Cobolimab with dostarlimab and docetaxel in patients with advanced non-small cell lung cancer (NSCLC): COSTAR Lung

Poster No. 1223

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Background

Immune checkpoint inhibitors targeting PD-(L)1 are approved in the first line setting for the treatment of lung cancer.[1] However, primary and acquired resistance to anti-PD-(L)1 therapy is common in solid tumors and novel immunotherapy combinations are needed.

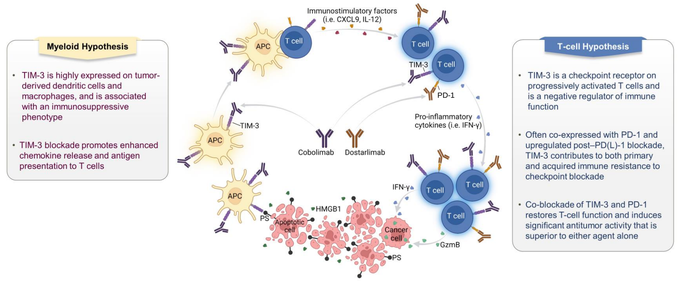
TIM-3 is an immune checkpoint receptor highly expressed on multiple immune cell types and is associated with suppressed anti-tumor responses.[2]

TIM-3 upregulation on PD-1 positive tumor infiltrating lymphocytes is associated with reduced proliferation and secretion of cytokines important for T cell-mediated anti-tumor activity.[3-5] Concurrent TIM-3 and PD-1 blockade is more effective at reducing tumor growth than blocking either pathway alone.[6]

Cobolimab (TSR-022/GSK4069889), a novel first-in-class anti-TIM-3 mAb, activates immune cell function and induces significant anti-tumor activity when combined with anti-PD-1 agents (**Figure**).

Early clinical studies show durable responses with an acceptable safety profile when cobolimab was administered in combination with an anti-PD-1 mAb, dostarlimab, in prior-treated or treatment-naïve advanced or metastatic NSCLC.[1]

Figure: Cobolimab Mechanism of Action



Objective

COSTAR Lung (NCT04655976) aims to compare the efficacy and safety of cobolimab plus dostarlimab plus standard of care chemotherapy (docetaxel; Arm A) versus dostarlimab plus docetaxel (Arm B) and docetaxel alone (Arm C) in patients with PD-1/PD-L1 relapsed/refractory NSCLC.

Methods

Study design

An **ongoing** study:

Multicenter | Global | Parallel group | Randomized | Phase II

With potential for **Phase III** expansion

Cobolimab dose of 300 mg is determined based on the Phase 1 study AMBER (GSK Study 213348; NCT02817633)[7]

Participants will be stratified according to:

- Prior lines of therapy: 1 prior line of therapy vs 2 prior lines of therapy
- PD-L1 status: tumor proportion score ≥50% vs <50%
- Histology: squamous vs non-squamous

This study will be completed in three phases: screening, treatment, and follow-up

Key inclusion/exclusion criteria:

Key inclusion criteria

- ≥18 years old
- Pathologically-proven advanced or metastatic NSCLC, and only squamous or non-squamous cell carcinoma
- Received ≤2 lines of therapy for advanced/metastatic disease
- Measurable disease per RECIST v1.1
- Documented radiographic disease progression on prior PBCT and on prior anti-PD-(L)1 therapy
- Agrees to submit an archival FFPE tumor tissue specimen that was collected on or after diagnosis
- Documented PD-L1 status
- ECOG PS of 0 or 1
- Life expectancy of at least 3 months and adequate organ function
- Participant has recovered from any prior treatment-related toxicities

Key exclusion criteria

- Previous treatment with an anti-PD(L)-1 agent that resulted in permanent discontinuation due to AE
- Previous treatment with an anti-TIM-3 or anti-CTLA-4 agent or docetaxel
- Documented sensitizing EGFR, ALK, or ROS-1 mutation
- Radiologic or clinical disease progression ≤8 weeks after initiation of prior anti-PD-1/PD-L1 antibody treatment
- Received >30 Gy RT to the lung within 6 months of first dose of study treatment
- New or progressive brain metastases and/or leptomeningeal metastases
- Active autoimmune disease or active infection
- Current interstitial lung disease, current pneumonitis, or history of pneumonitis

