BARCELONA 2024 ESMO congress

Scientific Congress highlights

Gastrointestinal tumors, upper digestive

Sarah Derks, Amsterdam UMC

The Netherlands

DECLARATION OF INTERESTS

Sarah Derks has received honoraria from:

Advisory board: Bristol-Myers Squibb

Speaker role: Bristol-Myers Squibb, Benecke, Servier research funding

Research funding and medication supply: Incyte

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Great year for Upper-GI cancers

491 abstracts:
15 selected for oral presentation
166 poster presentations

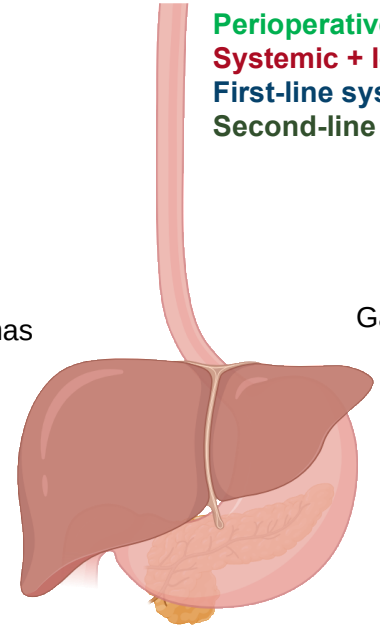
Perioperative/Adjuvant
Systemic + local therapy
First-line systemic
Second-line systemic

Hepatocellular carcinomas

IMbrave 50
LEAP_012
HIMALAYA
DUPHE-H-308
APOLLO
CheckMate 9DW

Gastro-esophageal cancer

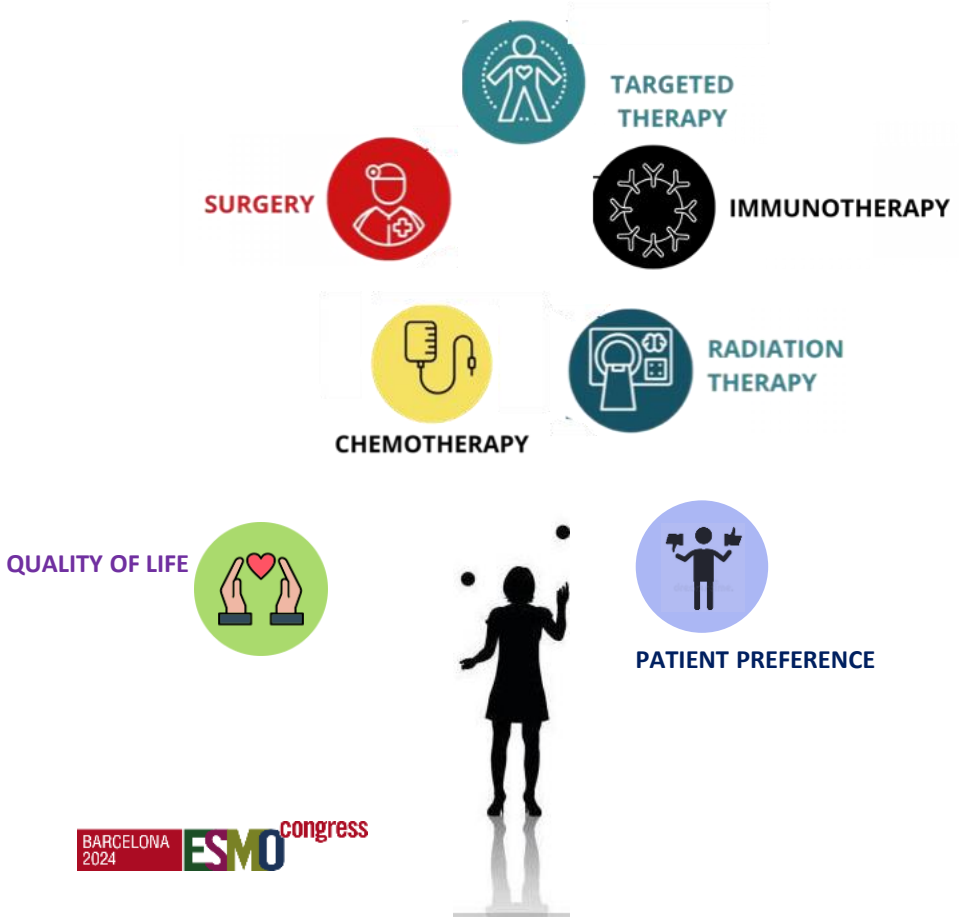
AGITG TOPGEAR
IKF628/Moonlight
KEYNOTE 811
DESTINY-Gastric03



Pancreatic cancer

PRODIGE 44
POLAR
NAPAN

Multimodality treatment in upper-GI cancer



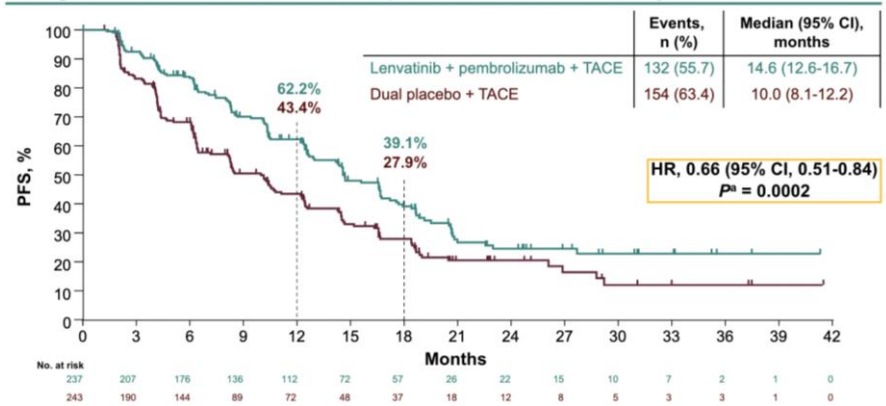
maximize treatment de-escalate when needed

