

THERAPEUTIC CANCER VACCINES: ELUCIDATING THE DIFFERENCES BETWEEN PASSIVE AND ACTIVE IMMUNOTHERAPY

by Lou Iovino



Despite several cancer therapeutic agents in Phase III development, there is still confusion surrounding the meaning of the terms “passive” and “active immunotherapy” vs. “cancer vaccines.”

The recent approval of Gardasil® (Quadrivalent Human Papillomavirus [Types 6, 11, 16, 18] Recombinant Vaccine, Merck & Co. Inc) has been hailed as a success story for cancer vaccines. However, this prophylactic vaccine against cervical cancer, precancerous and low-grade lesions, and genital warts caused by certain HPV types, has led to some confusion around cancer vaccine research, and has prompted cancer vaccine developers to launch educational initiatives to help clarify the differences.

According to the Cancer Vaccine Consortium, “Prophylactic vaccines, like childhood immunizations and the HPV vaccine, provide protective immunity before diseases occur, averting their full impact. Therapeutic cancer vaccines, however, seek to boost the immune system and are used after disease onset. The goal of these ‘active immunotherapies’ is to produce strong anti-tumor immunity, shrinking or delaying growth of tumors and initiating periods of remission and improved quality of life, while avoiding the side effects associated with surgery, radiation, or chemotherapy.”

Passive vs. Active Immunotherapy

Active immunotherapy is poised to change the face of cancer treatment. Before this can happen, however, there is a pressing need to educate the oncology and healthcare communities about the differences between passive and active immunotherapy and the potential benefits to patients.

Passive immunotherapy involves creating antibodies outside the body, then infusing them into the patient. The antibody binding to a specific cell surface protein triggers widespread wholesale killing of any antibody-bound cell.

“With passive immunotherapies, there is no immune system education. The immune system responds to the antibody-bound cells for as long as the infused antibody remains in the body; so this passive immunotherapy approach doesn’t provide true immune system education or memory,” said David Johnson, Director of Medical Liaisons for Favril Inc. “The goal of patient-specific active immunotherapy is to truly educate a patient’s own immune system to mount a vigorous, targeted, and sustained attack against only the cancer cells.”

To be successful, active immunotherapies must isolate a target that exists only on tumor cells and not on normal, healthy cells. The mechanism of action of the antibody rituximab [Rituxan®; Genentech] illustrates this point. “Rituximab targets CD20, which is also present on the great majority of all B cells,” according to Johnson. “When the immune system responds to the binding of CD20, it responds indiscriminately, whether the cells are malignant or normal, leading to the elimination of the majority of a patient’s normal B-cell population. Conversely, if you can isolate a homogenous target that only exists on the patient’s tumor cells, then you may have an ideal target for an active immunotherapy, which may offer a long-term immune system response against the tumor.”

Getting Closer

Cancer vaccine development today is analogous to where monoclonal antibody development was 10 years ago. There have been a lot of early-stage trials, the results of which indicate that the approach could work, but no company has been able to bring a product forward. However, advances in robotics that have spun out of the human genome project with regard to molecular biology, and our understanding of how the immune system works are helping to bring active immunotherapies closer to realization.

“We are learning that active immunotherapy products probably work best in a setting of low tumor burden,” said David Guy, Chief Commercial Officer of Favril Inc.



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Developers have also learned that it takes time for patients to develop an immune response. “For instance, with non-Hodgkin’s lymphoma,” said Guy, “you can cytoreduce quite effectively with a number of agents, get a patient into remission, administer an active immunotherapy product, and have time for an immune response to develop.”

Bringing an Active Immunotherapy to Market

While it is important, for active immunotherapy developers to differentiate their products from preventative vaccines among the scientific community, it is also a key initiative from a business perspective. “The payor knowledge and understanding of vaccines is in the preventative vaccines. So, that has implications with cost of therapy, duration of therapy, and expectations of efficacy or cure,” said Guy. “Therapeutic vaccines are very different. Because these active immunotherapies are individualized, the cost structure is totally different. We don’t want to spend time or resources engaging the payors on these differences, we’d rather recategorize the therapy.”

One aspect of cancer treatment today that is helping to make active immunotherapies commercially viable is that the annual pricing of novel oncology products is approximately \$50,000. At this pricing level, production of an individualized active immunotherapy becomes commercially viable. Furthermore, if this approach can put patients into long-term remissions, then it has the potential to become a cost-effective option to cancer treatment.

“Active immunotherapy will have an increasingly important role in the treatment of a variety of cancer types,” said Al Medwar, Head of Oncology Marketing, EMD Pharmaceuticals. “Given the significant number of approaches being explored, it is likely that some of these approaches will be effective and may dramatically change the treatment of both solid tumors and hematologic malignancies. This is important because despite recent advances in cancer treatment, patients and healthcare providers are still in need of additional treatment options.” ■■■■

DIFFERENCES BETWEEN ACTIVE AND PASSIVE IMMUNOTHERAPY

Passive Immunotherapy		Active Immunotherapy (Id-KLH)
Antibodies manufactured and administered to patient	Source of Immune Response	Patients own immune system
Humoral Antibodies	Type of Immune Response	Humoral (antibodies) and cellular (T cells)
Effective only while antibodies present	Duration of Immune Response	May persist for long time (immunologic memory)
Relapse if antigen changes	Specificity of Immune Response	Broad response (less prone to antigen mutational response)

Source: Favril Corporation