Figure: COSTAR Lung Study Schema

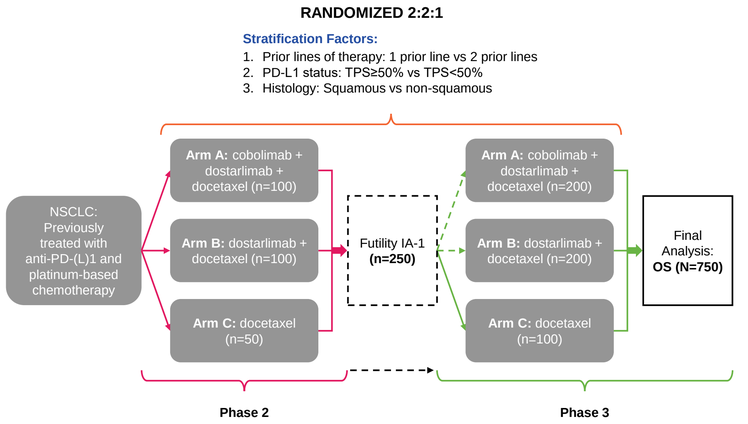
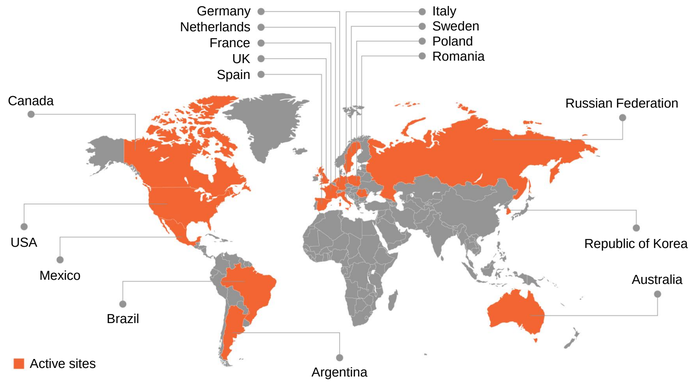


Figure: Trial Status



Study endpoints and assessments

Primary endpoints:

- OS for Arms A or B vs C
  - OS defined as survival from the date of randomization to the date of death by any cause

Secondary endpoints:

- Arms A vs B:
  - OS
- Arms A vs B, A vs C, and B vs C:
  - Confirmed ORR per investigator assessment based on RECIST v1.1
  - PFS per RECIST v1.1
  - DoR per RECIST v1.1
  - TTD: defined as time from randomization to meaningful deterioration on a composite endpoint of dyspnea, chest pain, and cough (from EORTC-QLQ-LC13 domains)
  - Change from baseline as assessed by EORTC-QLQ-C30 and EORTC-QLQ-LC13 domains
- Arms A and B vs C:
  - Safety and tolerability per incidence of TEAEs, SAEs, irAEs, TEAEs leading to death, and AEs leading to discontinuation

Exploratory endpoints:

- Confirmed ORR per investigator assessment and PFS (iRECIST)
- Pharmacokinetics
- Immunogenicity
- Biomarkers of response
- Patient-reported efficacy and tolerability
- Healthcare resource utilization

Statistical analyses

Futility analysis to assess ORR across the 3 arms in the Phase 2 portion.

Conducted after 250 participants are enrolled in total (Arm A and B: 100 each, Arm C: 50), and have been followed-up for a minimum period, have withdrawn from the study, or died.

An additional 500 patients may be included in the Phase 3 portion and final analysis will be conducted on OS primary endpoint.

Abbreviations

AE, adverse event; ALK, anaplastic lymphoma kinase; APC, antigen-presenting cell; CTLA-4, cytotoxic T-lymphocyte-associated protein 4; CXCL9, C-X-C Motif Chemokine Ligand 9;DoR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status;EGFR, epidermal growth factor receptor; EORTC-QLQ-C30, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire 30-Item Core Module; EORTC-QLQ-LC13, EORTC-QLQ 13-Item Lung Cancer Module; FFPE, formalin-fixed paraffin embedded; Gy, gray;GzmB, Granzyme B; HMGB1, high mobility group Box 1; IA, interim analysis; IFN, interferon;IL, interleukin; irAE, immune-related AE; iRECIST v1.1, immune-related RECIST version 1.1;mAb, monoclonal antibody; NSCLC, non-small cell lung cancer; ORR, objective response rate;OS, overall survival; PBCT, platinum-based chemotherapy; PD-1, programmed cell death protein-1;PD-L1, programmed cell death-ligand 1; PFS, progression-free survival; RECIST v1.1, ResponseEvaluation Criteria in Solid Tumors version 1.1; ROS-1, ROS proto-oncogene 1; RT, radiotherapy;SAE, serious adverse event; TEAE, treatment-emergent AE; TIM-3, T-cell immunoglobulin and mucin-domain containing-3; TPS, tumor proportion score; TTD, time to treatment discontinuation.