Patient selection is key

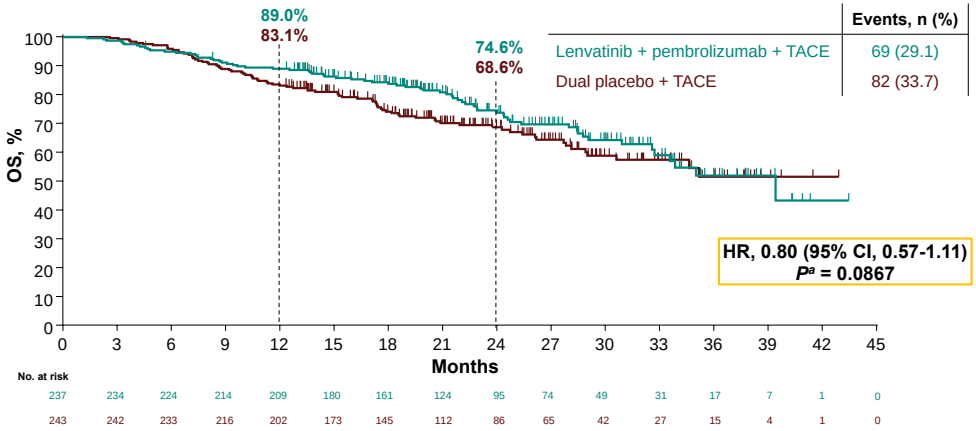
Phase III LEAP-012: TACE + lenvatinib and pembrolizumab

2nd phase III study: VEGF+PD-1 targeting combined with TACE this year (EMERALD-1)

Progression-Free Survival per RECIST v1.1 by BICR



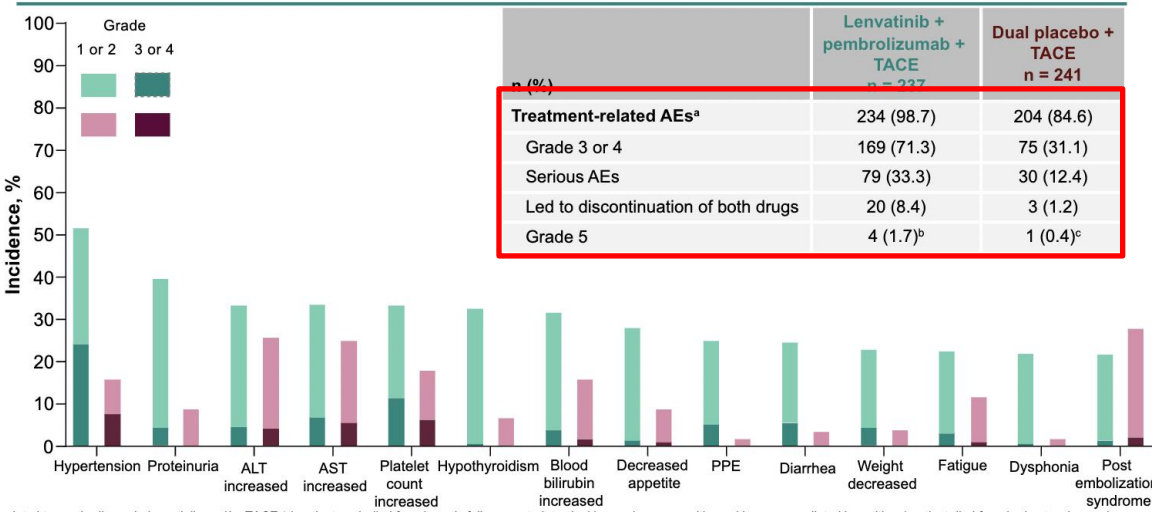
Overall Survival



[a]One-sided *P* from re-randomization test; threshold *P* = 0.025. Data cutoff date for IA1: January 30, 2024.

Phase III LEAP-012: TACE + lenvatinib and pembrolizumab

Most Common Treatment-Related Adverse Events[a] (≥25%)



n (%)	Lenvatinib + pembrolizumab + TACE n = 237	Dual placebo + TACE n = 241
Treatment-related AEs[a]	234 (98.7)	204 (84.6)
Grade 3 or 4	169 (71.3)	75 (31.1)
Serious AEs	79 (33.3)	30 (12.4)
Led to discontinuation of both drugs	20 (8.4)	3 (1.2)
Grade 5	4 (1.7)[b]	1 (0.4)[c]

Conclusion:

- TACE+ Lenvatinib and pembrolizumab is a potential new treatment option for intermediate stage HCC
- Challenge for physicians to select patients that will most likely benefit most from combination treatment vs sequential treatment

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Adjuvant treatment HCC: update survival Imbrave-050

Adjuvant atezolizumab-bevacizumab in resected or ablated high risk HCC

Patient population
- Confirmed first diagnosis of HCC and had undergone curative resection or ablation
- Disease free
- Child-Pugh class A
- High risk of recurrence[a]
- No extrahepatic disease or macrovascular invasion (except Vp1/Vp2)
- ECOG PS 0 or 1

