legacy

Gastric cancer in Chile

Molecular and clinical profiling of patients in a high incidence/high mortality country

Mauricio P. Pinto, PhD

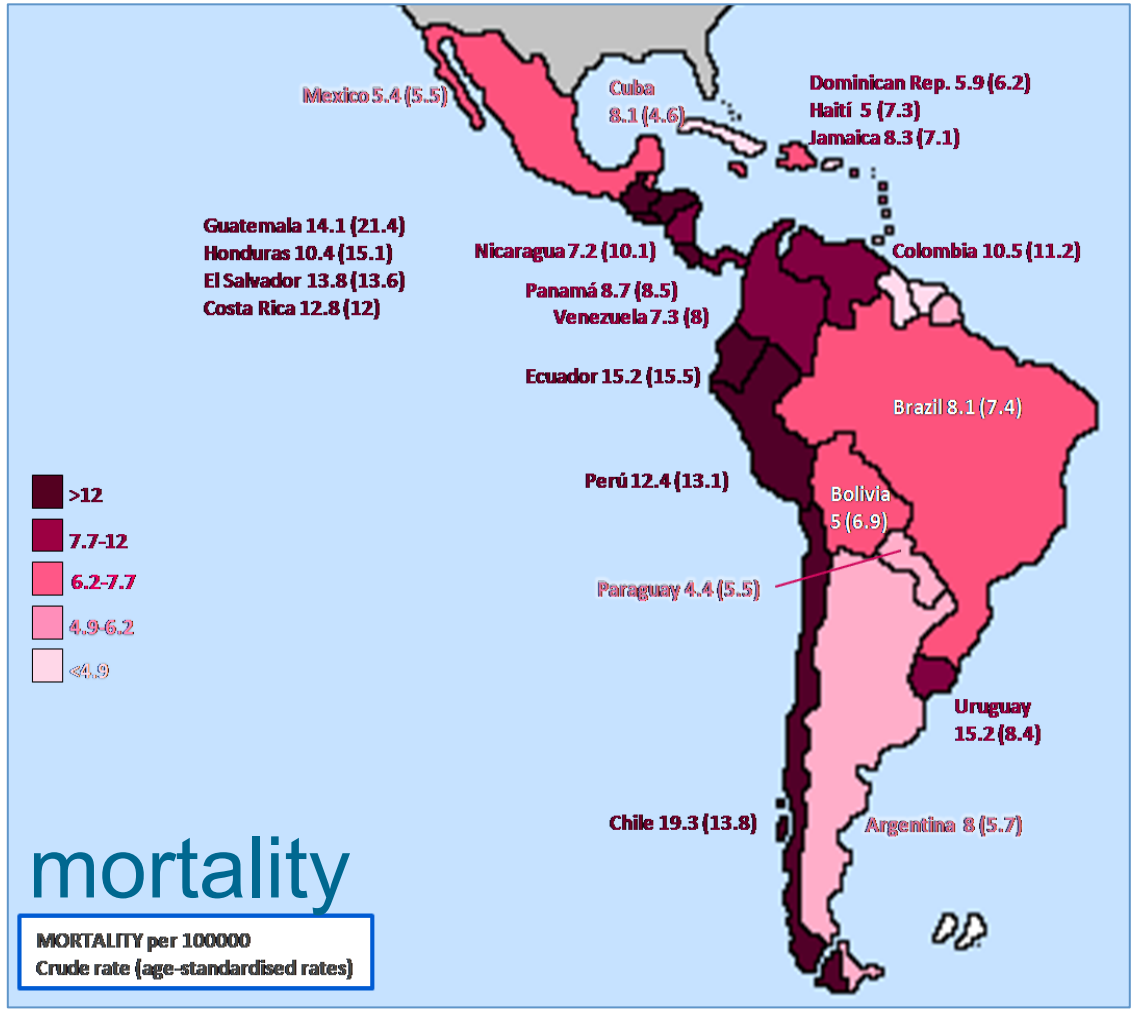
This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No GA825832

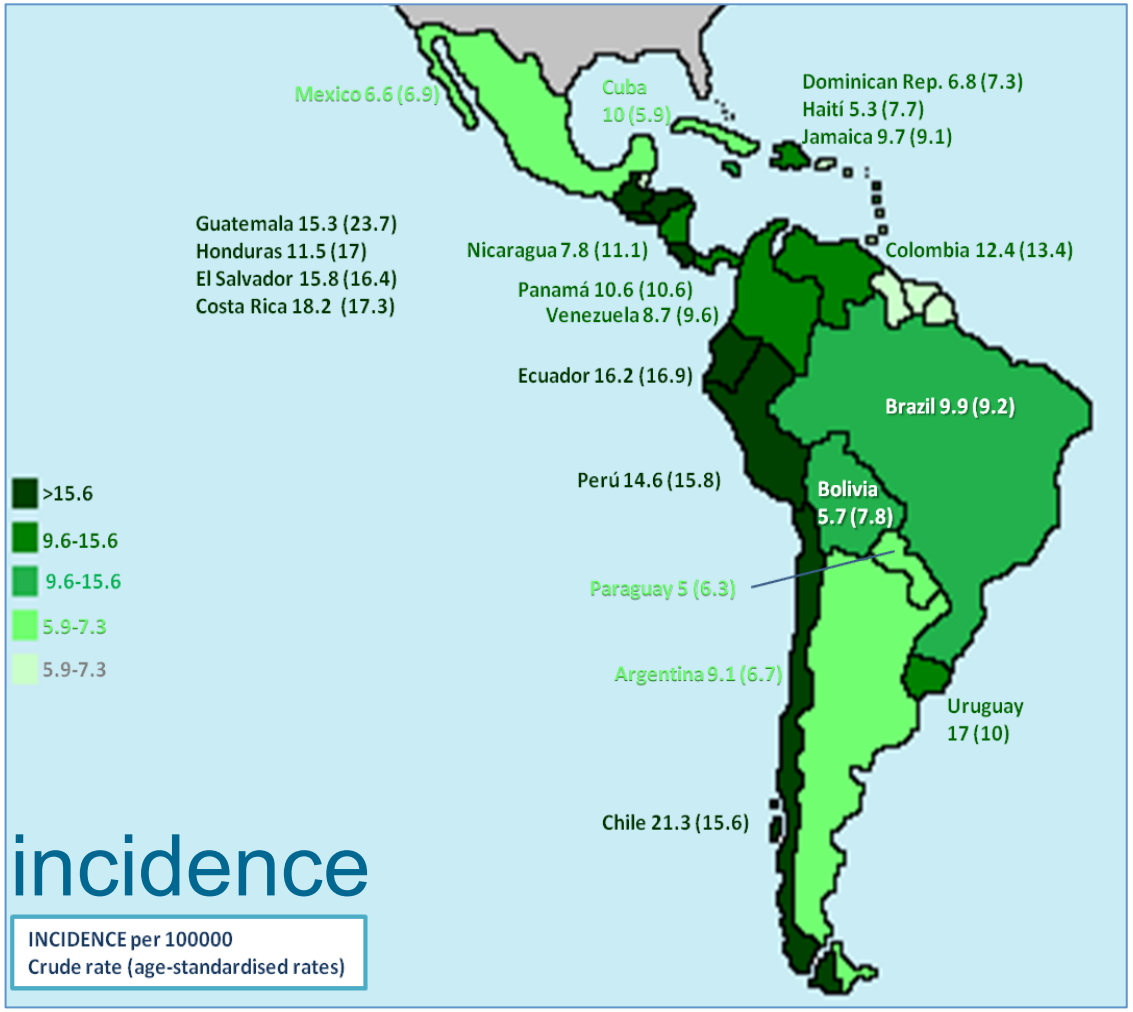
Gastric Cancer in Chile

- Facts & Figures
- Gastric Cancer Task Force One
- Clinical profiling
- Molecular profiling
- Molecularly-based stratification
- Future challenges

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No GA825832

GC mortality and incidence in Latin America





Garrido M. Journal of Cancer Therapy 2016; **7**, 1-12.

