Novel regimens versus standard-of-care in NSCLC: a phase II, randomized, open-label, platform trial using a master protocol

Introduction

Unmet need

Although the role of immunotherapy in NSCLC is well documented, a large unmet need following first-line PD-1/PD-L1 immunotherapy exists due to inherent or emerging resistance.

Study rationale

- Treatment regimens combining agents that target different processes within the cancer ecosystem have the potential to enhance responses in individual or refractory NSCLC patients.
- Advanced NSCLC is a potential candidate for combination therapy in NSCLC based on preclinical studies suggesting that ICOS may promote antitumor immune responses and longer survival.
- In murine tumor models (CT26 and EMT6), combination of an anti-ICOS agonist antibody that is designed to enhance ADCC with anti-PD-1/PD-L1 and platinum–based combination chemotherapies demonstrates improved efficacy relative to monotherapeutic approaches.

This trial (NCT03739710) is a

Randomized Phase II Open-label Platform trial

Sub-study 1 is ongoing and will evaluate

with Current SoC

No treatment crossover permitted

Study initiated in January 2019; 3, IP) alone or in combination with Kaplan–Meier plots illustrating the survival of CT26-bearing mice treated with either anti-ICOS (7E.17G9-mIgG1, Q4D x 100 µg anti-ICOS with anti-PD-1) or anti-ICOS & an IgG4 ICOS agonist (GSK3359609) + SoC, n=70. Participants in sub-study 1 will be randomized in a 1:2 ratio; randomization ratios for subsequent sub-studies will vary and are defined by the study protocol.

Additional sub-studies to be added based on emerging non-clinical and clinical data (see future protocol amendment).

This trial (NCT03739710) is a phase II, randomized, open-label, platform trial using a master protocol.

- Will consist of several sub-studies, with each sub-study comparing anti-ICOS (7E.17G9-mIgG1, Q4D x 100 µg anti-ICOS with anti-PD-1) or anti-ICOS & an IgG4 ICOS agonist (GSK3359609) + SoC, n=70.
- Participants in sub-study 1 will be randomized in a 1:2 ratio; randomization ratios for subsequent sub-studies will vary and are defined by the study protocol.

Key inclusion criteria

- ≥ 18 years with NSCLC and measurable disease
- Discontinued disease progression during or after a maximum of 2 lines of systemic treatment (for health/economic evaluation). Stage IIIB/IV or unresectable metastatic disease
- 2 lines of platinum-containing chemotherapy regimens
- RMD candidates must have had disease progression on at least 2 lines of treatment or are refractory to initial treatment

Key exclusion criteria

- Prior treatment with docetaxel or ICOS agonists
- 2 prior lines of therapy for NSCLC, including RMD–selected participants
- Known GFR<30/30 renal failure indications
- Symptomatic CNS metastases

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Sample size is not fixed in the SoC arm; however, there will be

105 patients in sub-study 1 (35 SoC, 70 experimental arm)

with a maximum of 70 patients in additional experimental arms — this will provide at least 81% power with a type I error of 0.025% for each pairwise comparison.

Advanced NSCLC

Progressed on prior anti-PD-1/PD-L1. 1: Platinum–based chemotherapies

- Stratiﬁed by histology (squamous vs. non-squamous)
- and line of PD-1/PD-L1 therapy (1st vs 2nd)

Randomization

- Sub-study 1: 1:1:1
- Randomization will be done at regular intervals
done at regular intervals

Follow-up:

- every 12 weeks by phone until death or patient withdraweled from further contact.

ClinicalTrials.gov Number: NCT03739710
EudraCT Number: 2018-001316-29

Acknowledgments