



BSMO

NEW DRUGS IN GI CANCER

**Joëlle Collignon
Wim Demey**



DISCLOSURES W. DEMEY

ADVISORY BOARD AND LECTURES:

MERCK, PFIZER

VIRTUAL CONGRES INSCRIPTION:

PFIZER, SERVIER, MERCK, MSD



OESOGASTRIC CANCER in BELGIUM 2022 IMMUNOTHERAPY

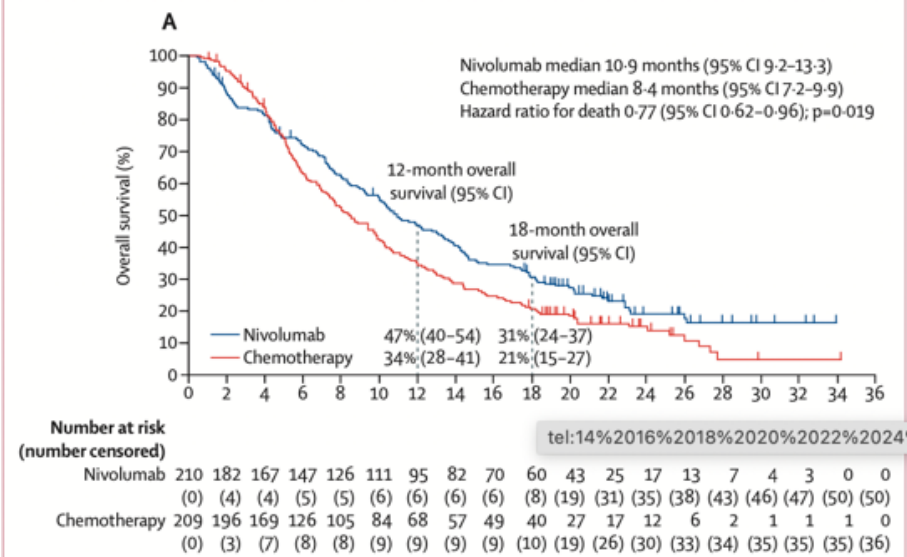
- **SECOND LINE NIVOLUMAB FOR METASTATIC ESCC**
- **First line PEMBROLIZUMAB plus chemotherapy for ESCC, ADK EC AND EGJC Sievert 1 PDL1-CPS ≥ 10**
- **First line NIVOLUMAB plus chemotherapy for GC EGJ ADK PDL1-CPS ≥ 5**
- **Adjuvant NIVOLUMAB for non pCR ESCC AND AC OESOPHAGEAL CANCER AND AC EGJC after surgery**

Nivolumab versus chemotherapy in patients with advanced oesophageal squamous cell carcinoma refractory or intolerant to previous chemotherapy (ATTRACTION-3): a multicentre, randomised, open-label, phase 3 trial



Ken Kato, Byoung Chul Cho, Masanobu Takahashi, Morihito Okada, Chen-Yuan Lin, Keisho Chin, Shigenori Kadowaki, Myung-Ju Ahn, Yasuo Hamamoto, Yuichiro Doki, Chueh-Chuan Yen, Yutaro Kubota, Sung-Bae Kim, Chih-Hung Hsu, Eva Holtved, Ioannis Xynos, Mamoru Kodani, Yuko Kitagawa

Belgium approval 2021

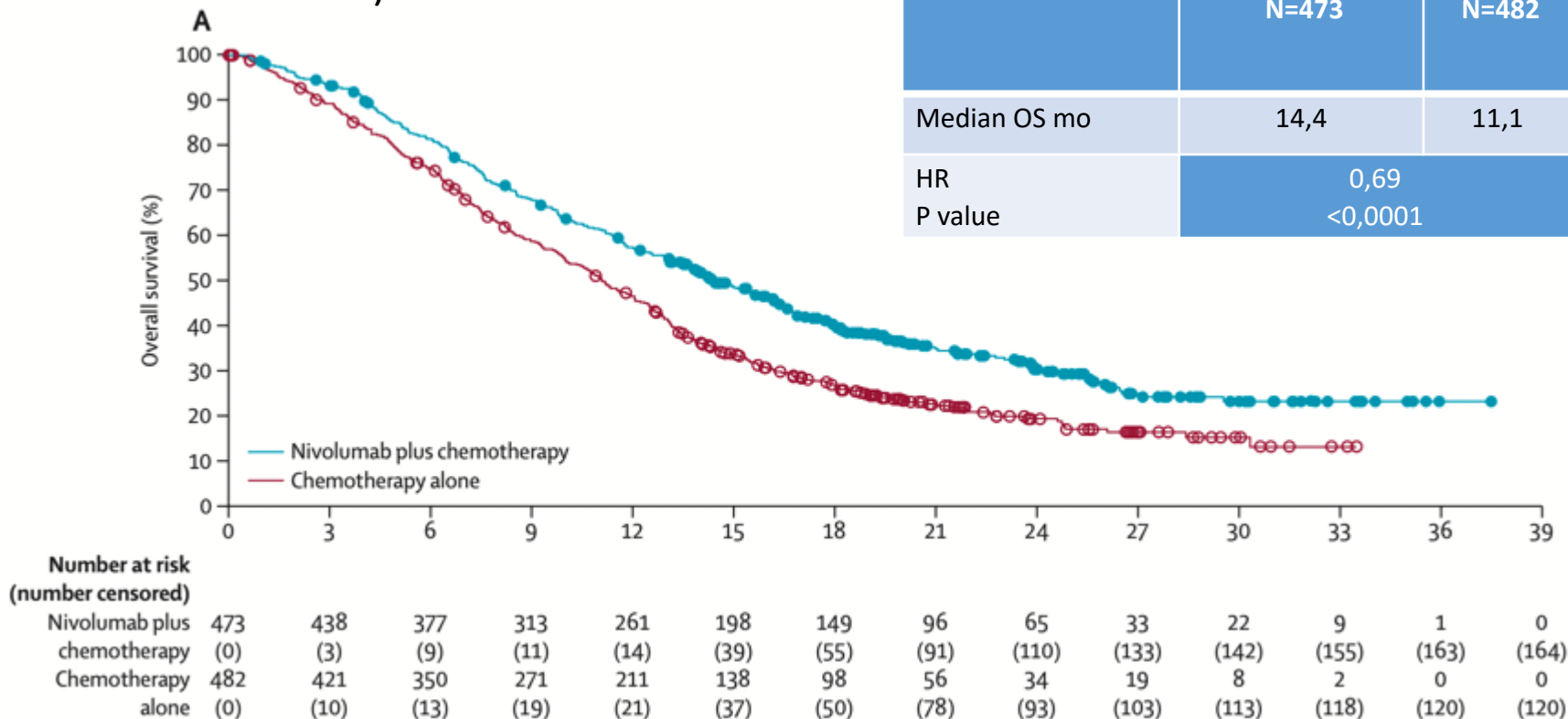


ATTRACTION-3 2d line	NIVO N=210	DOCET OR PACLI N=209
Median OS mo	10,9	8,4
HR	0,77	

TRIAL	CHECKMATE-649 L1	KEYNOTE 590 L1	Checkmate 577 adjuvant
DISEASE location	GC, EGJ, Esophagus	Esophagus, EGJ sievert 1	Esophagus, EGJ
Histology	ADK	ADK/SCC	ADK/SCC
Region	Global	Global	Global
PFS HR	0,68 CPS $\geq$ 5	0,62 CPS $\geq$ 10	0,69
ORR	45 vs 60 % (CPS $\geq$ 5)	30 vs 48 %	NA
OS difference	3,3 m (CPS $\geq$ 5) 2,7 m (CPS $\geq$ 1) 2,2 All patients	5,1 m ESCC (CPS $\geq$ 10) 2,8 m ESCC	NR but DFS X2
ESMO MCBS (Magnitude of Clinical Benefit Scale)	4 (CPS $\geq$ 5) 3 (CPS $\geq$ 1) 2 (all patients)	4 ESCC (CPS $\geq$ 10) 3 vs 4 all ESCC 3 vs 4 all pats	Grade A

PRIMARY ENDPOINT OS (PD-L1 CPS ≥

5)



