



## **GLOSSARY OF TERMS**

<b>Adjuvant therapy:</b>	Any treatment given after the primary treatment to improve the chances of increased benefit. Adjuvant therapy may include chemotherapy, immunotherapy, radiation therapy, hormone therapy, biological therapy or any and all of the above.
<b>Adverse event:</b>	An adverse event is any adverse change in health or side effect that occurs in a person who participates in a <a href="#">clinical trial</a> while the patient is receiving the treatment (study medication, application of the study device, etc.) or within a previously specified period of time after the treatment has been completed. Adverse events are graded 1-5 using standard common toxicity criteria developed by the United States National Institutes of Health. Grade 3-5 adverse events are defined as serious adverse events.
<b>Antigen:</b>	A protein that is recognized as foreign by the immune system and that has the ability to induce a specific immune response.
<b>Antigen specific effector (killer) T cells:</b>	Immune cells that are responsible for selectively killing and eliminating cancer cells and many infectious agents, including viruses, from the body. Along with antibodies, these cells are responsible for the immune protective and therapeutic effects of the adaptive immune system.
<b>Apheresis:</b>	A procedure during which blood is drawn and separated into its components by a process similar to dialysis where some components are retained and some are returned to the donor.
<b>Astrocytoma:</b>	A tumor that begins in the brain or spinal cord in small, star-shaped cells called astrocytes that are a subset of glial cells. Grade IV astrocytomas are generally referred to as glioblastoma multiforme.
<b>Autologous:</b>	Derived from the same individual. When used to describe a medical procedure such as a transplant, it means a body component that is removed and then returned to the same individual.
<b>B Cells</b>	One of the three main cell types contained in the portion of the immune system that is responsible for antigen-specific immunity. B cells produce antibodies, which mediate other functions of the adaptive immune system.
<b>Biopsy:</b>	A medical test involving the removal of cells or tissues for examination; the medical removal of tissue from a living subject for the purpose of determining the presence or extent of a disease.

<b>Biotherapeutics:</b>	The field encompassing therapeutic materials produced using biological means, including immunologic and recombinant DNA technology.
<b>Carcinoma:</b>	The most common type of cancer occurring in humans, a carcinoma is a cancer that begins in a tissue that lines the inner or outer surfaces of the body.
<b>Cell infusion:</b>	Delivery of cells by injection from an infusion bag into a blood vessel over a period of time.
<b>Cell mediated immune response:</b>	An adaptive immune response produced by antigen specific effector T cells.
<b>Clinical trial:</b>	Any investigation in humans intended to discover or verify the effects of an investigational drug or biological or new use of an already marketed drug or biological, and/or to identify any adverse reactions to the investigational drug or biological with the object of determining safety and/or efficacy of the studied use. The terms “clinical trial” and “clinical study” are synonymous.
<b>Common toxicity criteria (CTC):</b>	A standardized classification of side effects used in assessing toxicities during clinical trials.
<b>Conformal:</b>	Term used to describe image guided radiotherapy that is focused on the edges of surgically resected cancers. Designed to conform to the site and shape of the cancer so as to limit damage to normal tissue.
<b>Cytokine:</b>	Any of a number of substances, such as interferons, interleukins, and growth factors that control communications between cells. Distinguished from hormones by the fact that they only act locally on adjacent cells in the same area where they are produced.
<b>Cytotoxic:</b>	Toxic to living cells.
<b>Cytotoxic chemotherapy:</b>	Chemicals or drugs that kill cells, especially cancer cells. Their side effects are typically related to the fact that they kill healthy normal cells in addition to cancer cells.
<b>Delayed type hypersensitivity skin test:</b>	A skin test that is used to measure T cell-mediated immunity. The delayed type skin reaction typically takes 24 to 72 hours to develop. The best known example is the tuberculin skin test for tuberculosis. Called ‘delayed’ to distinguish it from immediate hypersensitivity, which typically takes minutes to a few hours to develop and is mediated by antibodies. The best known example of testing for immediate hypersensitivity is allergy testing.
<b>Dendritic cell:</b>	A type of immune cell that is specialized to process and present antigens to T cells. Therefore, also called antigen presenting cells. Dendritic cells are present in tissues in contact with the external environment, such as the skin and the inner lining of the nose, lungs, stomach and intestines and can also be found in an immature state in the blood. Dendritic cells carry antigens from body surfaces to lymphoid tissue where the processed antigen is presented to T cells in a form that leads to the generation of an

adaptive immune response.

**DNA (deoxyribonucleic acid):**

A linear polymer found in the nucleus of a cell that encodes the cell's genetic information.

**Efficacy:**

The ability to produce a desired favorable effect in treating or preventing the studied disease or condition.

***Ex vivo:***

Outside the living body

**Food and Drug Administration (FDA):**

The branch of the U.S. Department of Health and Human Services responsible for regulating the approval and use of drugs, medical devices, cosmetics, and foods.

**Glioma:**

A primary brain tumor that originates from non-neuronal supportive cells of the brain, called glial cells.

