A061 First-in-human hapten-enhanced stressed-ghost cell immunotherapy (STC-1010) for advanced colorectal cancer: preclinical and early clinical data

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Background

- **Colorectal cancer** (CRC) is the second leading cause of cancer-related deaths globally, with most metastatic cases (mCRC) being microsatellite stable (MSS) and **resistant to immunotherapy**.
- To address this, we developed STC-1010, an **allogeneic antigen-based immunotherapy** using the proprietary **Stimulated Ghost Cells** (SGC) **platform** targeting CRC patients.
- STC-1010 combine three human CRC lines (HCT116, HT-29, LoVo) conditioned by **controlled stress** to **reveal tumor plasticity and resistance antigens**, then **haptenated** for **enhanced immunogenicity**.
- STC-1010 educates the immune system by inducing T and B cell activation, designed to transform cold tumor into immunologically "hot" tumors. (Fig 1)

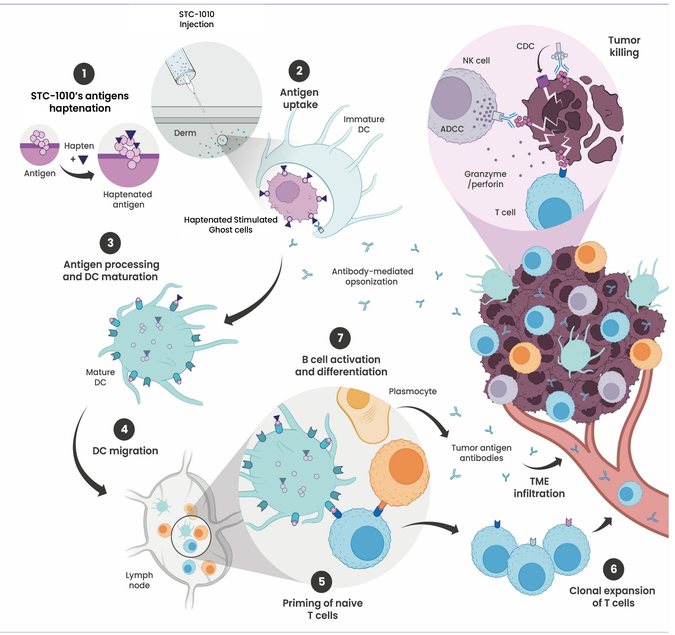


Figure 1: Immune mechanisms triggered by injection of STC-1010 leading to tumor cell death

(1) Haptenation of STC-1010 generating hapten-modified peptides
(2) Following intradermal injection, STC-1010 is phagocytosed by dendritic cells (DCs)
(3) Hapten-modified peptides are differentially processed compared to non-haptenated and presented by DCs on MHC class I and II molecules. Danger-associated molecular patterns (DAMPs) expressed by STC-1010 promote DCs activation
(4) Mature DCs migrate to the draining lymph nodes, where (5) they activate naïve T cells through MHC–TCR interactions
(6) Activated T cells undergo clonal expansion and subsequently infiltrate the tumor microenvironment (TME), where they mediate tumor cell killing
(7) Helper T cells also promote B cell activation and differentiation into plasma cells, leading to the secretion of tumor-specific antibodies. These antibodies bind to tumor cell antigens, contributing to tumor cell elimination through antibody-dependent cellular cytotoxicity.

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Results : Functionnal immune activation and tumor killing in ex vivo model

- Detection of hapten-modified peptides in mDCs after STC-1010 exposure confirms efficient uptake, antigen processing and presentation (Fig. 2B)
- mDCs exposed to STC-1010 showed an increased activation of key immune pathways compared to vehicle controls (Fig 2C)
- Autologous CD8⁺ T cells primed with STC-1010–mDCs induce robust apoptosis of HCT116 at 72 h, with consistent cytotoxicity across batches (Fig. 2D)