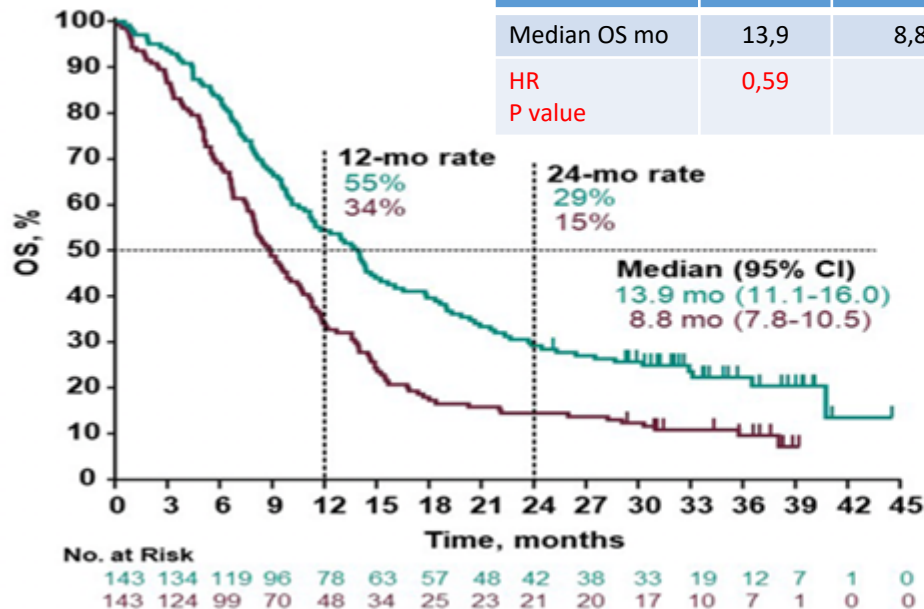
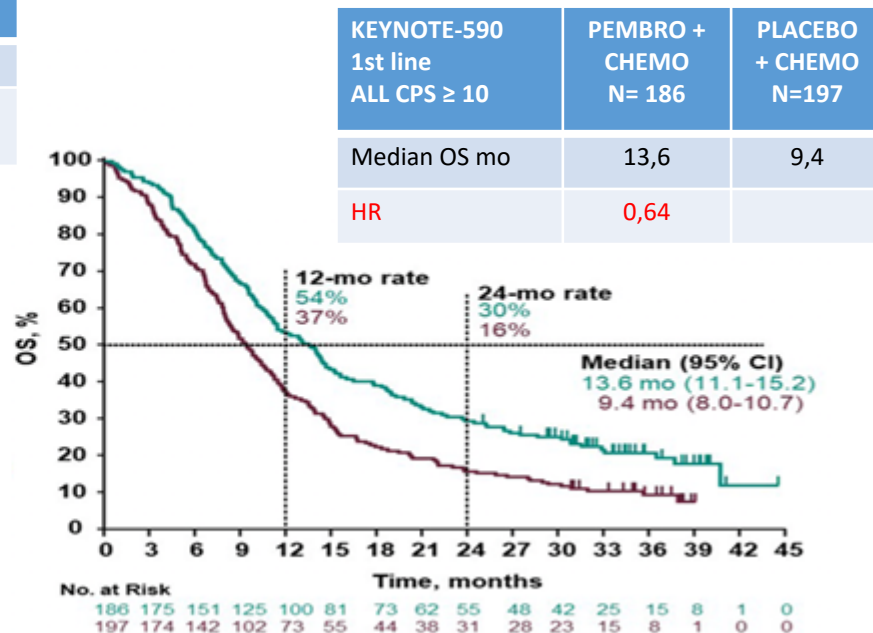
	NIVO+CHEMO N=473	CHEMO N=482
Median OS mo	14,4	11,1
HR	0,69	
P value	<0,0001	

TRIAL	CHECKMATE-649 L1	KEYNOTE 590 L1	Checkmate 577 adjuvant
DISEASE location	GC, EGJ, Esophagus	Esophagus, EGJ sievert 1	Esophagus, EGJ
Histology	ADK	ADK/SCC	ADK/SCC
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KEYNOTE-590

ASCO GI 2022 UPDATE

First line PEMBROLIZUMAB plus chemotherapy for ESCC, ADK EC AND EGJC
Sievrt 1 PDL1-CPS ≥ 10

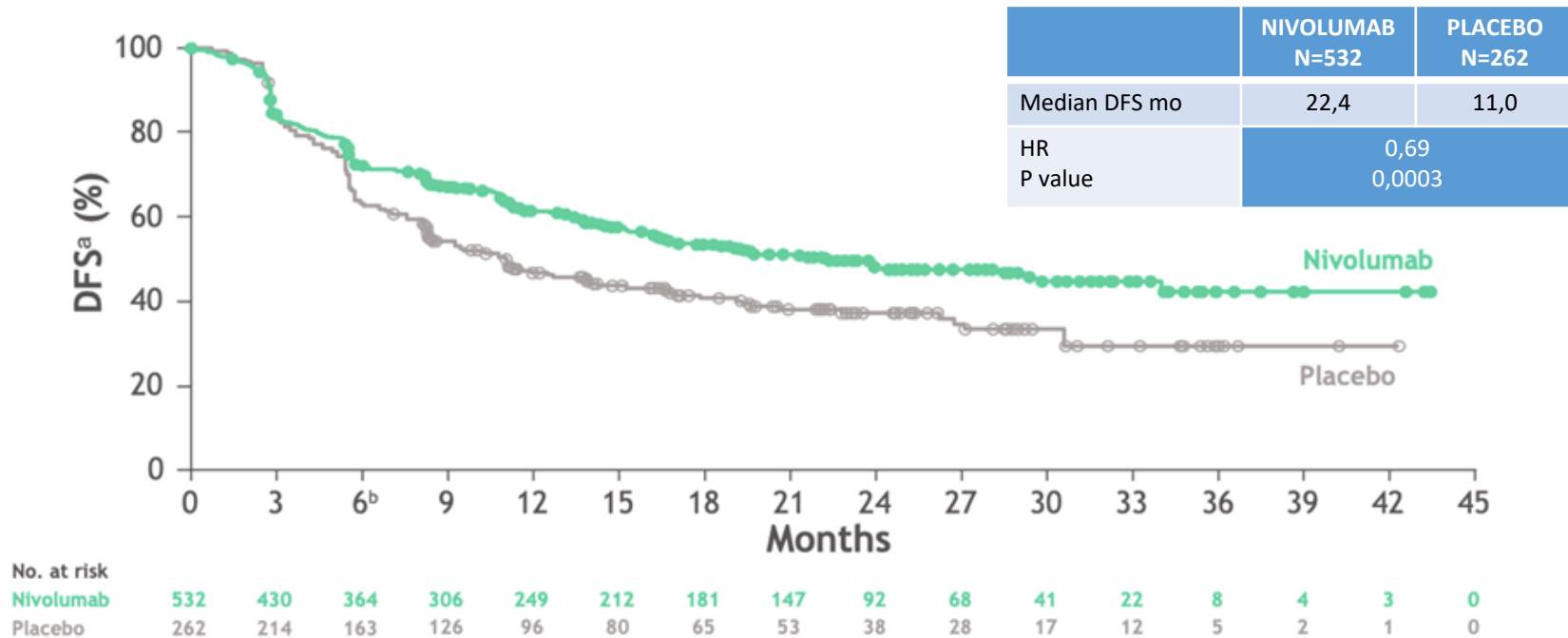
ESCC CPS ≥ 10 All patients CPS ≥ 10 

THIS RESULTS ARE INDEPENDANT OF CPS STATUS, ALTHOUGH SQUAMOUS HISTOLOGY
AND CPS ≥ 10 MAY GET A MAXIMUM BENEFIT

TRIAL	CHECKMATE-649 L1	KEYNOTE 590 L1	Checkmate 577 adjuvant
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Histology	ADK	ADK/SCC	ADK/SCC
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PRIMARY ENDPOINT DFS

FIRST POSITIVE TRIAL IN ADJUVANT SINCE CROSS AND FLOT TRIAL



- Nivolumab provided superior DFS with a 31% reduction in the risk of recurrence or death and a doubling in median DFS versus placebo

^aPer investigator assessment; ^b6-month DFS rates were 72% (95% CI, 68-76) in the nivolumab arm and 63% (95% CI, 57-69) in the placebo arm; ^cThe boundary for statistical significance at the pre-specified interim analysis required the P value to be less than 0.036.



NEW BELGIUM APPROVALS: INTEGRATION IN LINES OF THERAPY

ESOPHAGEAL OR EGJ ADK	ESOPHAGEAL SQUAMOUS CELL CARCINOMA
LOCALLY ADVANCED ESOPHAGEAL OR EGJ ADK CRT+ SURGERY NO PCR: ADJUVANT NIVOLUMAB	LOCALLY ADVANCED CRT+ SURGERY NO PCR: ADJUVANT NIVOLUMAB
1L METASTATIC NIVO + CHEMO (CPS $\geq$ 5) FOR GC ALSO PEMBRO + CHEMO (CPS $\geq$ 10) NOT FOR GC CHEMO + Tmab (HER2+) CHEMO ALONE (HER2- CPS <5)	1L METASTATIC PEMBRO + CHEMO (CPS $\geq$ 10)
2L METASTATIC TAXANE +/- RAMUCIRUMAB OR IRINOTECAN	2L METASTATIC NIVOLUMAB
3-4 L METASTATIC TRIFLURIDIN-TIPIRACIL OR IRINOTECAN OR BSC	3-4L METASTATIC TAXANE OR IRINOTECAN OR BSC



Importance of CPS?

