KY1044, a novel anti-ICOS antibody, elicits long term in vivo anti-tumour efficacy as monotherapy and in combination with immune checkpoint inhibitors

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

ICOS regulates both pro- and anti-inflammatory cytokine production by effector T-cells (T_Eff) and regulatory T-cells (TRegs), as well as T-cell proliferation and survival.

ICOS is involved in the interaction between T- and B-cells (lg class switching), and in antibody responses to T-cell dependent antigens.

ICOS expression levels vary in different immune cell subtypes (Fig. 1), being higher on immunosuppressive TRegs (CD4+/FOXP3+) than on CD8+ T-effector cells (CD8+ T_Eff), and higher in the tumour microenvironment (TME) than in the periphery (e.g., spleen).

High levels of intratumoral ICOS’ TRegs have been associated with poor survival in several cancer types such as head and neck, ovarian, hepatocellular carcinoma and gastric cancer [1-4].

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

**KY1044**

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

KY1044 is an anti-ICOS subclass G1 kappa monoclonal antibody that selectively binds to ICOS with an affinity of less than 2nM (as determined at neutral and acidic pH as in TME).

KY1044 binds human, cynomolgus monkey, rat and mouse ICOS with similar affinity.

KY1044 has a dual mechanism of action:

1. Preferential depletion of intratumoral ICOS+ TRegs resulting in an increase in T_Eff : TRegs ratio in the TME
2. Stimulation of ICOS+ T_Eff cells

**References**