

Information Sheet for Public

Target of the dissemination

The primary objective of the proposed clinical trial entitled : « **Phase II study evaluating the clinical efficacy of TG4010 (MVA-MUC1-IL2) in patients with metastatic renal cell carcinoma (RCC)** ».

Is to determine the clinical efficacy of subcutaneous injection of the product TG4010 in patients with metastatic renal cell carcinoma, after going through radical or partial nephrectomie as a treatment of this disease. TG4010 works as a vaccine by stimulation of the immune defense system. Therefore it is also to determine if the vaccine TG4010 is able to induce a tumor regression and to confirm the good tolerance of sub-cutaneous injection of this product, which has been well tolerated in other studies performed with the same preparation in intra-muscular injection.

This clinical trial will be conducted in the "Service d'Urologie de l'Hôpital Saint Luc" in Bruxelles. The principal investigator is Dr Bertrand TOMBAL, and the sponsor is Transgene, a company based in Strasbourg (France).

Brief description of the genetically modified organism

The product TG4010 is a suspension of a virus called MVA (Modified Virus Ankara) in which the genetic information coding for the MUC1 and the interleukin 2 proteins have been included. This product was specially developed for use in oncology patients whose tumors express the MUC1 antigen. The MUC1 protein is normally found at the surface of some cells in the breast but in tumor cells the form of the protein is slightly modified and the protein is present in a greater quantity. The MVA vector was developed in Germany in 1970's and was successfully used, without significant side effects, to vaccinate against smallpox in about 150.000 humans, including young children and person with high risk for vaccination. In the TG4010 product, the MVA vector is the carrier of the MUC1 antigen and interleukin 2.

Risk assessment for public health and environment

The MVA virus used as carrier of genes in the TG4010 product has several advantages: it is not able to propagate in human and most mammalian cells, which confer to MVA a good safety feature with respect the risk of dissemination. In addition, the virus presents several deletions in its genome which make it a non pathogenic virus for humans. MVA virus remains, however, able to produce large quantities of foreign proteins from infected cells and it keeps its ability to induce an immune response. The MVA cannot interact with the genome of the infected cells since it remains localized in the cytoplasm, outside of the nucleus until the cell is destroyed by MVA lytic effect. This limits the possibility of integration. TG4010 was already administered to humans during previous clinical trials. No dissemination of the vector was detected by relevant techniques (PCR) in treated patients, as had been previously confirmed in animals. The risk for the public health and the environment related to the TG4010 viral vector use is low due to the properties described above.

Methods and monitoring plans in case of emergency

In hospital services where the patients will be treated with TG4010, a detailed procedure for product preparation will be provided to the staff involved in the product preparation. A technical sheet describing procedure for injection, procedures to remove the wastes and procedures to follow, in case of accidental shedding of TG4010, will be put in the room. All wastes related to the product use should be stored in a specific closed container which will be decontaminated according to the standard hospital procedures.