Advanced Pancreatic and Biliary Track Cancers

An Update

Jaffer A. Ajani Oct 04, 2022
Acknowledging Dr. Javle for some slides

Jaffer Ajani Disclosures

Paid consultant (Ad hoc)

BMS
Merck
Astellas
Taiho
More
Zymeworks
Beigene
Dava
Astrazeneka
Acrotech
Daiichi
Vaccinogen
Innovent
Merck
Serrono
Oncotherics
Bayer
OncLive
FivePrime
Amgen
GRAIL
Novartis
Geneos
Arcus
Servier
BI
Gilead

Research Grants to UTMDACC

BMS
Merck
Astellas
Taiho
Delta Fly
Roche
Prolinx
Zymewors
Daiichi Leap
Gilead
LaNova
Turning point

Biliary Tract Cancers

Several areas of major interest

IDH mutations

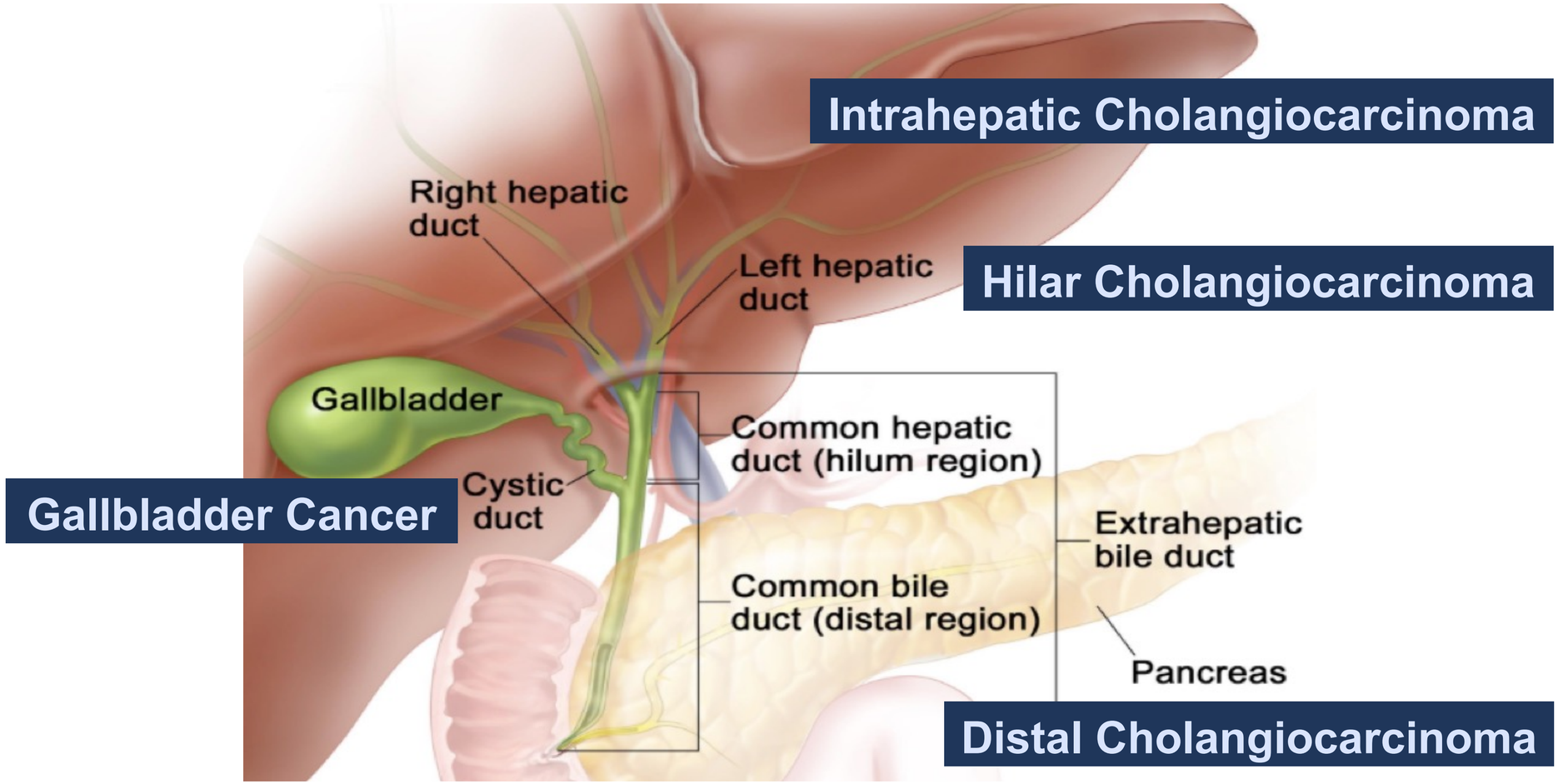
FGFR fusions and alterations

Immune modulations

Her2 over expression

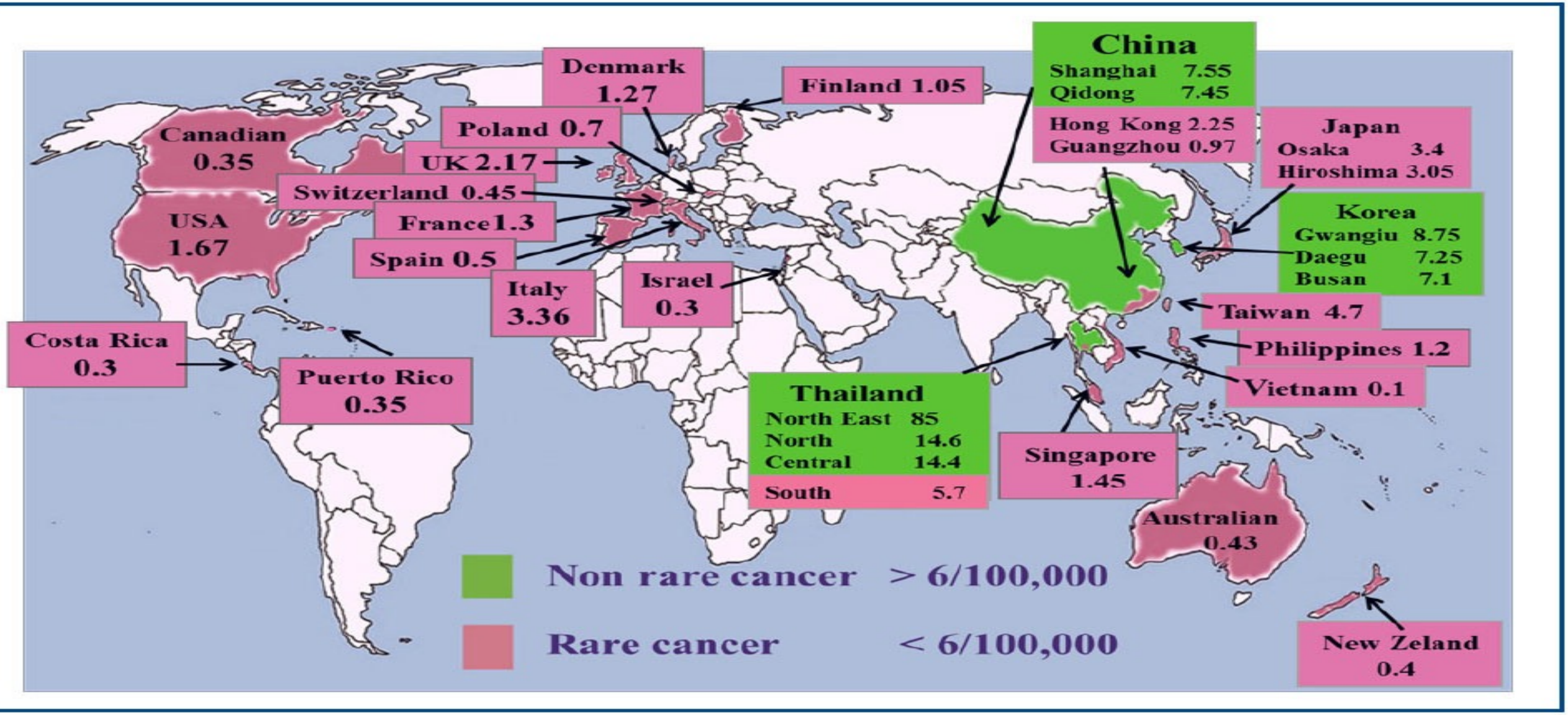
BRAF mutations

Biliary Tract Cancers (BTCs)

