Poster CT168

PHASE 1 STUDY OF COM701 (A NOVEL CHECKPOINT INHIBITOR OF PVRIG) IN PATIENTS WITH ADVANCED SOLID TUMORS.

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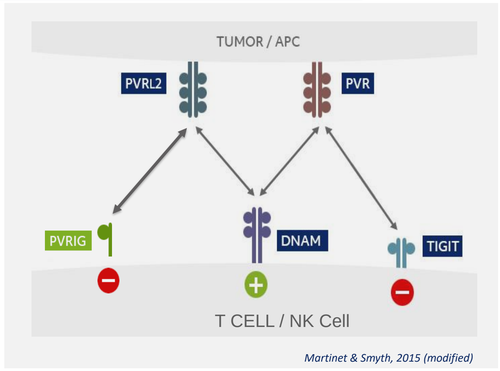
BACKGROUND

- There is a high unmet medical need for the treatment of pts with relapse/refractory disease following treatment with checkpoint inhibitors
- COM701 is a novel first-in-class checkpoint inhibitor and humanized IgG4 monoclonal antibody that binds with high affinity to poliovirus receptor related immunoglobulin domain containing (PVRIG) blocking its interaction with its ligand, PVRL2
- In non-clinical experiments we have demonstrated that inhibition of PVRIG leads to enhanced activation of T and NK cells and that knockout of PVRIG results in tumor growth inhibition in mouse tumor models
- We hypothesize that COM701 will be safe and tolerable and demonstrate antitumor activity in pts with R/R solid tumors
- We have reported on safety/tolerability in initial dose level cohorts[1]

PVRIG IS A Novel Checkpoint in the TIGIT/DNAM-1 AXIS

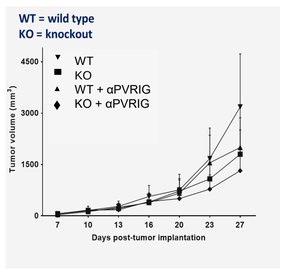
Two Parallel Inhibitory Pathways



Martinet & Smyth, 2015 (modified)

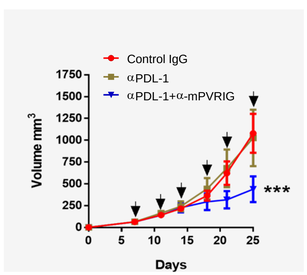
PVRIG INHIBITION REDUCES TUMOR GROWTH IN MOUSE CANCER MODELS

PVRIG KO MICE (MC38)



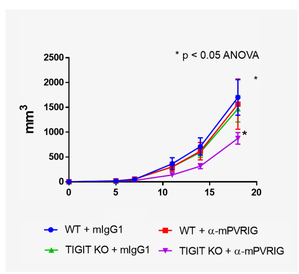
Reduced tumor growth in KO mice

anti-PVRIG + anti-PD1 (CT26)



Synergistic tumor growth inhibition with anti-PD1

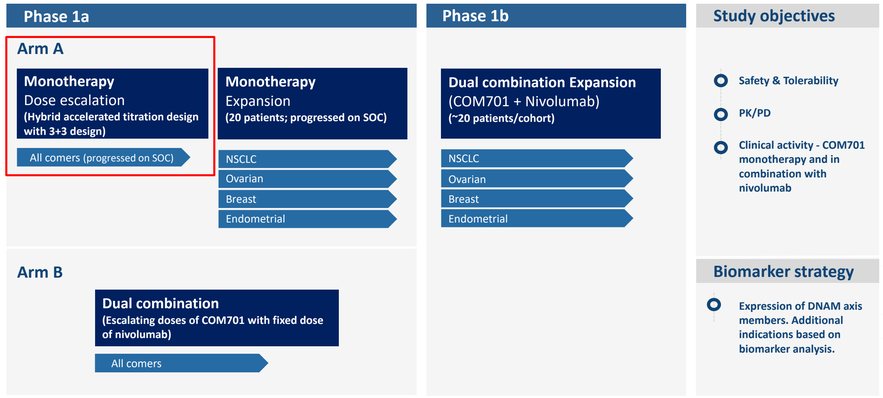
anti-PVRIG + TIGIT KO (B16)



PVRIG inhibition required for tumor growth inhibition in TIGIT KO mice

METHODS

- NCT03667716 is an ongoing open-label first-in-human phase 1 study in pts with R/R solid tumors
- We report on the initial part of this study (in red box) evaluating the safety and tolerability of escalating doses of COM701 monotherapy IV Q3 weekly



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-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 led to immunotherapy treatment discontinuation

ACCRUAL INFORMATION

- As of the date of this presentation the 5th dose level pt cohort has been filled
- No dose-limiting toxicities have been observed in the 5th dose level pt cohort and earlier dose level cohorts[1]
- Clinical and laboratory assessment for safety and tolerability is ongoing for the 5th and earlier pt dosing 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

REFERENCE

1. Drew W. Rasco, Kyriakos P. Papadopoulos, Adeboye H. Adewoye, John Hunter, Denise Ramsey, Adam ElNaggar, Amita Patnaik, Daniel A. Vaena. J Clin Oncol 37, 2019 (suppl 8; abstr TPS40). ASCO-SITC 2019.

Study sponsored by Compugen Ltd. For more information: www.cgen.com

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