GASTRO JournalClub

L'importanza della ricerca in Oncologia

10-11 OTTOBRE 2019 - ROMA

VOI Donna Camilla Savelli Hotel - Via Garibaldi, 27

MOLECULAR CHARACTERIZATION AND ITS CORRELATION TO CLINICAL OUTCOME IN ADVANCED GASTRIC CANCER: FROM BED TO BENCHSIDE

SALVATORE CORALLO

ISTITUTO NAZIONALE DEI TUMORI
MILANO

GASTRO JournalClub

THE UNMET NEED

BENCH

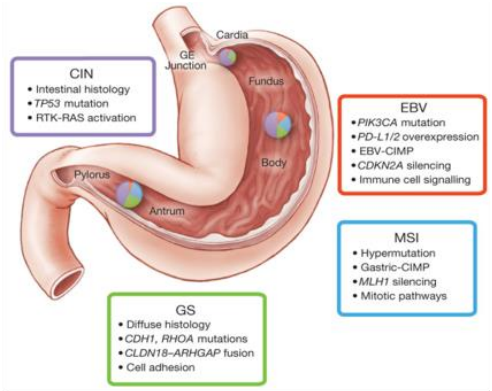
BEDSIDE

GASTRO JournalClub

Recent evolution of understanding the biology of gastroesophageal cancer

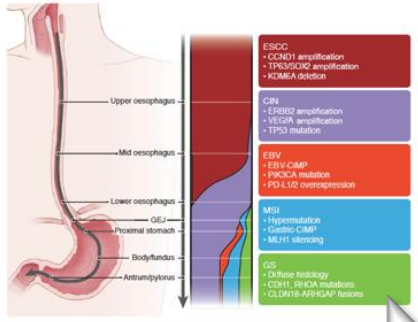
2011

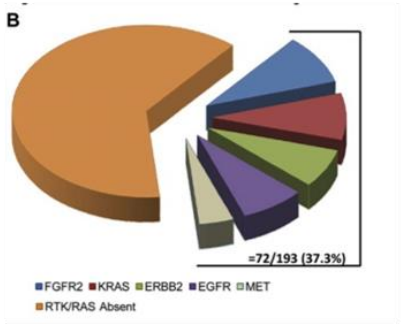
Identification of RTK amplification



2016

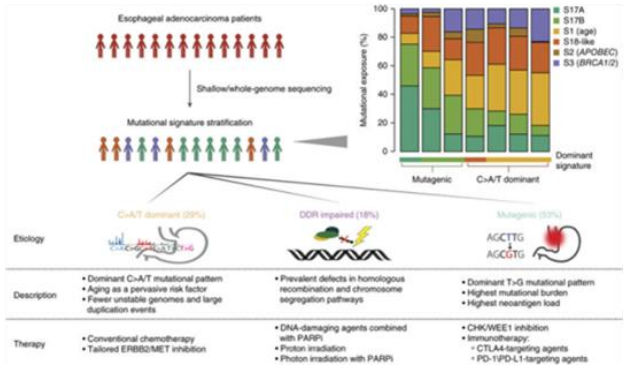
Subclassification of oesophageal adenocarcinoma





