PROGRAMA

Digestivo

– No colorrectal –

20 JUNIO 2024

XVII JORNADAS ONCOLÓGICAS

ARAGÓN · NAVARRA · RIOJA

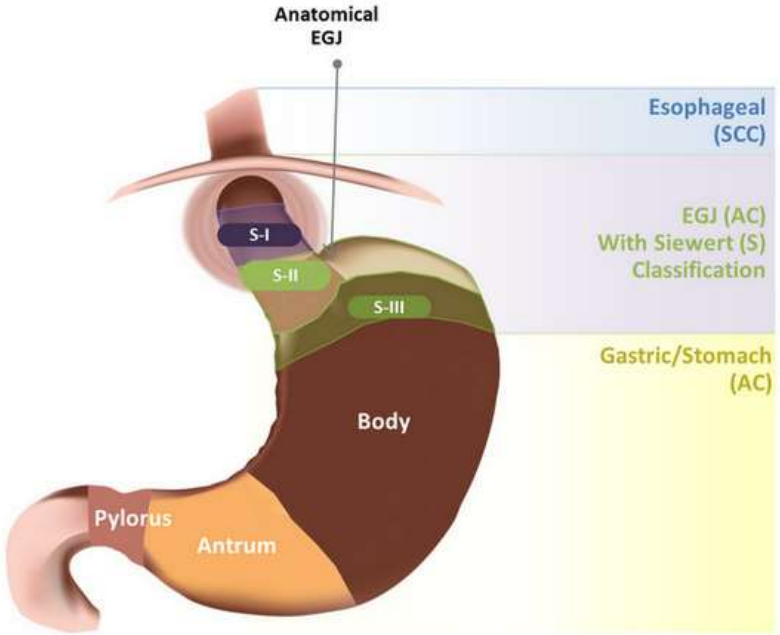
Dr. Alfonso Martín Carnicero

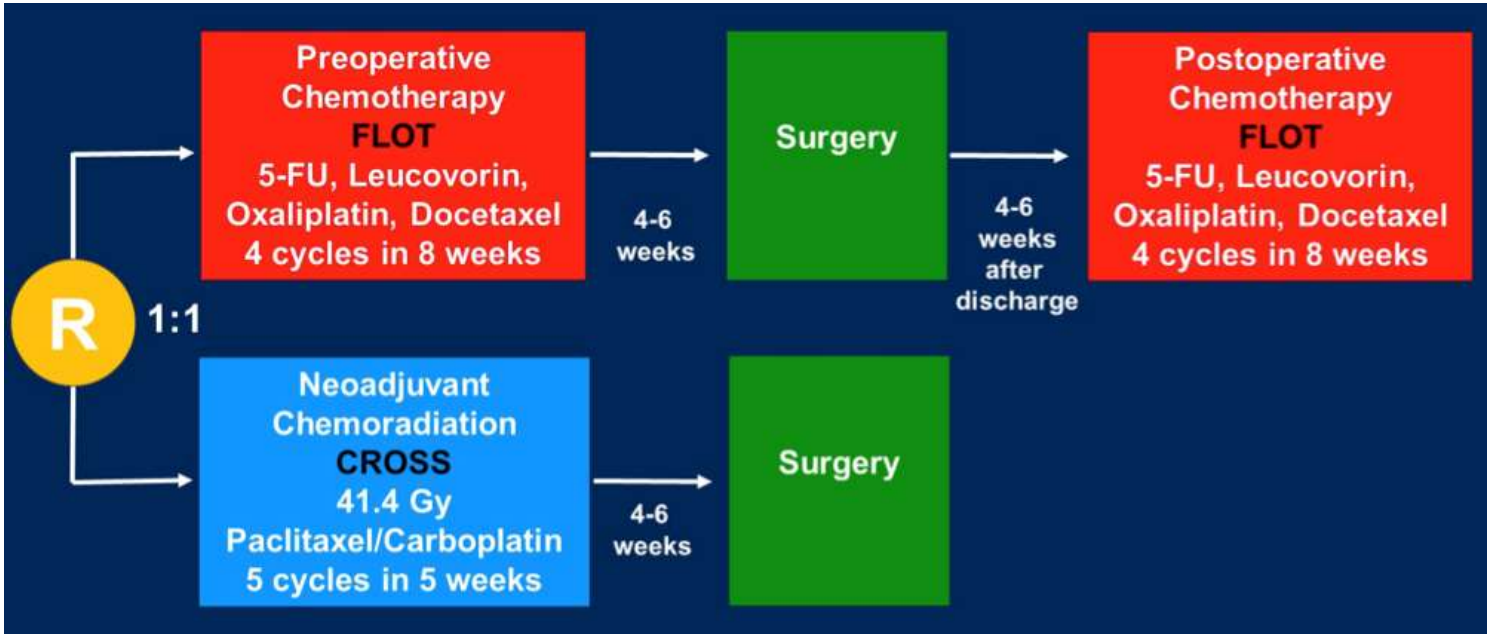
Hospital San Pedro. Logroño

Plenary Session

- **LBA1**. Prospective randomized multicenter phase III trial comparing perioperative chemotherapy (FLOT protocol) to neoadjuvant chemoradiation (CROSS protocol) in patients with adenocarcinoma of the esophagus (ESOPEC trial).

