



The Impact of Prior Treatment with a CD19 Targeting Monoclonal Antibody on Subsequent Treatment with CD19 Targeting CART Cell Therapy in Preclinical Models

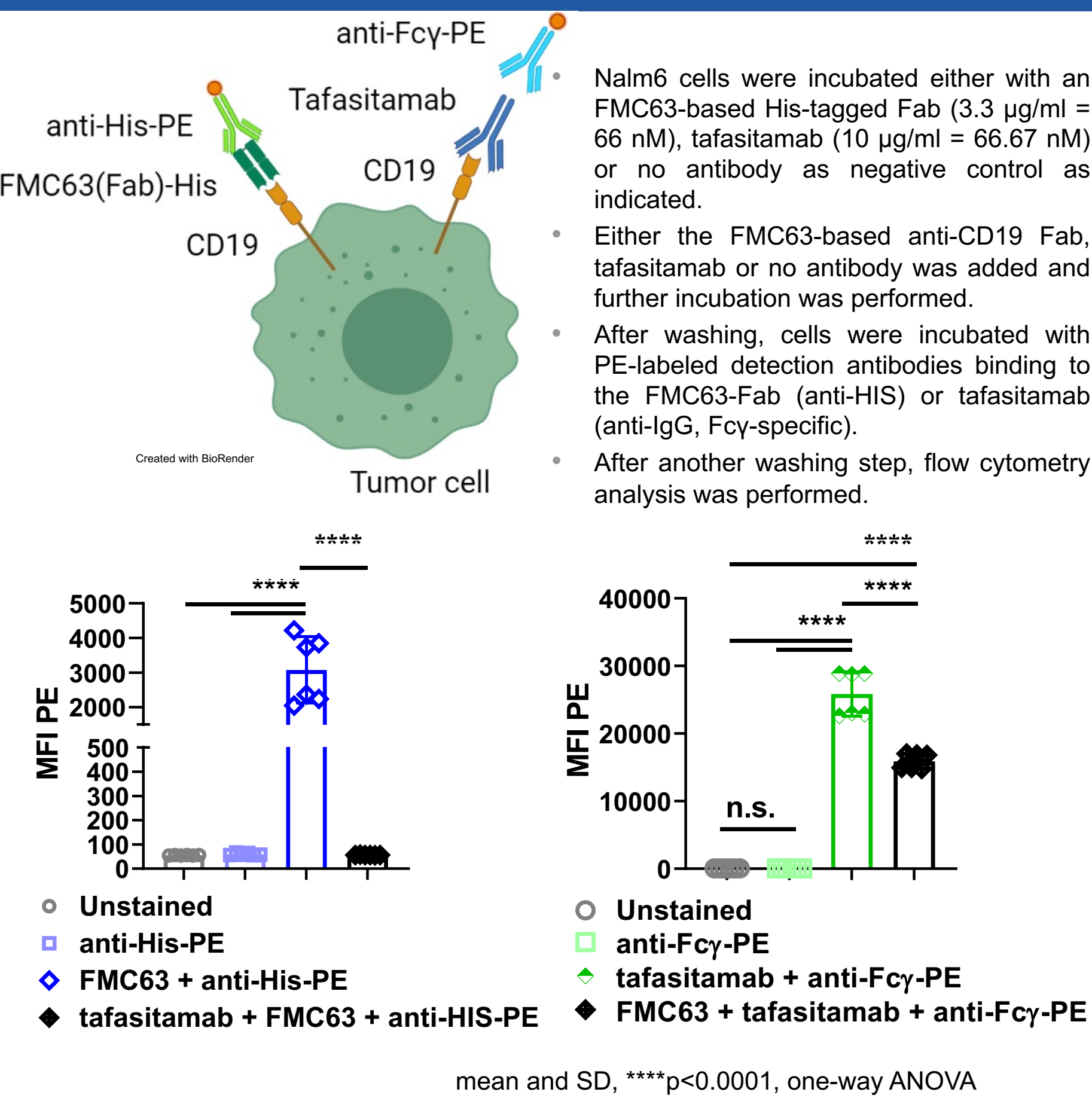
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Background

- CD19-directed chimeric antigen receptor T cell (CART19) therapy is highly effective and was FDA approved.
- CD19 is a key target for novel antibody-based approaches, including tafasitamab, loncastuximab tesirine, and blinatumomab.
- One of the major concerns is that CD19 targeting with a monoclonal antibody impairs subsequent CART19 cell therapy.
- In this study, we evaluated the potential interference between tafasitamab and CART19 (using a construct similar to the FDA approved therapy, FMC63-41BBζ, tisagenlecleucel) in preclinical lymphoma and leukemia models.

