BTK Inhibitors Resistant REC1 Lymphoma Cell Lines and Animal Models

2024.09

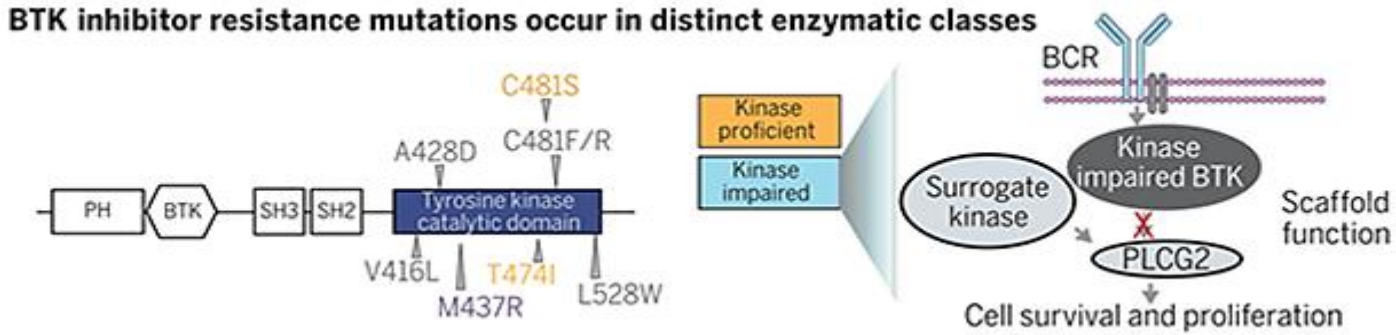
OncoWuXi Newsletter

Introduction

BTK and drug resistance

Bruton's tyrosine kinase (BTK) is a central mediator of B cell activation, proliferation, and signaling downstream of the B cell receptor (BCR), making it a key target for B cell neoplasms.

Despite excellent clinical outcomes for patients treated with covalent BTK inhibitors (BTKi), acquired resistance to covalent BTK inhibitors are a limitation of their clinical use. Acquired mutations at the C481 residue of BTK confer resistance to all covalent BTK inhibitors. BTK L528W is associated with reduced BTK enzymatic activity.



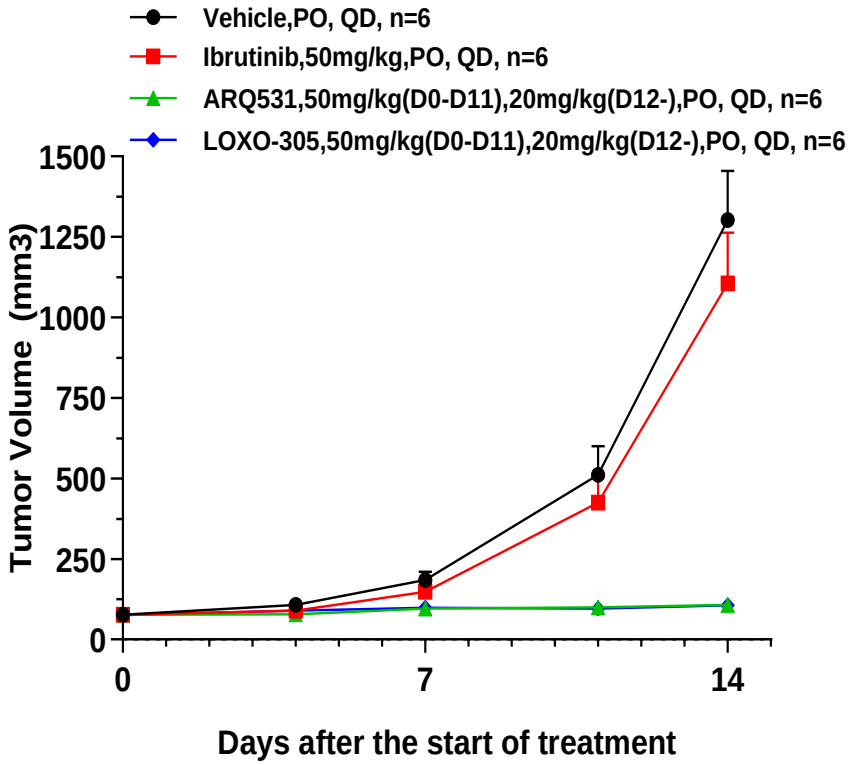
Science. 2024 Feb 2;383(6682):eadi5798.

