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Society for Immunotherapy of Cancer

First in Human Study with the CD40 Agonistic Monoclonal Antibody APX005M in Subjects with Solid Tumors

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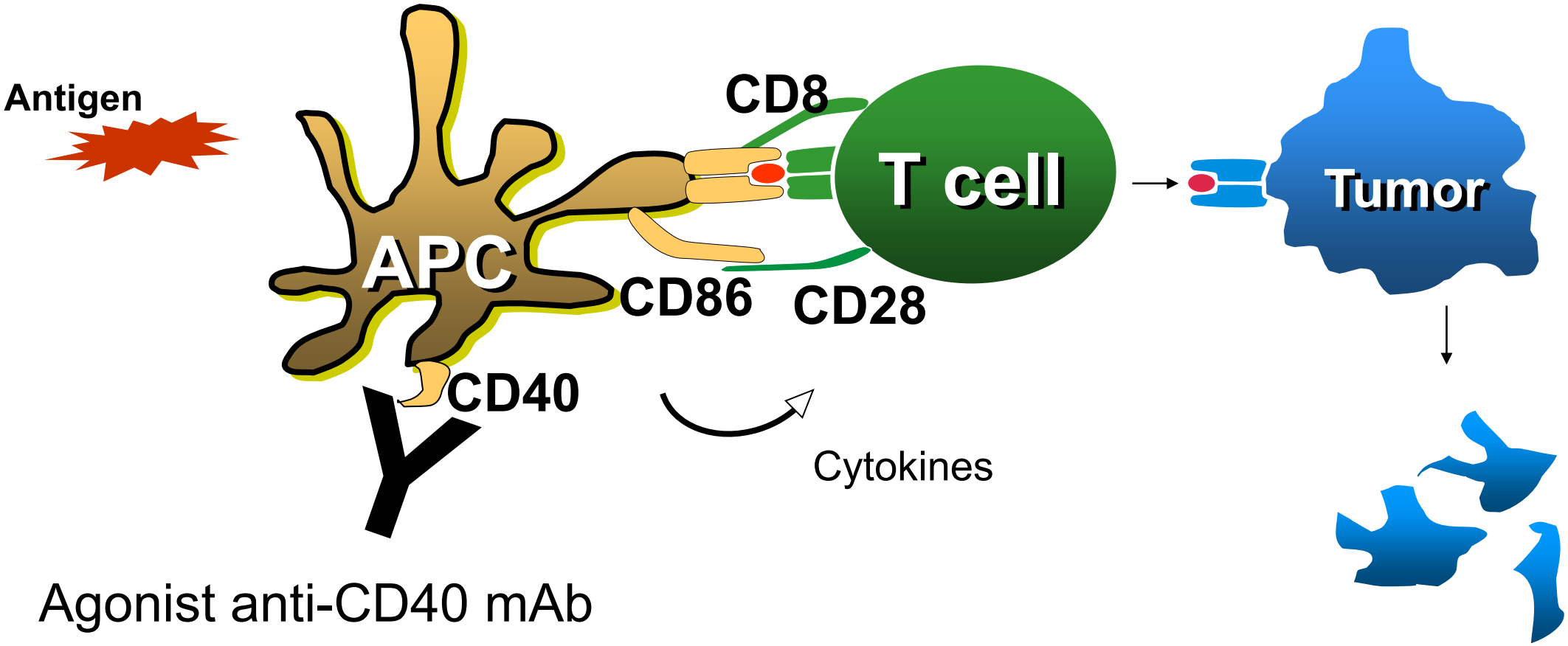
Presenter Disclosure Information

Robert H. Vonderheide

The following relationships exist related to this presentation:

-Investigator in the APX005M-001 study

CD40 as a Target for Cancer Treatment

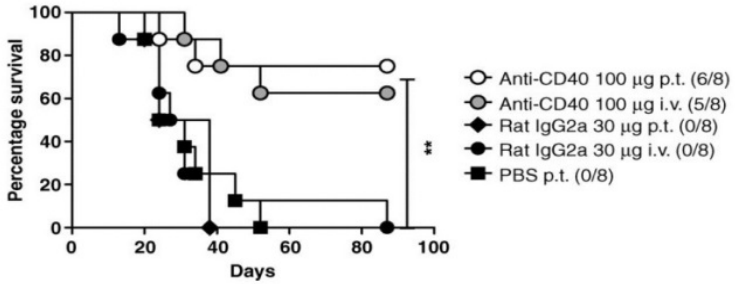


Agonist anti-CD40 mAb

Vonderheide and Glennie, Clin Can Res, 2013

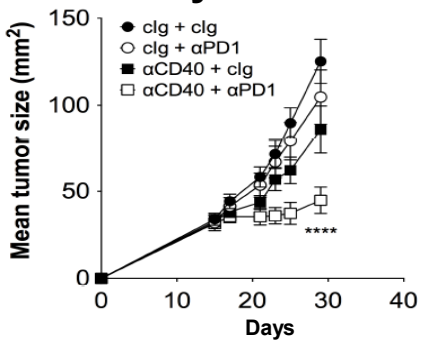
CD40 Activation Has Anti-tumor Effect in a Variety of Tumor Models