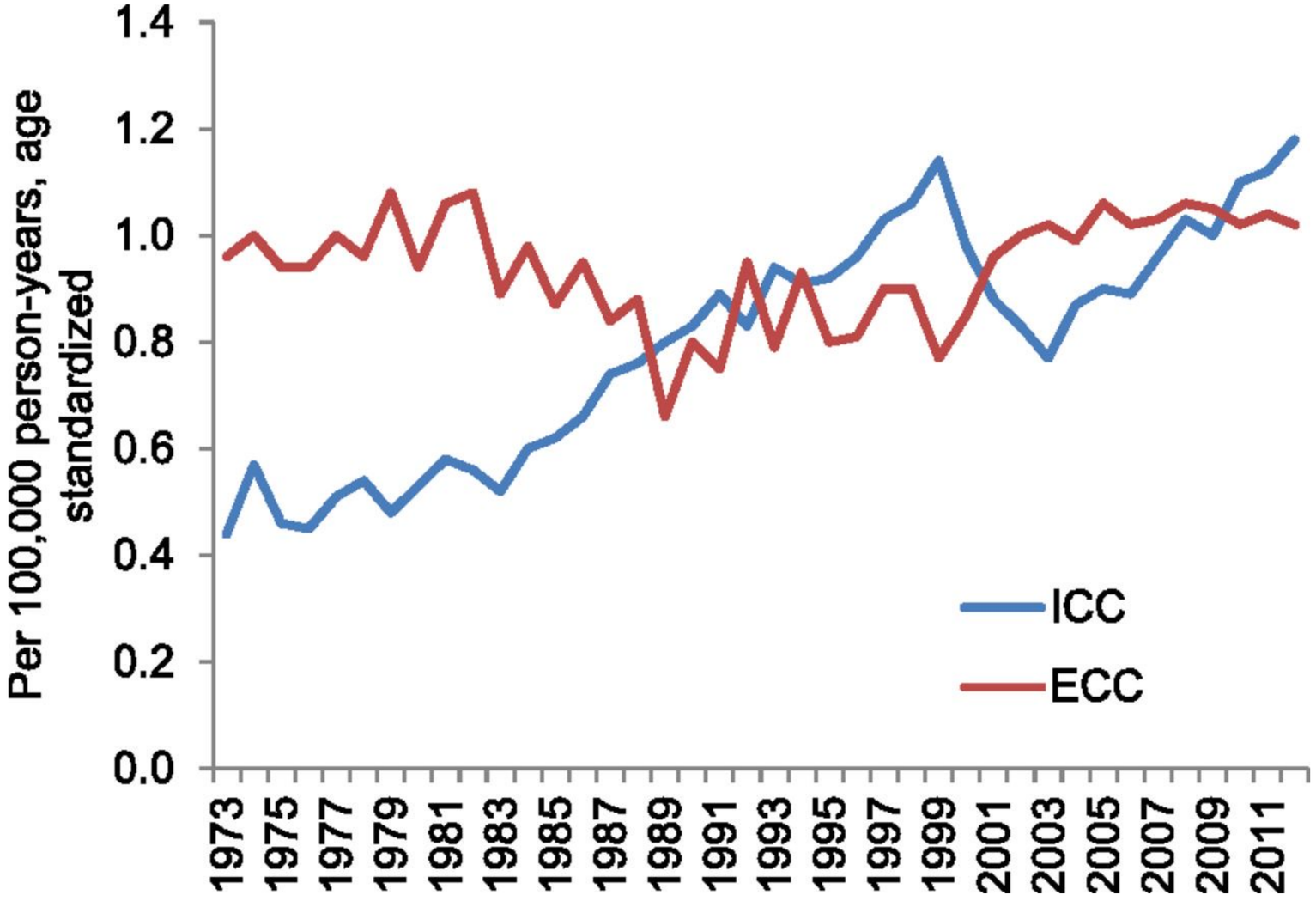


NCI Bile Duct Cancer PDQ 2017

Cholangiocarcinoma Worldwide



Age-adjusted incidence of intrahepatic cholangiocarcinoma and extrahepatic cholangiocarcinoma, 1973–2012..



