

Autologous glioblastoma tumor cells treated with an antisense oligonucleotide against insulin-like growth factor type 1 receptor protect mice against GL261 tumor challenge

Short title: GBM immunotherapy preclinical study

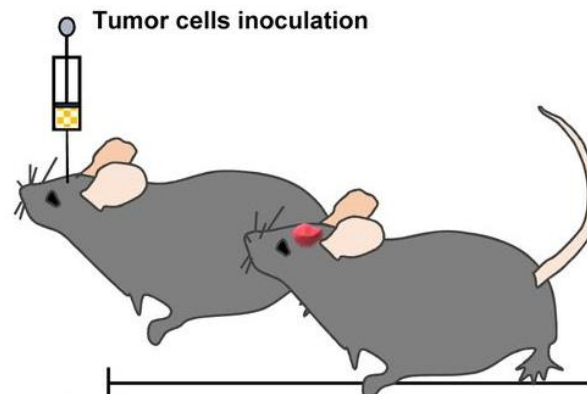
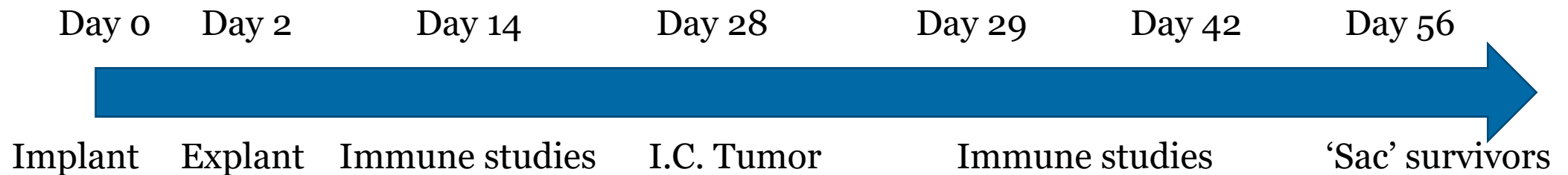
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Imvax Inc., Philadelphia, PA

*Presenter

Survival Study in the GL261 murine model

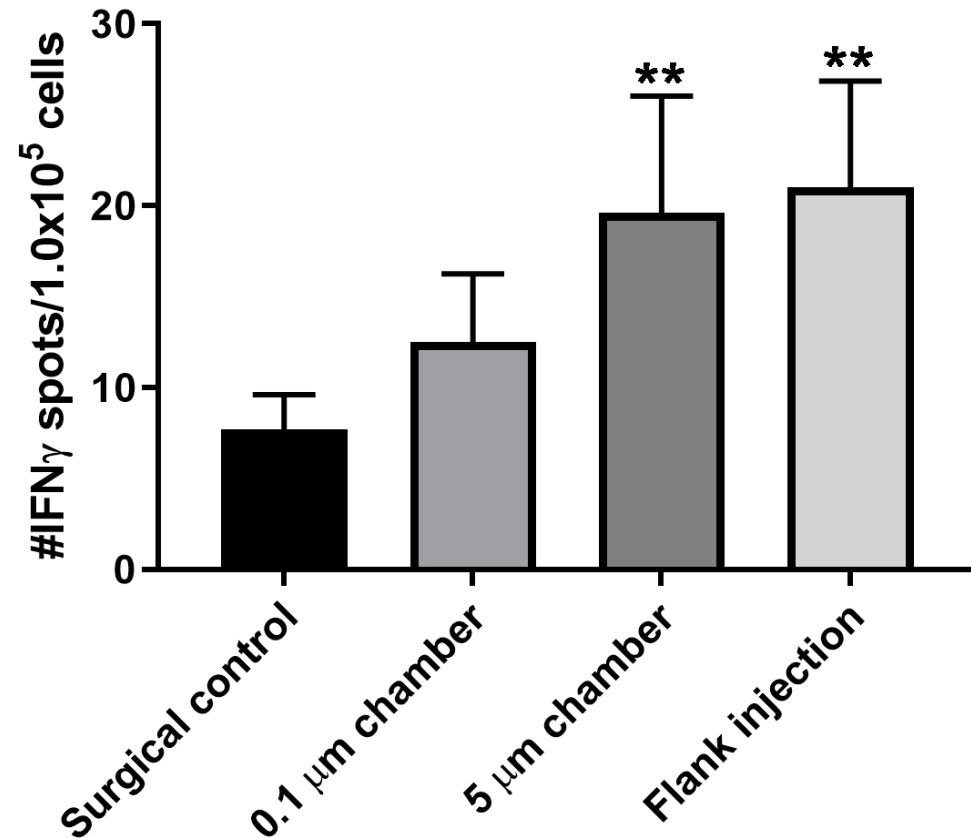
- Prophylactic approach.
- *Immuno-competent 'orthotopic' lethal intracranial tumor challenge*
- Mice / group: Surgical control = 12 mice, 0.5 μm -pore chamber = 20 mice, 0.1 μm -pore chamber = 20 mice
- Single chamber 2-day implant / mouse
- Luciferase⁺ tumor imaging



T cell immune response: anti-tumor Th1 IFN γ

(D27 post-chamber removal)