MB49 Bladder Carcinoma



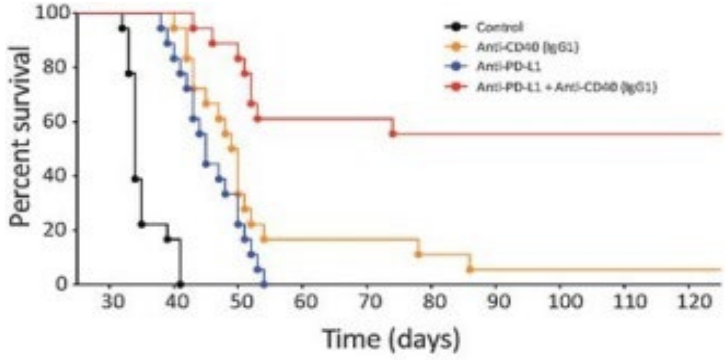
Sandin et al. Cancer Immunol Res 2014

AT3 Mammary Adenocarcinoma



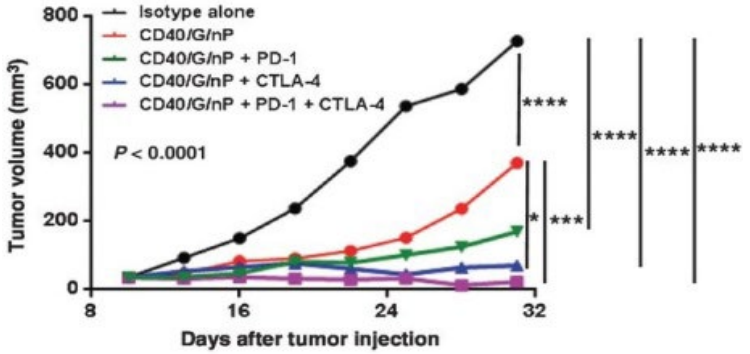
Ngiow et al. Cancer Res 2016

MC38 Colon Carcinoma



Zippelius et al. Cancer Immunol Res 2015

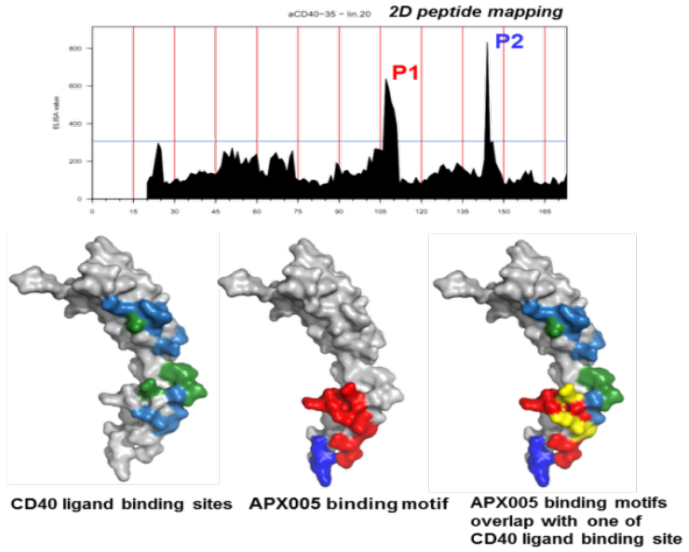
Pancreatic Ductal Adenocarcinoma

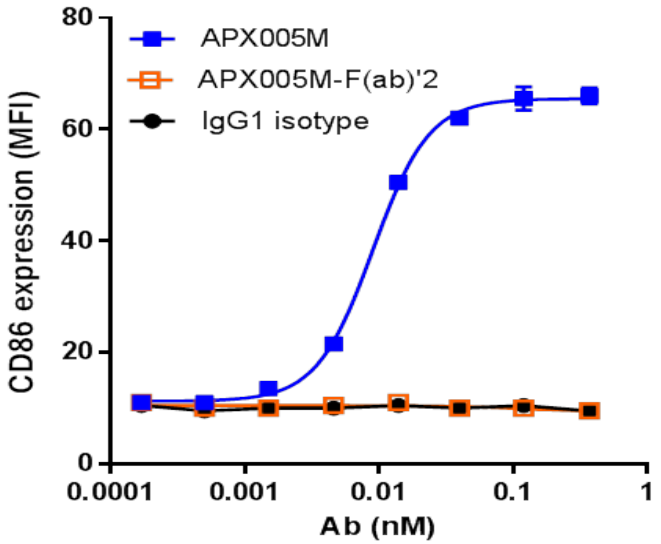


Winograd et al 2015. Cancer Immunol Res 2015

APX005M Profile

- Humanized IgG1κ mAb against human CD40
- Binds with high affinity (Kd = 1.2 x 10^{-10}M) to CD40 ligand binding domain on CD40
- Fc mutation increases binding affinity to FcγRIIb and decreases binding affinity to FcγRIIIa resulting in:
  - 20 fold increase in CD40 agonistic potency vs. non-mutated APX005
  - No effector function (ADCC, CDC)
- CD40 agonistic activity is dependent on FcγR crosslinking





