Lead Product Candidate: Toca 511 & Toca FC Preclinical Overview

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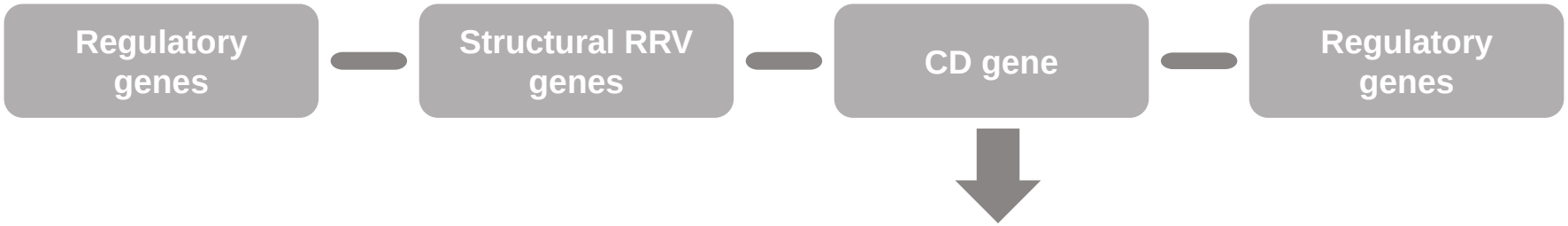
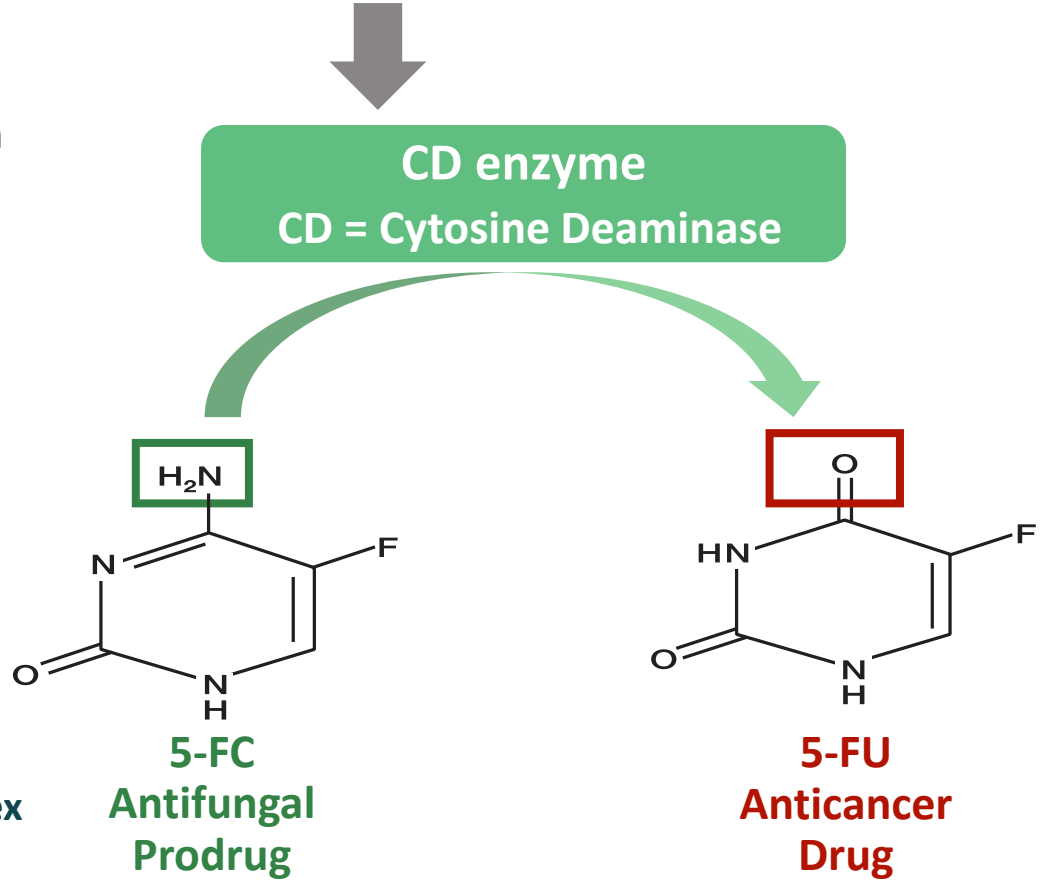
Toca 511, delivers CD prodrug activator gene selectively to cancer cells



- Toca FC is an extended-release formulation of 5-FC
- 5-FC is selectively converted to 5-FU via CD within infected cancer cells
- Humans do not have a CD gene
- 5-FU has a very short half-life, minimizing off-target effects
- 5-FU directly kills cancer cells and MDSCs within the tumor microenvironment
- In situ 5-FU production within infected cancer cells creates a high therapeutic index