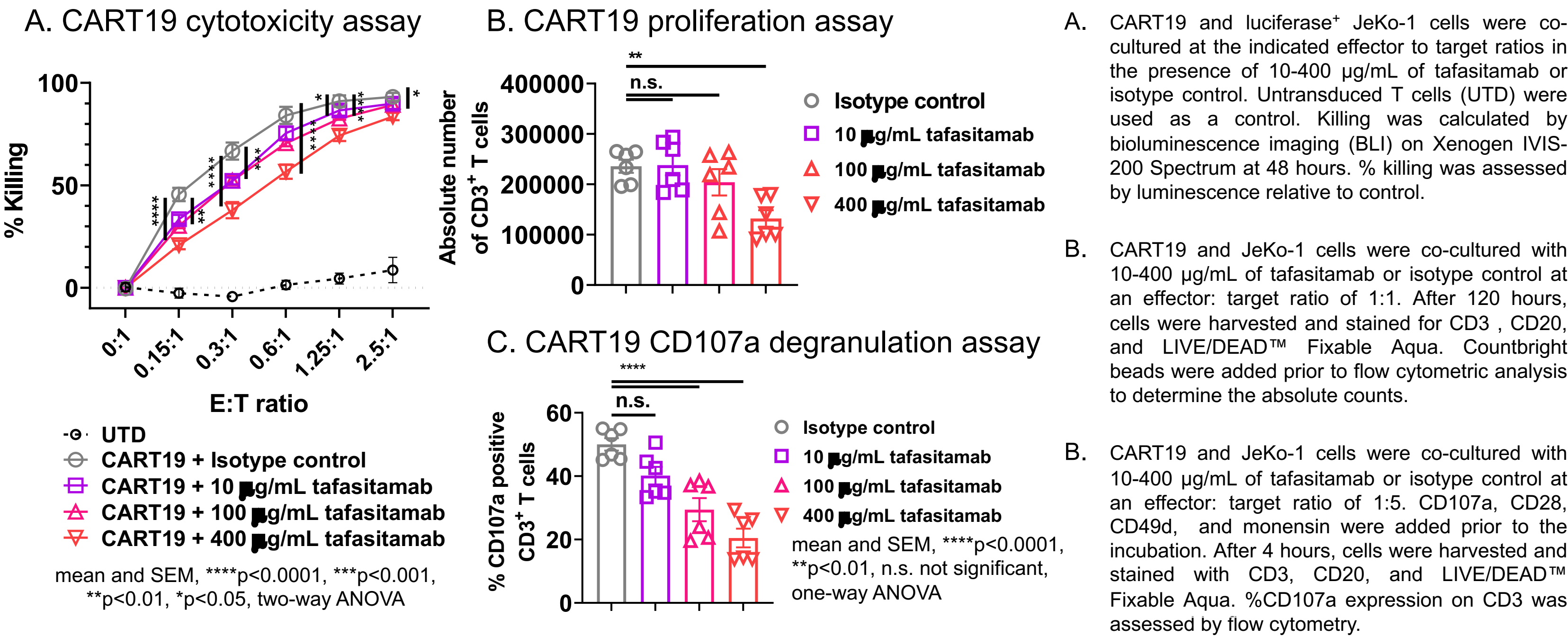
Tafasitamab and FMC63-based CART19 compete for binding to CD19



