Information Sheet for Public

Target of the dissemination

The primary objective of the proposed clinical trial entitled: **« Randomized, multicenter, phase II study evaluating two doses of TG4010 (MVA-MUC1-IL2) in patients with metastatic breast cancer »**

is to determine the efficacy of subcutaneous injections of TG4010 in metastatic breast cancer patients after no more than two chemotherapy regimens for the treatment of the disease. TG4010 acts as a vaccine which stimulates the immune system. The other objectives of the trial are to determine if TG4010 is able to decrease the size of the tumors and to confirm the safety of subcutaneous injections of the product which was administered by intramuscular route in previous clinical trials.

This clinical trial will be conducted in the Service d'Oncologie Médicale de l'Hôpital Erasme in Bruxelles.

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 developped 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 decontamined according to the standard hospital procedures.

Information Sheet for Public

Target of the dissemination

The primary objective of the proposed clinical trial entitled : « **Randomized Multicenter PHASE II study Evaluating The Clinical Efficacy of TG4010 (MVA-MUC1-IL2) in association with Chemotherapy in Patients with Non Small Cell Lung Cancer** » is to determine the efficacy of TG4010 in a defined population of patients with an advanced lung cancer (stage IIIB/IV) and having not received any treatment to treat this stage of the disease.

This study concerns a vaccine (TG4010), the target of which is to stimulates the immune system against a protein present on lung tumors; and to help the immune system to fight the cancer. This study could be determine if the vaccine TG4010 is able to induce a regression of the tumors (above mentioned) alone or in combination with a standard chemotherapy treatment. It is also to confirm the good tolerance of subcutaneous injections of the product which was well tolerated in previous clinical trials conducted with the same product in intramuscular injections.
This clinical trial will be conducted in the Service d'Oncologie Médicale de l'Hôpital Erasme in Bruxelles.

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 developped 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 decontamined according to the standard hospital procedures.