Gastroesophageal Carcinoma





Primary Endpoint

- Overall survival (OS)

Secondary Endpoints

- Progression free survival (PFS)
- Postoperative pathological stage
- Postoperative complications
- Adverse events
- Recurrence free survival
- Site of tumor recurrence
- Quality of life

Inclusion Criteria

- Histology: Adenocarcinoma
- Esophageal cancer according UICC (TNM7)[1,*]
- Clinical stage cT1N+ or cT2-4a, cN0/+, cM0

Exclusion Criteria

- Squamous or other non-adenocarcinoma histology
- Gastric cancer
- Clinical Stage cT1cN0 and cT4b
- Metastatic disease

Intention to treat (ITT) analysis of overall survival (primary endpoint) in all randomized patients

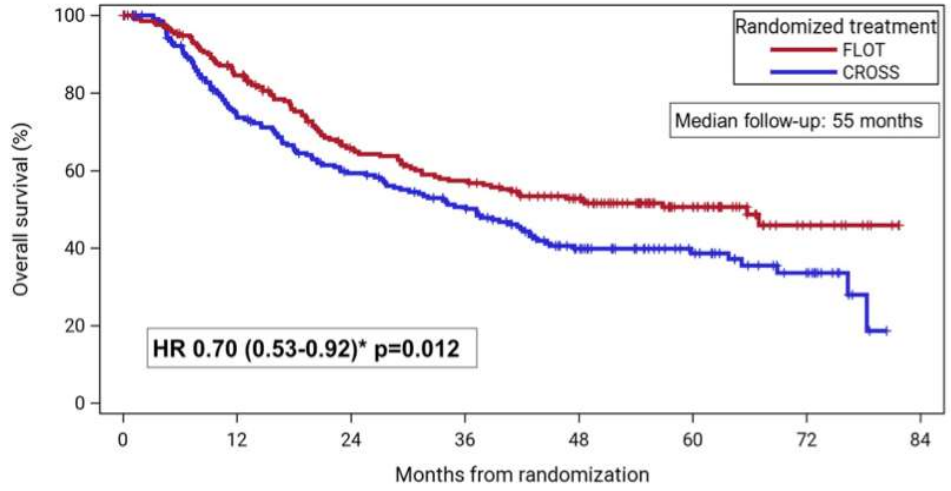
Assumptions on 3-year overall survival rates:
CROSS 55%, FLOT 68% (hazard ratio 0.645)

Characteristics of ESOPEC Trial Patients

	FLOT	CROSS
N	221	217
Age mean	63,1	62,6
Sex male	89,1%	89,4%
ECOG >0	26,7%	28,1%
Clinical T – Stage		
cT1 – 2	19,5%	17,1%
cT3 – 4	79,1%	81,9%
Clinical N – Stage		
cN0	22,2%	18,4%
cN+	77,8%	81,6%

Treatment Exposure

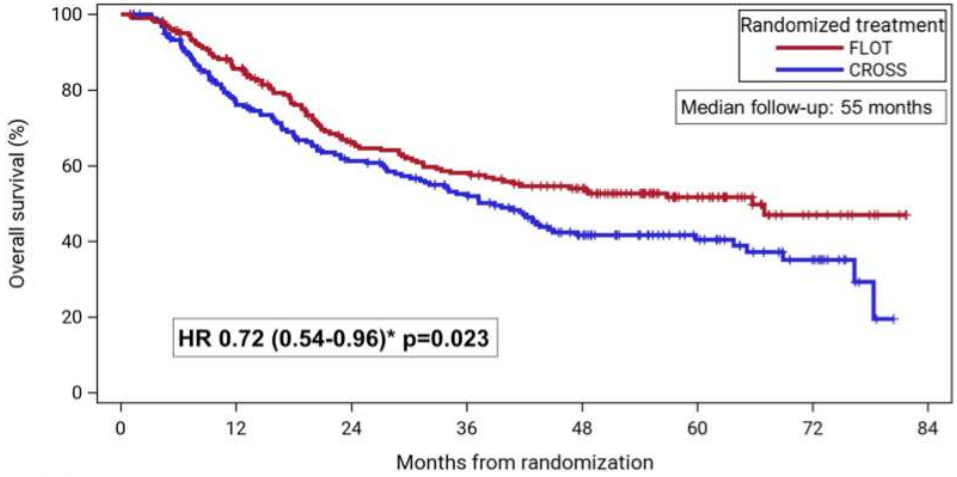
	FLOT Group	CROSS Group
N	221	217
Started neoadjuvant treatment (PP population*)	93.7 %	90.3 %
Completed neoadjuvant treatment	87.3 %	67.7 %#
Received neoadjuvant treatment plus surgery	86.0 %	82.9 %
Received adjuvant treatment	63.3 %	
Completed adjuvant treatment	52.5 %	



	FLOT	CROSS
Events	97	121
Median OS	66	35
3y OS Rate	57,4%	50,7%
5y OS Rate	50,6%	38,7%