T cells + Tumor lysate + IMV-001 + DCs + LPS

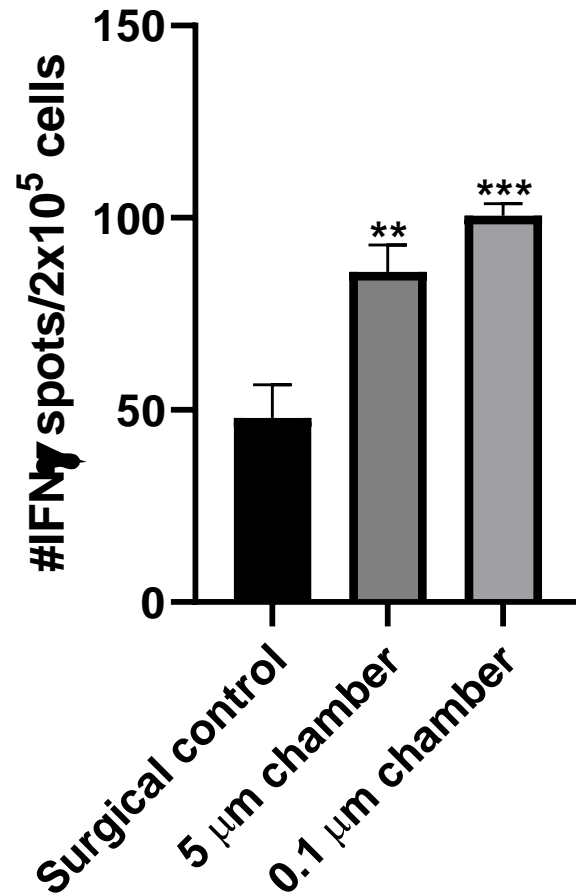


#IFN γ producing T cells from control and vaccinated mice (no tumor challenge). Stimulation was performed with dendritic cells pulsed with tumor lysate + oligo + LPS.

** $P=0.0064$ and ** $P=0.0025$ compared to surgical control group. One Way Anova, followed by Tukey's multiple comparisons test

T cell immune response: anti-tumor Th1 IFN γ

PBMCs + Tumor lysate + IMV-001 + DCs + LPS

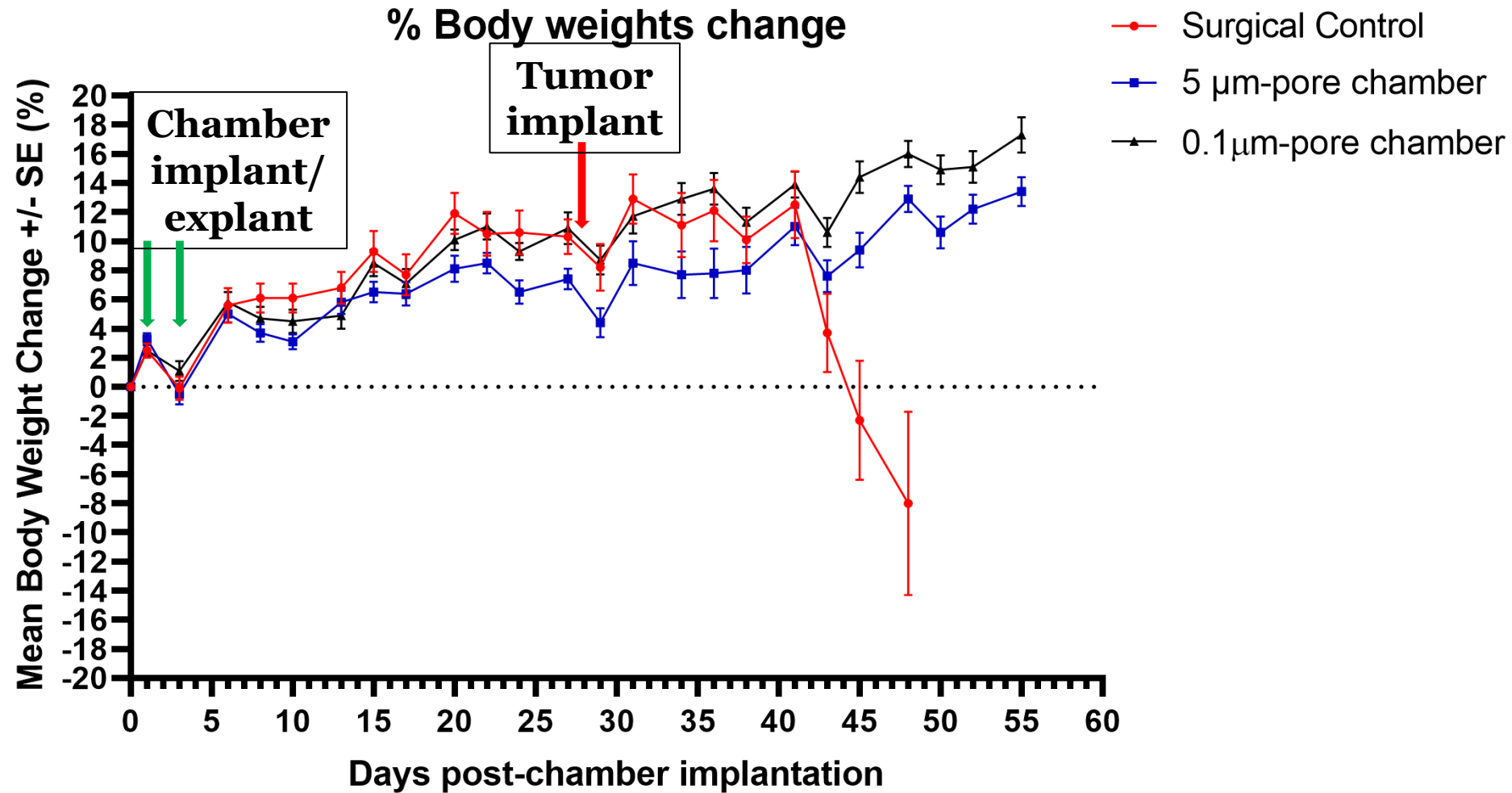


#IFN γ producing PBMCs from control and vaccinated mice, tumor challenged on D28. Stimulation was performed with dendritic cells pulsed with tumor lysate + IMV-001 and LPS

