

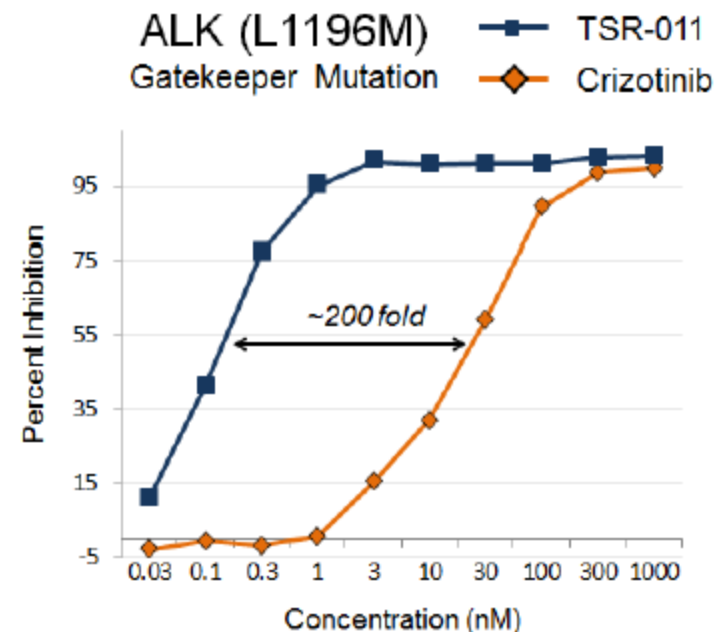
Is there a hope for TSR-011?



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- Pros – promising preclinical data
 - Higher potency vs. crizotinib – lower IC50
 - Differentiated activation against clinically resistant gatekeeper mutation
- Cons – complexity of the underlying mechanism for drug resistance
 - Difficult to identify suitable targets - complexity of the secondary ALK mutations
 - May have to be in a combination therapy in order to see clinical benefit

ALK Type	Cell Type	Assay	TSR-011 IC50 (nM)	Crizotinib IC50 (nM)
NPM-ALK	Karpas299 (ALCL)	pY-ALK	2	69
		Proliferation	1	16
EML4-ALK	H3122 (NSCLC)	pY-ALK	1	108
		Proliferation	1	25
ALK negative	HT	Proliferation	>1,000	>1,000



Source: **Front Oncol* (2012) 2:17; **2012 ASCO #3007; ****Sci Trans Med* (2012) 4:120; *****PNAS* (2011) 108:7535