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No GA825832

GC is the leading cause of cancer death in Chile

Variable	Chile	China	S. Korea
Incidence (per 100,000/year)	15.6	19.5	35.8
Mortality (per 100,000/year)	13.8	13.4	24.3

Chilean population: ~17.5 M
>73% is *H. pylori*+
High prevalence of EBV+
Incidence and mortality is higher in males
Total GC deaths: >3,300 a year

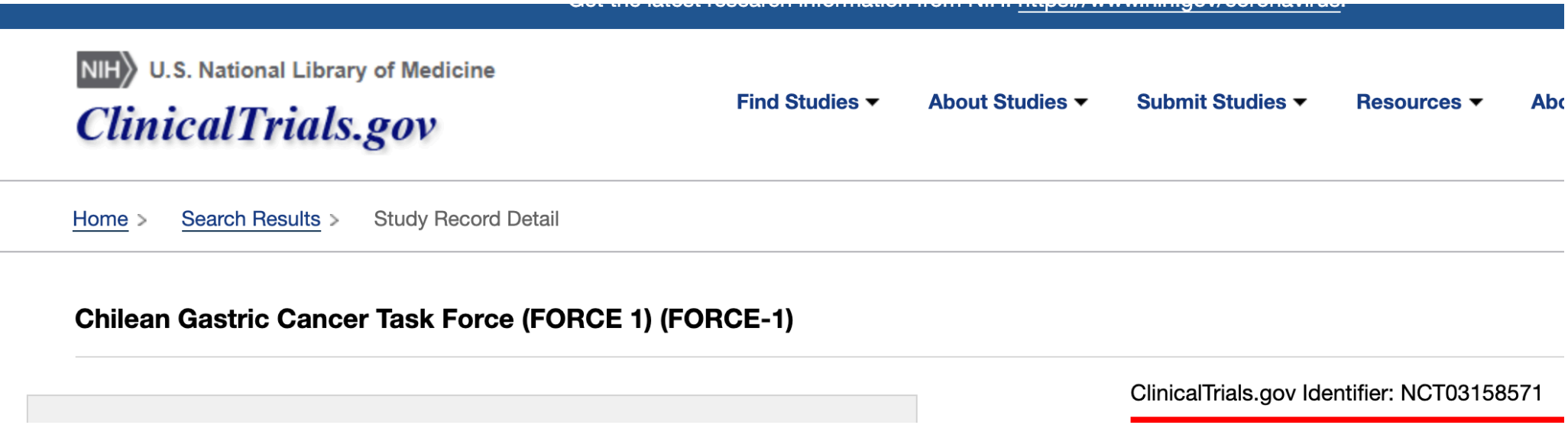
Caglevic, C., Silva, S., Mahave, M., Rolfo, C., & Gallardo, J. (2016). The current situation for gastric cancer in Chile. Ecancermedicalscience, 10, 707. https://doi.org/10.3332/ecancer.2016.707

Yang L, Zheng R, Wang N, et al. Incidence and mortality of stomach cancer in China, 2014. Chin J Cancer Res. 2018;30(3):291-298. doi:10.21147/j.issn.1000-9604.2018.03.01

Eom BW, Jung KW, Won YJ, Yang H, Kim YW. Trends in Gastric Cancer Incidence According to the Clinicopathological Characteristics in Korea, 1999-2014. Cancer Res Treat. 2018 Oct;50(4):1343-1350. doi: 10.4143/crt.2017.464.

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No GA825832

The Gastric Cancer Task Force One Study (FORCE1)

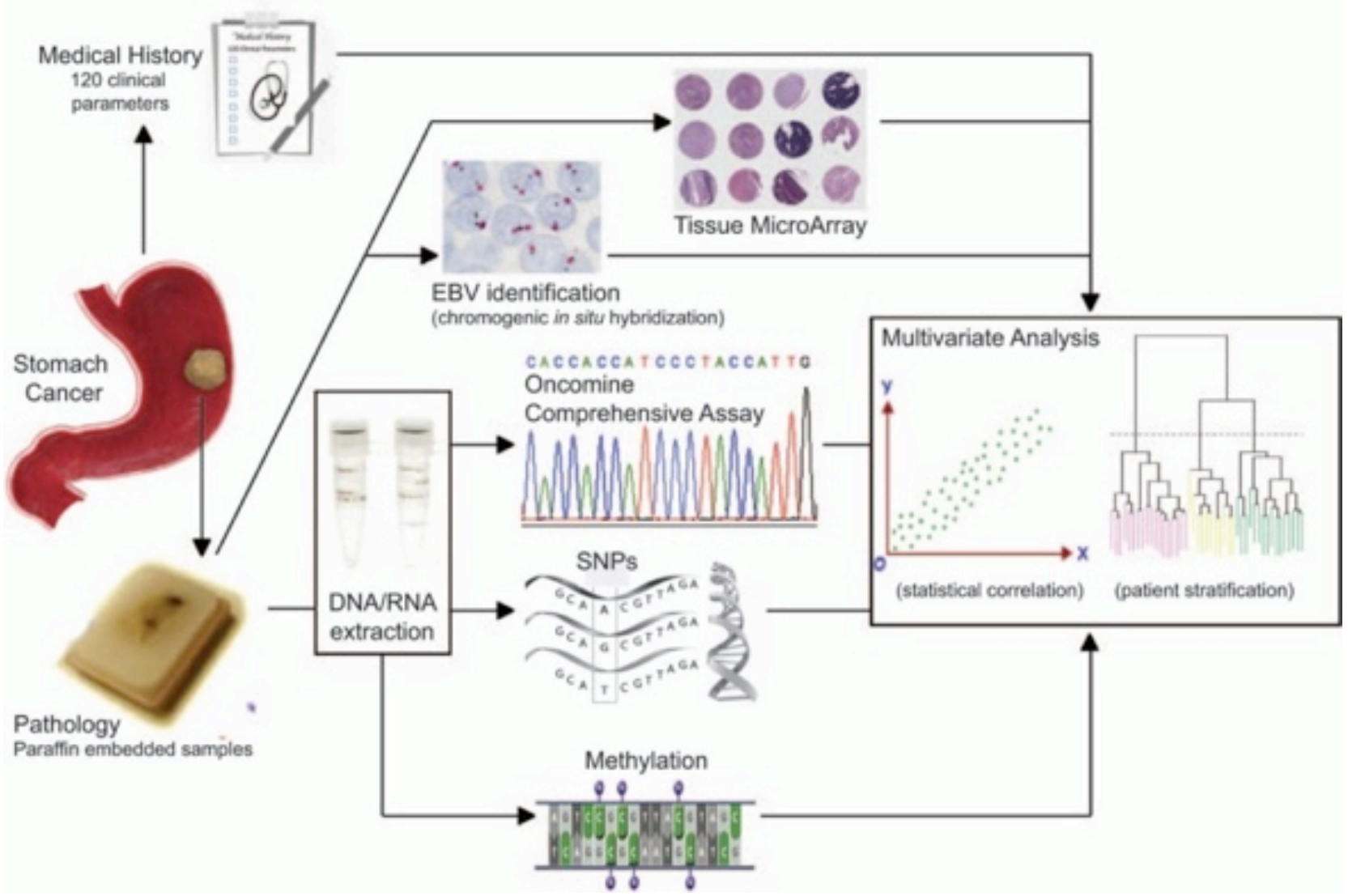


Started in 2015 this project sought to stratify GC patients according to their clinical and molecular charcateristics

Recruited a total of 224 patients

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No GA825832

The Gastric Cancer Task Force One Study (FORCE1)



Owen, G. I., Pinto, M. P., Retamal, I. N., … Garrido, M. (2018). Chilean Gastric Cancer Task Force: A study protocol to obtain a clinical and molecular classification of a cohort of gastric cancer patients. Medicine, 97(16), e0419. https://doi.org/10.1097/MD.0000000000010419

