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6314- Efficacy results of a novel vaccine composed of stimulated and haptenized tumours cells in BALB/c mice grafted with murine colon adenocarcinoma CT26 cells.

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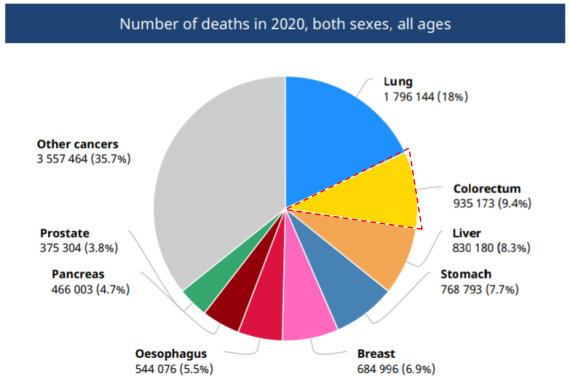
Background

- **Context**

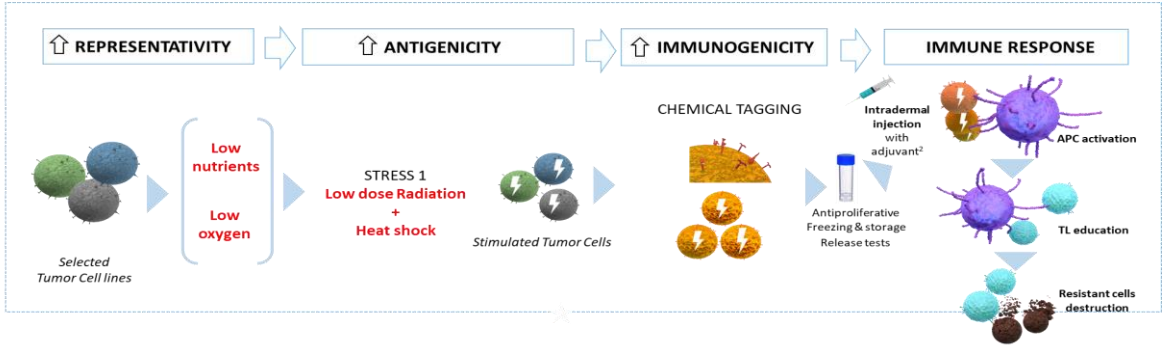
A need to turn cold tumor into hot tumor



mCRC MSS 95%	
WW	FR
917 505	20 584

mCRC MSI-H* 5%	
WW	FR
48 290	1084

- **STC technology = Stimulated Tumor cell lines**



- **Objectives: 2 studies (A and B).**
  - A) Evaluate efficacy of a one cell line-based product (CT26) physical stimulated (S=irradiation and heat shock) and/or haptenized (H) w/o immunostimulant (IS=cyclophosphamide + mGM-CSF w/o BCG)
  - B) Investigate a potential increase of antitumoral effect of 3 cell lines vaccine (3CL-SH made of CT26, CMT-93, LTPA)

Study Design & Methods

Female BALB/c mice were subcutaneously grafted with 5.10^4 CT26-WT cells
Treatment administered sub-cutaneously

- Study A
  - N=9 groups (10 mices / group)

G1) Control group,
G2) IS,
G3) CT26-S,
G4) CT26-H,
G5) CT26-SH,
G6) CT26-S+IS,
G7) CT26-H+IS,
G8) CT26-SH+IS,
G9) CT26-SH+IS+BCG