Supriya K. Saha et al. The Oncologist 2016;21:594-599

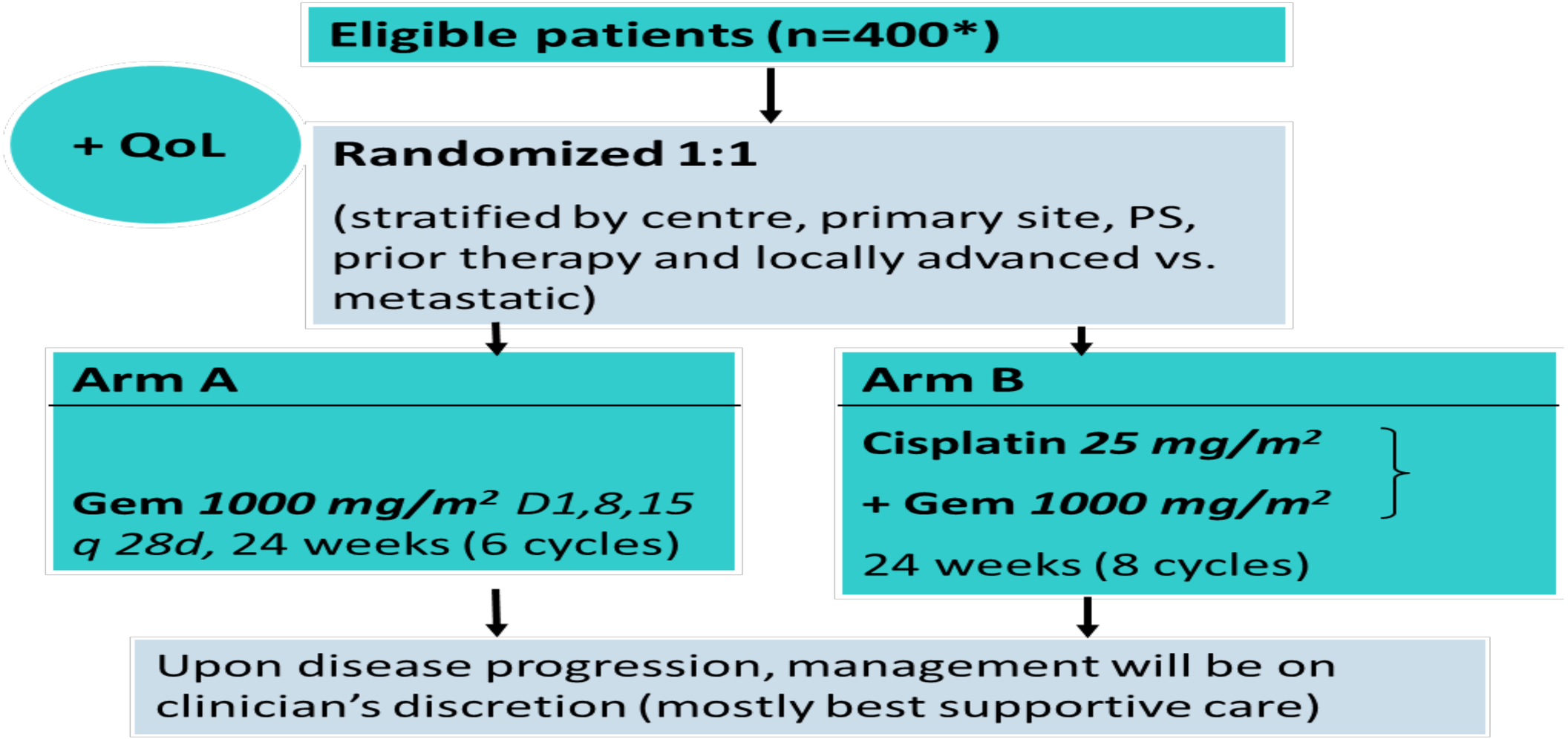
The Oncologist

Incidence of mutations in targetable pathways in biliary cancers

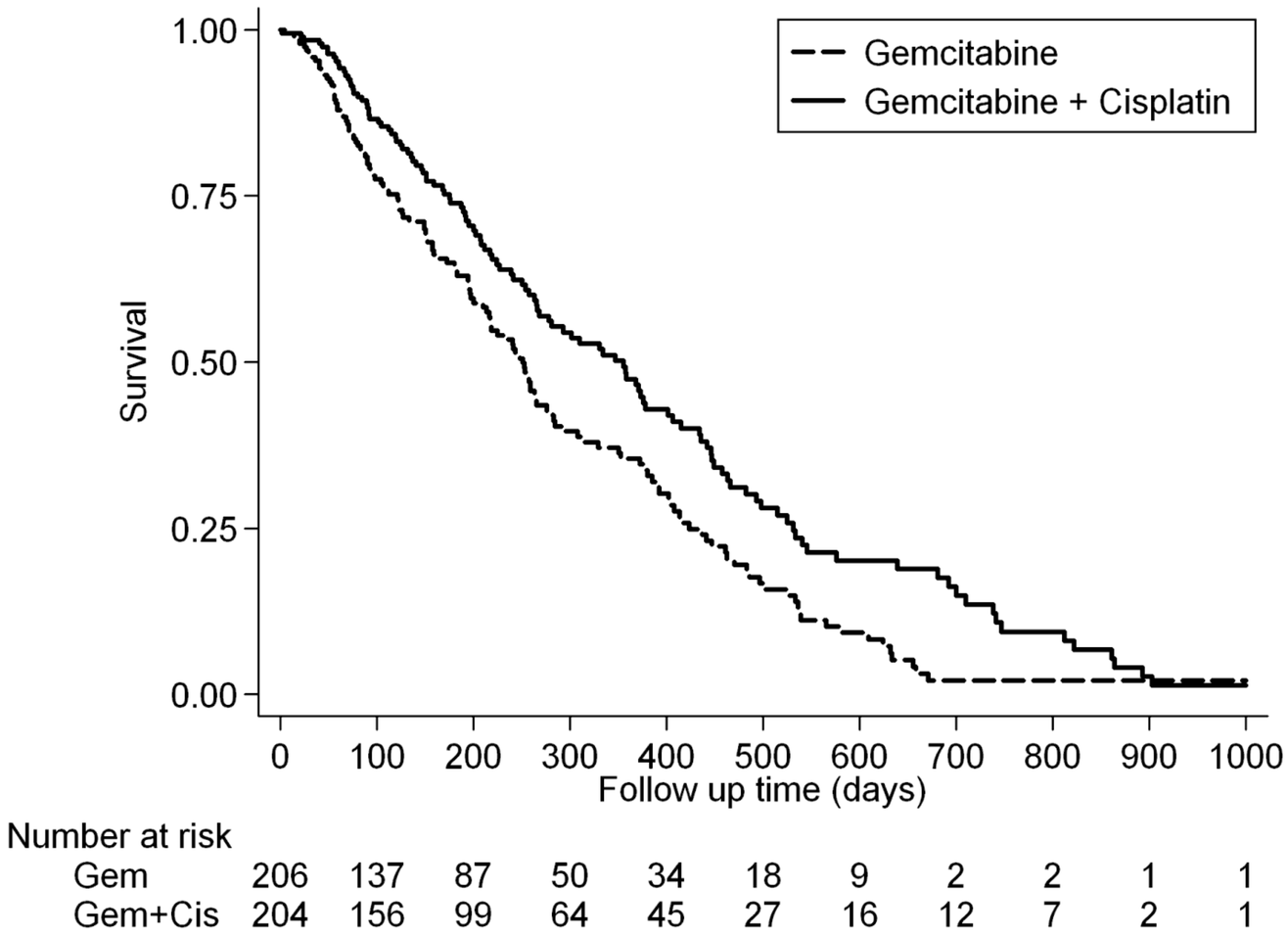
CGP findings	ICCA	
Total GA/patient	3.6	
CRGA/patient	2.0	
ERBB2 amplifications	4%	
BRAF substitutions	**5%**	
KRAS substitutions	22%	
PI3KCA substitutions	5%	
FGFR1–3 fusions and amplifications	**11%**	
CDKN2A/B loss	27%	
IDH1/2 substitutions	**20%**	
ARID1A alterations	18%	
MET amplifications	2%	

Javle M, et al. *Cancer* 2016;122:3838–3847

ABC-02 – ADVANCED BILIARY CANCER



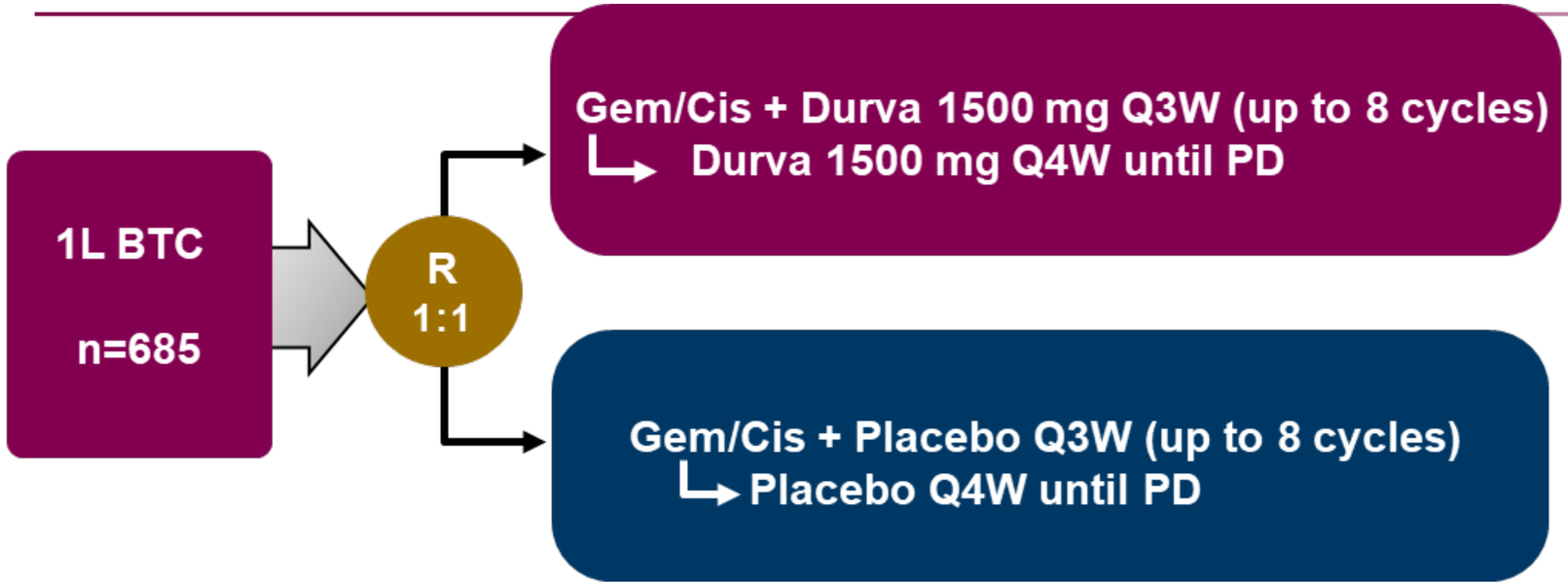
Phase 3 ABC-02 trial: survival data (ITT)



