Table: 1879P

Drugs	H-1703	Calu-1 IC50 (nM)	SK-Mes-1
PF-05212384 (PI3K/mTOR inhibitor)	18	26	335
AZD-2014 (Dual mTORC1/C2 inhibitor)	145	217	215
Everolimus (mTORC1 inhibitor)	Unable determine IC50	Unable determine IC50	Unable determine IC50
MK-2206 (pan-Akt inhibitor)	Unable determine IC50	Unable determine IC50	Unable determine IC50

Conclusions: Overall, the results of our study suggest the potential implication of PI3K/mTOR-Rictor pathway in SQLC oncogenesis, thus rendering it a promising target for a targeted approach. Among the mTOR components, RICTOR CNG seems to predict a higher sensitivity to PI3K/mTOR inhibition and might represent a potential biomarker to be explored as a stratification tool in clinical trials. Confirmatory RICTOR silencing experiments are currently ongoing.

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1879P Potential role of RICTOR copy number gain (CNG) as a key biomarker of mTOR activity: A comprehensive preclinical analysis in squamous cell lung cancer (SQLC) models

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Background: We previously performed a multi-step genomic study in almost 100 resected SQLC patients dichotomized according to the prognosis. Among the pathways with a biological impact on SQLC oncogenesis, PI3K/mTOR-Rictor emerged as a crucial axis [Pilotto WCLC 2016]. In order to explore the potentiality of mTOR inhibition, we present a set of in vitro experiments in RICTOR-aberrant SQLC preclinical models.

Methods: Next-generation sequencing (NGS), fluorescence in situ hybridization (FISH) and Western Blot were performed in 3 SQLC cell lines (H-1703, SK-Mes-1, Calu-1) for detecting CNG/protein profile of the PI3K/mTOR-Rictor components. The activity of PI3K/mTOR pathway targeted inhibitors in the SQLC cell lines was examined in short- (72 hours) and long-term (1 week) cell viability assays.

Results: NGS analysis revealed a different amount of RICTOR CNG among SQLC cell lines. FISH confirmed that H-1703 harbors the highest number of RICTOR copies (6) followed by SK-Mes-1 (4) and Calu-1 (3.5), suggesting polysomy of the short arm of chromosome 5 as the main mechanism of RICTOR gain. Although Rictor protein levels were similar among the cell lines, p-mTOR S2448 (active form of mTOR complexes) was higher in H-1703 than SK-Mes-1 and Calu-1. PI3K/mTOR inhibition proved more effective in H-1703, with lower IC50 values in short term treatment (Table). Similar findings were confirmed in long-term assays.