The combination of immune checkpoint blockers with the anti-ICOS KY1044 antibody results in a strong anti-tumour response

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Introduction

ICOS is an inducible T-cell costimulator that is structurally and functionally related to CD28/CTLA-4.

ICOS regulates both pro- and anti-inflammatory cytokine production by effector and regulatory T cells (TEff and TReg, as well as follicular helper T cells and dendritic cells) and is required for the maintenance of Treg homeostasis. It is involved in the interaction between T- and B-cells (class switching), and in antibody responses to T-cell dependent antigens.

By immunizing Kynmice™ in which endogenous ICOS gene has been knocked out [5], we have identified a novel, fully human antibody called KY1044 which cross-reacts with mouse ICOS facilitating in vivo studies in immune proficient mice.

KY1044 is a fully human anti-ICOS subclass G1 kappa monoclonal antibody that selectively binds to ICOS.

The preferential high expression of ICOS on intratumoural TReg makes this protein a strong candidate for a depleting antibody strategy.

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Increased efficacy at an intermediate dose

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ICOS/FOXP3 in cancer

Decreased efficacy of KY1044 in combination with anti-PD-L1

Conclusions

KY1044, a novel fully human anti-ICOS antibody has a dual mechanism of action. KY1044 has the ability of killing ICOS™ cells via ADCC. KY1044 also acts as an agonist antibody on ICOS® effector cells in vivo (IFNγ release).

As shown in different models, KY1044 strongly inhibits tumour growth as monotherapy & in combination with checkpoint inhibitors such as anti-PDL1. KY1044 increases intratumoral TReg depletion improves the T/Eff ratio and also induces the up-regulation of inflammatory cytokines in vivo.

Intratumoral TReg expression high levels of ICOS on their surface. ICOS/Foxp3 expression varies in human tumour types, showing high expression in head and neck cancers, and low expression in glioblastoma/glioma. ICOS is highly expressed in the TME and especially on Treg (e.g. Head and Neck Cancer)

In summary, our data demonstrates that targeting ICOS with KY1044 is a valid approach for manipulating the immune system and for inducing a strong anti-tumour response. The data presented here also warrant the assessment of KY1044 in cancer patients in a clinical trial.

References