Joint Team Effort Succeeds in Advancing First-in-Cass Triple Combination Immunotherapy to Studies in Patients with Colorectal Cancer

AMAL Therapeutics and ViraTherapeutics, in partnership with their common parent company, Boehringer Ingelheim, are very proud to announce that they have advanced their first-in-class heterologous prime-boost vaccine to Phase 1 studies in patients with colorectal cancer in combination with Ezabenlimab (BI 754091). This advancement is a result of several years of close and strong collaboration between the teams, which have recently also published their joint research in Nature Communications[1] and Cancers[2].

The heterologous prime-boost vaccine combines the therapeutic chimeric recombinant protein vaccine ATP128, designed using the KISIMA® platform from AMAL Therapeutics, with the viral vector VSV-GP128, a modified vesicular stomatitis oncolytic virus developed by ViraTherapeutics, both expressing shared tumor-associated antigens. Ezabenlimab is a humanized programmed cell death 1 (PD-1)-targeting monoclonal antibody developed by Boehringer Ingelheim. The combination of KISIMA® cancer vaccines with VSV-GP oncolytic viral therapy is a promising therapeutic approach to make 'cold tumors' that do not respond to immune-checkpoint blockade 'hot', aiming to improve the responsiveness to immune therapy and the outcomes of patients.

The KISIMA-01 trial was started in July 2019 and initially evaluated the safety, tolerability, and efficacy of ATP128 alone or in combination with Ezabenlimab in patients with stage IV colorectal cancer. Now, the heterologous prime-boost combination has entered this Phase 1 trial, by including VSV-GP128 together with ATP128 and Ezabenlimab in the treatment setting.

Cancer vaccines and oncolytic viruses are two of the four pillars of Boehringer Ingelheim's cancer immunology strategy. Along with T-cell engagers and immune/stromal modulators, the company believes that these four areas will potentially increase the "temperature" in the tumor microenvironment, offering the best chance to create durable treatments for patients.

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[1] Das, K., Belnoue, E., Rossi, M. *et al.* A modular self-adjuvanting cancer vaccine combined with an oncolytic vaccine induces potent antitumor immunity. *Nat Commun* **12,** 5195 (2021). https://doi.org/10.1038/s41467-021-25506-6

[2] Hofer, T.; Rossi, M.; Carboni, S.; Di Berardino Besson, W.; von Laer, D.; Wollmann, G.; Derouazi, M.; Santiago-Raber, M.-L. Heterologous Prime-Boost Vaccination with a Peptide-Based Vaccine and Viral Vector Reshapes Dendritic Cell, CD4+ and CD8+ T Cell Phenotypes to Improve the Antitumor Therapeutic Effect. *Cancers* **2021**, *13*, 6107. https://doi.org/10.3390/cancers13236107