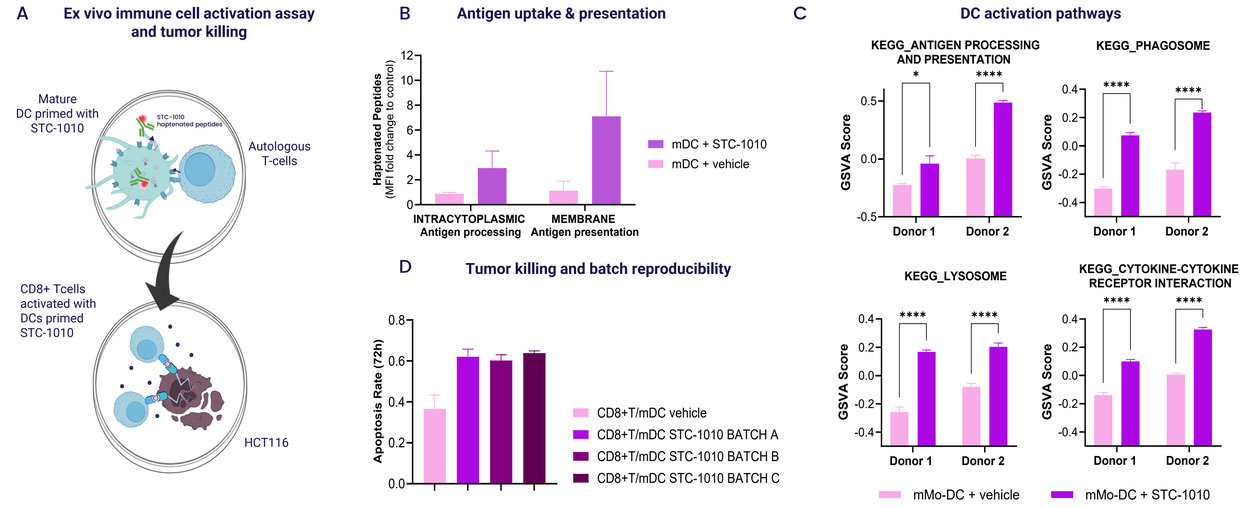


Figure 2: STC-1010 activates DCs to prime CD8⁺ T cells and drive robust tumor killing against CRC cells

***A** : Experimental design. Monocytes were differentiated into monocyte-derived dendritic cells (mDCs). These cells were and treated with STC-1010 (BATCH A/B: Pilot ; BATCH 3: GMP) or Vehicle (CS5). Haptenated peptides processed and presented by mDC were then detected using an anti-hapten antibody. The primed mDCs were co-cultured with autologous CD8⁺ T cells. Activated CD8+ T cells by mDC-STC-1010 were then co-cultured with HCT116 cells to induce tumor killing. **B**: Haptenated peptides were detected in mDCs by flow cytometry, at intracellular (processed antigen) and surface (presented antigen) levels (MFI : Mean Fluorescence Intensity) **C** : Transcriptomic (RNA-seq) GSVA analysis of KEGG pathways across different mDC subsets of two different donors (mean of technical triplicates). Two-way ANOVA with Holm-Šídák post-hoc test, *P<0.05, and ****P<0.0001; **D**: Apoptosis rate was quantified at 72 h using an IncuCyte S3™ Live Cell Imager across 3 different batches.*

Results : Anti-tumor activity in vivo CT26 syngeneic model

- mSTC-1010 (murine STC-1010) significantly reduces CT26 tumor growth (Fig. 3B) and extends survival by 40% (Fig. 3C)
- mSTC-1010 drives expansion of CD4⁺, CD8⁺ and B cells in draining lymph nodes (Fig. 3D)
- mSTC-1010 elicits a robust humoral response, with significantly elevated anti-hapten antibody levels measured by ELISA (Fig. 3E)

