

# ID8 SYNGENEIC OVARIAN CANCER MODEL RESPONSE TO CHECKPOINT INHIBITORS



Dylan Daniel, PhD  
*Director, Scientific Development*

In our November 2017 model spotlight, we described the development of a novel syngeneic mouse model of orthotopic ovarian cancer, ID8-Luc. Ovarian cancer remains a significant unmet medical need with a relative five-year survival rate of 17% in patients diagnosed with highly advanced stage IV ovarian cancer. While often initially responsive to platinum- and taxane-based chemotherapy, relapse is common in ovarian cancer.

We previously reported a median survival of 35-40 days in the orthotopic ID8 model accompanied by the development of peritoneal ascites. Further investigation of the disease progression in solid tissues using ex vivo bioluminescence imaging (BLI) in animals with advanced disease detected the highest disease burden to localize in the pancreas, spleen, ovaries and uterine horns.

## **Checkpoint Inhibitor Testing Using anti-mPD-1 Ab, anti-mPD-L1 Ab, and anti-mCTLA-4 Ab**

Syngeneic mouse models are of significant value in immuno-oncology research because the mice have an intact immune system that enables the therapeutic manipulation of the immune system to elicit anti-tumor responses. Based on their clinical benefit in human melanoma and non-small cell lung cancer, T cell checkpoint inhibitors, including anti-PD-1, are under active investigation in human ovarian cancer clinical trials. To determine if the ID8-Luc ovarian cancer model was responsive to checkpoint inhibition, we tested anti-mPD-1 Ab, anti-mPD-L1 Ab and anti-mCTLA-4 Ab in mice with established ID8 peritoneal tumor burden; using BLI to monitor therapeutic response (Fig. 1A). Robust tumor regression was observed in the mice treated with both anti-mPD-1 (100% TFS) or anti-mPD-L1 (100% TFS) (Fig. 1B). In stark contrast, anti-mCTLA-4 showed no significant activity above that of a rat isotype control antibody. Representative BLI images show extensive disease burden in control and anti-mCTLA-4 treated mice while anti-mPD-1 and anti-mPD-L1 have no detectable disease (Fig. 2). The lack of measurable disease was also confirmed by gross necropsy at the end of the study.

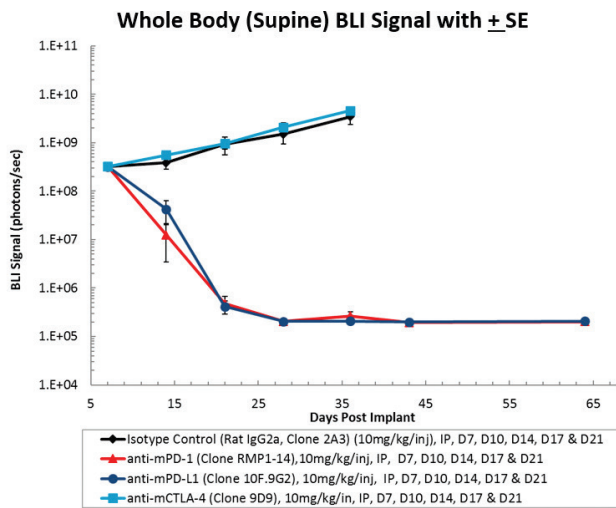


Figure 1A. Intraperitoneal ID8-luc: mean whole body BLI signal over time.