2014

Gastric cancer TCGA



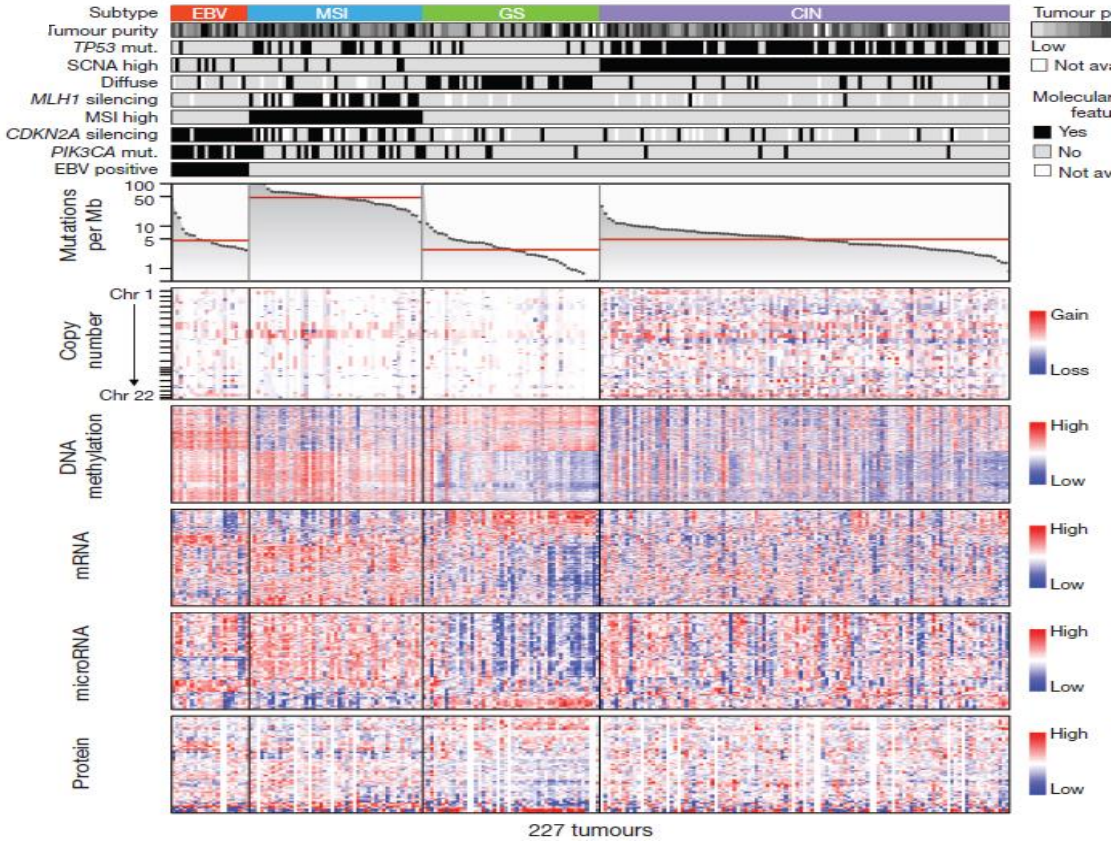
2017

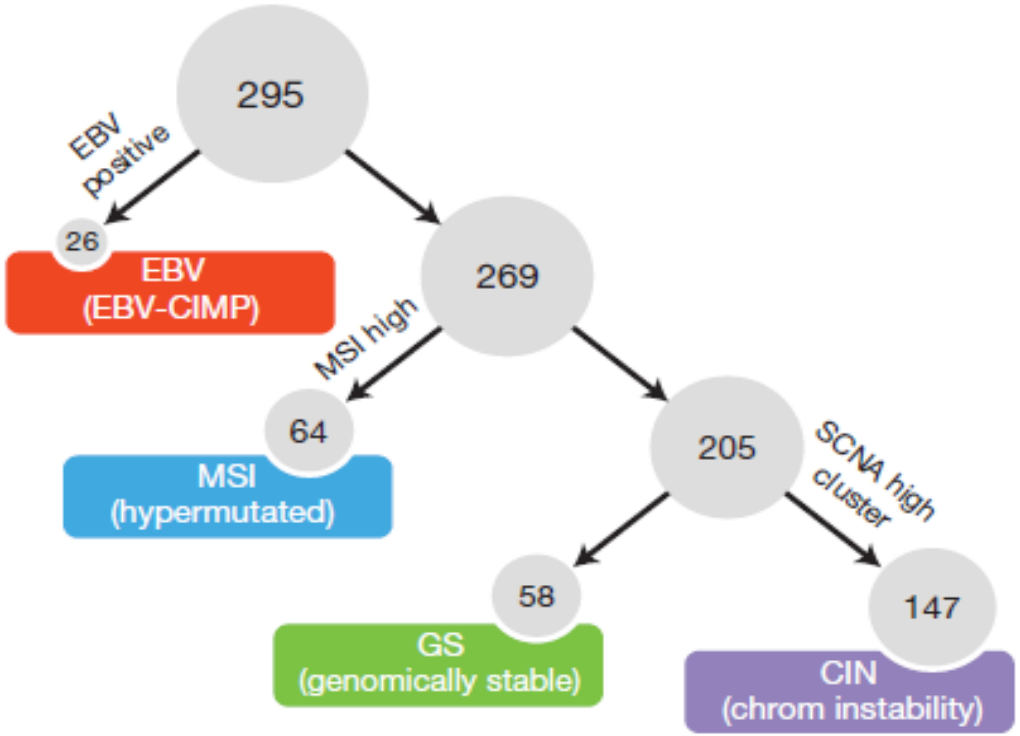
Oesophageal cancer TCGA

Deng et al, Gut 2011
Gastric Cancer TCGA, Nature 2014
Secrier et al, Nature Genetics 2016
Oesophageal Cancer TCGA, Nature 2017

GASTRO JournalClub

The TGCA classification: a Copernican Revolution?





The Cancer Genome Atlas Research Network, *Nature* 2014.