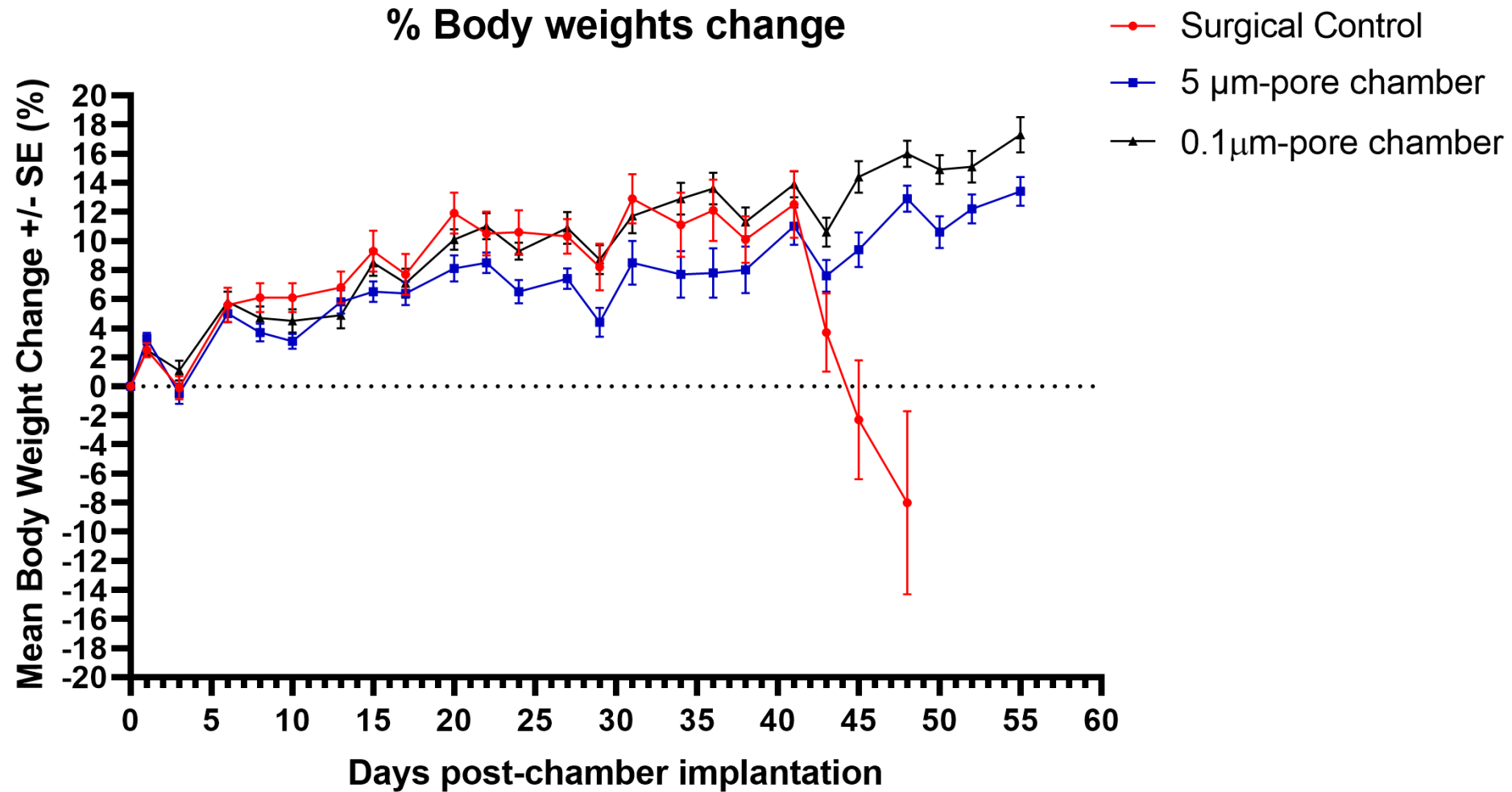
*** $P=0.0002$ and ** $P=0.001$ compared to surgical control group. One Way Anova, followed by Tukey's multiple comparisons test

(D27 post-chamber removal)