Treatment arm	Gem	Gem+Cis
Number of patients	n=206	n=204
Deaths, n (%)	141 (68.5)	122 (59.8)
Median survival, months	8.3	11.7
Log-rank p-value	0.002	
HR (95% CI)	0.70 (0.54–0.89)	

Valle J, et al. *N Engl J Med* 2010;362:1273–1281

TOPAZ-1 study design: durvalumab + chemotherapy in 1L BTC



PRIMARY ENDPOINT

OS

SECONDARY ENDPOINTS

PFS, ORR, DOR, PROs, Safety, Biomarkers (PD-L1), PK/ADA

Patient population

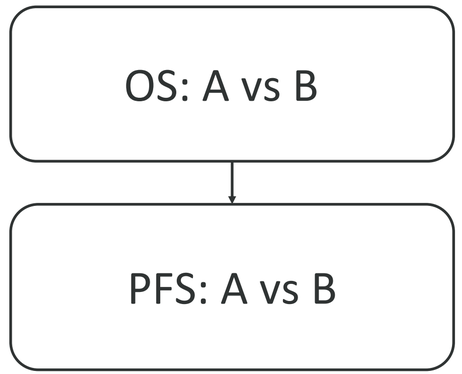
- Locally advanced, or metastatic BTC, or recurrence >6 months from curative surgery or last dose of adjuvant therapy
- Bili ≤2.0 × ULN,
- ECOG PS 0 and 1,
- Must have at least one measurable lesion by RECIST 1.1 at baseline
- Ampullary cancer excluded

Stratification factors

- Disease status (initially unresectable vs recurrent)
- Primary tumor location (ICC, ECC, GBC)

MTP at IA2

Statistical testing of PFS only if OS is statistically significant



1L, first line; ADA, anti-drug antibody; Bili, bilirubin; BTC, biliary tract carcinoma; DOR, duration of response; Durva, durvalumab; ECC, extrahepatic cholangiocarcinoma; ECOG PS, Eastern Cooperative Oncology Group performance score; GBC, gallbladder cancer; Gem/Cis, gemcitabine and cisplatin; ICC, intrahepatic cholangiocarcinoma; MTP, multiple testing procedure; ORR, overall response rate; OS, overall survival; PD, progressive disease; PD-L1, programmed cell death ligand-1; PFS, progression-free survival; PK, pharmacokinetics; PRO, patient-reported outcome; Q3W, every 3 weeks, Q4W, every 4 weeks; R, randomization; RECIST, Response Evaluation Criteria in Solid Tumors; ULN, upper limit of normal

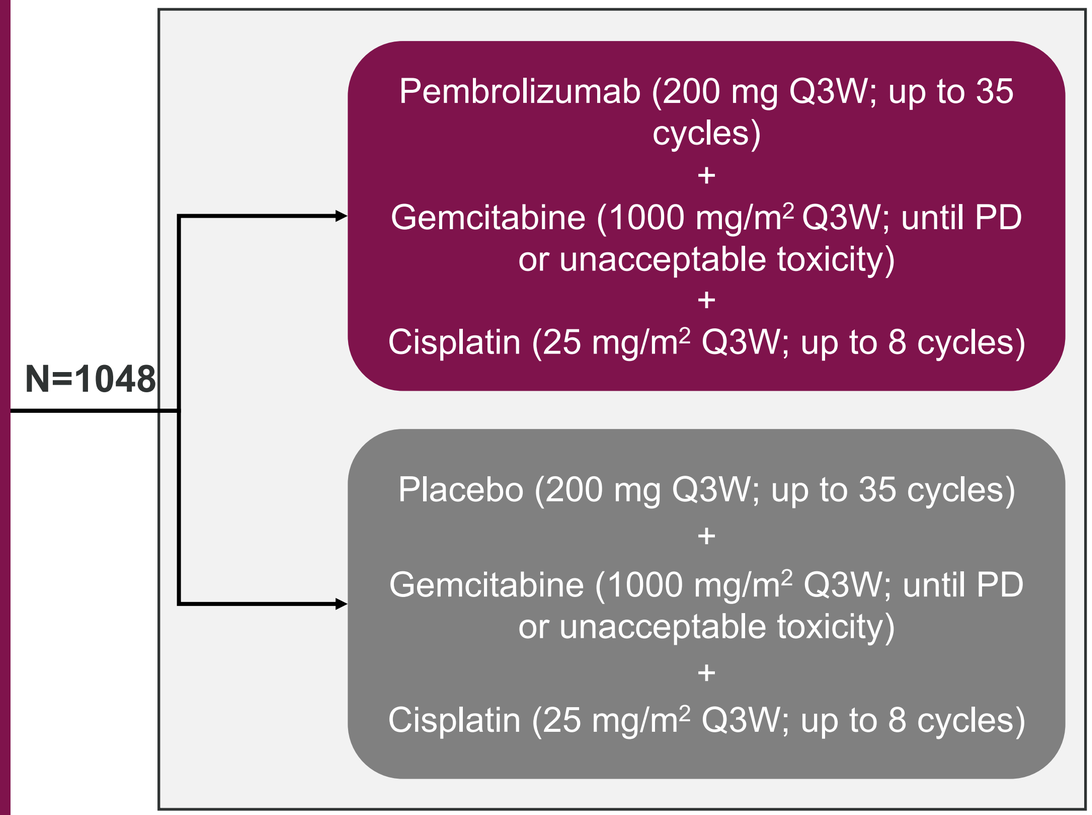
NIH 2021. NCT03875235. https://clinicaltrials.gov/ct2/show/NCT03875235. Accessed November 30, 2021; Data on file. AstraZeneca. 2021

	Durvalumab + GemCis (N=341)	Placebo + GemCis (N=344)
Median age (range), y	64 (20–84)	64 (31–85)
Female, %	50.4	48.8
ECOG PS 0, %	50.7	47.4
Median follow-up, mo	13.7	12.6
Median OS (95% CI), mo	12.8 (11.1–14.0)	11.5 (10.1–12.5)
18-month OS (95% CI), %	35.1 (29.1–41.2)	25.6 (19.9–31.7)
24-month OS (95% CI), %	24.9 (17.9–32.5)	10.4 (4.7–18.8)
Median PFS (95% CI), mo	7.2 (6.7–7.4)	5.7 (5.6–6.7)
Grade 3/4 AEs, n (%)*	256 (75.7)	266 (77.8)
TRAEs leading to death, n (%)*	2 (0.6)	1 (0.3)

*Safety data percentages are calculated from the safety population (n=338 for durvalumab + GemCis and n=342 for placebo + GemCis).