**Good Clinical Practices (GCP):**

National and international regulatory guidelines for the design, conduct, performance, monitoring, auditing, recording, analysis, and reporting of clinical trials that provides assurance that the data and reported results are credible and accurate, and that the rights, integrity, and confidentiality of trial participants are respected and protected.

**Good Manufacturing Practices (GMP):**

National and international regulatory guidelines designed to insure consistent manufacturing of safe and effective medical products.

**Grade:**

A description of a tumor based on how abnormal the cancer cells look under a microscope and how quickly the tumor is likely to grow and spread. Grading systems are different for each type of cancer but are generally scored from 1-4 with grade IV being the most malignant.

**Granulocyte Macrophage Colony Stimulating Factor (GM-CSF):**

A cytokine that functions as a white blood cell growth factor, specific for granulocyte and macrophage stem cells. GM-CSF also has the ability to activate dendritic cells. This latter property is responsible for GM-CSF's potency as an immunological adjuvant.

**Growth factor:**

A naturally occurring substance capable of stimulating cellular growth, proliferation and cellular differentiation.

**Immune:**

An individual's ability to protect itself from a disease causing agent by virtue of having or producing antibodies or lymphocytes capable of reacting with a specific antigen associated with that agent. Also, generally refers to an individual's ability to resist disease-causing agents by any means.

**Immunogenic:**

Relating to or denoting substances able to stimulate an immune response.

**Immunogenicity:**

Ability of a particular substance, specifically an antigen or complex of antigens, to provoke an immune response in the body.

<b>Immunotherapeutic:</b>	Treatment of disease by inducing, enhancing or suppressing an immune response.
<b>Institutional Review Board (IRB):</b>	Also known in some countries as the <b>Ethics Review Board</b> , or <b>ERB</b> . This is the panel of experts at a clinical trial site that conducts a scientific and ethical review of a study protocol and then authorizes that specific institution to participate in the study protocol. The IRB or ERB is charged with insuring that the rights of study participants are protected and that each participant enrolled in the trial has given their fully informed consent to participate in the clinical trial.
<b>Interleukin-2 (IL-2):</b>	A cytokine that is produced by T cells and stimulates T cells to multiply.
<b>Investigational New Drug Application (IND):</b>	Application to the FDA for authorization to begin to test a drug or biologic in humans. May be filed by individuals, research institutions or companies. The IND becomes effective, if the FDA does not disapprove it within 30 days or implement a 'clinical hold', which prevents the applicant from treating a patient until all issues have been resolved. The IND shows results of previous experiments; how, where and by whom the new studies will be conducted; a full description of the agent being evaluated; how it is thought to work in the human body; any toxic effects found in the animal studies; and how the agent is manufactured. All study protocols to test the agent are recorded under the IND number. All clinical trials being performed using one of those protocols must be reviewed and approved in advance by the IRB where the trials will be conducted (in Europe, the ERB).
<b>Investigator (or clinical investigator):</b>	A health care professional responsible for the conduct of a clinical trial at a clinical trial site and who coordinates with the study sponsor and the IRB. If a trial is conducted by a team of individuals at a trial site, the investigator is the responsible leader of the team and may also be called the principal investigator.
<b>Irradiated:</b>	Exposed to radiation, as for diagnostic or therapeutic purposes. Radiation damages DNA in such a way as to render cells replication incompetent. Cancer cells can be exposed to a sufficiently high dose of radiation to render them completely incapable of replicating.
<b>Killer T cell:</b>	A fully differentiated T cell that functions in cell-mediated immunity by attacking and killing target cells that have specific surface antigens. Also called cytotoxic T-cells.
<b>Macrophage:</b>	A multifunctional white blood cell that specializes in engulfing invading microorganisms. Additional functions of macrophages include the ability to be activated to kill cancer cells, the ability to function as antigen presenting cells (dendritic cells) and the ability to be activated to suppress immune responses.
<b>Malignancy:</b>	A tumor that is capable of spreading beyond its site of origin, often to other regions of the body and ultimately producing death, if left untreated. Compared to benign tumor that only grows locally and generally can be cured surgically.

Synonymous with cancer.

**Malignant transformation:**

The process by which normal cells become cancer cells.

**Metastatic:**

Cancer that has spread from its site of origin to another location in the body.

**Monoclonal antibodies:**

Antibodies that all have an identical structure because they are made by a population of identical immune cells that is a clone derived from a single parent cell.

**Mucositis:**

The inflammation and ulceration of the mucous membranes lining the digestive tract, usually as an adverse effect of chemotherapy and radiotherapy treatment for cancer.

**Mutation:**

A change in DNA structure of a particular gene that changes the genetic message carried by that gene when the cell duplicates itself. May occur spontaneously during cell replication or may be caused by external agents such as radiation that damage DNA.

**New Drug Application (NDA):**

An application to the FDA for marketing approval for a drug. Same as a BLA, but applies to drugs, not biologicals. Applications are reviewed by the Center for Drug Evaluation and Research (CDER) the division of the FDA that is responsible for drug regulation.

