Randomized phase II trial evaluating the combination of TG4001, a HPV16 therapeutic vaccine and avelumab (ave) in patients (pts) with immunotherapy-naïve recurrent and/or metastatic (R/M) HPV16-positive cervical or anogenital cancer

Background

Human papillomavirus (HPV) is a small DNA virus associated with cervical, anogenital (AG) cancers and squamous cell carcinoma of the head and neck.
TG4001 is a therapeutic vaccine based on modified vaccinia virus Ankara with insertion of modified non-oncogenic HPV-16 E6 and E7 antigens and interleukin-2 as adjuvant. The phase I trial of TG4001 combined with ave showed a favorable safety profile (Borcoman E. et al, 2023).

Patients and Methods

Pts with R/M cervical and anogenital cancer and who were checkpoint inhibitors naïve were randomized independent of PD-L1 expression between ave plus TG4001 or ave alone. Pts were required to have no more than one prior line of therapy for R/M disease and no liver involvement. Primary endpoint was PFS. Subgroup analysis (cervical, anal, other genital cancer) was preplanned in the protocol.

Results

90 pts were randomized between June 2021 and April 2024. 49 (54%), 27 (30%) and 14 (16%) pts had cervical, anal, and other genital cancers, respectively. Patients' demographics were well balanced between the 2 arms. Median PFS (mPFS) was 3.0 and 2.8 months (mo) in the experimental and control arm, respectively (HR=0.87 [90%CI: 0.59-1.29], p=0.28). In the cervical cancer subgroup, mPFS was 4.3 and 2.1 mo in the experimental and control arm, respectively (HR=0.58 [90%CI: 0.33-1.01], p=0.053). Overall Response Rate (ORR) in the whole population was 15.2% (7/46pts) in the experimental arm and 13.6% (6/44pts) in the control arm. In the cervical cancer subgroup ORR was 20% (5/25pts) in the experimental arm and 8.3% (2/24pts) in the control arm.

There were no new safety signals. Three pts (6.5%) in the experimental arm and 2 pts in the control arm (4.5%) presented grade 3 or 4 treatment-related AEs. Translational analysis including immunogenicity results will be presented.

Conclusion

TG4001 combined with ave did not improve PFS over ave alone in the whole patient population. Preplanned subgroup analysis in cervical cancer showed a positive efficacy signal in the combined arm.

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C. Le Tourneau[1] , F. Rolland[2] , O. Capitain[3] , P. Cassier[4] , J.-D. Fumet[5] , S. Salas[6] , A. Daste[7] , L. Manso Sánchez[8] , M.J. Bermejo-Pérez[9] , A. Casado Herraez[10] , L. Mansi[11] , P. Pautier[12] , O.Lantz[13] , E. Dochy[14] , C. Spring-Giusti[14] , K. Bidet Huang[14] , H. Makhloufi[14] , C. Halluard-Thin[14] , A. Tavernaro[14] , J.P. Delord[15]

[1]Department of Drug Development and Innovation (D3i), Institut Curie, Paris, France, [2]Institut de Cancérologie de l'Ouest - Site René Gauducheau, Saint Herblain, France, [3]Institut de Cancérologie de l'Ouest - Site Paul Papin, Angers, France, [4]Cancérologie Médicale - Centre Léon Bérard, Lyon, France, [5]Centre Georges-François Leclerc, Early phase unit, Dijon, France, [6]Centre d'Essais Précoces en Cancérologie de Marseille-Hôpital Timone, Marseille, France, [7]Hôpital Saint André, CHU de Bordeaux, Bordeaux, France, [8]Hospital Universitario 12 de Octubre, Madrid, Spain, [9]Hospital Universitario Virgen de La Victoria, Málaga, Spain, [10]Hospital Universitario Clinico San Carlos, Madrid, Spain, [11]CHU de Besançon, Service d'Oncologie Médicale, Besançon, France, [12]Institut Gustave Roussy, Centre de Lutte Contre le Cancer, Villejuif, France, [13]Laboratoire d'Immunologie, CIC-BT1428 et Unité Inserm 932, Institut Curie, Paris, France, [14]Transgene S.A. Illkirch –Graffenstaden, France, [15]Institut Universitaire du Cancer de Toulouse-Oncopole, Toulouse, France