APX005M-001 Phase 1 Study Design

APX005M-001

- Patients with solid tumors and no available treatment options
- (IV infusion, 60-90 minutes) 3-week treatment cycle
- 8 dose levels from 0.0001 to 1 mg/kg

Treatment until disease progression or unacceptable toxicity

Study Objectives:

- **Primary:** Establish MTD and recommended Phase 2 dose
- **Secondary:** Evaluate the PD, PK, ADA, and preliminary evidence of efficacy

APX005M-001 Study Population and Treatment

Patients

30 patients:

- Median age 65 years (range 37-79)
- 90% Caucasian
- 57% (17) female / 43% (13) male

Primary disease site/histology:

- 9 colorectal
- 8 pancreas
- 2 endometrial
- 2 salivary gland
- 1 each: adenocarcinoma of unknown origin, anus, kidney, liver adenocarcinoma, liver hepatocellular carcinoma, melanoma, penis, small intestine, parathyroid

Treatment

- 60-90 minute IV infusion
- All patients receiving APX005M at doses ≥ 0.3mg/kg were pre-medicated with oral H1 antagonist, NSAID, acetaminophen, optional H2 antagonist

Exposure

- 30 patients
  - 88 infusions
  - Median 3 (range 1-10)
- 8 dose levels
  - ranging from 0.0001 mg/kg to 1 mg/kg

Overall Safety

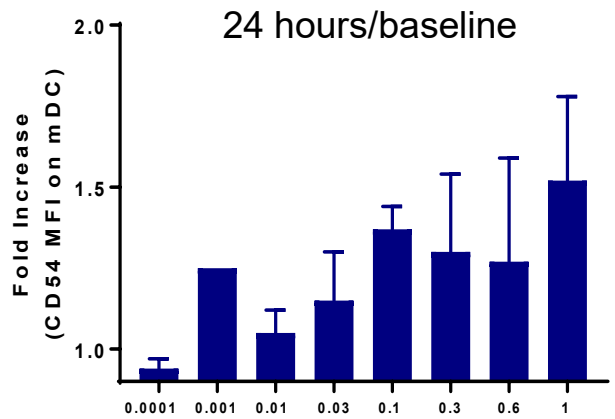
Adverse Events	%
≤ Grade 2	88% 406/462
Grade 3 or 4	12% 54/462
Considered unrelated by Investigator	48% 223/462
Serious	3.7% 17/462
Serious and considered related by Investigator	1.4% 6/462

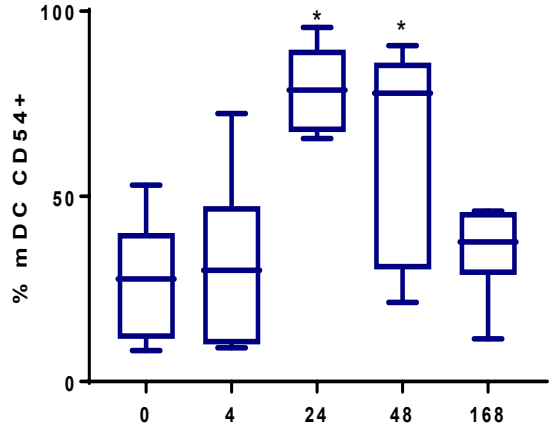
AEs of Special Interest

- On-target infusion reaction/cytokine release syndrome (CRS) Grade ≥ 2 has been observed at highest dose levels
- Transient elevation in LFTs (≤ Grade 3) observed in some patients with liver metastases
- Transient decreases in lymphocyte or platelet counts have been observed in some of the patients and are consistent with an on-target effect
- 2 DLTs
  - 1/6 patients (1 mg/kg)
    - Grade 4 CRS in Cycle 1
  - 1/6 patients (0.6 mg/kg)
    - Grade 3 CRS in Cycle 1

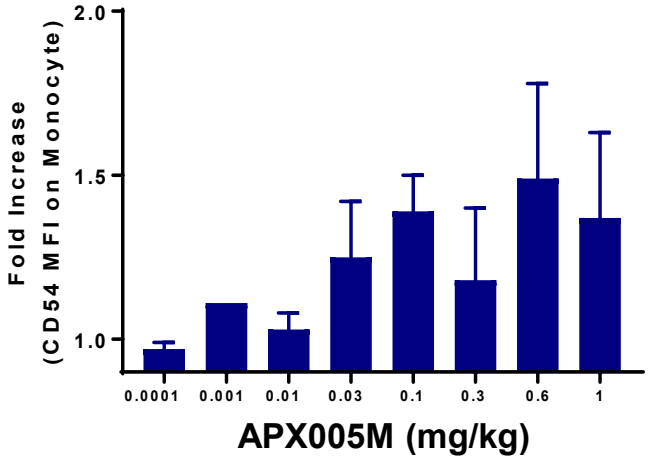
Maximum tolerated dose of APX005M is 1mg/kg body weight

