Annual report : 2010 / Gene Therapy Advisory Committee.

GTAC

GENE THERAPY ADVISORY COMMITTEE

SEVENTEENTH ANNUAL REPORT

Covering the period from January 2010 to December 2010

About the Gene Therapy Advisory Committee (GTAC)

The Gene Therapy Advisory Committee (GTAC) is a Non-Departmental Public Body (NDBP), acts independently of Ministers and is recognised as a Research Ethics Committee by the UK Ethics Committee Authority (UKECA). Under the the Medicines for Human Use (Clinical Trials) Regulations 2004, GTAC has UK-wide statutory responsibility for the ethical oversight of clinical trials involving gene therapy. GTAC's terms of reference also include the ethical oversight of clinical trials involving cell therapies derived from stem cell lines.

In July 2010 the Government's Advisory Non-Departmental Public Bodies Review concluded that the Gene Therapy Advisory Committee (GTAC) no longer needed to provide advice directly to Ministers and that responsibility for supporting its Research Ethics Committee (REC) statutory functions should be transferred to the National Research Ethics Service (NRES).

The Committee works with other Government agencies with an interest on the development and use of gene and stem cell therapies and this area, such as the Medicines and Healthcare products Regulatory Agency (MHRA), the Health and Safety Executive (HSE) and the Human Tissue Authority (HTA). GTAC's Secretariat is provided by the Department of Health for England.

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FOREWORD

This year we considered seven new protocols all of which received favourable opinions. The protocols included treatments for various cancers, haematopoietic stem cell transplantation, cardiovascular disease and Parkinson's disease. In addition, the Committee gave advice on four research projects undertaking preclinical research and also held discussions with three clinicians on using gene therapy investigational products in patients who do not meet the inclusion criteria of a study.

We held a discussion with The National Institute of Biological Standards and Controls which also runs the UK Stem Cell Bank, about the preparation of a seed stock of mouse 3T3 fibroblasts. These cells act as 'feeder cells' for human cell cultures used in certain healthcare applications, such as corneal stem cell transplantation and skin grafting. We were presented with the preparative methods and characterisation of a new 3T3 line. The new 3T3 line has been prepared to replace the various mouse 3T3 feeder cell lines in use around UK transplantation centres. GTAC endorsed the use of these new feeder cells for human stem cell cultures.

GTAC and the MHRA have worked together to produce advice for investigators in the UK wishing to conduct clinical trials involving cell therapy A 'Points to Consider' document was produced and although it is believed that it is still too early to offer prescriptive regulatory and ethical advice to stem cell researchers, it was felt that it might be helpful to set out some of the issues that need to be thought through before proceeding to a clinical trial involving stem cells. These include immunological responses of the patients and transplanted cells, the genetic stability of cells, long term monitoring, as well as age and gender issues in patients. This advice was prepared taking into account the EC consultation document 'Detailed Guidelines on Good Clinical Practice Specific to Advanced Therapy Medicinal Products'.

We also took part in a number of EC consultation processes relating to the production of guidelines relating to trials involving Advanced Therapies. These included, 'Guidelines on Good Clinical Practice Specific to Advanced Therapy Medicinal Products', 'Concept Paper on the Development of a Guideline on the Risk-Based Approach According to Annex 1, Part IV of DIR.2001/83/EC applied to Advance Therapy Medicinal Products', 'Concept Paper on the Revision of the Note for Guidance on the Quality, Pre-clinical and Clinical Aspects of Gene Transfer Medicinal Products', 'EMA Consultation paper: guideline on quality, non-clinical and clinical aspects of medicinal products containing genetically modified cells', 'CHMP/CAT Position statement on Crutzfeldt-Jacob Disease and advance therapy medicinal products', 'Committee for Medicinal Products for Human Use – Questions and Answers on Gene Therapy' a document which sets out a harmonized position on issues that can be subject to different interpretation or require clarification on gene therapy medicinal products and 'The European Medicines Agency Road Map to 2015: The Agency's Contribution to Science, Medicines, Health' which is a draft document setting out EMEA's longer term strategy on contributing to better promotion and protection of public health, improving the regulatory environment for medicinal products and helping to stimulate innovation, research and development in the EU.

This year saw a major change in GTAC's position and processes following a review by the Chancellor the Exchequer and the Chief Secretary of the Treasury of the number and cost of Arms Length Bodies (ALBs) and Advisory Non-Departmental Public Bodies (ANDPBs) of which GTAC is one. The major change for GTAC is our transfer from Health, Science and Bioethics Division of the Department of Health (DH) to the

National Research Ethics Service (NRES) which is accountable to the R&D Directorate, who lead on research ethics policy within DH. DH research ethics policy is set out in the Governance Arrangements for Research Ethics Committees (GAfREC) and applies to all NRES RECs. An updated harmonised UK-wide edition of GAfREC had been issued for consultation in 2009 and was now very close to being finalised for publication by RDD in collaboration with the Health Departments in the other UK countries and NRES. The policy in GAfREC will also apply to GTAC which is a new area for GTAC because up to now, GAfREC did not apply to GTAC. The plan is for us to adopt the NRES Standard Operating Procedures (SOPs) from 01 June 2011.

We will remain a specialist committee and potential investigators would still be encouraged to present novel strategies and accompanying preclinical work prior to formal submission of clinical proposals. We still intend to obtain external peer review of protocols and continue our close working relationship with MHRA. This is regarded as a source of strength in current arrangements and MHRA colleagues would continue to be welcome to observe GTAC meetings.

Finally I would like to express my personal thanks to past and present colleagues in the Health, Science and Bioethics Division of the Department of Health who have give GTAC such wonderful support over many years . Their knowledge, dedication and hard work have been central to the success and effectiveness of our work.

Professor Martin Gore

Chairman of GTAC

SUMMARY

In 2010, GTAC considered seven applications to conduct gene therapy clinical trials under its remit as the National Research Ethics Committee for gene and stem cell therapy clinical research.

As in previous years, the majority of applications 58% (4 studies) were for cancer with the other three single applications (14% each) in haematopoietic stem cell transplantation, cardiovascular disease and Parkinson's disease respectively. More detailed information on all applications is contained in Section 1.

In its lifetime to date, the Committee has reviewed 189 applications. Of these, 166 trials have come to fruition, with 109 closed to patient enrolment and 56 currently open or due to open for recruitment. The remaining 24 applications were either declined by the Committee or never recruited patients as they were withdrawn following initial GTAC approval. Short summaries on some of the studies which have closed during 2010 are given in Section 3.

Although there was a reduction in number of submissions in 2010 than in previous years which could be attributed to the general downturn in economic activity worldwide, four separate research teams brought their preclinical data to the Committee for further discussion and advice. The Committee has always supported early discussions with researchers who are very close to bringing their study to the clinic and look forward to reviewing formal clinical applications in the not too distant future. More detailed information on these discussions is given in Section 1.6.

On three occasions the Committee also informally discussed with clinicians the scientific and clinical implications of using gene therapy investigational medicinal products in patients who would not be eligible to meet the inclusion criteria for entry into a trial. Researchers value the opinion, expertise and advice that Committee members are able to provide in exploring both the benefits and possible risks that this may incur. More information on the three gene therapy products involved in these discussions are given in Section 1.5.

In September the Committee contributed to the Academy of Sciences independent review of the regulation and governance of UK medical research. This call for evidence will have a long term implication for medical research in the UK and is connected to the Department of Health's published 'Report on the arm's-length bodies review' on 26 July. The report set out the steps to abolish and reorganise arm's-length bodies in an attempt to: 'create a more streamlined sector'; ensure 'less bureaucracy'; 'reduce intervention'; and enable 'greater efficiency through contestability'. This reorganisation had already impacted on the Committee's standing as an advisory body to Ministers and it is also planned that overall accountability for the Committee would move to the National Research Ethics Service (NRES) in 2011. In order to enable GTAC to adopt the NRES SOPs in full, some adaptation will be required to reflect the special provisions for trials of medicinal products for gene therapy under the Clinical Trials Regulations. NRES were keen to ensure that the gene and stem cell therapy research community engaged in the discussions on this transition and in November opened a consultation process until 31 December 2010.

Over the years GTAC has continued to ensure delivery of high quality gene therapy research to patients. The Committee has seen and encouraged successful trials progress from the first in man stage through to the phase III stage where hundreds of patients may be treated in order to prove the safety and efficacy of the treatment. This commitment will continue into the future.

The final section of this report details GTAC's membership and external expert advisers who have so generously given of their time in providing expert comments on new applications. Between 1993 and 2010, GTAC has recorded the participation of over 2,000 patients in UK gene therapy trials.

SECTION 1: PROTOCOLS REVIEWED BY GTAC IN 2010

In 2010, GTAC reviewed seven applications. Included in this number were three resubmitted applications that had not commenced in over two years since being given a favourable opinion (GTAC 116, GTAC 128 and GTAC 136).

1.1 Cancer

1.1 Cancer

Cancer is a multi-factorial disease where cells escape the body's control mechanisms and invade, erode and destroy normal tissue. The driving forces in the development of cancer are the cell's genes which can become damaged by a variety of factors such as the environment, diet and life-style. The chance of developing cancer can also be increased by an individual's genetic make-up, for example, in the case of familial breast and ovarian cancer, due to mutations in the BRCA and other genes. There are over 200 different types of cancer that can occur anywhere in the body. Surgery is usually the treatment of choice, however, cancer is less amenable to curative surgery once it has spread beyond the original tumour (metastasised). Gene therapy offers a new, but still experimental, potential treatment that could complement conventional treatments such as surgery, chemotherapy and radiotherapy. In fact, approximately 70% of all gene therapy clinical trials in the UK aim to develop a treatment for cancer.

1.1.1 Melanoma

Melanoma is a very serious form of skin cancer. There are two main types of skin cancer, called melanoma and non-melanoma skin cancer. Melanoma, also known as malignant melanoma, is the more dangerous form of skin cancer. The main cause is exposure to intense sunlight. The number of cases of melanoma is on the increase. In the UK, there are around 40,000 new cases of non-melanoma skin cancer and around 6,000 new cases of malignant melanoma each year. Melanoma begins when the skin pigment (melanin) producing cells in the epidermal layer, called melanocytes, become cancerous. It occurs most commonly on the abdomen, head, neck or limbs. The chance of developing melanoma increases with age, but it affects all age groups and is one of the most common cancers in young adults. As with most tumours, affected cells display cancer specific proteins on their cell surface.

GTAC 172: A Phase I/II trial of SCIB1, a DNA immunotherapy, in the treatment of patients with malignant melanoma

This application wishes to determine the safety and tolerability of three dose levels of SCIB1. Part one will comprise a dose escalation in a cohort of patients with Stage IV or inoperable Stage III melanoma to determine the recommended dose (RD) for the second part of the study.

SCIB1 is a plasmid DNA which is designed to express an engineered human antibody molecule carrying an epitope derived from the TRP-2 melanoma antigen plus two

helper T cells. Injection of the DNA should result in the uptake of the plasmid and expression of the engineered antibody molecule to attack the tumour cells.

Patients will be recruited consecutively into three cohorts. Progression to the next dose of SCIB1 will only take place if adequate safety had been demonstrated at the previous dose. Part Two will then evaluate the safety and tolerability of the recommended dose.

This application was reviewed at the February meeting and received approval.

1.1.2 Blood cancer (leukaemia)

Leukaemia is a cancer of the white blood cells. White blood cells are produced by the bone marrow. There are two main types of white blood cell, lymphoid and myeloid, which are produced from different bone marrow populations. The lymphoid population includes all lymphocytes and plasma cells which are involved in antibody production and other roles in the immune system. All the other blood cells are grouped together as myeloid. The four main types of leukaemia are acute myeloblastic (AML), acute lymphoblastic (ALL), chronic lymphocytic (CLL) and chronic myeloid (CML).

GTAC 128: WT1 TCR gene therapy of leukaemia: A phase I/II safety and toxicity trial.

This application was initially reviewed in 2007 when it received a favourable opinion. As this study had not commenced within two years the Committee re-reviewed the application.

This trial is designed for patients who have either Acute Myeloid Leukaemia (AML) or Chronic Myeloid Leukaemia (CML). The study proposes a strategy of immunotherapy to combat leukaemic cells. These cells have on their surface a protein called Wilms Tumour antigen 1 (WT1). By modifying T cells so that they produce WT1, it is hoped that this will stimulate the immune system to mount an immune attack specifically against WT1 positive cancer cells without damaging normal tissue.

The vector is based on a retrovirus and contains the gene for WT1 as its therapeutic gene load. It is an ex vivo protocol where peripheral blood T cells are collected by leukapheresis before being transduced with the retroviral vector. Through transduction, the vector modifies the leukocytes to display WT1 on their surface. Before re-infusion of the modified T cells, patients will be given chemotherapy drugs. The main objective of the trial is to determine the feasibility of TCR gene transfer in a clinical setting.

The protocol was discussed at the July meeting and received approval.

GTAC 173: WT1 Immunity via DNA fusion gene vaccination in haematological malignancies by intramuscular injection followed by intramuscular electroporation

This is a phase II study in patients with CML and AML based on HLA A2 genotype. Eligible HLA A2 positive patients will be vaccinated with two DNA vaccines.

The aim of the study wishes to examine whether DNA vaccination against Wilms Tumour antigen 1 (WT1) is able to reduce the leukaemia load in patients with chronic myeloid leukaemia (CML) on a stable dose of imatinib by measuring the amount of BCR-ABL and WT-1 transcripts in the blood; to evaluate the effect the vaccination has on time to disease progression and relapse in patients with acute myeloid leukaemia (AML) and to evaluate whether the immune system can be activated by the vaccine. Up to 6 vaccination at monthly intervals will be given and patients who respond to the vaccine may continue receiving vaccinations at three monthly intervals for up to two years.

This application was reviewed at the April meeting and received approval.

1.1.3 Lung Cancer

There are approximately 37,700 people diagnosed with lung cancer each year. For these patients often the cancer is not found early and has already become malignant (it has spread to other parts of the body). This means that the prognosis for patients with such advanced lung cancer is not good and only around 5% of patients diagnosed with advanced lung cancer have a life expectancy greater than 5 years. There are two main types of lung cancer, non-small cell and small cell lung cancer.

GTAC 174: A Phase II trial to assess the safety, immunological activity of TroVax® plus Pemetrexed/Cisplatin in patients with malignant Pleural mesothelioma

This Phase II trial seeks to determine whether an improved response to the tumour associated antigen, 5T4, can be demonstrated in patients with mesothelioma after injection with TroVax. Patients who will be receiving pemetrexed-cisplatin chemotherapy as standard care will be recruited.

They will receive the vaccine alongside this chemotherapy. It is hoped that the vaccine will stimulate the immune system to attach on to mesothelioma cells carrying the 5T4 protein.

TroVax® is well known to the Committee who had reviewed several previous studies using this IMP. TroVax is based on modified Vaccinia Ankara Virus(MVA) which carries the gene for "oncofoetal antigen" or "5T4" which is found on the surface of many cancer cells. The strategy is to immunise patients against 5T4 in an attempt to alert the immune system to the presence of the cancer cells.

This application was reviewed at the December meeting and received approval.

1.2 Haematopoietic Stem Cell Transplantation

Bone Marrow Transplantation (BMT) is used to treat a wide range of conditions, including blood cell cancers, inherited abnormalities of the immune system and certain metabolic disorders. The process relies on the transfer of blood stem cells from a suitable donor to the patient. T cells, which are white blood cells, play a central role in helping the donor stem cells establish themselves in the recipient. T cells' job is to

eliminate foreign molecules (viruses, cancerous cells etc). In recipients of bone marrow transplants this feature of T cells can become a problem. T cells recognise small differences between the donor and the recipient, hence, donor T cells may start attacking normal tissues in their new host. This complication is called Graft-versus-Host-Disease (GvHD). Thus, unless the donor and recipient are very closely matched, T cells have to be removed from the graft, or are heavily suppressed using drugs. Under these circumstances, T cells' beneficial effects are lost and the risk of graft failure or infective problems increases.

GTAC 116 : Phase I/II clinical trial of T cell suicide gene therapy following haploidentical stem cell transplantation

This application was initially reviewed in 2006 when it received a favourable opinion. As this study had not commenced within two years the Committee re-reviewed the application.

Children who receive a bone marrow transplant are at risk of developing graft versus host disease (GvHD). In this study the T cells from the graft obtained from a haploidentical donor (usually a parent) are removed and modified to encode a suicide gene which allows the cells to be destroyed should they cause GvHD in the recipient. The donor T cells are modified using a retrovirus carrying thymidine kinase and can be removed by giving patients the drug Ganciclovir in case GvHD occurs.

This study wishes to recruit children who have primary immunodeficiencies, haematological malignancies or metabolic disorders. The objective is to demonstrate that modified cells safely improve cellular immune reconstitution after haploidentical stem cell transplantation.

This application was reviewed at the July meeting and received approval.

1.3 Cardovascular Disease

Cardiovascular disease is the name given to a wide range of different conditions that affect the heart and/or blood vessels. Examples would include coronary artery disease, stroke, and heart failure. It is the biggest killer in the world today and in Britain one person in three may die from cardiovascular disease (or heart disease). Cardiovascular disease can be acquired through certain behaviours such as smoking, a lack of exercise or a poor diet but it can also be caused through genetic familial factors.