Overall Survival

ITT

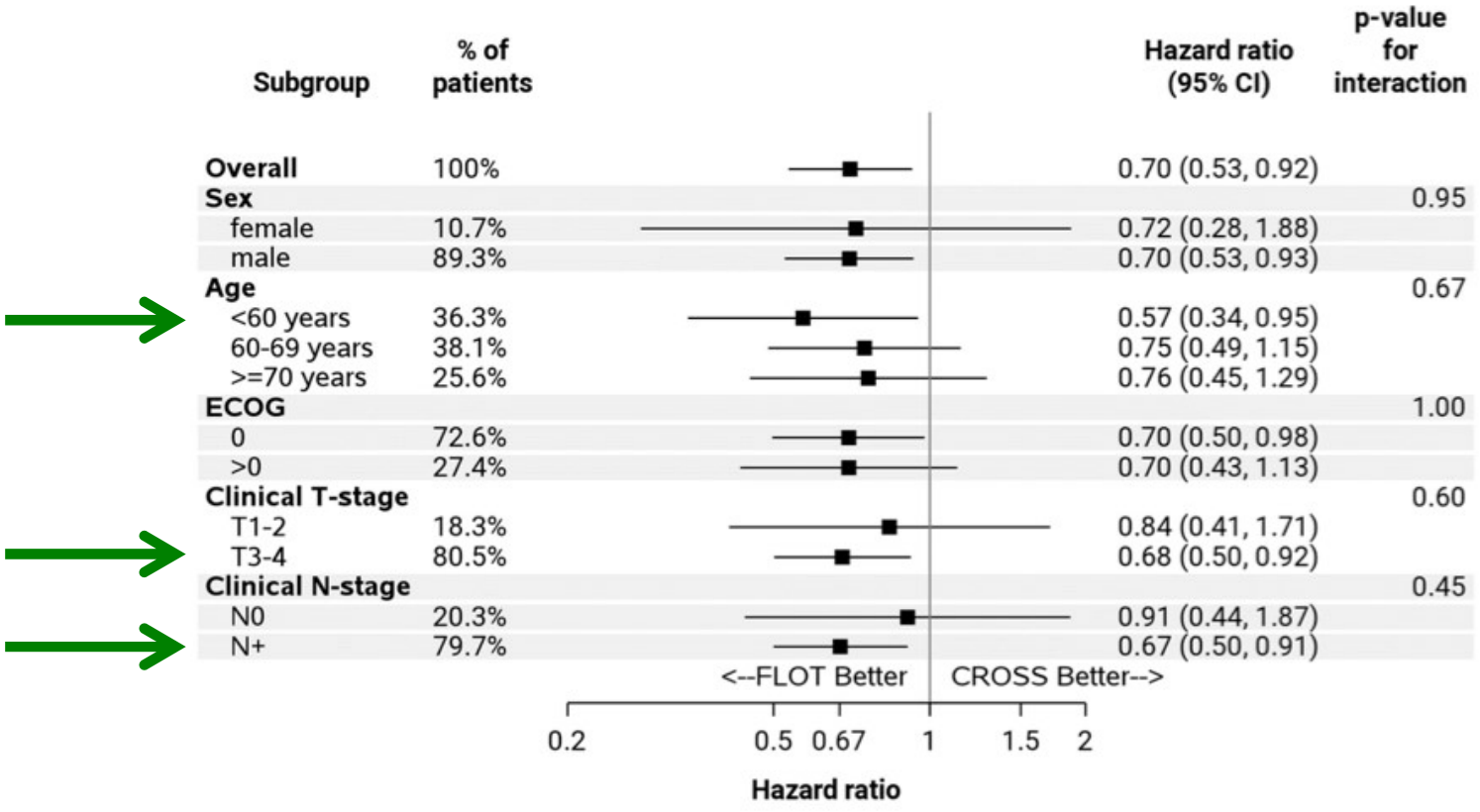


	FLOT	CROSS
Events	92	110
Median OS	66	39
3y OS Rate	58,1%	52,6%
5y OS Rate	51,8%	40,5%