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MDSCs = Myeloid Derived Suppressor Cells

Toca 511 & 5-FC yields sustained high levels of 5-FU in tumors while minimizing systemic exposure

Comparison of peak 5-FU levels in tumors and plasma after Toca 511 & 5-FC or systemic administration of 5-FU

Setting	Treatment	Tumor 5-FU (µg/g)	Plasma 5-FU (µg/g)
Rat F98 glioma	Toca 511 & 5-FC	69	0.4
Human Colon[1]	5-FU	0.1-2.8[2]	52

[1]Peters, et.al. Cancer Chemother Pharmacol, 1993. 31(4): p. 269-76
[2]The higher human tumor value of range was used for calculation of ratio

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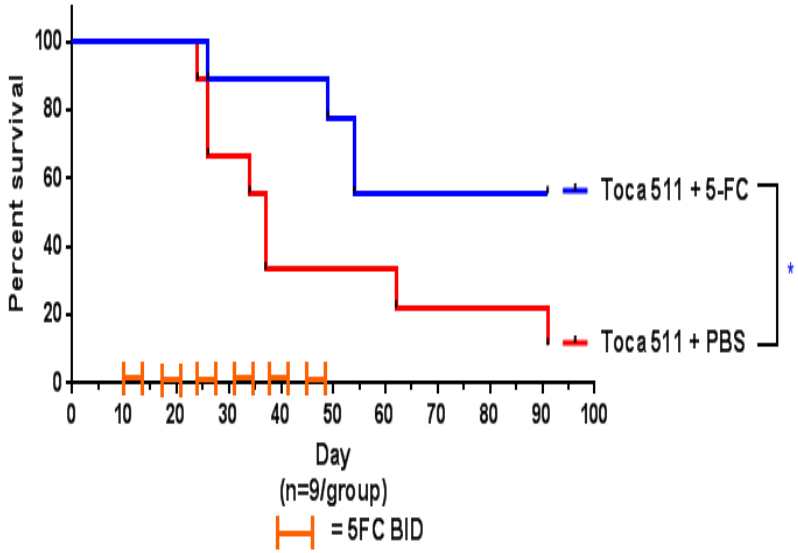
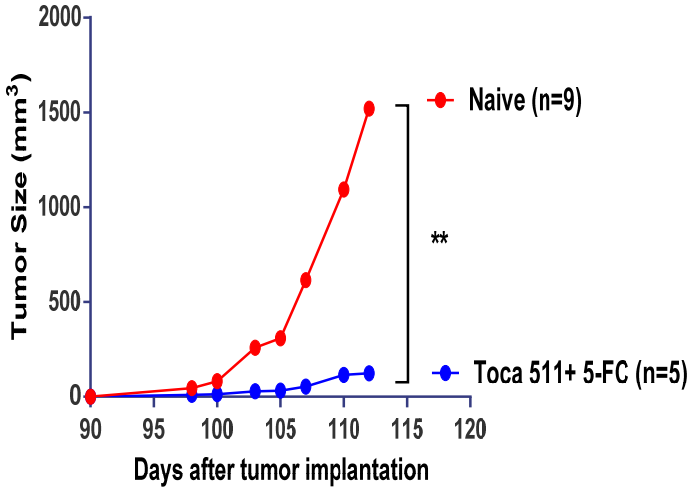
Toca 511 & 5-FC efficacy in CRC liver metastases model

Improved Median Survival, 50% Cure Rate,
Antitumor Immune Response, No Toxicity





CT26-luc liver metastases model treated with Toca 511 (IV) & 5-FC (500 mg/kg Q5D every 1W)

