

Appendix M-I-A Requirements for Protocol Submission

Non Technical Abstract

TroVax is a novel type of therapy, called an immunotherapy vaccine, which is designed to induce the bodies own immune system to attack and kill cancer cells. TroVax vaccine, is based on a safe and well known vaccine called vaccinia virus, which has been used for many years to give protection from smallpox i.e. the smallpox vaccine,. TroVax is based on the attenuated vaccinia virus strain called MVA, which is particularly safe for use in all cross sections of the public, including older people and children.

TroVax has been designed to enter cells at, or close to the injection site, and once inside the cells it produces a protein called 5T4. 5T4 is a specific protein which is usually present on the surface of cells within the placenta during pregnancy, and is also present in high levels on the surface of cancer cells e.g. colorectal, breast and renal cancer cells. The protein is produced in very low levels by a few normal tissues, such as pituitary gland or duodenum (intestines).

When TroVax produces 5T4, and it is displayed on the surface on the cell, the body's immune system becomes alerted to it as a "foreign" protein. This does not happen when 5T4 is on the surface of the placenta cells or tumour cells under "normal" conditions of pregnancy or disease. Once the immune system is alerted to 5T4 in this way, there is an expansion of the cells in the immune system, which are then targeted to recognise 5T4 protein on the cancer cells. We hope that this immune response will ultimately kill the cancer cells or inhibit their growth.

TroVax has demonstrated a good safety profile in both pre-clinical and clinical studies. In an early clinical trial, for patients with late stage colorectal cancer, TroVax was given as an injection into the arm muscle. At all three of the different dose strengths tested, it was found to be safe and well tolerated, producing only mild side effects, such as swelling at the injection site or mild "sweats". The vaccine was also shown to stimulate the immune response, 2-8 weeks after the start of vaccination in the vast majority of patients treated.

The proposed clinical trial in patients with renal cancer, will use the same route of injection for TroVax i.e. into the muscle at the 10x dose strength, which was shown to be safe in the previous clinical trial. TroVax will be given in combination with Interleukin 2 (IL-2), which is standard treatment for renal cancer. The main aims of this TroVax trial are summarised as follows:

Firstly

- To assess the safety and tolerability of TroVax injections when given as a therapeutic vaccine to patients with metastatic renal cell cancer
- To assess the immune responses induced by treatment with TroVax

Secondly

- To assess the effect of treatment with TroVax on tumour response rates, time to disease progression and two year survival.

If the first two criteria are met in that TroVax is safe, and induces immune responses in combination with IL-2, we will seek permission to undertake a larger study in this group of patients, to establish statistically significant data on clinical benefit.