1.3.1 Heart Failure

Heart failure is a condition resulting from any structural or functional cardiac disorder which impairs the ability of the heart to fill or pump enough blood around the body to satisfy bodily needs. It is not the same as cardiac arrest, which is the termination of normal heart function which can ultimately lead to death. Worldwide there are more than 500,000 new cases of heart failure each year and even with the best treatments, heart failure carries a yearly mortality rate of around 10%. There are many different causes for heart failure, including stress, smoking, old age (heart failure often occurs in the over 65s) and obesity. There is also the possibility of genetic family history of heart failure where there are thinner heart muscle walls, leading to a weak heart.

GTAC 136: Investigation of the safety and feasibility of SERCA gene transfer in the human failing heart using an adeno-associated viral vector

This study received a favourable opinion in March 2008 but was resubmitted for review as it had not yet commenced.

Participants in this study will have been fitted with a left ventricular assist devices (LVAD) which are implantable mechanical pumps to bridge them whilst they await a heart transplant (bridge-to-transplant).

The gene therapy vector used in this study is based on AAV6 (adeno-associated virus, serotype 6), which has a good safety record and tropism for the heart muscle. The therapeutic gene is "sarcoplasmic reticulum calcium ion adenosine tri-phosphatase 2a (ATPase 2a)" or SERCA2a. SERCA2a is an energy pump and the amount of calcium it stores determines the intensity of the heart pump. For those with heart failure the pump is poor due to low amounts of SERCA2a and thus a lower calcium store. It is hoped that increasing the amount of SERCA2a (and calcium held) will increase the power of the heart contraction.

The aim of the study is to determine the safety and feasibility of giving an AAV vector expressing SERCA2a to patients undergoing LVAD implantation.

This application was reviewed at the September meeting and approved.

1.4 Neurological Disorders

A neurological disorder is a disorder that involves the nervous system. A neurological disorder can be caused by either a disease, such as multiple sclerosis, or a trauma or injury to the nervous system. Neurological disorders can be remarkably difficult to treat and are often debilitating.

Symptoms of neurological disorders can include the slow loss of coordination, balance, or ability to speak clearly. Often symptoms start with a mild and intermittent twitching or numbness in one extremity, tremors, rigid muscles, slowed motion, difficulty swallowing, loss of automatic movements such as blinking, swinging the arms, and unconscious acts.

Diagnosing some neurological disorders may very well depend on symptoms evaluation alone. Parkinson's for example, has no definitive test and is more likely to be diagnosed through physical examination well after the initial onset of symptoms.

Treatment options vary greatly depending on the neurological disorder. Some neurological disorders become more difficult to treat as they progress. Physical therapy to retain as much physical dexterity as possible is nearly always prescribed. Medication such as dopamine agonists, Levodopa, carbidopa, selegiline, anticholinergics, or amantadine may help during various stages of neurological diseases. Surgery is an option for candidates who can withstand the surgical process and are able to progress through the physical therapy process. Surgical procedures include the destruction of very small amounts of brain tissue in the affected areas, or the stimulation of various parts of the brain.

1.4.1 Parkinson's Disease

Parkinson's disease (PD) belongs to a group of conditions called motor system disorders, which are the result of the loss of dopamine-producing brain cells in the nigrostriatal system of the brain. The four primary symptoms of PD are tremor (trembling) in hands, arms, legs, jaw, and face, stiffness of the limbs and trunk, slowness of movement; and impaired balance and coordination. As these symptoms become more pronounced, patients may have difficulty walking, talking, or completing other simple tasks. PD usually affects people over the age of 50. Early symptoms of PD are subtle and occur gradually. In some people the disease progresses more quickly than in others.

GTAC 170A: A multicentre, open-label study to determine the long term safety, tolerability and efficacy of ProSavin® in patients with bilateral, idiopathic Parkinson's disease

The clinical study investigating a gene therapy medicinal product in Parkinson's disease received GTAC approval in earlier in the year (GTAC 170). The applicants requested that GTAC review this application for a follow up study to assess the long term safety, tolerability and efficacy of ProSavin®

Patients who participated in the ProSavin trial will be eligible to enter into this observational study 12 months after completion of the main study. The participants will be assessed every six months for the second year and then annual monitoring will continue alongside the standard of care therapy for ten years. This follow up study will also be open to those patients who acted as controls in the main study by receiving placebo surgery.

At each visit patients will be given standard tests for Parkinson's disease using evaluation scales, questionnaires and activity tests which are standard for patients with this disease.

This application was given approval at the September meeting.

1.5 Compassionate Use Applications

Medicines legislation (specifically The Medicines for Human Use (Marketing Authorisations Etc.) Regulations 1994/SI 3144) requires that medicinal products are licensed before they are marketed in the UK. However, some patients may have special clinical needs that cannot be met by licensed medicinal products. UK law allows the manufacture and supply of unlicensed medicinal products (commonly known as "specials") subject to certain conditions. The term "compassionate use" refers to the treatment of a seriously ill patient using a new, unapproved drug when no other treatments are available or all treatment options have been tried but found not to be effective.

The Committee informally discussed with clinicians the scientific and clinical implications of using gene therapy investigational medicinal products in patients who would not be eligible to meet the inclusion criteria for entry into a trial.

1.5.1 Compassionate use of Trovax IMP

The investigational medicinal product (IMP) TroVax® is well known to the Committee who had reviewed several previous studies using this IMP. TroVax is based on modified Vaccinia Ankara Virus(MVA) which carries the gene for "oncofoetal antigen" or "5T4" which is found on the surface of many cancer cells. The strategy is to immunise patients against 5T4 in an attempt to alert the immune system to the presence of the cancer cells.

Following a request from the treating physician, the Sponsor sought advice from GTAC to provide TroVax on a compassionate basis to a patient who has advanced metastatic ovarian cancer and who has relapsed following a second course of chemotherapy.

This matter was discussed at the April meeting.

1.5.2 Compassionate use of gene therapy for GTAC 116

The researchers conducting study GTAC 116 discussed with the Committee the possibility of using this gene therapy protocol in a child who did not meet the study's inclusion criteria because the child had already undergone a procedure from a mismatched unrelated donor but has subsequently suffered a relapse of malignancy.

The GTAC 116 study involves children who receive half-matched bone marrow or blood stem cell transplants from a parent. To safeguard against Graft vs Host Disease (GvHD) the researchers wished to genetically modify the donor's T cells to encode a suicide gene mechanism which allows the cells to be destroyed if they cause GvHD in the recipient.

This matter was discussed at the April meeting.

1.5.3 Compassionate use of gene therapy for GTAC 132

The investigators conducting study GTAC 132 discussed with the Committee the implications of retreating a patient. This patient was the first to be treated on this study earlier this year. Sadly there has been limited immune recovery and the clinicians felt that the best option would be to implement a further procedure that may restore effective immune function before the patient's clinical state deteriorates.

This matter was discussed at the September meeting.

1.6 Pre-proposal Presentations

The Committee has always supported early discussions with researchers who are very close to bringing their research to the clinic. Such an exchange of information on the

preclinical research conducted and the data obtained to date, together with advice from both the GTAC Committee members and MHRA advisors enhances the quality of the research that will be conducted in the future. For a number of years MHRA and GTAC have worked collaboratively to meet with applicants who wish to hold such informal discussions.

1.6.1 Pre-proposal presentation on the clinical application of hydrodynamic gene delivery to the liver

Committee members were given a presentation on the pre-clinical work to date into regional hydrodynamic gene delivery to the liver.

The presentation was followed by a general discussion on the data obtained to date. The Committee was of the opinion that this research is still at a very early but pivotal stage and made several suggestions for further areas to be considered.

This matter was discussed at the February meeting.

1.6.2 Pre-proposal presentation on research in a coronary artery bypass graft

Coronary artery bypass graft (CABG) surgery remains the cornerstone of treatment for patients with severe multi-vessel coronary artery disease, particularly in patients with diabetes and impaired left ventricular function. Saphenous vein bypass grafts (SVG) are the most widely used grafts but the long term success of CABG is limited by SVG occlusion.

This team of researchers gave a presentation on their pre-clinical work to date in developing viral intervention strategies to block neointima formation associated with failure of CABG procedures. Ultimately they wish to undertake a randomised, placebo controlled clinical trial whose primary objective is to determine whether genetic modification of vein grafts to overexpress TIMP3 is safe and effective in reducing graft atherosclerosis in patients undergoing CABG surgery.

This matter was discussed at the April meeting.

1.6.3 Pre-proposal presentation on research into lentiviral vectors in ADA SCID

The researchers attended to give a presentation on their development of a lentiviral vector encoding the human ADA gene to replace the gammaretroviral vector which was used for previous studies of ADA SCID.

They presented data on preliminary studies which have shown that this vector is capable of efficient transduction of different haematopoietic cell lineages and of CD34+ cells from ADA deficient patients. The development of lentiviral vectors would improve the safety profile with regard to insertional mutagenesis which was seen as a possible adverse event in studies using a gammaretroviral vector.

This matter was discussed at the September meeting.

1.6.4 Pre-proposal presentation on survival motor neuron (SMN) replacement therapy for spinal muscular atrophy

Spinal muscular atrophy (SMA) is a recessive autosomal disorder, the infantile form being the most severe which is often fatal by 3 years of age. It is caused by mutation of the SMA gene which is characterised by degeneration of motor neurons causing muscle weakness and atrophy of the muscles.

The Committee received a presentation on the early pre-clinical research in this devastating disease for which there is no effective treatment. The investigator has developed a vector system based on self complementary adenoassociated virus (scAAV) that crosses the blood-brain barrier and allows fast, robust and long-lasting gene transfer.

The researcher discussed with the Committee his findings to date and also whether their current plan would deliver a product able to meet the regulatory requirements so that they may proceed to initiating a clinical trial.

This matter was discussed at the December meeting.

1.7 Amendments to Ongoing Protocols

In 2010, the GTAC Committee members reviewed over 50 applications for substantial amendments which were submitted for ongoing studies.

SECTION 2: REGULATORY AND GUIDANCE ISSUES

2.1 Public Consultations Considered

In 2010 GTAC discussed and contributed comments to the following consultations:

2.1.1 Detailed guidelines on good clinical practice specific to advance therapy medicinal products

These guidelines had been developed to address specific issues related to good clinical practice for clinical trials involving advanced therapy medicinal products and supplement the principles and detailed guidelines set out in the Directive.

Of particular relevance to GTAC was Section 10 on Ethics Committees which the Committee discussed in depth.

2.1.2 Concept Paper on the Development of a guideline on the Risk-Based approach according to Annex 1, Part IV of Dir 2001/83/EC applied to advanced therapy medicinal product

The EMEA issued a concept paper wishing to provide the background and rationale on drawing up a guideline to determine the extent of data required for a Marketing Authorisation Application for an advanced therapy medicinal product.

The Committee noted the content of this paper.

2.1.3 Concept paper on the revision of the note for guidance on the quality, pre-clinical, and clinical aspect of gene transfer medicinal products

The Committee discussed this concept paper which proposed a revision of the Note for guidance on the Quality, Preclinical and Clinical Aspects of Gene Transfer Medicinal Products that came into effect in 2001. The revised guideline referred to a number of recently developed scientific guidelines as well as complying with the Regulations on Advanced Therapy Medicinal Products.

2.1.4. Questions and answers on gene therapy paper

The EMEA have issued a document which sets out a harmonized position on issues that can be subject to different interpretation or require clarification on gene therapy medicinal products.

Committee members noted the content.

2.1.5 The European Medicines Agency Road Map to 2015: the Agency's contribution to science, medicines, health

The EMEA issued a draft document setting out its longer term strategy to contributing to better promotion and protection of public health, improving the regulatory environment for medicinal products and helping to stimulate innovation, research and development in the EU.

Committee members noted the content.

2.1.6 Consultation on Stem Cell-based Medicinal Products

The European medicines Agency (EMA) has issued a reflection paper on medicinal products covering specific aspects related to stem cells based medicinal products. The Committee members noted the content.

2.1.7 EMA Consultation paper: guideline on quality, non-clinical and clinical aspects of medicinal products containing genetically modified cells

The EMA Committee for the Medicinal Products for Human Use (CHMP) have issued a consultation paper on their proposed guidance for the development and evaluation of medicinal products containing genetically modified cells intended for use in humans. Its focus is on the quality, safety and efficacy requirements of genetically modified cells which are developed as medicinal products.

Committee members noted the content of this paper at the July meeting.

2.1.8 CONSULTATION: CHMP/CAT Position statement on Crutzfeldt-Jacob Disease and advance therapy medicinal products

The EMA Committee for the Medicinal Products for Human Use (CHMP) have issued a consultation paper on their proposed position statement on the possibility of transmitting CJD or vCJD agents into advanced therapy medicinal products (ATMP).

Committee members noted the content of this paper at the September meeting.

2.1.9 Consultation from the Academy of Medical Sciences - Call for evidence on the function and scope of a proposed 'single research regulator'.

In early 2010, the Academy of Medical Sciences was commissioned by Government to undertake an independent review of the regulation and governance of UK medical research. A first call for evidence inviting views on issues relevant across the regulation and
governance framework closed in June 2010.

Following the publication of the Department of Health's report on arm's-length bodies (ALB report) in July, the Academy issued a second call for evidence to provide all interested parties with an oopportunity to consider the proposals in the ALB report with direct relevance to the regulation of medical research.

The GTAC Committee contributed to this exercise in September 2010.

2.2 Issues specific to GTAC

2.2.1 Assessment of Mouse Feeder Cells

In previous years the Department of Health had asked the National Institute of Biological Standards and Controls (NIBSC), which also runs the UK Stem Cell Bank, to prepare a seed stock of mouse 3T3 fibroblasts. These cells act as "feeder cells" for human cell cultures used in both corneal stem cell transplantation and skin grafts. The

new bank has been prepared to replace the somewhat random collection of various mouse 3T3 feeder cell lines in use around UK transplantation centres. The NIBSC cell line appears to have been rigorously analysed under clean room facilities and has now been issued for release to a number of transplantation centres.

In 2009 the NIBSC asked GTAC to review the preparation of this seed stock for use in the culturing of cells that ultimately would be used in transplantation procedures. At the February meeting the Committee was given a presentation on the provenance of the 3T3 cells and it was agreed that a Sub-Committee would evaluate the data as these cells would be used in human embryonic stem cell research that the Committee would review in the future.

2.2.2 Guidance on Clinical Trials Involving Cell Therapy

Working with the Clinical Trials Unit of the MHRA, a 'Points to Consider' document for UK stem cell clinical trials was discussed at the February meeting. It is believed that it is still too early to offer prescriptive regulatory and ethical advice to stem cell researchers, but there are a number of issues that need to be thought through before proceeding to a clinical trial involving stem cells. These include immunological responses of the patients and transplanted cells, the genetic stability of cells, long term monitoring, as well as age and gender issues in patients. The recently issued EC consultation document 'Detailed guidelines on good clinical practice specific to advanced therapy medicinal products' is relevant to this guidance especially Section 10 in relation to GTAC's role.

Committee members discussed this draft document and commented that this would be a useful paper to guide researchers in developing cell therapy trials. Several minor suggestions regarding clarity of wording were recommended which would contribute to the document which would be published on the GTAC website in the near future.

SECTION 3: UPDATE OF CLOSED UK CLINICAL TRIALS

The following are short summaries provided by researchers of gene therapy trials that have closed in 2010. GTAC would like to thank all researchers who have contributed to this section, which builds on initiatives in previous reports. The summaries are essentially unedited and reflect the views of the researchers.

3.1 Cancer

3.1.1 GTAC 083: A Phase I/II safety study of MetXia-OB83 in patients with pancreatic cancer

Phase of Development: Phase I

Objectives:

Primary Objectives:
1. To assess the safety of ascending doses of MetXia administered via intra-arterial injection (percutaneous selective arterial catheterisation) into the pancreas of patients with adenocarcinoma of the head of the pancreas, requiring bypass for biliary or gastric obstruction.

2. To assess the optimal dose of cyclophosphamide (CPA) delivered by intra-arterial infusion into the tumour for use with MetXia in this patient group.

Secondary Objectives:
1. To assess the clinical response (tumour response rates, time to disease progression and median survival) of tumours in non-resectable patients receiving MetXia in combination with CPA delivered to the tumour by local intra-arterial infusion.

2. To assess the immunological response to tumour antigens.

Number of Patients:

A total of 35 patients were enrolled in the study of which 26 (74%) were included in the intent-to-treat (ITT) population and 14 (40%) were included in the per-protocol (PP) population. The most common reason for exclusion from the ITT population was that the patients did not receive MetXia (1 patient in Part 1 and 8 patients in Part 2).

Diagnosis and Main Criteria for Inclusion:

Patients were eligible for the study if there was strong evidence of inoperable adenocarcinoma of the pancreas; had stage III, IVa or IVb unresectable disease; were aged 18 years or more; were Karnofsky performance status >70%; were fit for surgery (if bypass surgery required); were expected to survive longer than 3 months; had no other 2.0≥known malignancy; had total white blood cell (WBC) count x 109/L, platelet 100 x 10≥count 9/L and serum creatinine 0.15 mmol/L; and were able to give written≤ informed consent and to comply with the protocol.
Patients were excluded from the study if they were pregnant, lactating, or not using effective contraception if applicable; had undergone major surgery within the previous 14 days; had undergone radiotherapy or chemotherapy in the previous 4 weeks; had an intercurrent serious infections within the previous 28 days; had a life threatening illness unrelated to cancer; had clinical evidence of cerebral metastases; had a previous history of significant cardiovascular disease, epilepsy, allergy or major psychiatric illness; had renal or hepatic insufficiency; or were unable to give informed consent.

