

High Proportion of Potential Candidates for Immunotherapy in a Chilean Cohort of Gastric Cancer Patients: Results of the FORCE1 Study

Miguel Cordova-Delgado, Mauricio P. Pinto, Ignacio N. Retamal, Matías Muñoz-Medel, María Loreto Bravo, Mariía F. Fernández, Betzabé Cisternas, Sebastian Mondaca, Cesar Sanchez, Hector Galindo, Bruno Nervi, Carolina Ibáñez, Francisco Acevedo, Jorge Madrid, José Peña, Erica Koch, Maria José Maturana, Diego Romero, Nathaly de la Jara, Javiera Torres, Manuel Espinoza, Carlos Balmaceda, Yuwei Liao, Zhiguang Li, Matías Freire, Valentina Gárate-Calderón, Javier Caceres, Gonzalo Sepúlveda-Hermosilla, Rodrigo Lizana, Liliana Ramos, Rocío Artigas, Enrique Norero, Fernando Crovari, Ricardo Armisen, Alejandro H. Corvalán, Gareth I. Owen and Marcelo Garrido

Table S1. Demographic and clinico-pathological characteristics of HER2+ subgroup ($n = 12$), EBV+ subgroup ($n = 12$), PDL1+ subgroup ($n = 26$) and MSI+ subgroup ($n = 13$) populations.

Characteristic	HER2+ n (%)	EBV+ n (%)	PDL1+ n (%)	MSI+ n (%)
n	12	12	26	13
Gender				
Male	7 (58.3)	11 (91.7)	21 (80.8)	7 (53.8)
Female	5 (41.7)	1 (8.3)	5 (19.2)	6 (46.2)
Stage at diagnosis				
I	2 (16.7)	1 (8.3)	3 (11.5)	2 (15.4)
II	3 (25.0)	5 (41.7)	9 (34.6)	6 (46.2)
III	6 (50.0)	4 (33.3)	12 (46.2)	4 (30.8)
IV	1 (8.3)	2 (16.7)	2 (7.7)	1 (7.7)
Location of primary tumor				
Distal esophagus and GEJ	3 (25.0)	6 (50.0)	7 (26.9)	1 (7.7)
Fundus	0	3 (25.0)	3 (11.5)	0
Corpus	4 (33.3)	2 (16.7)	8 (30.8)	3 (23.0)
Antrum	1 (8.3)	1 (8.3)	7 (26.9)	7 (53.8)
Pylorus	1 (8.3)	0	0	1 (7.7)
Multiple	2 (16.7)	0	1 (3.9)	1 (7.7)
NA	1 (8.3)	0	0	0
Lauren histological type				
Intestinal	8 (66.7)	4 (33.3)	6 (23.1)	3 (23.0)
Diffuse	2 (16.7)	2 (16.7)	9 (34.6)	6 (46.2)
Mixed	1 (8.3)	1 (8.3)	3 (11.5)	2 (15.4)
NA	1 (8.3)	5 (41.7)	8 (30.8)	2 (15.4)
WHO histological type				
Adenocarcinoma	10 (83.3)	9 (75.0)	21 (80.8)	12 (92.3)
Undifferentiated carcinoma	0	2 (16.7)	1 (3.9)	1 (7.7)
Adenosquamous cell carcinoma	0	0	1 (3.9)	0
NA	2 (16.7)	1 (8.3)	3 (11.5)	0
Signet-ring cell presence				
No	6 (50.0)	11 (91.7)	21 (80.8)	6 (46.2)
Yes	5 (41.7)	0	4 (15.4)	5 (38.5)
NA	1 (8.3)	1 (8.3)	1 (3.9)	2 (15.4)
Median/average age at diagnosis (years)	62.5/60.3 (39–83)	57.0/57.7 (36–75)	59.0/61.3 (33–84)	66.0/65.0 (26–82)
Median overall survival (months)	30	NR	66	NR

GEJ Gastroesophagic junction, NA Not available, NR Not reached.

Table S2. Driver mutations affecting FORCE1 patients.

Gene	Driver Mutation ^a	Affected Patients (n)
<i>BRAF</i>	p.D594G	3
<i>CTNNB1</i>	p.D32Y	1
<i>FBXW7</i>	p.R465H	1
<i>KRAS</i>	p.G13D	1
<i>NRAS</i>	p.G12D	2
<i>PIK3CA</i>	p.E545K	2
<i>RHOA</i>	p.Y42C	3
<i>TP53</i>	p.R175H	2
	p.R181C	1
	p.R248Q	2
	p.R248W	2
	p.R273C	4
	p.R273H	1
	p.R282W	1
	p.C135Y	1
	p.C176F	1
	p.Q144H	1
	p.P152L	1
	p.Y205S	1
	p.Y220H	2
	p.V173L	1
	p.V272M	1

^a Driver mutations identified using sequence-based and structure-based approaches.