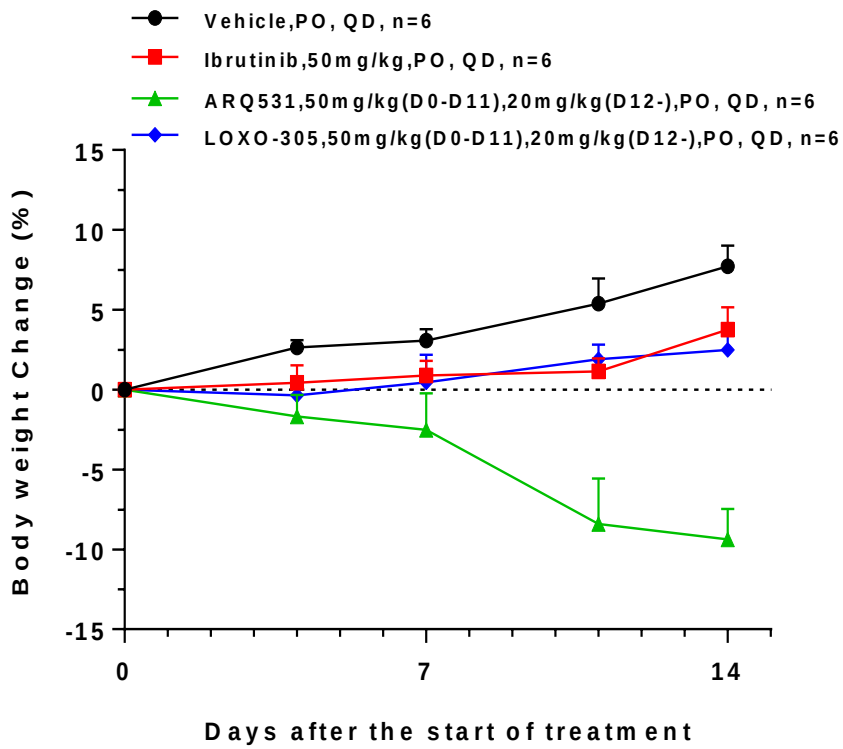
To empower the discovery of new therapies targeting BTK and overcoming drug resistance, WuXi Biology has established **REC1 lymphoma cell lines carrying BTK C481S or L528W mutation**. Both cell lines have been well-validated *in vitro* and *in vivo*.

Model ID
REC1 BTK C481S
REC1 BTK L528W

Anti-tumor efficacy of BTKi in the REC1 BTK C481S model

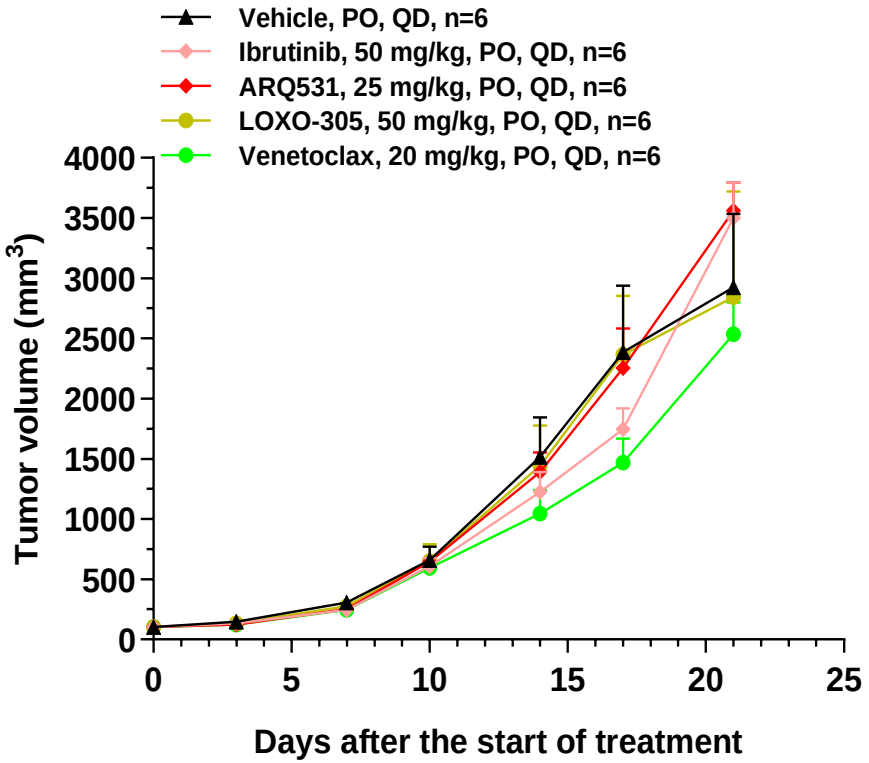
Model ID	Drugs tested	Dosage	TGI (%)
REC1 BTK C481S	Ibrutinib	50 mg/kg, PO,QD*2W	16.05
	ARQ531	50 mg/kg, (D0-D11), 20mg/kg, (D12-), PO*QD	97.51
	LOXO-305	50 mg/kg, (D0-D11), 20mg/kg, (D12-), PO*QD	97.48

