

Appendix 3 Non Technical Abstract

Appendix M-I-A Requirements for Protocol Submission

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, which has been used for many years to give protection from smallpox i.e. the smallpox vaccine, which is produced using a modified vaccinia virus. TroVax is based on the modified vaccinia virus, Ankara, known as 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 also produced in very low levels by a few normal tissues, such as pituitary gland or oesophagus (gullet).

When TroVax produces 5T4, the bodies 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 early stage clinical trials, for patients with colorectal cancer or renal cancer, TroVax was given as an injection into the muscle. At the dose strength tested, it was found to be safe and well tolerated, producing only mild side effects, such as swelling at the injection site or mild fever. The vaccine was also shown to stimulate an immune response to the 5T4 protein, 2-8 weeks after the start of vaccination in all patients treated.

The proposed clinical trial will be in men with prostate cancer who have failed to respond to prior hormone or chemotherapy. The same route of injection i.e. into the muscle, and the TroVax dose strength, which was shown to be safe in the previous clinical trial will be used. TroVax will be given in combination with GM-CSF, which is another treatment for prostate cancer. The main aims of this TroVax trial are summarised as follows:

Firstly

- To assess the safety and tolerability of TroVax alone and in combination with GM-CSF
- To evaluate whether GM-CSF markedly increases the cellular or humoral anti-5T4 responses to TroVax

Secondly

- To evaluate the objective response frequency of TroVax alone and in combination with GM-CSF

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