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No GA825832

Clinical profiling

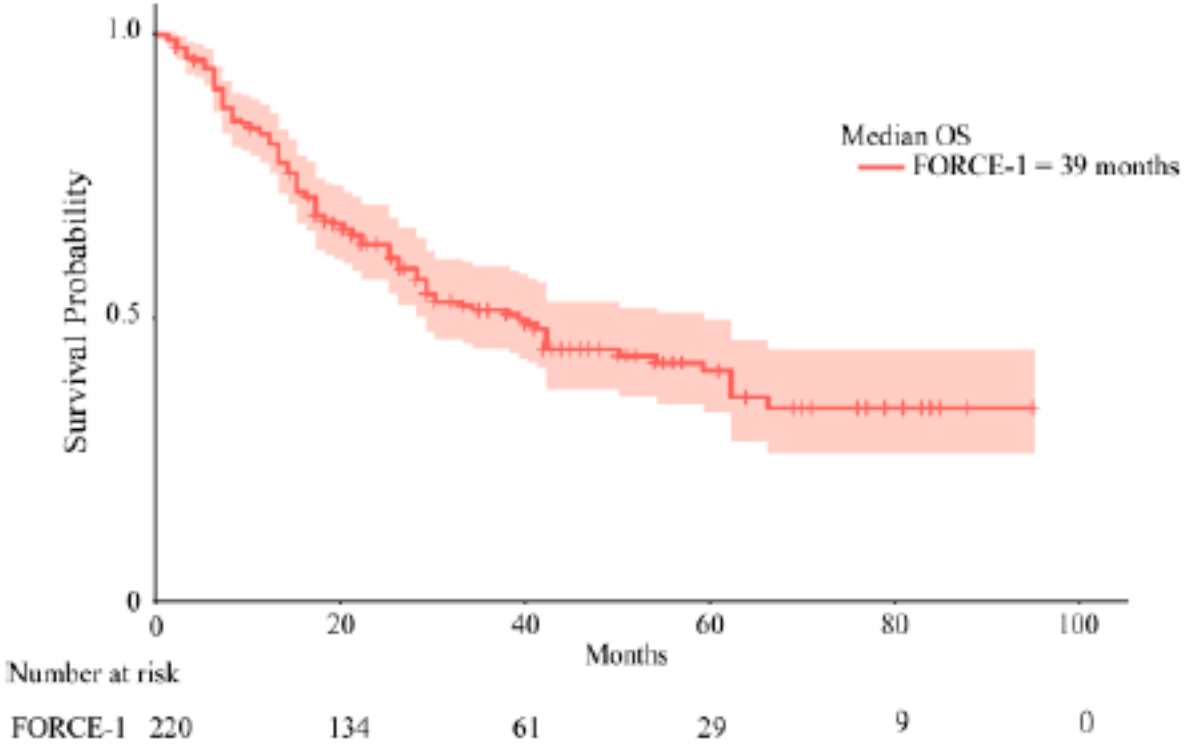
Characteristic	FORCE-1 *n* (%)
Gender	
Male	142 (63.4)
Female	82 (36.6)
Stage at diagnosis	
I	30 (13.4)
II	57 (25.4)
III	88 (39.3)
IV	49 (21.9)
ECOG Performance Status	
0	69 (30.8)
1	69 (30.8)
2	6 (2.7)
≥3	1 (0.4)
NA	79 (35.3)
Location of primary tumor	
Distal esophagus and GEJ	49 (21.9)
Fundus	12 (5.3)
Corpus	86 (38.4)
Antrum	54 (24.1)
Pylorus	8 (3.6)
Multiple	9 (4.0)
NA	6 (2.7)

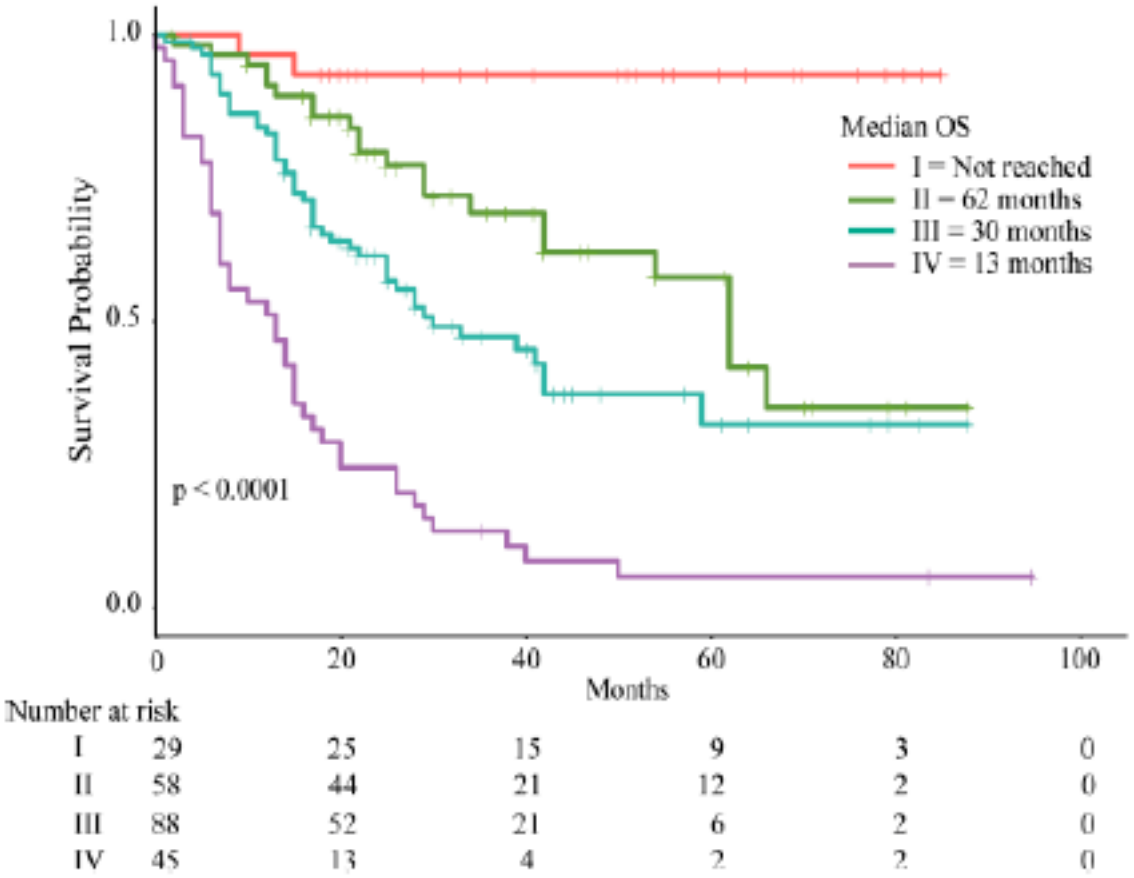
Characteristic	FORCE-1 *n* (%)
Lauren histological type	
Intestinal	76 (33.9)
Diffuse	61 (27.2)
Mixed	17 (7.6)
NA	70 (31.3)
WHO histological type	
Adenocarcinoma	171 (76.3)
Undifferentiated carcinoma	9 (4.0)
Adenosquamous cell carcinoma	3 (1.3)
NA	41 (18.3)
Signet-ring cell presence	
No	122 (54.5)
Yes	74 (33.0)
NA	28 (12.5)
Comorbidities at diagnosis	
Two or less	192 (85.7)
Three or more	32 (14.3)
Age	
Mean, median (range)	61.4, 62 (26–89)

Cordova-Delgado M, Pinto MP, …, Garrido M. High Proportion of Potential Candidates for Immunotherapy in a Chilean Cohort of Gastric Cancer Patients: Results of the FORCE1 Study. Cancers (Basel). 2019 Aug 30;11(9):1275. doi: 10.3390/cancers11091275. PMID: 31480291; PMCID: PMC6770659.