GASTRO JournalClub

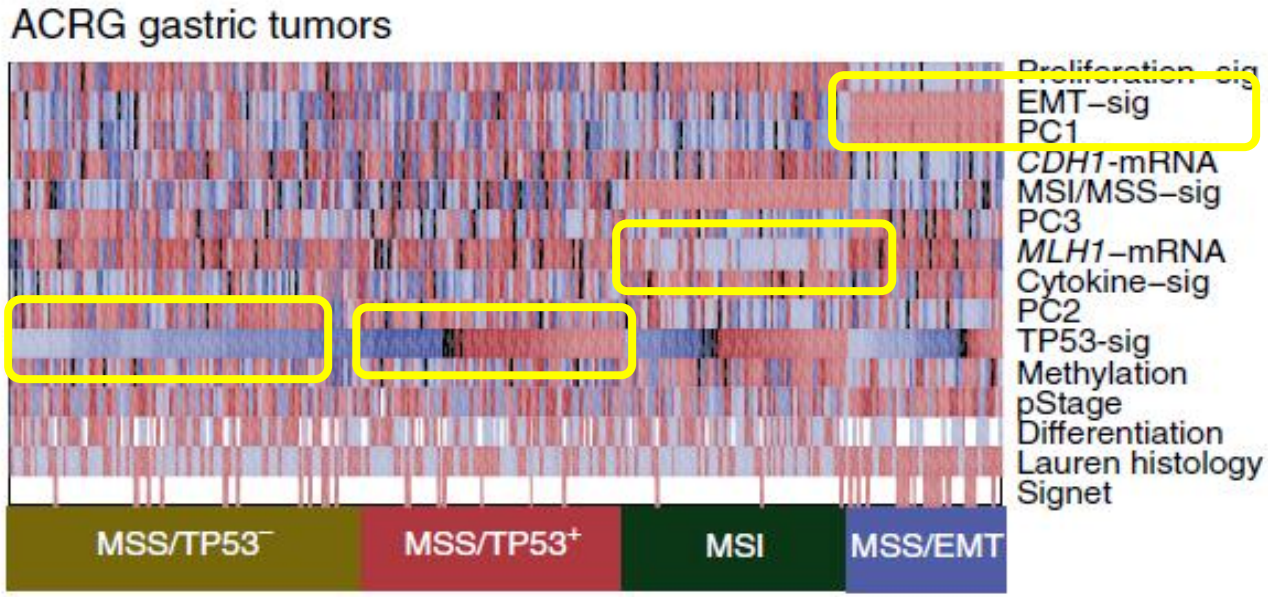
Limits of the TGCA classification

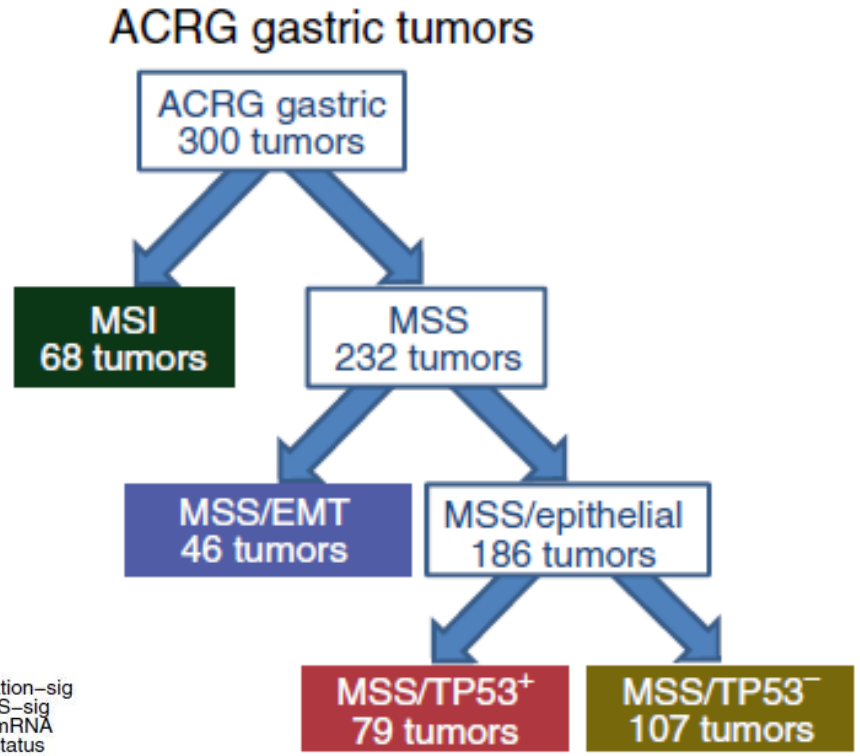
- Lack of prognostic/predictive impact (only few follow-up data from patient in the TGCA cohort are available)
- Uncertain applicability in the metastatic setting
- Low reproducibility in clinical practice (need of multple genomic and proteomic data sets).

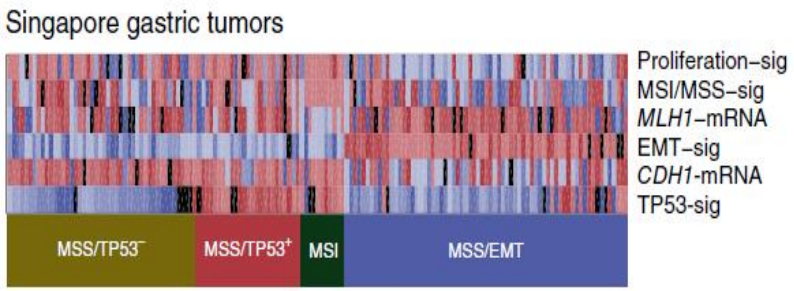
Overcoming the limits of the TGCA classification: the ACRG proposal