Re-implantation of cancer cells into naïve or cured animals

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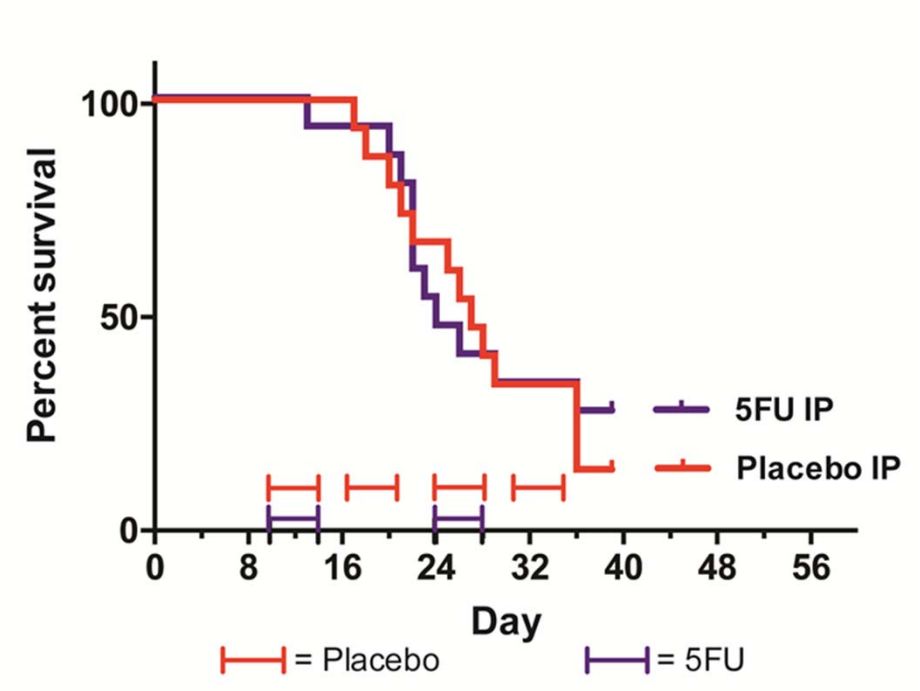
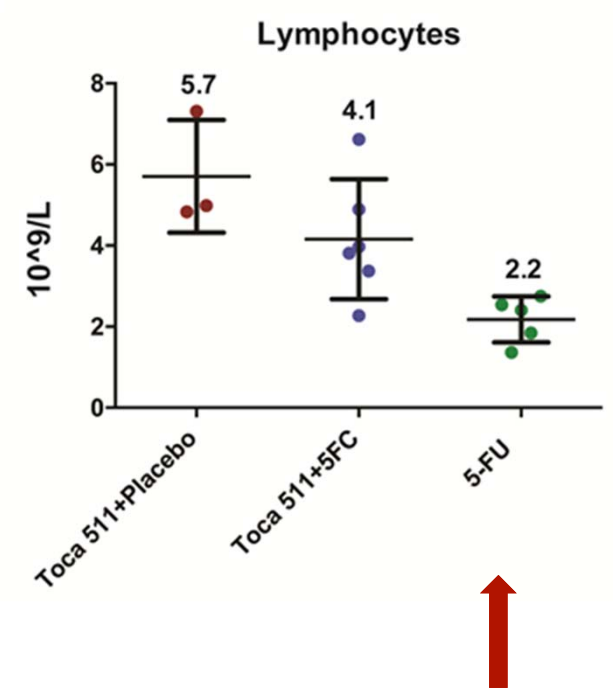
In contrast to Toca 511 & 5-FC, systemic 5-FU does not increase survival and is toxic to lymphocytes



CT26-luc liver metastases model treated with systemic 5-FU



Blood lymphs drop with systemic 5-FU

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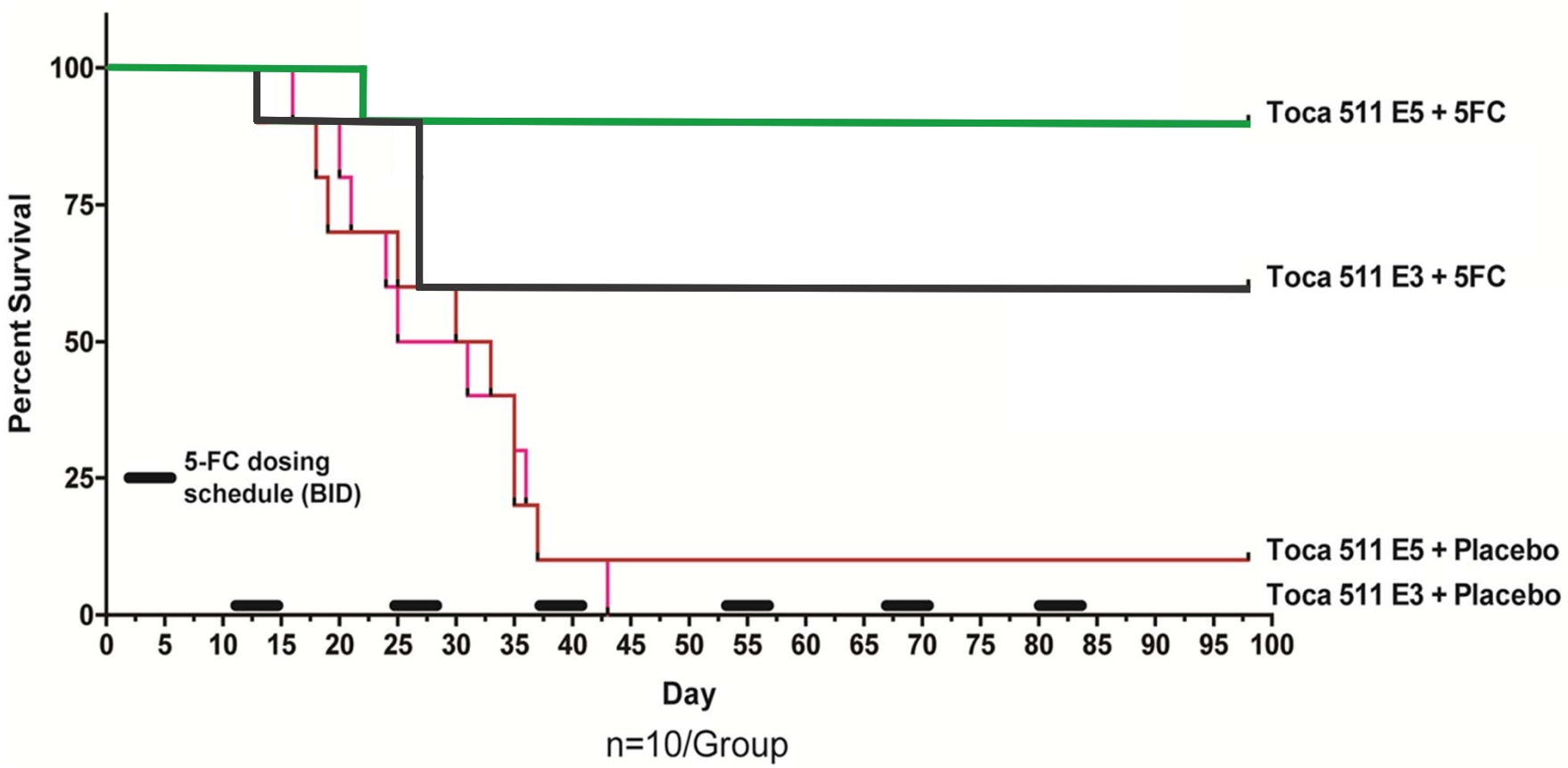
Toca 511: Dose dependent increase of survival