Table S3. Actionable mutations affecting FORCE1 patients.

Gene	Druggable Mutation	Drug Associate	Level of Evidence ^a	Cancer Type	Affected Patients (N)
<i>ALK</i>	Fusion	Crizotinib, Alectinib, Ceritinib	1	NSC Lung	4
<i>ATM</i>	p.S2017fs				1
<i>ATM</i>	p.L581fs	Olaparib	4	All solid tumors	1
<i>ATM</i>	p.D2725fs				1
<i>BRAF</i>	p.D594G	PLX8394	4	All tumors	3
<i>BRCA1</i>	Fusion	Cobimetinib, Trametinib	3A	Melanoma	1
<i>BRCA1</i>	p.Q1111fs	Rucaparib, Niraparib	1	Ovarian	1
<i>BRCA2</i>	p.E2258*	Talazoparib, Olaparib	2A	Breast/Ovarian	1
<i>BRCA2</i>	Deletion (CNV)				2
<i>CDKN2A</i>	p.R131C	Abemaciclib, Palbociclib,			1
<i>CDKN2A</i>	p.R87Q	Ribociclib	4	All solid tumors	1
<i>CDKN2A</i>	p.Q50*				1
<i>ERBB2</i>	Amplification (CNV)	Trastuzumab	1	Esophagogastric	3
<i>ERBB2</i>	p.R678Q	Neratinib	3A	Breast	2
<i>FGFR2</i>	p.P253R	AZD4547, BGJ398, Erdafitinib, Debio1347	4	All solid tumors	1
<i>HRAS</i>	p.G12D	Tipifarnib	3A	Head and Neck	1
<i>HRAS</i>	p.Q61H	Panitumumab, Cetuximab	R1	Colorectal	1
<i>KRAS</i>	p.G12A				1
<i>KRAS</i>	p.G12D	Cobimetinib, Binimetinib, Trametinib	4	All tumors	3
<i>KRAS</i>	p.G13D				1
<i>KRAS</i>	p.G12D	Panitumumab, Cetuximab	R1	Colorectal	1
<i>NRAS</i>	p.G12D	Binimetinib, Binimetinib + Ribociclib	3A	Melanoma	1
<i>NRAS</i>	p.E542K				4
<i>NRAS</i>	p.K111E				1
<i>NRAS</i>	p.G118D	Buparlisib, Alpelisib,			1
<i>PIK3CA</i>	p.T1025A	Fulvestrant, Serabelisib,	3A	Breast	2
<i>PIK3CA</i>	p.H1047R	Copanlisib, GDC-0077, Taselisib			1
<i>PIK3CA</i>	p.E545G				3
<i>PIK3CA</i>	p.R88Q				2
<i>PIK3CA</i>	p.T319fs				1
<i>PTEN</i>	p.T167fs	GSK2636771, AZD8186	4	All tumors	1
<i>PTEN</i>	p.R335*				1
<i>PTEN</i>	p.R173H				1
<i>ROS1</i>	Fusion	Crizotinib	1	NSC Lung	1

^a Downloaded from OncoKB database *NSC* Non-Small cell, *CNV* Copy number variation.