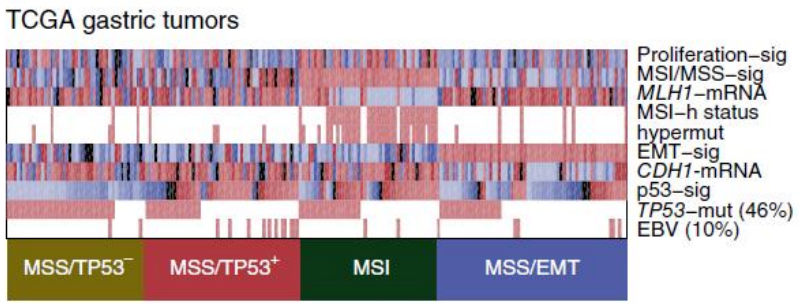
GASTRO JournalClub

The ACRG classification





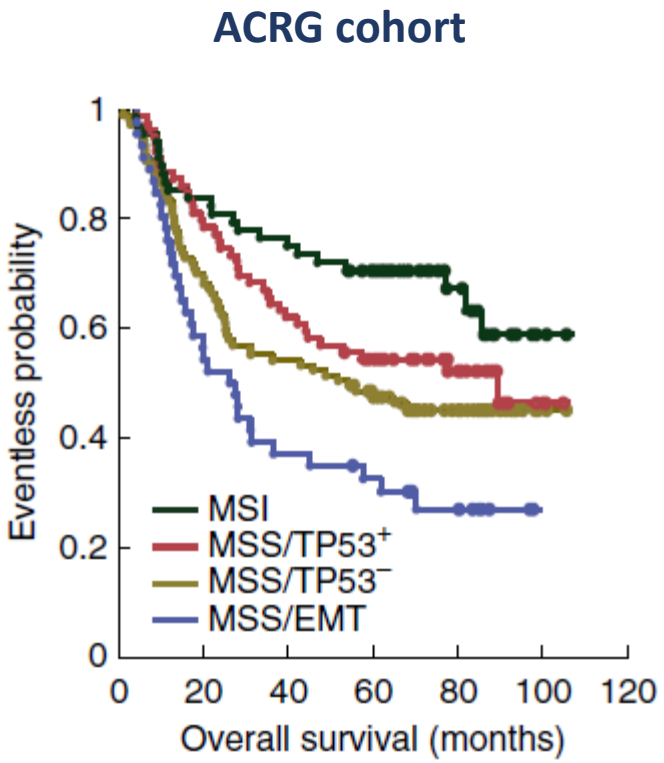


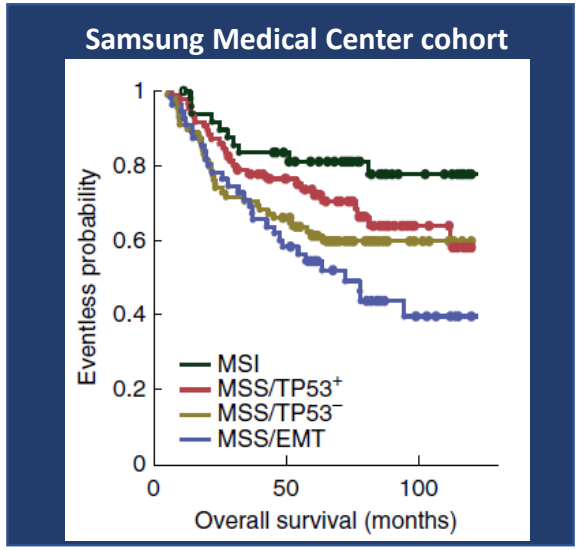


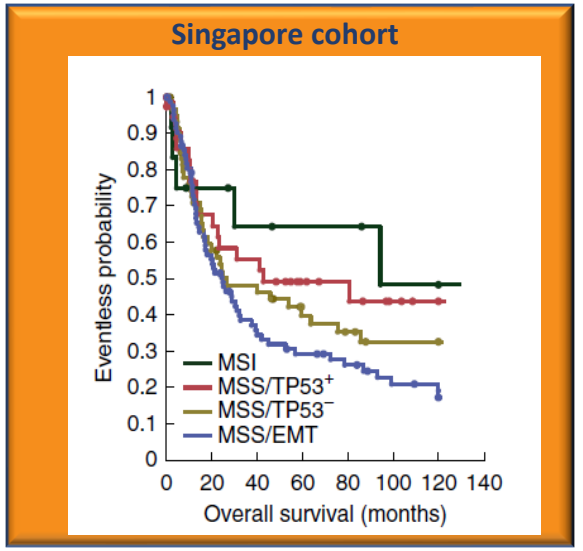
Cristescu R, *Nature Medicine* 2015.

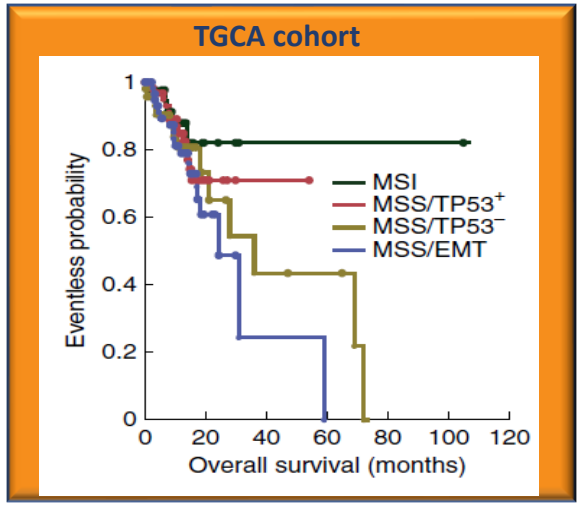
GASTRO JournalClub

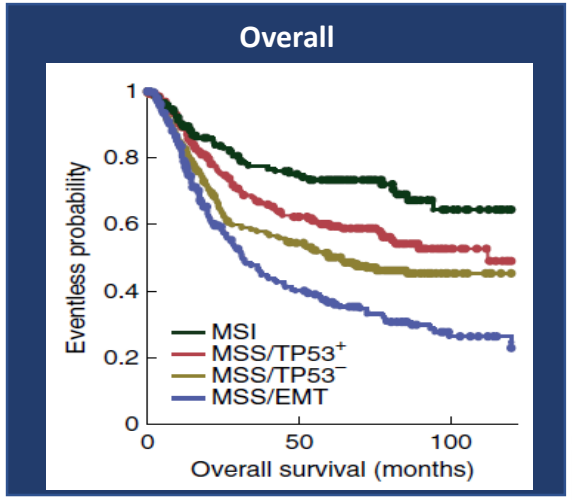
ACRG classification and its prognostic significance











Cristescu R, *Nature Medicine* 2015.