E3, E5 = 10^3, 10^5 TU/ gm brain
Tu-2449 glioma cells in B6C3 F1 mice

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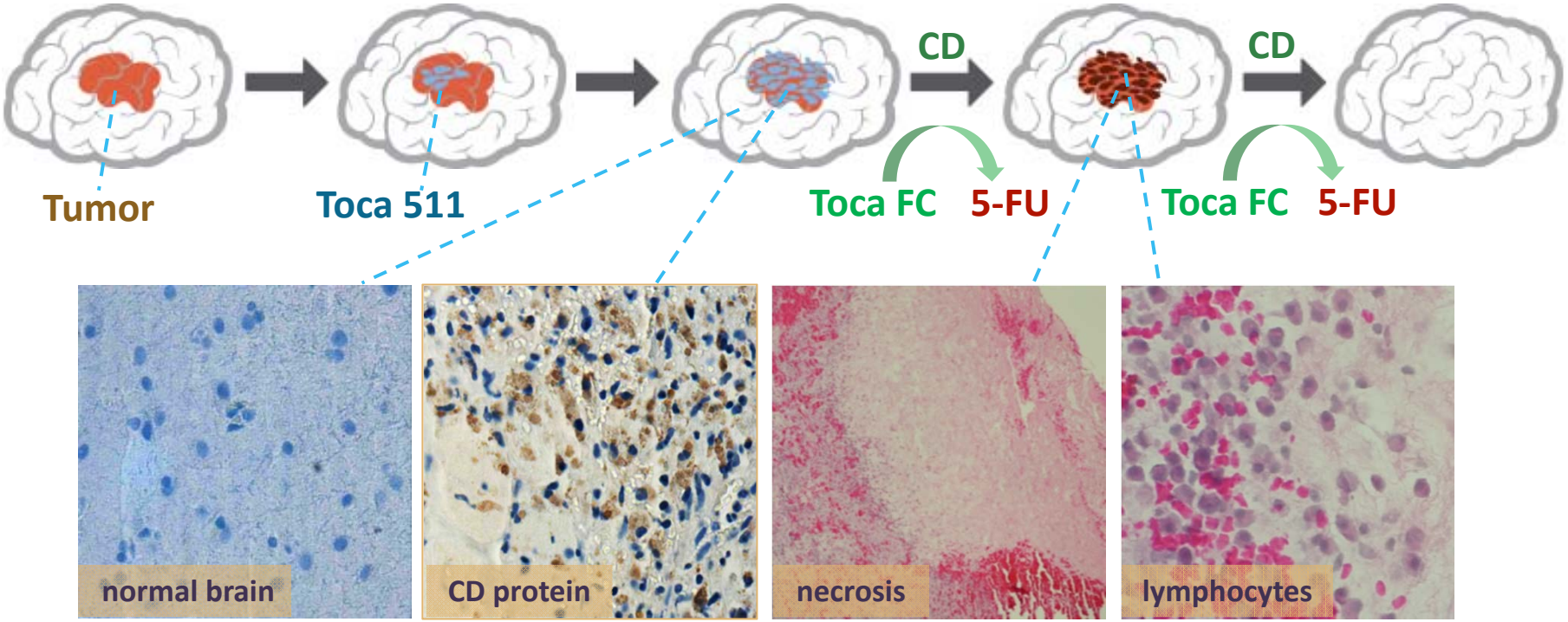
Modified from Ostertag et al. Neuroonc. 2015.