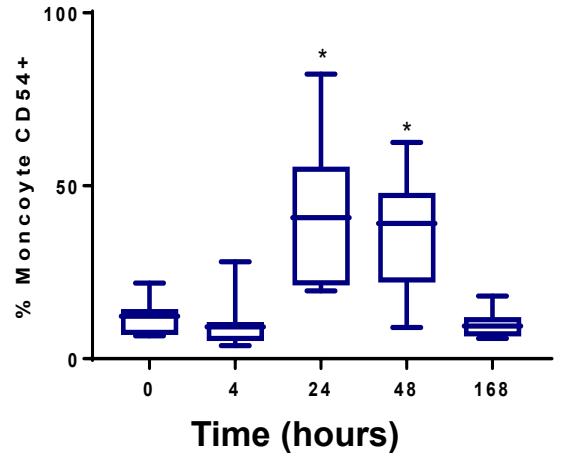
APX005M Activates Dendritic Cells and Monocytes in Cancer Patients





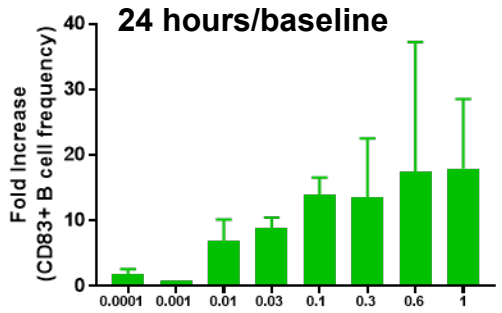
N =8
Dose range: 0.3 to 1mg/kg
* T-test vs. baseline p<0.05

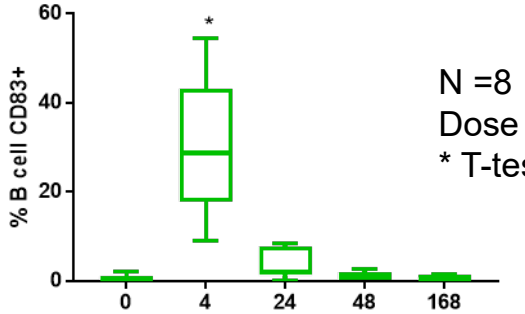




APX005M Activates B Cells in Cancer Patients

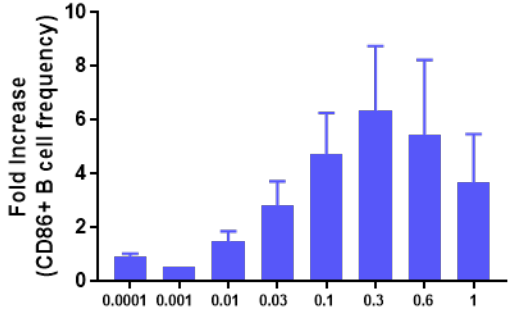
CD83

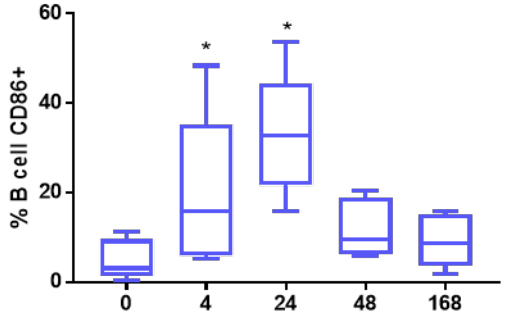




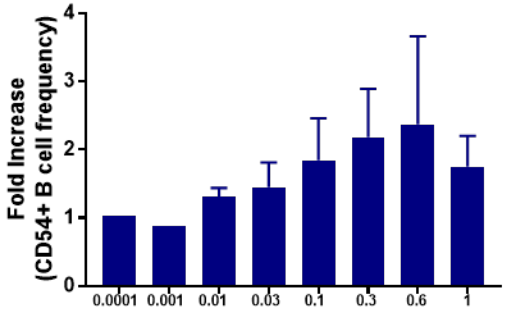
N =8
Dose range: 0.3 to 1mg/kg
* T-test vs. baseline p<0.05

CD86

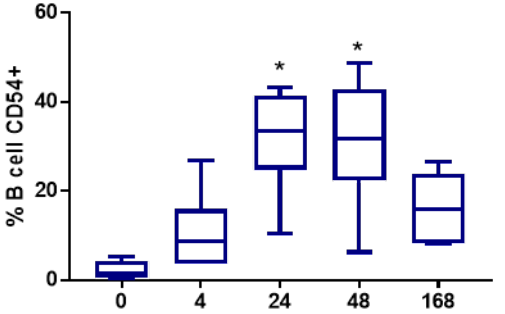




CD54



APX005M (mg/kg)

