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Efficacy of STC-1010, a new allogenic cancer vaccine in colorectal cancer models.

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Background: Colorectal cancer (CRC) is the second cause of cancer-related death worldwide. Recent tremendous progresses have installed immunotherapy as a treatment option and opened multiple ways to address therapeutic challenges for MSI or MSS CRC patients. Accordingly, Brenus-Pharma developed a therapeutic cancer vaccine, the STC-1010, basing on the technology by stimulating tumor cells (STC) with physical (irradiation and heat shock) and chemical (via standard-of-care (SoC) chemotherapy) stress, coupled with the haptenization for overexpressing tumor-related antigens. **Methods:** The mouse version of STC-1010 (mSTC-1010) vaccine prepared using two CRC mouse cell lines (CT26 and CMT93) and one pancreatic cancer mouse cell line (LTPA), previously showed encouraging results in pre-clinical studies on MSS CT26 'cold-tumor' and anti-PD1 resistant MSI MC38 'hot-tumor' murine models. mSTC-1010 associated with immunostimulant (cyclophosphamide and GM-CSF at low doses), combined or not with chemotherapy (FOLFOX or FOLFIRI) led to a significant decrease of tumor volume, a M1-oriented macrophage response (immunohistochemical, iNOS/CD163 $>$ 1), and an increase of T lymphocyte infiltration. **Results:** We confirmed these proof-of-concept efficacy with the human STC-1010 using three CRC human cell lines (HCT116, HT29 and Lovo). STC-1010 favored ex vivo an immune stimulation on human dendritic cells (DCs) which further primed CD8+ T cells to induce massive apoptosis of CRC cells (versus control). In HT29 *in-ovo* chicken embryo Chorio-Allantoid Membrane (CAM) assay, STC-1010 significatively increased IL-12, IL-2 and IFN-gamma expression (versus control) ($p < 0.02$). Results from this immune reactive model showed significant increase of tumor necrosis ($p = 0{,}0267$), metastasis regression (-49%), and increase infiltration of CD4+, CD8+ compared to control group. **Conclusions:** The good tolerability of the STC-1010 vaccine in different models allows to plan a first-in-human phase I/II clinical trial with MSS and MSI-H metastatic CRC (mCRC) patients. A dose-escalation phase Ia (STC-1010 plus immunostimulant, associated to mFOLFOX6 w/o bevacizumab) will be performed with MSS mCRC patients to evaluate the safety and the recommended phase 2 trial dose (RP2D). A subsequent expansion phase IIa part will assess STC-1010 efficiency, associated with SoC in first-line setting for MSS patients, and in second-line setting after immunotherapy for MSI-H, dMMR or Lynch syndrome mCRC patients. Research Sponsor: Brenus Pharma.