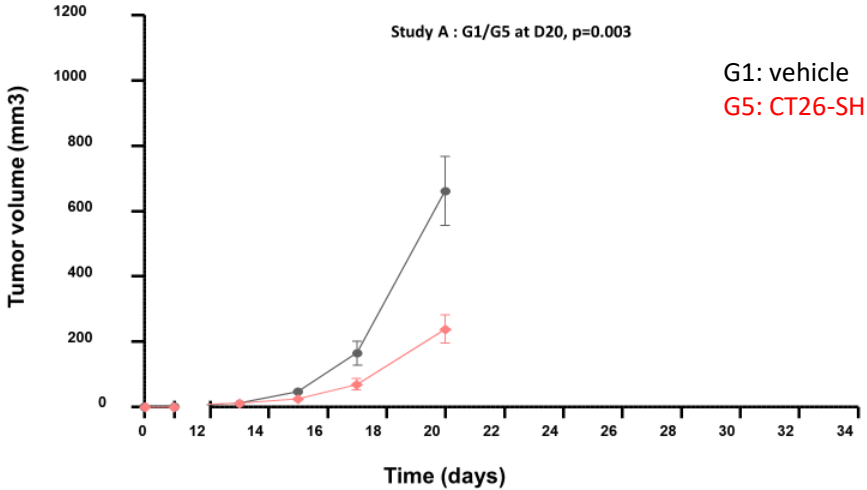
- Study B
  - N=5 groups (20 mices / group)

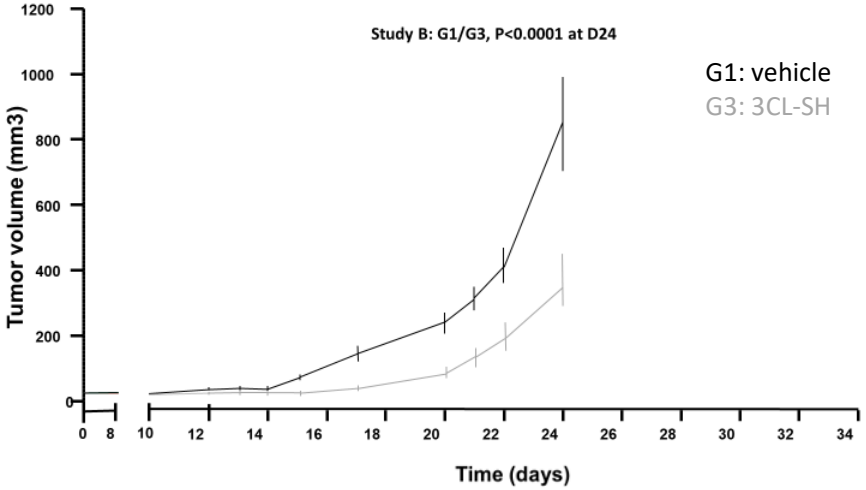
G1) Control group,
G2) CT26-SH + IS,
G3) 3CL-SH,
G4) 3CL-SH + IS once a week for 3 weeks
G5) 3CL-SH + IS twice a week for 4 weeks

- Endpoints
  - Overall survival (OS) and tumour growth (TG) were recorded until 1000 mm^3, safety endpoint or on D41 (study A) or D50 (study B)

Results

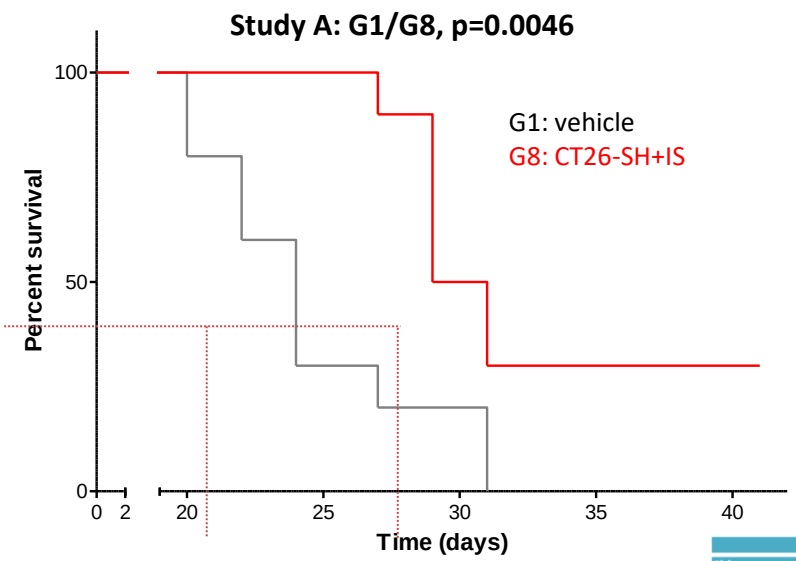
- Results showed a significant impact on TG when cells were **both physically stimulated then haptenized**, such as CT26-SH (study A: G1/G5, p=0.003 at D20) or 3CL-SH (study B G1/G3 P<0.0001 at D24) compared to the control group.