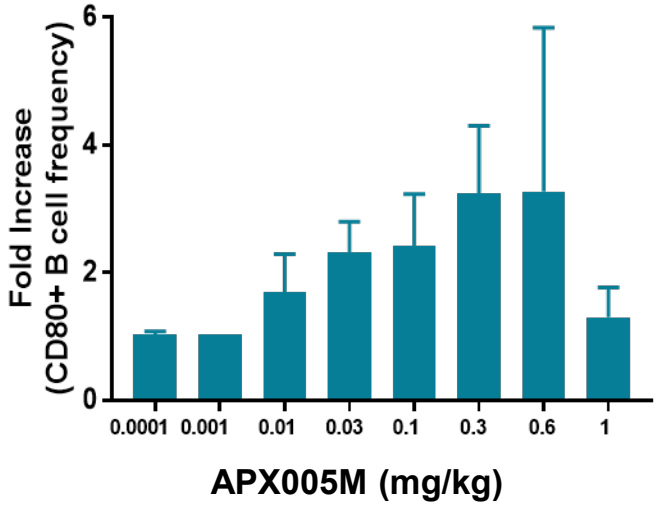


Time (hours)

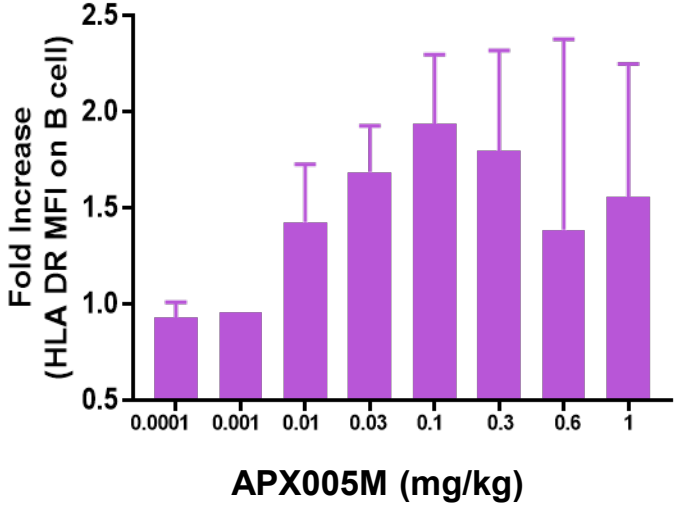
APX005M Activates B Cells in Cancer Patients