Disclosures

HRK is a consultant and on advisory board for Merck, Bristol Myers Squibb (BMS), Ono, Takeda and AstraZeneca, receives payment or honoraria for speaker's bureau from Merck, BMS, Ono, Takeda and AstraZeneca, **CG** served at a speaker's bureau and advisory board and received honoraria from AstraZeneca, BMS, Merck Sharp & Dohme, and Roche. **DK** declares no conflicts interest. **AT** declares no conflicts of interest. **EF** declares advisory board participation for AbbVie,. Amgen, AstraZeneca, Bayer, Beigene, Blue Print Medicines, Boehringer Ingelheim, BMS, Lilly, GlaxoSmithKline (GSK), Janssen, Medical Trends, Merck KGaA, Merck Sharp & Dohme, Novartis, Peptomyc, Pfizer, Puma Biotechnology, Regeneron, Roche, Sanofi Genzyme, Syneos Health, Takeda, and Grifols; speaker bureau participation for AstraZeneca, Boehringer Ingelheim, BMS, Lilly, Merck Sharp & Dohme, Novartis, Peervoice, Pfizer, prIME Oncology, Roche, Takeda, Touchmedical, and CME Outfitters; research funding from Fundación Merck Salud and a grant for oncology innovation; and is an independent member of the Board at Grifols. **VV** has received fees for consulting or serving on advisory boards for BMS, Merck, GSK, Foundation Medicine, AstraZeneca, EMD Serono, Novartis, and Novocure. **YJK** declares no conflicts of interest. **TOG** declares no conflicts of interest. **PGL** discloses a financial relationship with Roche, MSD, BMS, Boehringer Ingelheim, Pfizer, AbbVie, Guardant Health, Novartis, Lilly, AstraZeneca, Janssen, Systimc, Blueprint Medicines, Takeda, Gilead, and Rova. **RC** discloses a financial activity with AstraZeneca, BMS, Roche, Boehringer Ingelheim, Takeda, and Pfizer. **KP** reports grants from AbbVie, Novartis, Pfizer, AstraZeneca, Roche, Nektar, BioGene, MSD, H3B, Prestige Biopharma, Janssen and GSK; **RA, BDP, TB, DL, JC** and **AW** are employees of GSK with stock/other ownership interests. **WL** is an employee of GSK with stock/other ownership interests in GSK and Takeda. **AD** is an employee of GSK with stock/other ownership interests in GSK and BMS. **SN** reports personal payment or honoraria for lectures, presentations, speaker's bureaus, manuscript writing, or educational events from AbbVie, AstraZeneca, BeiGene, Boehringer Ingelheim, BMS, Eli Lilly, Pfizer, PharmaMar, Roche, and Takeda; and personal fees for participation on a data safety monitoring board or advisory board from AstraZeneca, Bayer, Daiichi Sankyo, Eli Lilly, Pfizer, Roche, Sanofi, and Takeda.

Acknowledgments

This study (GSK 213410) was funded by GSK. Editorial support provided by Nathan Ley and Ailthne Atkinson of Fishawack Indicia Ltd., UK, part of Fishawack Health, and funded by GSK.

References

1. Moreno V, Roda D, Pikiel J *et al.* Safety and efficacy of dostarlimab in patients with recurrent/advanced non-small cell lung cancer: Results from cohort E of the phase I GARNET trial. *Clin Lung Cancer* 2022; DOI: 10.1016/j.cllc.2022.05.013.
2. de Mingo Pulido Á, Gardner A, Hiebler S *et al.* TIM-3 regulates CD103+ dendritic cell function and response to chemotherapy in breast cancer. *Cancer Cell* 2018; **33**: 60-74. e6.
3. Dardalhon V, Anderson AC, Karman J *et al.* Tim-3/galectin-9 pathway: regulation of Th1 immunity through promotion of CD11b+Ly-6G+ myeloid cells. *J Immunol* 2010; **185**. 1383-92.
4. Ngiow SF, von Scheidt B, Akiba H *et al.* Anti-TIM3 antibody promotes T cell IFN-γ-mediated antitumor immunity and suppresses established tumors. *Cancer Res* 2011; **71**. 3540-51.
5. Sakuishi K, Apetoh L, Sullivan JM *et al.* Targeting Tim-3 and PD-1 pathways to reverse T cell exhaustion and restore anti-tumor immunity. *J Exp Med* 2010; **207**. 2187-94.
6. Falchook GS, Ribas A, Davar D *et al.* Phase 1 trial of TIM-3 inhibitor cobolimab monotherapy and in combination with PD-1 inhibitors nivolumab or dostarlimab (AMBER). *J Clin Oncol* 2022; **40**(16_suppl): abstract 2504.
7. Ribas A, Eroglu Z, Perez JMMT *et al.* AMBER parts 1c and 1e: A phase 1 study of cobolimab plus dostarlimab in patients (pts) with advanced/metastatic melanoma. *J Clin Oncol* 2022; **40**(16_suppl): abstract 9513.

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Presented at IASLC-WCLC, Vienna, Austria, August 6–9, 2022