4-12 weeks

1 cycle of TACE, if indicated

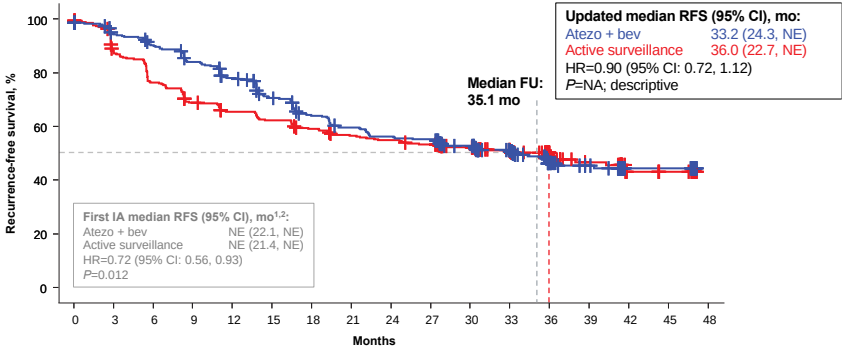
R 1:1

12 months or 17 cycles

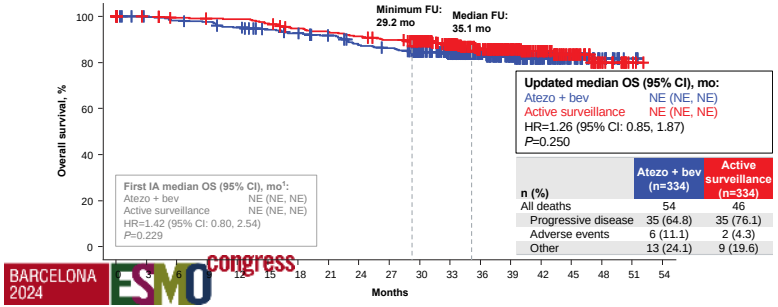
Atezolizumab 1200 mg q3w + bevacizumab 15 mg/kg q3w (n=334)

Active surveillance (n=334)

Early RFS benefit was not maintained with longer follow-up



Updated OS remained immature but showed numerical improvement from the first IA



n (%)	Atezo + bev (n=334)	Active surveillance (n=334)
All deaths	54	46
Progressive disease	35 (64.8)	35 (76.1)
Adverse events	6 (11.1)	2 (4.3)
Other	13 (24.1)	9 (19.6)

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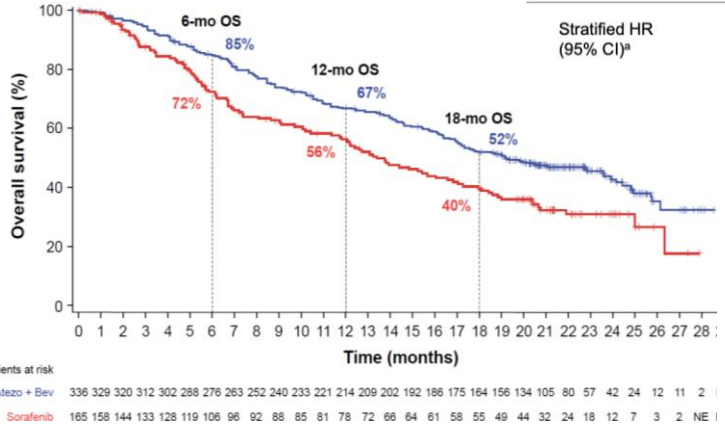
Conclusion:
- Survival benefit did not sustain overtime
- Alternative treatment approaches are needed

1th line treatment HCC:

IMbrave 150: atezolizumab-bevacizumab as first-line treatment for unresectable HCC



Updated OS	Atezo + Bev (n = 336)	Sorafenib (n = 165)
OS events, n (%)	180 (54)	100 (61)
Median OS, mo (95% CI)	**19.2** (17.0, 23.7)	**13.4** (11.4, 16.9)
Stratified HR (95% CI)[a]	**0.66** (0.52, 0.85) *P* = 0.0009[b]	

Finn et al, NEJM, 2020
Finn, ASCO-GI, 2021

HIMALAYA study:
tremelimumab plus durvalumab
5-year OS 28.7% vs 12.7% (sorafenib)

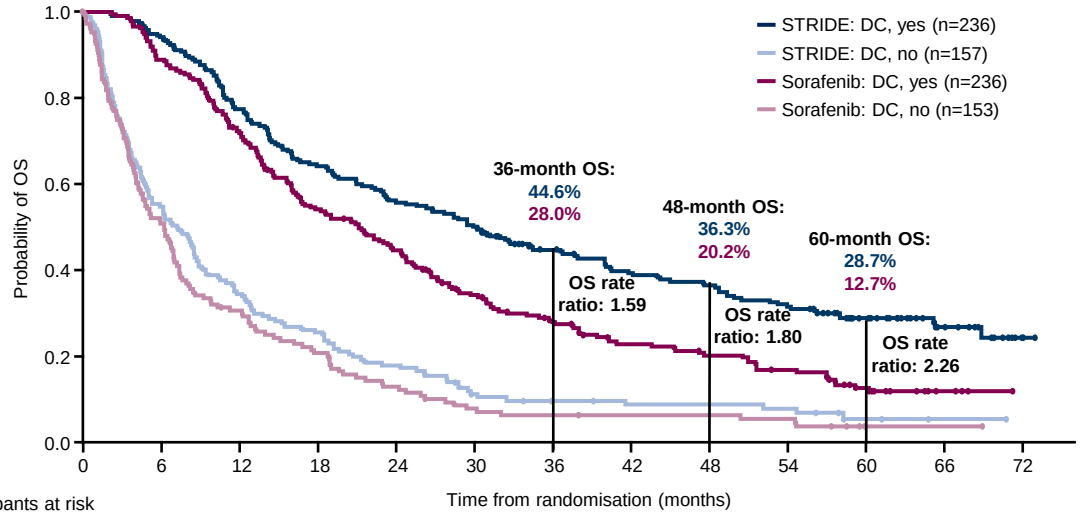
CheckMate 9DW study:
Nivolumab (NIVO) plus ipilimumab (IPI)