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No GA825832

Clinical profiling





Cordova-Delgado M, Pinto MP, …, Garrido M. High Proportion of Potential Candidates for Immunotherapy in a Chilean Cohort of Gastric Cancer Patients: Results of the FORCE1 Study. Cancers (Basel). 2019 Aug 30;11(9):1275. doi: 10.3390/cancers11091275. PMID: 31480291; PMCID: PMC6770659.

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No GA825832

legacy Molecular profiling

Mutation Gene	Frequency *n* (%)	Mutation Gene	Frequency *n* (%)
SNVs		CNVs	
TP53	49 (48.51)	*MYC* [a]	5 (4.95)
PIK3CA	15 (14.85)	*CCND1* [a]	4 (3.96)
VHL	6 (5.94)	*CCNE* [a]	4 (3.96)
NRAS	7 (6.93)	*FGFR2* [a]	4 (3.96)
KRAS	6 (5.94)	*ERBB2* [a]	3 (2.97)
BRAF	5 (4.95)	*MDM2* [a]	3 (2.97)
APC	5 (4.95)	*CDKN2A* [b]	2 (1.98)
PTEN	5 (4.95)	*KRAS* [a]	2 (1.98)
RHOA	4 (3.96)	*AKT1* [a]	1 (0.99)
CDKN2A	3 (2.97)	*CDK6* [a]	1 (0.99)
CTNNB1	3 (2.97)	*GAS6* [a]	1 (0.99)
ATM	2 (1.98)	*ZNF217* [a]	1 (0.99)
PIK3R1	2 (1.98)		
PTPN11	2 (1.98)	Fusions	
ERBB3	1 (0.99)	*EML4_ALK*	4 (4.65)
FBXW7	2 (1.98)	*EGFR_EGFR*	1 (1.16)
DNMT3A	2 (1.98)	*SLC34A2_ROS1*	1 (1.16)
SMAD4	2 (1.98)	*TBL1XR1_ETV1*	1 (1.16)
CDH1	2 (1.98)	*TRIM24_BRAF*	1 (1.16)
ERBB2	2 (1.98)		

Owen, G. I., Pinto, M. P., Retamal, I. N., … Garrido, M. (2018). Chilean Gastric Cancer Task Force: A study protocol to obtain a clinical and molecular classification of a cohort of gastric cancer patients. Medicine, 97(16), e0419. https://doi.org/10.1097/MD.0000000000010419

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No GA825832

Molecular profiling

Gene	Aminoacidic Mutational Change	Total Samples *n* / Function	101 Chilean FORCE-1 *n* (%)	100 UHK TCGA *n* (%)	30 UTOKIO TCGA *n* (%)	295 TCGA Nature 2014 *n* (%)	66 Brazil TCGA *n* (%)
TP53	R273C	Missense	4 (4.0%)	4 (4.0%)	NR	6 (2.0%)	1 (1.5%)
	R213 *	Nonsense	3 (3.0%)	1 (1.0%)	NR	5 (1.7%)	NR
	R175H	Missense	2 (2.0%)	NR	1 (3.3%)	6 (2.0%)	1 (1.5%)
	R248Q	Missense	2 (2.0%)	4 (4.0%)	NR	5 (1.7%)	3 (4.5%)
	R248W	Missense	2 (2.0%)	1 (1.0%)	NR	1 (0.3%)	NR
	P98S	Missense	2 (2.0%)	NR	NR	NR	NR
	Y220H	Missense	2 (2.0%)	NR	NR	NR	2 (3%)
	C242F	Missense	2 (2.0%)	NR	NR	NR	NR

Some TP53 variants in the Chilean population have not been previously reported

Owen, G. I., Pinto, M. P., Retamal, I. N., … Garrido, M. (2018). Chilean Gastric Cancer Task Force: A study protocol to obtain a clinical and molecular classification of a cohort of gastric cancer patients. Medicine, 97(16), e0419. https://doi.org/10.1097/MD.0000000000010419

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No GA825832

Molecular profiling

Gene	Aminoacidic Mutational Change	Total Samples *n*	101	100	30	295	66
		Function	Chilean FORCE-1 *n* (%)	UHK TCGA *n* (%)	UTOKIO TCGA *n* (%)	TCGA Nature 2014 *n* (%)	Brazil TCGA *n* (%)
PIK3CA	E542K	Missense	4 (4.0%)	NR	NR	5 (1.7%)	2 (3%)
	C378R	Missense	2 (2.0%)	NR	NR	1 (0.3%)	NR
	E545K	Missense	2 (2.0%)	NR	NR	11 (3.7%)	2 (3%)
	R88Q	Missense	2 (2.0%)	NR	NR	4 (1.4%)	1 (1.5%)
	T1025A	Missense	2 (2.0%)	NR	NR	NR	NR
VHL	S68L	Missense	6 (5.9%)	NR	NR	NR	NR
NRAS	G13V	Missense	5 (5.0%)	NR	NR	NR	NR
	G12D	Missense	2 (2.0%)	NR	NR	NR	NR
KRAS	G12D	Missense	3 (3.0%)	2 (2%)	NR	7 (2.4%)	1 (1.5%)
BRAF	D594G	Missense	3 (3.0%)	NR	NR	NR	NR
RHOA	Y42C	Missense	3 (3.0%)	NR	4 (13.3%)	3 (1%)	NR
APC	D156fs	Frameshift deletion	2 (2.0%)	NR	NR	NR	NR

Owen, G. I., Pinto, M. P., Retamal, I. N., … Garrido, M. (2018). Chilean Gastric Cancer Task Force: A study protocol to obtain a clinical and molecular classification of a cohort of gastric cancer patients. Medicine, 97(16), e0419. https://doi.org/10.1097/MD.0000000000010419