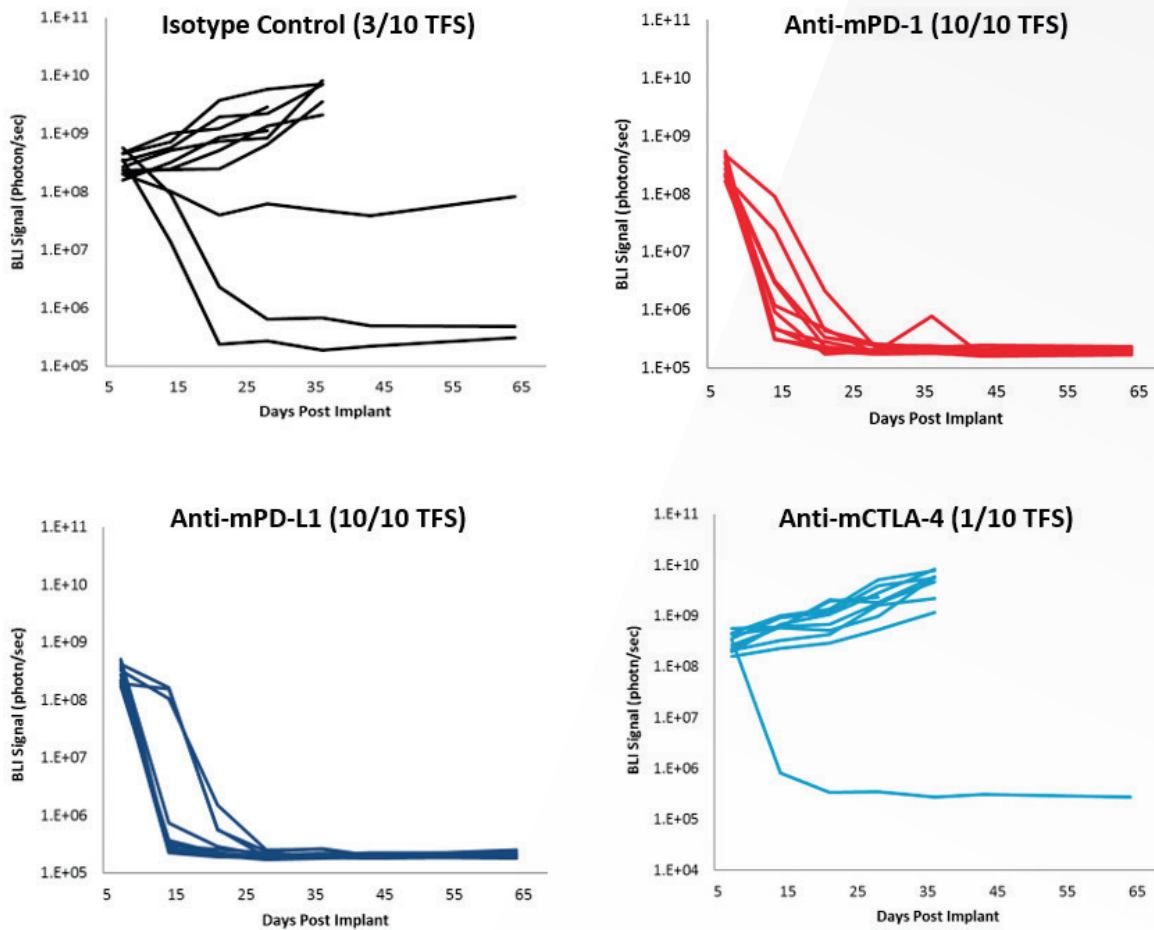


Figure 1B. Intraperitoneal ID8-luc: individual animal whole body BLI signal over time.