Toca 511 & Toca FC selectively turns tumor into 5-FU factory

Dual Actions: 5-FU Kills Tumor **and** Activates Immune System Against Cancer



Brain and tumor samples from Tocagen clinical trial patients

CD = cytosine deaminase

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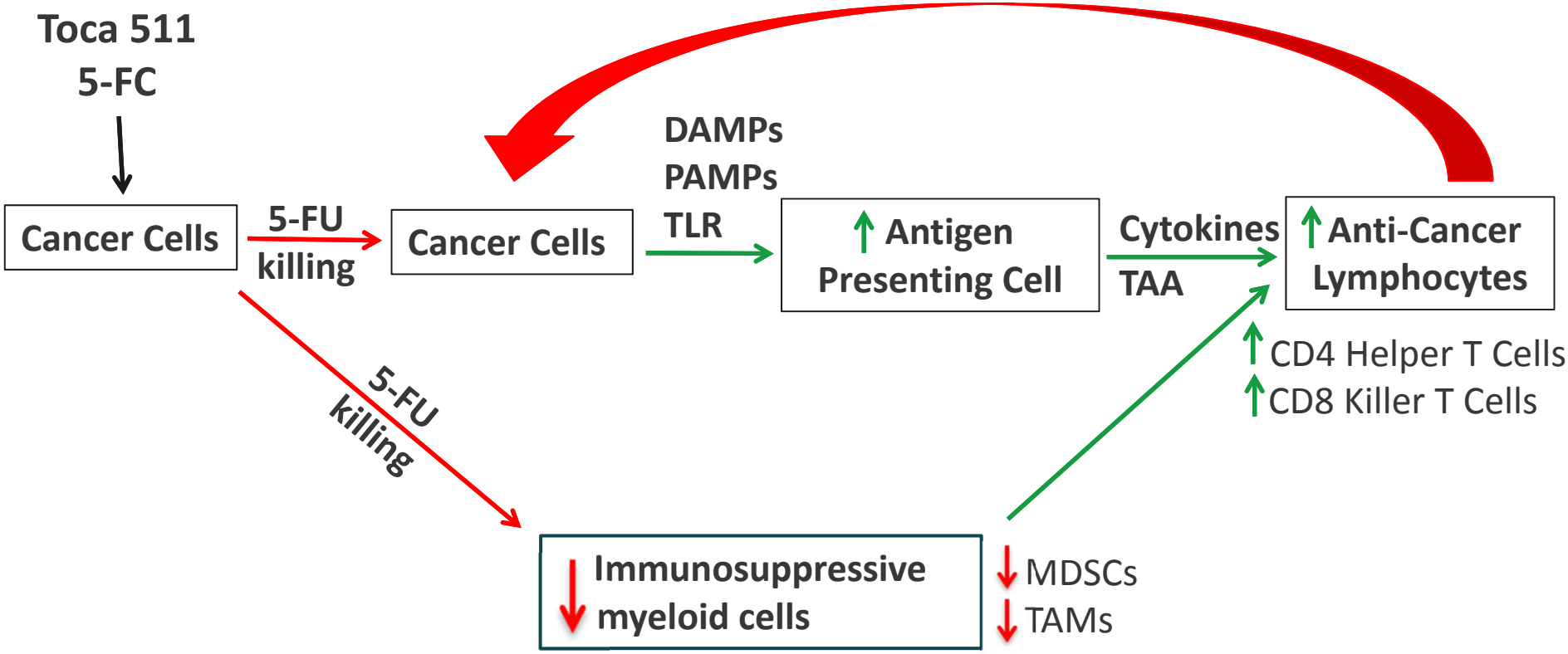
5-FU selective immunotherapeutic

Directly kills tumor cells leading to immune activation



DAMPs = Danger Associated Molecular Patterns
PAMPs = Pathogen Associated Molecular Patterns
TLR = Toll Like Receptors

TAA = Tumor Associated Antigens
MDSCs = Myeloid Derived Suppressor Cells
TAMs = Tumor Associated Macrophages

