



IMT-1012 Cancer Immunotherapy Clinical Trial Overview

COMPANY OVERVIEW

Immunotope is a clinical stage biotechnology company dedicated to developing and commercializing new approaches to the diagnosis, treatment and prevention of recurrence of cancer and infectious diseases.

Our comprehensive approach to cancer therapy focuses on effective treatments that **destroy tumors** and **prevent metastasis**, and the critical, unmet need to diagnose cancer at the very earliest stages.

Immunotope's immunotherapeutic vaccine products are designed to cure the patient, because once immunized, the patient develops long-lasting immunity that recognizes and destroys recurrent or metastatic tumor cells whenever and wherever they may arise, even at distal locations.

- DIRECT TARGETING OF CRITICAL TUMOR PATHWAYS
- TARGETING THE IMMUNOPROTEOME – THE ONLY ANTIGENS RECOGNIZED BY THE IMMUNE SYSTEM
- RAPID TIMELINE FROM DISCOVERY TO CLINIC
- EARLY-STAGE DIAGNOSTICS

IMT-1012 IMMUNOTHERAPEUTIC VACCINE PHASE I CLINICAL TRIAL IN OVARIAN AND BREAST CANCER

Immunotope's lead product is the IMT-1012 immunotherapeutic vaccine, a formulation of twelve different novel antigens. Each antigen in the vaccine targets a separate, critical tumor pathway including malignant transformation, activation of oncogenesis, metastasis, inhibition of tumor suppressors, apoptosis, DNA replication and repair, and cell cycle regulation (Figure 1).

This multi-targeting strategy affords broad coverage to account for tumor complexity and heterogeneity, and significant minimization of the potential for tumor escape. The vaccine targets essential pathways known to be present in aggressive tumors.

An Investigational New Drug (IND) application has been cleared by FDA to evaluate safety, efficacy and antigen-specific T cell responses in advanced Stage III/IV postsurgical ovarian cancer patients and in node positive, Her2 negative breast cancer patients. In this two-dose study, the primary endpoints are safety and T cell response, with a secondary endpoint evaluating the delay in recurrence of disease.

The Phase I trial is being conducted at the Duke University Cancer Center.

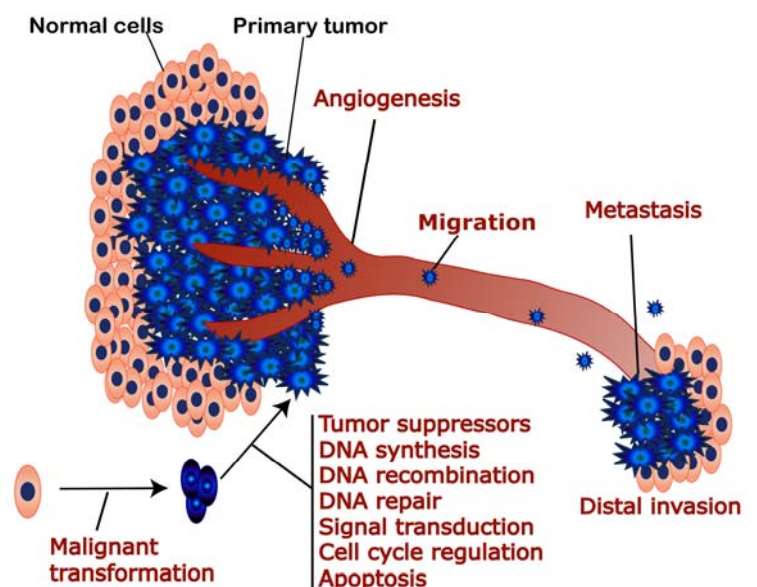


Figure 1. The IMT-1012 vaccine targets twelve different cancer pathways (red font) essential to many cancer processes including malignant transformation, survival and metastasis. Each of these antigens acts on a pathway or process that is also targeted by various small molecule therapeutics and monoclonal antibodies. We are investigating whether paired combinations of antigens and targeted therapeutics synergize to enhance tumor killing. (Figure adapted from Chambers and Matrisian J Natl Cancer Inst. 1997;89:1260-70.)