KEYNOTE-966: pembrolizumab plus GemCis versus GemCis alone in first-line advanced and/or unresectable BTC

Screening/baseline:
- Histologically confirmed diagnosis of advanced (metastatic) and/or unresectable (locally advanced) BTC (ampullary cancer excluded)
- Measurable disease based on RECIST v1.1, as determined by the site investigator
- No prior systemic therapies
- No CNS metastases and/or carcinomatous meningitis
- Participants with a history of hepatitis B/C can be enrolled if they meet study criteria
- Availability of archival tumor tissue sample or newly obtained core or excisional biopsy of a tumor lesion
- Life expectancy >3 months
- Adequate organ function



Primary objective:
- OS

Secondary objectives:
- ORR (RECIST v1.1; BICR)
- DOR (RECIST v1.1; BICR)
- PFS (RECIST v1.1; BICR)

Safety outcomes:
- Number of patients experiencing more than one adverse event
- Discontinuations due to adverse events

Status	Active, not recruiting
Estimated completion date	August 31, 2023

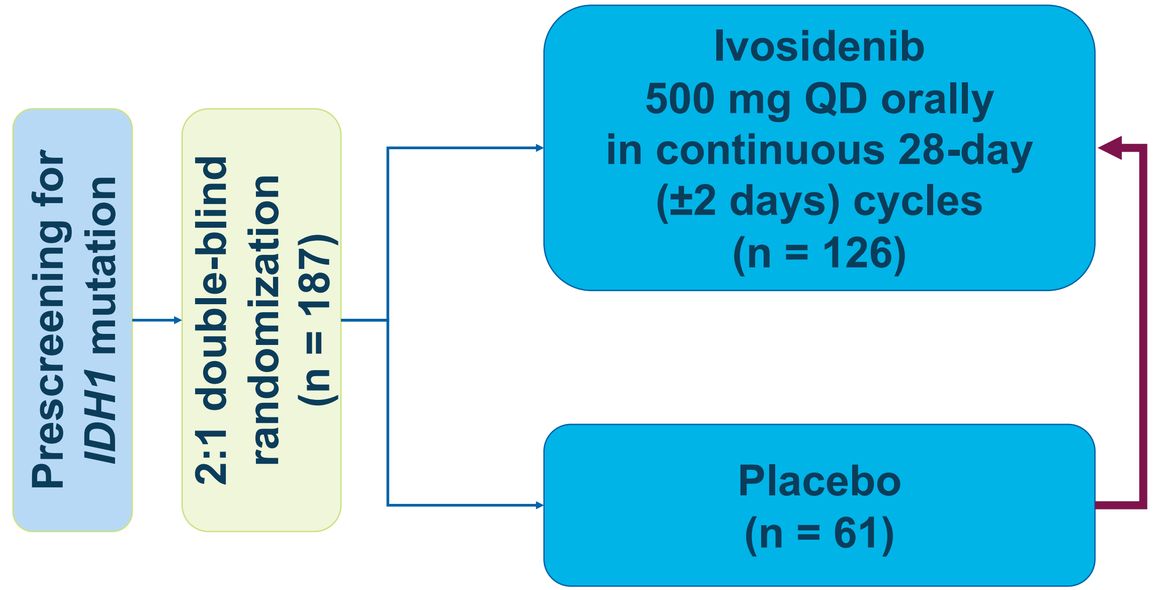
BICR, blinded independent central review; BTC, biliary tract carcinoma; CNS, central nervous system; DOR, duration of response; GemCis, gemcitabine-cisplatin; ORR, objective response rate; OS, overall survival; PD, progressive disease; PFS, progression-free survival; Q3W, every 3 weeks; RECIST, Response Evaluation Criteria in Solid Tumors

NIH 2021. NCT04003636. https://clinicaltrials.gov/ct2/show/NCT04003636. Accessed November 17, 2021

ClarIDHy: Study design and endpoints

Key eligibility criteria

- ≥ 18 years of age
- Histologically confirmed diagnosis of CCA
- Centrally confirmed m*IDH1*[a] status by NGS
- ECOG PS score 0 or 1
- 1−2 prior therapies (at least 1 gemcitabine- or 5-FU-containing regimen)
- Measurable lesion as defined by RECIST v1.1
- Adequate hematologic, hepatic, and renal function

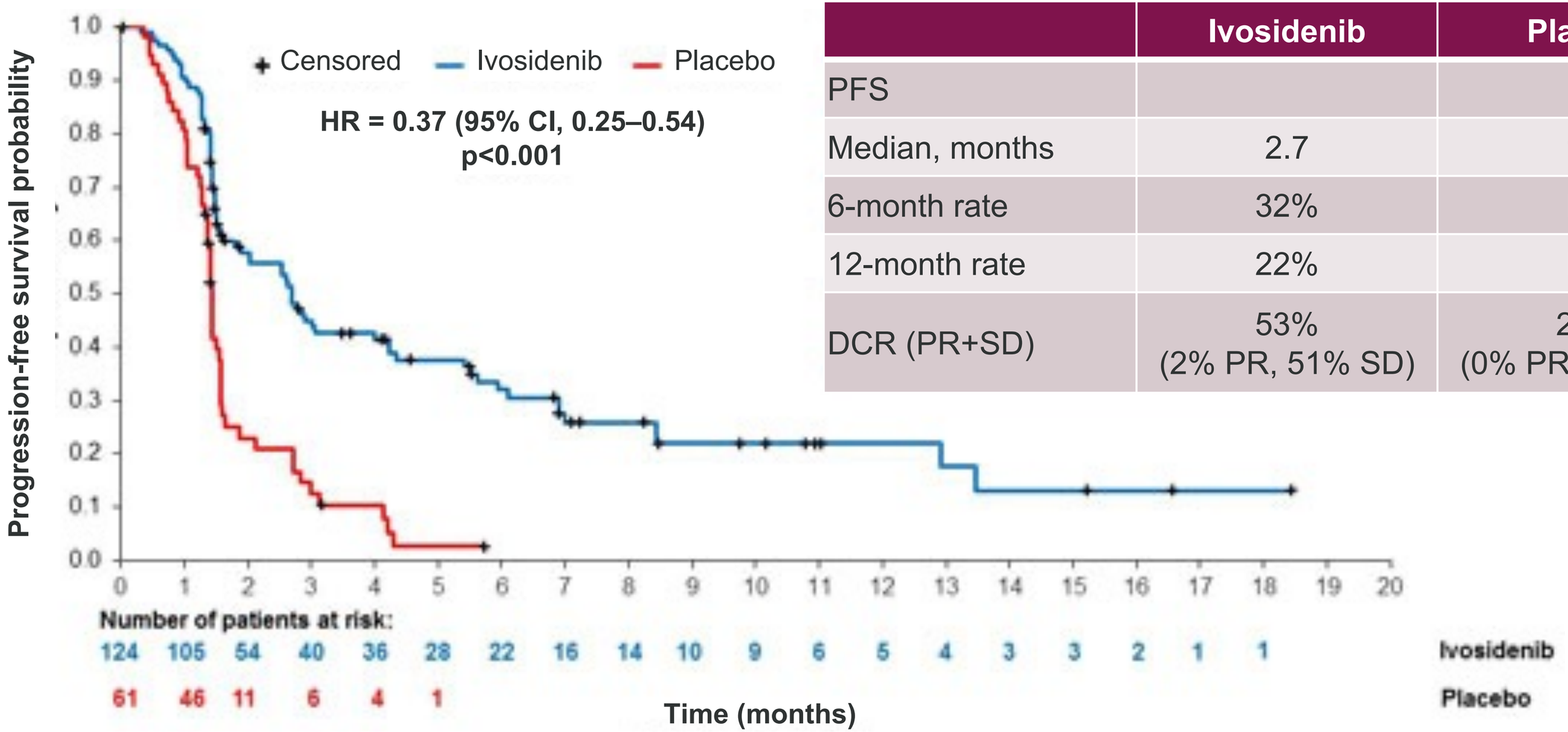


[b]Assessed using EQ-5D-5L, EORTC QLQ-C30, EORTC QLQ-BIL21, and PGI questions

ECOG PS = Eastern Cooperative Oncology Group Performance Status; EORTC = European Organisation for Research and Treatment of Cancer; EQ-5D-5L = 5-level EuroQoL-5 Dimension questionnaire; FU = fluorouracil; NGS = next-generation sequencing; PGI = Patient Global Impression; QD = once daily; QLQ-BIL21 = Cholangiocarcinoma and Gallbladder Cancer module; QLQ-C30 = Quality of Life Questionnaire Core 30; RECIST = Response Evaluation Criteria in Solid Tumors

Abou-Alfa GK et al. *Lancet Oncol*. 2020;21:796-807.