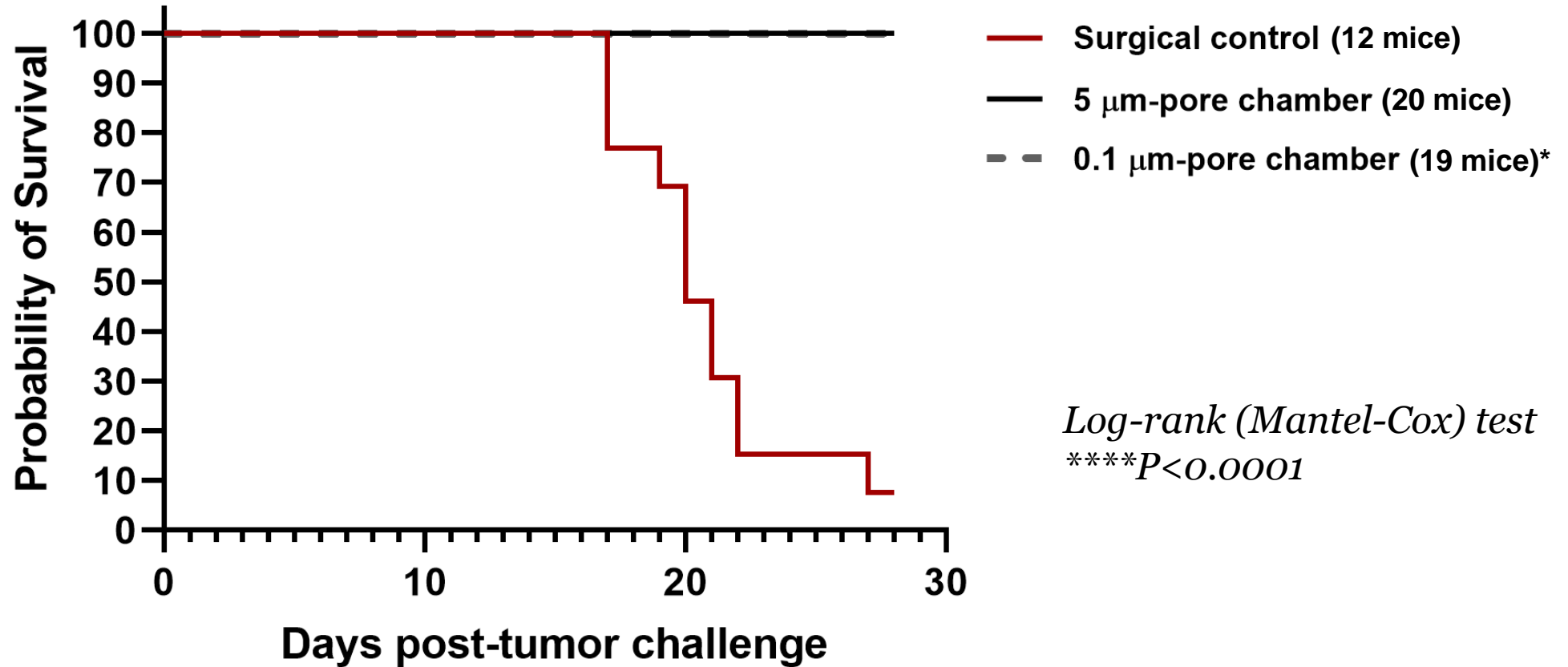
Tumor challenge: mouse weight change



Tumor challenge: mouse weight change



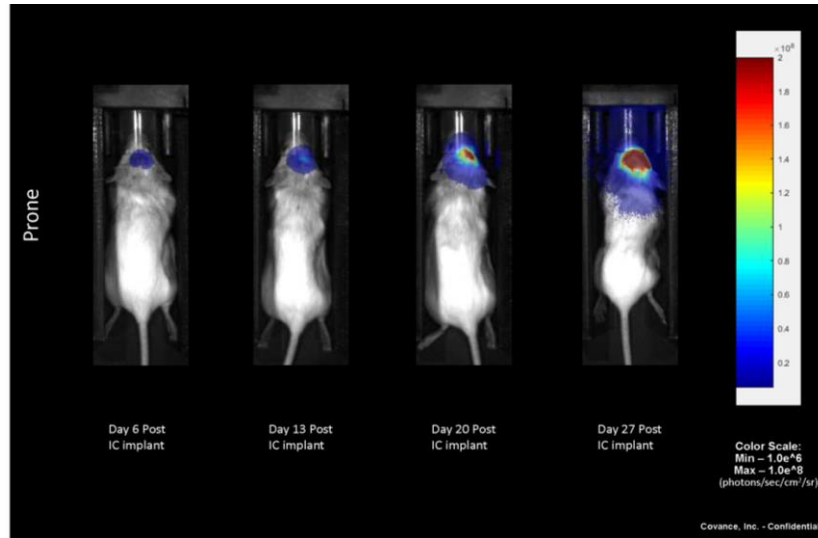
Overall Survival, day 0 = tumor challenge