IMMUNOTOPE TECHNOLOGY: THE RIGHT ANTIGENS ARE KEY TO SUCCESSFUL IMMUNOTHERAPY

Immunotope's proprietary immunoproteomics platform identifies novel antigens that are critical to effective immunotherapy and diagnosis for all solid tumor cancers. We directly extract and characterize the immunoproteome- a subset of proteins representing less than 1% of all proteins present in tumor cells. Although tens of thousands of tumor proteins have been identified, only a very few- the proteins of the immunoproteome- are processed and presented in such a way that cytotoxic T cells of the immune system can recognize and can be activated against the tumor. Immunoproteomics identifies the tumor cell 'signature' associated with Major Histocompatibility Complex (MHC) molecules (Figure 2). These antigen complexes are the signals recognized by cytotoxic T lymphocytes (CTL) that instruct the CTL to destroy cells presenting the tumor signature. Immune system recognition is essential to immunotherapeutics development because a positive clinical outcome will only be realized if the immune system is activated against the tumor signature that is actually presented on diseased cells in the patient's body. Each IMT-1012 antigen is a component of the immunoproteome.

THE CLINICAL SIGNIFICANCE OF IMMUNOTOPE'S IMT-1012 TUMOR ANTIGENS

Ovarian cancer remains the most lethal gynecologic malignancy and a leading cause of cancer death in Western industrialized countries. Although a majority of women with advanced ovarian cancer achieve complete clinical remission after surgery and chemotherapy, most develop fatal recurrences. And while localized breast cancer is curable in a high percentage of patients, those with four or more positive axillary lymph nodes or spread to supraclavicular nodes, or metastatic disease also experience a high rate of relapse. The IMT-1012 vaccine is the first multivalent vaccine for ovarian and breast cancer that contains twelve antigens in the that are confirmed to be present in ovarian and breast tumor signatures. Each antigen acts on an essential tumor pathways. Examples of antigens and their targets are illustrated in Figure 1 (Table 1).

Table 1. Examples of IMT-1012 antigens and their targeted antitumor mechanisms.

| Source Protein | Targeted Mechanism (Pathway) |
|------------------------------|-----------------------------------|
| Cyclin I | Cell cycle regulation |
| Topoisomerase II | DNA synthesis |
| TACE/ADAM17 | Angiogenesis |
| EDDR1 | Malignant transformation |
| Cyclin-Dependent Kinase CDC2 | Cell cycle regulation |
| Replication Protein A | DNA replication and recombination |

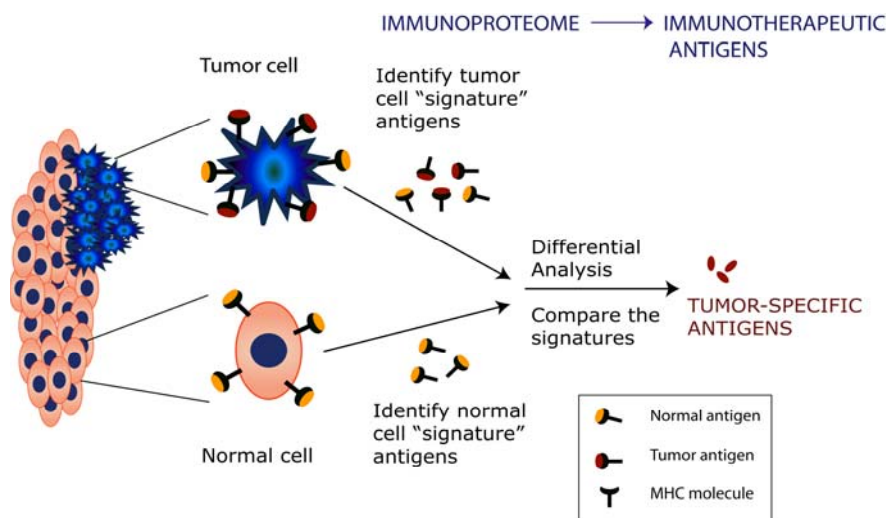


Figure 2. Immunotope directly extracts MHC-antigen complexes from tumor and normal cells to identify the antigens that comprise the tumor cell immunoproteome, the subset of less than 1% of cellular proteins that only occur on tumors and can be recognized by cytotoxic T lymphocytes. The tumor-specific response can only be activated against antigens that are actually presented by MHC molecules on cells in the patient's body.

APPLICATIONS FOR ALL SOLID TUMOR CANCERS

While the IMT-1012 clinical study will be conducted in ovarian and breast cancer patients, the concept of indication-optimized multivalent vaccines is broadly applicable to the treatment of many types of solid tumors. Several of the antigens in the IMT-1012 vaccine are present in multiple tumor types.

FOR MORE INFORMATION CONTACT

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