- Keynote 590: 22C3 IHC pharmaDX assay
- Checkmate 649: Dako 28-8 pharmaDX assay

$$\text{CPS} = 100 \times \frac{\text{PD-L1 staining cells (tumor cells, lymphocytes, macrophages)}}{\text{total viable tumor cells}}$$

- RIZIV/INNAMI: no mention of which assay
→ to discuss with your pathologist...

HER2 + OESOGASTRIC CANCER in BELGIUM 2022

TRASTUZUMAB DERUXTECAN (ENHERTU)

PENDING

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Trastuzumab Deruxtecan in Previously Treated HER2-Positive Gastric Cancer

K. Shitara, Y.-J. Bang, S. Iwasa, N. Sugimoto, M.-H. Ryu, D. Sakai, H.-C. Chung, H. Kawakami, H. Yabusaki, J. Lee, K. Saito, Y. Kawaguchi, T. Kamio, A. Kojima, M. Sugihara, and K. Yamaguchi, for the DESTINY-Gastric01 Investigators*

6.4 mg per kilogram of body weight every 3 weeks

Therapy with trastuzumab deruxtecan led to significant improvements in response and overall survival, as compared with standard therapies, among patients with HER2-positive gastric cancer. Myelosuppression and interstitial lung disease were the notable toxic effects. (Funded by Daiichi Sankyo; DESTINY-Gastric01 ClinicalTrials.gov number, NCT03329690.)

- pathologically documented unresectable or metastatic gastric or GEJ cancer
- Centrally confirmed HER2 positive on biopsy after progression on first line trastu containong regimen
- ECOG PS 0 or 1

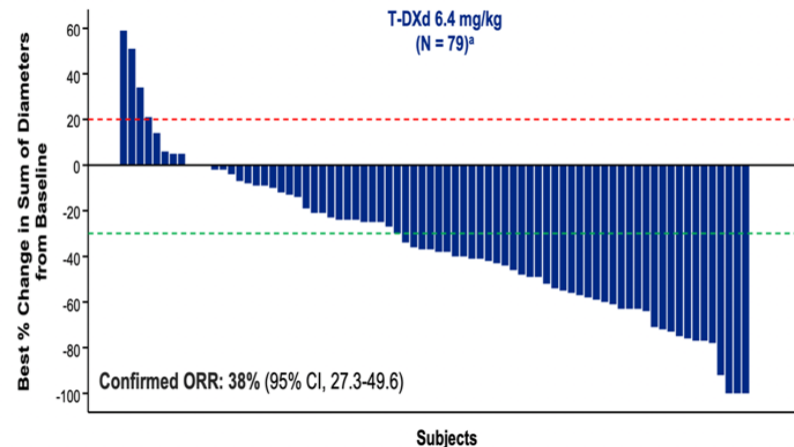
T-DX
6,4 mg/Kg / 3 W
N=79

PRIMARY ENDPOINT:
Confirmed ORR by IRR

SECONDARY ENDPOINTS:
PFS by ICR
OS
DOR by ICR
Safety and tolerability

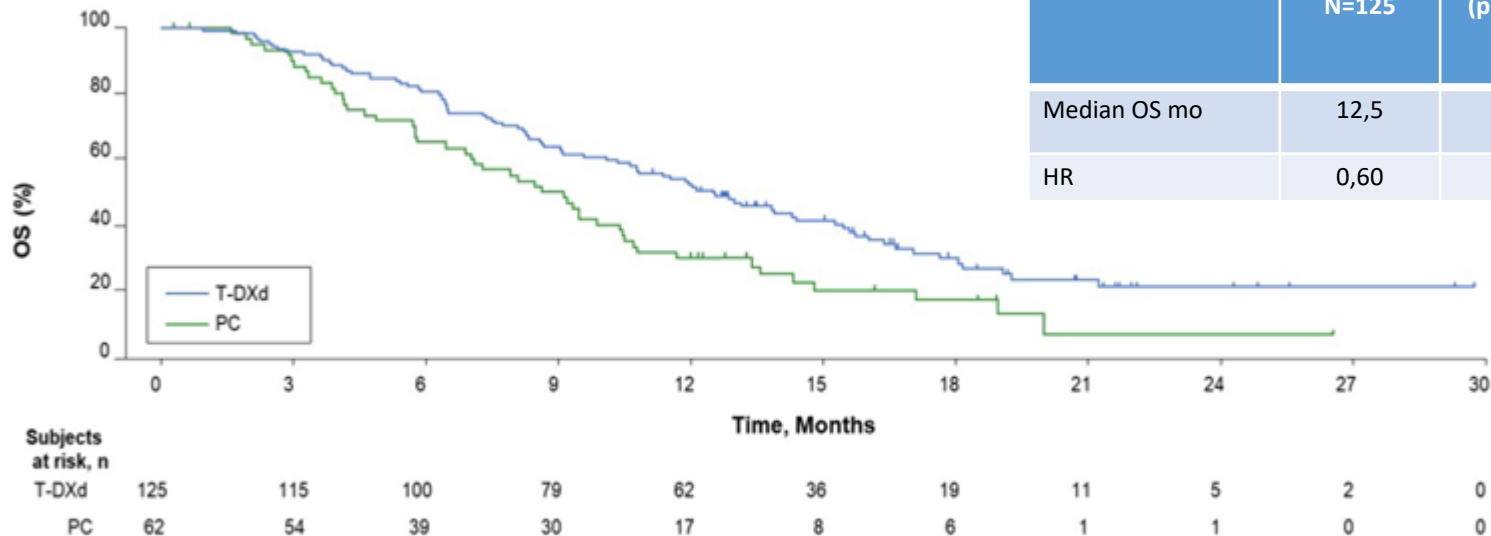
DESTINY-Gastric02 is the first study focused only on second-line T-DXd monotherapy in Western patients with HER2+ gastric/GEJ cancer who have progressed on a trastuzumab-containing regimen

	N=79
Confirmed ORR %	30
CR	3,8
PR	34,2
SD	43
Median DOR ,mo	8,1
Confirmed DCR %	64 %
Median PFS mo	5,5



Overall Survival

Kaplan-Meier Analysis of OS



DESTINY GC	T-DXd N=125	Chemo (physician 's choice) N=62
Median OS mo	12,5	8,9
HR	0,60	

As in the primary analysis (101 OS events; 54.0% maturity), in this updated analysis (133 OS events; 71.1% maturity), T-DXd showed superior antitumor activity compared to PC

HR, hazard ratio; OS, overall survival; PC, physician's choice; T-DXd, trastuzumab deruxtecan.

*In the T-DXd arm, 41 patients (32.8%) were censored.

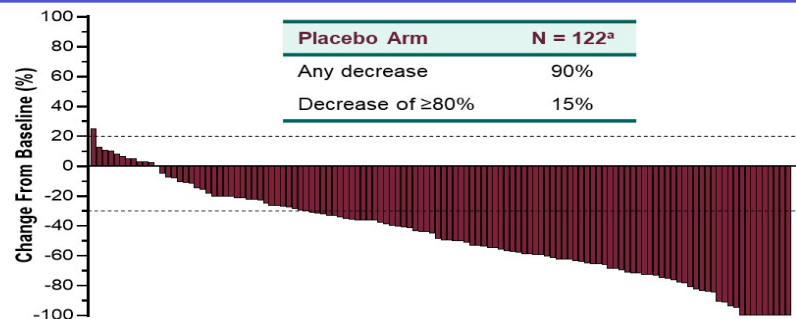
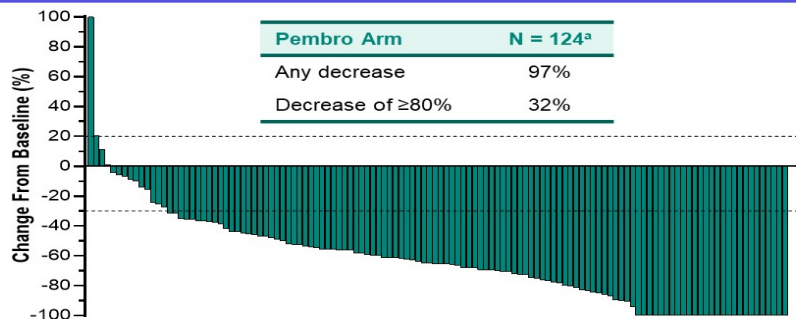
*In the PC arm, 13 patients (21.0%) were censored.

*1 patient in the PC arm received crossover treatment of T-DXd.

*HR and corresponding 95% CI were estimated using Cox proportional hazards model stratified by region.