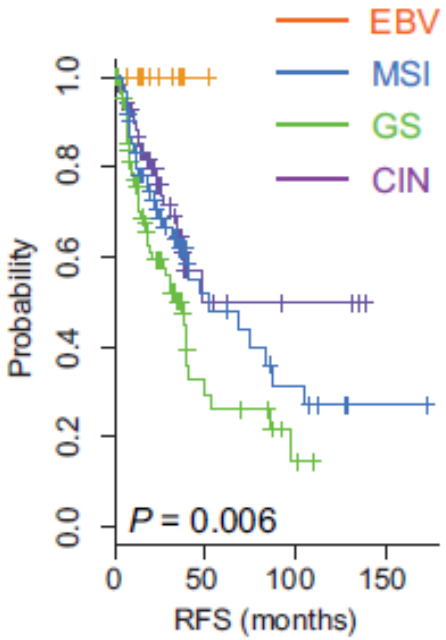
GASTRO JournalClub

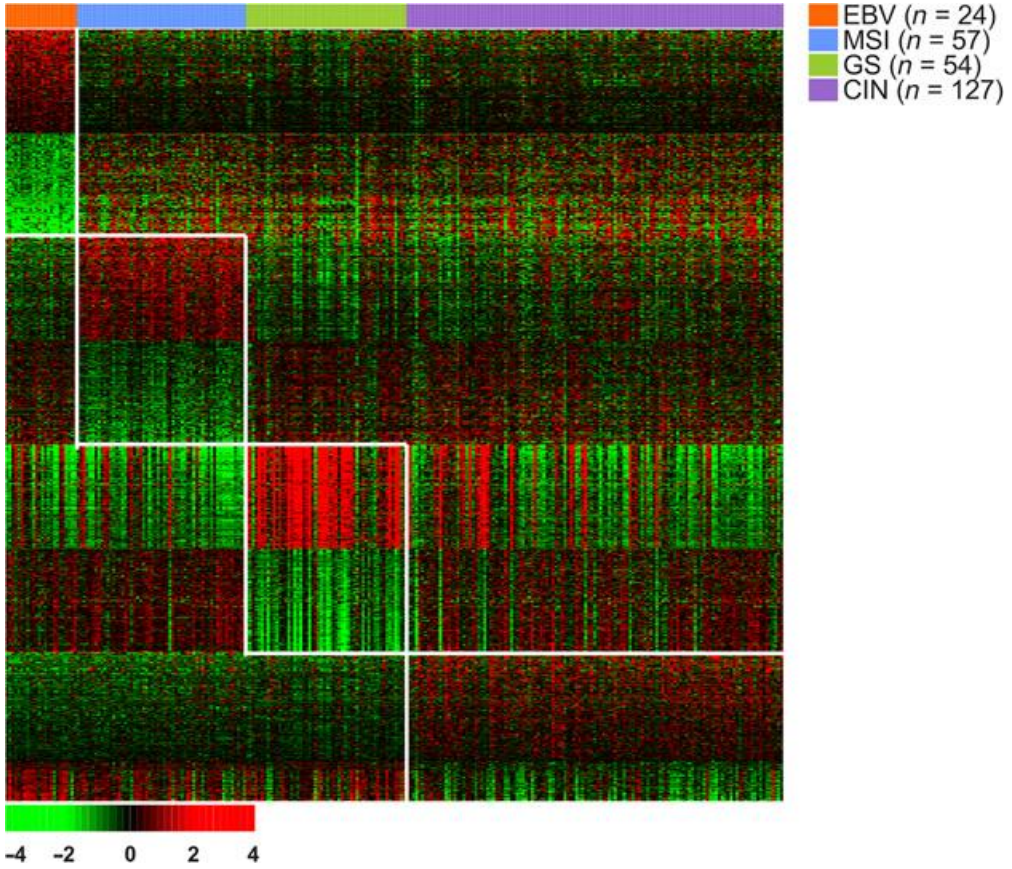
TGCA *vs* ACRG

GASTRO JournalClub

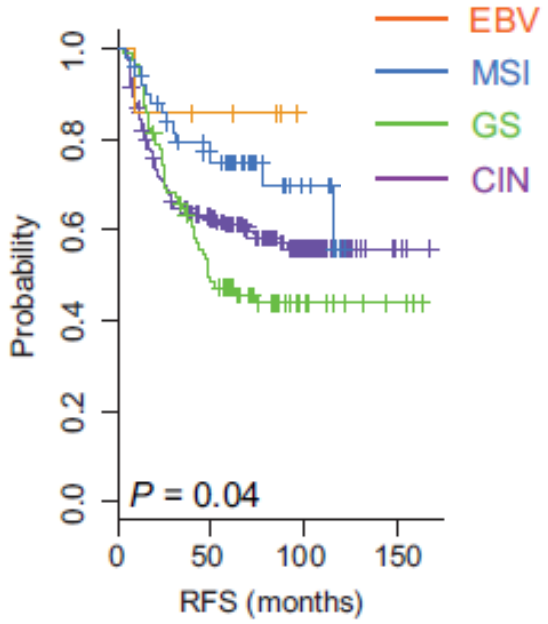
TGCA classification and its prognostic significance

MDACC





Samsung



Sohn et al, Clin Cancer Res, 2017; 23:4441

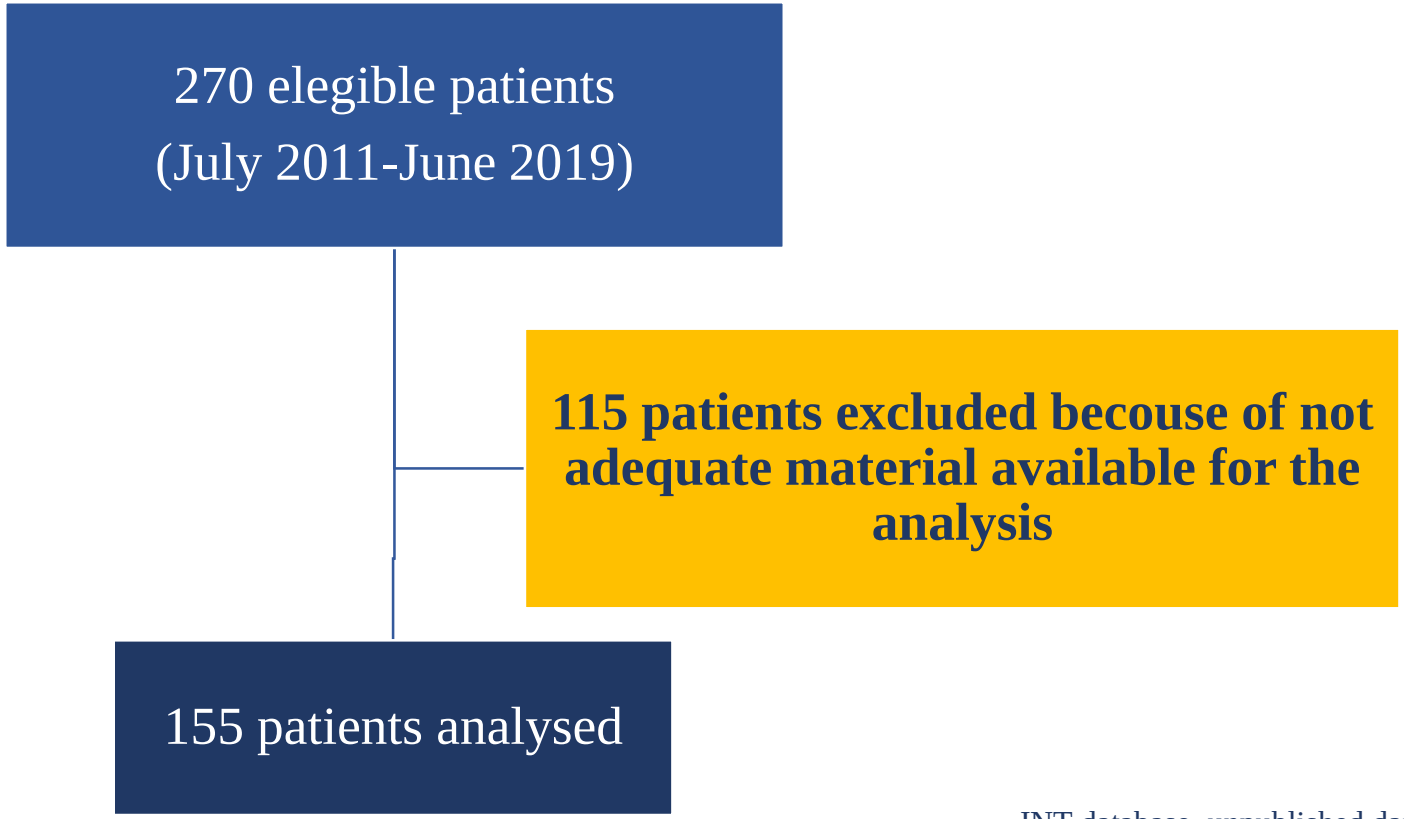
GASTRO JournalClub

Limits of the TGCA classification:

- Lack of prognostic/predictive impact (only few follow-up data from patient in the TGCA cohort are available)
- Uncertain applicability in the metastatic setting
- Low reproducibility in clinical practice (need of multple genomic and proteomic data sets).