Statistical Methods:

This was a pilot study; therefore, no formal statistical analysis was planned or performed. The data were summarised descriptively. Survival was measured from the day of the first administration of MetXia until the date of death.

Summary of the Results (ITT Population):

Three (38%) of the patients in Part 1 of the study and 11 (61%) of the patients in Part 2 were male. The mean ages of the patients were 64.5 years (Part 1) and 63.4 years (Part 2). All of the patients were white.

Safety:
Of the 26 patients in the ITT population, 25 (96%) patients experienced a total of 365 treatmentemergent AEs: 7 (88%) patients in Part 1 experienced 119 AEs and 18 (100%) patients in Part 2 experienced 246 AEs. The most frequently reported AEs were abdominal pain and vomiting (both reported by 6 [75%] patients in Part 1 and 8 [44%] patients in Part 2) followed by nausea (5 [63%] patients in Part 1 and 6 [33%] patients in Part 2) and hypokalaemia (4 [50%] patients in Part 1 and 6 [33%] patients in Part 2). Nineteen (73%) patients experienced SAEs (5 [63%] patients in Part 1 and 14 [78%] patients in Part 2) and 10 (38%) patients experienced a total of 16 AEs that resulted in death (4 [50%] patients with 10 AEs in Part 1 and 6 [33%] patients with 6 AEs in Part 2). Ten (38%) patients experienced AEs for which dosing was interrupted or discontinued (2 [25%] patients in Part 1 and 8 [44%] patients in Part 2). None of the AEs were considered related to MetXia. Thirteen (50%) patients experienced AEs that were considered related to CPA (no patients in Part 1; 13 [72%] patients in Part 2) and 25 patients experienced AEs that were considered related to disease (7 [88%] patients in Part 1 and 18 [100%] patients in Part 2). There were no unexpected findings in laboratory variables and no clinically meaningful changes in vital signs in the 3 hours after dosing with MetXia. The Karnofsky performance scores of 8 of the 10 patients with follow-up information were lower at follow-up than at screening; 1 patient had no change and 1 patient had an improvement from 80% at screening to 90% at follow-up.

3.1.2 GTAC 105: An exploratory study of the safety and biological activity of OncoVex^{GM-CSF} in combination with radiotherapy and cisplatin in the treatment of locally advance epithelial cancer of the head and neck.

This trial was to find out more about a new biological therapy called OncoVEX^{GM-CSF} to treat head and neck cancer. Doctors usually treat head and neck cancer with surgery, radiotherapy or chemotherapy.

OncoVEX^{GM-CSF} was injected directly into the cancer. The treatment used a virus which had been changed to make a natural substance called GM-CSF. The virus was a form of the common cold sore virus. The normal strain of the virus had been changed so that it was unlikely to be at all harmful, except to cancer cells. The researchers hoped that the virus would kill cancer cells and the GM-CSF would boost the immune system to help fight the cancer.

In this trial they were using OncoVEX^{GM-CSF} alongside radiotherapy and chemotherapy. The aims of the trial were to find out

- The best dose of OncoVEX^{GM-CSF} to give

- How well OncoVEX^{GM-CSF} worked alongside radiotherapy and chemotherapy for advanced head and neck cancer

Recruitment
Start 01/11/2005
End 29/02/2008

Phase
Phase 1/2

Summary of results
The trial team worked out the highest dose of OncoVEX^{GM-CSF} that could be given safely in this situation. They also found that by having these injections alongside standard treatment, cancer came back in fewer people than would usually be expected.

The trial recruited 17 people who had a head and neck cancer that had spread to their lymph nodes. Everybody taking part had treatment with radiotherapy and cisplatin chemotherapy.

The researchers also injected OncoVEX^{GM-CSF} directly into each person's cancer on up to 4 separate occasions.

- Scans showed that the cancer had got smaller or disappeared in 14 people
- Out of 15 people who had surgery to remove the lymph nodes in the neck (a neck dissection), the researchers found cancer in the lymph nodes of only 1 person

The trial team followed up the people in the trial for an average of just under 2½ years. They found that the cancer hadn't come back in the head and neck area in any of the people taking part, but in 4 people, the cancer had spread somewhere else in the body.

The researchers concluded that OncoVEX^{GM-CSF} injections can be given safely alongside radiotherapy and chemotherapy. Although this study was small, cancer did respond to treatment in 14 people. So the researchers plan to look at this treatment in trials involving larger numbers of people.

We have based this summary on information from the team who ran the trial. The information they sent us has been reviewed by independent specialists (peer reviewed) and published in a medical journal. The figures we quote above were provided by the trial team. We have not analysed the data ourselves.

3.2 Infectious Disease

3.2.1 GTAC 118: Phase I study evaluating the safety and immunogenicity of a new TB vaccine, MVA85A, in healthy volunteers who are infected with HIV.

MVA85A is a novel viral vector vaccine against tuberculosis designed to act as a boosting immunisation in people who have already received BCG. In clinical trials it has

been found to be safe in healthy BCG naïve people, people who are BCG vaccinated, and also people with latent TB infection.

In this phase I trial the primary objective was to assess its safety for the first time in HIV infected adults. The secondary objective was to measure the strength and breadth of the immune response generated by the vaccine in these volunteers. This is an important group of people to study because in parts of the globe where a better TB vaccine is most needed, there is a high incidence of TB, and co-infection with HIV and TB is common and devastating.

HIV infected volunteers were recruited from four hospitals in southern England, but were excluded if they had advanced HIV disease or were already on anti-retroviral treatment. To recruit 20 volunteers into two groups of 10, it was necessary to screen 35 people. The first group received a single low dose intradermal injection of MVA85A and the second group received a single standard dose by the same route. Volunteers were followed up for one year. Five of the volunteers also had latent TB infection.

The results showed that the vaccine was well tolerated and the occurrence and severity of side effects was similar at the two doses. Volunteers experienced a local reaction at the vaccine site just as expected with intradermal injection of MVA85A but it was not substantially different from HIV negative people. To find out if the vaccine had any effect on the progression of HIV infection in these people, the amount of circulating virus and the level of immune cells was measured throughout the trial, and no effect was seen.

The vaccine-specific immune responses measured in these volunteers were strong and long lasting. The pattern of immune responses was similar to previous trials with MVA85A, but overall the responses were not quite as strong as in HIV negative people. This raises the possibility that a second boosting dose of the vaccine might be beneficial in HIV infected people.

It is not known yet if MVA85A might give protection against TB. Nevertheless, demonstrating that this vaccine is safe and well tolerated in an important target population is crucial. It paves the way for further safety and efficacy trials of MVA85A to take place in HIV and TB endemic areas.

The main challenge of this trial was recruitment. It took 32 months to complete enrolment having increased the number of trial sites from one to four. It turned out that the majority (85%) of the volunteers were male although both groups were comparable. Coordinating the volunteers' routine clinical care at multiple sites with their trial visits also required careful planning.

The analysis of the completed trial will shortly be published in a peer review journal.

SECTION 4: ANNEXES

ANNEX A: GTAC MEMBERS AND ATTENDEES IN 2010

- Professor Martin Gore (Chairman), Consultant Medical Oncologist, The Royal Marsden Hospital, London.
- Professor Andrew Baker, Professor of Molecular Medicine, University of Glasgow.
- Professor Kathleen Bamford, Consultant Medical Microbiologist and Visiting Professor, Imperial College Healthcare NHS Trust and Imperial College
- Mrs Deborah Beirne, Nurse Consultant and Assistant Director of Clinical Research, St James Hospital, Leeds.
- Professor Hilary Calvert, Director of Anticancer Drug Discovery and Development at University College London Partners.
- Professor Mary Collins, Division of Infection and Immunity, Royal Free and University College Medical School.
- Professor Steven Dunnett, Cardiff School of Biosciences, University of Cardiff .
- Ms Claire Foster-Gilbert, Chief Executive The Ethics Academy.
- Professor Terence Hamblin, Professor of Immunohaematology, University of Southampton; Consultant Haematologist with Southampton University Hospitals and Kings College Hospital, London.
- Dr Peter Harris, Vice President Oncology and Renal Medicine, Genzyme Europe Research .
- Mrs Rachel Haynes, Director of Public Affairs, Arthritis Care, London
- Mr Alastair Kent, Director Genetic Interest Group, London .
- Dr Adrian Lepper, Retired Chartered Engineer, Hertfordshire.
- Dr Stephen Minger, Head of Research and Development for Cell Technologies, GE Healthcare.
- Mrs Fiona Sandford, Patient Advocate, Hertfordshire.
- Dr Justin Turner, Queen's Counsel.
- Dr Michael Waterhouse, Television Producer and Author, Southborough.

Observers

Department of Health:

- Miss Angelica Belen
- Miss Tara George

Health and Safety Executive:

- Dr David Brown
- Dr Paul Logan
- Dr Michael Paton

Medicines and Healthcare products Regulatory Agency (MHRA):

- Dr Elaine Godfrey
- Mr David Jones
- Dr Jimmy McBlane
- Dr Riaz Zuhrie

National Research Ethics Service (NRES):

- Mr David Neal

Secretariat (Department of Health)

- Dr Mark Bale
- Dr John Connolly
- Mrs Mamta Malhotra-Bajaj
- Mr Colin Pavelin
- Dr Suzanne Paylor
- Mrs Halina Pounds

Payment of members

Fees are payable to Members at a rate of £148.59 per meeting, £180.40 per meeting for the Chair, and members are reimbursed for all reasonable travelling expenses.

ANNEX B: MEMBERS' ATTENDANCE IN 2010

Name	Meetings attended in 2009
Professor Martin Gore	April, July, September, December
Professor Mary Collins	February, (from item 2.3 and up to item 4.0)April (up to item 7.0), July, September (from item 2.0)
Professor Andrew Baker	February, April, September (up to item 8.0) , December (up to item 8.0)
Dr Kathleen Bamford	February, April, July, December
Ms Deborah Beirne	February, April, July, September, December
Professor Hilary Calvert	February, April, July, September, December
Professor Steven Dunnett	February, September, December
Ms Claire Foster	February, April (up to item 8.0), September, December
Professor Terry Hamblin	February, December
Dr Peter Harris	February (up to item 4.0), April, July, September, December
Mrs Rachel Haynes	February, April (up to item 3.0), July (up to item 3.0), September, December
Mr Alastair Kent	February, (up to item 3.0), April, July, December
Dr Adrian Lepper	February, April, July, September, December
Dr Stephen Minger	September, December
Mrs Fiona Sandford	February, July, December
Dr Justin Turner	February, April, September (from item 3.0), December
Dr Michael Waterhouse	February, April, September, December

ANNEX C: REGISTER OF MEMBERS INTERESTS IN 2010

GTAC MEMBER	DECLARED INTEREST
Professor Andrew Baker	None
Prof Kathleen Bamford	Chair HHT Gene therapy and genetic modification safety committee Companies who have paid expenses or provided financial support for attendance at meetings, or paid honoraria include Pfizer/Pharmacia Ltd, Gilead Ltd, Wyeth Ltd, Bayer Ltd, Baxter. Research funding: Pfizer Advisory boards: Pfizer, Baxter Fundraising committee: International Child Care Trust
Mrs Deborah Beirne	Post is supported by Cancer Research UK. Work involves gene therapy trials
Professor Hilary Calvert	Occasional Advisory boards for: Astex, Astellas, Clovis Oncolgy and GSK.
Professor Mary Collins	None
Professor Steven Dunnett	None
Ms Claire M Foster-Gilbert	Chief Executive, the Ethics Academy (registered charity no 1108210) Member Unilever's Central Research Ethics Advisory Group Member British Medical Associations' Medical Ethics Committee
Professor Martin Gore	Speaker bureau and advisory boards: Roche, GSK, Novartis, Bayer, Pfizer, Schering Plough, Bristol Myers Squibb, Aveo, AstraZeneca, Astellas
Professor Terence Hamblin	Ad hoc consultant to Genzyme and Advancell. Paid employment as Editor of Leukemia Research by Elsevier Publications. Ad hoc medico-legal consultant.
Dr Peter Harris	Genzyme employee and share option holder No other consultancies
Mrs Rachel Haynes	None
Mr Alastair Kent	Patient representative on the Committee for Advanced Therapies. Member of Clinigene International Advisory Committee
Dr Adrian Lepper	Independent consultancy assignments. Director and Trustee– Chiltern Society Ltd. Director and Trustee – Chiltern Woodland Project Ltd. Wife has a small shareholding in Glaxo Smith Kline

	01 June 2009 – Governor of Royal Brompton and Harefield NHS Foundation Trust. Chair of Organ Donation Committee.
Dr Stephen Minger	PhD studentships jointly funded by GSK/MRC and Novartis/MRC, received honoraria for research seminars from GSK, Novartis, Merck until August 2009 Co-Organiser of London Regenerative Medicine Network which is partially funded by GSK until August 2009 Member of Progress Educational Trust Advisory Panel until August 2009 Paid consultant to Vertex Pharmaceutical Company (fees placed into research accounts) until August 2009 Unpaid advisor to Nikon Corp until August 2009
Mrs Fiona Sandford	None
Dr Justin Turner	None
Dr Michael Waterhouse	None

ANNEX D: EXTERNAL EXPERT ADVISERS TO GTAC IN 2010

GTAC is extremely grateful to all its expert advisers for their support in the review of applications and for their input of expertise and advice in 2009. These included:

Dr Adil Daud, Melanoma Clinical Research, University of California, San Francisco, USA

Prof Farzin Farzaneh, Kings College London

Prof Christian Ottensmeier, Southampton University Hospitals, Southampton

Prof Viggo Van Tendeloo, University of Antwerp, Belgium

ANNEX E: SUMMARY OF UK GENE THERAPY CLINICAL RESEARCH 1993-2010

GTAC NO.	PROTOCOL NAME	DETAILS	CENTRE	OUTLINE APPROVAL	VECTOR	GENE	CELL LINE	NO. OF PATIENTS
01	Adenosine deaminase gene transfer in a child with severe combined immunodeficiency syndrome	SCID-ADA	Institute of Child Health/Great Ormond Street Hospital	1-93	Retrovirus	ADA	pOAM-P1	1 CLOSED
02	Gene Therapy Research for Cystic Fibrosis	CF Nasal trial	Royal Brompton Hospital	3-93	Plasmid	CFTR	*E. coli* DM5α	15 CLOSED
03	A pilot study of idiotypic vaccination for follicular B-cell lymphoma using a genetic approach	B-cell lymphoma	MRC Cambridge	7-93	Plasmid	anti-idiotype immunoglobulin	*E. coli*	7 CLOSED
04	Use of gene transfer to determine the role of tumour cells in bone marrow used for autologous transplantation and the efficiency of immunomagnetic "purging" the bone marrow	Neuroblastoma	ICRF Bristol	2-94	Retrovirus	LNL-6/neo G1N-neo	PA317	Trial withdrawn
05	Gene Therapy for metastatic melanoma: Assessment of expression of DNA constructs directly injected into metastases	Metastatic melanoma	ICRF Oxford	5-94	plasmid	IL-2	*E. coli* JM109	23 CLOSED
06	The treatment of	Metastatic	Institute of Cancer	2-94	Retrovirus	IL-2	GP+env AM12	12

GTAC NO.	PROTOCOL NAME	DETAILS	CENTRE	OUTLINE APPROVAL	VECTOR	GENE	CELL LINE	NO. OF PATIENTS
	metastatic malignant melanoma with autologous melanoma cells that have been genetically engineered to secrete IL-2	melanoma	Research; Royal Marsden Hospital					CLOSED
07	Towards gene therapy for cystic fibrosis	CF Nasal trial	Oxford; Cambridge	2-94	Plasmid	CFTR	*E. coli*	18 CLOSED
08	Gene Therapy Research for Cystic Fibrosis	CF Nasal trial	Edinburgh	5-94	Plasmid	CFTR	*E. coli*	16 CLOSED
09	Gene Therapy Research for Cystic Fibrosis	CF Lung trial	Royal Brompton Hospital	9-94	Plasmid	CFTR	*E. coli*	16 of 16 CLOSED
10	Transfer of the Human Multi-drug Resistance Gene into the Haemopoietic Cells of Patients Undergoing High Dose Therapy and Autologous Stem Cell Transplantation for Malignant Lymphoma	Lymphoma	University College London Medical School	12-94	Retrovirus	MDR-1	AMI2M1	3 CLOSED
11	Genetic prodrug activation therapy for breast cancer	Breast Cancer	Hammersmith Hospital	10-95	plasmid	Cytosine deaminase	*E. coli*	12 CLOSED
12	Use of a recombinant vaccinia virus for therapy of cervical cancer	Cervical Carcinoma	University of Wales, Cardiff	6-95	Vaccinia	TA-HPV	MRC5	1+8 CLOSED
12A	Use of a recombinant Vaccinia vaccine (TA-HPV) to treat Cervical intraepithelial neoplasia III	Cervical intraepithelial neoplasia III	University of Wales, Cardiff	5-96	Vaccinia	HPV E6 and E7	MRC5	12 CLOSED
12B	Use of a recombinant	Cervical	University of Wales,	8-97	Vaccinia	HPV E6	MRC5	8

