CDK4/6 INHIBITION WITH LEROCICLIB (G1T38) DELAYS ACQUIRED RESISTANCE TO TARGETED THERAPIES IN PRECLINICAL MODELS OF NON-SMALL CELL LUNG CANCER

ABSTRACT #4415

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OBJECTIVES

• Assess the ability of lerociclib to enhance and tumor efficacy of TKIs in preclinical models of NSCLC harboring various oncogenic alterations
• Determine whether lerociclib delays or acquires resistance to TKIs in NSCLC models with various oncogenic alterations
• Identify the nature of resistance mechanisms that can be addressed with lerociclib + TKI combination treatment

RESULTS

• Lerociclib significantly delays acquired resistance to new-generation targeted therapies in NSCLC cell lines, resulting in 100% complete responses and 0% tumor cures in the corresponding osimertinib monotherapy group.
• Seven days of combination treatment with lerociclib + osimertinib resulted in 100% complete responses and 0% tumor cures in the corresponding osimertinib monotherapy group.
• Lerociclib delays acquired resistance to targeted therapies in NSCLC cell lines harboring a variety of oncogenic alterations, including EGFR, ALK, and RET.

SUMMARY

• EGFR-mutant NSCLC harbors a variety of oncogenic alterations, including EGFR, ALK, and RET.
• Seven days of combination treatment with lerociclib + osimertinib resulted in 100% complete responses and 100% tumor cures after 17 days in preclinical NSCLC models.
• Combination treatment with lerociclib + osimertinib effectively delay resistance to targeted therapies in NSCLC cell lines.

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REFERENCES