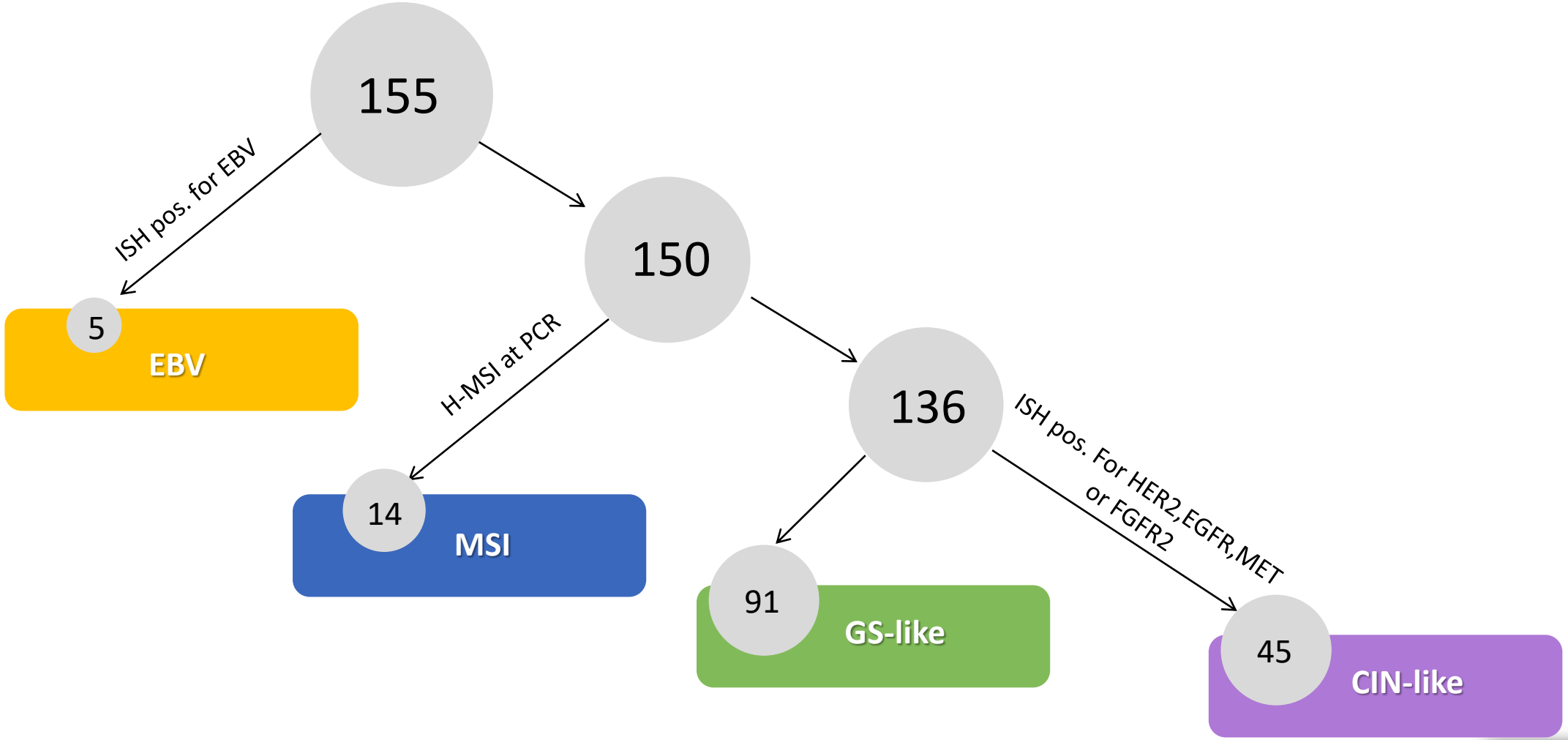
Study Design

Samples from metastatic GC patients were analysed via bright-field ISH for HER2/EGFR/FGFR2/MET amplifications and EBV infection and PCR for MSI.