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No GA825832

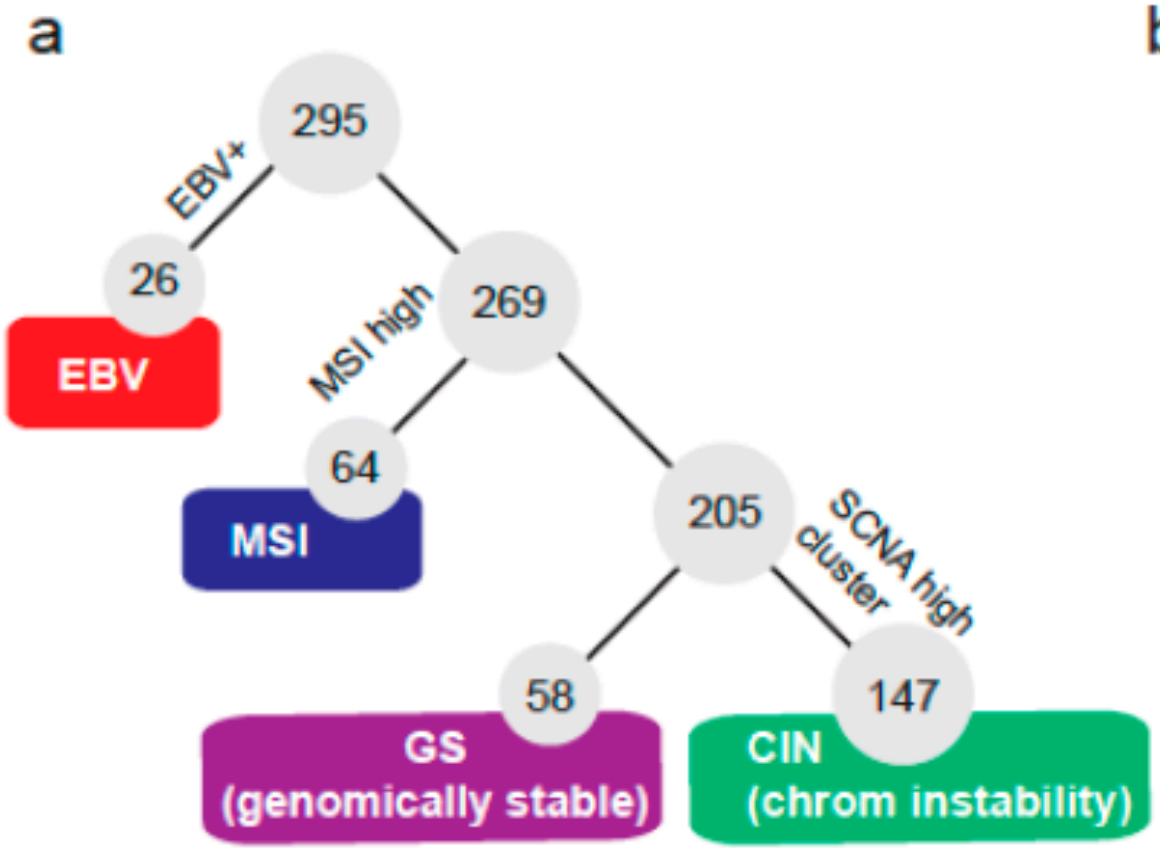
legacy

Given the existence of specific variants on the Chilean population

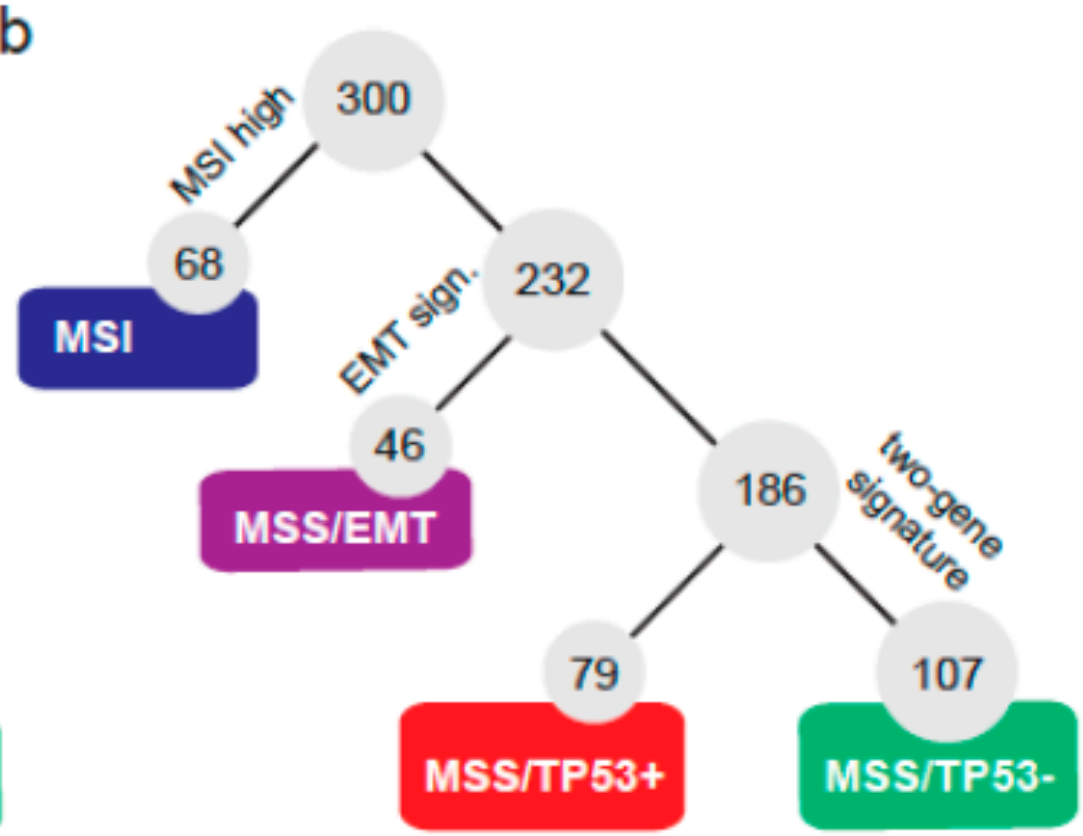
Can we define molecular subtypes?

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No GA825832

GC molecular subtypes



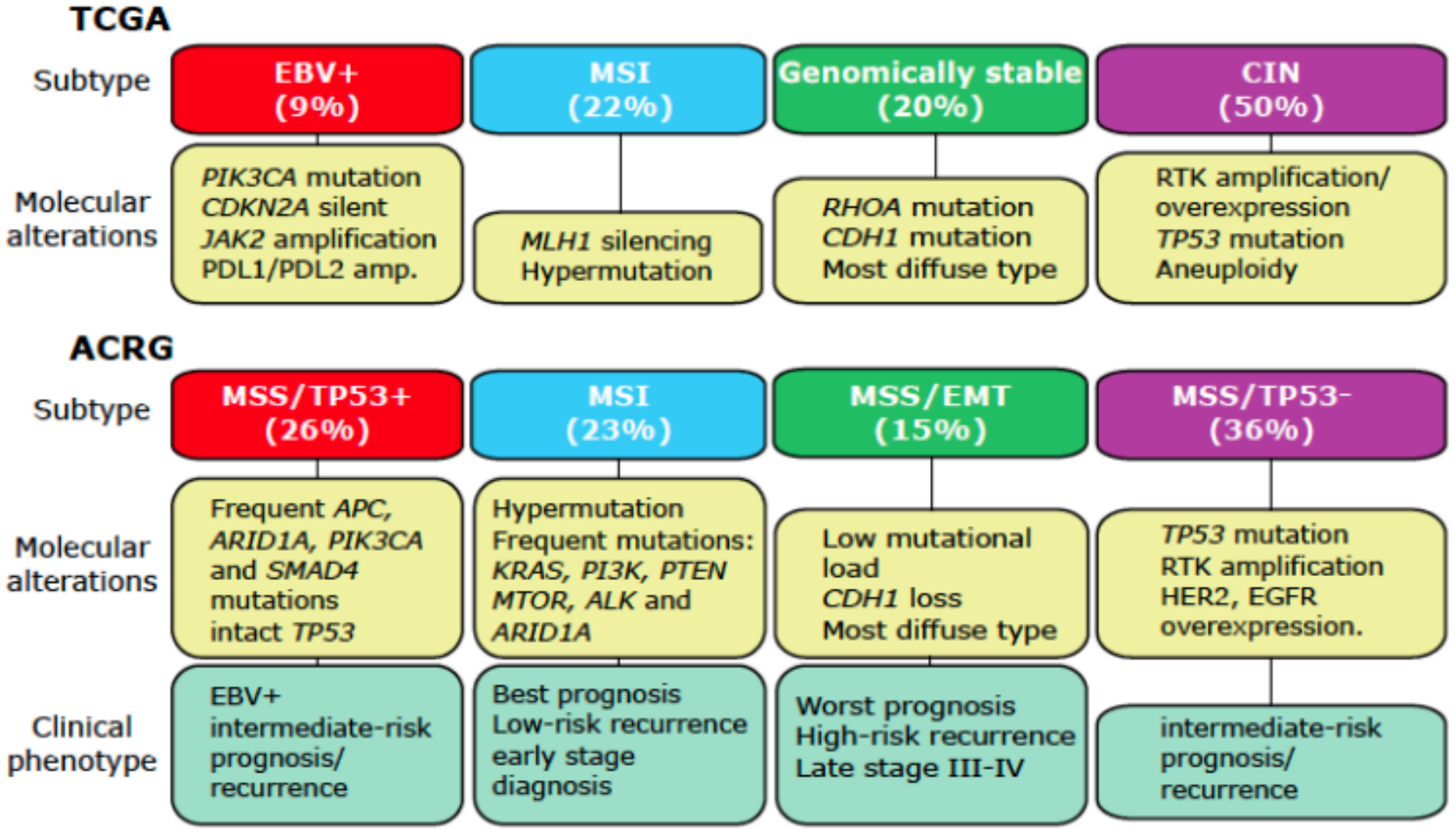
The Cancer genome Atlas



Asian Cancer Research Group

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No GA825832

legacy



This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No GA825832

ACRG and TCGA are too expensive and hard to apply into the clinic

Is it possible to elaborate a molecular stratification based on IHC/ISH?