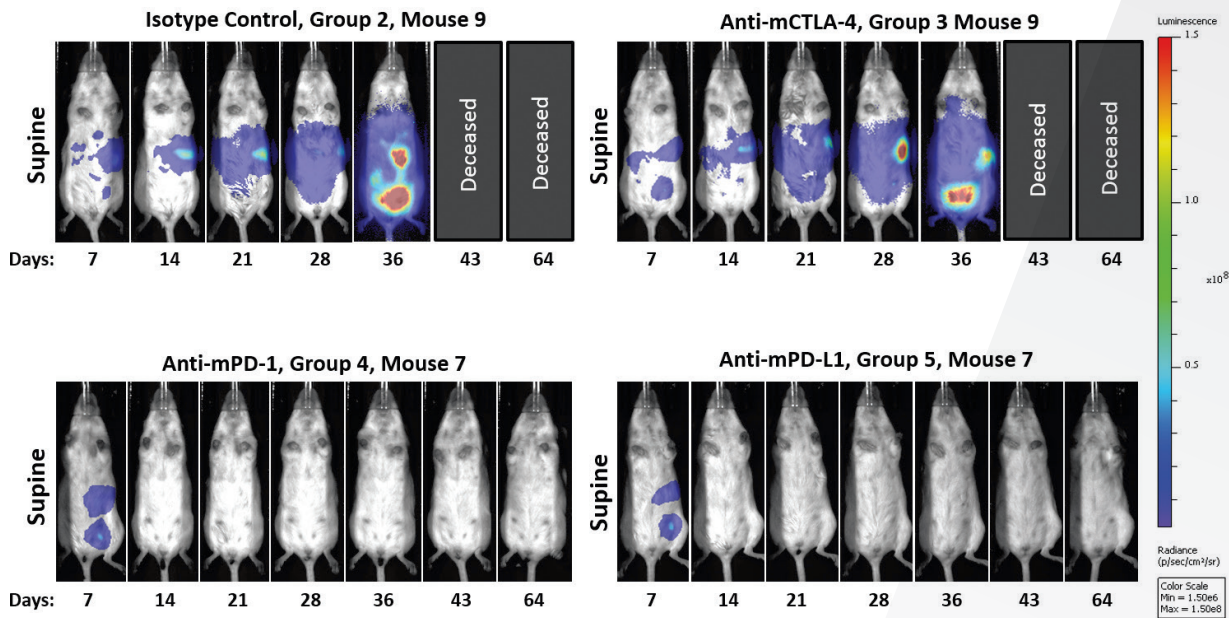


Figure 2. Intrapерitoneal ID8-luc: representative BLI images over time.

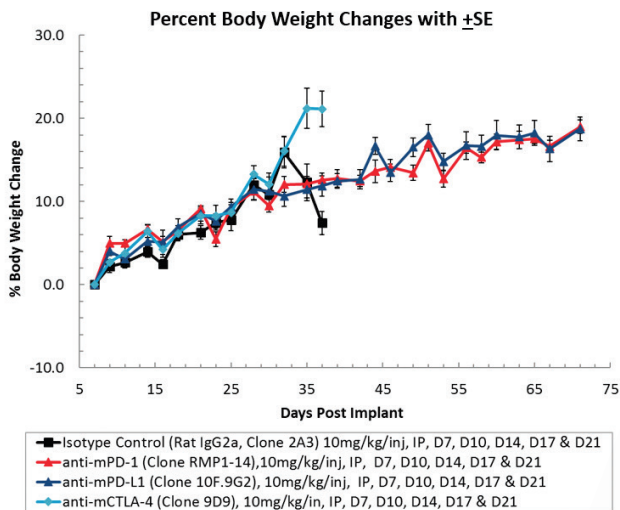


Figure 3A. Intrapерitoneal ID8-luc: mean body weight change over time.

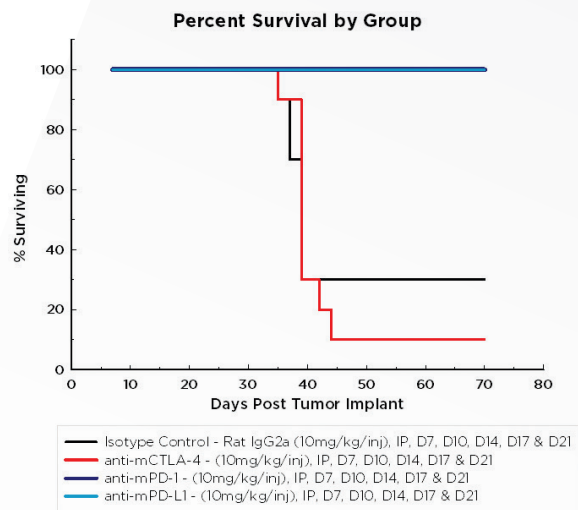


Figure 3B. Orthotopic ID8-luc: overall survival (morbidity/mortality).

## Continued Assessment of anti-mPD-1 and anti-mPD-L1 Therapy

Mice randomized for initiation of treatment on day 7 post implant have a 10-20% rate of spontaneous regression (Fig. 1B). To reduce the incidence of spontaneous regression and determine if anti-mPD-1 and anti-mPD-L1 therapy will be as effective with more advanced tumor burden, we are currently assessing the activity of these checkpoint inhibitors on animals randomized and treated 14 days post implant. We think that these studies will provide data to enable rational combinations with client compounds.

Contact Covance to speak with one of our scientists to see how ID8 or one of our other syngeneic models can be used for your next immuno-oncology study.

*Note: Studies were performed in accordance with applicable animal welfare regulations in an AAALAC-accredited facility.*

Learn more about our drug development solutions at [www.covance.com/preclinical-oncology](http://www.covance.com/preclinical-oncology)

Covance is the drug, medical device and diagnostics business segment of LabCorp, a leading global life sciences company. COVANCE is a registered trademark and the marketing name for Covance Inc. and its subsidiaries around the world.

**The Americas** +1.888.COVANCE (+1.888.268.2623) +1.609.452.4440

**Europe/Africa** +00.800.2682.2682 +44.1423.500888

**Asia Pacific** +800.6568.3000 +65.6.5686588

© Copyright 2019 Covance Inc. ARTNON018-0418

**COVANCE**<sup>®</sup>  
SOLUTIONS MADE REAL<sup>®</sup>