****1 mouse post-I.C. surgical death in 0.1 μm group***

Imaging the tumors

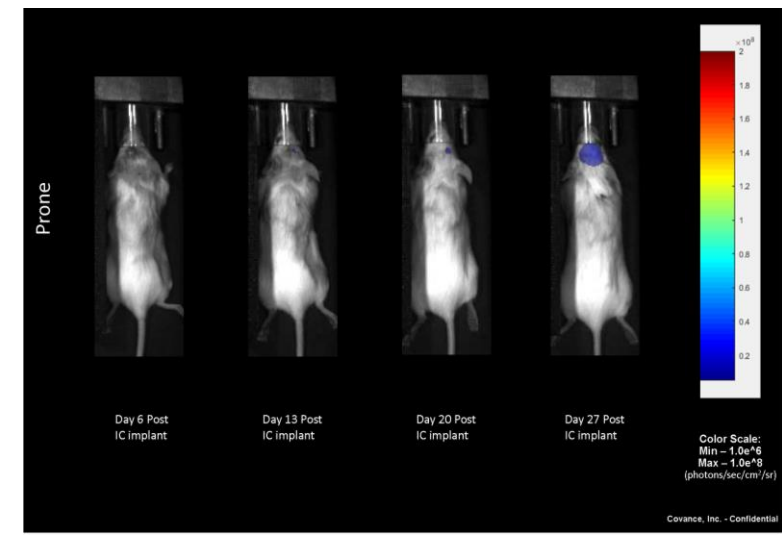
Surgical control, Mouse#4



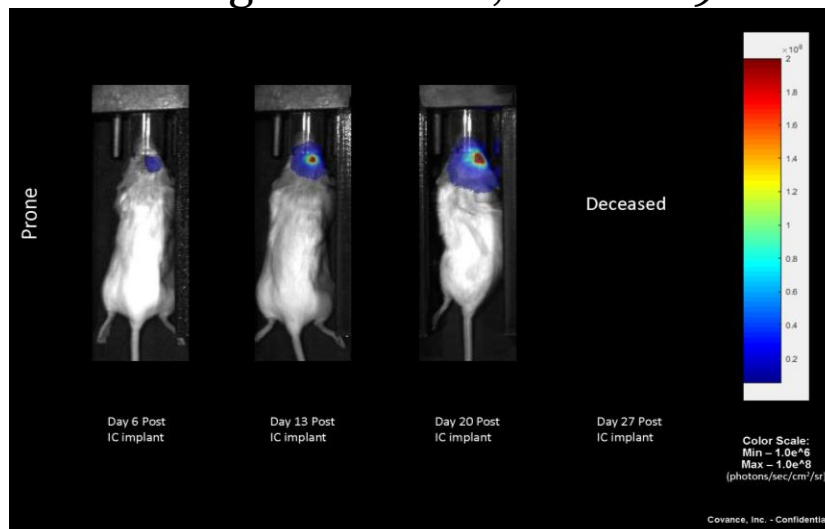
5 μ m-pore chamber, Mouse#2