24 hours/baseline

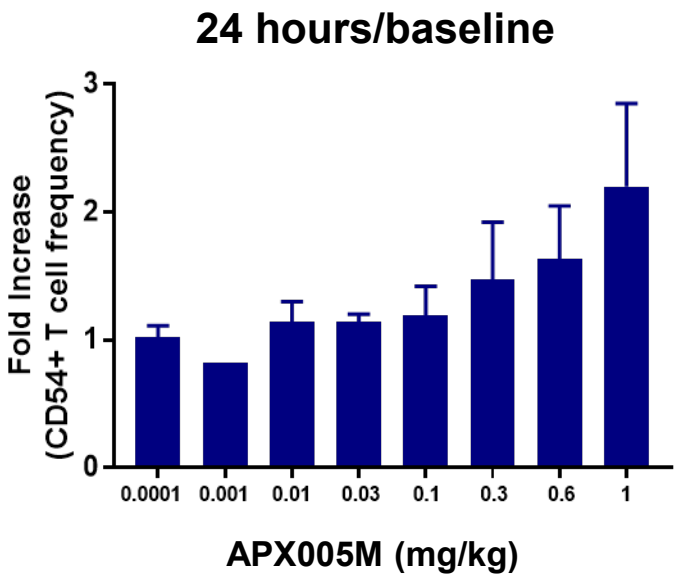
CD80

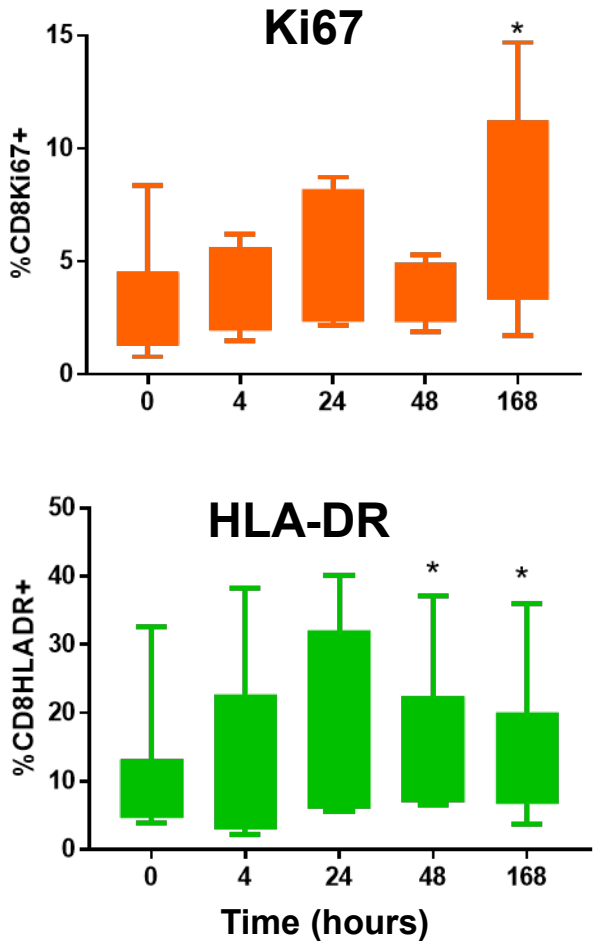


HLA-DR



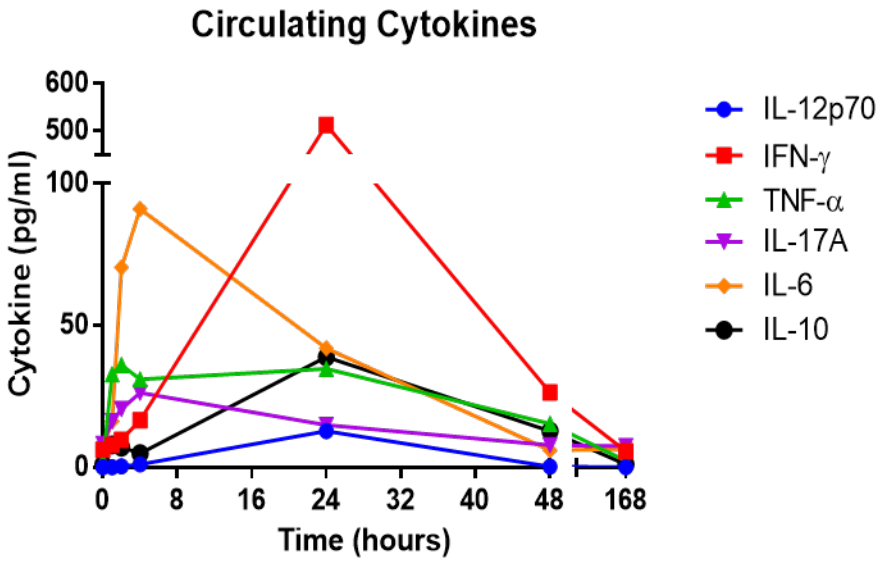
APX005M Activates T Cells in Cancer Patients



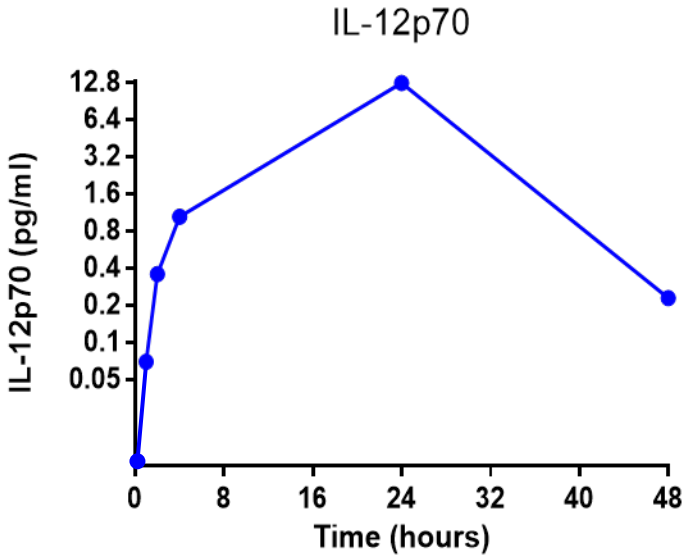


N =7
Dose range: 0.03 to 1mg/kg
* T-test vs. baseline p<0.05

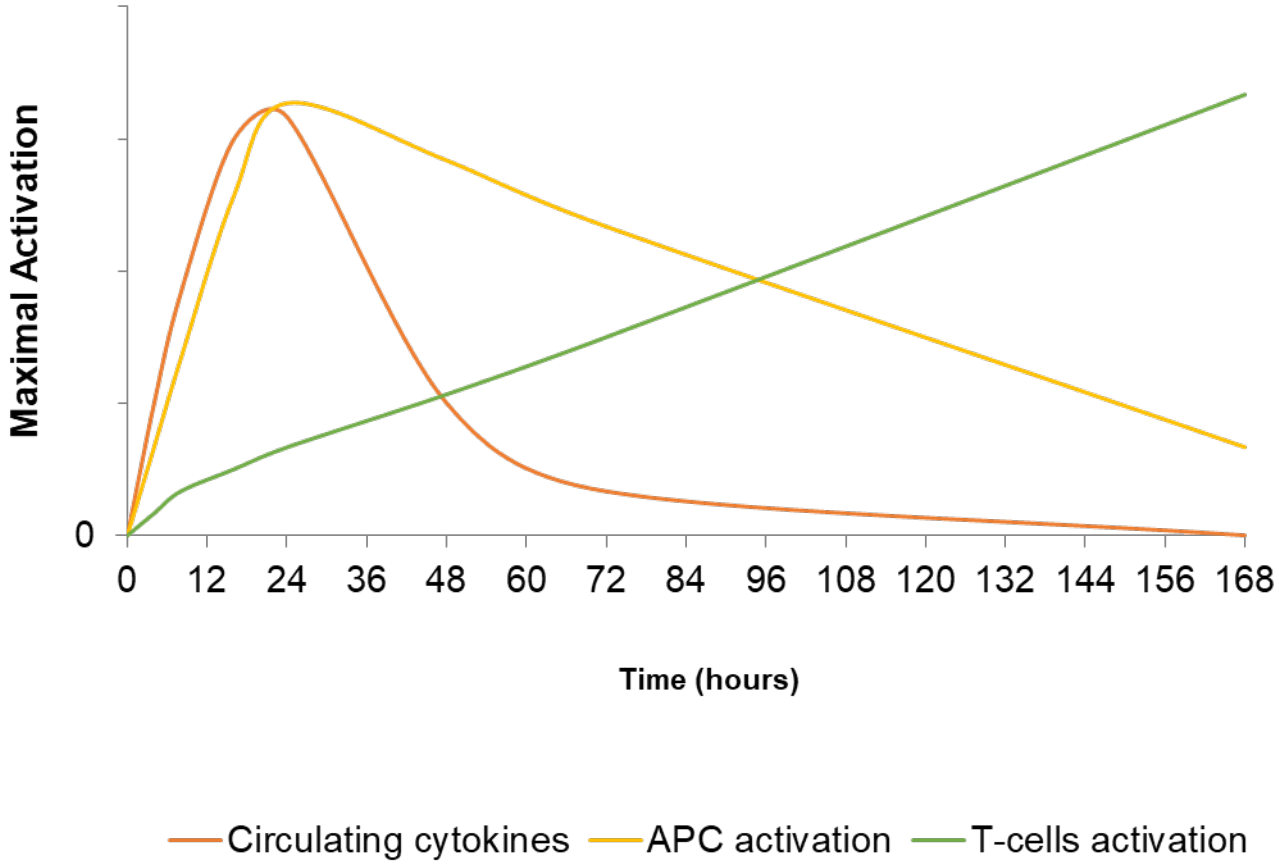
APX005M Stimulates Cytokine Production in Cancer Patients



