**Abstracts**

**1341 CD27 AN EMERGING IMMUNO-ONCOLOGY TARGET AT THE CROSSROADS OF INNATE AND ADAPTIVE ANTITUMOR IMMUNE RESPONSES**

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**Background** CD27 is a member of the TNF-Receptor superfamily expressed on CD4+ and CD8+ T cells, on NK and NKT cells and on B cells. It promotes T cell co-activation, proliferation, clonal expansion and differentiation into antigen specific cytotoxic and memory T cells after stimulation with its ligand CD70. Its stimulatory signal is mediated via the NFkB pathway, but also via the phosphatidylinositol 3 kinase and the protein kinase B. Moreover, CD27 signaling influences the innate immune response via a direct activation of NK cells and a subsequent secretion of interferon-gamma (IFN-γ). CD27 plays a central role in immunological responses and by promoting T cell and NK cell activation it contributes to antitumor immunity. Previous studies have demonstrated tumor growth inhibition with anti-CD27 agonistic monoclonal antibodies in different mice models for solid and hematological tumors. This mechanism of action can be partly explained by the recruitment of IFN-γ producing CD8+ T cells within the tumor. CD27 is a promising target for antitumor therapy.

**Methods** Kineta has generated a library of 147 fully human anti-CD27 monoclonal antibodies after immunization of Trianni mice.

**Results** From this library, a lead candidate with strong agonistic proprieties has been selected. This anti-CD27 antibody originates from a unique clade after alignment of the variable heavy chains. Kineta’s lead candidate demonstrates selectivity and cross-reactivity with Non-Human Primate (NHP)-CD27 but not with the mouse-CD27. It also induces strong NFkB signaling in a Jurkat T cell-reporter, either soluble or cross-linked. It also induces T cell proliferation and secretion of pro-inflammatory cytokines in vitro. This T cell activation occurs only in the presence of a TCR engagement preventing future risks of spontaneous activation of naïve T cells in vivo. Our lead antibody also induces direct activation of NK cells demonstrated by the expression of CD69 on their surface. We have evaluated the antitumor properties of our lead antibody as a single agent in vivo in human CD27 Knock-In (KI) mice. Our anti-CD27 candidate induces a significant anti-tumor activity in the EG7 thymoma model. We have also demonstrated the anti-tumor efficacy of this lead candidate in Raji cells implanted in Scid mice. Preliminary experiments performed in human CD27 KI mice have demonstrated a long half-life of our antibody at different concentrations.

**Conclusions** Epitope characterization, NHP pharmacokinetic analysis and additional in vivo studies of our lead anti-CD27 antibody in different tumor models use as a single agent and in combination with different check-point inhibitors are ongoing.