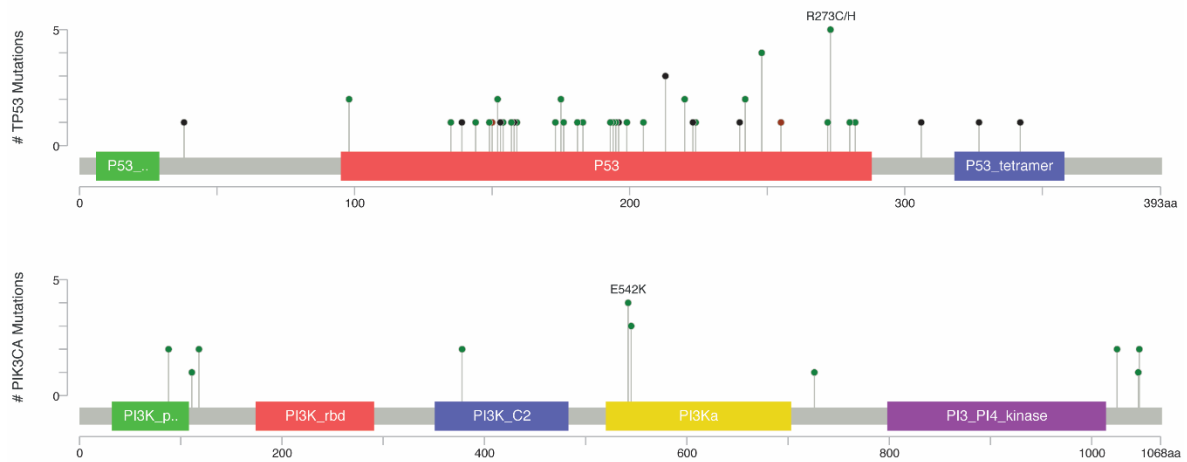


Figure S1. Lollipop diagram showing *TP53* and *PIK3CA* gene mutations found in the GCTF.

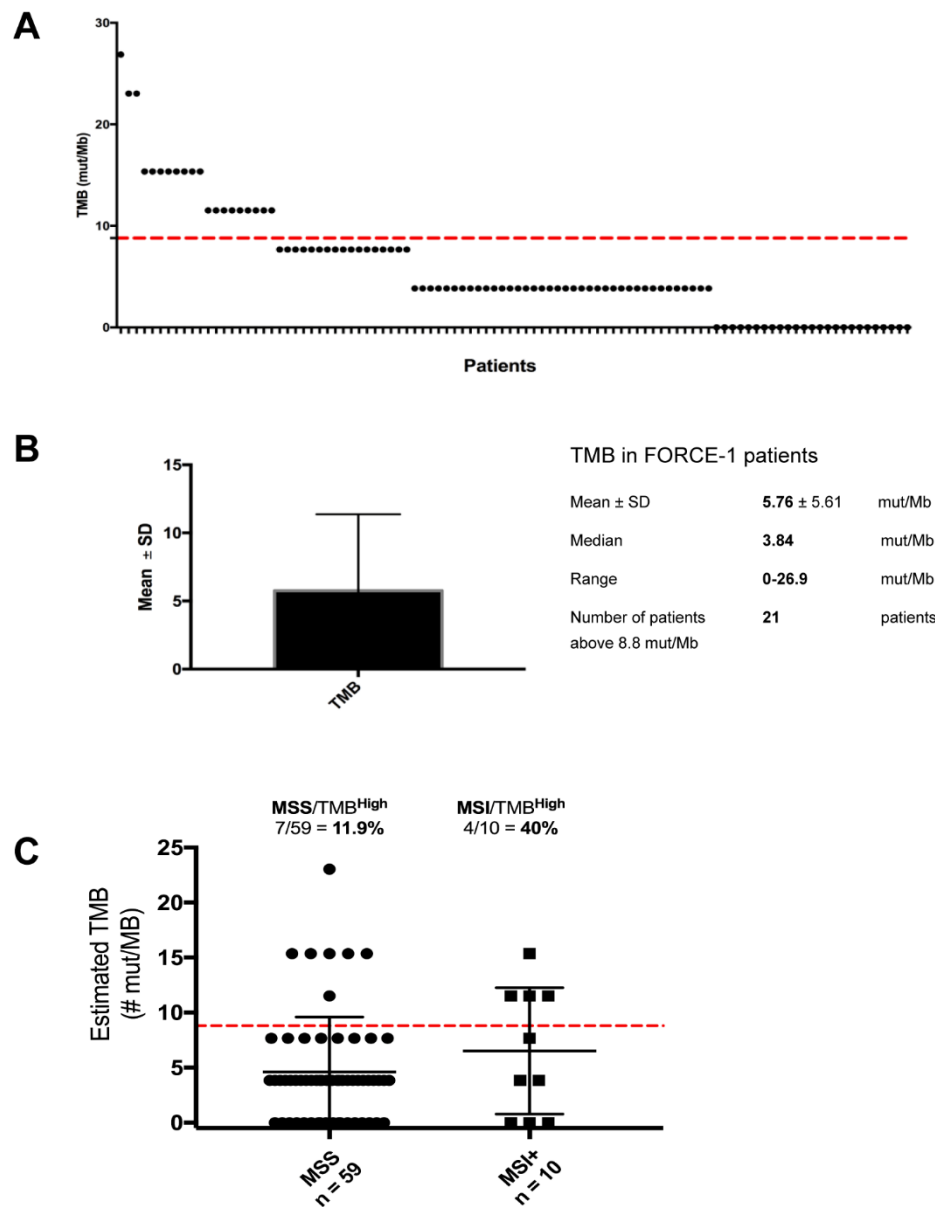


Figure S2. Estimated TMB and TMB levels in MSI+ or MSS patients.