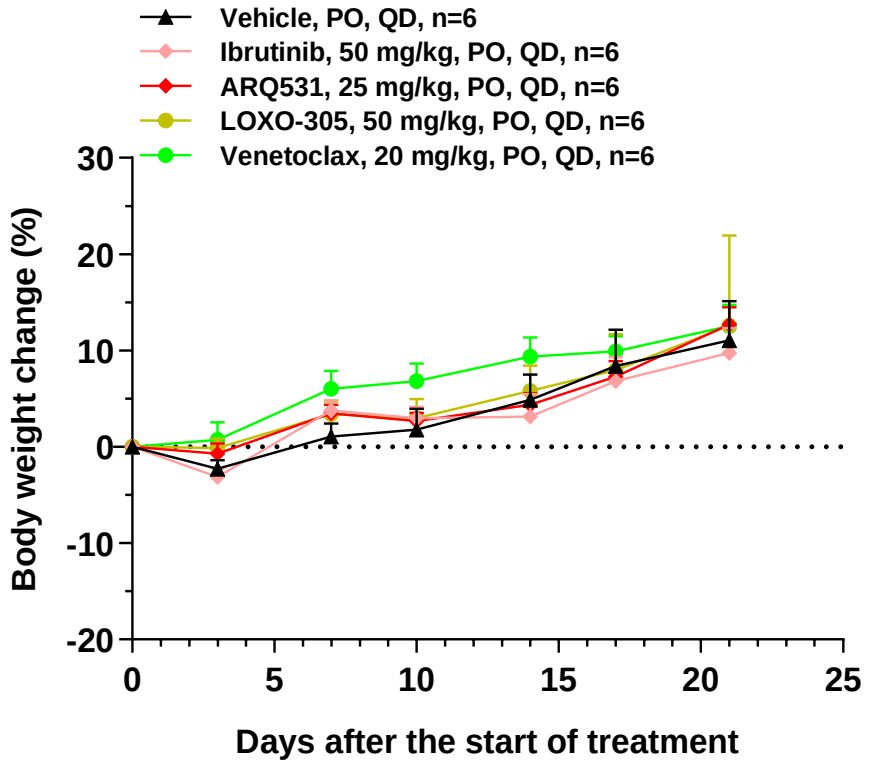




Anti-tumor efficacy of BTKi in the REC1 BTK L528W model

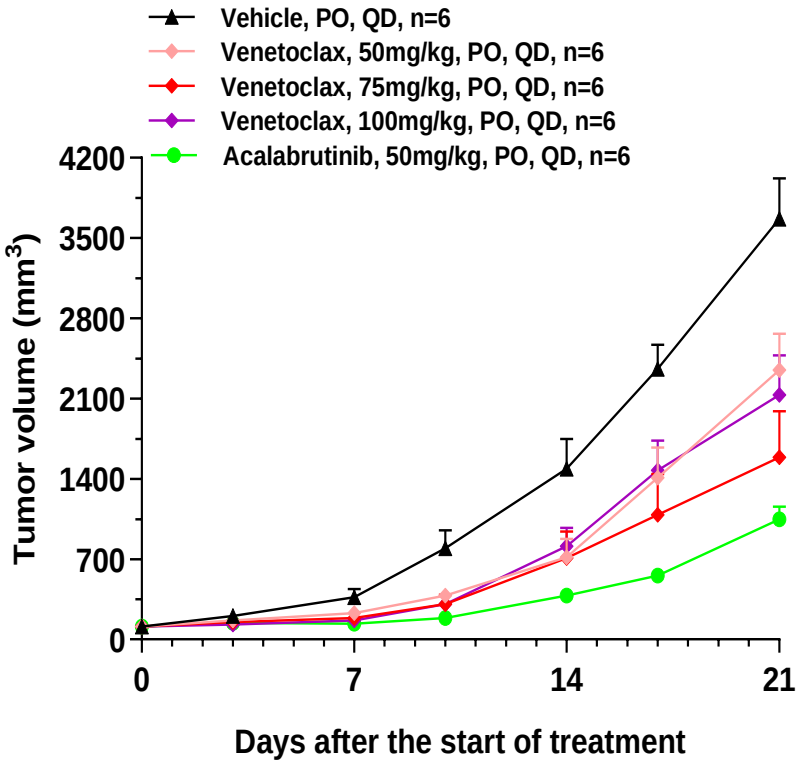
Model ID	Drugs tested	Dosage	TGI (%)
REC1 BTK L528W	Ibrutinib	50 mg/kg, PO, QD*3W	28.13
	ARQ531	25mg/kg, PO, QD*3W	5.89
	LOXO-305	50 mg/kg, PO, QD*3W	0.95
	Venetoclax	20mg/kg, PO, QD*3W	40.29