PEMBRO+Trastuzumab+Chemo as first line in Her2positive in Gastric/GE Junction tumors, Keynote-811

Confirmed Response at IA1



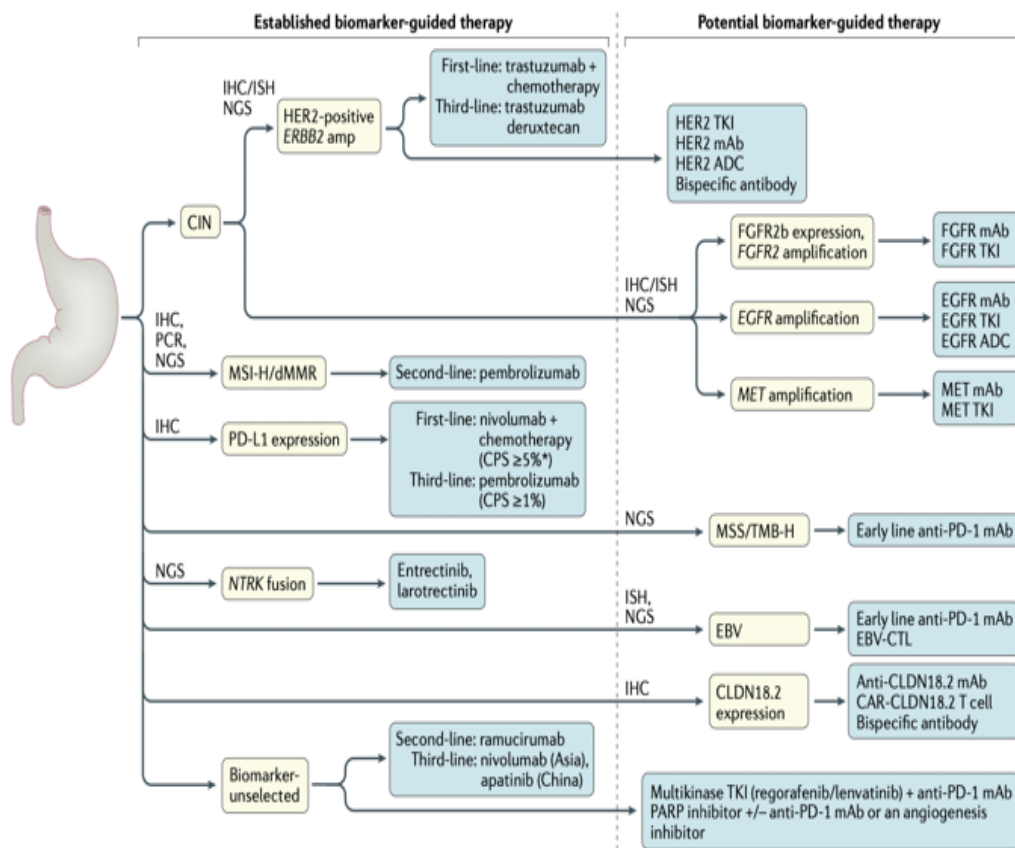
ORR and DCR, % (95% CI)	Pembro Arm (N = 133)	Placebo Arm (N = 131)
ORR	74.4% (66.2-81.6)	51.9% (43.0-60.7)
ORR difference ^b	22.7% (11.2-33.7) P = 0.00006	
DCR	96.2% (91.4-98.8)	89.3% (82.7-94.0)

Best Response, n (%)	Pembro Arm (N = 133)	Placebo Arm (N = 131)
CR	15 (11%)	4 (3%)
PR	84 (63%)	64 (49%)
SD	29 (22%)	49 (37%)
PD	5 (4%)	7 (5%)
Not evaluable	0	2 (2%)
Not assessed	0	5 (4%)

Duration of Response ^c	Pembro Arm (N = 99)	Placebo Arm (N = 68)
Median ^d	10.6 mo	9.5 mo
Range	1.1+ to 16.5+	1.4+ to 15.4+
≥6-mo duration ^d	70.3%	61.4%
≥9-mo duration ^d	58.4%	51.1%

^aParticipants with RECIST-measurable disease at baseline and ≥1 post-baseline measurement evaluable for change from baseline in target lesions. ^bCalculated using the Miettinen and Nurminen method stratified by the randomization stratification factors. ^cCalculated in participants with best response of CR or PR. ^dKaplan-Meier estimation. The treatment regimen in both arms included trastuzumab and chemotherapy. Data cutoff date: June 17, 2020.

OESOGASTRIC CANCER in BELGIUM 2022



EGC	THERAPY	FDA	BELGIQUE
L1	NIVO or PEMBRO + CHEMO (CK 649/KN 590)	YES	Yes End 2021
HER2 POSITIVE L1	TRASTUZUMAB +PEMBROLIZUMAB (KEYNOTE 811)	YES	pending😞
HER2 POSITIVE ≥ L2	TRASTUZUMAB DERUXTECAN (DESTINY)	YES	Pending😞
MSI-H ≥ L2	PEMBROLIZUMAB	YES	Pending😞
NTRK 1-3 < 1% (ALL TOMOR)	LAROTRECTINIB ENTRECTINIB	YES	YES



DISCLOSURES J. COLLIGNON

ADVISORY BOARD AND LECTURES:

AMGEN, SERVIER, BAYER, MERCK, ROCHE, LILLY, SANOFY, SIRTEX, CELGENE,
PFIZER, IPSEN, NOVARTIS, BMS, ASTRA-ZENECA

(~~TRAVEL AND ACCOMMODation~~) VIRTUAL CONGRES INSCRIPTION:

ROCHE, AMGEN, PFIZER, MSD, BMS

BILIARY TRACT CANCER WHICH TARGETS?

GENOMIC FINDINGS		IHCCA N=412 %	EHCCA N=57 %	GBCA N=85 %
ERB2 amplification		4	11	16
BRAF substitution		5	3	1
KRAS substitution		22	42	11
PI3CA substitution		5	7	14
FGFR 1-3 Fusions/amplifications		11	-	3
CDKN2A/B loss		27	19	17
IDH1/2 mutations		20	—	—
ARID1A alterations		18	12	13
TP53		2-29	40-55	25-46

BILIARY TRACT CANCER PLACE OF TARGETED THERAPY

A LOT OF DRUGS ARE STILL PENDING AND ONE MNP

NGS in BELGIUM
TRIALS only for BTC



REVIEW

Recommendations for the use of next-generation sequencing (NGS) for patients with metastatic cancers: a report from the ESMO Precision Medicine Working Group

»Summary of recommendations. **Tumour multigene NGS could be used to detect level I actionable alterations in cholangiocarcinoma.** Given that they are unlikely to be cost-effective in these cases, larger panels can be used only on the basis of specific agreements with payers taking into account the overall cost of the strategy (including off-label use of drugs) and pending a needed before implementing TMB in all cancers where anti-PD(L)1 antibodies are not approved «

Do not forget **MSI and NTRK** (standard) and **ERBBR2** (clinical trial)

Table 10. List of genomic alterations level I/II/III according to ESCAT in advanced cholangiocarcinoma (CC)

Gene	Alteration	Prevalence	ESCAT	References
IDH1	Mutations	20%	IA	Abou-Alfa G. K, et al. <i>Ann Oncol.</i> 2019 ¹²⁹
FGFR2	Fusions	15%	IB	Vogel A, et al. <i>Ann Oncol.</i> 2019 ¹³⁰
	MSI-H	2%	IC	Marabelle A, et al. <i>J Clin Oncol.</i> 2020 ¹³¹
NTRK	Fusions	2%	IC	Doebbele RC, et al. <i>Lancet Oncol.</i> 2020 ⁵⁰
BRAF ^{V600E}	Mutations	5%	IIB	Wainberg Z, et al. <i>J Clin Oncol.</i> 2019 ¹³²
ERBB2	Amplifications	10%	IIIA	Javle MM, et al. <i>J Clin Oncol.</i> 2017 ¹³³
	Mutations	2%		
PIK3CA	Hotspot mutations	7%	IIIA	André F, et al. <i>N Engl J Med.</i> 2019 ⁷²
BRCA 1/2	Mutations	3%	IIIA	De Bono J, et al. <i>N Engl J Med.</i> 2020 ⁹³
HRD in 5-15 % of all BTC				
MET	Amplifications	2%	IIIA	Camidge D, et al. <i>J Clin Oncol.</i> 2018 ⁵²

ESCAT, European Society for Medical Oncology (ESMO) Scale for Clinical Actionability of molecular Targets.

