A PHASE 1 STUDY EVALUATING COM701 MONOTHERAPY AND IN COMBINATION WITH NIVOLUMAB IN PATIENTS WITH ADVANCED SOLID MALIGNANCIES.

Abstract TPS23

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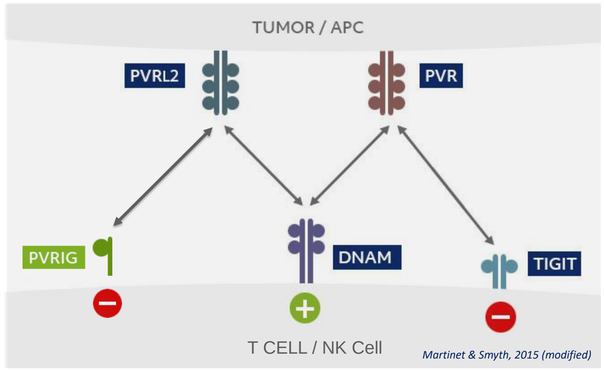
BACKGROUND

- COM701 is a novel first-in-class humanized IgG4 monoclonal antibody that binds with high affinity to poliovirus receptor related immunoglobulin domain containing (PVRIG) blocking its interaction with its ligand, PVRL2
- Inhibition of PVRIG leads to enhanced activation of T and NK cells leading to tumor growth inhibition in mouse tumor models[1]
- There is a high unmet medical need for the treatment of patients who are refractory to or relapse following treatment with checkpoint inhibitors
- We have previously reported on the preliminary antitumor activity of COM701 monotherapy[2]
- We hypothesize that COM701 monotherapy and in combination with nivolumab will be safe and tolerable and demonstrate antitumor activity in pts with R/R solid tumors

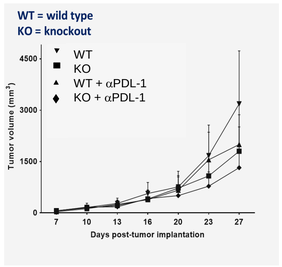
PVRIG IS A NOVEL CHECKPOINT IN THE TIGIT/DNAM-1 AXIS

Two Parallel Inhibitory Pathways



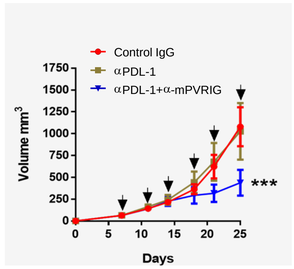
PVRIG INHIBITION REDUCES TUMOR GROWTH IN MOUSE CANCER MODELS1

PVRIG KO MICE (MC38)



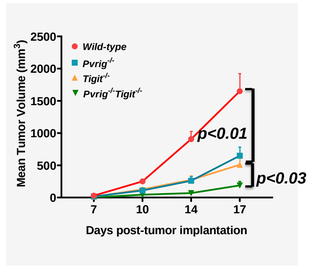
Reduced tumor growth in KO mice

anti-PVRIG + anti-PD1 (CT26)



Synergistic tumor growth inhibition with anti-PD1

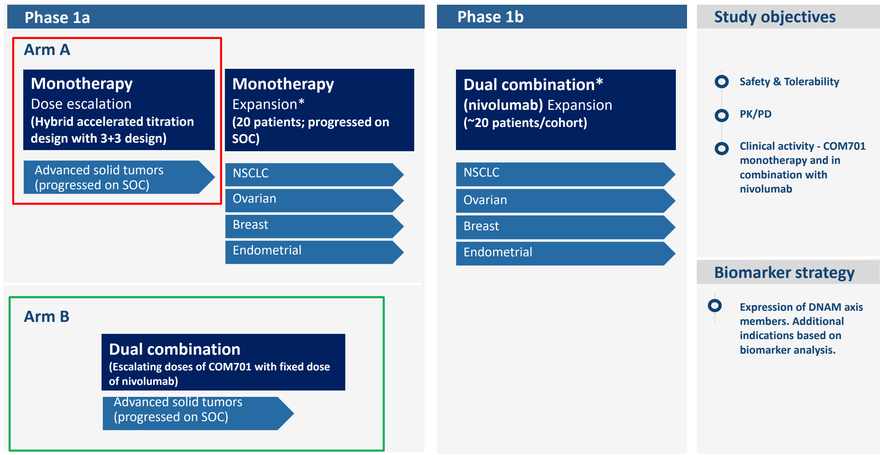
PVRIG KO+ TIGIT KO (B16)



PVRIG inhibition and TIGIT inhibition required for tumor growth inhibition

METHODS

- NCT03667716 is an ongoing open-label first-in-human phase 1 study in pts with R/R solid tumors
- Arm A (red box) evaluates escalating doses of COM701 monotherapy
- Arm B (green box) evaluates escalating doses of COM701 and a fixed dose of nivolumab
- We provide an update on the ongoing study evaluating the safety and tolerability of escalating doses of COM701 monotherapy and in combination with nivolumab



Study drugs (COM701 monotherapy or in combination with nivolumab) administered IV Q3 weeks or Q 4 weeks.
*Also includes colorectal cancer (CRC-MSS, CRC-KRAS mutation)

PRIMARY OUTCOME MEASURES

- To evaluate the safety profile of COM701 as monotherapy and in combination with nivolumab in subjects with advanced solid tumors
- The incidence of adverse events and dose-limiting toxicities (21 or 28-day DLT window) graded as per CTCAE v4.03
- To identify the maximum tolerated dose and/or the recommended dose for expansion
- To characterize the PK profile of COM701 as monotherapy and in combination with nivolumab

SECONDARY OUTCOME MEASURES

- To characterize the immunogenicity of COM701 alone and in combination with nivolumab
- To evaluate preliminary antitumor activity of COM701 in combination with nivolumab (Phase 1b only) responses as per RECIST v1.1

EXPLORATORY OUTCOME MEASURES

- To evaluate preliminary antitumor activity of COM701 as monotherapy
- To assess any association of DNAM axis members with clinical outcome
- To explore evidence of COM701-mediated PD effect in blood as monotherapy as well as in combination with nivolumab

KEY INCLUSION CRITERIA

- Age ≥18 yrs
- Histologically or cytologically confirmed, locally advanced or metastatic solid malignancy and has exhausted all the available standard therapy or is not a candidate for the available standard therapy
- ECOG performance status 0-1
- Prior anti-PD-1, anti-PD-L1, anti-CTLA-4, OX-40, CD137 permissible
- Adequate hematological, hepatic and renal function

KEY EXCLUSION CRITERIA

- Active autoimmune disease requiring systemic therapy in the last 2 years prior to the first dose of COM701
- Symptomatic interstitial lung disease or inflammatory pneumonitis
- Untreated or symptomatic central nervous system metastases
- History of immune-related events that lead to immunotherapy treatment discontinuation

ACCRUAL INFORMATION

- As of the date of this presentation enrollment is ongoing in patient dose cohort 8 20mg/kg IV Q 4 weeks (Arm A – red box)
- Enrollment into patient dose cohort 4 (Arm B – green box) has been completed with no dose-limiting toxicities reported
- No DLTs have been reported in lower patient dose cohorts

ACKNOWLEDGMENT

- We thank the patients for participating in this clinical trial and their families
- The investigators and clinical trial sites
- Study NCT03667716 is in collaboration with Bristol-Myers Squibb

REFERENCES

1. Ganguly and Pardoll, Johns Hopkins Univ. MC38 model
2. Dumbrava E, Fleming G, Hamilton E et al. Journal for ImmunoTherapy of Cancer 2019, 7(Suppl 1):P421. SITC Nov 2019.