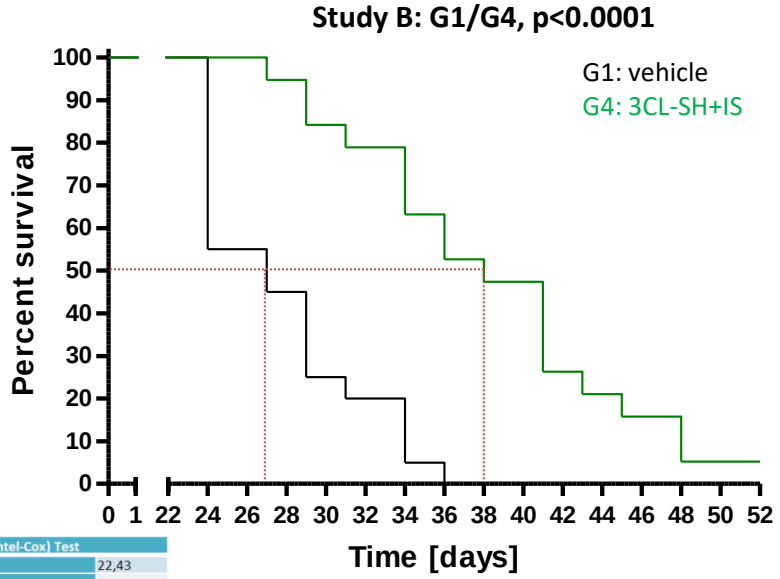




Results - OS

- **Stimulated cell-based treatments with IS** (CT26-SH + IS) significantly **increases OS** compared to control group (Study A: G1/G8 p=0.0046 & study B: G1/G2 p=0.0023).



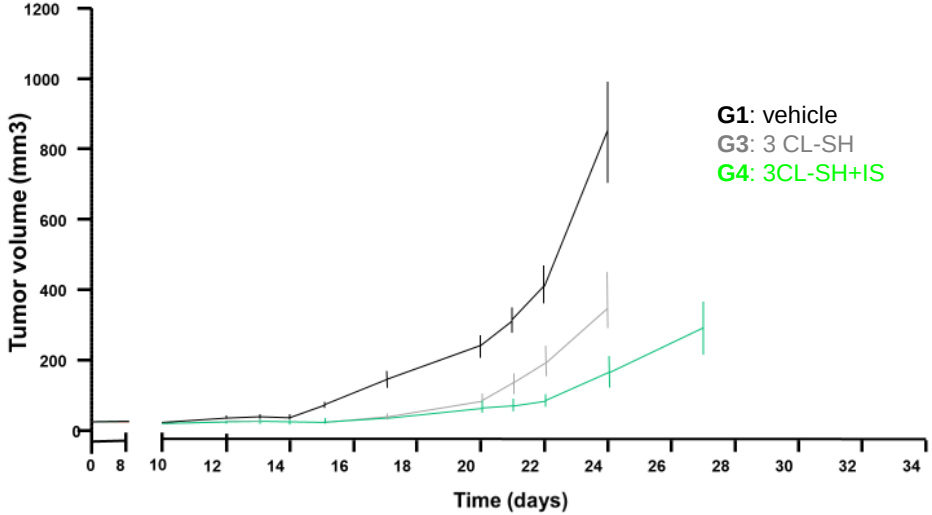


Log-rank (Mantel-Cox) Test	
Chi square	22,43
df	1
P value	< 0,0001
P value summary	***
Are the survival curves sig different?	Yes