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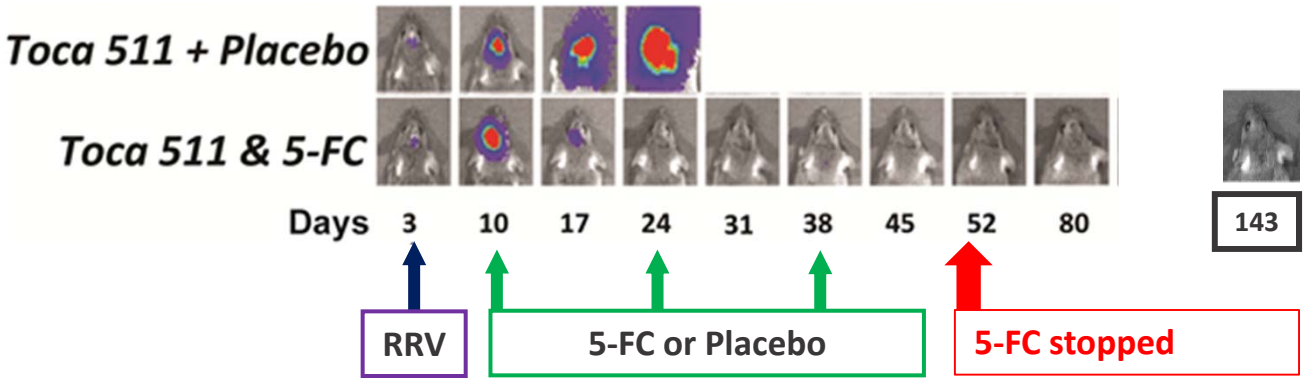
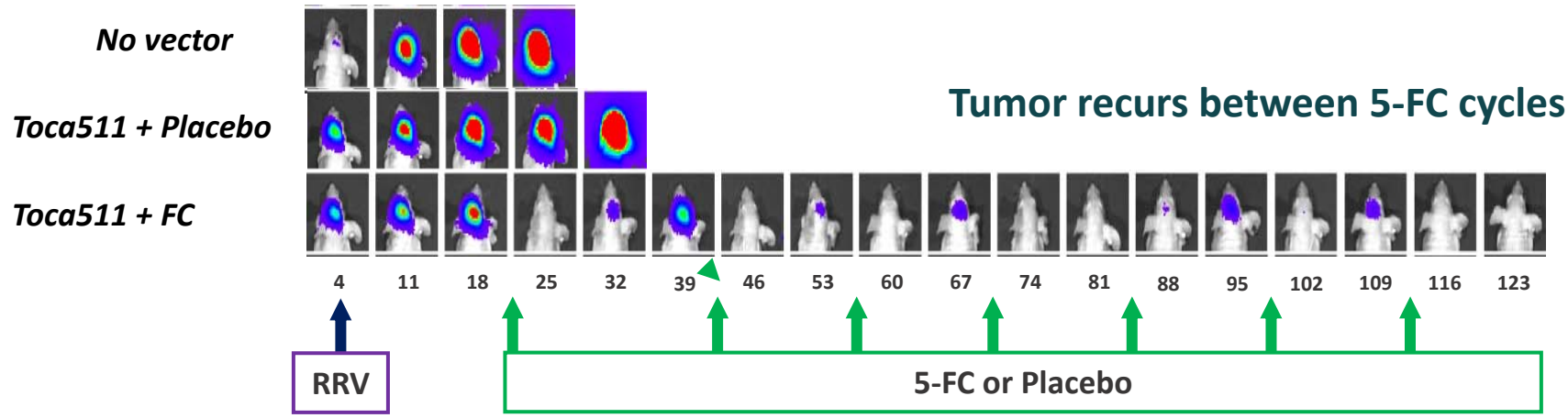
Toca 511 & 5-FC activates a durable immune response against cancer only in immune competent mice