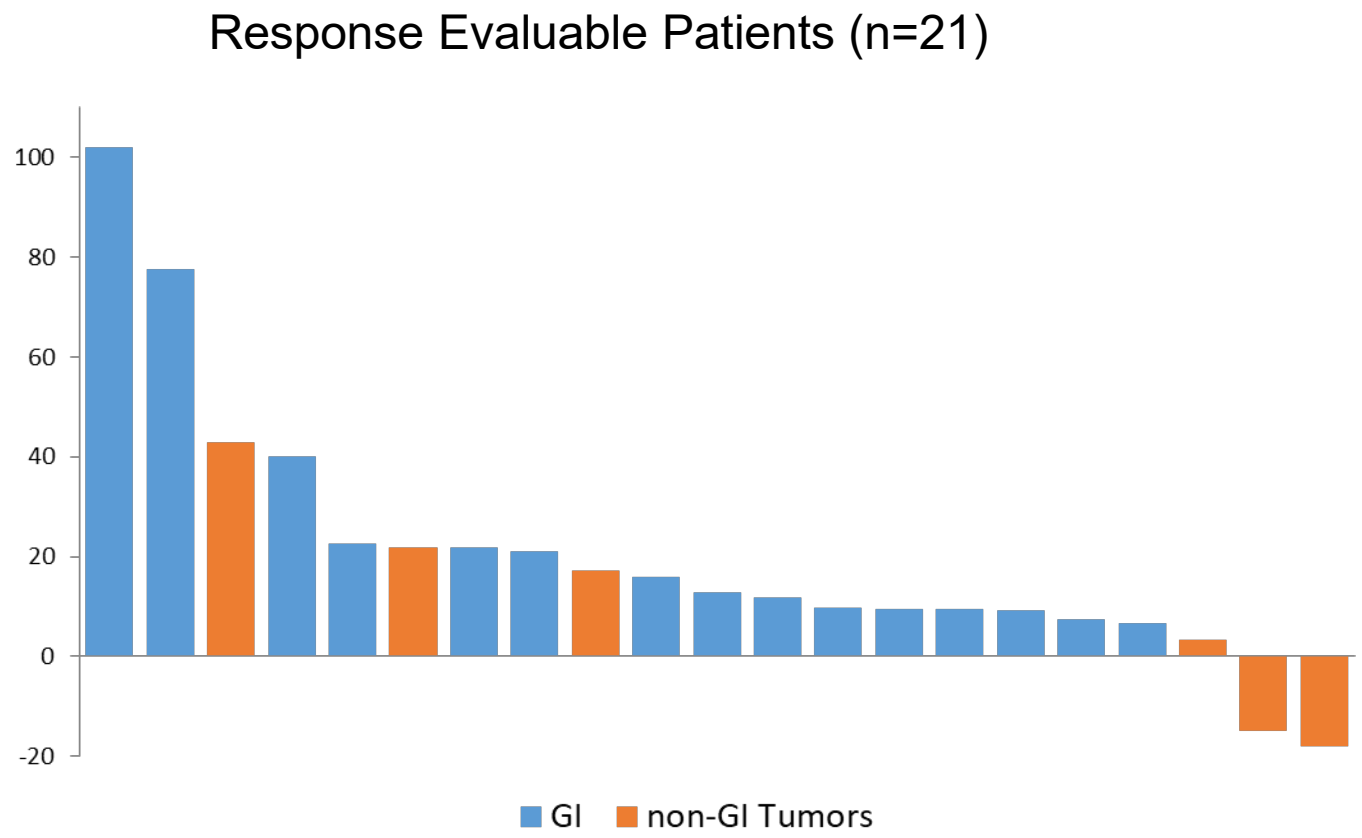
Average value for all patients treated at ≥ 0.1mg/kg (N=14)