GTAC NO.	PROTOCOL NAME	DETAILS	CENTRE	OUTLINE APPROVAL	VECTOR	GENE	CELL LINE	NO. OF PATIENTS
	Vaccinia vaccine (TA-HPV) to treat Cervical intraepithelial neoplasia III	intraepithelial neoplasia III	Cardiff; University of Manchester			and E7		CLOSED
12C	Use of recombinant Vaccinia vaccine (TA-HPV) to treat Vulval intraepithelial neoplasia III	Vulval Intraepithelial Neoplasia III	St Mary's Hospital, Manchester	1-00	Vaccinia	HPV E6 and E7	MRC5	18 CLOSED
12 D	Use of a recombinant Vaccinia vaccine (TA-HPV) to treat Ano-genital intraepithelial neoplasia III	Ano-genital intraepithelial neoplasia III	Addenbrooke's Hospital, Cambridge	4-00	Vaccinia	HPV E6 and E7	MRC5	12 CLOSED
13	A proposal to study the efficacy of transplantation of autologous retroviral transduced bone marrow in patients homozygous for the W402X mutation (Hurlers syndrome)	Hurlers Syndrome	Royal Manchester Children's Hospital, Manchester	12-95	Retrovirus	pLX	GP+env AM12	3 CLOSED
14	Phase I, Open-Label, Dose-Escalation Trial of Intra-Tumoral Injection with an E1B Attenuated Adenovirus ONYX-015, into Recurrent and Locally Advanced p53(-) Squamous Cell Tumours of the Head and Neck	Head and Neck Cancer	Beatson Oncology Centre, Glasgow	1-96	Adenovirus	E1B deleted	HEK293	22 CLOSED
14A	A phase II trial of intravenous cisplatin, 5-FU and intratumoral	Head and Neck Cancer Phase II Study	Beatson Oncology Centre, Glasgow	7-97	Adenovirus	E1B deleted	HEK293	37 CLOSED

GTAC NO.	PROTOCOL NAME	DETAILS	CENTRE	OUTLINE APPROVAL	VECTOR	GENE	CELL LINE	NO. OF PATIENTS
	injection with ONYX-015 into recurrent, chemotherapy naive squamous cell tumours of the head and neck							
14 B	Phase I, Open-Label, Dose-Escalation Trial of Intraperitoneal Injection with an E1B Attenuated Adenovirus in patients with recurrent/refractory ovarian carcinomas	Recurrent/ refractory ovarian cancer	Beatson Oncology Centre, Glasgow	2-97	Adenovirus	E1B deleted	HEK293	12 CLOSED
15	Towards gene therapy for Cystic Fibrosis	CF Nasal Trial	Oxford/Cambridge/Leeds/ Manchester Consortium	5-96	Plasmid	CFTR	*E. COLI*	11 CLOSED
16	Phase I study in patients with recurrent metastatic squamous cell carcinoma of the head and neck using SCH 58500 (rAd/p53)	Head and Neck Cancer	Institute of Cancer Research; Royal Marsden Hospital	9-96	Adenovirus	p53	HEK293	Trial never commenced in UK CLOSED
17	Gene therapy for Cystic Fibrosis Delivery to nasal epithelium and lung by nebulisation of the pCFICFTR/#67	CF Lung and Nasal Trial	Royal Brompton Hospital	11-96	Plasmid	CFTR # 67	*E. COLI* TGI	16 CLOSED
18	A Phase I dose-escalation study of intratumoral injection with modified HSV Type I (ICP 34.5$^-$) into primary and recurrent malignant glioma	Glioblastoma	Beatson Oncology Centre, Glasgow	12-96	HSV	ICP34.5 deleted	BHK 21/C13	9 CLOSED

GTAC NO.	PROTOCOL NAME	DETAILS	CENTRE	OUTLINE APPROVAL	VECTOR	GENE	CELL LINE	NO. OF PATIENTS
18A	A Phase I dose-escalation study of intratumoral injection with modified HSV Type I (ICP 34.5⁻) into primary and recurrent malignant glioma	Glioblastoma	Beatson Oncology Centre, Glasgow; Institute of Neurological Sciences, Glasgow; Queen Elizabeth Hospital, Birmingham	7-99	HSV	ICP34.5 deleted	BHK 21/C13	12 CLOSED
18B	A study of the safety of the modified Herpes simplex virus (HSV 1716) when injected into tumour bearing brain following resection of recurrent or newly diagnosed high grade glioma	Glioblastoma	Beatson Oncology Centre, Glasgow.	11-00	HSV	ICP34.5 deleted	BHK 21/C13	8 CLOSED
19	GTI 0115 radiation and infection of murine cells producing HSV TK vector followed by intravenous ganciclovir against the efficacy of surgery and radiation in the treatment of newly diagnosed previously untreated glioblastoma (tumour site).	Glioblastoma	Beatson Oncology Centre, Glasgow; Institute of Neurological Sciences, Glasgow	3-97	Retrovirus	TK	PA317	Trial withdrawn CLOSED
20	A clinical trial with Ad-5CMV-p53 vector in patients with ascites formation.	Gastrointestinal cancer, malignant cancer ascites	Royal Marsden Hospital, London	4-97	Adenovirus	P53	Hek293	1 CLOSED
21	Phase II study of immunotherapy of advanced breast cancer by repeated intramuscular injection of recombinant	Breast Cancer	Guy's Hospital, London	11-97	Vaccinia	MUC-1 IL2	-	14 CLOSED

GTAC NO.	PROTOCOL NAME	DETAILS	CENTRE	OUTLINE APPROVAL	VECTOR	GENE	CELL LINE	NO. OF PATIENTS
	vaccinia viruses containing sequences coding for human MUC-1 and IL2 (TG1031).							
22	A multiple ascending dose study evaluating the safety and the gene transduction into malignant cells after the administration of EIA-lipid complex by intra-peritoneal administration in patients with epithelial ovarian cancer who over express HER-2/neu.	Ovarian Cancer	The John Radcliffe Hospital, Oxford; Guy's and St Thomas's Cancer Centre, London; Royal Marsden Hospital, London; St George's Medical School, London.	9-97	Plasmid	E1A HER2/ neu	*E. coli* STBL2	22 CLOSED
23	A pilot study of recombinant CEA vaccinia virus vaccine with post vaccination CEA peptide challenge in combination with 5-fluorouracil and folinic acid in the treatment of colorectal cancer (Phase I subcutaneous).	Colorectal Cancer	Queen Elizabeth Hospital, Birmingham	3-98	Vaccinia	CEA	CV1	0 CLOSED
24	A phase I study of intraperitoneal administration of a replication deficient adenovirus carrying a nitroreductase gene in ovarian cancer patients.	Ovarian Cancer	City Hospital NHS Trust and University Hospital NHS Trust Birmingham	3-98	Adenovirus	Nitroreductase	HEK-293	0 CLOSED

GTAC NO.	PROTOCOL NAME	DETAILS	CENTRE	OUTLINE APPROVAL	VECTOR	GENE	CELL LINE	NO. OF PATIENTS
25	A multiple ascending dose study evaluating the safety and gene transduction into malignant cells after administration of E1A-lipid complex by intratumoral injection with unresectable or metastatic head and neck tumours.	Head and Neck	Royal London Hospital; Charing Cross Hospital	Submission withdrawn	Plasmid	E1A	HEK293	Application withdrawn
26	A study of dose requirements, safety and local efficacy of intratumoral injection of the genetically modified non-virulent herpes simplex virus HSV ICP 34.5 negative mutant 1716 into accessible soft tissue nodules of secondary malignant melanoma.	Malignant Melanoma	Glasgow Western Infirmary and Southern General Hospital, Glasgow	9-98	HSV	ICP34.5 deleted	BHK-21/C13	5 CLOSED
27	The use of MetXia-P450 for the treatment of advanced breast cancer (Phase I/II intratumoral).	Breast Cancer	The Churchill Oxford	10-98	Retrovirus	Cytochrom e P450	TEFLY-A	12 CLOSED
28	A phase I/II study of hepatic artery infusion with WTP53-CMV-AD in primary metastatic malignant liver tumours.	Liver Cancer	Hammersmith Hospital, London	Application Withdrawn	Adenovirus	p53	HEK293	Application withdrawn
29A	A Phase I/II pilot study of idiotypic vaccination for follicular B-cell	B-cell lymphoma	Royal Bournemouth Hospital; Southampton General Hospital; Christie	5-99	Plasmid	Idiotypic DNA vaccination	*E. coli* JM109	25 of 25 CLOSED

GTAC NO.	PROTOCOL NAME	DETAILS	CENTRE	OUTLINE APPROVAL	VECTOR	GENE	CELL LINE	NO. OF PATIENTS
	lymphoma using a genetic approach (LIFTT). EudraCT: 2005-002967-99		Hospital Manchester					
29B	A pilot study of donor idiotypic vaccination for the purpose of targeted post-transplant immunotherapy following allogenic bone marrow transplantation for multiple myeloma "EDLI"	Multiple myeloma	Southampton General Hospital; Nottingham City Hospital; University College London	5-00	Plasmid	Idiotypic DNA vaccination	*E. coli* JM109	3 of 5-10
29C	Phase I/II study of idiotypic vaccination for multiple myeloma using a genetic approach (MMIFTT)	Multiple myeloma	Royal Bournemouth Hospital; Southampton General Hospital; Nottingham City Hospital	4-00	Plasmid	Idiotypic DNA vaccination	*E. coli* JM109	13 of 15 – 20
29D	Phase I/II study of idiotypic vaccination for chronic lymphocytic leukaemia using a genetic approach (CLLIFTT)	Chronic lymphocytic leukaemia	Royal Bournemouth Hospital; Southampton General Hospital	4-00	Plasmid	Idiotypic DNA vaccination	*E. coli JM109*	2 of 10 CLOSED
30	Use of a retrovirus carrying human cytochrome p450 for the treatment of ovarian cancer (Phase I intra-abdominal).	Ovarian Cancer	Northern General Hospital, Sheffield	2-00	Retrovirus	Cytochrom e P450	TEFLY-A	6 CLOSED
31	Gene directed enzyme prodrug therapy for the treatment of head and neck cancer (Phase I intratumoral)	Head and Neck Cancer	Queen Elizabeth Hospital, Birmingham; Royal Marsden Hospital, London	7-99	Adenovirus	Nitroreduct ase	PER-C6	7 of 30 CLOSED

GTAC NO.	PROTOCOL NAME	DETAILS	CENTRE	OUTLINE APPROVAL	VECTOR	GENE	CELL LINE	NO. OF PATIENTS
32	Gene directed enzyme prodrug therapy for the treatment of liver cancer (Phase I intratumoral)	Liver Cancer	Queen Elizabeth Hospital, Birmingham	7-99	Adenovirus	Nitroreductase	Per-c6	25 of 30 CLOSED
33	Phase I trial of immunotherapy with adenovirus-interferon-γ in malignant melanoma (intratumoral)	Malignant Melanoma	St. George's Hospital	7-99	Adenovirus	IFN-γ	-	1 CLOSED
34	A phase II/III trial of chemotherapy alone versus chemotherapy plus Adp53 in ovarian and primary intraperitoneal cancer (intraperitoneal)	Ovarian Cancer	Royal Marsden Hospital, Christie Hospital/ CRC Institute for Cancer Studies, John Radcliffe Hospital	7-99	Adenovirus	p53	HEK293	1 CLOSED
35	Phase II trial of pre-operative intratumoral injection with an E1B attenuated adenovirus in patients with resectable head and neck tumours	Head and Neck Cancer	Beatson Oncology Centre, Glasgow	7-99	Adenovirus	E1B deleted	HEK293	15 CLOSED
36	The safety and effects of Ad5.1 mediated human FGF-4 gene transfer in patients with peripheral arterial occlusive disease (PAOD)	Peripheral Arterial Occlusive Disease	St George's Hospital, London	10-00	Adenovirus	FGF-4	PER-C6	13 (2 UK) of 30 CLOSED

GTAC NO.	PROTOCOL NAME	DETAILS	CENTRE	OUTLINE APPROVAL	VECTOR	GENE	CELL LINE	NO. OF PATIENTS
37	A Phase III study of quadruple HAART followed by double-blind randomisation to HIV vaccination with ALVAC-HIV and Remune or placebo	HIV	Chelsea & Westminster Hospital, Royal Free Hospital, Brighton General Hospital, University Hospital of Wales Cardiff	5-00	Canarypox	HIV-1 *env, gag*	AVIAN	8 of 15 CLOSED
38	A Phase I, open label, dose escalation trial to assess the safety and immunogenicity of DISC-GMCSF in patients with metastatic melanoma	Malignant melanoma	Churchill Hospital, Oxford Royal Marsden Hospital, London	5-00	HSV	hGMCSF	CR2C9 (Vero-derived)	10 CLOSED
39	Gene therapy protocol for the evaluation of the safety, biodistribution and efficacy of TroVax in patients with metastatic colorectal cancer (Phase I i.m.)	Colorectal cancer	Christie Hospital NHS Trust, Manchester	10-00	Vaccinia	Human oncofoetal antigen 5T4	CEF	22 of 22 CLOSED
40	A Phase I dose escalation trial of an E1B attenuated adenovirus as an intravesical therapy for recurrent superficial/muscle invasive bladder cancer	Bladder cancer	St James's University Hospital, Leeds	Conditional Approval 7-00	Adenovirus	E1B deleted	HEK293	Trial withdrawn
41	Randomised multi-centre trial evaluating two different vaccination schedules of MVA-MUC-1-IL-2 in women with metastatic	Breast cancer	Guy's Hospital, London	Application withdrawn	Vaccinia	MUC-1, IL-2	CEF	Application withdrawn

GTAC NO.	PROTOCOL NAME	DETAILS	CENTRE	OUTLINE APPROVAL	VECTOR	GENE	CELL LINE	NO. OF PATIENTS
	breast cancer (Phase II i.m.)							
42	Phase I study of melanoma poly-epitope DNA and melanoma poly-epitope modified vaccinia Ankara in patients with melanoma	Melanoma	The Churchill Hospital, Oxford	7-00	Vaccinia DNA	Mel3 (melanoma antigens)	CEF	12 of 20 CLOSED
43	A phase I/II trial of polyHER2neu-a polyepitope DNA vaccine encoding HER-2 epitopes in the treatment of epithelial cancers (i.m.)	Breast cancer	St James's University Hospital, Leeds	Application Declined	Plasmid	HER-2 epitopes	*E. coli*	Application Declined
44	Treatment of leukaemic relapse after allogenic stem cell transplantation by HSV-tk transduced donor lymphocyte transfusions.	Chronic myeloid leukaemia	Hammersmith Hospital, London	10-00	Retrovirus	HSV -tk	AM12	0 of 10-20
45	Phase I clinical gene therapy protocol for X-SCID	X-SCID	Institute of Child Health, London	01-01	Retrovirus	Common gamma chain	PG13	11 of 20 CLOSED
46	Phase I gene therapy protocol for X-CGD	X-CGD	Institute of Child Health, London; Royal Free Hospital, London Great Ormond Street Hospital Royal Free Hospital	12-00	Retrovirus	Gp91-phox	HEK293	3 of 5 CLOSED
47	A phase I, Randomised, Double-blind, Placebo Controlled, Escalating	Coronary artery disease	John Radcliffe Hospital, Oxford; King's College Hospital, London	12-00	Adenovirus	HIF-1α/VP16	HEK293	4 UK patients CLOSED

GTAC NO.	PROTOCOL NAME	DETAILS	CENTRE	OUTLINE APPROVAL	VECTOR	GENE	CELL LINE	NO. OF PATIENTS
	Dose, Multicentre Study of Ad2/Hypoxia Inducible Factor Gene Transfer Administered by Intramyocardial Injection During Coronary Artery Bypass Grafting Surgery in Patients with Incomplete Revascularisation							
48	A randomised phase I trial of intravenous CI-1042 with or without entanercept in patients with metastatic carcinoma	Metastatic carcinoma	Hammersmith Hospital, London	12-00	Adenovirus	p53	HEK293	Application withdrawn
49	A phase I/II Study of Immunotherapy for Patients with Metastatic Melanoma Using Dendritic Cells Transfected with a Plasmid Encoding Two Melanoma Antigens	Metastatic Melanoma	CRC Institute for Cancer Studies, Birmingham	02-01	Plasmid complexed with peptide	MART-1 gp-100	*E. coli*	Trial never opened CLOSED
50	A Phase II Trial of Preoperative intratumoural Injection with HSV1716 in Patients with Resectable Squamous Cell Tumours of the Head and Neck	Head and Neck Cancer	Southern General Hospital, Glasgow	05-01	HSV	ICP34.5 deleted	BHK-21/C13	20 of 20 CLOSED
51	A multinational multicenter, randomised, double-blind, placebo	Coronary Artery Disease	Papworth Hospital NHS Trust; Royal Sussex County Hospital; Royal Infirmary of Edinburgh;	05-01	Adenovirus	FGF-4	HEK293	17 of 60 in UK 116 of 450 world-wide CLOSED

GTAC NO.	PROTOCOL NAME	DETAILS	CENTRE	OUTLINE APPROVAL	VECTOR	GENE	CELL LINE	NO. OF PATIENTS
	controlled study to evaluate the efficacy and safety of Ad5FGF-4 in patients with stable angina		Hammersmith Hospital, London; King's College Hospital, London; Royal Free Hospital, London; St Thomas' Hospital, London; The London Chest Hospital; Wythenshawe Hospital, Manchester; Nottingham City Hospital; University Hospital Wales, Cardiff; Queen Elizabeth Hospital, Birmingham (to be confirmed)					
52	A phase I study to evaluate the safety, tolerability and immunogenicity of two administrations of either plasmid DNA (pSG.HBs) versus placebo or modified vaccinia virus Ankara (MVA.HBs) versus placebo, followed by two boost administrations of MVA.HBs expressing hepatitis B surface antigen in healthy male volunteers	Hepatitis B Vaccine Trial	TNO BIBRA International, Surrey; University of Oxford; Central Middlesex Hospital	08-01	Vaccinia & plasmid	HBsAg	MVA: Chicken embryo fibroblasts; Plasmid in *E. coli*	18 of 18 CLOSED
53	A pilot study of the safety and immunogenicity of a candidate HIV-1 clade A DNA vaccine, pTHr.HIVA, given by	HIV	John Radcliffe Hospital, Oxford	05-01	Plasmid	HIV-1 clade A *gag* and 25 HIV-1 *gag, pol, env, nef*	I DH1	10 of 10 CLOSED