Phase 3 ClarIDHy trial: IDH1 inhibitor ivosidenib vs placebo in second-line setting: PFS by IRC

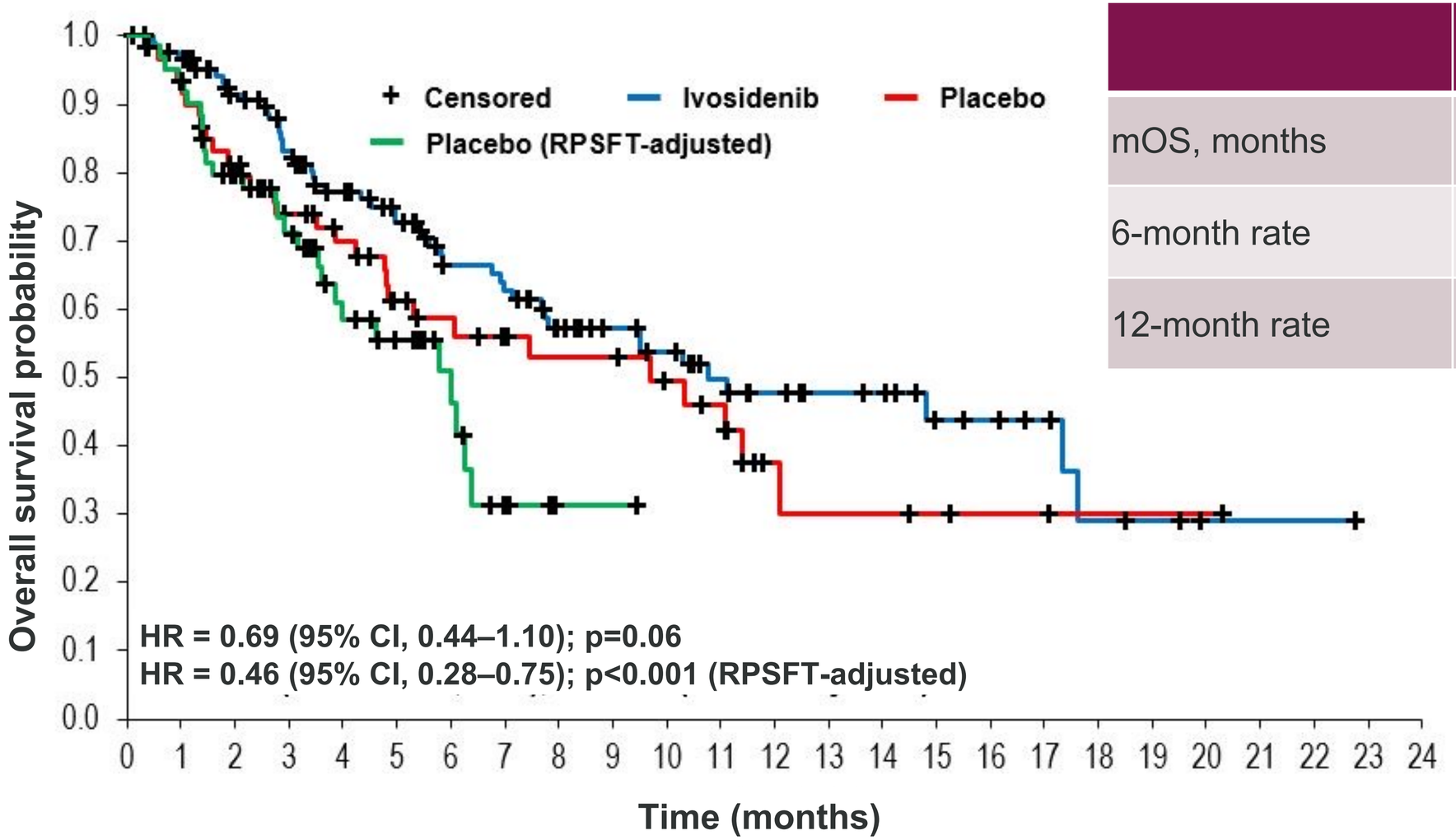


	Ivosidenib	Placebo
PFS		
Median, months	2.7	1.4
6-month rate	32%	NE
12-month rate	22%	NE
DCR (PR+SD)	53% (2% PR, 51% SD)	28% (0% PR, 28% SD)

Abou-Alfa GK, et al. Presented at: ESMO Congress 2019; 27 September–01 October 2019; Barcelona, Spain. Abs LBA10

NE, not estimated

Phase 3 ClarIDHy trial: IDH1 inhibitor ivosidenib versus placebo in second-line setting: OS by ITT

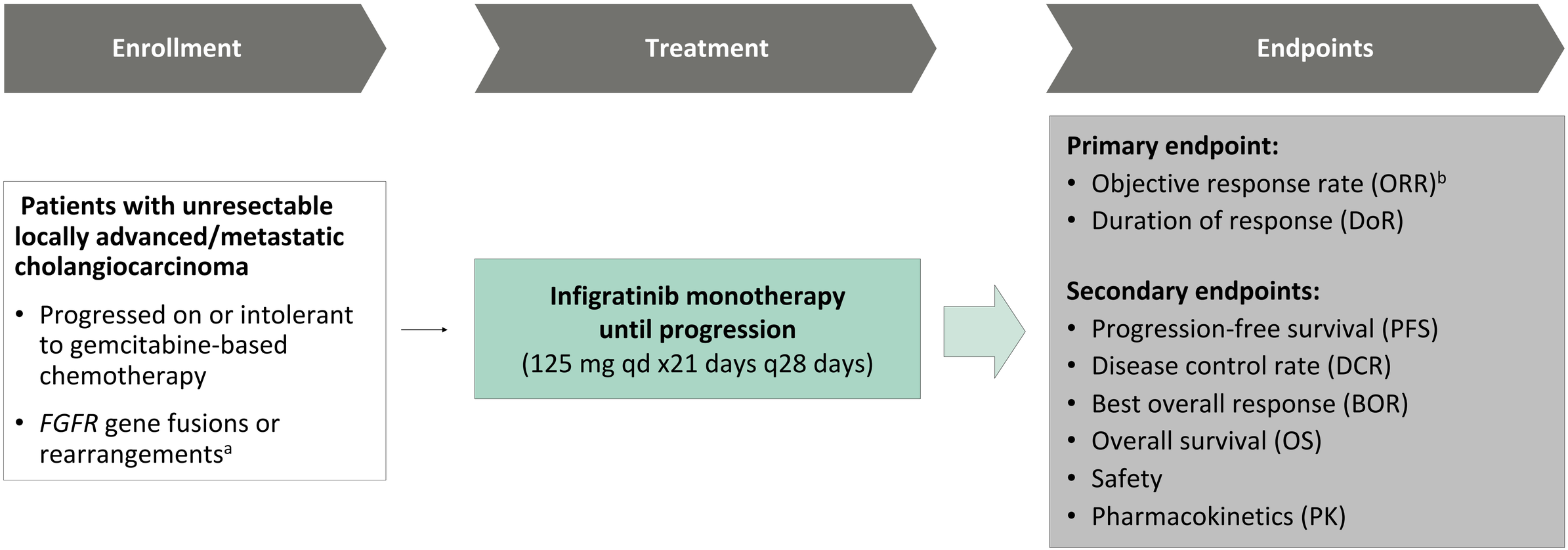


	Ivosidenib	Placebo
mOS, months	10.8	9.7
6-month rate	67%	59%
12-month rate	48%	38%

RPSFT method used to reconstruct the survival curve for the placebo-treated patients as if they had never crossed over to ivosidenib; with this method, the mOS with placebo adjusts to 6 months