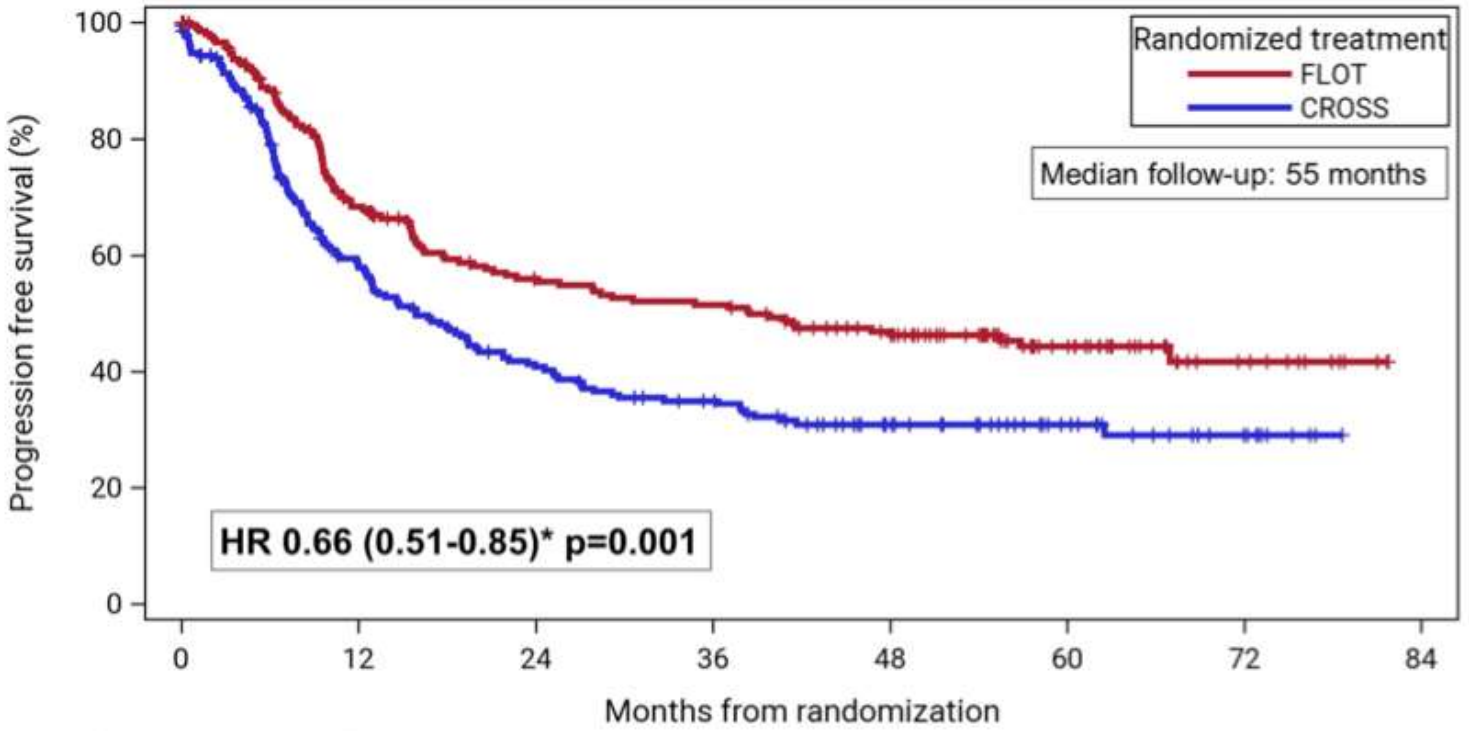
Overall Survival

PP

Overall Survival in Exploratory Subgroups



Progression Free Survival – ITT Population

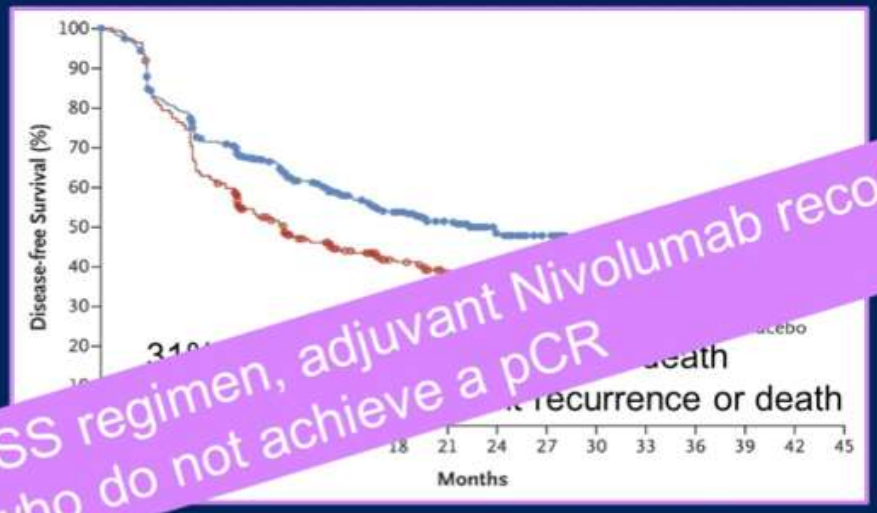


	FLOT	CROSS
Events	107	137
Median PFS	38	16
3y PFS Rate	51,6%	35%
5y PFS Rate	44,4%	30,9%

Pathology Results– Surgery Population	FLOT Group	CROSS Group
N	191	180
Resection status		
No resection	0.5%	1.1%
R0	94.2%	95.0%
R1	5.2%	3.9%
Postoperative N-Stage		
ypN-	50.8%	54.4%
ypN+	48.7%	44.4%
Pathological complete remission		
ypT0 ypN0	16.8%	10.0%
Tumor regression grade (Becker[1])		
Complete regression	18.3%	13.3%
Near complete regression (<10% vital tumor)	25.1%	39.4%

	ESOPEC Trial				
	FLOT Group	CROSS Group	CROSS Trial (CRT Group - AC)	Neo-AEGIS Trial (CRT Group)	FLOT-4 (FLOT Group)
Completed **pre-op** treatment	87.3%	**67.7%**	92%	87% (RT - 99%)	90%
Completed **post-op** treatment	52.5%				46%
pCR	16.8%	**10%**	23%	12%	16%
Median OS	66 mos	**39 mos**	43 mos	49 mos	50 mos
3-year OS	57.4%	50.7%	54%	57%	57%

CheckMate 577 Trial: Adjuvant Immunotherapy



If using CROSS regimen, adjuvant Nivolumab recommended for patients who do not achieve a pCR

DFS	Nivo	Placebo	HR
Median DFS	**22.4 mos**	11 mos	0.69
Median DFS (AC)	**19.4 mos**	11.1 mos	0.75
3-year DFS (AC)	**44%**	32%	