GTAC NO.	PROTOCOL NAME	DETAILS	CENTRE	OUTLINE APPROVAL	VECTOR	GENE	CELL LINE	NO. OF PATIENTS
	needle injection into the deltoid muscle in HIV-1-seropositive subjects receiving highly active anti-retroviral therapy					CTL epitopes		
54	A Phase II, Randomised, double-blind, Placebo-controlled, Parallel Group, Efficacy and Safety Study of NV1FGF in Patients with Severe Peripheral Artery Occlusive Disease	Peripheral Artery Occlusive Disease	St. George's Hospital, London; Royal Bournemouth Hospital; Leicester Royal Infirmary; Wythenshawe Hospital, Manchester; Freeman Hospital, Newcastle; Royal Free Hospital, London; Bristol Royal Infirmary (CLOSED); Leeds General Infirmary; Southampton General Hospital	08-01	Plasmid	FGF-1	I XAC-1	11 CLOSED
55	Gene directed enzyme prodrug therapy for the treatment of prostate cancer (Phase I intratumoral)	Prostate Cancer	Queen Elizabeth Hospital, Birmingham; Freeman Hospital Newcastle; St James's University Hospital, Leeds	04-01	Adenovirus	Nitro reductase	PER-C6	39 of 44 CLOSED
56	A Phase II, Multicentre, double-blinded, Placebo-Controlled, Dose-Finding Study of ZYC101a in the Treatment of high-grade Squamous Intra-Epithelial Lesions of the Uterine Cervix.	Ano-genital Neoplasia III	Hammersmith Hospital, London	11-01	Plasmid	HPV E6 & E7	*E. coli*	0 of 5 CLOSED
57	A Phase I, Multidose Study to Evaluate the Safety of Intramuscular Injections of HER-2 DNA in Patients with	Breast Cancer	Hammersmith Hospital, London	11-01	Plasmid	HER-2	*E. coli*	27 of 27 CLOSED

GTAC NO.	PROTOCOL NAME	DETAILS	CENTRE	OUTLINE APPROVAL	VECTOR	GENE	CELL LINE	NO. OF PATIENTS
	Metastatic Breast Cancer.							
58	The Use of a cDNA Vaccine Encoding the Human MUC1 Gene in the Treatment of Patients with Advanced Breast Cancer – A Phase I/II Study	Breast Cancer	ICRF, Guy's Hospital, London	08-01	Plasmid	MUC-1	*E. coli*	6 of 12-28
59	A phase IIa, open label trial to assess the safety, immunogenicity and efficacy of a prime-boost strategy of TA-CIN administered in associated with TA-HPV to patients with high grade ano-genital intraepithelial neoplasia (AGIN)	Cervical Cancer	University of Wales, Cardiff; St. Mary's Manchester; Addenbrooke's, Cambridge.	07-01	Vaccinia	E6 & E7 HPV	MR-5	29 CLOSED
60	Study of Transfection Efficacy and Safety of MetXia-OB83 in patients with cutaneous lesions of breast cancer or melanoma	Breast Cancer	Churchill Hospital, Oxford; Queen Elizabeth Hospital, Birmingham	07-01	Retrovirus	P450	TEFLYRD	8 of 8 CLOSED
61	An upward titration study of transfection efficacy and safety of Metxia-OB83 in patients with adenocarcinoma of the prostate	Prostate Cancer	The Churchill Hospital, Oxford.	08-01	Retrovirus	P450	TEFLYRD	CLOSED
62	First Administration to Man of an Oncolytic Herpes virus Vector Containing a	Melanoma, Breast, Head & Neck, cancer, Non-Hodgkins	Hammersmith Hospital, London; St George's Hospital, London; CR-UK Institute for Cancer	11-01	HSV	ICP34.5-deleted ICP47-deleted	BHK 21c13	30 CLOSED

GTAC NO.	PROTOCOL NAME	DETAILS	CENTRE	OUTLINE APPROVAL	VECTOR	GENE	CELL LINE	NO. OF PATIENTS
	Transgene for Granulocyte Macrophage Colony Stimulating Factor (OncoVex^{GM-CSF}) – A Study of its Safety, Biodistribution and Biological Activity.	Lymphoma	Studies, University of Birmingham			Human GM-CSF		
63	VTP-1/01: A Phase I/II Trial of Intravenous vs. Hepatic Arterial Infusion of an E1A-CR2 Deleted Adenovirus (VTP-1) in Patients with Inoperable, Metastatic Colorectal Carcinoma.	Metastatic colorectal carcinoma	Hammersmith Hospital, London	Application withdrawn	E1A conserved region 2 deleted & E3B RID gene region deleted	N/a	HEK-293	Application withdrawn
64	A Phase I trial of replication-competent herpes simplex virus (ICP 34.5 null mutant 1716) in patients with inoperable malignant pleural mesothelioma.	Malignant pleural mesothelioma	University of Glasgow, Beatson Oncology Centre, Glasgow	02-02	HSV HSV1716	ICP34.5 deleted	BHK-21/C13	0 CLOSED
65	A Phase I trial of PolyMEL, a polyepitope DNA vaccine in the treatment of metastatic melanoma patients.	Melanoma	St James Hospital, Leeds	01-02	Plasmid DNA (polyMEL)	Multiple melanoma epitopes	*E. coli*	9 of 12 CLOSED
66	A recombinant vaccinia Ankara (MVA)-based vaccine encoding Epstein-Barr Virus target antigens: phase I	Naso-Pharyngeal carcinoma	Queen Elizabeth Hospital, Birmingham; Royal Marsden Hospital, London	02-02	DNA plus MVA	EBV epitopes (EBNA1 and LMP2A)	CEF	16 of 19-22

GTAC NO.	PROTOCOL NAME	DETAILS	CENTRE	OUTLINE APPROVAL	VECTOR	GENE	CELL LINE	NO. OF PATIENTS
	dose escalation trial to determine immunogenicity and toxicity in patients with EBV+ malignancy EudraCT: 2004-001931-46							
67	Percutaneous Intramyocardial Gene Therapy against myocardial ischaemia with phVEGF-A165SR – A double-blind placebo controlled study	Coronary Artery Disease	Wythenshawe Hospital, Manchester	Application Pending	plasmid	VEGF	*E. coli*	Application withdrawn
68	A Phase I trial of polyHER2neu – a polyepitope DNA vaccine encoding HER-2 epitopes in the treatment of breast cancer.	Breast Cancer	The Leeds Teaching Hospital NHS Trust, Leeds	01-02; Re-validated 06/06	Plasmid DNA	Poly epitopes of HER-2	*E. coli*	3 of 12-15 CLOSED
69	A phase I/II study of vaccination with a DNA fusion gene containing an epitope of CMV in allograft donors and patients awaiting renal transplantation	CMV infection following transplant	Southampton General Hospital; Royal Free Hospital London; University College London Hospital	02-02	Plasmid DNA (pcDNA3)	Peptide from pp65 from CMV	*E. coli*	4 of 15 pairs (8 patients)
70	NUMBER NOT ALLOCATED							
71	A Phase I/II prospective study of immuno gene therapy with a liposomally encapsulated replication incompetent	Glioma	University of Liverpool	Application withdrawn	Replication disabled Semliki Forest Virus, liposome encapsulated	Human IL-2	Baby hamster kidney (BHK)	Trial withdrawn

GTAC NO.	PROTOCOL NAME	DETAILS	CENTRE	OUTLINE APPROVAL	VECTOR	GENE	CELL LINE	NO. OF PATIENTS
	Semliki Forest Virus (SFV) vector carrying the human interleukin-12 gene and administered intratumorally in patients with recurrent or progressing glioblastoma multiforme.							
72	Phase I/II study to determine the optimum dose and dosing regimen then to assess the efficacy of a poly-epitope pharmaccine, involving pSG2.Mel3 and MVA.Mel3, in patients with Stage III or Stage IV metastatic melanoma	Metastatic melanoma	Christie Hospital, Manchester; Churchill Hospital Oxford; Western General, Edinburgh; Southampton General Hospital	09-02	DNA and MVA	Multiple melanoma epitopes	CEF	41 of 41 CLOSED
73	Phase I clinical gene therapy protocol for adenosine deaminase deficiency GTX 8000/0041	Severe Combined Immunodeficiency	Great Ormond Street Hospital, London	12-02	Retrovirus (spleen focus forming virus)	Adenosine Deaminase	PG13	8 of 10
74	A Randomised Efficacy Trial of Herpes Simplex Virus HSV1716 in Recurrent Glioblastoma Multiforme (EudraCT: 2004-000097-32)	Glioblastoma multiforme	University Hospital Birmingham NHS Trust; Southern General Hospital, Glasgow; Sheffield Teaching Hospitals NHS Foundation Trust; Brighton & Sussex University Hospitals NHS Trust; Lancashire Teaching	07-04	HSV	ICP34.5 deleted	BHK21.c13	11 of 100

GTAC NO.	PROTOCOL NAME	DETAILS	CENTRE	OUTLINE APPROVAL	VECTOR	GENE	CELL LINE	NO. OF PATIENTS
			Hospitals NHS Foundation Trust; Leeds Teaching Hospitals NHS Trust					
75	A Phase I study of NYVAC C in healthy volunteers at low risk of HIV infection (EV01)	HIV-1	Imperial College London	02-03	MVA	HIV-1 Clade C *gag, pol, nef, env,* (NYVAC C)	Chick Embryo Fibroblasts	12 of 12 CLOSED
76	A phase I/II study of anti-CEA DNA vaccine (ACVA) with a CEA/pDOM fusion gene in patients with carcinoma expressing CEA EudraCT: 2004-00193221	Carcinoma	Southampton University Hospital NHS Trust, Western General Hospital Edinburgh, Portsmouth Hospitals NHS Trust, Leeds Teaching Hospitals NHS Trust	02-03	Plasmid DNA (pcDNA3)	CAP-1 peptide from CEA	*E. coli*	27 of 30
77	An open label study of Trovax given in conjunction with 5-fluorouracil/leukovorin (de Gramont regimen) plus irinotecan: safety and immunogenicity before during and after Chemotherapy. (Short title:Gene therapy protocol for the evaluation of the safety and efficacy of TroVax in conjunction with chemotherapy in patients with metastatic colorectal cancer)	Metastatic colorectal cancer	Christie Hospital Manchester; Queen Elizabeth Hospital, Birmingham	02-03	MVA	Human Oncofoetal Antigen 5T4	Chick Embryo Fibroblasts	19 of 19 CLOSED
78	A phase I clinical gene therapy trial for X-SCID	X-SCID	Institute of Child Health, London	02-03	Retrovirus (Moloney	Common gamma	PG13	0 of 10 CLOSED

GTAC NO.	PROTOCOL NAME	DETAILS	CENTRE	OUTLINE APPROVAL	VECTOR	GENE	CELL LINE	NO. OF PATIENTS
	using umbilical cord blood				murine leukaemia virus)	chain		
79	A pilot study to evaluate the safety, tolerability and immunogenicity of a candidate HIV-1 vaccine, MVA.HIVA delivered to HIV-1 sero-positive adults receiving HAART EudraCT: 2006-000484-29	HIV-1	MRC Human Immunology Unit, John Radcliffe Hospital, Oxford	07-03	MVA	HIV-1 clade A *gag, pol, nef* and *env*	CEF	16 of 20 CLOSED
80	Phase I/II study – first administration of Dendritic cells transduced with ImmunoVEX$^{TRI\text{-}Melan}$ to patients with metastatic or inoperable melanoma	metastatic or inoperable melanoma	St George's Hospital Medical School, London	Application declined	HSV	hTyrosinase, hMART1, hGP100	*Vero (MEVP16/M4 F6A)*	Application declined
81	An open label study of TroVax given in conjunction with 5-Fluorouracil/ Leukovorin/Oxaliplatin: safety and immunogenicity before, during and after chemotherapy (TV2)	Colorectal cancer	University of Leeds School of Medicine; Hammersmith Hospital, London	05-03	MVA	Human oncofoetal antigen 5T4	CEF	17 of 17 CLOSED
82	A phase II trial to evaluate efficacy and safety of intramuscular injections of HER-2 DNA Autovac™ in patients with metastatic	Breast cancer	Hammersmith Hospital	07-03	Plasmid	HER-2 with T cell epitopes P2 and P30 derived from	*E. coli*	Trial withdrawn

GTAC NO.	PROTOCOL NAME	DETAILS	CENTRE	OUTLINE APPROVAL	VECTOR	GENE	CELL LINE	NO. OF PATIENTS
	or locally advanced breast cancer					tetanus toxin		
83	A Phase I/II safety study of MetXia-OB83 in patients with pancreatic cancer	Pancreatic cancer	Royal Liverpool University Hospital; Hammersmith Hospitals, London	10-03	Retrovirus (Moloney murine leukaemia virus)	cytochrome P450	FLY RD83	31 of 27 CLOSED
84	A Phase I study of immunotherapy for patients with metastatic melanoma using dendritic cells transfected with a plasmid encoding two melanoma antigens	Malignant melanoma	Hammersmith Hospital Site	07-03	Plasmid DNA	MART-1 and gp-100	*E. coli*	27 CLOSED
85	A phase I trial to assess the safety of DNA C, and the safety and immunogenicity of DNA C followed by NYVAC C in an open, randomised comparison to NYVAC C alone in healthy volunteers at low risk of HIV infection (EV02) (EudraCT: 2004-001802-28)	HIV-1	Imperial College London, St's Mary's Hospital	10-03	Plasmid pORT1 And MVA	HIV-1 clade C *gag, pol, nef, env*	*E. coli*	15 CLOSED
86	First administration of dendritic cells transduced with ImmunoVEX$^{Tri\text{-}Melan}$ to patients with metastatic or inoperable melanoma, preliminary assessment of safety, biodistribution and	metastatic or inoperable melanoma	St George's Hospital Medical School, London & CRUK Oncology Unit, Southampton; Southampton University Hospital NHS Trust; Moorfields Eye Clinic at St George's Hospital Medical School;	10-03	HSV	hTyrosinase, hMART1, hGP100	Vero (MEVP16/M4 F6A)	19 CLOSED

GTAC NO.	PROTOCOL NAME	DETAILS	CENTRE	OUTLINE APPROVAL	VECTOR	GENE	CELL LINE	NO. OF PATIENTS
	indicators of efficacy		St Lukes Cancer Centre, Royal Surrey County Hospital					
87	A Phase II Study Immunologically Evaluating 5T4-MVA (TroVax) in Patients undergoing Surgical Resection of Colorectal Liver Metastases	Metastatic colorectal cancer	Christie Research Centre, Manchester; North Manchester General Hospital	01-04	MVA	Human Oncofoetal Antigen 5T4	Chick Embryo Fibroblasts	20 of 20 Study closed November 2006
88	A Cancer Research UK Phase I Trial of AEG35156/GEM640 (XIAP antisense) administered as a 7 day continuous intravenous infusion in patients with advanced tumours EudraCT: 2004-000448-26	Advanced tumours	Christie Hospital NHS Trust, Edinburgh Royal Infirmary	12-03	N/a	Antisense DNA to human X-linked inhibitor of apoptosis	*N/a*	11 of 18-46
89	A Phase I/II Trial of a DNA vaccine with a $PSMA_{27}$/ pDom fusion gene given by intramuscular injection in HLA A2+ patients with prostate carcinomas with or without electroporation CI/2004/0011	Prostate cancer	Southampton University Hospitals NHS Trust; Royal Marsden Foundation Trust, London	02-04	DNA with and without electroporation	1st domain of Tetanus toxin fragment C, 9 amino acid peptide from PSMA	*E. coli*	32 of 32
90	A Controlled, Randomised, Parallel Group, Multicentre Study of the Efficacy and Safety of Herpes Simplex Virus-	Operable primary or recurrent high grade glioma	Walton Centre for Neurology and Neurosurgery, Liverpool (withdrawn); Queen's Medical Centre, Nottingham;	04-04	Adenovirus type 5, E1 and E3 deleted	Herpes simplex virus-thymidine kinase gene (HSV-	HEK293	5 CLOSED