Pre-incubation with tafasitamab abolished FMC63 binding to CD19

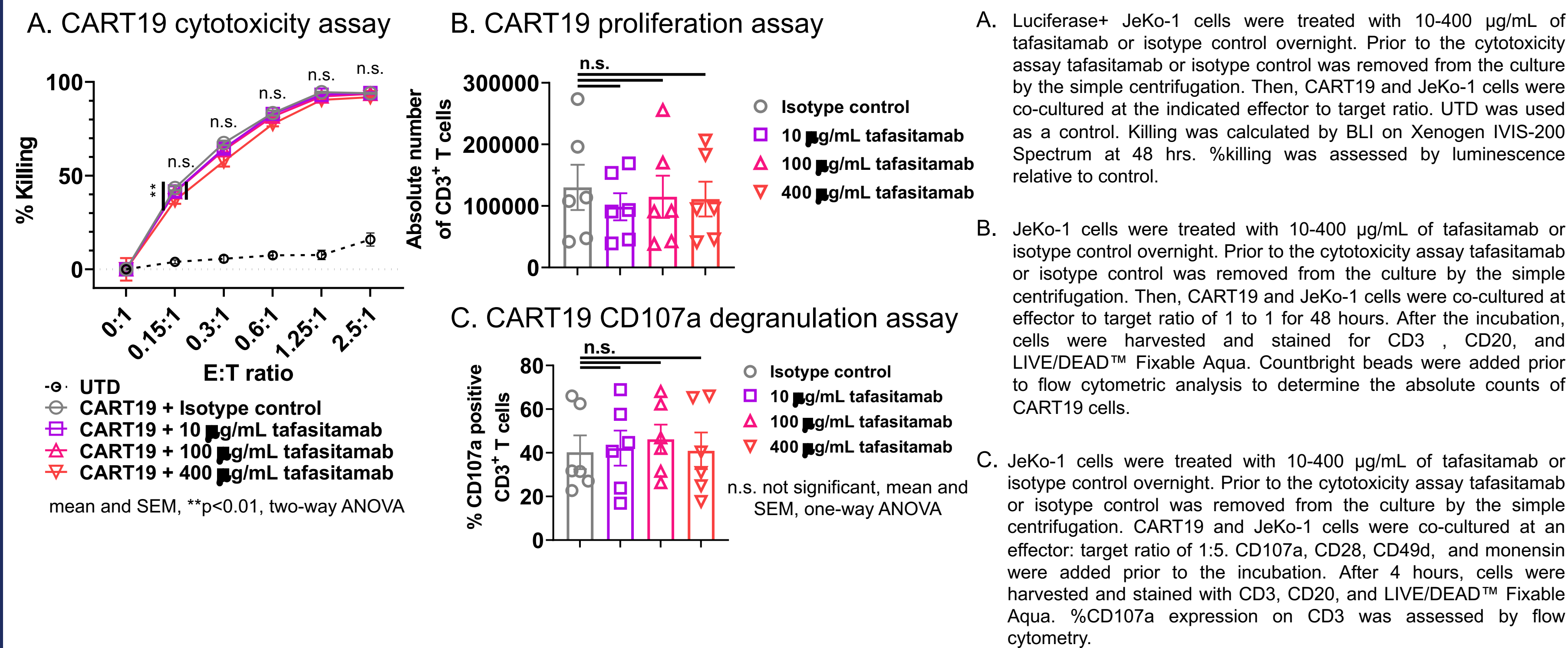
Pre-incubation with FMC63 partially prevented tafasitamab binding to CD19

Concomitant treatment with tafasitamab and CART19 impairs CART cell functions *in vitro*