Kelly RJ, N Engl J Med, 2021

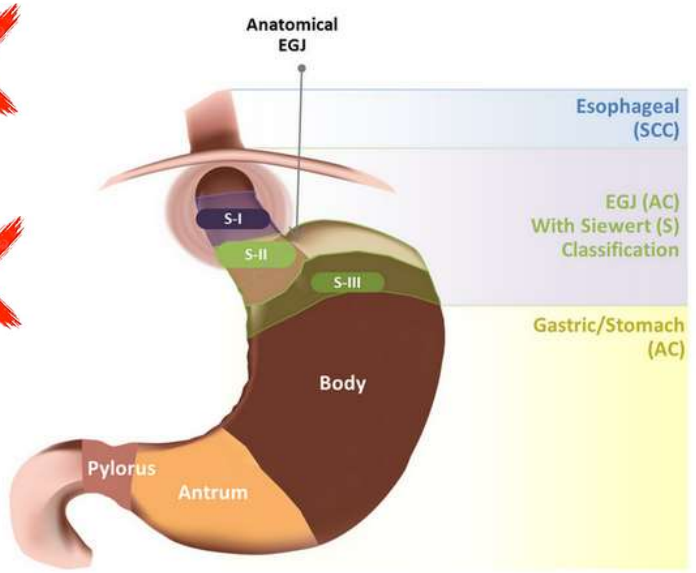
Oral Abstract Session

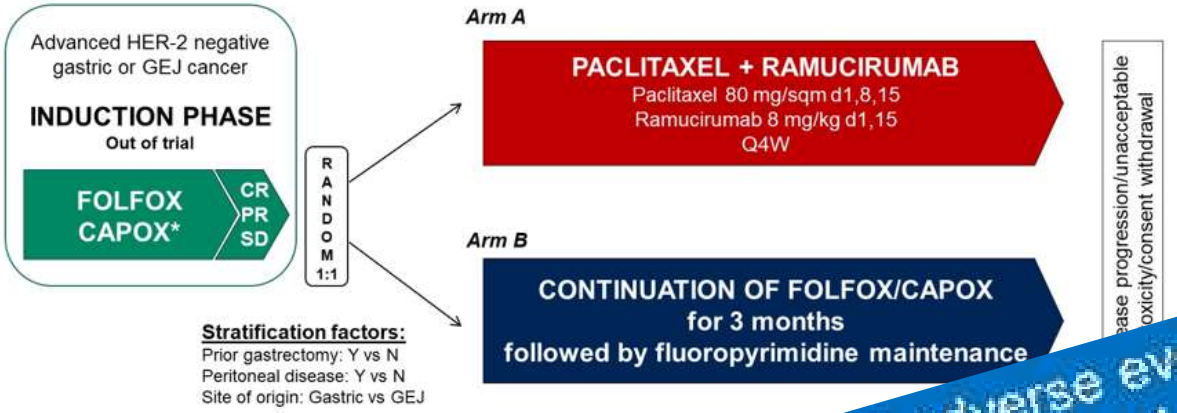
Gastroesophageal Carcinoma

- **4000**. A phase II/III study of peri-operative nivolumab and ipilimumab in patients with locoregional esophageal and GEJ adenocarcinoma: Results of the neoadjuvant pathologic complete response rate (ECOG-ACRIN EA2174).

- **4001**. Effect of Chemotherapy/targeted therapy alone vs. Chemotherapy/targeted therapy followed by radical surgical resection on survival and QoL in patients with limited-metastatic ADC of the stomach or EGJ: The IKF-575/RENAISSANCE phase III trial.

- **4002**. Ramucirumab plus paclitaxel as switch maintenance versus continuation of oxaliplatin-based chemotherapy in patients with advanced HER2-negative gastric or GEJ cancer: The ARMANI phase III trial.

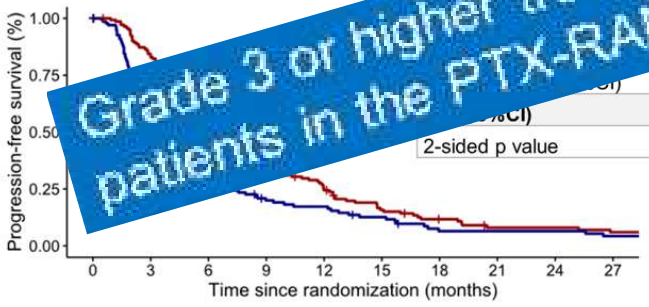




	Arm A n=95[a]	Arm B n=102[a]
ORR, %	18.9	15.7
DCR, %		
CR		(12.8%)
	%)	39 (38.2%)
	9 (**9.5%**)	33 (**32.3%**)
	5 (5.3%)	14 (13.7%)

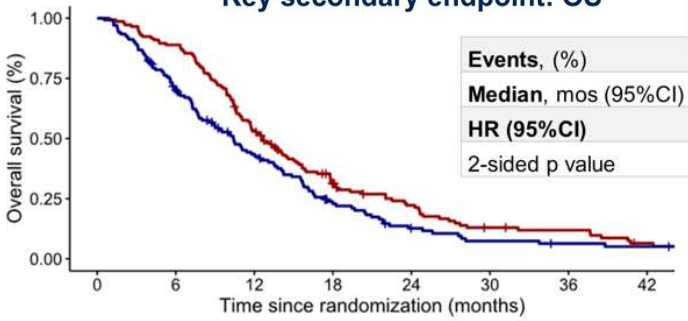
Grade 3 or higher treatment-related adverse events were observed in 40.4% of patients in the PTX-RAM arm versus 20.7% of patients in the FOLFOX/CAPOX arm

Primary endpoint: PFS



		X/CAPOX) n=136
	%	90%
	6.6 (6.0-7.8)	**3.5** (2.8-4.2)
%CI)	**0.64 (0.49-0.81)**	
2-sided p value	**P<0.001**	

Key secondary endpoint: OS



	Arm A (PTX-RAM) n=144	Arm B (FOLFOX/CAPOX) n=136
Events, (%)	86%	85%
Median, mos (95%CI)	**12.6** (11.5-15.0)	**10.4** (8.0-13.1)
HR (95%CI)	**0.75 (0.58-0.97)**	
2-sided p value	**P=0.028**	

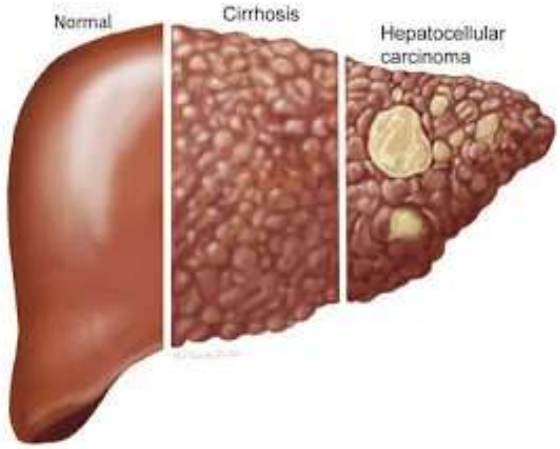
Oral Abstract Session

Hepatobiliary Carcinoma

- **4006**. A Addition of stereotactic body radiotherapy (SBRT) to systemic chemotherapy in locally advanced cholangiocarcinoma (ABC-07): Results from a randomized phase II trial.

- **4007**. International, open-label phase 2 study of regorafenib plus pembrolizumab in patients with advanced hepatocellular carcinoma (HCC) previously treated with immune checkpoint inhibitors (ICI).