Abou-Alfa GK, et al. Presented at: ESMO Congress 2019; 27 September–01 October 2019; Barcelona, Spain. Abs LBA10

Open-label, phase 2 study design (NCT02150967)



[a]Study cohorts (planned enrollment):
Cohort 1 (n=120): patients with *FGFR2* gene fusions/rearrangements
Cohort 2 (n=20): patients with *FGFR1&3* gene fusions/rearrangements and/or *FGFR* mutations (prior selective FGFR inhibitors are not permitted in Cohorts 1&2)
Cohort 3 (n=20): patients with *FGFR2* gene fusions who have received prior treatment with a selective FGFR inhibitor other than infigratinib

[b]ORR assessed by blinded independent central review (BICR, per RECIST v1.1)

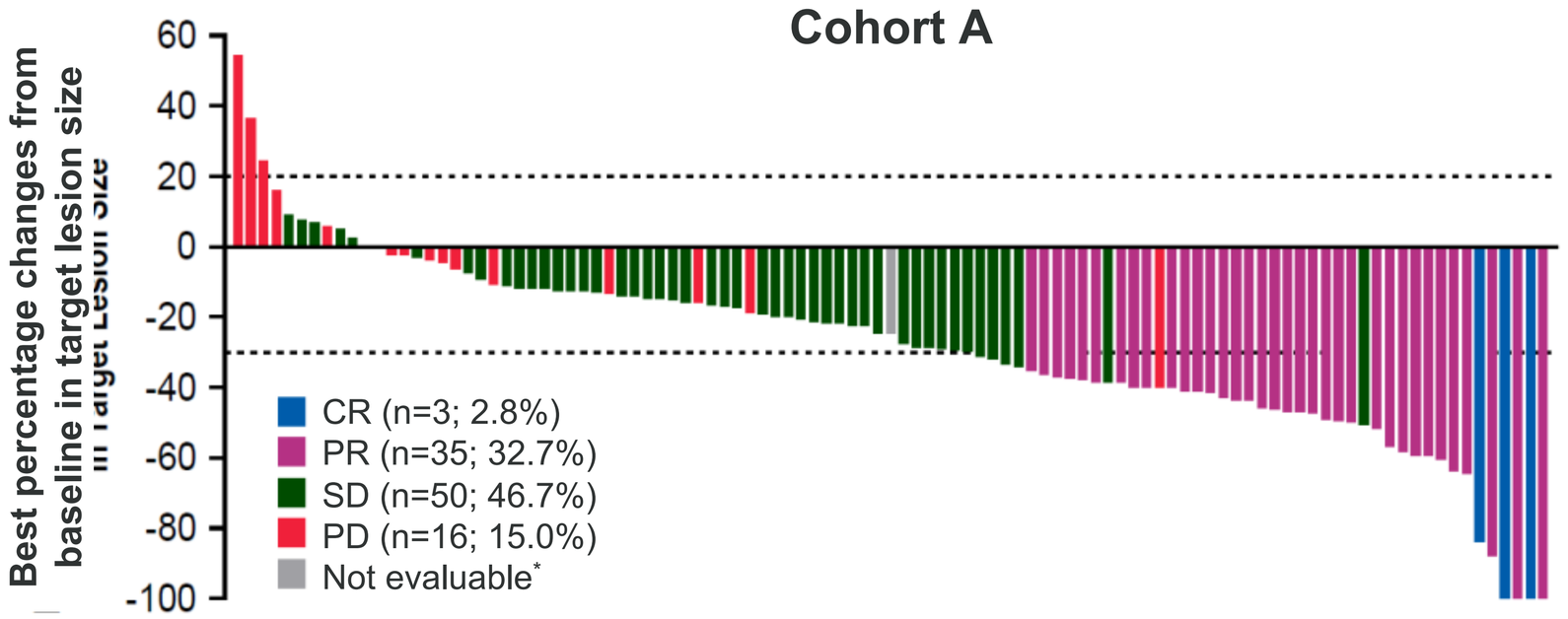
Javle M, et al. Presented at ASCO-GI, January 17, 2021. Abstract 265.

Clinical activity of infigratinib by prior lines of therapy

	Patients with ≤1 line of prior therapy (n=50)	Patients with ≥2 lines of prior therapy (n=58)
Objective response rate (confirmed), % (95% CI)	**34.0** (21.2–48.8)	**13.8** (6.1–25.4)
Complete response, n (%)	0	1 (1.7)
Partial response, n (%)	17 (34.0)	7 (12.1)
Stable disease, n (%)	27 (54.0)	39 (67.2)
Progressive disease, n (%)	4 (8.0)	7 (12.1)
Unknown, n (%)	2 (4.0)	4 (6.9)
Best overall response (confirmed/unconfirmed), % (95% CI)	**42.0** (28.2–56.8)	**27.6** (16.7–40.9)
Disease control rate, % (95% CI)	**88.0** (75.7–95.5)	**81.0** (68.6–90.1)
Median progression-free survival, months (95% CI)	**7.3** (5.6–9.3)	**7.4** (5.6–7.7)

Javle M, et al. Presented at ASCO-GI, January 17, 2021. Abstract 265.

Phase 2 FIGHT-202 trial: pemigatinib in locally advanced or metastatic CCA



Variable	Cohort A (n=107) *FGFR2* fusions/rearrangements	Cohort B (n=20) Other *FGF/FGFR* genetic alterations	Cohort C (n=18) No *FGF/FGFR* genetic alterations
ORR, % (95% CI)	35.5 (26.50–45.35)	0	0
Best OR,[a] n (%)			
CR	3 (2.8)	0	0
PR	35 (32.7)	0	0
SD	50 (46.7)	8 (40.0)	4 (22.2)
PD	16 (15.0)	7 (35.0)	11 (61.1)
Not evaluable[a]	3 (2.8)	5 (25.0)	3 (16.7)
Median DoR, months (95% CI)	7.5 (5.7–14.5)	—	—
DCR (CR + PR + SD), % (95% CI)	82 (74–89)	40 (19–64)	22 (6–48)

*Patient had a decrease in target lesion size but was not evaluable for response per RECIST v1.1

Vogel A, et al. ESMO Congress 2019; 27 September–01 October 2019; Barcelona, Spain. Abs LBA40

FGFR Inhibitors
FGFR2 Fusion–Positive Cholangiocarcinoma[1-9]

	Infigratinib (N = 108)	Pemigatinib (N = 107; Cohort A)	Futibatinib; TAS 120 (N = 103)[a]	Deranzantinib (N = 103)
Patient demographics				
Prior treatment lines, % 1 2+	 34 14 30	 51 32 17	 47 31 24	 52 30 17
Stage IV at enrollment, %	96	66	Not reported	Not reported
Outcomes				
ORR, %	23.1 2L: 34% 3L+: 16%	35.5	42	21
DCR, %	84.3	82	78.6	76
mPFS, mo	7.3	6.9	9	8
mOS, mo	12.5	21.1	21.7	16

Futibatinib: Selective Covalent FGFR1–4 Inhibitor

- In contrast to other FGFR inhibitors, futibatinib demonstrates:
  - Covalent irreversible binding to a conserved cysteine in the FGFR kinase domain P-loop[13]
  - Robust inhibition of FGFR2 kinase domain mutants resistant to reversible ATP-competitive inhibitors[13–15]