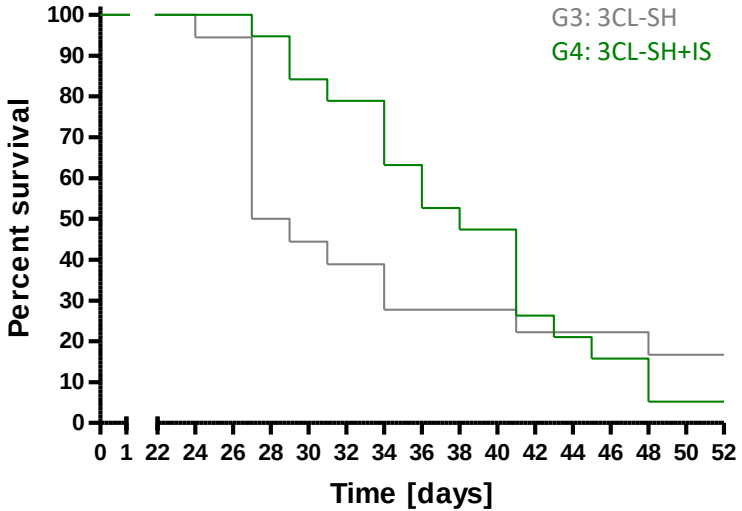
Results

- In addition, **IS reinforced the effect of cell-based treatment**, with CT26-SH (Study A: G1/G8, p<0.0001 at D20, Study B: G1/G2 p<0.0001 at D24) and with 3CL-SH (Study B: G4/G3 p=0.0004).

Study B: G1/G4/G3



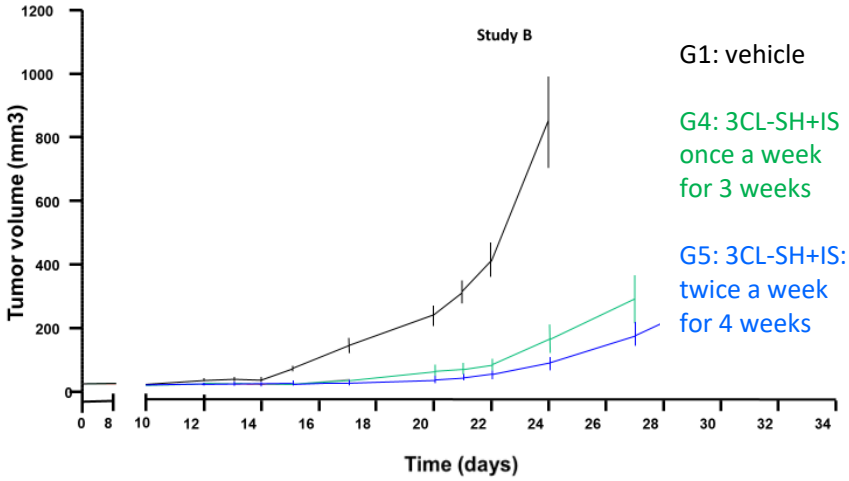
Study B: G4/G3, p=0.0004

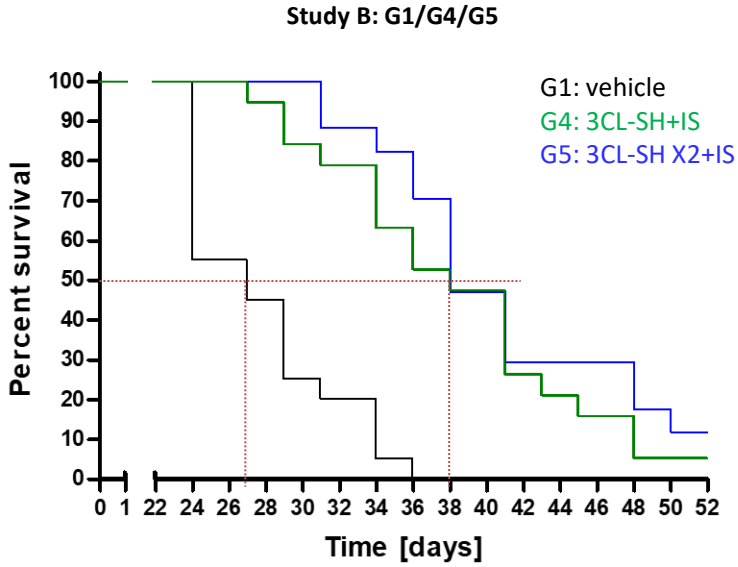


- Addition of BCG to CT26-SH+IS does not improve efficacy (Study A: G8/G9 p=NS).data not shown

Results

- 3CL-SH+IS exhibits a significant efficacy on TG (Study B: G1/G4 p=0.0053 or G1/G5 p=0.0018) and OS whatever the administration schedule.

