Safety and Efficacy of an Inactivated, Unadjuvanted Vaccine Against the Novel Influenza A Variant (H1N1v) in Renal Transplant Recipients (Transfluvac Study)

F Thibault1,2, C Noble3,4, E Morelon4,5, S Daoud5, R Cahen3, C Dollinger5, N Lecorre6, I Charreau7, V Meiffredy7, J Aboulker7, B Autran2,6*, B Barrou1,2 1Service Urologie, GH Pitié Salpêtrière-Assistance Publique Hôpitaux de Paris, France; 2Université Pierre et Marie Curie Paris VI, Paris, France; 3Néphrologie, Centre Hospitalier Lyon-Sud, Lyon, France; 4Université de Lyon, Lyon, France; 5Néphrologie, Transplantation et Immunologie Clinique, Hôpital Edouard Herriot Lyon France; 6Laboratoire d’Immunologie Cellulaire et Tissulaire, Inserm U 543, GH Pitie Salpetriere, Assistance Publique - Hôpitaux de Paris, France; 7Inserm SC 10, Hopital Paul Brousse, Inserm, Villejuif, France

Background: A novel influenza A virus (H1N1v) led to a pandemic in 2009. Among the high risk population are the transplant recipients for whom few data are available. They are known to be difficult to immunize, and it is feared that vaccination could trigger allograft rejection episodes. The goal of this study was to assess the efficacy and safety of a new monovalent, inactivated, and unadjuvanted vaccine against H1N1v in a renal transplant population. Materials and Methods: 121 renal transplant recipients (> 6 month follow-up, median age of 51 years) under triple immunosuppression (Prednisone, Tacrolimus or Cyclosporine, Mycophenolate Mofetil or Mycophenolic acid) were immunized against influenza H1N1v in an open label, interventional study. Vaccination consisted of 2 injections at day 0 and day 21 of an inactivated, unadjuvanted H1N1v vaccine containing 15 μg/ml hemagglutinin (HA) (Sanofi Pasteur, France). The primary endpoint was the assessment of the humoral immunity on day 0, 21, and 42: the seroprotection rate (SP) was defined as the percentage of patients with an antibody title against HA ≥ 1/40e post vaccination; the seroconversion rate (SC) was defined as the percentage of patients with an prevaccine antibody title against HA < 1/10e and ≥ 1/40e after or with a prevaccine title ≥1/10e increasing at least 4 fold after immunization; the seroconversion factor (SCF) was defined as the ratio between pre and post vaccine geometrical means of the antibody titles. Secondary endpoints were the number and severity of clinical and biological adverse events, number of cases of pandemic H1N1v influenza biologically confirmed, and the function of the grafts. Results: The SP rate was 20% (95% CI: 13-28%) at day 0 (n = 117), 53 % (95% CI: 43-62%) at day 21 (n = 118), and 60% (95% CI: 51-69) at day 42 (n = 116). The SC rate was 24% (95% CI: 17-33%) after the first injection and 32% (95% CI: 24-42%) after the second injection. The SCF was 3.7 (95% CI: 2.8-5) after the first injection and 4.5 (95% CI: 3.4-5.9) after the second injection. Three clinical episodes of influenza A infection occurred, one at day 3 (biologically confirmed) and 2 at day 23 and day 27 (unconfirmed). Of the 121 patients, 20% reported at least one local adverse event, 23% at least systemic adverse event, and 35% at least one local or systemic adverse event. The majority of these events (95%) were minor to mild. No serious adverse events or adverse events of special interest were reported. As expected, graft function remained unchanged throughout the study. No rejection episodes were recorded. Conclusions: the SP rate at baseline was 20%, higher than anticipated. SP and SC rates post vaccination remained low as compared to those obtained in the general population or even in an HIV infected cohort receiving the same vaccine. The tolerability of this vaccine was excellent. These preliminary results confirm that immunizing transplant recipients against infectious agents remain a challenge requiring new strategies.