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No GA825832

legacy

The answer is YES

Published: 01 April 2016

A protein and mRNA expression-based classification of gastric cancer

Namrata Setia, Agoston T Agoston, Hye S Han, John T Mullen, Dan G Duda, Jeffrey W Clark, Vikram Deshpande, Mari Mino-Kenudson, Amitabh Srivastava, Jochen K Lennerz, Theodore S Hong, Eunice L Kwak & Gregory Y Lauwers

Modern Pathology **29**, 772–784(2016) | Cite this article

1629 Accesses | **60** Citations | **17** Altmetric | Metrics

ORIGINAL ARTICLES

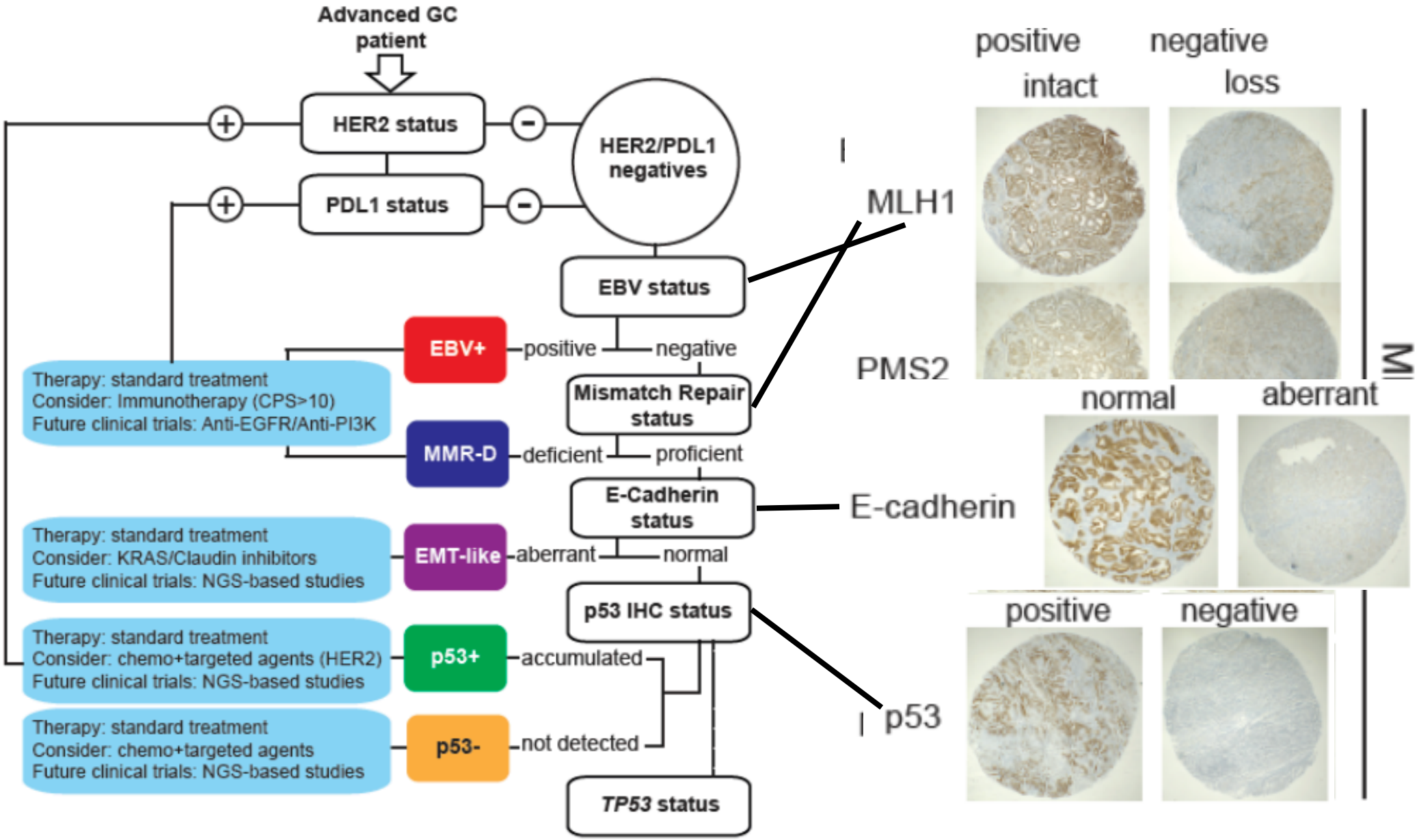
High-throughput Protein and mRNA Expression–based Classification of Gastric Cancers Can Identify Clinically Distinct Subtypes, Concordant With Recent Molecular Classifications

Ahn, Sangjeong MD, PhD[*,†]; Lee, So-Jeong MD[*]; Kim, Yonugkeum MD[*]; Kim, Ahrong MD[*]; Shin, Nari MD[‡]; Choi, Kyung Un MD, PhD[*]; Lee, Chang-Hun MD, PhD[*]; Huh, Gi Yeong MD, PhD[§]; Kim, Kyong-Mee MD, PhD[‖]; Setia, Namrata MD[¶]; Lauwers, Gregory Y. MD[#]; Park, Do Youn MD, PhD[*]

Author Information

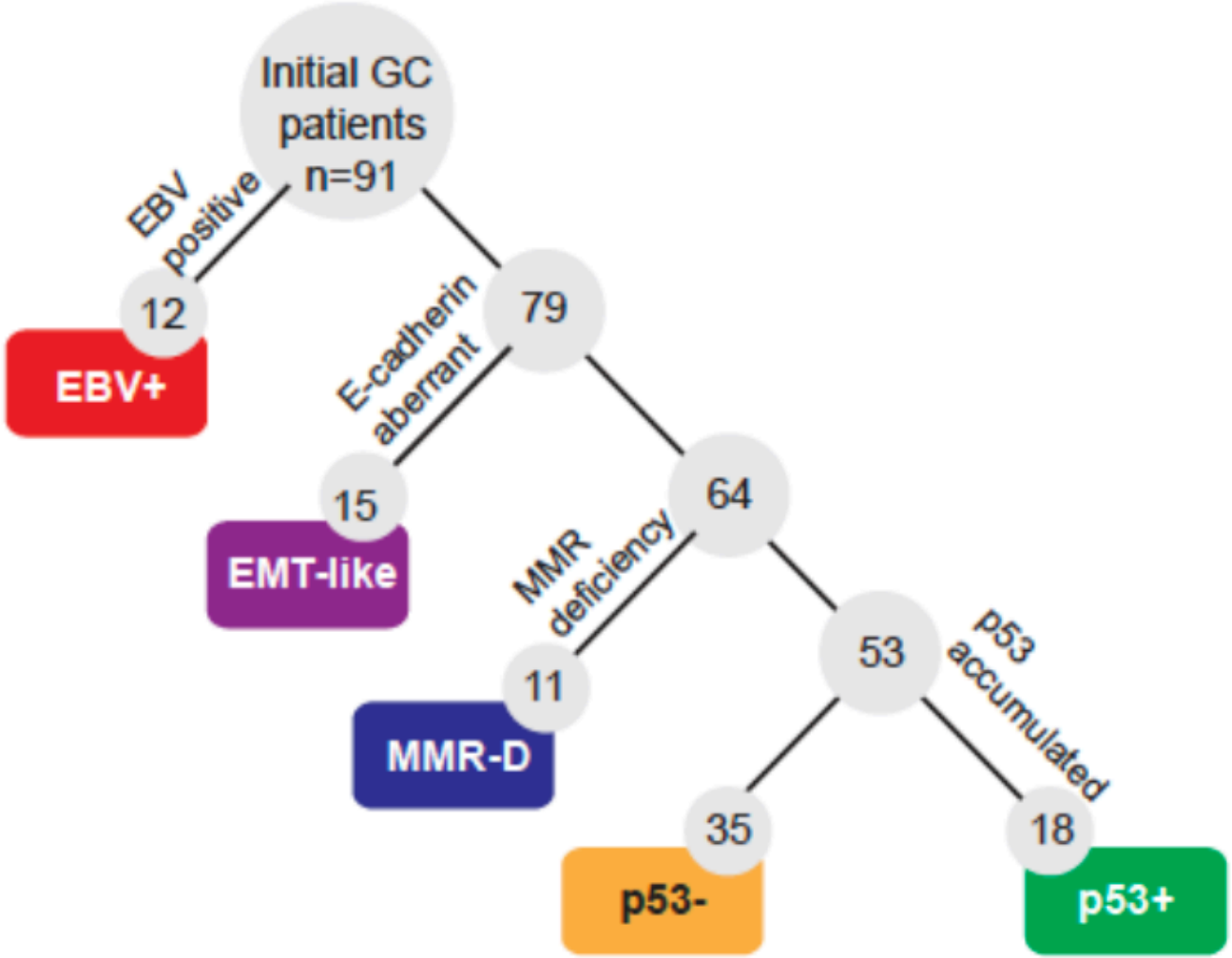
The American Journal of Surgical Pathology: January 2017 - Volume 41 - Issue 1 - p 106-115
doi: 10.1097/PAS.0000000000000756