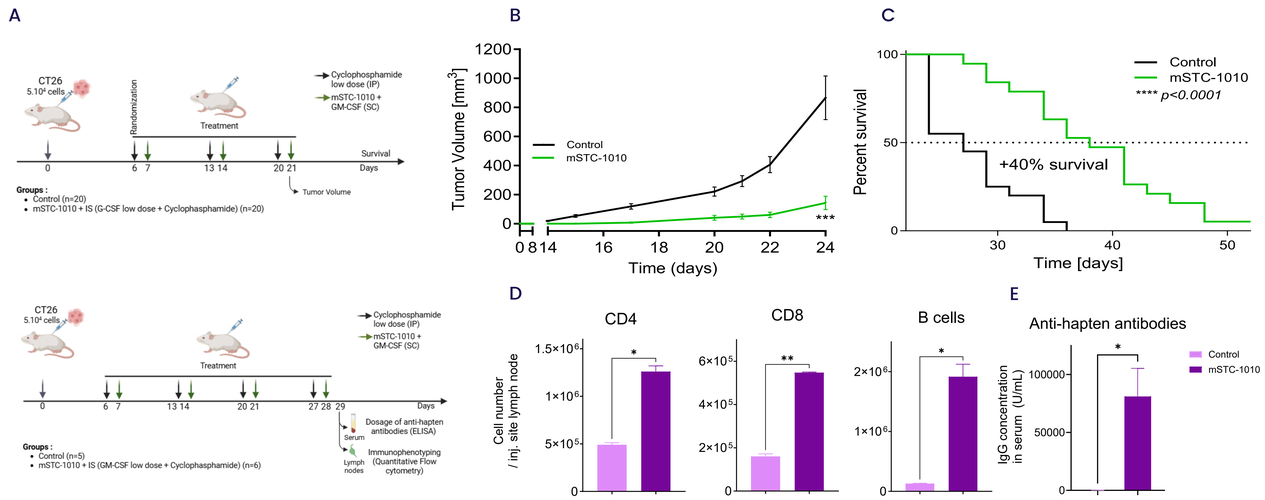


Figure 3: Murine surrogate of STC-1010 (mSTC-1010) induces an anti-tumor immune response in CT26 colorectal syngeneic model

A.** Experimental studies design. **B.** Tumor volume (p=0,0001 Unpaired non parametric t test with Welch correction) **C.** Survival analysis (p<0,0001, Log-rank (Mantel-Cox) test) **D**. The Immunophenotyping of immune cells (CD4, CD8 and B cells) in lymph node near the injection site (n=3 / group – pool of 2 lymph nodes) was performed by quantitative flow cytometry (* p<0,05 ; ** p<0,005, Brown-Forsythe and Welch anova tets) **E.** Dosage of anti-hapten antibodies was assessed by ELISA (* p=0,02 Unpaired non parametric t test with Welch correction) .*

Clinical outlook

- **STC-1010 is evaluated in the first-in-human BreAK CRC 001 phase I/IIa trial in patients with unresectable, metastatic, or locally advanced CRC** (NCT06934538).
- This multicenter study includes a phase I dose-escalation and expansion followed by a phase IIa cohort expansion. Phase I assesses the safety of STC-1010 combined with standard-of-care, aiming to establish the maximum tolerated dose (MTD) and recommended phase II dose (RP2D). Phase IIa evaluates preliminary efficacy
- **Preliminary data in MSS + KRAS-mutant CRC patients** (primary colon/rectum with metastatic involvement of lung, liver, lymph nodes, peritoneum) **indicated a good safety profile, with no dose-limiting toxicities** (DLTs) **and a 100% response rate in disease control rate** (DCR).

Conclusion

- mSTC-1010 **induced significant tumor growth inhibition** and **extended survival** in syngenic CRC model, driven by coordinated humoral and cellular responses.
- STC-1010–primed dendritic cells **efficiently process and present haptenated peptides, activating autologous CD8⁺ T cells to mediate robust, reproducible tumor killing** against colorectal cancer cells across multiple production batches
- First-in-human **BreAK CRC 001** planned readouts in Q2 2026 : complete safety data from Phase Ia and exploratory efficacy across dose cohorts.
- **Altogether, these data support STC-1010 as a promising therapeutic option for patients with MSS, immune-cold colorectal cancer, addressing a major unmet clinical need**.

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Figure 1 was designed in collaboration with illustrator Diane ROTTNER, and image rights belong to Brenus Pharma.
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