MODEL COHORT

CTG-2992: A NSCLC EGFR Exon 20 Mutant, Osimertinib Insensitive PDX Model

The patient-derived xenograft model, CTG-2992, was established from a poorly differentiated metastatic NSCLC adenocarcinoma collected from a pre-treated, 33 year old female patient, whose smoking history is unknown.

The patient received 4 lines of therapy prior to model establishment as displayed in this table.

Line of Therapy	Treatment	Treatment Duration	Response
First	Cisplatin/Pemetrexed	<1 Month	N/A
Second	Gefitinib	N/A	No Response
Third	Docetaxel	<1 Month	N/A
Fourth	Gemcitabine/Vinorelbine	2 Months	N/A

EGFR Status of CTG-2992 Confirmed by Next Generation Sequencing (NGS)

Sequencing of the patient tumor revealed an EGFR exon 20 insertion mutation, D770_N771insG, located in the molecule's protein tyrosine kinase domain. After PDX model establishment, whole exome sequencing and RNA sequencing were performed, which revealed maintenance of the EGFR exon 20 insertion mutation.

This mutation is generally considered to render tumors resistant to EGFR tyrosine kinase inhibitors, potentially explaining the patient's lack of response to Gefitinib.

Other potentially deleterious genomic alterations identified in the model are listed in the table below.

Gene	Alteration	Impact
TP53	H178Q (DNA Binding Domain)	Loss of function; Likely Oncogenic*
EGFR	CNV; Amplification (4 Copies)	Likely Oncogenic
MET	CNV; Amplification (4 Copies)	Likely Oncogenic
RET	Overexpression (6-fold)	Unknown
ALK	Overexpression (6.6-fold)	Unknown

*according to OncoKB

In order to identify PDX models insensitive to EGFR inhibition, which can be used to facilitate discovery of novel therapies targeting exon 20 mutations, an in vivo study was performed. This study assessed the activity of the third generation inhibitor, Osimertinib, in CTG-2992.

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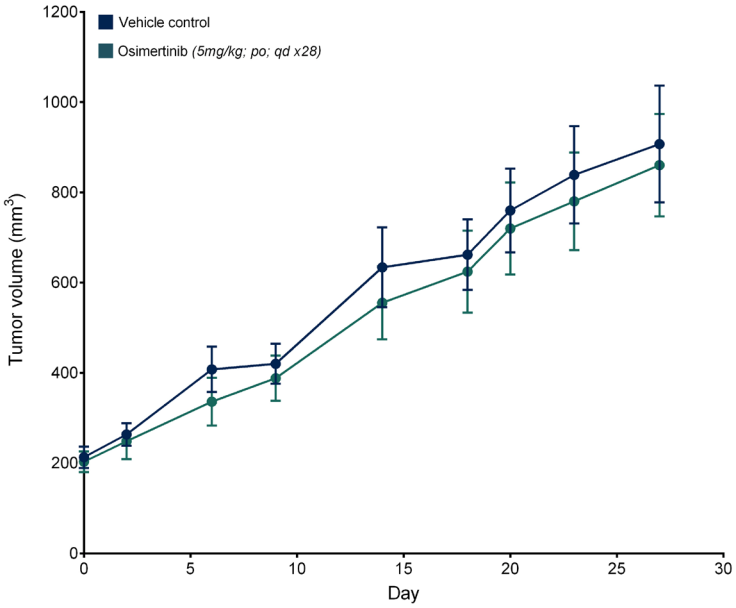
In Vivo Response to Osimertinib

Nu/Nu nude mice subcutaneously implanted with CTG-2992 were treated daily with 5mg/kg Osimertinib orally for 28 days.

CTG-2992 showed continued growth in the presence of Osimertinib, with an overall mRECISIT of progressive disease (PD) and a tumor growth inhibition of 22% (treatment vs. vehicle control).

As a result, CTG-2992 is a robust model for testing novel therapies to overcome the resistance seen in Exon 20 EGFR mutations. Champions Oncology is currently building an expanded cohort of EGFR mutant PDX models established from patients who have progressed on EGFR therapy. A detailed list of the currently available models is displayed below.



Additional EGFR Mutant NSCLC PDX Models Available*

	EGFR Mutation Status	Patient EGFR Treatment History (Pre-Collection)	WES/RNA-Seq Available	Commercial Availability
CTG-2695	Exon 19 del E746_A750del	Afatinib (Response, then PD), Osimertinib (PD)	Both	Available
CTG-2803	Exon 19 del L747fs, T571fs	Gefitinib (PD), Osimertinib (PD)	Both	Available
CTG-2839	Exon 19 del E746_A750del	Osimertinib (Response, then PD), Afatinib (PD)	Both	*Pending*
CTG-2842	Exon 20 Ins A767_V769dup	Erlotinib (PD)	Both	Available
CTG-2934	Exon 19 del (L747_S752del) T790M	Osimertinib (Response, then PD)	Both	Available
CTG-2939	Exon 19 del E746_A750del	Gefitinib (PD), Experimental EGFR inhibitor (continuation)	Both	Available
CTG-2992	Exon 20 Ins D770_N771insG	Gefitinib (PD)	Both	Available
CTG-3160	Exon 19 del (E746_A750del) T790M	Erlotinib (Response, then PD)	Both	Available
CTG-2790	Exon 19 del E746_A750del	Gefitinib (PD), Experimental EGFR inhibitor (PD)	Both	Available
CTG-1014	L858R/T790M	Erlotinib (PD)	Both	Available
CTG-2534	G719C/S768I	Erlotinib (Response, then PD)	Both	Available
CTG-2535	E746_A750del	Erlotinib/Sorafenib (Response, then PD)	Both	Available
CTG-2537	L858R/T790M	Gefitinib (Response, then PD)	Both	Available
CTG-3192	E746_A750del	Gefitinib (Response, then PD); Osimertinib/Experimental MET inhibitor (Response, then PD)	Both	Available
CTG-3196	L858R	Afatinib (Response, then PD); Experimental EGFR inhibitor (Response, then PD)	Both	Available
CTG-3271	L747_P753delinsS/T790M	Osimertinib (Response, then PD)	Both	Available
CTG-3320	E746_A750del/L49F	Gefitinib (Response, then PD)	Both	Available
CTG-3470	E746_A750del	Gefitinib (Response, then PD); Osimertinib (Response, then PD)	Both	Available
CTG-3477	L747_P753delinsS/E865G/T790M	Experimental EGFR inhibitor (Response, then PD); Gefitinib (PD); Experimental EGFR inhibitor (Response, then PD); Osimertinib (PD)	Both	Available

*as of August 2021

Please visit www.ChampionsOncology.com for access to the Champions Model Select® and updated information about Champions Oncology's PDX Models.

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