**Objective response rate**

The percentage of patients who cancer shrinks or disappears after treatment

**Orphan product designation:**

A special status granted by the Orphan Drug Act (“ODA”) to a product to treat a rare disease or condition upon request from a sponsor. Orphan Product Designation generally requires either of the following: (1) the disease or condition for which the product is intended has a prevalence that totals fewer than 200,000 people in the United States or, if the drug is a vaccine, diagnostic drug or preventive drug, the persons to whom the drug will be administered in the United States are fewer than 200,000 per year, or (2) for a drug intended for diseases or conditions affecting 200,000 or more people, or for a vaccine, diagnostic drug, or preventive drug to be administered to 200,000 or more persons per year in the United States, there is no reasonable expectation that costs of research and development of the drug for the indication can be recovered by sales of the drug in the United States. Orphan product status gives a product certain benefits, the most important of which is a period of seven years of marketing exclusivity following FDA marketing approval. Similar regulations exist in the European Union.

**Phase in product development:**

Therapeutic development is divided into phases that are determined by the main objectives of the development process.

**Phase I:**

A phase I clinical trial is the first step in testing a new investigational medication (or new use of a marketed medication) in humans. Phase I studies are mainly concerned with evaluating a medication’s safety, including the safe dosage range. Except for medications used to treat cancer, phase I clinical trials are usually conducted in healthy individuals and

are not intended to treat disease or illness. Because cancer can be such a life-threatening condition and many effective anti-cancer agents have high toxicity, phase I trials with anti-cancer medications are usually carried out in patients who already have the disease and who have failed standard of care treatments. Phase I studies may provide a preliminary insight into the medication's efficacy.

**Phase II:**

Phase II clinical trials involve subjects who have the disease or condition to be treated with the test medication. These trials are designed to acquire more information on the safety of the new treatment and to begin to determine how effective the new treatment could be in the targeted disease or condition. Phase II studies may also be performed to determine optimal dosing and delivery regimens. Many different study designs may be employed in Phase II, including small randomized studies. Patients are carefully monitored for side effects and for any improvement in their illness, symptoms, or both.

**Phase III:**

After a treatment has been shown to have positive safety and efficacy results in small groups of patients, it may be studied in a larger Phase III trial to confirm efficacy and identify adverse events from long-term use. A Phase III trial usually compares how well the study treatment works with an inactive placebo and/or another approved medication. Usually subjects are randomly entered into comparator study arms and, optimally, study participants (subjects and investigators), will be blinded with regard to which study treatment a particular subject is receiving. Phase III studies generally also are multi-center, meaning that subjects are treated at multiple clinical trial sites in order to minimize the bias that might occur through the treatment of all subjects at a single trial site by a single clinical investigator. Phase III trials are generally designed to obtain definitive outcome data for the purposes of submitting a BLA or NDA for marketing approval from the FDA or other regulatory authority.

**Pivotal study:**

Typically a Phase III study which is designed to generate the data required by a regulatory agency to decide whether or not to approve a drug.

**Preclinical study:**

A laboratory or animal study of a biological, drug, device, or procedure to find out if the new treatment shows enough promise to be studied in humans.

**Progression free survival:**

A term used to describe the length of time during and after treatment during which the disease being treated (usually cancer) does not get worse.

**Protocol:**

A written action plan for a clinical trial. The plan states what will be done in the study and why. It outlines how many participants will take part in the study, what types of patients may take part, what tests they will receive and how often, what the treatment plan is, and the sponsor's plan to analyze the data when the study is completed.

**Radiographic:**

The use of X-rays to view a non-uniformly composed material such as the human body.

<b>Radiotherapy:</b>	The treatment of disease, such as cancer, by exposure to a radioactive substance.
<b>Receptors (T cell)</b>	A molecule found on the surface of T lymphocytes (or T cells) that is responsible for recognizing antigens bound to major histocompatibility complex (MHC) molecules.
<b>Resection:</b>	Removal of an organ, lesion or cancerous tumor by cutting it away from the body or the remainder of the tissue.
<b>Stable disease:</b>	Progression-free survival greater than six months.
<b>Stage</b>	The extent of a cancer in the body. Staging is usually based on the size of the tumor, whether lymph nodes contain cancer, and whether the cancer has spread from the original site to other parts of the body.
<b>T cell:</b>	A white blood cell responsible for cell-mediated immunity, the process that is responsible for attacking and destroying virus-infected cells, foreign tissue and tumor cells. T cells are one of three main cell types (others are B cells and macrophages) of the portion of the immune system that is responsible for adaptive immune responses and antigen-specific immunity.
<b>Time to progression</b>	A measure of time after a disease is diagnosed (or treated) until the disease starts to get worse
<b>Tumor:</b>	An abnormal mass of tissue. Tumors can be benign or malignant (cancerous).
<b>TVAX Immunotherapy<sup>®</sup></b>	General treatment approach that employs the combination of vaccination to induce an immune response against the disease causing agent and intravenous infusion of blood derived antigen specific effector T cells that TVAX founders have tested in university-sponsored and company sponsored clinical trials.
<b>WHO:</b>	World Health Organization.