Apollo study:
Anlotinib plus Penpulimab vs sorafenib

- **DUPH-H-308** study:
QL1706 (**anti-PD1** (iparomlimab) and **anti-CTLA4** (Tuvonralimab)) + **bevacizumab** +chemo

1th line treatment HCC:

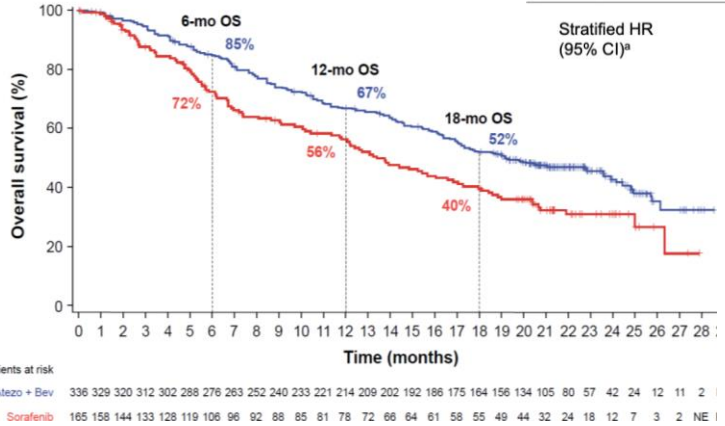
HIMALAYA: tremelimumab + durvalumab vs sorafenib



No. of participants at risk													
STRIDE: DC, yes	236	222	181	150	130	116	93	80	74	64	43	19	2
STRIDE: DC, no	157	86	54	40	28	15	11	9	9	8	3	1	0
Sorafenib: DC, yes	236	209	167	125	102	73	57	43	37	30	17	5	0
Sorafenib: DC, no	153	74	44	30	19	11	9	8	8	7	1	1	0

1th line treatment HCC:

IMbrave 150: atezolizumab-bevacizumab as first line treatment for unresectable HCC



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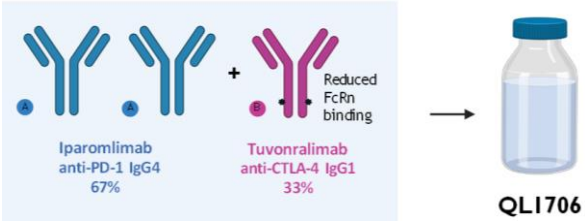
1th line treatment HCC: DUPH-H-308

Phase II (ongoing): QL1706+- bevacizumab +- chemo



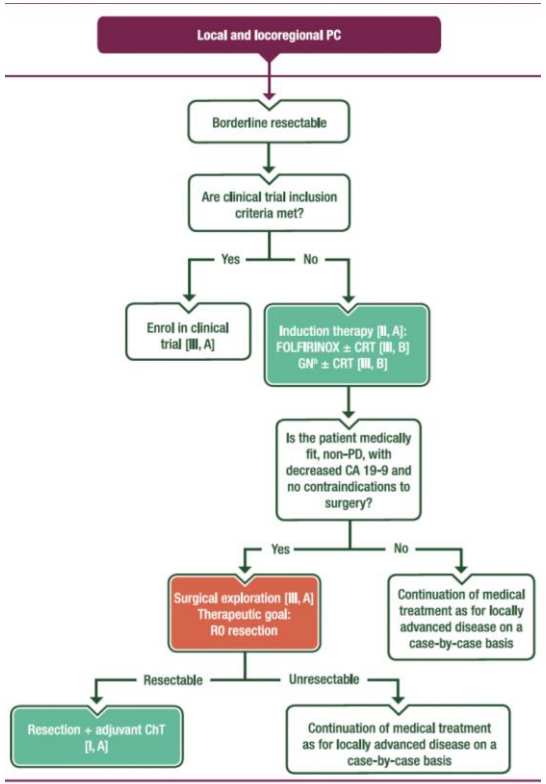
	QL1706 Arms			Control
	QL1706+bev+ chemo (n=31)	QL1706+bev (n=30)	QL1706+chemo (n=30)	Sintilimab+bev (n=29)
Best overall response, n (%)				
CR	2 (6.5)	0	1 (3.3)	0
PR	10 (32.3)	13 (43.3)	13 (43.3)	8 (27.6)
SD	15 (48.4)	11 (36.7)	12 (40.0)	13 (44.8)
PD	2 (6.5)	5 (16.7)	3 (10.0)	5 (17.2)
Not done	2 (6.5)	1 (3.3)	1 (3.3)	3 (10.3)
ORR, % (95% CI)	38.7 (21.8-57.8)	43.3 (25.5-62.6)	46.7 (28.3-65.7)	27.6 (12.7-47.2)
DCR, % (95% CI)	87.1 (70.2-96.4)	80.0 (61.4-92.3)	86.7 (69.3-96.2)	72.4 (52.8-87.3)
Median TTR (range), months	1.5 (1.3-5.5)	2.7 (1.3-4.1)	2.2 (1.3-8.2)	4.2 (1.4-7.0)
Median DoR, months	Not reached			