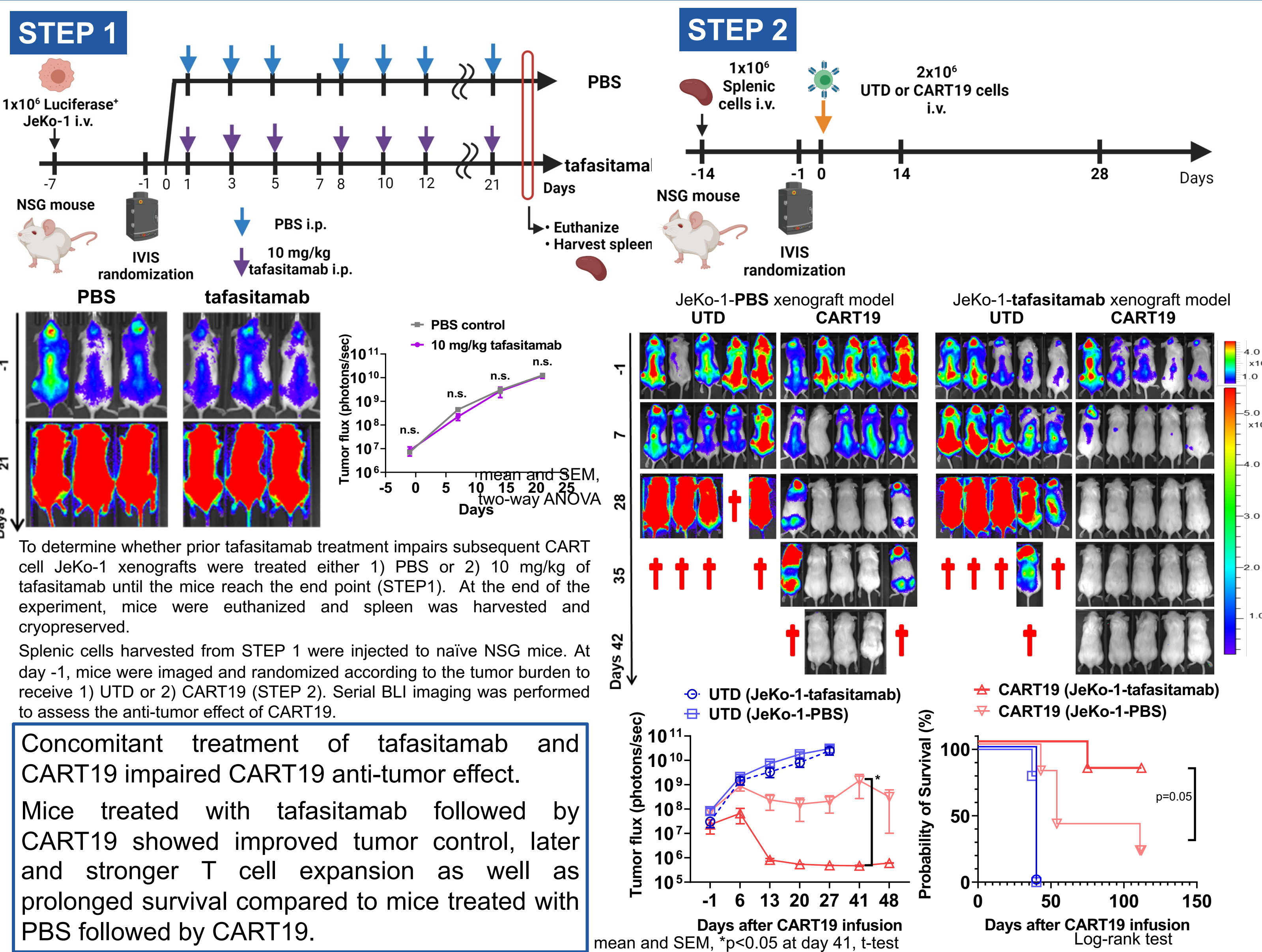
CART19 cytotoxicity, proliferation, and degranulation were significantly reduced in the presence of high dose tafasitamab.

Prior tafasitamab treatment does not impair CART cell functions *in vitro*



CART19 cytotoxicity, proliferation, and degranulation were not affected by prior treatment with tafasitamab.

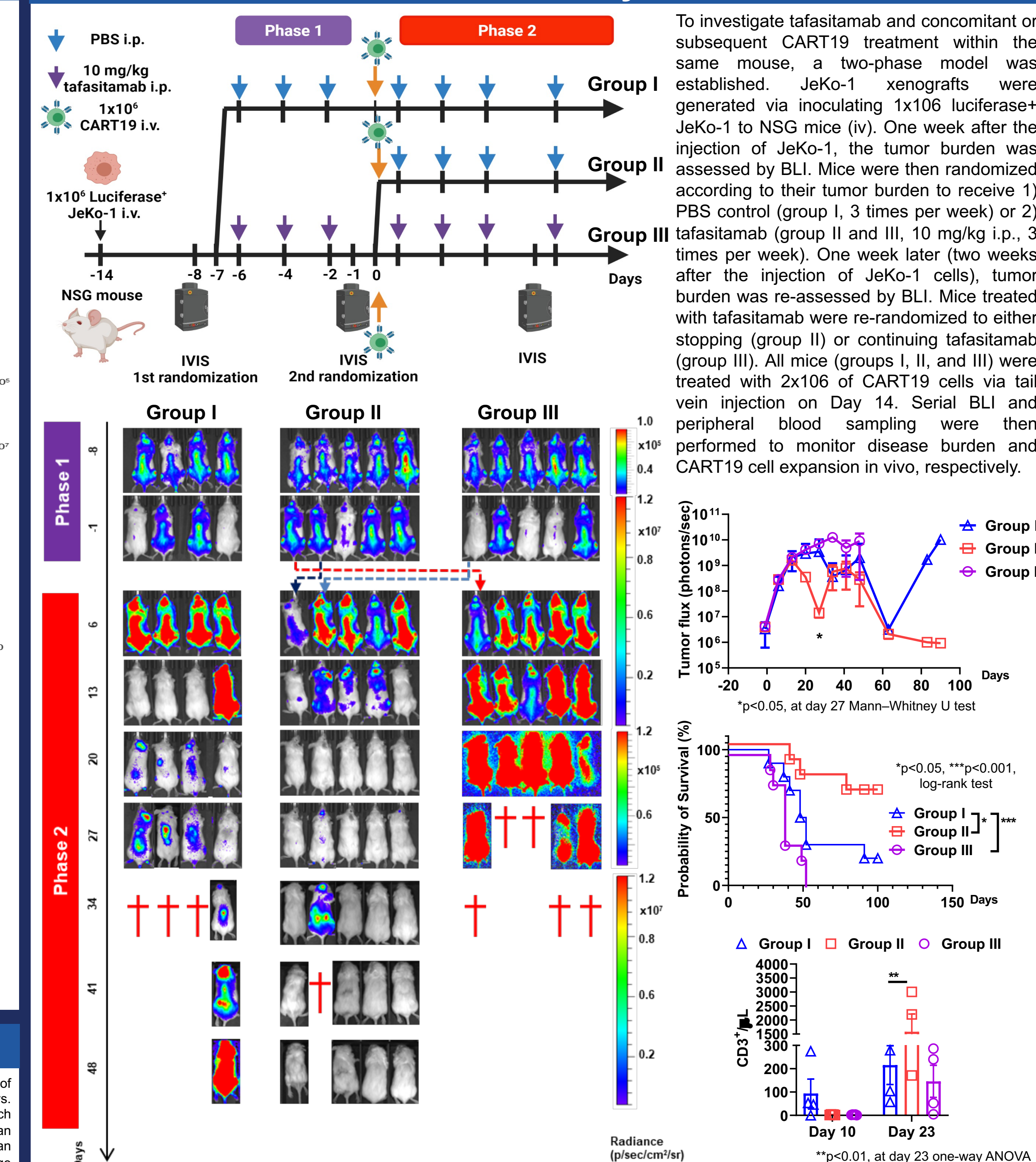
Prior tafasitamab treatment does not impair CART cell functions *in vivo*