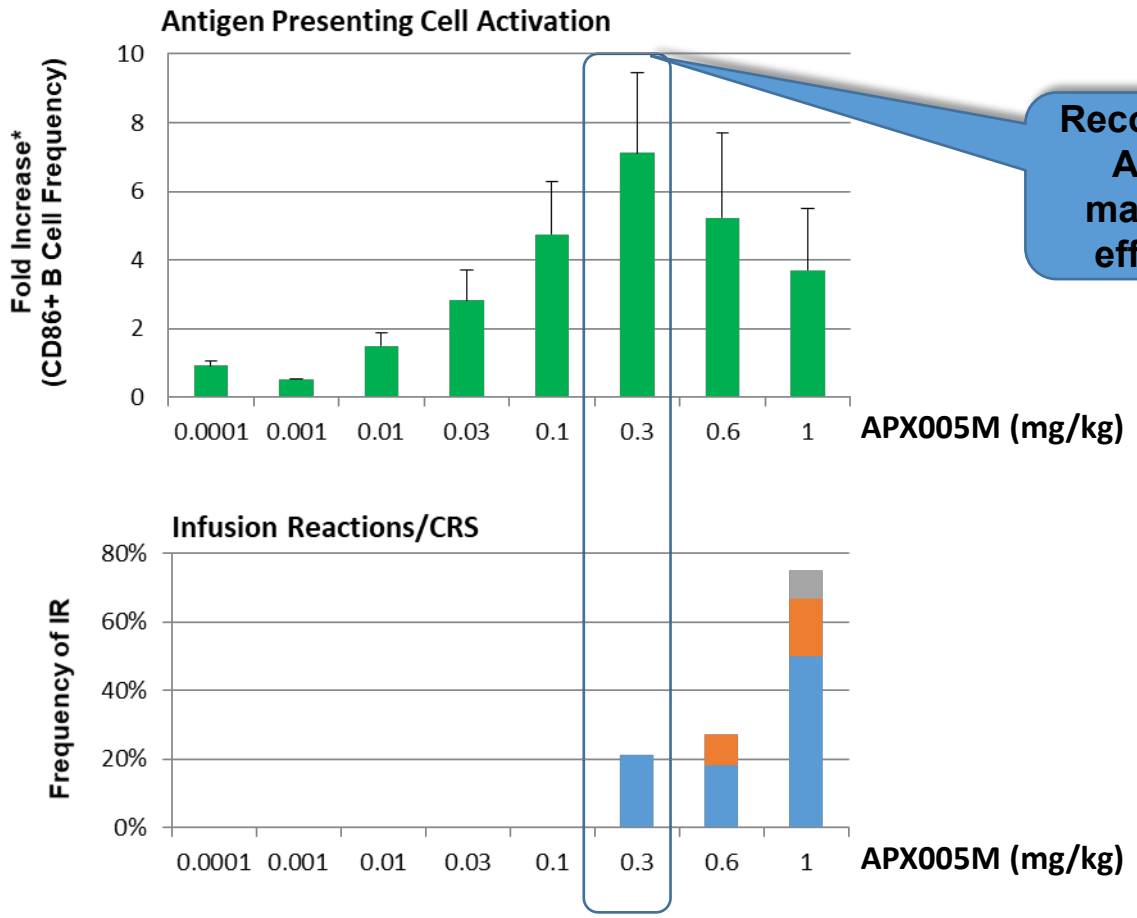
Model of Pharmacodynamic Changes Following Therapy with APX005M



Best Tumor Response



Recommended Phase 2 Dose



Recommended Phase 2 Dose of APX005M is the dose with maximum pharmacodynamic effect and toxicity ≤ Grade 2

Ongoing Clinical Trials with APX005M (N~290)

Apexigen IND

- NCT02482168: Single agent APX005M in patients with selected solid tumors (P252)

- NCT03123783: APX005M in combination with nivolumab in immunotherapy naïve NSCLC and PD-1/PD-L1 failing metastatic melanoma (P251)

Other INDs

- NCT02706353: Intratumoral AP005M in combination with systemic pembrolizumab in 1st line metastatic melanoma (P230)

- NCT03214250: APX005M in combination with gemcitabine and nab-paclitaxel with or without nivolumab in untreated metastatic pancreatic cancer (254)

- NCT03165994: APX005M in combination with chemoradiation in neoajuvant esophageal and GE junction cancers (P232)

Conclusions

- APX005M has demonstrated single agent robust immune pharmacodynamic effects in cancer patients
- APX005M exhibits a good overall safety profile with expected on-target toxicities
- APX005M is currently investigated in combination with immunotherapy and other cancer treatment modalities in a variety of solid tumors.