KISIMA-01: A first-in-human trial of the heterologous prime-boost vaccine ATP128/VSV-GP128 with ezabenlimab (BI 754091) in patients with stage IV colorectal cancer

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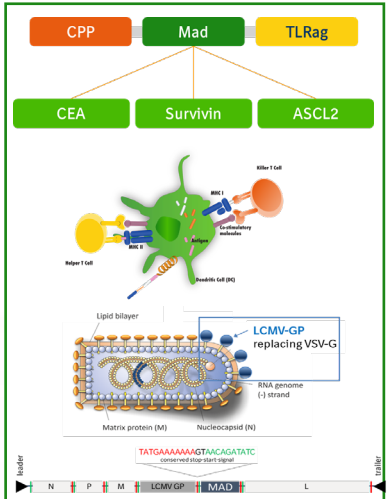
Background

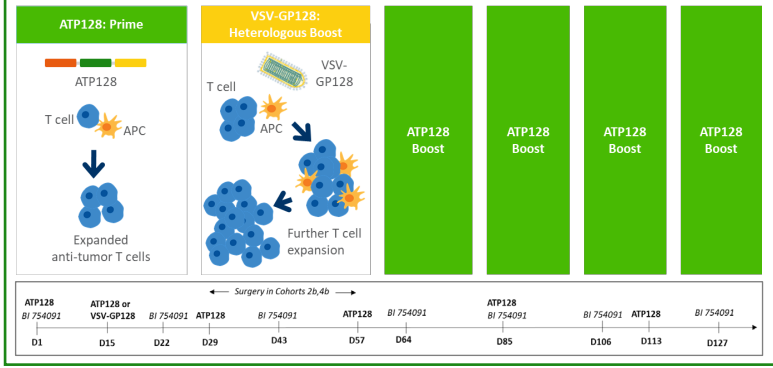
Most microsatellite stable/mismatch repair proficient (MSS/MMRp) stage IV colorectal cancers (CRC) do not respond to PD-1 inhibition. **ATP128**, based on the KISIMA™ platform, is a single chimeric fusion protein, composed of 3 elements essential to generate potent antitumoral cellular immunity: a proprietary cell-penetrating peptide (CPP) for antigen delivery, a proprietary Toll-like receptor (TLR)-peptide agonist with self-adjuvant properties and a modulable multi-antigenic domain (Mad), where the Mad includes 3 CRC antigens: carcinoembryonic antigen (CEA), survivin, achaete-scute complex homolog 2 (ASCL2).

VSV-GP128 is a recombinant vesicular stomatitis virus (VSV) carrying the glycoprotein (GP) of a non-neurotropic strain of lymphocytic choriomeningitis virus (LCMV) instead of the native VSV-GP to abrogate neurotoxicity. As viral vector, VSV-GP128 expresses a Mad with identical sequence to ATP128 integrated in a linear, negative-sense, single-stranded RNA genome. Preclinical data have shown that priming with KISIMA vaccine followed by VSV-GP boost induced a large pool of polyfunctional and persistent antigen-specific cytotoxic T cells in the periphery as well as within the tumor in several tumor models. Combining heterologous vaccination with a PD-1 inhibitor further improved its therapeutic efficacy in preclinical studies[1].

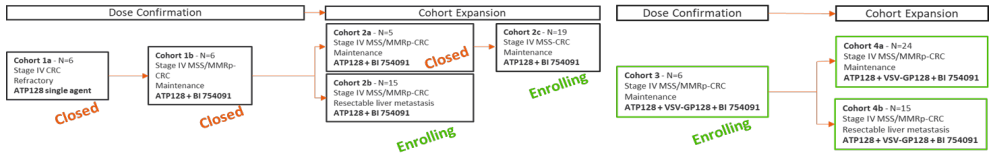
[1] Das et al. A modular self-adjuvanting cancer vaccine combined with an oncolytic vaccine induces potent antitumor immunity. Nature Communication 2021; 12:5195



Heterologous prime-boost vaccination with ATP128 (above) and VSV-GP128 (below) is superior to homologous vaccination with either vaccine platform. Heterologous prime-boost vaccination induced a potent $CD8^+$ T cell response against tumor-associated and tumor-specific antigens and favored the development of immunological memory while dampening antiviral immunity in preclinical studies[1].



KISIMA-01 dosing schedule. ATP128 is given subcutaneously on day 1 (prime); VSV-GP128 is administered intravenously on day 15 as the heterologous boost. ATP128 is again administered on day 29 (injection 3) and then every 4 weeks for the last 3 immunizations. Ezabenlimab is administered every 3 weeks starting with the first ATP128 administration. Blood and tissue samples are collected before, during and after ATP128/VSV-GP128 treatment to monitor the induction of a tumor associated antigen-specific immune response and immune-related changes.



KISIMA-01 trial design. KISIMA-01 (NCT04046445) is an open-label, multi-center Phase 1b umbrella trial to investigate the safety, tolerability and immunogenicity of the heterologous prime-boost vaccine AT128/VSV-GP128 in combination with the anti-PD1 ezabenlimab in patients with stage IV MSS CRC. Two different patient populations are currently investigated: 1) maintenance setting (during a chemotherapy free period) after a minimum of 4 months of 1st line standard chemotherapy with clinical benefit (defined as PR or SD) (n=30; Cohorts 3 and 4a); 2) resectable liver-limited disease (n=15; Cohort 4b). The heterologous prime-boost cohorts (ATP128/VSV-GP128) of the KISIMA-01 trial will be recruiting in the US, Switzerland and Belgium.