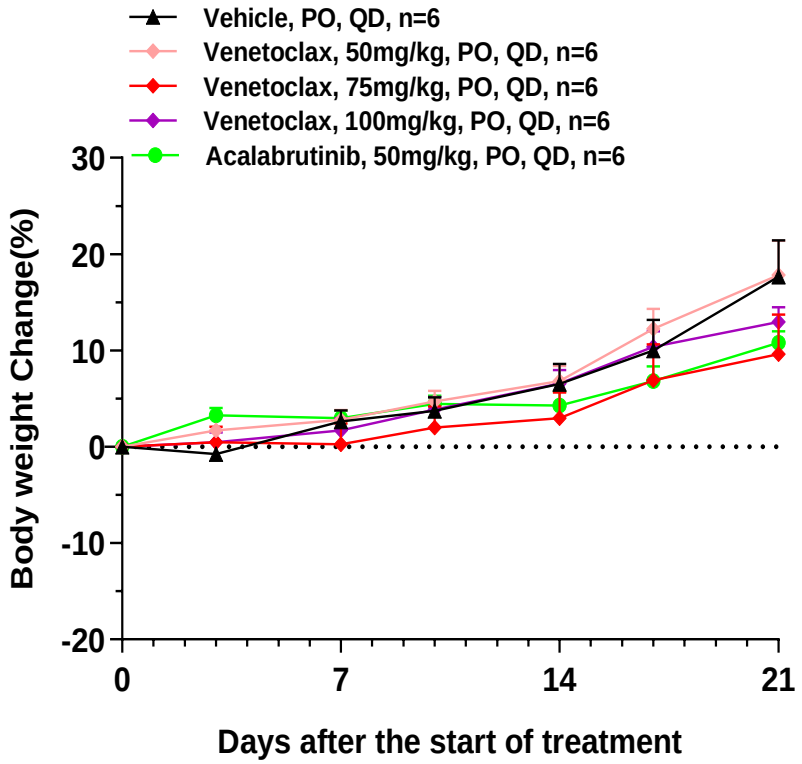




Anti-tumor efficacy of BTKi in the REC1 BTK L528W model

Model ID	Drugs tested	Dosage	TGI (%)
REC1 BTK L528W	Venetoclax	50 mg/kg, PO, QD*3W	37.12
	Venetoclax	75 mg/kg, PO, QD*3W	58.48
	Venetoclax	100 mg/kg, PO, QD*3W	43.24
	Acalabrutinib	50 mg/kg, PO, QD*3W	73.65





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