INT database, unpublished data

Study Design: Methods

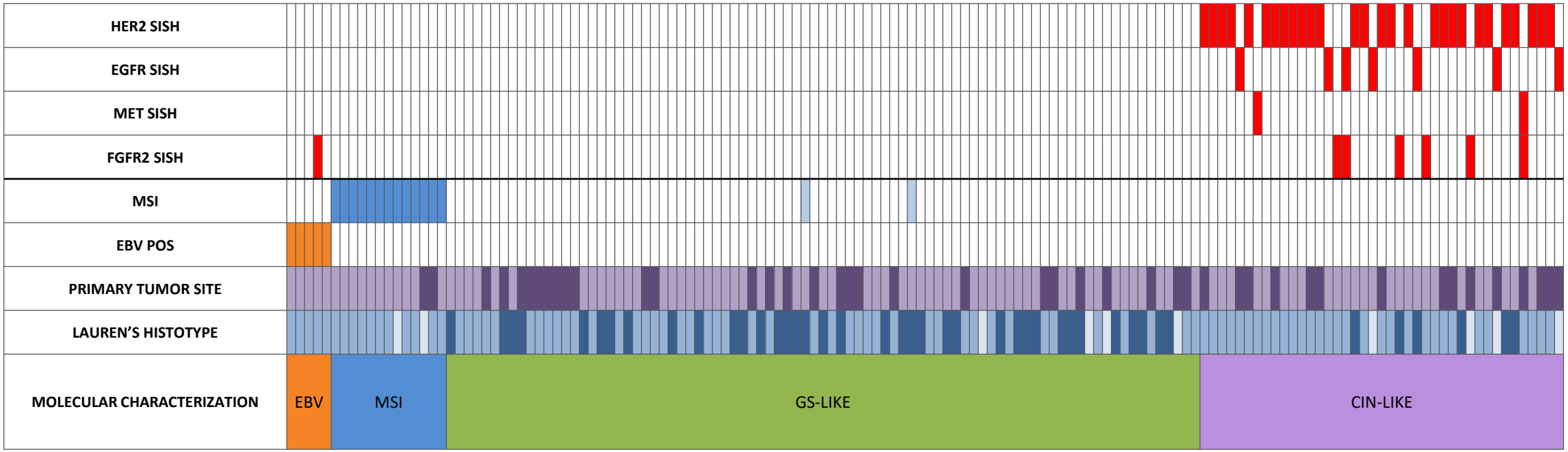


INT database, unpublished data

Patient Characteristics

Patient Characteristics	CIN-LIKE n=45 (29%)	GS-LIKE n=91 (58.7%)	MSI n=14 (9%)	EBV positie n=5 (3.2%)	Overall n=155(%)
Age, median (IQR)	60 (48-71)	62 (50-69)	66 (58-72)	68 (61-78)	62 (51-70)
< 65	28 (62.2)	36 (39.6)	6 (42.9)	1 (20)	90 (58)
≥ 65	17 (37.8)	55 (60.4)	8 (57.1)	4 (80)	65 (42)
Sex					
Male	30 (66.7)	55 (60.4)	7 (50)	4 (80)	96 (62)
Female	15 (33.3)	36 (39.6)	7 (50)	1 (20)	59 (38)
Site					
Gastro-oesophageal junction	16 (35.6)	29 (31.9)	2 (14.3)	0	47 (30)
Gastric body or antrum	29 (64.4)	62 (68.1)	12 (85.7)	5 (100)	108 (70)
Histotype					
Intestinal	35 (77.8)	47 (51.6)	12 (85.7)	4 (80)	98 (63.2)
Diffuse	7 (15.6)	40 (44.0)	0	0	47 (30.3)
Mixed	3 (0.6)	4 (4.4)	2 (14.3)	1 (20)	10 (6.5)
Metastatic disease at diagnosis					
Yes	34 (75.6)	75 (82.4)	10 (71.4)	4 (80)	123 (79.4)
Not	11 (24.4)	16 (17.6)	4 (28.6)	1 (20)	32 (20.6)
Site of metastases					
Liver metastases	20 (44.4)	21 (23.1)	1 (7.1)	0	42 (27.1)
Peritoneal metastases	16 (35.6)	47 (51.6)	8 (57.1)	3(60)	74 (47.7)