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No GA825832



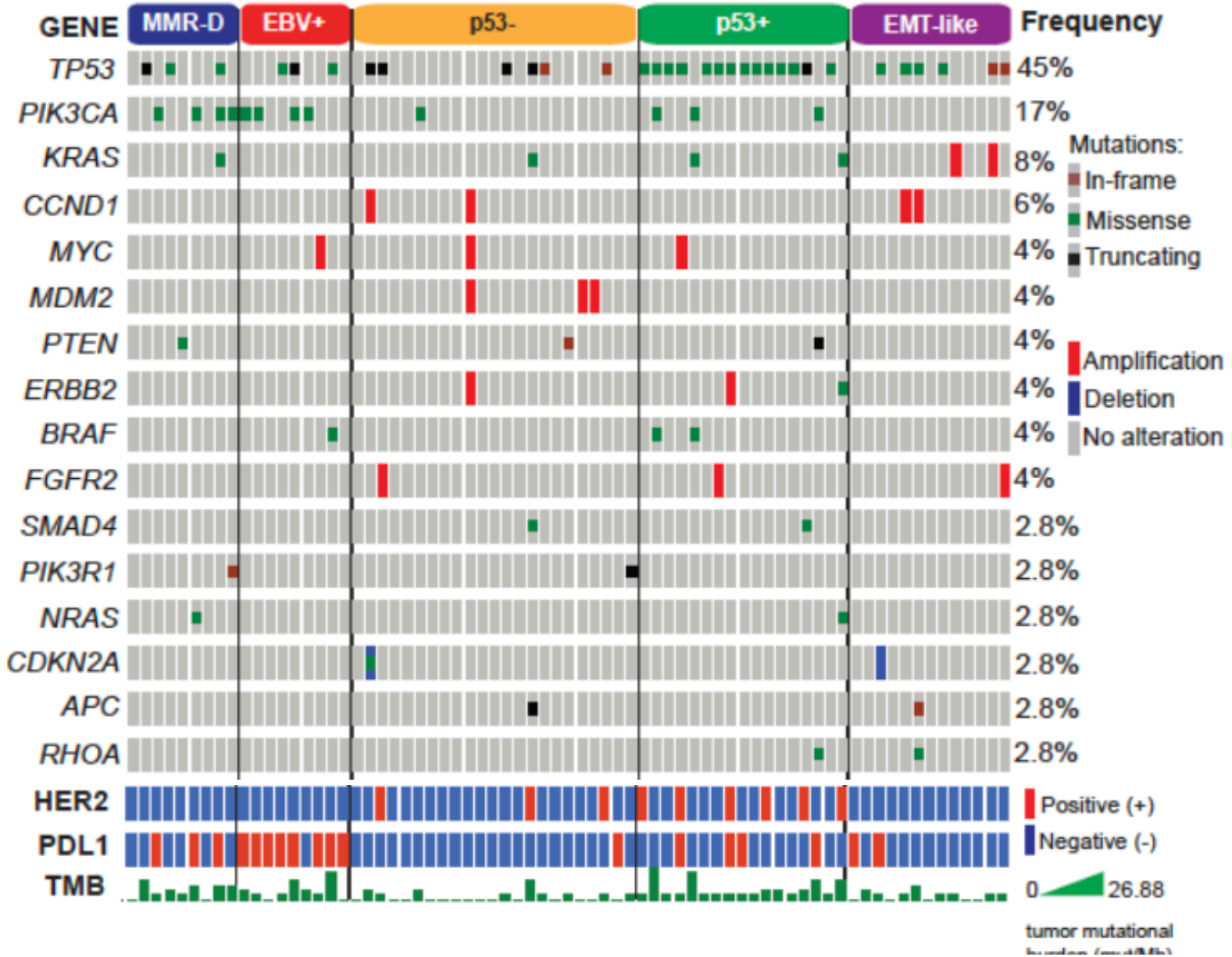
Pinto, M.P.; Córdova-Delgado, M.; Retamal, I…; Garrido, M. A Molecular Stratification of Chilean Gastric Cancer Patients with Potential Clinical Applicability. Cancers 2020, 12, 1863.

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No GA825832



Pinto, M.P.; Córdova-Delgado, M.; Retamal, I…; Garrido, M. A Molecular Stratification of Chilean Gastric Cancer Patients with Potential Clinical Applicability. Cancers 2020, 12, 1863.

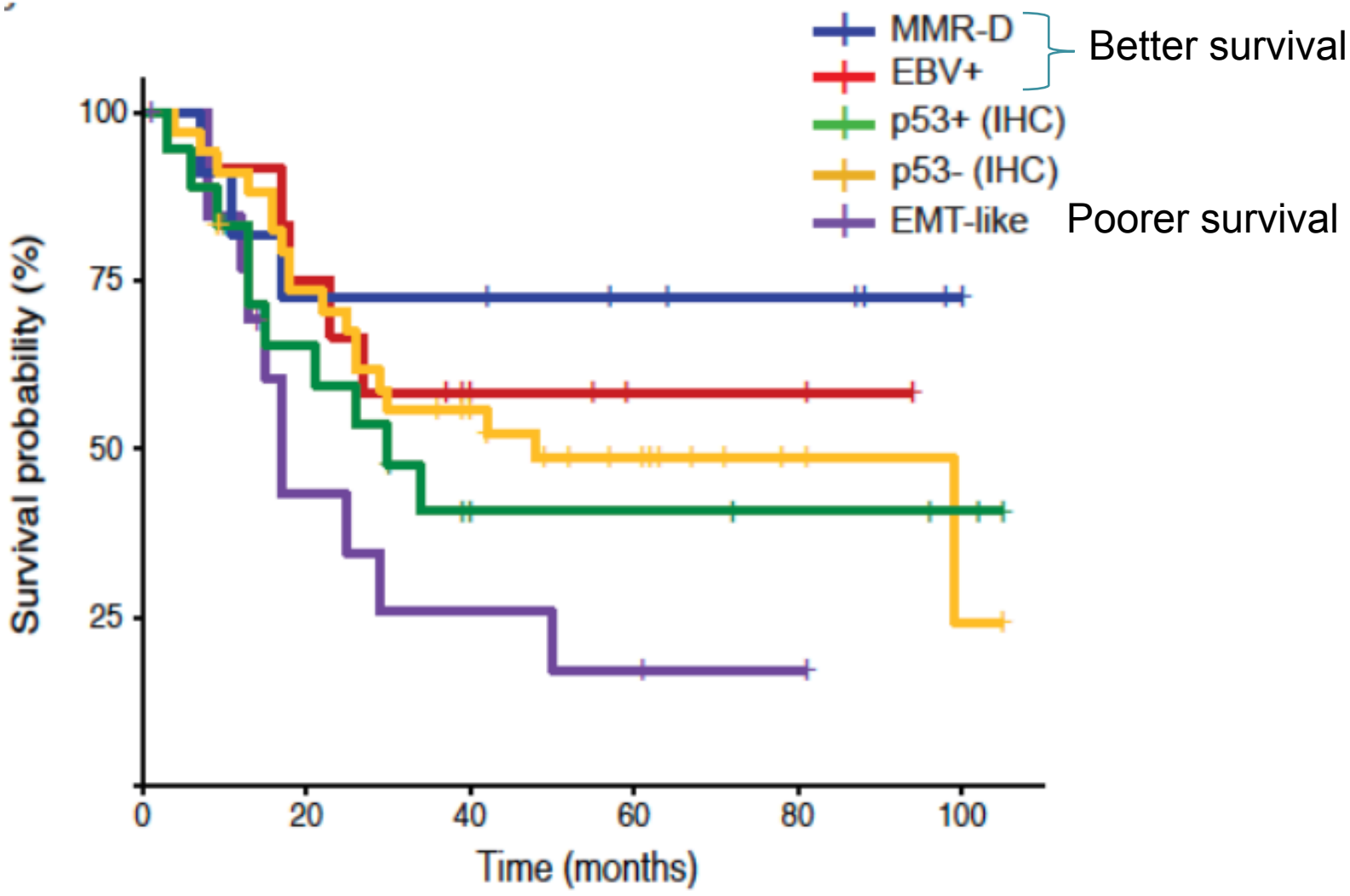
This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No GA825832



