Overview

The tyrosine kinase receptor AXL is overexpressed in a variety of cancer, stromal, and select immune cells in tumors, and has been implicated in resistance to chemotherapy, targeted therapies, and immunotherapies. AXL has recently been described as a highly potent and selective small molecule AXL inhibitor1. This poster describes the preclinical evaluation of AB801 in vitro & in vivo models.

AXL Signaling Supports Therapeutic Resistance in Tumors

AXL expression correlates with proliferation, migration/invasion, and epithelial-mesenchymal transition (EMT) in cancer cells. Overexpression results in drug resistance and amplified immune responses.1,2

Activation of AXL can occur in a ligand-dependent manner via its ligand, growth arrest specific protein 6 (Gas6) and AXL can also signal independently of Gas6, via homodimerization or heterodimerization with other receptor tyrosine kinases, leading to activation.

AXL phosphorylation facilitates signaling cascades that promote cancer cell proliferation, survival, migration, EMT, and an immunosuppressive microenvironment.

High AXL Expression Is Associated With Resistance to TKI Therapies

AB801 In Combination With Osimertinib Causes Significant Tumor Regression in PC9 EGFR™/NSCLC Xenografts

AB801 In Combination With Sunitinib Significantly Reduces Tumor Growth in 786-O CRC Xenografts

AB801 Treatment Sensitizes Cancer Cells to Chemotherapy & Immunotherapy

Summary

Resistance to TKI therapies is associated with high AXL expression in vitro and in patients. AB801 inhibits both Gas6-dependent and independent AXL phosphorylation in a concentration-dependent manner. In vivo, AB801 in combination with TKI therapies significantly reduces tumor volume, cell mitosis, and increases necrosis.

AB801 was well-tolerated as a single agent & in combination with TKI therapies in vivo.

AB801 in combination with docetaxel upregulates proteins and genes that will increase responses to chemotherapy and immunotherapy.

References

1. Mee D. et al. EORTC-NCI-AACR 2020 Ref 230

We Are Hiring!

Susan L. Paprocka, Subhasree Sridhar, Armon Goshayeshi, Eugene Park, Suan Lu, Ruben Flores, Lauren Rocha, Dillon Miles, Manjunath Lamani, Sean Cho, Ning Wang, Yang Guan, Saranya Chandrasekar, Ritu Kushwaha, Salena Jaffe, Angelo Kaplan, Enzo Stagnaro, Lisa Seitz, Janine Köhle, Estera Fernández-Sala

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AB801 is a Potent and Selective AXL Inhibitor That Demonstrates Significant Anti-Tumor Activity In Combination With Standard of Care Therapeutics

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2022 EORTC-NCI-AACR Drug Resistance & Modifiers
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Board Number P808

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