PHASE IIIb
2023

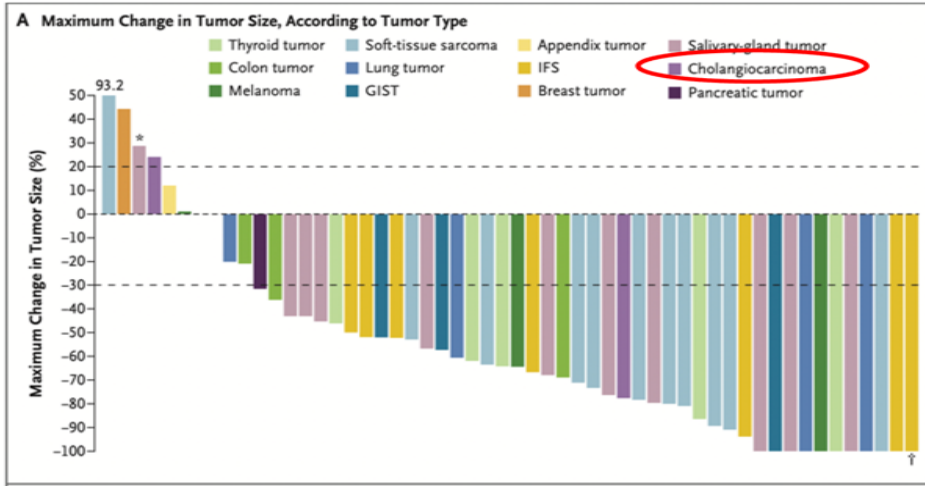
MNP

Reimbursed

Clinical trial

NTRK fusion target

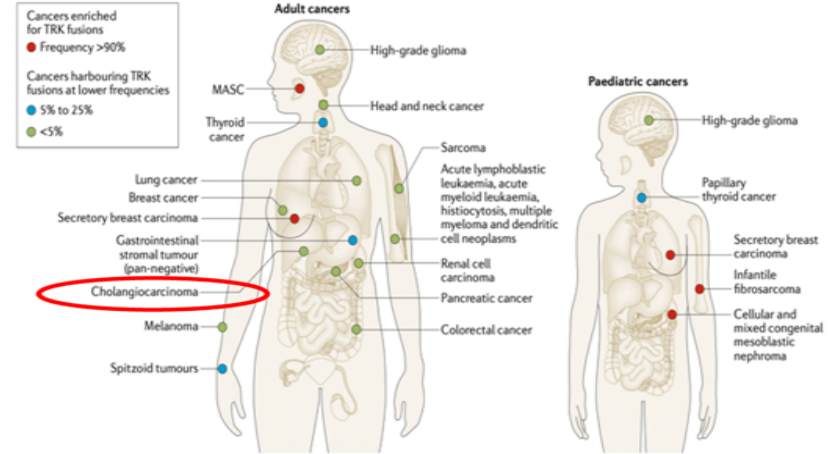
April 2018 LAROTRECTINIB FDA approval Second tissue agnostic FDA approval for treatment of cancer



**HIGH RESPONSE RATE AND DURABLE ACTIVITY
INDEPENDANT OF AGE AND TUMOR TYPE**

Drilon, NEJM 2018

IN BELGIUM 2 NTRK

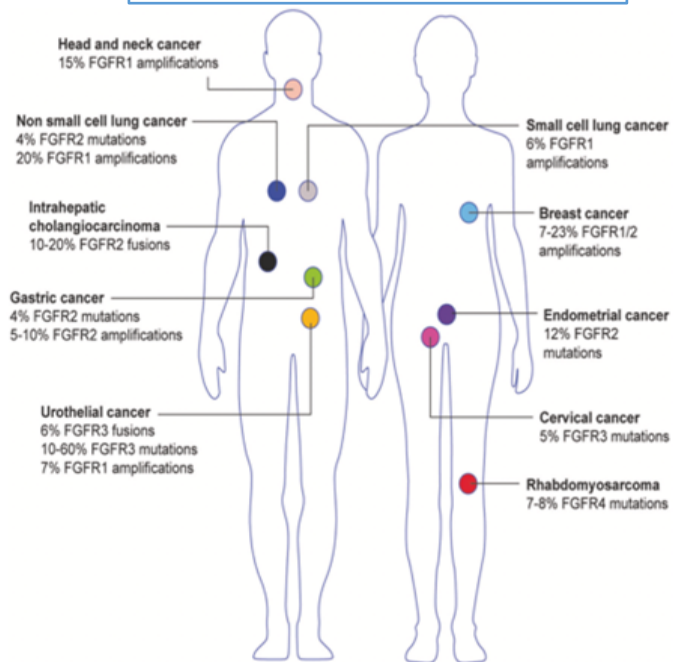


**NTRK fusion to check in
all tumor for fit patient**

E. Coco, Nature Review. Clinical Oncology 2018

**BEGIUM ACCESS (REIMBURSED)
LAROTRECTINIB: VITRAKVI
ENTRECTINIB: ROZLYTREK**

FGFR alterations



Seen 5–10% of all human cancers, although this frequency increases to 10–30% in urothelial carcinoma and intrahepatic cholangiocarcinoma.

MA KROOK, BJC 2021

**Pemigatinib
(Pemazyre)
FDA/EMA
BELGIUM
MNP**

adults with locally advanced or metastatic cholangiocarcinoma with a fibroblast growth factor receptor 2 (FGFR2) fusion or rearrangement that is **relapsed or refractory after at least one line of systemic therapy**

FIGHT-202: A PHASE 2 STUDY OF PEMIGATINIB IN PATIENTS WITH PREVIOUSLY TREATED LOCALLY ADVANCED OR METASTATIC CHOLANGIOCARCINOMA

Pemigatinib is a selective, potent, oral inhibitor of FGFR1, 2, and 3

FGF/FGFR status
Progression after ≥ 1 prior therapy
ECOG PS ≤ 2

Oral pemigatinib
13,5 mg QD
2 W on 1 week off

Cohort A (planned N=100)
FGFR2 fusion/rearrangements

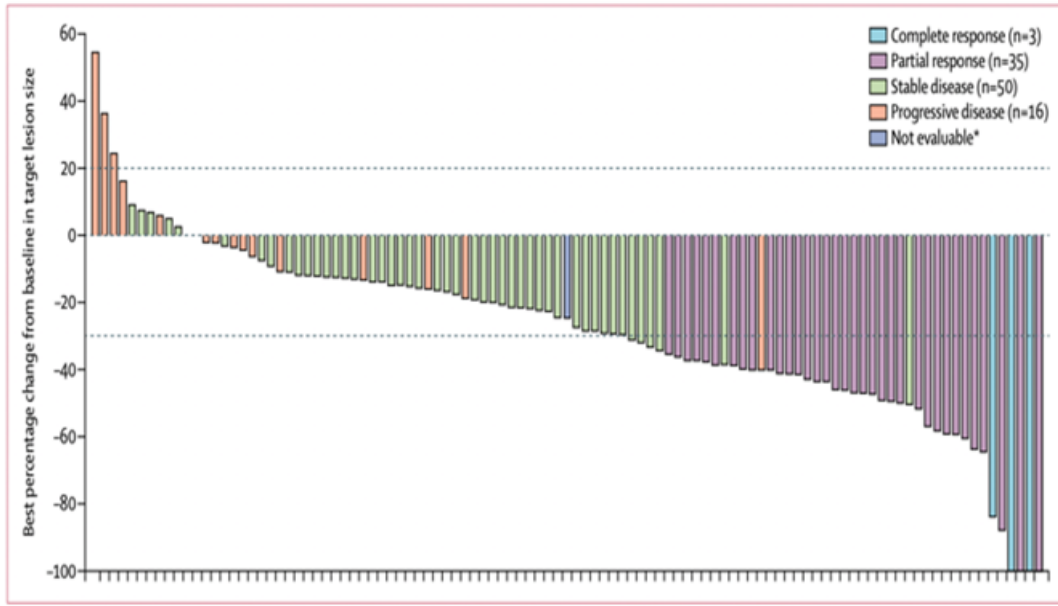
Cohort B (planned N=20)
Other FGF/FGFR genetic alterations

Cohort C (planned N=20)
NO FGF/FGFR genetic alterations

Primary endpoint: ORR in cohort A

- **Secondary endpoints** ORR in cohorts B, A + B, and C; duration of response, disease control rate, PFS, OS, and safety in all cohorts

