Highlight Therapeutics & Cima announce positive results from pre-clinical study combining BO-112 + STING agonist published in Journal for ImmunoTherapy of Cancer

Intratumoral co-injection of BO-112 and a STING agonist synergize to achieve local and distant anti-tumor efficacy

Pre-clinical study data follow publication of positive Phase 2 results of BO-112 + pembrolizumab in melanoma at SITC

Madrid, Spain, 2 December, 2021 – Highlight Therapeutics, ("Highlight"), a clinical-stage biopharmaceutical company developing RNA-based therapies against cancer, and the Spanish research institute Cima Universidad de Navarra today announced that positive results from a pre-clinical study of intratumoral administration of BO-112 with a STING agonist have been published in the Journal for ImmunoTherapy of Cancer (JITC, Impact Factor 13.75). [1]

BO-112 is a dsRNA agonist which is in development to target anti-PD1 resistance. Positive preliminary results of a phase 2 study of intratumoral administration of BO-112 with pembrolizumab in patients with advanced melanoma that have progressive disease on anti-PD-1-based therapy were presented at The Society for Immunotherapy of Cancer (SITC) in Washington, D.C. on Nov. 12.

Results of a pre-clinical in vivo study of intra-tumoral co-injections of BO-112 and the DXMAA STING agonist conducted by Cima demonstrated synergistic efficacy with the ability to eradicate distant, uninjected tumor lesions. The combination of BO-112 and DMXAA was chosen because of its excellent efficacy, and the requirements for antitumor effects were studied on selective depletion of immune cell types and in gene-modified murine strains lacking BATF3, IFNAR or STING.

"These results, following the positive Phase 2 data on the combination of BO-112 and anti-PD1 therapies, are very encouraging," ***said Dr. Marisol Quintero, CEO of Highlight Therapeutics****. "We have been collaborating with Dr. Melero to better understand BO-112's Mode of Action. The main objective has been to achieve both local control of the disease and, more importantly, efficacy against distant tumor lesions. The work published in the Journal for ImmunoTherapy of Cancer shows that co-injections of BO-112 and a STING agonist attain synergistic efficacy, enabling distant uninjected tumor lesions to be eradicated. There may also be further opportunities involving irradiation of locally injected lesions and we look forward to continuing this work."*

"We believe this combined intratumoral approach should be feasible in the clinic, since both BO-112 and several STING agonists have been injected into patients' tumors in clinical trials. We have consistently observed synergistic therapeutic effects on a variety of transplantable murine tumor models, showing complete regressions of the injected and non-injected concomitant tumor lesions" commented ***Dr. Ignacio Melero, senior researcher in immunotherapy at Cima and co-director of the Department of Immunology at Clínica Universidad de Navarra****."*

Abstract published in JITC

Background BO-112 is a nanoplexed form of polyinosinic:polycytidylic acid that acting on TLR3, MDA5 and PKR elicits rejection of directly injected transplanted tumors, but has only modest efficacy against distant untreated tumors. Its clinical activity has also been documented in early phase clinical trials. The DMXAA STING agonist shows a comparable pattern of efficacy when used via intratumoral injections.

Methods Mice subcutaneously engrafted with bilateral MC38 and B16.OVA-derived tumors were treated with proinflammatory immunotherapy agents known to be active when intratumorally delivered. The combination of BO-112 and DMXAA was chosen given its excellent efficacy and the requirements for antitumor effects were studied on selective depletion of immune cell types and in gene-modified mouse strains lacking BATF3, IFNAR or STING. Spatial requirements for the injections were studied in mice bearing three tumor lesions.

Results BO-112 and DMXAA when co-injected in one of the lesions of mice bearing concomitant bilateral tumors frequently achieved complete local and distant antitumor efficacy. Synergistic effects were

contingent on CD8 T cell lymphocytes and dependent on conventional type 1 dendritic cells, responsiveness to type I IFN and STING function in the tumor-bearing host. Efficacy was preserved even if BO-112 and DMXAA were injected in separate lesions in a manner able to control another untreated third-party tumor. Efficacy could be further enhanced on concurrent PD-1 blockade.
Conclusion Clinically feasible co-injections of BO-112 and a STING agonist attain synergistic efficacy able to eradicate distant untreated tumor lesions.

Next steps in the development of BO-112 include:

- Initiation of a pivotal Phase 3 study in 2nd-line melanoma is planned in 2022 following discussions with regulatory agencies in the US and Europe
- Highlight Therapeutics has initiated strategic partnerships discussions with anti-PD1 companies interested in enhancing their anti-PD1 market potential
- Initial data from a sponsor-initiated Phase 1B trial by UCLA evaluating BO-112 + pembrolizumab in anti-PD1 resistant hepatocellular carcinoma currently recruiting patients is expected in 2022

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1. Alvarez M, Molina C, De Andrea CE, et al
Intratumoral co-injection of the poly I:C-derivative BO-112 and a STING agonist synergize to achieve local and distant anti-tumor efficacy
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https://jitc.bmj.com/content/9/11/e002953.info

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Notes to editors

About Highlight Therapeutics

Highlight Therapeutics, formerly known as Bioncotech Therapeutics, is a private, clinical-stage company dedicated to unlocking the full potential of immuno-oncology. Our lead drug candidate BO-112 is a best-in-class RNA-based therapy which has been demonstrated to initiate a powerful immune response, leveraging a unique multi-target approach to turn 'cold' tumors 'hot' and therefore visible to the immune system. It has the potential to rescue patients who are resistant to current checkpoint inhibitor therapy, a very large market opportunity. BO-112 is currently being investigated in a range of clinical trials as a monotherapy and in combination with checkpoint inhibitors. In addition to in-house research, Highlight Therapeutics has a number of external collaborators, including Merck & Co and UCLA.

For more information, please visit www.highlighttherapeutics.com

About Cima Universidad de Navarra

Cima Universidad de Navarra is a biomedical research institution of the Universidad de Navarra. Our mission is to conduct translational research of excellence, based on novel biological knowledge and aimed at finding therapeutic solutions to patients' needs. To translate the results of basic research into clinical applications, Cima has a Translation and Transfer unit that seeks to establish collaborations with biotechnology and pharmaceutical companies to ensure patients can benefit from scientific innovation.

We specialize in cancer, heart and liver diseases, immunotherapy and gene therapy research.

More information: www.cima.unav.edu/en/