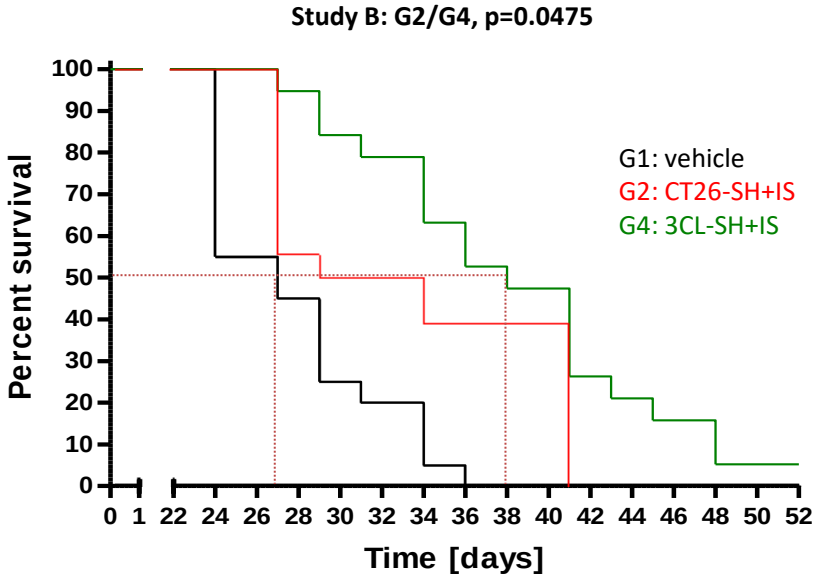


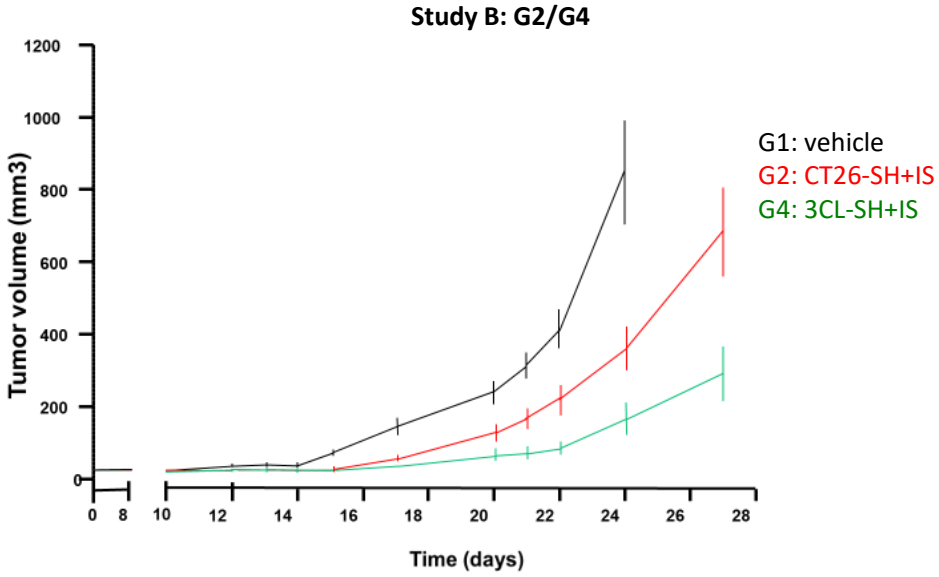


- No side effect or inflammatory reaction towards the vaccines have been evidenced

Results- OS

- A direct comparison of 3CL-SH+IS and CT26-SH+IS confirmed **a significant added benefit in favour of the 3 cell lines vaccine** (Study B: G2/G4 p=0.0475) **compared to** the **one cell line** treatment.





Conclusion

- **Brenus Pharma STC vaccine** based on physical stimulation and haptenization **demonstrated a significant anticancer effect in mice with immunostimulant** and confirmed **a better efficacy of the 3 cell lines vaccine versus a single cell line vaccine**.
- Further studies are ongoing to test the efficacy of STC vaccine in PD1 resistant preclinical model and in combination with Standard of Care (Chemotherapies).

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