Abou-Alfa, Lancet onco, 2020



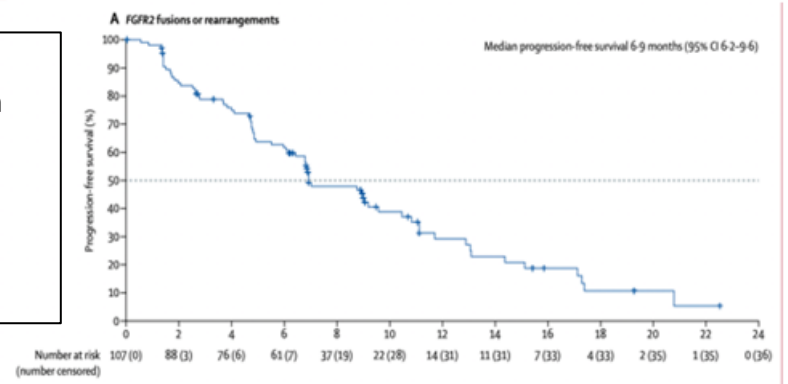
**1206 screened
N cohort A=107**

**Primary endpoint
ORR cohort A**

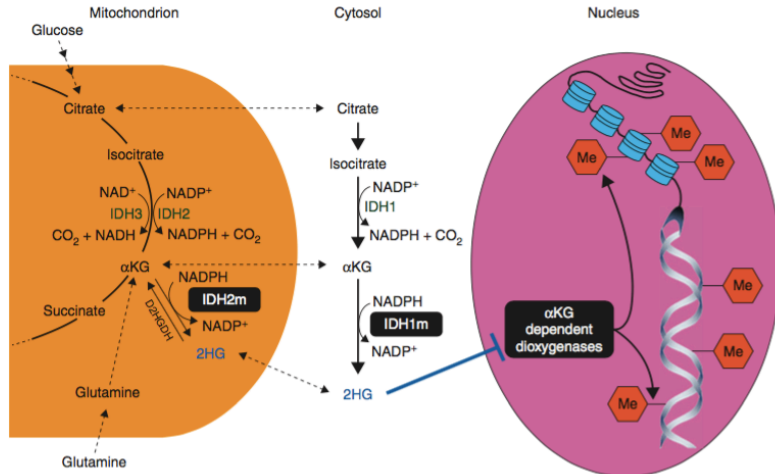


FIGHT 202	PEMIGATINIB
mPFS	6,9
ORR	35,5 %
mOS	21,1
DCR	82 %

FIGHT 302 PHASE III
 pemigatinib vs gemcitabine-cisplatin
PROOF PHASE III
 infigratinib vs gemcitabine-cisplatin
FOENIX-CCA3
 Futimatinib vs gemcitabine-cisplatin



IDH 1 MUTATIONS: IVODISENIB (TIBSOVO)



IDH= isocitrate dehydrogenase

Dang, Annals of onco, 2016

FDA approval: augustus 2021
PHASE 3b BELGIUM Q2 2023?

N=181

- **BTS**
- **Centrally confirmed mIDH1 status by NGS**
- **ECOG PS 0-1**
- **1-2 prior therapies**

ClarIDHy trial

Lancet Oncol 2020; 21: 796–807

Ivosidenib 500 mg QD orally
in continuous 28-day cycles
N=124

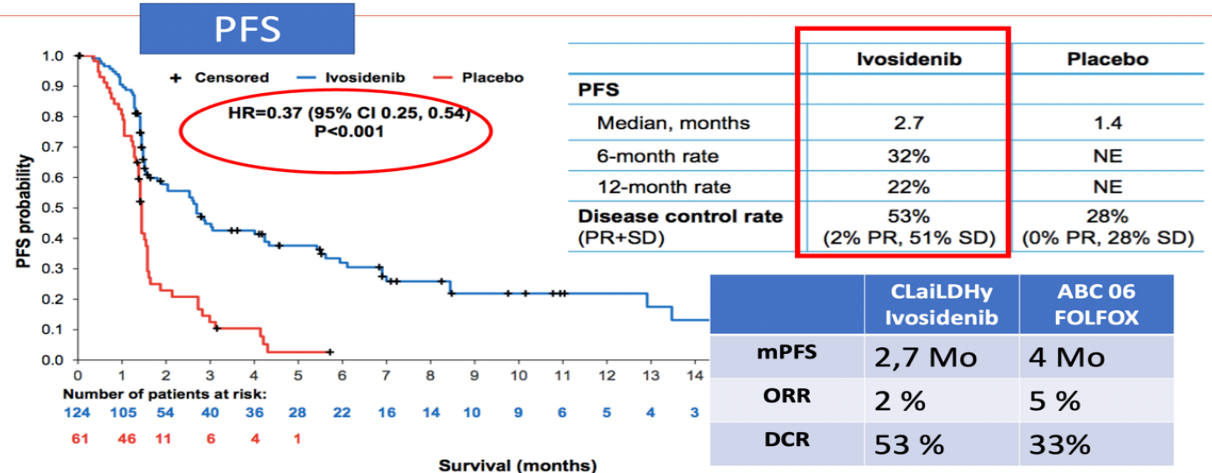
Double blind
rando
R2:1

Placebo
N= 61

**Cross over permitted
after progression**

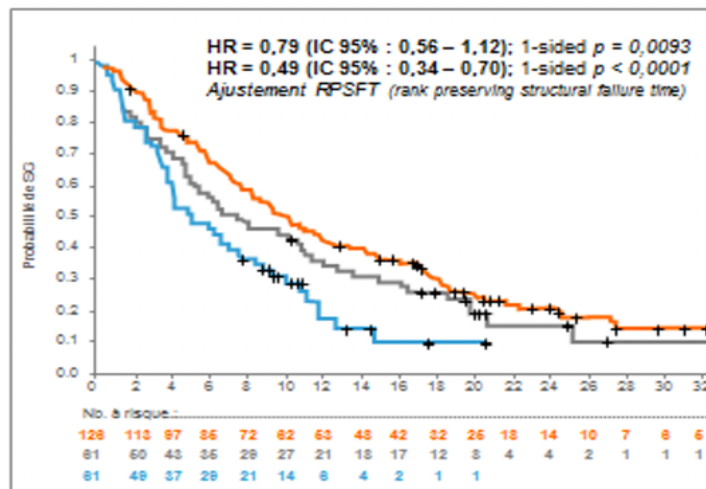
Primary endpoint: PFS by blinded independent radiology center (IRC)

- **Secondary endpoints included:** safety and tolerability; PFS by local review; OS; objective response rate; quality of life (QoL)†; pharmacokinetics/pharmacodynamics



IDH 1 MUTATIONS: IVODISENIB

ClarIDHy: final OS analysis after RPSFT adjustment
for crossover (70% of the patients in placebo arm)



MEDIAN OS FOR PLACEBO AFTER ADJUSTMENT FOR CROSSOVER = 5,1 months ($p < 0.0001$) vs 10.3 (ivosidenib)

+ Censored
 — Placebo
 — Placebo RPSFT adjusted
 — Ivosidenib

	Ivosidenib (n=126)	Placebo (n=61)
Number of events (%)	100 (79,4%)	50 (82,0%)
Median OS (months)	10,3	7,5
6 month rate	69%	57%
12 month rate	43%	36%

PANCREATIC CANCER in BELGIUM 2022

OLAPARIB (LYNPARZA)

PENDING (SOON reimbursed)

IN BELGIUM
NGS ACCESS



REVIEW

Recommendations for the use of next-generation sequencing (NGS) for patients with metastatic cancers: a report from the ESMO Precision Medicine Working Group

» tumour multigene NGS in patients with advanced PDAC not yet in daily practice but ESMO considers it is the mission of clinical research centres and their networks to propose multigene sequencing to patients with advanced PDAC in the context of molecular screening programmes, in order for patients to get access to innovative drugs. If multigene sequencing is not carried out, **detection of MSI and NTRK** fusions should be done using cheaper standard methods, pending drugs are approved and reimbursed. «



Table 8. List of genomic alterations level I/II/III according to ESCAT in advanced pancreatic ductal adenocarcinoma (PDAC)

Gene	Alteration	Prevalence	ESCAT	References
BRCA1/2	Germline mutations	1%–4%	IA	The Cancer Genome Atlas Research Network. <i>Cancer Cell</i> . 2017 ¹¹¹ Golan T, et al. <i>N Engl J Med</i> . 2019 ¹¹²
	Somatic mutations	3%	IIIB	Shroff R, et al. <i>JCO Precis Oncol</i> . 2018 ¹¹³
	MSI-H	1%–3%	IC	Pihlak R, et al. <i>Cancers</i> . 2018 ¹¹⁵ Marcus L, et al. <i>Clin Cancer Res</i> . 2019 ⁹⁷
NTRK	Fusions	<1%	IC	Cocco E, et al. <i>Nat Rev Clin Oncol</i> . 2018 ¹¹⁴ Doebele RC, et al. <i>Lancet Oncol</i> . 2020 ⁵⁰
KRAS	Mutations	90%	IIIA	Zeitouni D, et al. <i>Cancers</i> . 2016 ¹¹⁶
PIK3CA	Hotspot mutations	3%	IIIA	Heestand G, et al. <i>Oncotarget</i> . 2015 ¹¹⁷ Payne S, et al. <i>J Clin Oncol</i> . 2015 ¹¹⁸
BRAF ^{V600E}	Mutations	3%	IIIA	Hyman D, et al. <i>N Engl J Med</i> . 2015 ¹¹⁹
MDM2	Amplifications	2%	IIIA	Azmi A, et al. <i>Eur J Cancer</i> . 2010 ¹²⁰
ERBB2	Amplifications/ mutations	1%–2%	IIIA	Waddell N, et al. <i>Nature</i> . 2015 ¹²¹ Harder J, et al. <i>Br J Cancer</i> . 2012 ¹²² Hyman D, et al. <i>Nature</i> . 2018 ⁵⁵
NRG1	Fusions	1%	IIIA	Jones M, et al. <i>Clin Cancer Res</i> . 2019 ¹²³
ALK	Fusions	<1%	IIIA	Singhi A, et al. <i>J Natl Compr Canc Netw</i> . 2017 ¹²⁴
RET	Fusions	<1%	IIIA	Drilon A, et al. <i>J Clin Oncol</i> . 2018 ²¹
ROS1	Fusions	<1%	IIIA	Pishvaian M, et al. <i>J Clin Oncol</i> . 2018 ¹²⁵

