemeneur[3], K. Onoue[4], Y. Yamashita[4], N. Yamagata[4], K. Onoguchi[4], I. G. Pait[4], B. Malone[5], O. Baker[6], P. Brattas[5], O. Lantz[1], K. Bendjama[5], C. Ottensmeier[7]

1. Institut Curie, Paris, France
2. IUCT Oncopole, Toulouse, France
3. Transgene SA, Illkirch-Graffenstaden, France
4. NEC Corporation, Tokyo, Japan
5. NEC Oncoimmunity AS, Oslo, Norway
6. NEC Laboratories Europe GmbH, Heidelberg, Germany
7. The Clatterbridge Cancer Centre NHS Foundation Trust, Liverpool, UK

Randomized phase I trial of adjuvant individualized TG4050 vaccine in patients with locally advanced resected HPV-negative head and neck squamous cell carcinoma (HNSCC)

Background: T cells targeting tumor specific mutations drive anti-tumor immune responses. TG4050 is a novel viral-based personalized cancer vaccine, encoding up to 30 patient- and tumor-specific sequences bearing in-silico predicted class I and class II epitopes. TG4050 may prime an adaptive immune response against tumor antigens and prevent relapse in patients with locally advanced resected HNSCC. (NCT04183166)
Methods: Eligible patients with resected stage III or IV HPV-negative HNSCC were randomized after completion of standard of care adjuvant (chemo)radiotherapy to receive TG4050 immediately (arm A) or upon relapse (arm B). TG4050 was administered subcutaneously weekly for 6 weeks, then every 3 weeks for a total of 20 doses. Safety, efficacy and immunogenicity were evaluated. Longitudinal vaccine response was assessed by tetramer staining against target epitopes. In selected patients we explored tumor specificity and clonal expansion using bulk and single-cell (sc)TCR sequencing.
Results: 17 patients were randomized in arm A and 16 in arm B. All TG4050-related adverse events were mild to moderate. Disease-free survival data after a median follow-up of 24 months will be presented. Immune response was assessed after vaccination with TG4050 in 16 patients as monotherapy and in 2 at relapse in combination with chemoimmunotherapy. ELISPOTs evidenced priming of neoantigen-specific T cells in 17/18 (94%) patients. T-cell responses were either *de novo* (undetectable prior to vaccination) (82%) or amplification of pre-existing responses (18%). The median number of neoantigen responses was 6 (0 – 19). Frequency of tetramer positive $CD8^+$ T cells was evaluated in 9 patients and increased by 100 to 1000-fold as early as 8 days after initiation, reaching a plateau by day 22 and sustained over the follow-up period. Moreover, we identified clones targeting vaccine epitopes by scTCR sequencing of tetramer positive cells (10 tumoral specificities in 5 patients). Using bulk TCR sequencing data in 2 patients, we show that these antigen specific clones were found in TILs at baseline in the tumor but absent in the periphery prior to vaccination and were significantly expanded after treatment.
Conclusion: TG4050 design was well tolerated in patients with locally advanced resected HNSCC and induced sustained immune responses. Efficacy data will be presented.