GTAC NO.	PROTOCOL NAME	DETAILS	CENTRE	OUTLINE APPROVAL	VECTOR	GENE	CELL LINE	NO. OF PATIENTS
	Thymidine Kinase Gene Therapy (Cerepro™), with Subsequent Ganciclovir, for the Treatment of Patients with Operable High Grade Glioma. EudraCT: 2004-000464-28		Addenbrooke's NHS Trust, Cambridge; Queen Elizabeth Hospital, Birmingham			tk)		
91	Double-blind, randomised, placebo-controlled, parallel group and dose-finding, multicentric, safety and efficacy study with intramuscular injections of NV1FGF in subjects with intermittent claudication.	Peripheral artery occlusive disease in patients with intermittent claudication	Royal Bournemouth Hospital; Gloucestershire Hospitals NHS Foundation Trust, Cheltenham; Newcastle Upon Tyne Hospitals NHS Trust;	03-04	Plasmid	FGF-1	*E coli* XAC-1	0 -118 subjects world-wide. CLOSED
92	A Randomised Phase II Trial of PANVAC Vaccination in the Adjuvant Treatment of Stage II Colorectal Cancer. (EudraCT: 2004-001734-16)	Colorectal Cancer	Oxford Radcliffe Hospitals NHS Trust & CRUK Medical Oncology Unit, Oxford	06-04	Vaccinia and fowlpox virus,	Carcino-embryonic antigen, Mucin-1, B7-1, ICAM-1 and LFA-3		0 of 40 CLOSED
93	An open, randomised, parallel group study to evaluate the safety, tolerability and immunogenicity of the	HIV	Addenbrooke's Hospital Cambridge; Chiltern International, Slough	06-04	Plasmid on gold particles	Reverse transcriptase, nef, gag of HIV-1	E. coli DH1	37 CLOSED

GTAC NO.	PROTOCOL NAME	DETAILS	CENTRE	OUTLINE APPROVAL	VECTOR	GENE	CELL LINE	NO. OF PATIENTS
	GW825780 DNA immunotherapeutic when delivered using the PowderJect ND5.5 device to healthy adult volunteer subjects. (EudraCT: 2004-000251-41)							
94	A Phase II exploratory study of the efficacy and safety of OncoVEX GM-CSF in combination with Arimidex in the neoadjuvant treatment of breast cancer in post menopausal women with oestrogen receptor positive tumours (EudraCT: 2004 – 01938-16)	Breast Cancer	Hammersmith Hospitals NHS Trust	Application declined	HSV	ICP34.5-deleted ICP47-deleted Human GM-CSF	BHK 21c13	Declined
95	Safety and immunology evaluation of TroVax produced by the Baxter synthetic route in patients with stage IV colorectal cancer (EudraCT: 2004-002251-13)	Colorectal cancer	Christie Hospital NHS Trust, Manchester; The Leeds Teaching Hospitals NHS Trust	11/04	MVA	Human Oncofoetal Antigen 5T4	Chick Embryo Cells	Application withdrawn
96	A Phase I Study of Adoptive Transfer of Autologous Tumour Antigen-Specific T Cells with Pre-conditioning Chemotherapy and Intravenous IL2 in	CEA positive malignancies	Christie Hospital NHS Trust, Manchester	11-04	Retrovirus	MFE23 specific for carcinoembryonic antigen; CD3ζ	Murine PG13	15 of 22 CLOSED

GTAC NO.	PROTOCOL NAME	DETAILS	CENTRE	OUTLINE APPROVAL	VECTOR	GENE	CELL LINE	NO. OF PATIENTS
	Patients with Advanced CEA Positive Tumours. EudraCT: 2005-004085-16							
97	A multicenter, randomised, double-blind, placebo-controlled study evaluating the efficacy of BIOBYPASS (ADGVVEGF121.10NH) delivered by NOGATM - Guided/myostar catheter in no option patients with class II-IV stable angina. EudraCT: 2004-001250-91	Stable angina	King's College Hospital, Barts and the London NHS Trust	11-04	Adenovirus type 5	VEGF	human embryonic retinoblasts (PER.C6)	0 of 129 CLOSED
98	A pilot study of lentivirus transduced acute myeloid leukaemia (AML) blasts expressing B7.1 (CD80) and IL-2, for the induction of graft verses leukaemia (GVL) effect in poor prognosis, relapsed AML. EudraCT: 2005-000806-29	Acute myeloid leukaemia	King's College London	11-04 Full approval Dec 07	Lentivirus (HIV-1)	CD80 (B7.1) and IL-2	human embryonic kidney 293T	2 of 24.
99	A Phase 2, Randomized, Double-blind, Placebo controlled, Parallel-group, Multicenter,	Peripheral artery disease: Intermittent Claudication	Ninewells Hospital, Dundee; St George's Hospital and Medical School; Freeman Hospital,	11-04	Adenovirus (E1 and E4 deleted)	HIF-1α (Hypoxia-Inducible Factor-1)	human 293 cells	33 of 35 CLOSED

GTAC NO.	PROTOCOL NAME	DETAILS	CENTRE	OUTLINE APPROVAL	VECTOR	GENE	CELL LINE	NO. OF PATIENTS
	Dose-Selection Study of Ad2/Hypoxia Inducible Factor HIF-1α/VP16 in Patients with Intermittent Claudication. EudraCT: 2004-002508-13		Newcastle (withdrawn); Belfast City Hospital Trust; Ealing Hospital NHS Trust, Hull and East Yorkshire NHS Trust & University of Hull, University Hospital Birmingham Foundation Trust, Hammersmith Hospitals NHS Trust					
99A	Extended Follow-up Program EudraCT No: 2007-004610-14	Follow up to Peripheral artery disease: Intermittent Claudication (GTAC 099A)	NHS Tayside; St George's Hospital and Medical School; Ealing Hospital.	Full approval May 08				CLOSED
100	A phase II study of NY-ESO-1 ISCOMATRIX® vaccine followed by recombinant fowlpox NY-ESO-1 (rF-NY-ESO-1) or NY-ESO-1 ISCOMATRIX® vaccine alone in patients with high risk resected NY-ESO-1 positive melanoma and prostate cancer. EudraCT: 2004-004991-36	Melanoma or prostate carcinoma	Oxford Radcliffe Hospitals NHS Trust, Southampton University Hospitals NHS Trust, Mount Vernon Hospital,	Conditional approval, 03-05; Approval 05-05	Recombinant fowlpox virus	NY-ESO-1 tumour specific antigen	Chicken embryo dermal (CED) cells	2 - of 40
101	An Ascending Dose Trial of the Safety, Tolerability and Biological Effect of intra-arterial Injection of	Hepatocellular Carcinoma	Royal Infirmary of Edinburgh,	Declined 04-05	HSV1716	HSV deleted in both copies of RL1 gene	BHK21.c13	Application Declined

GTAC NO.	PROTOCOL NAME	DETAILS	CENTRE	OUTLINE APPROVAL	VECTOR	GENE	CELL LINE	NO. OF PATIENTS
	the Selectively Replication-Competent Herpes Simplex Virus HSV1716 in Patients with Unresectable Hepatocellular Carcinoma. EudraCT: 2005-000133-38							
102	A Phase I Trial of Intra-Peritoneal Ad-hTR-NTR and CB 1954, an Adenovirus-Delivered Telomerase-Directed Enzyme-Prodrug Therapy, in Patients with Advanced Intra-Abdominal Cancer. EudraCT: 2005-003294-24	Intra-Abdominal Cancer	Beatson Oncology Centre, Western infirmary, Glasgow;	Conditional approval, 04-05.	Adenovirus (E1/E3 deleted)	Bacterial nitroreductase gene	Human 293 cells	0 - of 8-12
103	A Phase I Study of Adoptive Transfer of Autologous Tumour Antigen-Specific T Cells with Pre-conditioning Chemotherapy and Intravenous IL2 in Patients with CD19 Positive Malignancy.	CD19 positive cancer	Christie Research Centre, Manchester	06-05	Retrovirus	Chimeric Immune Receptor CD19-z cDNA.	Murine PG13	5- of 24
104	Safety, Immunology And Efficacy Evaluation Of TroVax In Patients With Stage IV Clear Cell Renal Carcinoma (TV2). EudraCT: 2005-	Renal carcinoma	Christie Research Centre, Manchester; Institute for cancer studies, Birmingham	Conditional approval, 04 -05	Attenuated vaccinia virus vector MVA	Human Oncofoetal Antigen 5T4	Chick Embryo Cells (CECs)	0 of 10 Application withdrawn

GTAC NO.	PROTOCOL NAME	DETAILS	CENTRE	OUTLINE APPROVAL	VECTOR	GENE	CELL LINE	NO. OF PATIENTS
	000088-24							
105	An exploratory study of the safety and biological activity of OncoVex^{GM-CSF} in combination with radiotherapy and cisplatin in the treatment of locally advance epithelial cancer of the head and neck. EudraCT: 2005-000777-21	Head and Neck cancer	Royal Marsden Hospital NHS Foundation Trust, London, Barts and the London NHS Trust;	Conditional approval, 04-05; Approval 08-05	HSV	ICP34.5-deleted ICP47-deleted Human GM-CSF	BHK 21c13	17 of 35 CLOSED
106	Phase I/II clinical trial of T cell suicide gene therapy following allogeneic haematopoietic stem cell transplantation EudraCT: 2005-001925-27	To prevent GvHD in children and adults undergoing DLI after bone marrow transplant	Great Ormond Street Hospital NHS Trust; Royal Free Hospital, London	Declined	Retrovirus	HSV-TK (herpes simplex thymidine kinase – splice corrected version)	PG13	Declined
107	A multicenter, randomized, double blind, placebo-controlled study to evaluate the safety, tolerability, and efficacy of BHT-3009 when administered intramuscularly to patients with relapsing remitting multiple sclerosis (Protocol No. BHT-3009-03). EudraCT: 2005-	Multiple Sclerosis	Guy's and St Thomas' NHS Foundation Trust; Royal Hallamshire Hospital, Sheffield; Walton Neurology Centre, Liverpool; Queens Medical Centre, Nottingham Barking, Havering and Redbridge Hospitals NHS Trust; Royal Victoria Infirmary, Newcastle;	06-05	Plasmid DNA	human myelin basic protein (hMBP)	*E. Coli*	4 CLOSED

GTAC NO.	PROTOCOL NAME	DETAILS	CENTRE	OUTLINE APPROVAL	VECTOR	GENE	CELL LINE	NO. OF PATIENTS
	001340-22							
108	An open-labelled, international, multicenter, dose escalating, phase I/II Study of SPC2996, an LNA antisense molecule against Bcl-2, in patients with relapsed or refractory Chronic Lymphocytic Leukaemia EudraCT: 2004-004741-17	Chronic lymphocytic leukaemia	Christie Hospital NHS Trust, Manchester; Barts and the London NHS Trust, London; Leeds Teaching Hospitals NHS Trust; UHL NHS Trust, Leicester Royal Marsden NHS Foundation Trust	Conditional approval 06-05; Approval 08-05	n/a	Antisense DNA binding to mRNA of Bcl-2	n/a	35 of 42 CLOSED
109	A phase I, dose-escalating trial of JX-594 (thymidine kinase-deleted vaccinia virus encoding GM-CSF) administered by intravenous infusion in patients with refractory solid tumours EudraCT: 2005-002015-25	Solid tumours	Radcliffe Infirmary, Oxford	06-05	Replication-selective oncolytic vaccinia virus (TK depleted)	GM-CSF	Vero cells	0 of 20-30
110	A Single Arm Open-Label Phase I study of an injectable replication-incompetent adenoviral vector encoding a factor VII immunoconjugate to induce a cytolytic immune response against the vasculature of carcinoma of the bowel with metastatic	Liver and colorectal cancer	Hammersmith Hospital, London	Declined	Adenovirus	Factor VII		Declined

GTAC NO.	PROTOCOL NAME	DETAILS	CENTRE	OUTLINE APPROVAL	VECTOR	GENE	CELL LINE	NO. OF PATIENTS
	lesions to the liver							
111	A Phase II Double Blind, Cross–Over Study to Compare the Safety and Efficacy of 125, 250 and 500 ug/kg Monarsen (EN101) administered to Patients with Myasthenia Gravis. EudraCT: 2005–002740–26	Myasthenia Gravis	Hope Hospital, Salford; The Walton Centre, Liverpool	09/05	N/a	antisense oligodeoxynucleotide against Acetylcholinesterase	N/a	10 of 30 CLOSED
112	A Phase III Randomized, Open-Label Study of Docetaxel in Combination with CG1940 and CG8711 versus Docetaxel and Prednisone in Taxane-Naïve Patients with Metastatic Hormone-Refractory Prostate Cancer With Pain. EudraCT: 2005-003275-20	Prostate cancer	Royal Marsden Hospital; Cambridge University Hospitals NHS Foundation Trust; Nottingham University Hospitals NHS Trust; Royal Surrey County Hospital, Guildford; East & North Hertfordshire Hospitals NHS Trust; Lancashire Teaching Hospitals NHS Foundation Trust; Leeds Teaching Hospitals NHS Trust; Scunthorpe General Hospital, Christie Hospital NHS Foundation Trust, Manchester, Hammersmith Hospital, Clatterbridge Centre for Oncology NHS Foundation Trust, Lincoln County Hospital	09/05	AAV	Granulocyte macrophage colony stimulating factor (hgGM-CSF)	human kidney cells	0 of 100 approx 600 worldwide CLOSED

GTAC NO.	PROTOCOL NAME	DETAILS	CENTRE	OUTLINE APPROVAL	VECTOR	GENE	CELL LINE	NO. OF PATIENTS
113	A Phase III Randomized, Open-Label Study of CG1940 and CG8711 Versus Docetaxel and Prednisone in Patients with Metastatic Hormone-Refractory Prostate Cancer who are Chemotherapy-Naïve. EudraCT: 2005-002738-36	Prostate cancer	North Glasgow University Hospitals Division, Glasgow;; The Leeds Teaching Hospitals NHS Trust; Newcastle Hospitals NHS Trust; East & North Hertfordshire Hospitals NHS Trust; Nottingham City Hospital NHS Trust, Sheffield Teaching Hospitals NHS Trust; Churchill Hospital, Oxford; Hammersmith Hospitals NHS Trust; Cambridge University Hospitals NHS Foundation Trust; Northampton General Hospital NHS Trust; Northern Lincolnshire & Goole Hospitals NHS Trust, Scunthorpe; Conwy & Denbighshire NHS Trust; Greater Glasgow & Clyde, The Beatson WOS Cancer Centre	09/05	AAV	Granulocyte macrophage colony stimulating factor (hgGM-CSF)	human kidney cells	of 50 (600 worldwide) CLOSED
114	A Phase 2 Randomized, Double-Blind, Placebo-Controlled, Parallel-Group, Multi-Center Study of Ad2/Hypoxia Inducible Factor (HIF)-1α/VP16 Administered	Critical Limb Ischemia	Ninewells Hospital, Dundee	12/05	Adenovirus (E1 and E4 deleted)	HIF-1α (Hypoxia-Inducible Factor-1)	human 293 cells	0 of 90 CLOSED

GTAC NO.	PROTOCOL NAME	DETAILS	CENTRE	OUTLINE APPROVAL	VECTOR	GENE	CELL LINE	NO. OF PATIENTS
	by Intramuscular Injection to Patients with No or Poor Option Chronic Critical Limb Ischemia. EudraCT: 2005-004068-21							
115	An open-label dose-escalation study of a self complementary adeno-associated viral vector (scAAV2/8-LP1-hFIXco) for gene transfer in subjects with hemophilia B EudraCT No: 2005-005711-17	HAEMOPHILIA B	Royal Free Hospital, London Guy's and St Thomas' NHS Foundation Trust, London Basingstoke and North Hampshire NHS Foundation Trust	Conditional approval 03/06 Resubmitted in May 08 – Provisional opinion July 08 **Favourable Opinion May 2009**	Recombinant adeno-associated virus (rAAV).	Human FIX gene	293T	3 of 6
116	Phase I/II clinical trial of T cell suicide gene therapy following haploidentical stem cell transplantation EuraCT: 2005-001925-27 Application re-reviewed in July 2010 as the study has not yet commenced.	To prevent GvHD	UCL Institute of Child Health, London	06/06 Further information requested 07/10 Favourable Opinion 11/10	Retrovirus	HSV-TK (herpes simplex thymidine kinase – splice corrected version)	PG13	
117	A Phase I/II feasibility	Renal Cancer	Christie Hospital NHS	Conditional	Vaccinia	Human	Chicken	11 of 20

GTAC NO.	PROTOCOL NAME	DETAILS	CENTRE	OUTLINE APPROVAL	VECTOR	GENE	CELL LINE	NO. OF PATIENTS
	trial to assess the safety, immunological activity and efficacy of TroVax plus interferon-alpha (INF-a) in patients with advanced or metastatic renal cell cancer. EudraCT: 2006-000753-22		Trust, Manchester	approval 04/06; Approval 06/06		oncofoetal antigen 5T4	embryo fibroblasts	CLOSED
118	A Phase I study evaluating the safety and immunogenicity of a new TB vaccine, MVA85A, in healthy volunteers who are infected with HIV. EudraCT: 2006–000076–32	Tuberculosis	The Oxford Radcliffe Hospitals NHS Trust; University of Oxford; Great Western Hospital, Swindon & Marlborough NHS Trust St Mary's Hospital NHS Trust	Conditional approval 04/06; Approval 05/06	MVA	Antigen 85A of M. tuberculosis	Chicken embryo fibroblasts	20 of 20 CLOSED
119	An open-label dose escalation study of an adeno-associated virus vector (AAV2/2-hRPE65p-hRPE65) for gene therapy of severe early onset retinal degeneration. EudraCT: 2006-001571-37	Early-onset retinal degeneration	Moorfields Eye Hospital.	Conditional approval 04/06; Full approval 09/06	AAV2	human RPE65	293T	10 of 12
120	A Phase I trial of AEG35156 administered by 2-hour intravenous infusions in patients with advanced cancers. EudraCT: 2006-001361-42	Advanced cancers	Wythenshawe Hospital & Christie Hospital; South Manchester University Hospitals NHS Trust	Conditional approval 04/06; Approval 05/06	N/a	Antisense DNA to human X-linked inhibitor of apoptosis	*N/a*	29 of 30 CLOSED