INT database, unpublished data-4449



Gene amplification

Gastroesophageal junction

Gastric body or antrum

Intestinal

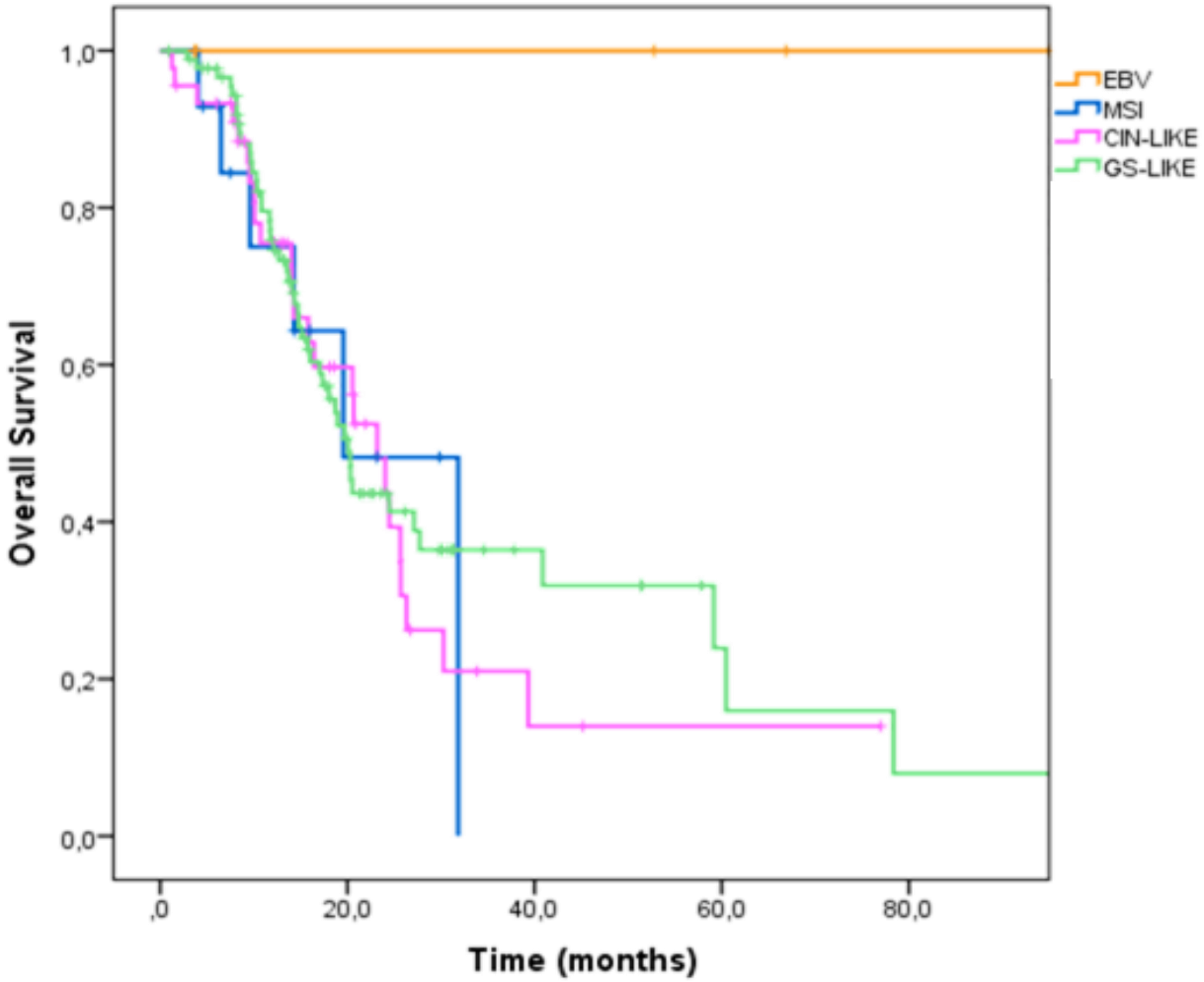
Mixed

Diffuse

INT database, unpublished data

GASTRO JournalClub

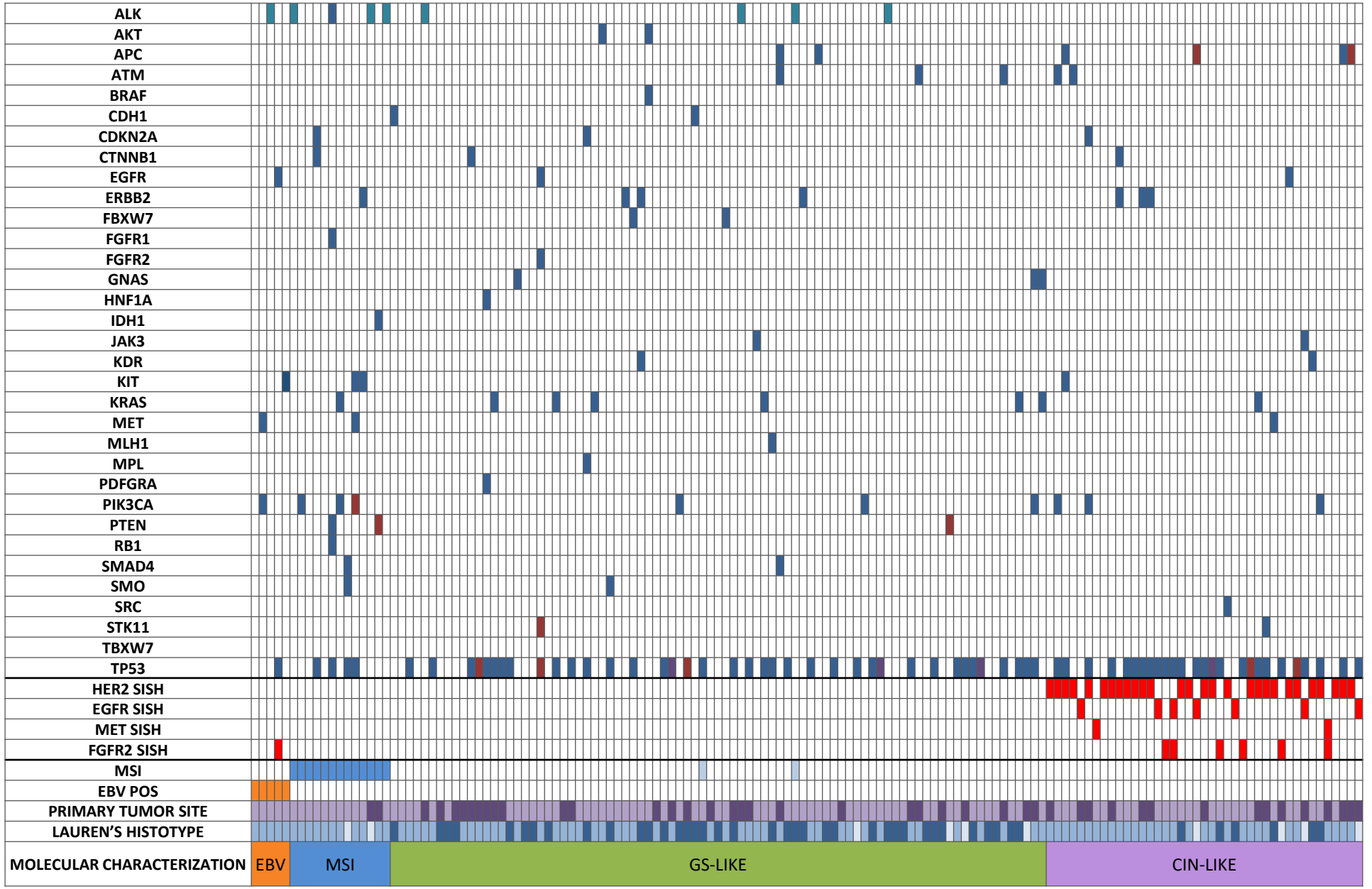
Survival Analysis



MOLECULAR SUBGROUPS	MEDIAN OS (MONTHS)
EBV	NR
MSI	31.8
CIN-LIKE	23.2
GS-LIKE	19.7
OVERALL	20.3
p value (Chi Square test): 0.2	

INT database, unpublished data

GASTRO JournalClub



INT database, unpublished data

GASTRO JournalClub

CONCLUSIONS

• Selected molecular alterations might be used to characterize in clinical practice GC patients identifying potentially targetable molecular alterations, subgroups of patients sensible to check-point inhibitors and EBV positive patients with good prognosis.

•Given their extraordinary sensibility to immuno-checkpoint inhibitors, the greater effort should be done to characterize MSI e EBV+ GC patients.

MOLECULAR CHARACTERIZATION AND ITS CORRELATION TO CLINICAL OUTCOME IN ADVANCED GASTRIC CANCER: FROM BED TO BENCHSIDE

salvatore.corallo@istitutotumori.mi.it

GASTRO JournalClub