**INTRODUCTION**

The pharmacokinetic (PK) profile is a determining factor in both the safety and efficacy of a drug or therapeutic regimen. PK profiles can vary significantly between patients and between humans and pre-clinical animal species.

Mouse xenograft models are ubiquitous in oncology research, widely utilized to study single agents, combinations and scheduling. Differences in PK between mouse and human are one factor limiting the translational relevance of xenograft studies. Additionally, studies to assess combinations and/or scheduling quickly require large numbers of animals owing to the many possible permutations.

Here we describe a device capable of recapitulating PK-like profiles in vitro, and explore the effects of PK on the treatment of non-small-cell lung carcinoma by erlotinib alone and in combination with pemetrexed.

**AIM**

Utilise a microfluidic addition and removal platform to i) recapitulate PK profiles in vitro; ii) model combinations of erlotinib and pemetrexed

**MATERIALS & METHODS**

The microfluidic addition and removal device, termed the MicroFormulator, was developed by Prof J. Wikswo and colleagues at VIBRNE, Vanderbilt University (USA). Prior to dosing of cells the device was assembled in a microbiological safety cabinet and the fluids sterilised with 70% ethanol and flushed with PBS.

Non-small-cell lung cancer lines (NSCLC) H322, H1299, A549, Calu-6 were obtained from Public Health England and cultured in 24-well plates in RPMI supplemented with 10% FCS. Cell viability was assessed using CellTiterBlue (Promega, U.K.). Microscope images were acquired using an Leica DM IL LED inverted microscope.

**RESULTS**

**IN VITRO PK MODELLING**

Utilising the device, drug inputs are added to well plates and the cell culture growth assessed. Dosing schedules can be varied to reflect therapeutic use.

**CONCLUSIONS**

The microfluidic device is able to aspirate and then add defined volumes of one or more fluids to individual wells of a multi-well plate. This enables the recollection, using sequential steps, of PK like profiles in vitro. As a consequence the culture medium within each well is replaced, every few hours, this reduces cell growth, in a cell line dependent manner.

Wells are individually addressable, allowing multiple different compounds, PK profiles, combinations or dosing schedules to be assessed on a single plate. Differences to PK profiles and other compounds, can be observed and determined using PK profiles. Further experiments in vitro will be necessary to determine whether these are recapitulated in vivo.

**ACKNOWLEDGEMENTS AND DISCLOSURES**

The authors would like to acknowledge the support of CN Bio Innovations, John Wikswo, Ron Reiserer, David Schaffer, Clayton Britt, and Greg Gerken at VIIBRE, and Prof. John Wikswo (Vanderbilt, U.S.A) for his support. CN Bio Innovations licenses from Vanderbilt University intellectual property related to the MicroFormulator.