	QL1706 Arms			Control
	QL1706+bev+ Chemo (n=30)	QL1706+bev (n=30)	QL1706+chemo (n=30)	Sintilimab+bev (n=29)
TEAEs, n (%)	30 (100.0)	30 (100.0)	30 (100.0)	28 (96.6)
Treatment-related, n (%)	30 (100.0)	27 (90.0)	29 (96.7)	25 (86.2)
Grade≥3 TEAEs, n (%)	16 (53.3)	19 (63.3)	20 (66.7)	18 (62.1)
Treatment-related, n (%)	14 (46.7)	16 (53.3)	17 (56.7)	13 (44.8)
Serious TEAEs, n (%)	9 (30.0)	15 (50.0)	15 (50.0)	13 (44.8)
Treatment-related, n (%)	7 (23.3)	11 (36.7)	7 (23.3)	5 (17.2)
TEAEs leading to death, n (%)	3 (10.0)	3 (10.0)	3 (10.0)	6 (20.7)
Treatment-related, n (%)	0	0	0	1 (3.4)
TEAEs leading to interruption of any treatment, n (%)	16 (53.3)	16 (53.3)	24 (80.0)	12 (41.4)
Treatment-related, n (%)	14 (46.7)	12 (40.0)	20 (66.7)	11 (37.9)
TEAEs leading to discontinuation of any treatment, n (%)	4 (13.3)	4 (13.3)	5 (16.7)	3 (10.3)
Treatment-related, n (%)	2 (6.7)	4 (13.3)	5 (16.7)	2 (6.9)

QL1706/CAPOX/bevacizumab selected for phase III

Pancreatic Cancer (BRPC)

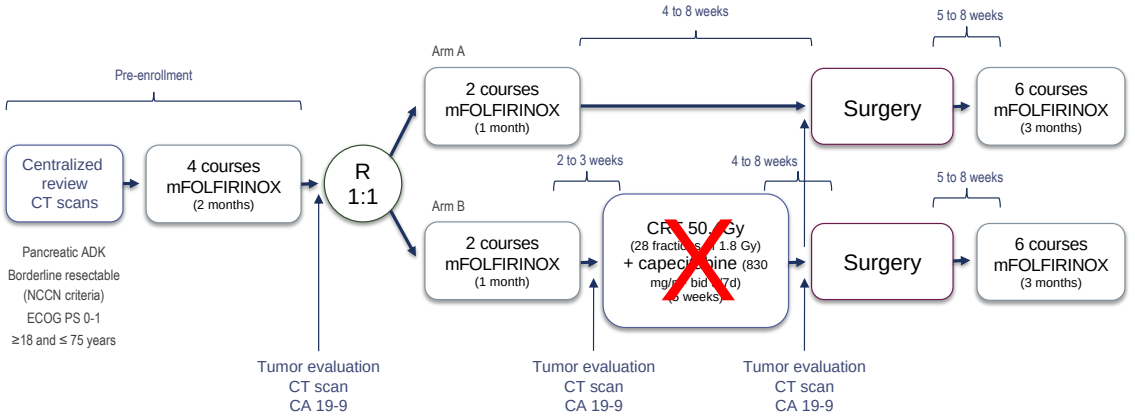
Additive effect of neoadjuvant chemoradiation: PANDAS/PRODIGE 44 trial



Vogel et al. Annals of Oncol, 2023

There is no place for neoadjuvant CRT in BRPC

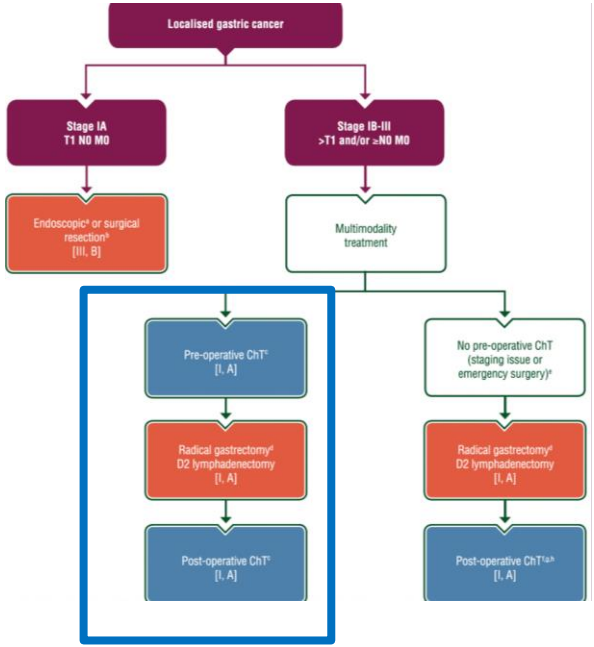
STUDY DESIGN



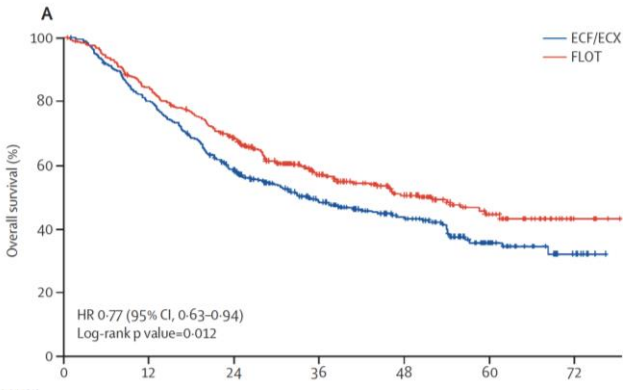
No benefit of CRT in R0 resection
No benefit of CRT in OS

