Immunophotonics, Inc.
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Interventional immuno-oncology: a transformational approach to treat solid tumors

Immunophotonics aims to revolutionize cancer immunotherapy with a novel and simple approach to achieve patient-specific anticancer immunity.

Despite recent advances in cancer treatment and immuno-oncology (IO) drugs, there remains a significant unmet need to effectively treat metastatic cancers. In response, Immunophotonics is developing IP-001, an immune-stimulating drug designed to induce potent antitumor immune activation when administered with standard-of-care interventional oncology procedures that utilize energy to destroy tumors.

Tumor ablation, and ablative radiation therapies such as stereotactic body radiation therapy (SBRT), are mainstays of minimally invasive solid cancer treatment that use physical means such as heat or radiation to destroy tumors. In addition to the primary function of killing tumor cells, ablation and radiation may expose tumor-associated antigens (TAAs) to the immune system, as well as release immunogenic damage-associated molecular patterns (DAMPs) and heat shock proteins along with other immunogenic cell death markers. However, despite these immunogenic ablation by-products, a meaningful or long-lasting antitumor immunity that can eliminate distant tumors or reduce recurrence is rare, especially in a clinical setting.

With the proprietary drug IP-001, Immunophotonics is set to revolutionize the field of interventional oncology. Because of a unique combination of physiochemical and immune-stimulatory properties, an intra-tumoral injection of IP-001 as an adjunct to ablation both prolongs the availability of TAAs to the immune system and activates antigen-presenting cells (APCs), especially dendritic cells, that enter the post-ablation tissue. Optimally, IP-001 induces a systemic T cell response against the cancer that enables control of distant tumors, reduction in local recurrence, and generates a long-term memory response (Fig. 1).

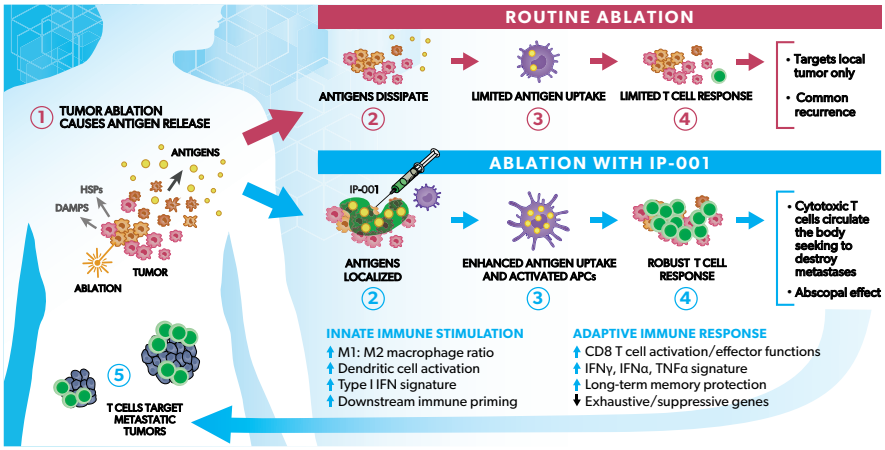

Fig. 1 | IP-001 drives both innate and adaptive anti-tumor immune responses: IP-001 captures antigens and enhances the post-ablation innate immune response by prolonging tumor antigen availability and modulation of the tumor microenvironment. Stimulation of antigen uptake by APCs leads to the adaptive response, abscopal effect, and long-term anticancer memory. APC, antigen-presenting cell; DAMPs, damage-associated molecular patterns; HSPs, heat shock proteins; IFN, type-I interferon; TNF, tumor necrosis factor.

IP-001 ignites innate and adaptive immunity

IP-001 has been studied in a variety of tumor models including melanoma, breast, liver, lung, prostate, pancreatic and other cancers, with evidence of wide applicability. For example, in experiments in which two tumors are implanted on opposite flanks, and only one is treated with ablation in conjunction with IP-001, a sufficient antitumor immune response is generated that has been shown to eliminate the untreated, distant tumor and increase long-term survival. In essence, IP-001 drives the elimination of tumors beyond the ablation site by systemically directing cellular immunity towards these tumors.

Mechanistically, IP-001 affects several steps in the cancer-immunity cycle. It stimulates the innate compartment of the immune system by increasing the exposure and uptake of TAAs liberated by the ablation procedure, by attracting and activating APCs, and driving a pro-inflammatory type-I interferon (IFN) response. This creates a favorable tumor microenvironment for downstream immune priming and tumor rejection, which drives the adaptive compartment of the immune system to initiate a systemic cytotoxic T lymphocyte (CTL) and T-helper 1 (Th-1) type T cell response. As a result, tumor-specific effector T cells infiltrate tumors throughout the body effectively turning 'cold' tumors 'hot', which in turn can lead to elimination of metastases as well as block tumor recurrence locally and systemically.

In addition to these effects, IP-001 also appears to reduce the number of immunoregulatory myeloid-derived suppressor cells and regulatory T cells, which is particularly important because the quality, magnitude, and persistence of an antitumor immune response is governed by the net balance of promoting and dampening the immune response. IP-001, unlike other IO drugs that often target single pathways, has an impact on multiple cancer–immunity interactions, which offers a compelling rationale for its anticancer action.

Clinical strategy drives significant opportunity

In humans, IP-001 appears to be well tolerated and has demonstrated excellent safety. Anecdotal results from investigator-initiated trials in patients with advanced cancer suggest a possible abscopal effect. A phase 1b/2a trial to further assess the safety and preliminary efficacy is ongoing (NCT03993678), with strong interest to expand into additional indications.

Leading experts in interventional oncology and immuno-oncology see IP-001 as a unique therapeutic opportunity to improve clinical outcomes. By combining the individual benefits of each of the respective fields, IP-001 sets the stage for a new discipline: interventional immuno-oncology (IIO). With IP-001-augmented ablation as its leading IIO program, Immunophotonics is pioneering an efficient and practical approach to train the immune system to fight cancer in a way that fits well in the existing clinical work flow.

IP-001 is the first asset from Immunophotonics' broad intellectual property, and offers a unique therapeutic opportunity in a complementary and non-competitive manner to ablation and other IO interventions. In doing so, adding IP-001 to existing ablation procedures represents an estimated US$13 billion *de novo* market opportunity. Immunophotonics welcomes discussions with investors and strategic partners who are interested in facilitating the technology through commercialization.

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