GTAC NO.	PROTOCOL NAME	DETAILS	CENTRE	OUTLINE APPROVAL	VECTOR	GENE	CELL LINE	NO. OF PATIENTS
121	An Open Label Phase I Study of CGT-A310, A Tropism Mediated Oncolytic Adenovirus, in Patients with Treatment-Refractory Metastatic Tumours (EudraCT: 2006-002097-21)	Metastatic Tumours	Barts and The London Hospital	Conditional approval 07/06	Ad5/35	TRAIL and Ad5 E1A	CGT-C905	0 - of 30
122	A Randomised Double Blind Dose Ranging Study to Assess the Safety Tolerability and Immunogenicity of a Monovalent H5 DNA Influenza Vaccine (A Vietnam/1194/2004) Administered by Particle Mediated Epidermal Delivery (PMED) to Healthy Adults (EudraCT - 2006-001501-29)	Avian Flu	GDRU (Guy's hospital, London campus)	07/06	Plasmid	Haemagglutinin antigen from influenza strain H5N1	*E. coli*	75 of 75 CLOSED
123	A prospective Randomised Double Blind Placebo Controlled Study to Assess the Efficacy of a Trivalent DNA Influenza Vaccine Administered by Particle Mediated Epidermal Delivery (PMED) Against a Controlled Influenza Virus Challenge (EudraCT: 2006-	Influenza	GDRU (Guy's hospital, London campus) Retroscreen Virology Ltd. Queen Mary, University of London, Barts and the London	Conditional approval 07/06; Approval 08/06.	Plasmid	Haemagglutinin antigen (HA) from three different influenza virus strains	*E. coli*	105 of 105 CLOSED

GTAC NO.	PROTOCOL NAME	DETAILS	CENTRE	OUTLINE APPROVAL	VECTOR	GENE	CELL LINE	NO. OF PATIENTS
	001501-92)							
124	An International, Randomised, Double-Blind, Placebo Controlled, Parallel Group Study to Investigate Whether TroVax Added to First Line Standard of Care Therapy Prolongs the Survival of Patients with Locally Advanced or Metastatic Clear Cell Renal Adenocarcinoma. (TRIST) EudraCT: 2006-001246-13	Renal Cancer	Christie Hospital NHS Trust, Manchester; The Leeds Teaching Hospitals NHS Trust, Leeds Nottingham University Hospitals NHS Trust, NHS Greater Glasgow & Clyde WOS Centre, Sheffield Teaching Hospitals NHS Foundation Trust, Royal Surrey County Hospital NHS Trust, Clatterbridge Centre for Oncology NHS Foundation Trust, South Tees Hospitals NHS Trust, East & North Herts NHS Trust, The Royal Wolverhampton Hospitals NHS Trust, NHS Greater Glasgow & Clyde, Beatson WOS Cancer Centre, Swansea NHS Trust, Churchill Hospital, Oxford Radcliffe Hospitals NHS Trust, University Hospitals of Leicester NHS Trust, Royal Bournemouth and Christchurch Hospitals NHS Foundation Trust,	09/06	Vaccinia	Human oncofoetal antigen 5T4	Chicken embryo fibroblasts	53 - CLOSED

GTAC NO.	PROTOCOL NAME	DETAILS	CENTRE	OUTLINE APPROVAL	VECTOR	GENE	CELL LINE	NO. OF PATIENTS
			Belfast City Hospital Trust,					
124A	TRIST-IR – Analysis of immune responses in a sub-set of patients enrolled into an international, randomised, double blind, placebo controlled, parallel group study to investigate whether TroVax® added to first-line standard of care therapy, prolongs the survival of patients with locally advanced or metastatic clear cell renal adenocarcinoma EudraCT No: 2007-002244-19	Sub-study of 124. Taking extra blood samples on some patients only	Christie Hospital NHS Trust, Manchester;	Conditional approval 10/07 Full App Dec 07				CLOSED
125	Restoring Dystrophin Expression in Duchenne Muscular Dystrophy: A Phase I/II Clinical Trial using Antisense Oligonucleotides. EudraCT: 2006-003833-33	Duchenne Muscular Dystrophy	Depts of Paediatrics, Imperial College London Hammersmith Hospital Campus & St Mary's Hospital Campus, London, Newcastle Upon Tyne Hospitals NHS Foundation Trust; Dubowitz Neuomuscular Centre, Hammersmith Hospital NHS Trust; Leeds Teaching Hospital NHS Trust; Royal Preston Hospital, Royal Manchester	09/06	N/a	Antisense oligonucleotide designed to induce exon skipping" in exon 51 of the DMD gene	*N/a*	8 CLOSED

GTAC NO.	PROTOCOL NAME	DETAILS	CENTRE	OUTLINE APPROVAL	VECTOR	GENE	CELL LINE	NO. OF PATIENTS
			Children's Hospital, Robert Jones Orthopaedic Hospital, Oswestry, Birmingham Heartlands Hospital, Sheffield Children's NHS Foundation Trust, Evelina Children's Hospital, London					
126	A Phase II Study of the Efficacy, Safety and Immunogencity of OncoVEX in Patients with Stage IIIc and Stage IV Malignant Melanoma. EudraCT: 2006-003841-17	Malignant Melanoma	Southampton University Hospitals; Royal Marsden Hospital, London.	Conditional approval 09/06; Approval 11/06	HSV	Human GM-CSF	WHO Vero cell line	50– 50 CLOSED
127	A phase III randomized, open-label and multicentre study with early stopping rules, testing TG4010 subcutaneous injections at the dose of 10^8 pfu in combination with chemotherapy treatment verses chemotherapy alone. EudraCT: 2005-001015-22	Lung cancer	Guy's and St Thomas NHS Foundation Trust, London, Clatterbridge Centre for Oncology NHS Foundation Trust	Conditional approval 09/06; Approval 01/07	MVA	Human MUC1 antigen and human Interleukin-2	Chicken embryo fibroblasts	0 - of 140; STUDY WITHDRAWN IN UK
128	WT1 TCR Gene Therapy of Leukaemia: A Phase I/II Safety and Toxicity Trial. EudraCT: 2006-	Leukaemia	The Royal Free Hospital; University College London Hospital University Hospitals Birmingham NHS Trust	Conditional approval 12/06 Full Approval Dec 07	Retrovirus	T cell receptor specific for Wilms' . Tumour	PG13	- of 18

GTAC NO.	PROTOCOL NAME	DETAILS	CENTRE	OUTLINE APPROVAL	VECTOR	GENE	CELL LINE	NO. OF PATIENTS
	004950-25 Application re-reviewed in July 2010 as the study has not yet commenced			Further information requested 07/10		antigen 1		
129	An Ascending Dose Trial of the Safety, Tolerability and Biological Effect of Intra-arterial Injection of the Selectively Replication-Competent Herpes Simplex Virus HSV1716 in Patients with Unresectable Hepatocellular Carcinoma. EurdraCT: 2005-000133-38	Liver cancer	Queen Elizabeth Hospital,, Birmingham	Approval 02/07 Full Approval 04/07	HSV	n/a	BHK21.c13	- of 9
130	A phase I study to assess the safety and immunogenicity of new TB vaccine candidates FP85A and MVA85A, in healthy adults who have previously been immunized with BCG, using a prime-boost delivery schedule. EurdraCT: 2007-000014-37	Tuberculosis	Churchill Hospital, Oxford	Approval 02/07 Full Approval 03/07	MVA and fowlpox	*M. tuberculosis* antigen 85A	Chicken Embryo Fibroblasts	31 – 36 CLOSED
131	A phase I/II trial to compare the immunogenicity and	HIV infection	St Mary's Hospital, London	Approval 02/07	Vaccinia	HIV-1 *gag, pol, nef,*	Chick Embryo Fibroblasts	22 of 22 CLOSED

GTAC NO.	PROTOCOL NAME	DETAILS	CENTRE	OUTLINE APPROVAL	VECTOR	GENE	CELL LINE	NO. OF PATIENTS
	safety of 3 DNA C prime followed by 1 NYVAC C boost to 2 DNA C prime followed by 2 NYVAC C boost. EudraCT: 2006-006 141-13			Full Approval 04/07		*env, (gp120),* NYVAC C		
132	Gene therapy for SCID-X1 using (SIN) gammaretroviral vector. EudraCT Number: 2007-000684-16	X-linked SCID	Great Ormond Street Hospital	Approval 05/07 Full Favourable Opinion 03/10	Gammaretro virus	Human common cytokine receptor gamma chain (γc)	293T	0 of 10
133	A phase I study to assess the safety and immunogenicity of a new candidate malaria vaccine, AdCh63 ME-TRAP alone and with MVA ME-TRAP, using a prime boost delivery schedule. EudraCT: 2006-005966-37	Malaria	Churchill Hospital, Oxford, Northwick Park Hospital, Harrow,	Approval 06/07 Full Approval 06/07	AdCh63, MVA	ME-TRAP	HEK 293 cells and CEF cells	34 of 32
134	Measurement of human T-cell turnover following vaccination with the tuberculosis vaccine MVA85A. EudraCT: 2007-001293-85	Tuberculosis	Churchill Hospital, Oxford	Approval 05/07	MVA	Antigen 85A	Chicken Embryo Fibroblasts	12 – 12 CLOSED
135	A randomised double-blind placebo-controlled study to evaluate the safety and immunogenicity of a candidate HIV-1	HIV	John Radcliffe Hospital, Oxford	Approval 07/07	MVA	Combinatio n of HIV derives antigens	Chicken Embryo Fibroblasts	0 of 30 Study withdrawn

GTAC NO.	PROTOCOL NAME	DETAILS	CENTRE	OUTLINE APPROVAL	VECTOR	GENE	CELL LINE	NO. OF PATIENTS
	vaccine, MVA.RENTA, delivered intradermally by needle injection, alone or in combination with MVA.HIVA, to HIV-1 seropositive adult subjects receiving Highly Active Antiretroviral Therapy (HAART). EudraCT: 2007-002865-11							
136	Investigation of the safety and feasibility of SERCA gene transfer in the human failing heart using an adeno-associated viral vector EudraCT: 2007-002809-48 Application re-reviewed in September 2010 as study had not yet commenced	Heart disease	Royal Brompton and Harefield NHS Trust, London; Papworth Hospital Cambridge	Approval 07/07 Full approval 03/08 Further info requested 09/10 Favourable opinion 11/10	AAV	Sarco(endo)plasmic reticulum calcium ion adenosine triphosphat ase 2a (SERCA2a)	HEK293	- of 16
137	A randomised, open-labelled, Phase II non-inferiority clinical study between two manufacturing processes for the tuberculosis vaccine, MVA85A EudraCT: 2007-001729-92	Tuberculosis	Churchill Hospital, Oxford	Approval 07/07	MVA	Antigen 85A	Chicken Embryo Fibroblasts	- 30 Study withdrawn February 2008
138	A randomised double-blind placebo-	Critical Limb Ischemia	The Freeman Hospital, Newcastle upon Tyne	Full approval 10/07	Plasmid	FGF1	*E.coli*	9 - 8 in UK 523 - 490 globally

GTAC NO.	PROTOCOL NAME	DETAILS	CENTRE	OUTLINE APPROVAL	VECTOR	GENE	CELL LINE	NO. OF PATIENTS
	controlled parallel group study of the efficacy and safety of 4 administrations of XRP0038/NV1FGF 4mg at 2-week intervals on amputation or any death in critical limb ischemia patients with skin lesions EudraCT: 2006-006277-24		Wythenshawe Hospital Manchester Site Closed 25 September 2009 NHS Tayside , Belfast City Hospital, Royal Bournemouth Foundation NHS Hospital, St George's Healthcare NHS Trust, UH Bristol NHS Foundation Trust, Imperial College Healthcare NHS Trust, Ealing Hospitals NHS Trust					
139	A Phase 1 open-label, dose-escalating study of the safety, tolerability and tumour-specific replication of the intravenous administration of green fluorescent protein encoded genetically engineered attenuated vaccinia virus GL-ONC1 with real-time imaging in patients with advanced solid organ cancers EudraCT: 2007-004228-18	Advance-stage solid tumours with green fluorescent protein (GFP)	Royal Marsden Hospital, Sutton	Conditional approval 10/07 Full Approval December 07	Attenuated vaccinia virus	GFP	Chicken embryo fibroblasts	27 of 60

GTAC NO.	PROTOCOL NAME	DETAILS	CENTRE	OUTLINE APPROVAL	VECTOR	GENE	CELL LINE	NO. OF PATIENTS
140	Evaluation of safety and gene expression with a single dose of pGM169/GL67A administered to the nose and lung of individuals with cystic fibrosis EudraCT 2007-004050-85	Cystic Fibrosis	National Heart & Lung Institute, London (Study conducted at the Royal Brompton Hospital)	Approved 10/07 Full Approval Oct 08	Lipid GL67	CFTR		38 - of 27
141	QUASAR V: A multi-centre randomised placebo-controlled trial of TroVax® vaccination in the adjuvant treatment of stage II and stage III colorectal cancer EudraCT: 2007-005099-15	Colorectal cancer	School of Medical Sciences, University of Oxford, Radcliffe Infirmary, Oxford	Conditional approval 10/07 Resubmitted 10/08 Conditional approval given	MVA	Tumour-associated antigen 5T4	Chick Embryo Fibroblasts	- 2786
142	A phase 1 study to assess the safety and imunogenicity of a new candidate malaria vaccine AdCh63 AMA1 EudraCT 2007-004567-21 **<u>Resubmitted Feb 2009</u>** A phase 1 study to assess the safety and immunogenicity of a new malaria vaccine	Malaria Malaria	Churchill Hospital, Oxford	No decision pending further info 10/07 Provisional Opinion 04/09 Favourable Opinion 06/09	AdCh63, AdCh63	AMA1 AMA1	HEK293 HEK293	0 - 24 13 of 16 CLOSED

GTAC NO.	PROTOCOL NAME	DETAILS	CENTRE	OUTLINE APPROVAL	VECTOR	GENE	CELL LINE	NO. OF PATIENTS
	candidate AdCh63 AMA1 alone and with MVA AMA1 EucraCT No: 2007-004567-21							
143	A Phase 1 study to assess the safety and immunogenicity of a new influenza vaccine candidate MVA-NP+M1 in healthy adults. EudraCT 2007-003970-24	Influenza	Centre for Clinical Vaccinology and Tropical Medicine, Churchill Hospital, Old Road, Headington, Oxford OX3 7LJ	Approval Dec 07 Full Approval February 08	MVA	H3N2	Chick Embroyo Fibroblasts	66 of 58
144	A Phase 1 study to assess the safety and immunogenicity of new Hepatitis C virus vaccine candidate AdCh3NSmut and Ad6NSmut. EudraCT 2007-004259-12	Hepatitis C	Centre for Clinical Vaccinology and Tropical Medicine, Churchill Hospital, Old Road, Headington, Oxford OX3 7LJ, Welcome Trust Clinical Research Facility, University Hospital Birmingham NHS Trust	Conditional Approval Dec 07 Full Approval May 08	Ad6 AdCh3	Multiple hepatitis antigens	PER.C6	40 of 50
145	A randomised, open labelled, phase I, safety, toxicity and exploratory immunogenicity evaluation of therapeutic immunisation +/- IL-2,GM-CSF and growth hormone in HIV-1 infected subjects	HIV-1	Chelsea and Westminster Hospital 369 Fulham Road London SW10 9NH	Conditional Approval Dec 07 Full approval June 08	Plasmid	Multiple HIV antigens	Bacterial cells (E.coli)	10 of 30

GTAC NO.	PROTOCOL NAME	DETAILS	CENTRE	OUTLINE APPROVAL	VECTOR	GENE	CELL LINE	NO. OF PATIENTS
	receiving highly active anti-retrovial therapy (HAART) EudraCT 2008-00575-24							
146	Phase I/II clinical trial of haematopoietic stem cell gene therapy for Wiskott-Aldrich Syndrome EudraCT 2007-004308-11	Wiskott-Aldrich Syndrome	Great Ormond Street Hospital	Conditional Approval Feb 08 **Favourable Opinion Dec 2009**	Lentivirus	Human WAS gene	293 T Cells	- of 5
147	Immunotherapy with CD19ζ gene-modified EBV-specific CTLs after stem cell transplant in children with high-risk acute lymphoblastic leukaemia EudraCT 2007-007612-29	Acute lymphoblastic leukaemia	Great Ormond Street Hospital, University Hospitals Bristol NHS Foundation Trust Marlborough Street	Approval Feb 08 Full Approval 09/08	Retrovirus	CD19 antigen	PG13	- of 30
148	A Phase I randomized, double-blind, placebo-controlled trial to evaluate the safety and immunogenicity of TBC-M4, an env, *gag, tat-rev* and *nef*-RT MVA HIV vaccine and a prime-boost regimen with ADVAX, an *env, gag, nef-tat* and *pol* DNA HIV Vaccine and TBC-M4 EudraCT No: 2007-	HIV	Chelsea and Westminster Hospital	Approval Feb 08 Full Approval April 08	MVA with DNA	Multiple HIV antigens		32 of 35 1300 worldwide