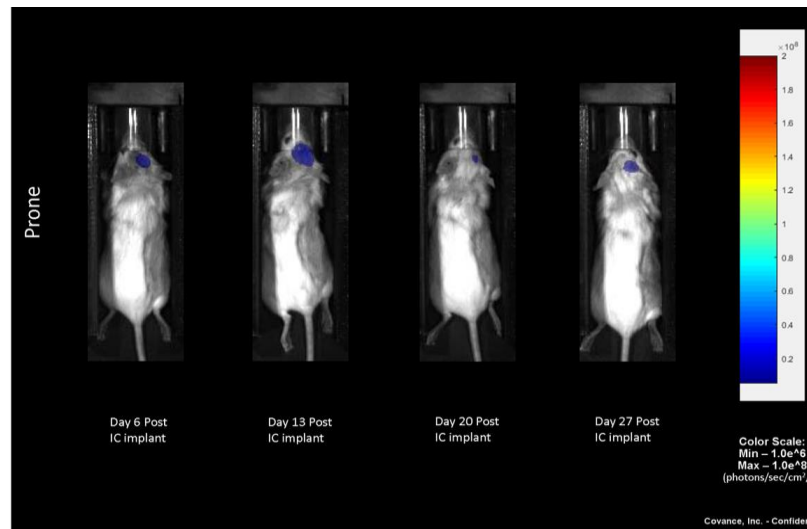
0.1 μ m-pore chamber, Mouse 10



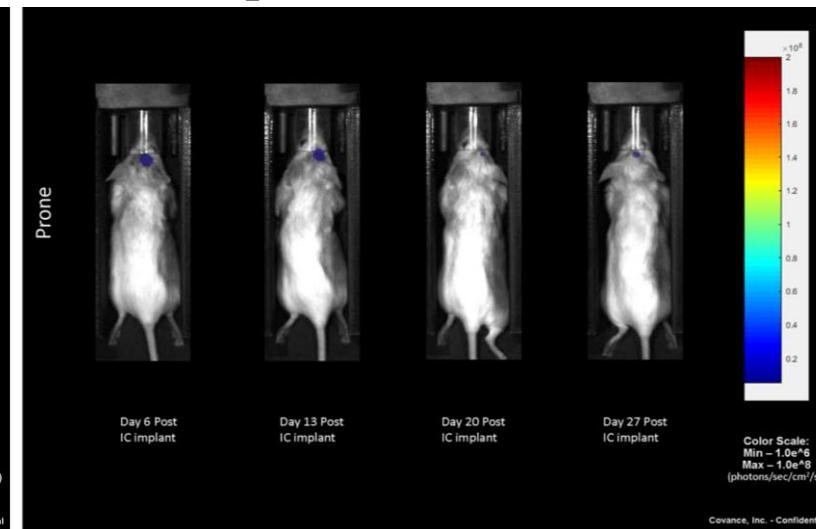
Surgical control, Mouse#9

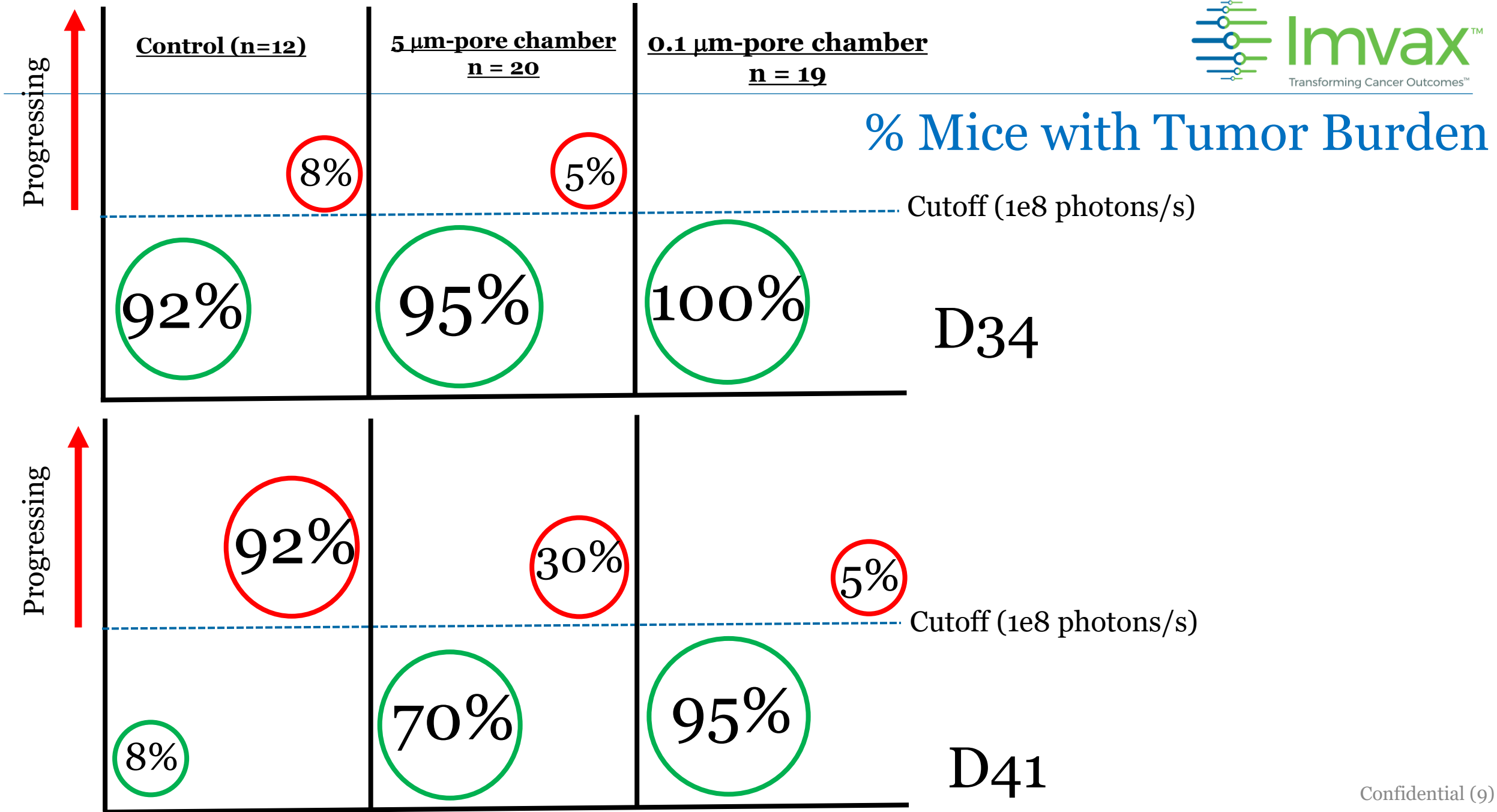


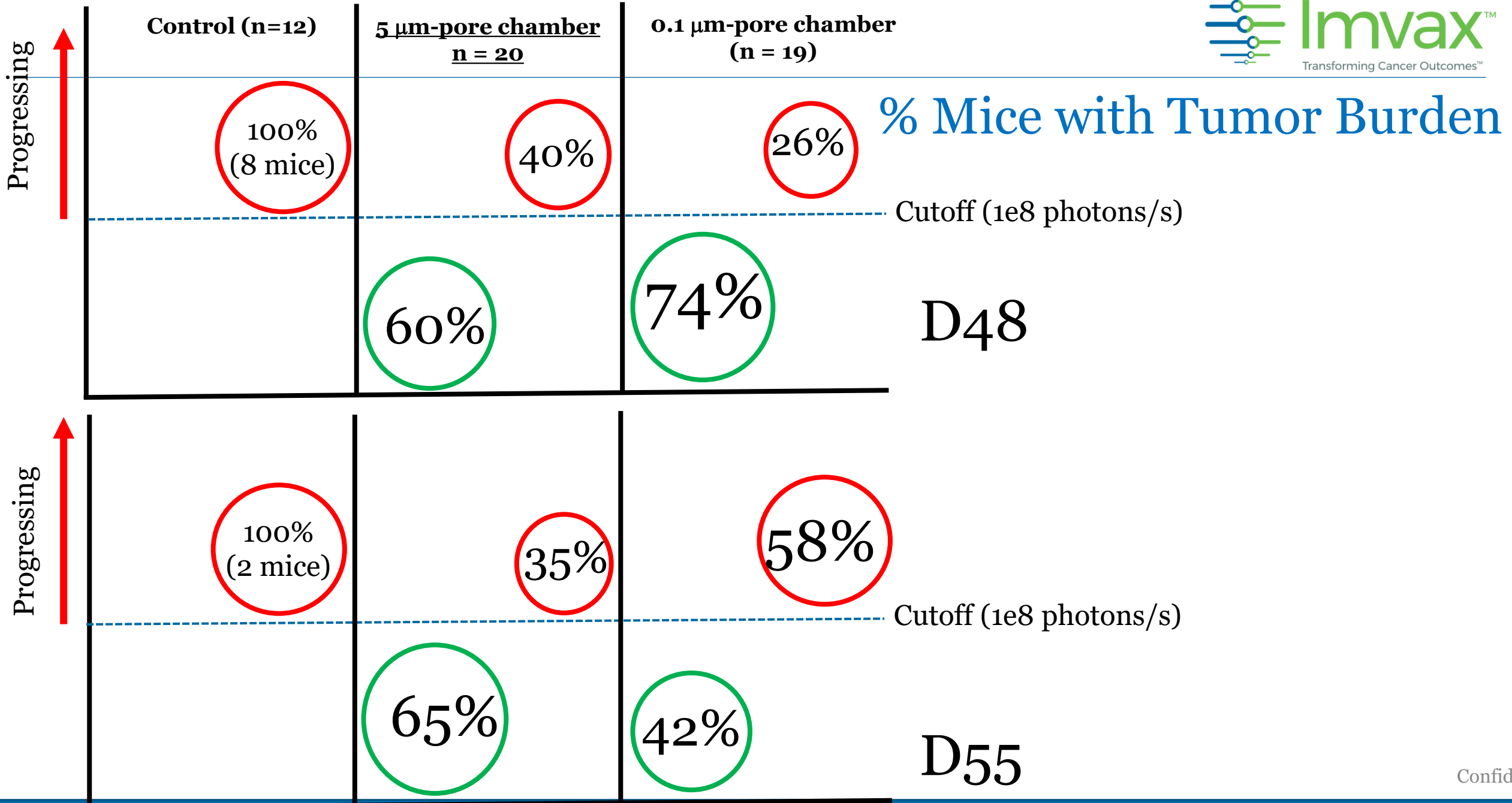