Concomitant treatment of tafasitamab and CART19 impaired CART19 anti-tumor effect.

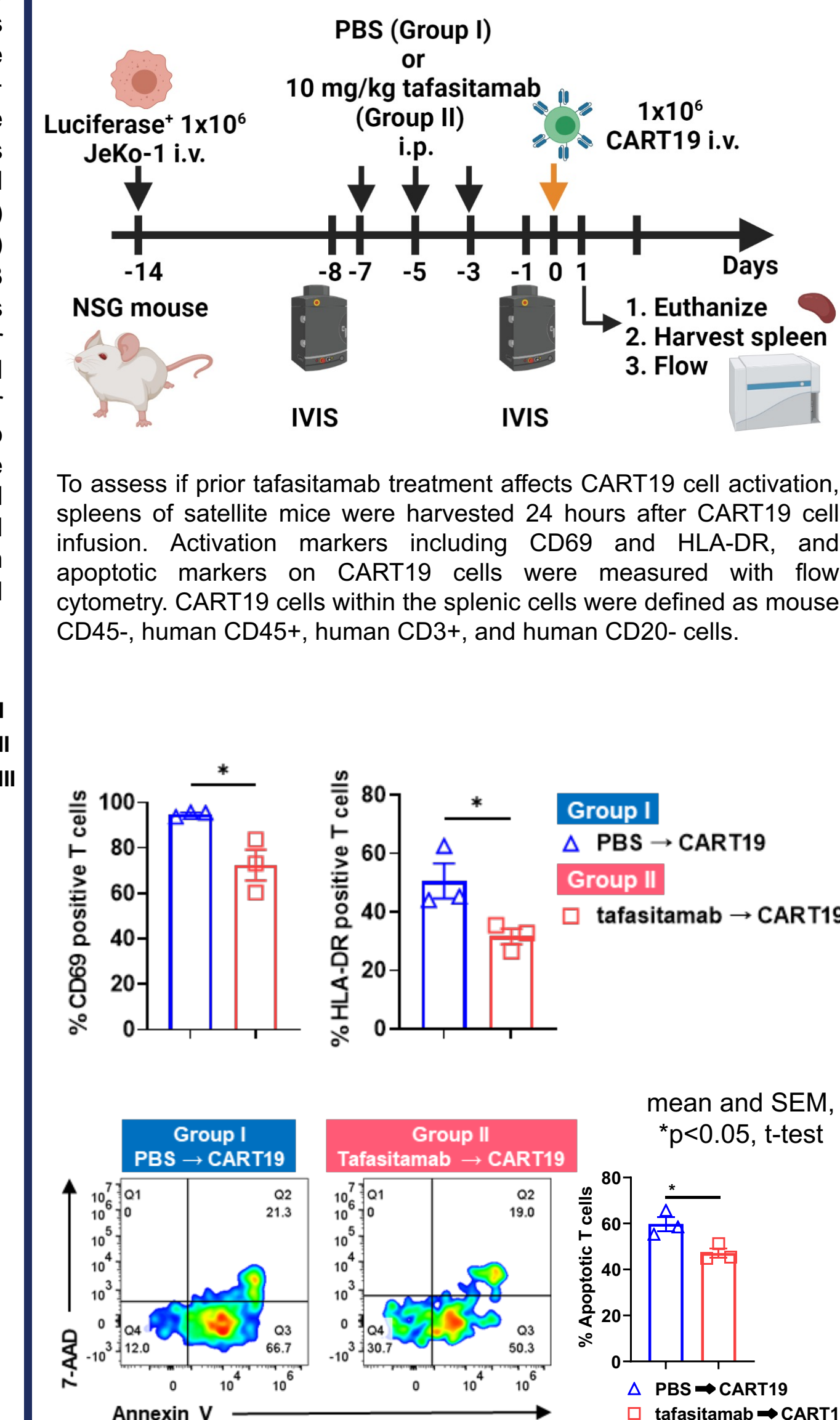
Mice treated with tafasitamab followed by CART19 showed improved tumor control, later and stronger T cell expansion as well as prolonged survival compared to mice treated with PBS followed by CART19.