- **4008**. Nivolumab plus ipilimumab vs lenvatinib or sorafenib as first-line treatment for unresectable HCC: First results from CheckMate 9DW.



Key eligibility criteria
- Unresectable HCC[b]
- At least 1 measurable lesion (RECIST v1.1)
- Systemic therapy naive
- Child-Pugh score 5 or 6
- ECOG PS 0 or 1
- No main portal vein invasion (Vp4)

Stratification factors:
- Etiology (HBV vs HCV vs uninfected)[c]
- MVI/EHS (present vs absent)
- AFP (< 400 vs ≥ 400 ng/mL)

N = 668, R 1:1

- n = 335: NIVO 1 mg/kg IV + IPI 3 mg/kg IV Q3W (up to 4 cycles) then NIVO 480 mg Q4W[d]
- n = 333: Investigator's choice of LEN 8 mg[e] or 12 mg[f] PO QD or SOR 400 mg PO BID

Treatment until disease progression, unacceptable toxicity, withdrawal of consent (all arms), or a maximum treatment duration of 2 years (NIVO + IPI arm only)

Among 325 patients treated with LEN/SOR: 275 (85%) received LEN and 50 (15%) received SOR

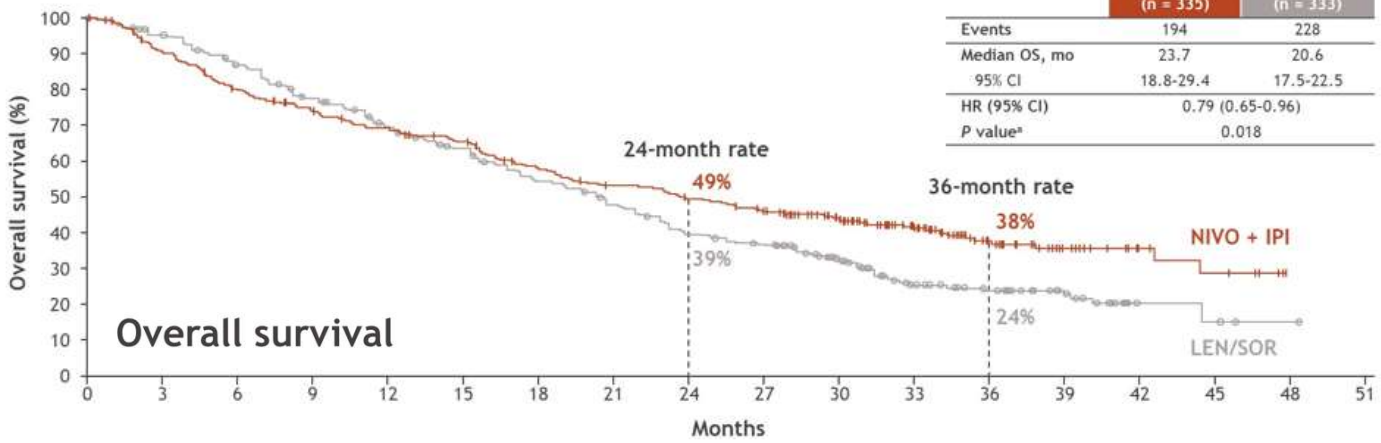
Primary endpoint:
- OS

Secondary endpoints:
- ORR and DOR by BICR per RECIST v1.1
- Time to symptom deterioration[g]

Key exploratory endpoints:
- PFS by BICR per RECIST v1.1
- Safety

Progression-free survival	NIVO + IPI (n = 335)	LEN/SOR (n = 333)
Events	219	215
Median PFS,[a] mo	9.1	9.2
95% CI	6.6-10.5	7.9-11.1
HR (95% CI)	0.87 (0.72-1.06)	

Duration of response	NIVO + IPI (n = 121)[d]	LEN/SOR (n = 44)[d]
Events	48	22
Median DOR,[a] mo	30.4	12.9
95% CI	21.2-NE	10.2-31.2



	NIVO + IPI (n = 335)	LEN/SOR (n = 333)
Events	194	228
Median OS, mo	23.7	20.6
95% CI	18.8-29.4	17.5-22.5
HR (95% CI)	0.79 (0.65-0.96)	
P value[a]	0.018	

	NIVO + IPI (n = 335)	LEN/SOR (n = 333)
ORR,[a] %	36	13
95% CI	31-42	10-17
P value[b]	< 0.0001	
Best overall response,[a] %		
Complete response	7	2
Partial response	29	11
Stable disease[c]	32	62
Progressive disease	20	14
Not evaluable	12	11
Median TTR (range),[a] mo	2.2 (1.1-11.6)	3.7 (0.6-11.2)