Mut KRAS G12C: recent data with ADAGRASIB (ASCO GI 2022)

GENETIC and PC



National
Comprehensive
Cancer
Network®

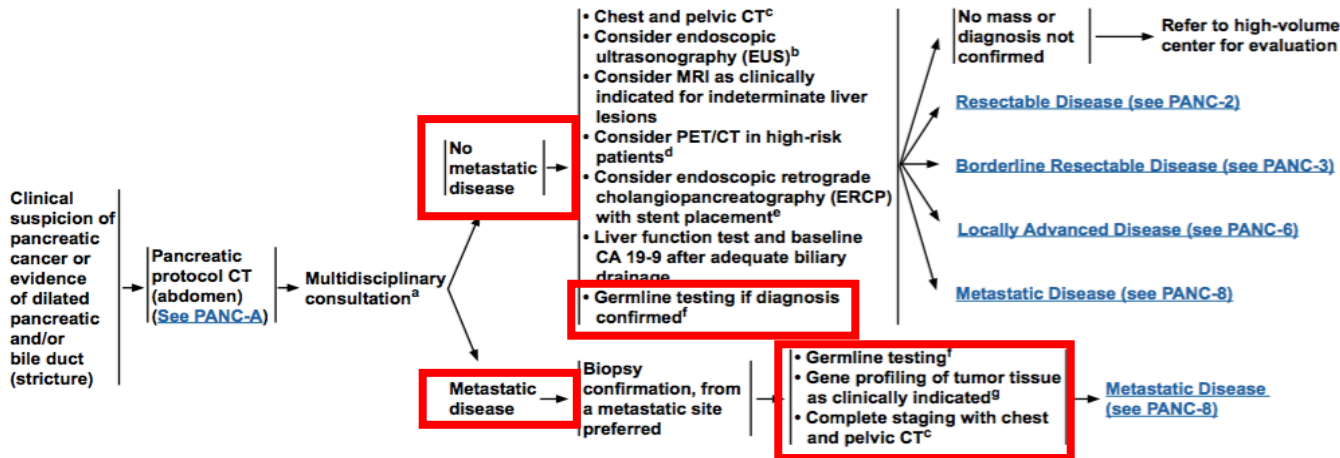
NCCN Guidelines Version 1.2020 Pancreatic Adenocarcinoma

[NCCN Guidelines Index](#)

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[Discussion](#)

CLINICAL PRESENTATION AND WORKUP



^f Germline testing is recommended for any patient with confirmed pancreatic cancer, using comprehensive gene panels for hereditary cancer syndromes. Genetic counseling is recommended for patients who test positive for a pathogenic mutation or for patients with a positive family history of cancer, especially pancreatic cancer, regardless of mutation.

^a Multidisciplinary review should ideally involve expertise from diagnostic imaging, interventional endoscopy, medical oncology, radiation oncology, surgery, pathology, geriatric medicine, and palliative care. Consider consultation with a registered dietitian. See [NCCN Guidelines for Older Adult Oncology](#) and [NCCN Guidelines for Palliative Care](#).

^b EUS to confirm primary site of involvement; EUS-guided biopsy if clinically indicated.

^c Imaging with contrast unless contraindicated.

^d PET/CT scan may be considered after formal pancreatic CT protocol in high-risk patients to detect extra pancreatic metastases. It is not a substitute for high-quality, contrast-enhanced CT. See [Principles of Diagnosis, Imaging, and Staging \(PANC-A\)](#).

^e See [Principles of Stent Management \(PANC-B\)](#).

SOMATIC GENE PROFILING

SEARCH FOR ACTIONABLE MUTATIONS LIKE FUSION (NTRK,ROS, ALK,NRG1) MUTATIONS (BRAF,BRCA1/2,PALB2,HER2,KRAS...) MMR DEFICIENCY



BRCA MUTATED METASTATIC PANCREATIC CANCER

FISRT LINE
MAINTENANCE

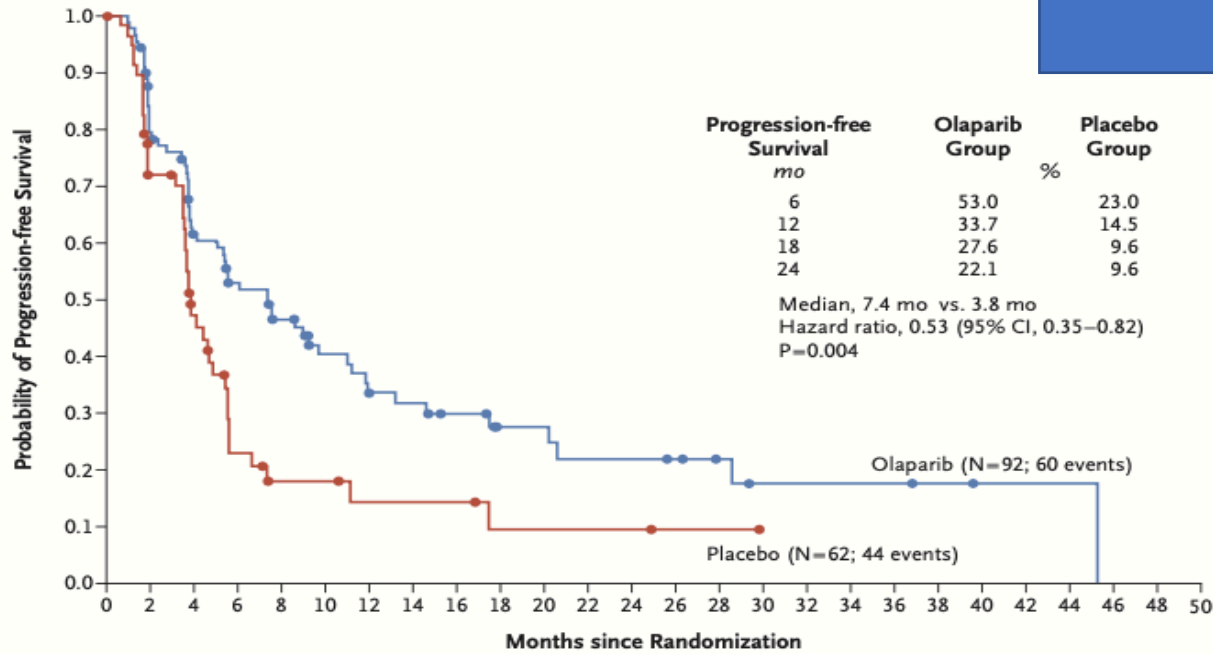
4-7 % OF PC HAVE A GERMLINE BRCA MUTATION

CELLS HAVE A DEFICIENCY IN HOMOLOGOUS RECOMBINATION AND ARE MORE SENSITIVE TO PARP INHIBITOR (poly(adenosine diphosphate–ribose polymerase)

PARP inhibitors cause an accumulation of DNA damage and tumor-cell death. In a phase 2 trial, olaparib had antitumor activity in heavily pretreated patients with a germline *BRCA* mutation and metastatic pancreatic cancer.

BRCA MUTATED METASTATIC PANCREATIC CANCER

A Progression-free Survival



No. at Risk

Olaparib	92	69	50	41	34	24	18	17	14	10	10	8	8	7	5	3	3	3	3	2	1	1	1	0
Placebo	62	39	23	10	6	6	4	4	4	2	2	2	2	1	1	0								

MEDIAN PFS 7,4 MO VS 3,8
HR 0,53

PANCREATIC ADENOCARCINOMA

STAGING: TDM(+/- echo-endo, laparoscopy)

clinical trials with
targeted treatment in
adjuvant and metastatic
lines

**RESECTABLE
(10-15%)**

**borderline
RESECTABLE**

**LOCALLY ADVAN
NON RESECTA**

**MMR/MSI testing
BRCA
Germline testing
Somatic testing**

**NAD
in some indications**

if ICTERE, BILIARY DRAINAGE

**NAD
+/- RT
prefer FOLFIRINOX**

**CHEMO
6 MONTHS**

**AGNOSTIC THERAPY:
MSI-H: PEMBROLIZUMAB
NTRK FUSION: LAROTRECTINIB/ENTRECTINIB
GERMLINE BRCA MUTATED: OLAPARIB MAINTENANCE
SOMATIC MUTATION: ACTIONABLE TREATMENT IN
CLINICAL TRIALS**

