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5660 / 21 - Characterisation of novel CD73 antibodies as a therapeutic method of adenosine regulation

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Presenter/Authors

Grainne Gernon, *Suzanne Grooby*, *Louise Tonkin*, *Anja-Christina Bitterwolf*, *Lorna Stewart*, *Marcel Deken*, *Pritom Shah*, *Katherine Ewings*, *Zoe Johnson*.

Cancer Research UK, United Kingdom, iOnctura SA, Switzerland

Disclosures

G. Gernon: None. **S. Grooby:** None. **L. Tonkin:** None. **A. Bitterwolf:** ; iOnctura SA. **L. Stewart:** None. **M. Deken:** ; iOnctura SA. **P. Shah:** None. **K. Ewings:** None. **Z. Johnson:** ; iOnctura SA.

Abstract

CD73 is a membrane-bound nucleotidase receptor which is frequently overexpressed in the tumour microenvironment and can be found on both tumour and immune cell types. Its function is to catalyse the conversion of adenosine monophosphate (AMP) to adenosine and phosphate and it has been proposed as a therapeutic target in cancer due to adenosines role in tumour immune suppression.

Using multiple approaches, a series of novel CD73 antibodies have been characterised for their therapeutic potential and benchmarked against agents currently undergoing clinical evaluation Inhibition of CD73 activity was evaluated using an Amplex Red-based coupled adenosine assay against both human and mouse CD73, and kinetics of antibody binding were determined using BioLayer Interferometry. Cellular assays were then utilised to further evaluate the antibodies *in vitro*. The ability of the CD73 antibodies to internalise was evaluated using two different methods, a Fab-ZAP killing assay and the IncuCyte™ FabFluor internalisation assay. The antibodies have also undergone functional studies, investigating the ability of the CD73 antibodies to disrupt the production of adenosine in tumour cells. We demonstrate that the novel CD73 antibodies inhibit CD73 function by two different mechanisms; direct inhibition of enzyme activity and modulation of cell surface expression, both of a which have therapeutic potential to disrupt CD73-mediated adenosine production and therefore reduce antitumor immune responses. Ongoing studies are investigating the *in vitro* and *in vivo* efficacy of the clone selected for further development as a monotherapy and in combination with a novel small molecule inhibitor in murine models of cancer.