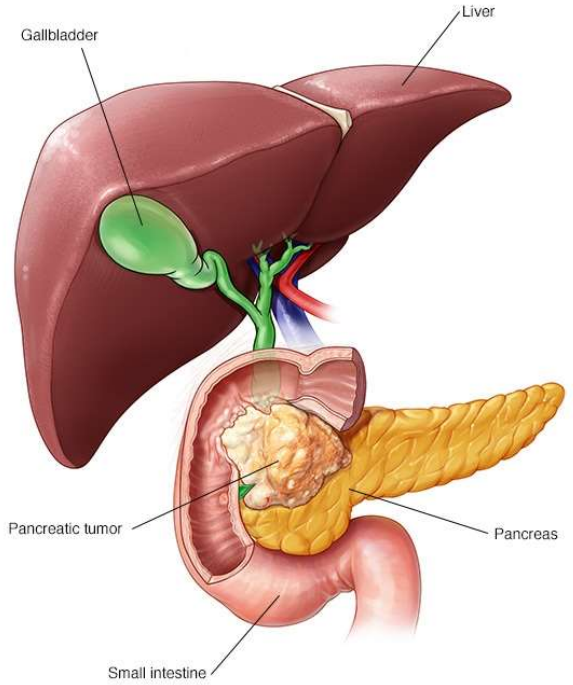
Oral Abstract Session

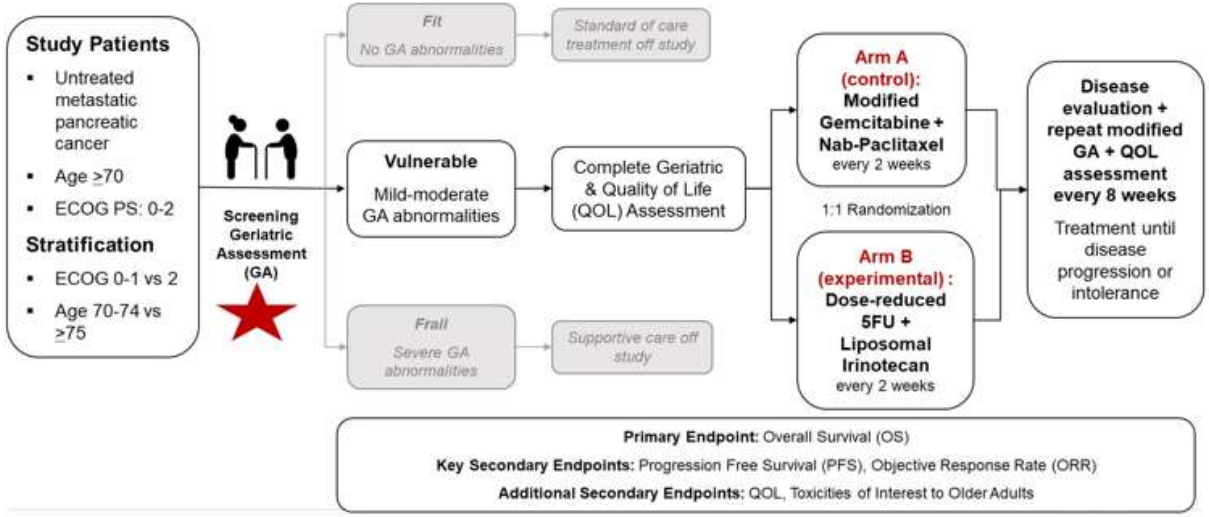
- **4003**. A randomized phase II study of gemcitabine and nab-paclitaxel compared with 5- fluorouracil, leucovorin, and liposomal irinotecan in older patients with treatment- näıve metastatic pancreatic cancer (GIANT): ECOG-ACRIN EA2186.

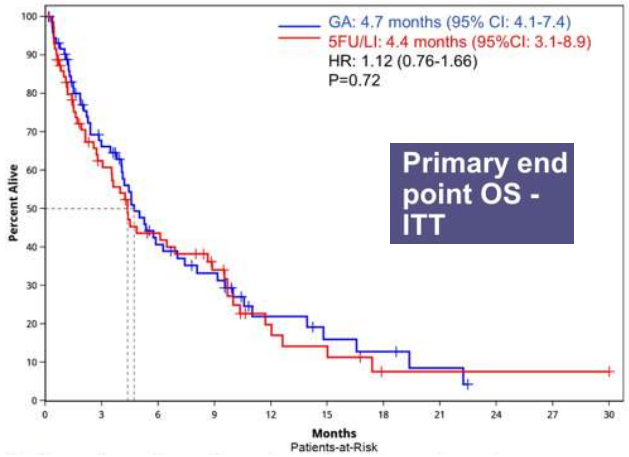
- **4004.** Early results of the PASS-01 trial: Pancreatic adenocarcinoma signature stratification for treatment-01.

- **4005**. NRG Oncology/RTOG 0848: Results after adjuvant chemotherapy +/- chemoradiation for patients with resected periampullary pancreatic adenocarcinoma (PA).

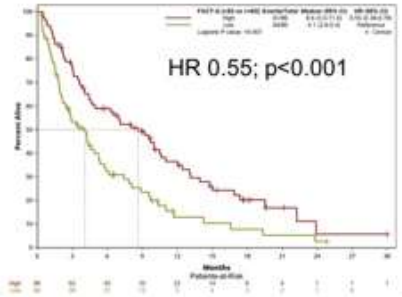
Pancreatic Carcinoma



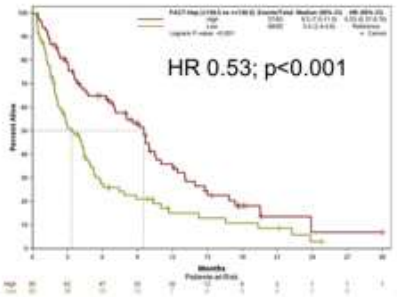




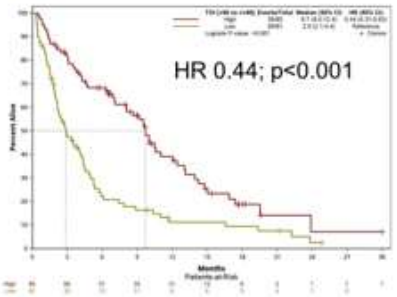
FACT- G

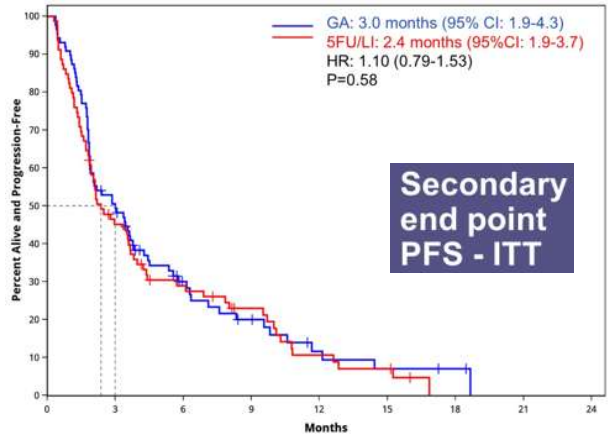


FACT- Hep 4



Physical/Functional well being





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Organizador:
Fundación Biomédica Miguel Servet