Sequential therapy of tafasitamab followed by CART19 enhances anti-tumor activity of CART19 cells



Mice treated with tafasitamab followed by CART19 showed improved tumor control, later and stronger T cell expansion as well as prolonged survival compared to mice treated with PBS followed by CART19.

Sequential therapy of tafasitamab followed by CART19 reduces early CART cell activation and apoptosis



Treatment of mice with tafasitamab followed by CART19 resulted in significantly lower CD69 and HLA-DR expression on CART19 cells as well as reduced apoptosis compared to PBS followed by CART19 treatment.

Summary

- Concomitant treatment of tafasitamab and CART19 leads to impaired anti-tumor activity due to antigen competition.
- Prior treatment with tafasitamab does not impact CART19 cell functions.
- Sequential therapy of tafasitamab followed by CART19 cell leads to superior anti-tumor activity in lymphoma xenograft models.
- Sequential therapy reduces early CART19 cell activation and apoptosis.

Conflict of Interest

Sakemura: Humanigen: Patents & Royalties; Cox: Humanigen: Patents & Royalties; Augsberger: Employee of Morphosys; Schanzer: Employee of Morphosys; Patra-Kneuer: Employee of Morphosys; Heitmüller: Employee of Morphosys; Steidl: Employee of Morphosys; Endell: Employee of Morphosys; Ding: Merck: Membership on an entity's Board of Directors or advisory committees; Agos Pharma: Membership on an entity's Board of Directors or advisory committees; AstraZeneca: Research Funding; AbbVie: Research Funding; Octapharma: Membership on an entity's Board of Directors or advisory committees; MEI Pharma: Membership on an entity's Board of Directors or advisory committees; aleon: Membership on an entity's Board of Directors or advisory committees; Beigene: Membership on an entity's Board of Directors or advisory committees; Parikh: GlaxoSmithKline: Honoraria; Verastem Oncology: Honoraria; Genentech: Honoraria; Ascentage Pharma: Research Funding; AbbVie: Research Funding; Merck: Research Funding; TG Therapeutics: Research Funding; AstraZeneca: Honoraria; Research Funding; Janssen: Research Funding; Morphosys: Research Funding; Pharmacia: Research Funding; Morphosys: Research Funding; Kay: Research Funding; Rigil: Membership on an entity's Board of Directors or advisory committees; Oncotracker: Membership on an entity's Board of Directors or advisory committees; Dava Oncology: Membership on an entity's Board of Directors or advisory committees; Juno Therapeutics: Membership on an entity's Board of Directors or advisory committees; Kenderian: MetLife: Patents & Royalties; Lentigen: Research Funding; Morphosys: Research Funding; Sunesis: Research Funding; Toler: Research Funding; BMS: Research Funding; Juno: Research Funding; Gilead: Research Funding; Kite: Research Funding; Novartis: Patents & Royalties; Research Funding; Torque: Consultancy; Humanigen: Consultancy; Patents & Royalties; Research Funding.