5 μ m-pore chamber, Mouse#4



0.1 μ m-pore chamber, Mouse#2

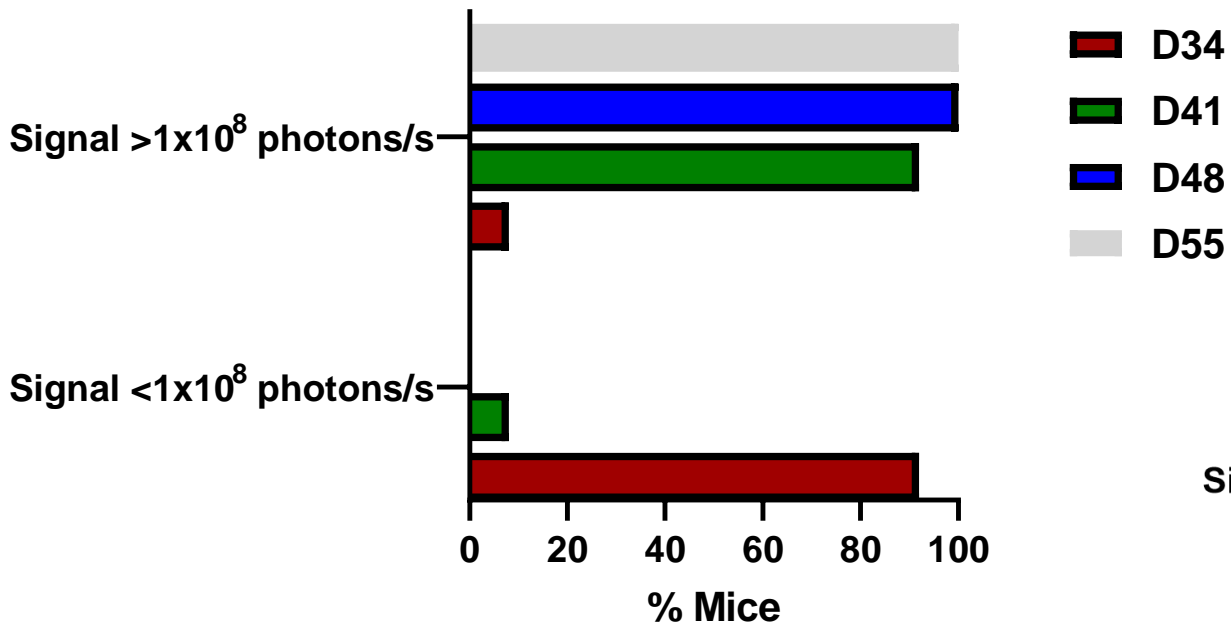




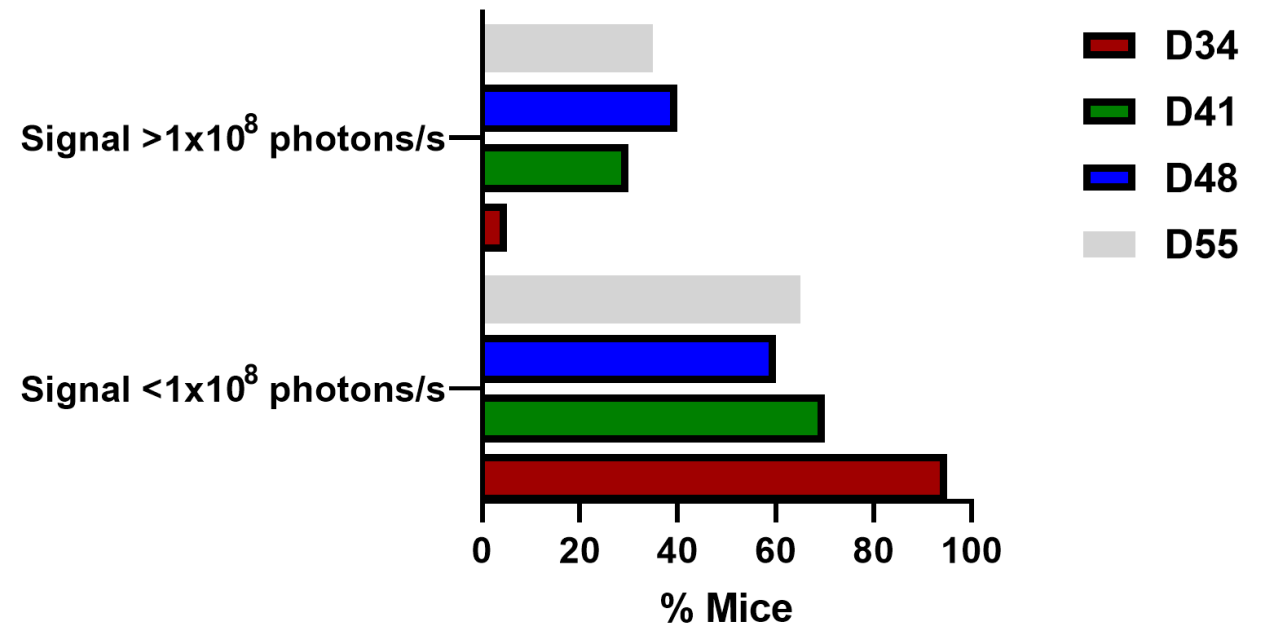


% Mice with Tumor Burden (another way to present the data)