Gastric and esophageal cancer

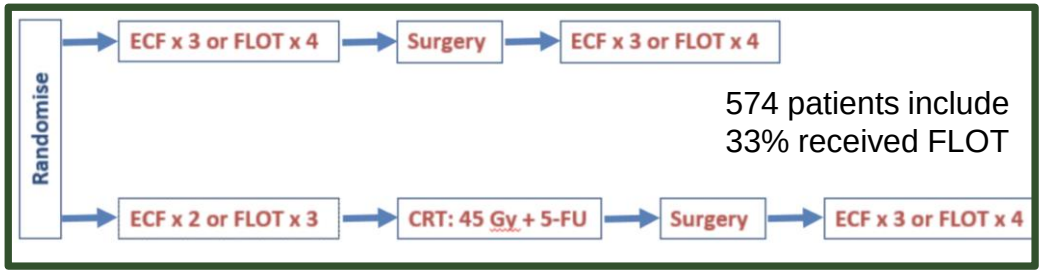
TOPGEAR: First phase III RCT testing complimentary CRT in perioperative treatment:



Perioperative FLOT



not a study to test FLOT vs chemoradiotherapy…



574 patients include
33% received FLOT

Lordick et al, Annals of Oncol 2022
Al-Batran, The Lancet, 2019

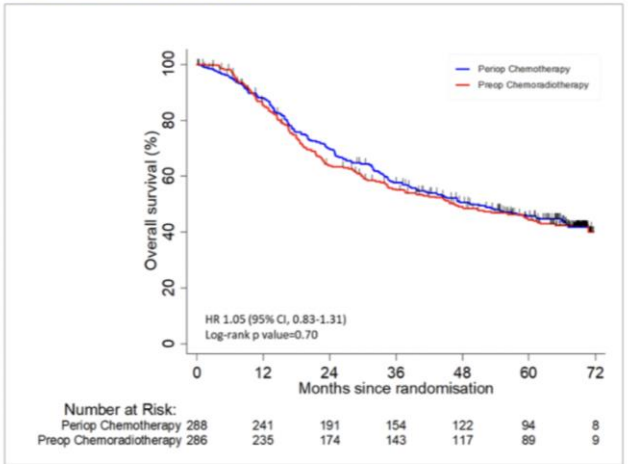
The NEW ENGLAND JOURNAL of MEDICINE

Gastric and esophageal cancer

TOPGEAR: First phase III RCT testing complimentary CRT in perioperative treatment:

Treatment	Preop CRT		Periop CT		P-value
	N	n (%)	N	n (%)	
Received preop chemotherapy	286	270 (94.4%)	288	263 (91.3%)	0.15
Received postop chemotherapy					
pati					
all r					
Receiv					
com					
Receiv					
all r					
cura					

Overall survival



	Preop CRT	Periop CT
Median OS	46.4 mths	49.4 mth
3-yr OS	55.1%	57.7%
5-yr OS	44.4%	45.7%

	Preop CRT N=286	Periop CT N=288	P-value
D1+ or D2 lymphadenectomy	188 (83.6%)	192 (81.0%)	
RO resection	208 (92.4%)	206 (87.7%)	0.09
R1 resection	15 (6.7%)	29 (12.3%)	
ypTNM stage:	(N=231)	(N=247)	
ypT0, ypTis	38 (16.5%)	18 (7.3%)	<0.001
ypT1/2	73 (31.6%)	62 (25.2%)	
ypT3/4	120 (51.9%)	166 (67.5%)	
[illegible]	125 (54.1%)	104 (42.3%)‡	<0.01
	106 (45.9%)	142 (57.7%)	
sponse:			
% residual tumour (pCR)	36 (16.8%)	18 (8.0%)	<0.0001
10% residual tumour	70 (32.7%)	48 (21.3%)	
50% residual tumour	61 (28.5%)	69 (30.7%)	
0% residual tumour	47 (22.0%)	90 (40.0%)	

RT adverse events	Preop CRT N=259	Periop CT N=287	P-value
greater toxicity	172 (66.4%)	176 (61.3%)	0.22
tologic toxicity:	**119 (45.9%)**	**119 (41.5%)**	**0.29**
tropenia	19 (7.3%)	26 (9.1%)	0.47
a without infection or fever	101 (39.0%)	93 (32.4%)	0.11
	17 (6.6%)	12 (4.2%)	0.22
topenia	13 (5%)	6 (2.1%)	0.06
ointestinal toxicity:	**73 (28.2%)**	**72 (25.1%)**	**0.41**
			.33
			.99
			.73
			.08
			007
			.08
			.06

No benefit in OS
No place for CRT in neoadjuvant treatment of gastric cancer

Gastric and esophageal cancer

SPACE-FLOT trial: Response to neoadjuvant FLOT predicts succes of adjuvant FLOT

Study Design

SPACE-FLOT is an international cohort study of real-world data

43 Hospitals
12 Countries

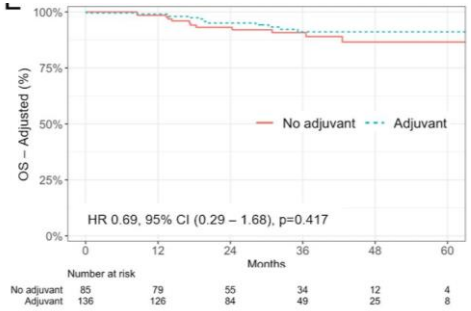
Australia
New Zealand
England
Ireland
Sweden
France
Italy
Netherlands
India
Malaysia
Singapore
Canada