Patients with resected pancreatic head adenocarcinomas

REGISTER

FIRST STEP: ADJUVANT SYSTEMIC TREATMENT*

Arm 1:
Gemcitabine alone

Arm 2:
Gemcitabine + Erlotinib x 5 cycles (Arm 2 closed to accrual effective 4/02/14)

REASSESS AND IF NO PROGRESSION, THEN:

STRATIFY

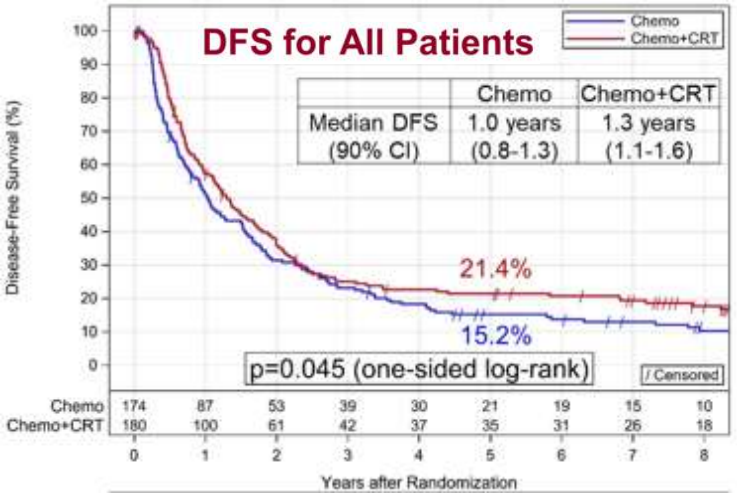
Nodal Status:
1: involved
2: uninvolved
CA19-9 result:
1: ≤ 90
2: > 90 – 180
Surgical margins:
1: positive (R1)
2: negative (R0)
Adjuvant Systemic Treatment:
1. Gemcitabine alone
2. FOLFIRINOX or mFOLFIRINOX
3. Non-oxaliplatin gemcitabine combinations

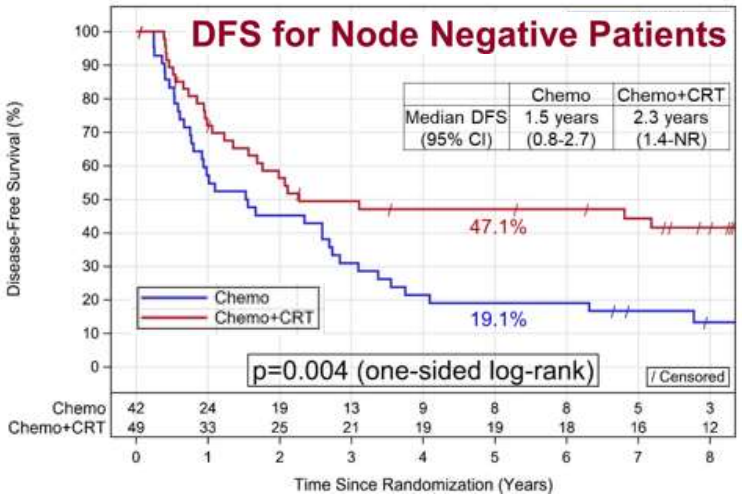
RANDOMIZE

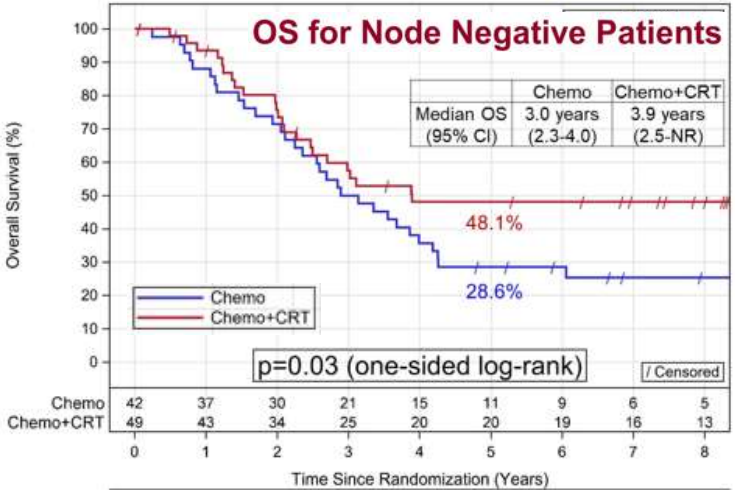
SECOND STEP: RT RANDOMIZATION For Non-Progressing Patients

Arm 3:
1 month of gemcitabine or combination chemotherapy

Arm 4:
1 month of gemcitabine or combination chemotherapy followed by XRT with either capecitabine or 5-FU







Conclusiones

1) FLOT es un nuevo estándar en ADC esofágico localmente avanzado.

2) Pacli/Ramu como switch de mantenimiento en Cancer G/UGE Her2- aumenta PFS/OS.

3) Nivo/Ipi nueva 1ª línea estándar en Hepatocarcinoma avanzado.

4) Gem/Abraxane es similar a NALIRI/5FU en pacientes ancianos con mPDAC avanzado.

5) La QRT de consolidación en PDAC localizado parece aumentar la DFS en toda la población así como la DFS y la OS en la población con ganglios negativos.

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