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Authors:, C. Ottensmeier[1], JP Delord[2], , A. Lalanne[3], O. Lantz[3], Camille Jamet [3], A. Tavernaro[4], M. Brandely[4], B. Grellier[4], B. Bastien[4], H. Makhloufi[4], T. Huss[4], Y. Yamashita[5], K. Onoue[5], N. Yamagata[5], Y. Tanaka[5], B. Malone[6], O. Baker[7], E. Quemeneur[4], K. Bendjama[4], C. Le Tourneau[3]

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

Safety and Immunogenicity of TG4050; a personalized cancer vaccine in head and neck carcinoma.

Background: Despite adjuvant therapy, over 50% of surgically treated head and neck squamous cell carcinoma (HNSCC) patients (pts) experience a recurrence of disease. Systemic stimulation of cellular immunity against tumor mutations using a viral vaccine may be an ideal modality to clear residual cancer cells. For this purpose, we developed a pipeline for the design of TG4050, a personalized cancer vaccine (PCV) using a Modified Vaccinia Ankara (MVA) viral vector. We report here preliminary safety and immunogenicity data from a phase I TG4050 study.

Methods: Surgically resected stage III or IV, HPV negative HNSCC pts were enrolled in the study. pts must have achieved clinical remission after adjuvant chemoradiotherapy. A PCV for each pt was manufactured with up to 30 neoantigens identified using a state-of-the-art machine learning algorithm, from next generation sequencing (NGS) data. Pts randomized to arm A received the PCV after completion of primary treatment. Pts randomized to arm B received the PCV in the event of relapse, in conjunction with second line therapy. The PCV schedule consisted of an induction period of 6 weekly administrations, followed by booster doses once every 3 weeks for up to one year. Immune cells were collected by leukapheresis at baseline and at day 64. Primary endpoint was safety. Secondary endpoints included feasibility, disease free survival and immune response as assessed by ex-vivo IFNg-ELISPOT.

Results: At the time of data cut-off, a total of 31 pts were randomized, 15 in arm A and 16 in arm B. A vaccine was successfully designed for all randomized pts. Pts had no evidence of disease at baseline either at the clinical or molecular level, as assessed by ctDNA assessment. All adverse events (AEs) were mild to moderate and most were injection site reactions. Median follow-up was 9.2 months in arm A vs 7.6 months in arm B. None of the pts in arm A experienced relapse vs. 2 in the arm B. Immune monitoring demonstrated priming of a polyepitopic T cell response against the PCV in 100% of pts in arm A, among pts evaluated to date, with a mean of 9 responses per pt (6-19). Responses were observed regardless of HLA genotype, and without cross-reactivity to the wildtype antigen. Baseline tumor analyses revealed challenging genomic and immune profiles such as low TMB (avg of 3.06 ± 0.86 Mut/Mb), a majority of immune-desert tumors, and a low expression of important immune related factors including PD-L1 (16 pts out of 17 had a negative to moderate PD-L1 expression).

Conclusions: Our preliminary data demonstrate that TG4050 is safe, well tolerated, and capable of inducing T cell responses in cold tumors. In summary viral based, PCVs designed to induce tumor-specific neoantigen may be associated with a safe tolerance and an improved outcome in HNSCC pts.