Eligible Population
N=1887

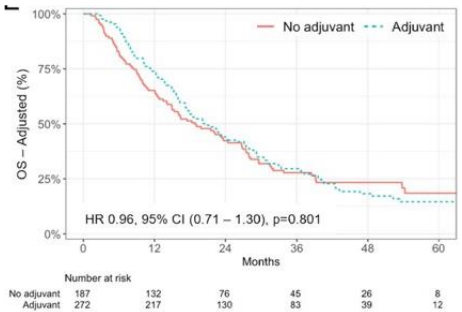
- Non metastatic GEJ/gastric adenocarcinoma
- Neoadjuvant FLOT chemotherapy
- Curative resection

Minimal pathological response N=459	Adjuvant FLOT N=272 / No adjuvant N=187
Partial pathological response N=1207	Adjuvant FLOT N=847 / No adjuvant N=360
Complete pathological response N=221	Adjuvant FLOT N=136 / No adjuvant N=85

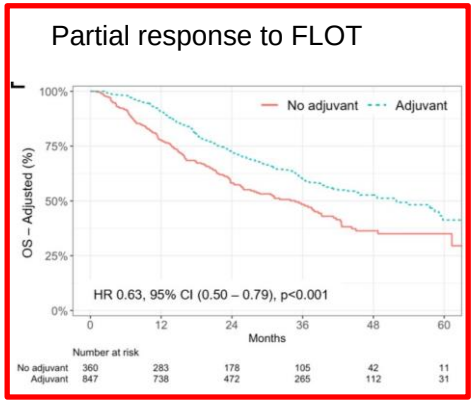
Complete response to FLOT



No response to FLOT



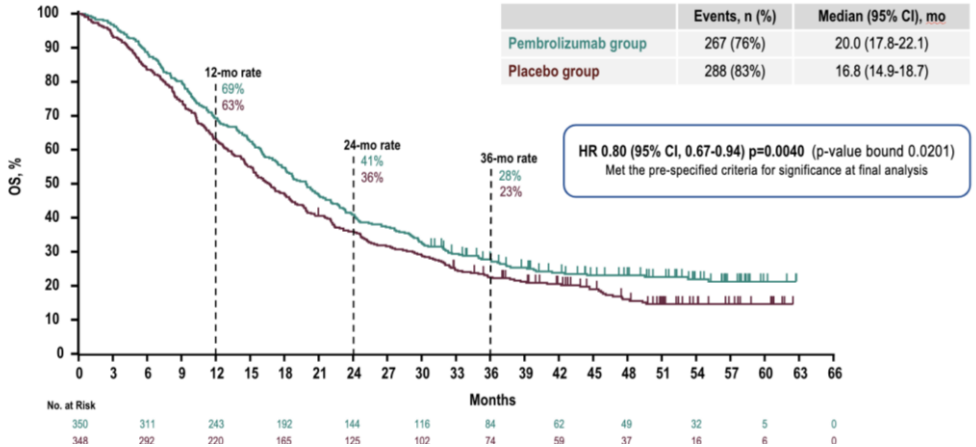
Partial response to FLOT



Gastric and esophageal cancer

First-line **HER2 positive disease**: final analysis **KEYNOTE 811**

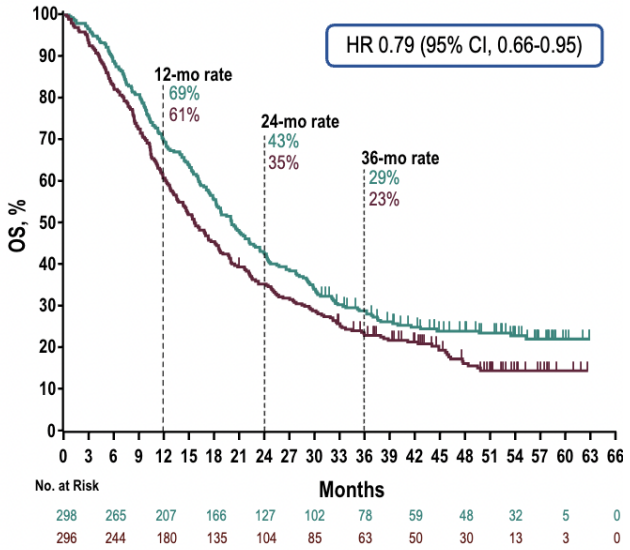
Overall Survival at Final Analysis (ITT)



	Events, n (%)	Median (95% CI), mo
Pembrolizumab group	267 (76%)	20.0 (17.8-22.1)
Placebo group	288 (83%)	16.8 (14.9-18.7)

OS PD-L1 CPS>1

	Events, n (%)	Median (95% CI), mo
Pembrolizumab group	226 (76%)	20.1 (17.9-22.9)
Placebo group	244 (82%)	15.7 (13.5-18.5)