**GEM or FU
NEW: GEM/CAPE
(ESPAC 4)**

**total of 6 months
chemo with NAD**

**SECOND LINE if patient still FIT
and according to first line
GEM, Nanolrinotecan, FOLFOX, (FOLFIRI)**



mCRC
in BELGIUM 2022
PLACE OF TARGETED
THERAPY

A LOT OF DRUGS ARE STILL
PENDING

BIOMARKERS testing for mCRC in 2021 (SOC belgium access)

aberration	%	Therapeutic option
KRAS/BRAF/NRAF WT	40	Cetuximab panitumumab
BRAF V600E mut	8	Encorafenib + cetuximab Encorafenib + panitumumab
HER2 positive IHC 3+/2+ with +ISH or NGS	3(all) 5-10 (RAS WT)	If KRAS-NRAS WT Trastuzumab + pertuzumab Trastuzumab + lapatinib Trastuzumab + tucatinib Trastuzumab deruxtecan
MSI-high (PCR or NGS panel)/Deficient Mismatch Repair	8	Pembrolizumab Nivolumab Nivo+Ipi
NTRK gene fusion	< 0,5	Larotrectinib/Entrectinib
KRAS G12 C mutation	3	AMG 510: sotorasib
BRAF non V600E mut	4	
Pole mutation	<1	
Others rare like FGFR fusion, RET fusion, ALK fusion	<1	RET inhibition PRALSETINIB/SELPERCATINIB

MSI-H mCRC in BELGIUM 2022

PEMBROLIZUMAB FIRST LINE (KEYTRUDA)

MSI-H

KEYNOTE-177 design

mCRC MSI

Key eligibility criteria

- MSI-H (PCR)/dMMR (IHC)
- Stage 4 CRC
- ECOG PS 0-1
- Treatment naive
- Measurable disease Recist V1.1

R 1:1

N=153

Pembro 200 mg IV Q3W for ≤ 35 cycles

N=154

Investigator choice chemotherapy

Optional PEMBRO at PD (60 %)

SOC CHEMO (N=143)	%
FOLFIRI	11,2
FOLFIRI + BEVA	25,2
FOLFIRI+CETUX	7,7
mFOLFOX 6	7,7
mFOLFOX 6+BEVA	44,8
mFOLFOX 6 +CETUX	3,5

Stratification factors

- ASIA vs non-ASIA region
- ECOG PS 0 vs 1
- ESCC vs EAC

Dual primary: OS and PFS (RECIST 1.1,BICR)

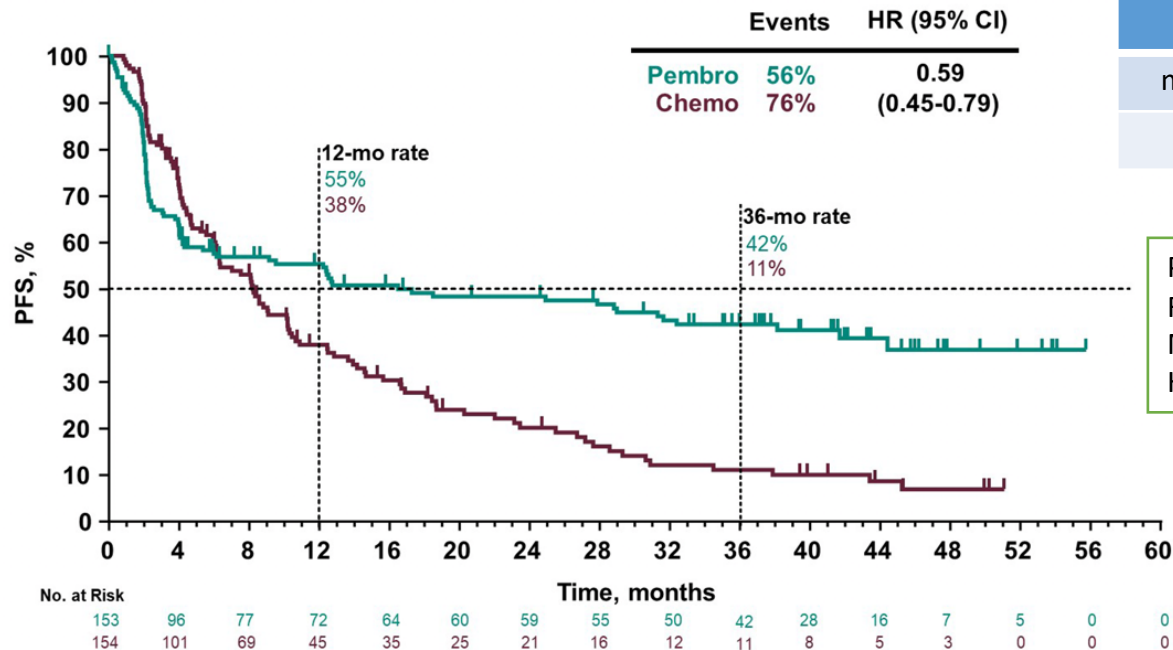
Secondary endpoints: ORR (RECIST 1.1,BICR),PFS2,HRQoL,safety

Tumor response assesed at 9 and Q9W

	STAGE II	STAGE III	STAGE IV
MSI-H CRC	22 %	12 %	3,5 %

ABSTRACT 3500
Update ASCO 2021
T Andre

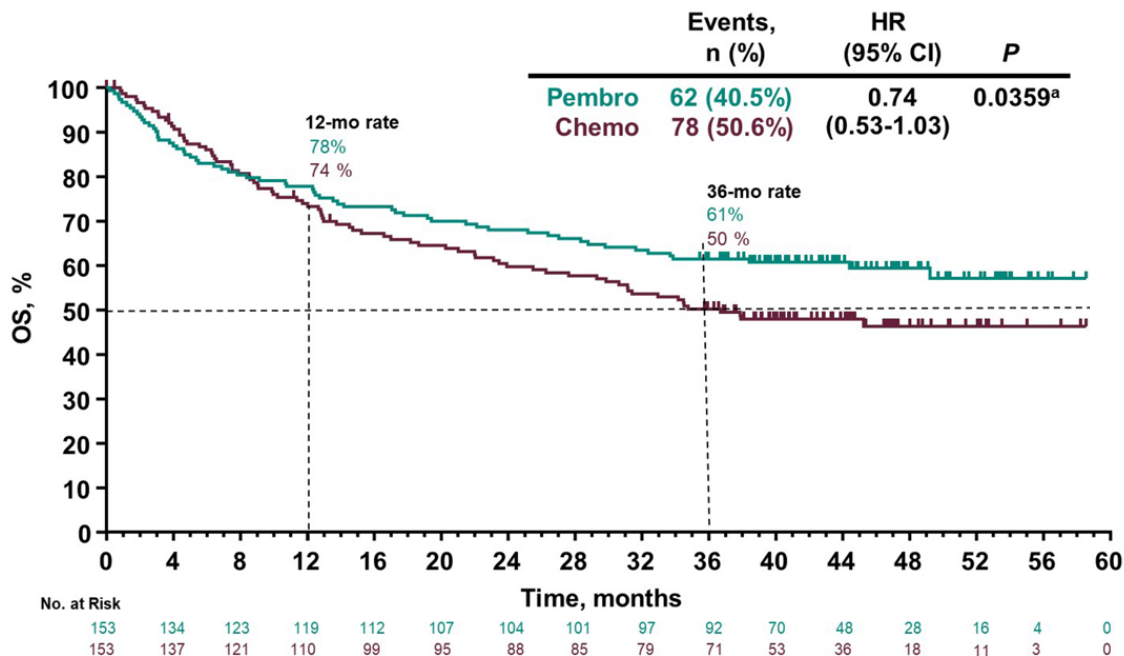
Progression-Free Survival



	PEMBRO	CHEMO
mPFS mo	16,5	6,1
HR	0,59	

PRESPECIFIED STATISTICAL CRITERIA
FOR SUPERIORITY OF PEMBRO WAS
MET: HR FOR PFS 0,59
HIGHLY SIGNIFICANT P VALUE

Overall Survival



**Non statistically significant
reduction in mortality BUT HIGH
CROSS OVER RATE (60 %)**

^aPembrolizumab was not superior to chemotherapy for OS as one-sided $\alpha > 0.0246$. Pre-specified sensitivity analyses to adjust for crossover effect by rank-preserving structure failure time model and inverse probability of censoring weighting showed OS HRs of 0.66 (95% CI 0.42-1.04) and 0.77 (95% CI 0.44-1.38). Data cut-off: 19Feb2021.



CONCLUSIONS



GI cancers current situation in **BELGIUM**

- **Trastuzumab in GC HER2 + cancer (waiting T-DxD,immunotherap))**
- **IMMUNOTHERAPY NOW IN EGC,HCC,MSI-H CRC (discussed criteria)**
- **BTC: MNP for Pemigatinib in FGFR2 fusion**
- **Pancreatic cancer maintenance: olaparib in BRCA PC very soon`**
- **Reimbursed Larotrectinib and Entrectinib in all NTRK fusion + tumors**



GI cancers in **BELGIUM GO FURTHER**

**VERY IMPORTANT TO FIND THE GOOD TARGET AND THE
GOOD TRIALS OR MNP**





BSMO



Joëlle Collignon, Wim Demey
BSMO BOARD