Surgical control

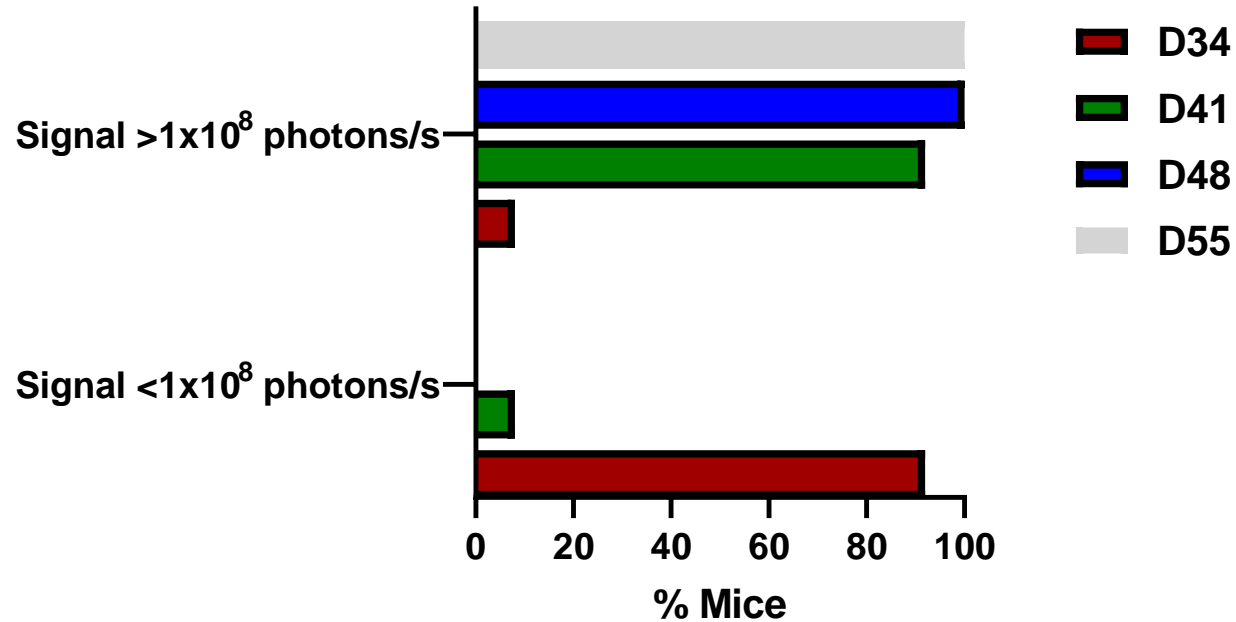


5 μm-pore chamber

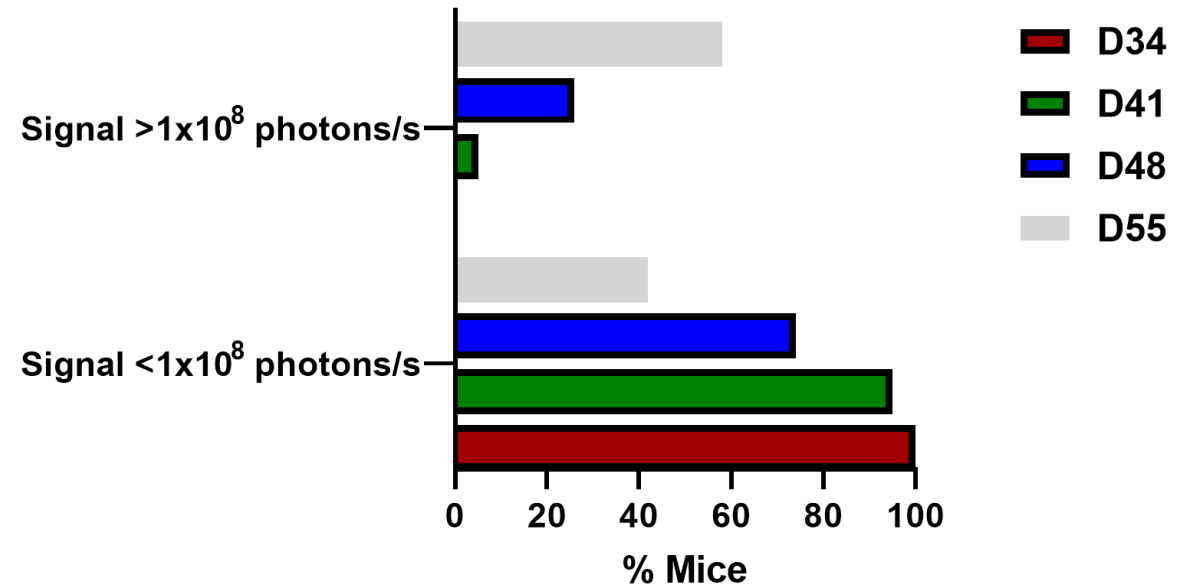


% Mice with Tumor Burden

Surgical control



0.1 μm-pore chamber



- Both standard 0.1 μm pore chambers and 5 μm treated mice survived with modest tumor burden in some, undetectable in others as long as studied
- Evidence of immune response in treated mice

Moving forward: #2005

- #2005 independently repeats 0.1 μm chambers compared to original 'Abraham' chambers
- Look at T cell exhaustion. What is the difference between treated mice that are showing progression (Photon Flux $>1\text{E}8$ by day 55) and mice that are not?
- Refine ELISPOT to ensure we are capturing the individual responses (pooled samples combines responders vs. Non-responders)
- Extend length of experiment, taking out from 1 to 2 months to capture MST.

Q&As ?