How about CPS>5 or CPS>10?
Not a preplanned analyses

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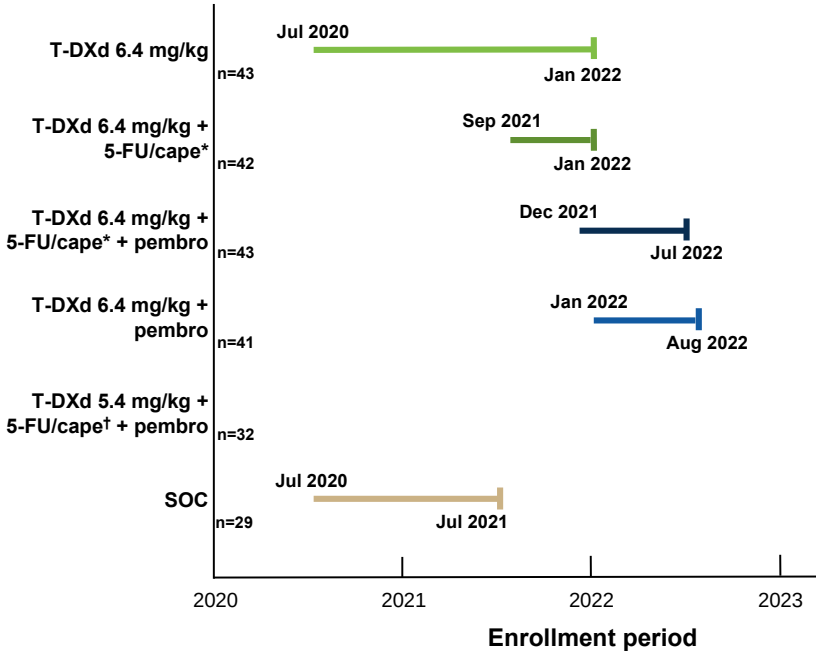
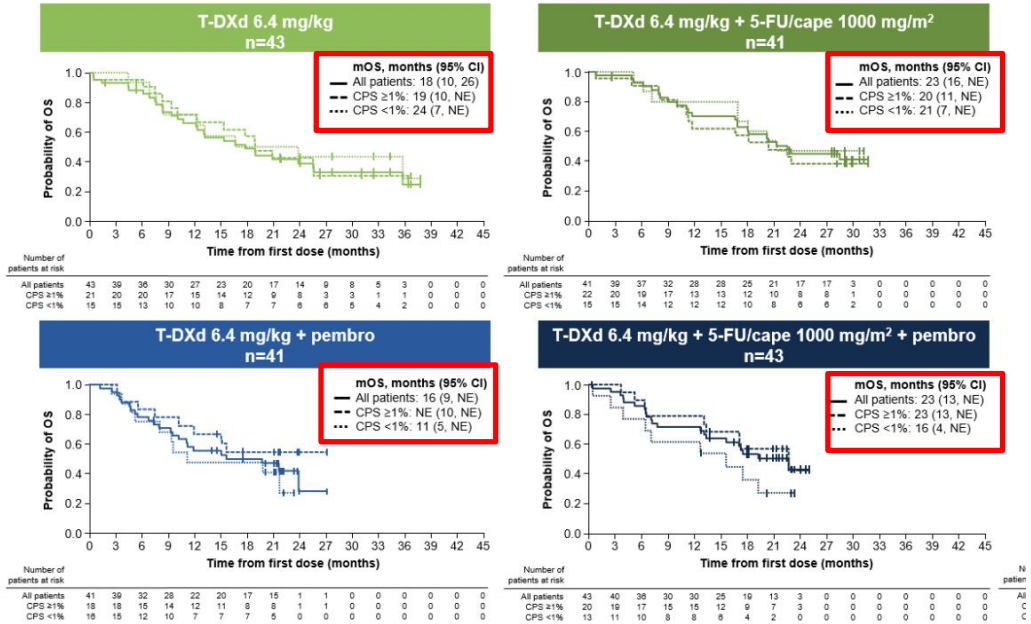
Gastric and esophageal cancer: HER2+

Phase 1b/2 DESTINY-Gastric -03: Trastuzumab-deruxtecan in first-line



Overall survival in all patients and by PD-L1 status



Best results + fluoropyrimidine

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Gastric and esophageal cancer

DESTINY-Gastric -03: Trastuzumab-deruxtecan in first-line

Adverse events summary

	T-DXd 6.4 mg/kg n=42*	T-DXd 6.4 mg/kg + 5-FU/cape 1000 mg/m² n=42	T-DXd 6.4 mg/kg + 5-FU/cape 1000 mg/m² + pembro n=43	T-DXd 6.4 mg/kg + pembro n=41	T-DXd 5.4 mg/kg + 5-FU/cape 750 mg/m² + pembro n=32	SOC n=29
Median follow-up, months	17	21	17	15	5	18
~~All-causality AEs, n (%)~~	~~42 (100)~~	~~42 (100)~~	~~43 (100)~~	~~41 (100)~~	~~27 (84)~~	~~29 (100)~~
Grade ≥3 AEs	27 (64)	**32 (76)**	**39 (91)**	33 (80)	**11 (34)**	17 (59)
Adjudicated drug-related ILD/pneumonitis§	4 (10)	5 (12)	8 (19)	5 (12)	0	NA
Grade ≥3 drug-related ILD/pneumonitis	0	0	3 (7)	1 (2)	0	NA
Death due to drug-related ILD/pneumonitis	0	0	2 (5)	1 (2)	0	NA
Left ventricular dysfunction	1 (2)	2 (5)	3 (7)	2 (5)	1 (3)	NA

Gastric and esophageal cancer

Educational session: personalized treatment beyond biomarkers

Oligometastatic disease

omec

To operate or not to operate?

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A good collaborating MDT is key

ACKNOWLEDGEMENT

UPPER GI SCIENTIFIC COMMITTEE MEMBERS

Sarah Derks
Tania Fleitas
Yelena Janjigian
Angela Lamarca
Rupert Langer
Trevor Leong
Sylvie Lorenzen
Shiraz Marker
Davide Melisi
Magnus Nilsson
Radka Obermannova
Filippo Pientrantionio
Arndt Vogel

Thank you for your kind attention