

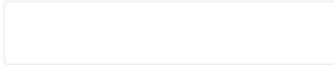


Session PO.ET06.06 - PI3K/AKT/mTOR Inhibitors

## 666 / 13 - A novel, highly selective PI3K $\delta$ inhibitor for the treatment of solid malignancies that express high levels of target protein as assessed by immunohistochemistry

📅 June 22, 2020, 9:00 AM - 6:00 PM

📍 Virtual Meeting II: E-Posters



### Presenter/Authors

Amy R. MacQueen, Giuditta Viticchie, Karolina Niewola, Francesca Finotello, Ian Powley, Pritom Shah, Lars Van der Veen, Michael Lahn, Zoe Johnson. Cancer Research UK, United Kingdom, Leicester Cancer Research Centre, United Kingdom, iOnctura SA, Switzerland, Medical University of Innsbruck, Austria

### Disclosures

**A.R. MacQueen:** None. **G. Viticchie:** None. **K. Niewola:** ; iOnctura SA. **F. Finotello:** None. **I. Powley:** None. **P. Shah:** None. **L. van der Veen:** ; iOnctura SA. **M. Lahn:** ; iOnctura SA. **Z. Johnson:** ; iOnctura SA.

### Abstract

The inhibition of PI3K $\delta$  preferentially targets regulatory T cells and myeloid derived suppressor cells, breaking tumour-induced immune tolerance and restoring anti-tumour immunity. Bioinformatics and protein expression studies have shown that PIK3CD/PI3K $\delta$  is also highly expressed in certain solid malignancies. IOA-244 is a novel, highly selective PI3K $\delta$  inhibitor, with the unique property of being ATP non-competitive. In addition to the effects of PI3K $\delta$  inhibition on the balance of CD8<sup>+</sup> T cells and T regulatory cells in the tumour microenvironment, we have recently demonstrated that IOA-244 effectively controls the growth of tumour cells with high levels of PI3K $\delta$  *in vivo* in T-cell deficient hosts.

Analysis of TCGA datasets shows that certain solid tumours express high levels of PIK3CD transcript, comparable to that of diffuse large B cell lymphoma. Of these indications, cutaneous and uveal melanoma are amongst the highest expressers. To support the clinical development of IOA-244, we demonstrate that patient-derived melanoma cells with a high expression of PIK3CD are susceptible to treatment with IOA-244 in a mouse patient-derived xenograft model. Furthermore, *in vitro* explant studies using clinical biopsy material demonstrates that PI3K $\delta$  expression can be detected in tumour tissue and that IOA-244 has an anti-proliferative function when added to these samples. Based on these and other supporting data, IOA-244 has received clinical trial approval in Europe and phase I clinical testing is underway in solid tumours with an anticipated high Treg:CD8 ratio and/or high protein expression of PI3K $\delta$ .