GTAC NO.	PROTOCOL NAME	DETAILS	CENTRE	OUTLINE APPROVAL	VECTOR	GENE	CELL LINE	NO. OF PATIENTS
	007195-42							
149	A multicenter, double blind, placebo controlled, randomized study of TroVax vs placebo in the first line treatment of patients with metastatic colorectal cancer receiving standard of care EudraCT No: 2007-005639-26	Colorectal cancer	Queen Elizabeth Hospital, Birmingham Sheffield Teaching Hospital NHS Foundation Trust St James's University Hospital, Leeds Teaching Hospitals NHS Trust, The James Cook University Hospital (South Tees NHS Trust) Nottingham University Hospitals NHS Trust - City Campus,	Approval Feb 08 Full Approval April 08	Vaccinia	Human onocofoetal antigen 5T4	Chicken embryo fibroblasts	- of -
150	Assessment of protection against malaria by sporozoite challenge of healthy adults vaccinated with AdCh63 ME-TRAP and MVA ME-TRAP EudraCT No: 2007-004360-44	Malaria challenge	Churchill Hospital, Oxford	No decision Feb 08 Full Approval 10/08	MVA	ME-TRAP	HEK 293 cells and CEF cells	- of 26 WITHDRAWN 04.12.08 and Transferred to Oxford A REC
151	A Phase 1, multicentre, randomised study to assess the immunogenicity and tolerance of a combination regime of trivalent DNA influenza vaccine administered by particle mediated	Influenza vaccine	Chiltern Clinical Research Unit, Berks; Chiltern Early Phase Unit, Ninewells Hospital & Medical School, Dundee	Provisional Opinion April 08 Full Approval June 08	DNA	Haemagglutinin antigen from three different influenza strains	*E.coli*	0 - of 200 CLOSED

GTAC NO.	PROTOCOL NAME	DETAILS	CENTRE	OUTLINE APPROVAL	VECTOR	GENE	CELL LINE	NO. OF PATIENTS
	epidermal delivery (PMED) and a standard protein influenza vaccine in healthy elderly adults EudraCT No: 2008-01244-40							
152	A Phase 1-2 multicentre, open-label study of the X-linked inhibitor of apoptosis (XIAP) antisense AEG35156 given in combination with Gemcitabine in patients with advanced pancreatic cancer EudraCT No: 2007-005971-36	Pancreatic cancer	Christie Hospital NHS Foundation Trust	Provisional Opinion April 08 Favourable Opinion August 08	None	Antisense to XIAP gene	none	0 Trial not commenced CLOSED
153	Adoptive immunotherapy for adenovirus (Ad) infection in stem cell transplant recipients EudraCT No: 2008-001207-30			Provisional Opinion April 08	Replication defective Adenovirus Type 5	Not applicable	PERC.6	Notified Jan 09 that study not yet open
154	A Phase 1 clinical trial of a replication defective Ad5 vector expressing nitroreductase and GMCSF (AdNRGM)	Prostate cancer	Queen Elizabeth Hospital at UHB NHS Foundation Trust	Provisional Opinion April 08 Favourable Opinion July 08	E1-E3 deleted replication deficient Adenovirus type 5	E. coli NTR and human GM-CSF	PERC.6	

GTAC NO.	PROTOCOL NAME	DETAILS	CENTRE	OUTLINE APPROVAL	VECTOR	GENE	CELL LINE	NO. OF PATIENTS
	given via brachytherapy, followed by CB1954 in patients with locally relapsed, prostate cancer. EudraCT No: 2007-007041-13							
155	An ascending dose trial of the safety, tolerability and biological effect of a single intratumoural administration of the selectively replication-competent herpes simplex virus HSV1716 in patients with inoperable malignant pleural mesothelioma EudraCT No: 2007-007646-35	Mesothelioma		Provisional Opinion April 08	Oncolytic herpes simplex virus type 1 containing deletion of the RL1 gene encoding ICP34.5	None	BHK21/C13	
156	Registration Phase III Study of Lucanix™ (Belagenpumatucel-L) in advanced non-small cell lung cancer: an international multicentre, randomized, double-blind, placebo-controlled study of Lucanix™ maintenance therapy for stages	Non-small cell lung cancer	Clatterbridge Centre for Oncology NHS Foundation Trust, NHS Tayside Guy's & St Thomas' NHS Foundation Trust The Beatson West of Scotland Cancer Centre	Provisional Opinion July 08 Favourable Opinion 11/08	pCEP4/HBA2 plasmid	Antisense to TGF-β2	Four irriadted non-small cell lung cancer cell lines: H460/HBA2; H520/HBA2; SKLU-1/HBA-2 & RH2/HBA-2.	8 - 162

GTAC NO.	PROTOCOL NAME	DETAILS	CENTRE	OUTLINE APPROVAL	VECTOR	GENE	CELL LINE	NO. OF PATIENTS
	III/IV NSCLC subjects who have responded to or have stable disease following one regimen of front-lone, platinum-based combination therapy. EudraCT No: 2007-005234-36							
157	Dose-Ranging Study of AVI-4658 to Induce Dystrophin Expression in Selected Duchenne Muscular Dystrophy (DMD) Patients EudraCT NO: 2007-004695-30	Duchenne Muscular Dystrophy	UCL Institute of Child Health & Great Ormond Street Hospital for Children, Institute of Human Genetics, Newcastle Hospitals NHS Trust	Provisional Opinion Oct 08 Favourable Opinion Dec 08	None	Antisense targeted to exon 51 of dystrophin gene	None	19 of 17
158	A phase 1/2a randomized, double-blind, placebo-controlled, dose-escalation study To evaluate the safety, tolerability, immunogenicity and vaccine-like viral shedding Of MEDI-534 a live, attenuated intranasal vaccine against respiratory syncytial virus (RSV) and parainfluenza virus type 3 (PIV3) in	Respiratory syncytial virus and parainfluenza virus type 3	Bristol Royal Hospital for Children Upper Maudlin Street,Bristol, Glasgow & Clyde Primary Care, Community & Mental Health Trust, The Leeds Teaching Hospital NHS Trust, Sheffield Children's Hospital, Western Bank, Sheffield, NHS Grampian, Glasgow Health Board, Alder Hey Children's NHS Foundation Trust, Southampton University Hospital NHS Trust, Oxford Vaccine Group,	Provisional Opinion Oct 08 Favourable Opinion Dec 08	Live attenuated vaccine with PIV backbone	Fusion of protein consisting of sequences of RSV with PIV F and HN regions	AGM kidney vero cells	0 of 70

GTAC NO.	PROTOCOL NAME	DETAILS	CENTRE	OUTLINE APPROVAL	VECTOR	GENE	CELL LINE	NO. OF PATIENTS
	healthy 6 to <24 month-old children and in 2 month-old infants EudraCT No: 2008-002651-24		St. George's, University of London Southfields Group Practice, London					
159	A phase II, multic enter, randomized and controlled open-label trial comparing the safety and efficacy of bilateral intraputaminal (IPu) administration of CERE-120 (adeno-associated virus serotype 2 [AAV2] – neurturin [NTN]) combined with best medical therapy (BMT) versus BMT-alone in subjects with idiopathic Parkinson's Disease EudraCT NO: 2007-006721-27	Parkinson's disease	National Hospital for Neurology, London	Provisional Opinion Oct 08	AAV2	Neuturin (NTN)	Not available	STUDY WITHDRAWN
160	**PREFIXED NUMBERS ARE TO BE USED FOR APPLICATIONS THAT ARE TRANSFERRED OUT FROM GTAC TO OTHER DELEGATED COMMITTEES**							
160-01	Study 08/H0707/178 A Randomized Phase 3 Clinical Trial to Evaluate the Efficacy and Safety of Treatment with OncoVEX$^{GM\text{-}CSF}$ Compared to	Melanoma	Senior Lecturer & Hot Consultant in Clinical Oncology Head and Neck Unit Royal Marsden Hospital Fulham Road London SW3 6JJ	Transferred to Hammersmith REC 22.10.08	Not available	Not available	Not available	

GTAC NO.	PROTOCOL NAME	DETAILS	CENTRE	OUTLINE APPROVAL	VECTOR	GENE	CELL LINE	NO. OF PATIENTS
	Subcutaneously Administered GM-CSF In Previously Treated Melanoma Patients with Unresectable Stage IIIb, IIIc and IV Disease EudraCT No: 2008-006140-20							
160-02	09/H0604/9 Assessment of protection against malaria by sporozoite challenge of healthy adults vaccinated with AdCh63 ME-TRAP and MVA ME-TRAP EudraCT No: 2008-006804-46	Malaria Challenge	Oxford Radcliffe NHS Trust Centre for Clinical Vaccinology and Tropical Medicine Churchill Hospital Old Road, Headington Oxford OX3 7LJ	Transferred to Oxford A REC 04.12.08	Not available	Not available	Not available	
160-03	(09/H0604/51) A phase IIa study to assess the safety and efficacy of a new influenza candidate vaccine MVA-NP+M1 in healthy adults EudraCT No: 2009-010334-21	Influenza challenge	Centre for Clinical Vaccinology and Tropical Medicine Churchill Hospital Old Road Headington Oxford OX3 7LJ	Transferred to Oxford A REC 06.03.09	Not available	Not available	Not available	
160-04	A Phase 3 randomised trial of concurrent cisplating and radiotherapy with or without OncoVEX GM-CSF in previously	Carcinoma	Royal Marsden Hospital Head and Neck Unit Fulham Road London SW3 6JJ	Transferred to Hammersmith, Q Charlotte's & Chelsea REC 08.03.10	Herpes simplex virus type 1	ICP34.5-deleted ICP47-deleted Human GM-CSF	BHK 21c13	

GTAC NO.	PROTOCOL NAME	DETAILS	CENTRE	OUTLINE APPROVAL	VECTOR	GENE	CELL LINE	NO. OF PATIENTS
	untreated patients with locally advanced squamous cell carcinoma of the head and neck EudraCT 2010-019071-29							
161	A Phase 1 safety trial of CTX0E03 drug product delivered intracranially in the treatment of patients with stable ischaemic stroke EudraCT No2008-00696-19	Ischaemic Stroke	Southern General Hospital Glasgow	Deferred 02/09 Provisional Opinion 04/09 Fav Opinion with conditions 07/09 Fav Opinion 02/10	Not applicable	Not applicable	CTXOE03	2 - 12
162	A phase 1 study to assess the safety and immunogenicity of Ad6NSmut and AdCh3NSmut in patients with hepatitis C virus infection EurdraCT No: 2008-006127-32	Hep C	John Radcliffe Hospital Headington Oxford OX3 9DZ Queen Elizabeth's Hospital, University Hospital Birmingham NHS Foundation Trust Wolfson Drive Edgbaston, Birmingham B15 2TH	Provisional Opinion 04/09 Favourable Opinion 06/09	Human Adenovirus Type 6 serotype pluse Chimpanzee Adenovirus Type 3 serotype	Encoding mutated non-structural region of Hepatitis C Virus	PERC.6	31 of 34
163	A phase II immunogenicity trial of AlphaVax Cytomegalovirus vaccine in allograft candidate recipients	CMV	UCL Medical School Rowland Hill Street London NW3 2PF	Provisional Opinion 04/09	Alphavirus	Encoding a fusion protein of glycoprotei n B, phosphopro	Vero	Notified August 09 that study has been put on hold.

GTAC NO.	PROTOCOL NAME	DETAILS	CENTRE	OUTLINE APPROVAL	VECTOR	GENE	CELL LINE	NO. OF PATIENTS
	EurdraCT No: 2009-009905-24					tein 65 and Immediate Early gene product 1		
164	A phase II prospective randomised double-blind placebo controlled study to assess the efficacy of the influenza vaccine BHG1L1 administered intranasally against a controlled influenza virus challenge in healthy adults EudraCT No: 2009-011529-15	Influenza challenge		Provisional Opinion 07/09 Favourable Opinion 02/10	Replication defective H5N1 influenza virus containing deletion of NS1 gene	None	Vero	CLOSED
165	HIV-CORE 001 – A randomised placebo-controlled study to evaluate the safety and immunogenicity of a candidate HIV-1 vaccine, MVA.HIVconsv, delivered by intramuscular needle injection to HIV-1 seropositive adult subjects receiving antiretroviral therapy (ART) EudraCT No: 2009-012662-31	HIV		Provisional Opinion 07/09 Favourable opinion 09/09	Modified Vaccinia Virus Ankara (MVA)	Encoing HIV conserved regions	HEK293	9 - 20

GTAC NO.	PROTOCOL NAME	DETAILS	CENTRE	OUTLINE APPROVAL	VECTOR	GENE	CELL LINE	NO. OF PATIENTS
166	A phase I/IIa study to assess the safety and immungenicity of new malaria vaccine candidates AdCh63 MSP1 alone and with MVA MSP1 EudraCT No: 2009-012591-27	Malaria	Centre for Clinical Vaccinology and Tropical Medicine Churchill Hospital Oxford Imperial College, London	Provisional Opinion 07/09 Full Favourable Opinion 09/09	Chimpanzee Adenovirus pluse Modified Vaccinia Virus Ankara (MVA)	Merozoite Surface Protein-1 (MSP-1)	HEK 293	16 of 15
167	A Phase 2 study of JX-594 (Thymidine Kinase-deleted vaccinia virus plus GM-CSF) administered by intratumoural injection in patients with metastatic colorectal tumours within the liver EudraCT No: 2009-014814-86	Liver Cancer	Oxford Radcliffe Hospital Trust Dept of Medical Oncoloy Churchill Hospital Headington Oxford OX3 7LJ	Favourable Opinion subject to Conditions 09/09	TK-deleted Vaccinia Virus	GM-CSF	HeLA	
168	A Phase 1 dose escalation trial of a group B oncolytic adenovirus (Co1oAd1) Administered by intrahepatic artery infusion in patients With primary or secondary liver cancer EudraCT No: 2009-014919-12	Liver Cancer	Oxford Radcliffe Hospital Trust Dept of Medical Oncoloy Churchill Hospital Headington Oxford OX3 7LJ	Favourable Opinion subject to Conditions 12/09 Favourable Opinion 01/10	Group B Adenovirus containing multiple deletions	None	A549 human lung carcinoma	
169	CMV TCR Gene	Stem Cell	University College London	Favourable	Retrovirus	Fusion of	PG20	- 10

GTAC NO.	PROTOCOL NAME	DETAILS	CENTRE	OUTLINE APPROVAL	VECTOR	GENE	CELL LINE	NO. OF PATIENTS
	Therapy: A phase 1 safety, toxicity and feasibility study of adoptive immunotherapy with CMV TCR-transduced donor-derived T Cells for recipients of allogeneic haematopoietic stem cell transplantation EudraCT No: 2008-006649-18	Transplantation	Royal Free Campus London NW3 2PF	Opinion subject to Conditions 12/09 Favourable opinion given 06/10	pMP71	alpha and beta genes encoding CMV T-cell receptor		
170	A phase 1/11 study of the safety, efficacy and dose evaluation of ProSavin®, administered using stereotactic injection to the striatum of patients with bilateral, idiopathic Parkinson's Disease EudraCT No: 2007-001109-26	Parkinson's Disease	University of Cambridge Centre for Brain Repair Cambridge CB2 0PY	Favourable Opinion subject to Conditions 12/09 Full favourable opinion 05/10	Equine Infectious Anaemia Virus (EIAV)	Tyrosine hydroxylase, aromatic L-amino acid decarboxylase and GTP-cyclohydrolase 1	HEK 293T	
170 A	A multicentre, open-label study to determine the long term safety, tolerability and efficacy of ProSavin® in patients with bilateral, idiopathic Parkinson's disease	Parkinson's Disease long term follow up		Provisional Opinion 10/10 Favourable Opinion 02/11				

GTAC NO.	PROTOCOL NAME	DETAILS	CENTRE	OUTLINE APPROVAL	VECTOR	GENE	CELL LINE	NO. OF PATIENTS
	EudraCT No: 2007-017253-35							
171	An open label dose escalation Phase 1 clinical trial of retinal gene therapy for choroideraemia using an adeno-associated viral vector (AAV2) encoding Rab-escort protein 1 (REP1) EudraCT No: 2009-014617-27	Choroideraemia	John Radcliffe Hospital Oxford OX3 9DU	Provisional Opinion 12/09 Favourable opinion 02/11	AAV2	Rab Escort Protein 1 (REP-1)	HEK293	
172	A Phase I/II trial of SCIBI, an DNA immunotheraepy, in the treatment of patients with malignant melanoma EudraCT No: 2009-017355-10	Malignant Melanoma	City Hospital Hucknall Road Nottingham NG5 1PB Freeman Hospital Freeman Road Newcastle-upon-Tyne NE7 7DN The Christie NHS Foundation Trust Wilmslow Road Withington Manchester M20 4BX	Provisional Opinion 10/03/10 Favourable opinion 27/04/10	Plasmid	IgG1 light and heavy chains		6 - 22
173	WT1 Immunity vis DNA fusion Gene Vaccination in Haematological Malignancies by intramuscular injection	Leukaemia	Southampton General Hospital	Provisional Opinion 05/10 Favourable Opinion 09/10		WTI-37 DNA vaccine		1 - 184

GTAC NO.	PROTOCOL NAME	DETAILS	CENTRE	OUTLINE APPROVAL	VECTOR	GENE	CELL LINE	NO. OF PATIENTS
	followed by intramuscular electroporation EudraCT No:2009-017340-14							
174	A Phase II trial to assess the safety, immunological activity of TroVax® plus Pemetrexed/Cisplatin in patients with malignant pleural mesothelioma EudraCT No: 2010-023230-22	Mesothelioma		Provisional Opinion 12/10	Vacinnia virus Ankara (MVA)	Human tumour associated antigen 5T4	Chick embryo cells	