Syngeneic glioma in immune competent mice: **5-FU plus immune activation**



Mice are "cured" despite stopping 5-FC

Human GBM in immune deficient mice: **5-FU only action**



Tumor recurs between 5-FC cycles

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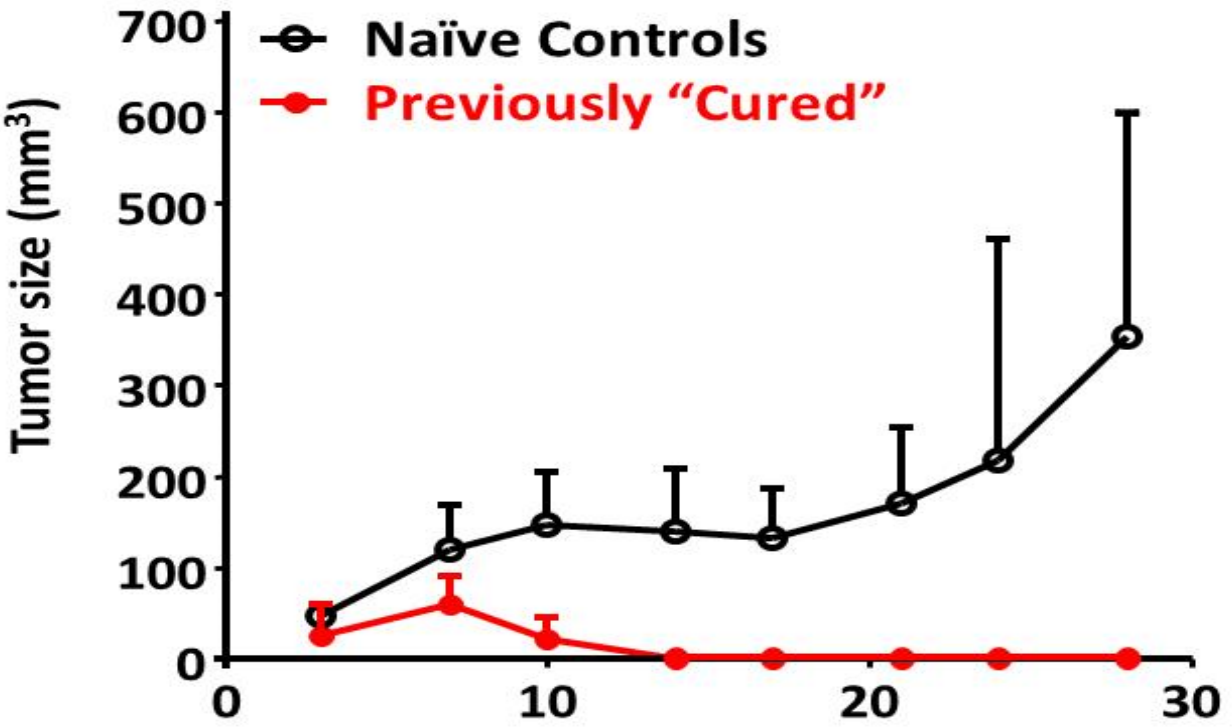
“Cured” mice develop systemic immunity



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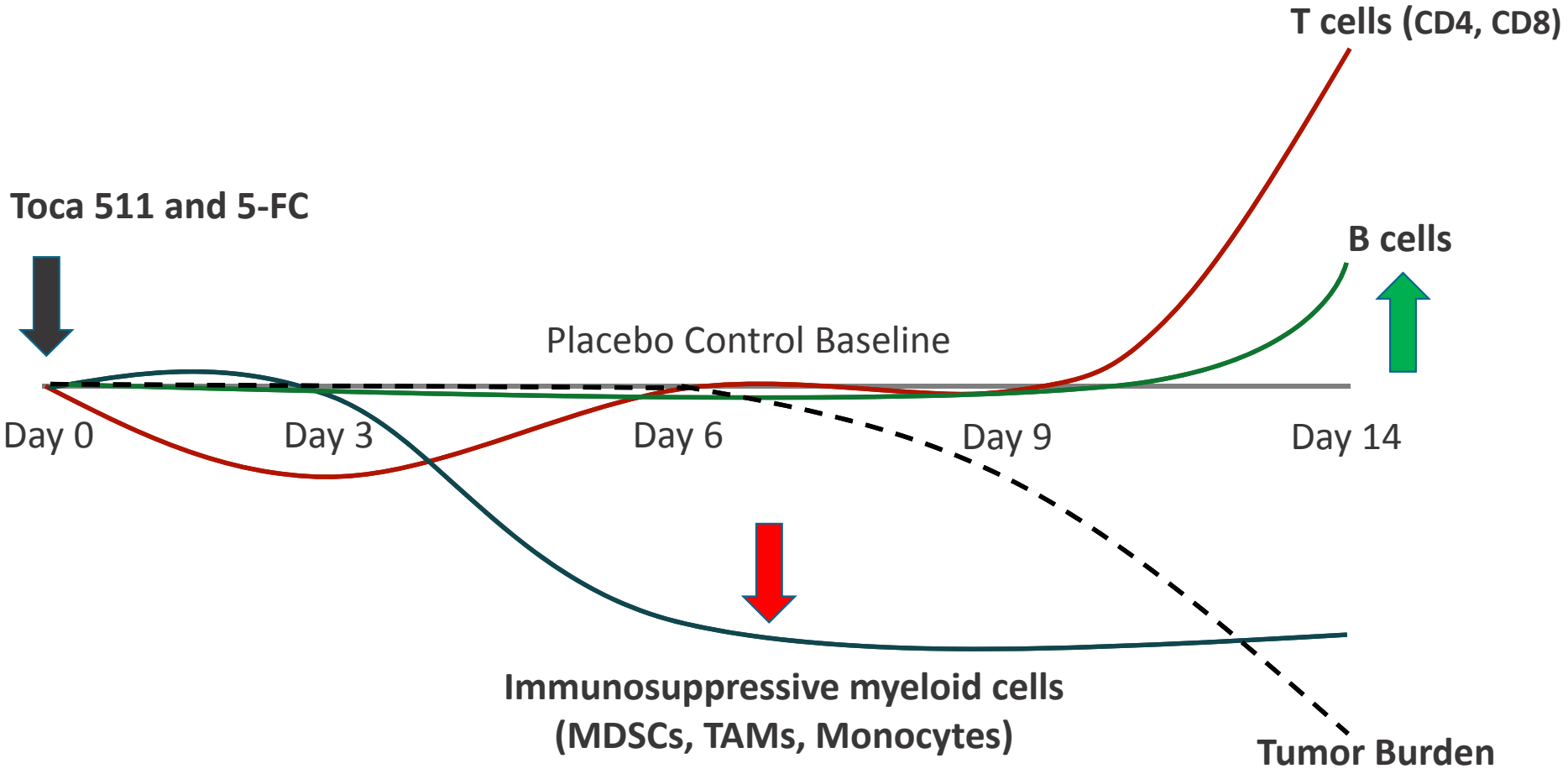
Toca 511 & 5-FC activate immune system in tumor microenvironment