Pinto, M.P.; Córdova-Delgado, M.; Retamal, I…; Garrido, M. A Molecular Stratification of Chilean Gastric Cancer Patients with Potential Clinical Applicability. Cancers 2020, 12, 1863.

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No GA825832

Molecular subtypes correlate with survival



Pinto, M.P.; Córdova-Delgado, M.; Retamal, I…; Garrido, M. A Molecular Stratification of Chilean Gastric Cancer Patients with Potential Clinical Applicability. Cancers 2020, 12, 1863.

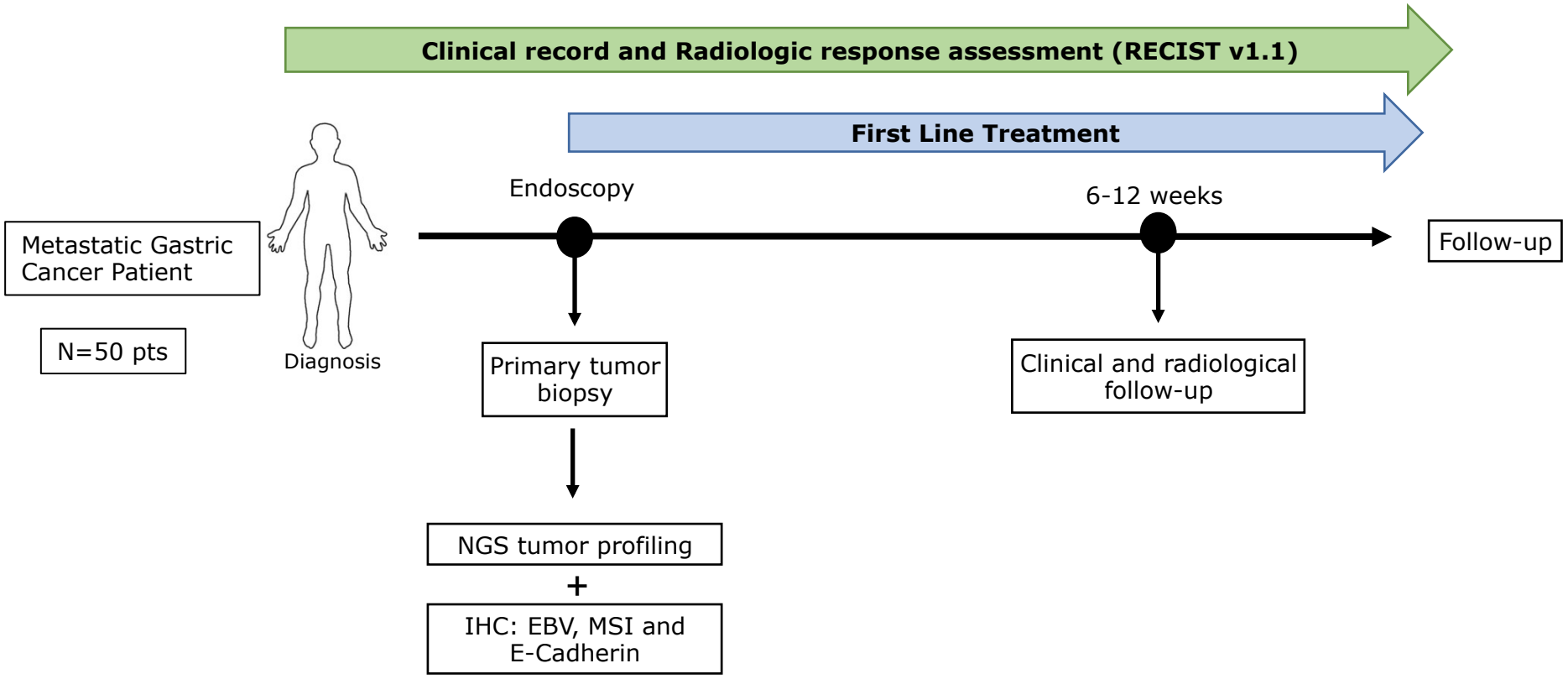
This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No GA825832

Distribution of GC subtypes

Pinto, M.P.; Córdova-Delgado, M.; Retamal, I…; Garrido, M. A Molecular Stratification of Chilean Gastric Cancer Patients with Potential Clinical Applicability. Cancers 2020, 12, 1863.

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No GA825832

Future challenges



This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No GA825832

Acknowledgements: Gastric Cancer Research Team

Clinical Trials Team

- María Fernanda Fernández, Study Coordinator
- Alejandra Daza, Study Coordinator
- Helda González, Study Coordinator
- Valentina Garate, Study Coordinator
- Bernardita Montt, Study Coordinator
- Liliana Bravo, Regulatory Affairs
- Lisseth Escobar, Study Coordinator
- Cesar Bravo, Study Coordinator
- Karla Ramos, Quality Control
- Daniela Araya, Data Entry
- Joyce Cisternas, Data Entry
- Yorkally Riquelme, Study Coordinator
- Gonzalo Peterli, Administrative Coordinator
- Valeska Borquez, Nurse Technician
- Francisco Gajardo, Administrative Coordinatur

GI Clinical Team

- Marcelo Garrido, GI Oncology
- Arnoldo Riquelme, Gastroenterology
- Allan Sharp, Digestive surgery

Biomarkers and Registry Team

- Ignacio Retamal, PhD Study Coordinator
- Francisco Villanueva, PhD Registry Coordinator
- Gareth Owen, PhD Chief Preclinical Lab
- Valentina Ortiz, Nurse Technician
- Margarita Pizarro, Biochemistry
- Matías Muñoz, Data Entry Senior
- Mauricio Pinto, PhD Protocol and Paper Writter
- María Loreto Bravo, PhD Study Coordinator

Diffussion and Project Manager Team

- Piga Fernandez, Patients Foundation
- EDUMED, Educational web resources
- Wladimir Flores, Project Manager in Oncology

Precision Oncology and Artificial Inteligence Team

- Nicolás Monge, MSc, innovation & AI Specialist
- Miguel Córdova, PhD Genomic and Ph specialist

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No GA825832

legacy

THANK YOU!!

2020 was crazy

Let’s hope 2021
Will bring

PEACE and
SANITY

This project has received funding from the European Union’s Horizon 2020 research and innovation programme under grant agreement No GA825832

legacy

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No GA825832

legacy

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No GA825832