Preclinical model.

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Preclinical efficacy is supported in many cancers

- brain cancer
- colorectal cancer
- pancreatic cancer
- breast cancer
- prostate cancer
- lung cancer
- bladder cancer
- ovarian cancer

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Clinical Data Summary for Toca 511 & Toca FC

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Toca 511 & Toca FC

- 128 patients with recurrent high grade glioma have been enrolled in Tocagen's ongoing investigational Phase 1 trials
- A favorable safety and tolerability profile has been observed to date
- Extended overall survival (OS) has been reported compared to historical benchmarks
- In 43 patients with recurrent HGG, mostly with glioblastoma, where Toca 511 was administered at the time of tumor removal, survival at 12 and 24 months was 52.5 percent and 31.6 percent, respectively
- Stable disease, partial and complete responses have been observed
- Based on these data, Toca 511 & Toca FC has advanced into a pivotal Phase 2/3 study in patients with recurrent glioblastoma or anaplastic astrocytoma
- Fast Track designation for the treatment of recurrent HGG and Orphan drug designation for the treatment of glioblastoma, a subset of HGG

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Modified from M.K. Aghi, MD, SNO, Nov. 18th, 2015.

Phase 2/3 Randomized, Controlled Trial of Toca 511 & Toca FC versus SOC in Patients with Recurrent Glioblastoma or Anaplastic Astrocytoma

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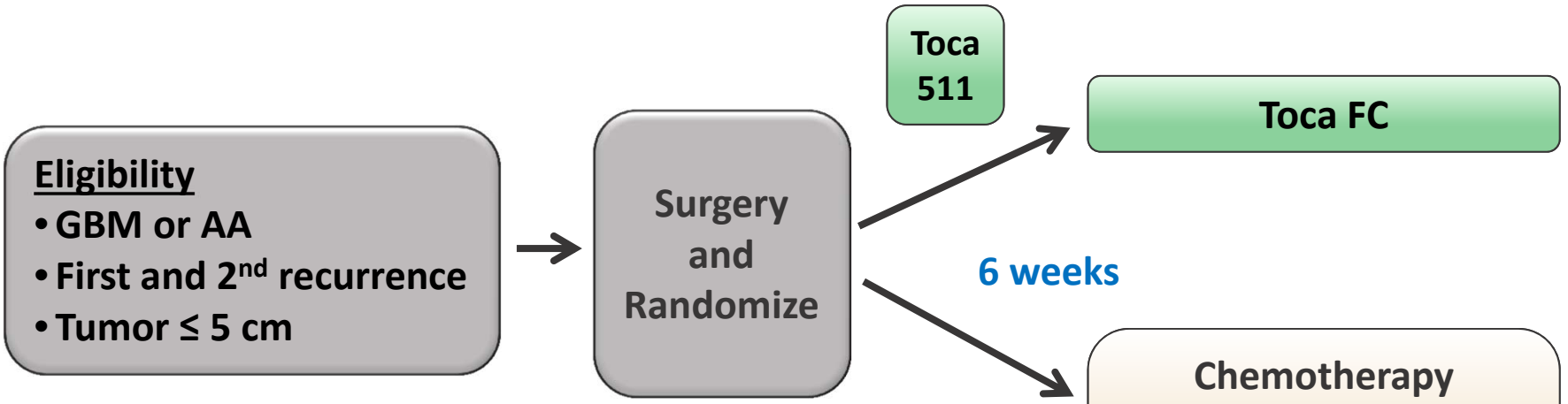
TOCA5 Pivotal Phase 2/3 Study Schema



Stratify by IDH mutation status
KPS (70-80 vs 90-100) and region

Primary endpoint: Overall Survival
Phase 2, N=170, 1:1 randomization

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ClinicalTrials.gov Identifier: NCT02414165
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