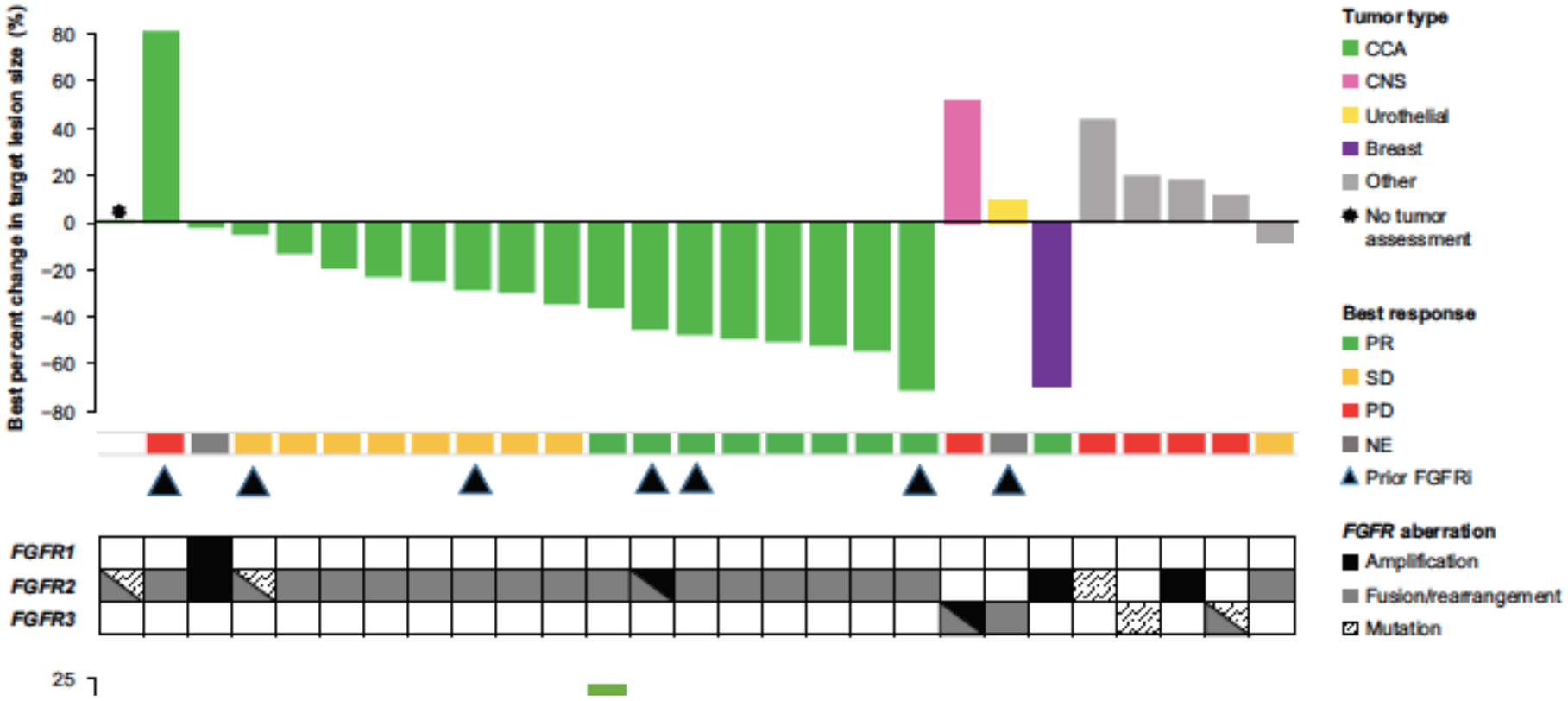
Inhibitory activity against *FGFR2* kinase domain mutations[15]

FGFR2 WT or mutants	Fold difference in IC_{50} vs WT FGFR2		
	Futibatinib	Erdafitinib	Pemigatinib
WT	1	1	1
N549D	2	10	102
N549K	8	13	164
V564I	4	1	42
V564L	44	23	335
E565A	3	1	8

Values in cells with yellow and red shading represent 5–15-fold and >15-fold attenuation with respect to wild-type inhibition, respectively.

FGFR, fibroblast growth factor receptor; IC_{50}, half-maximal inhibitory concentration; iCCA, intrahepatic cholangiocarcinoma; WT, wild-type.

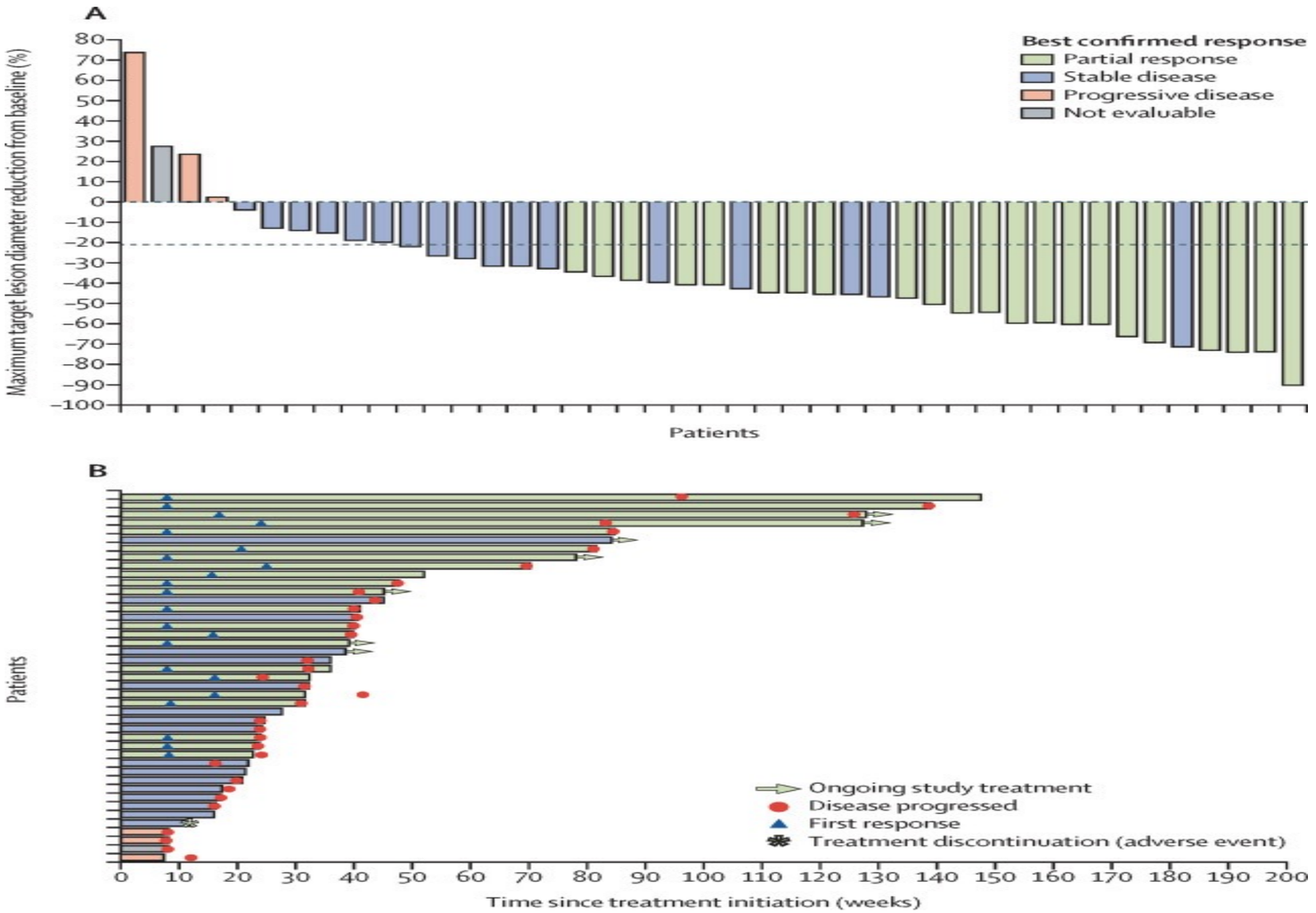
Activity of Futibatinib in Patients with Prior FGFRi



Meric-Bernstam F, Cancer Discov. 2021 Sep 22

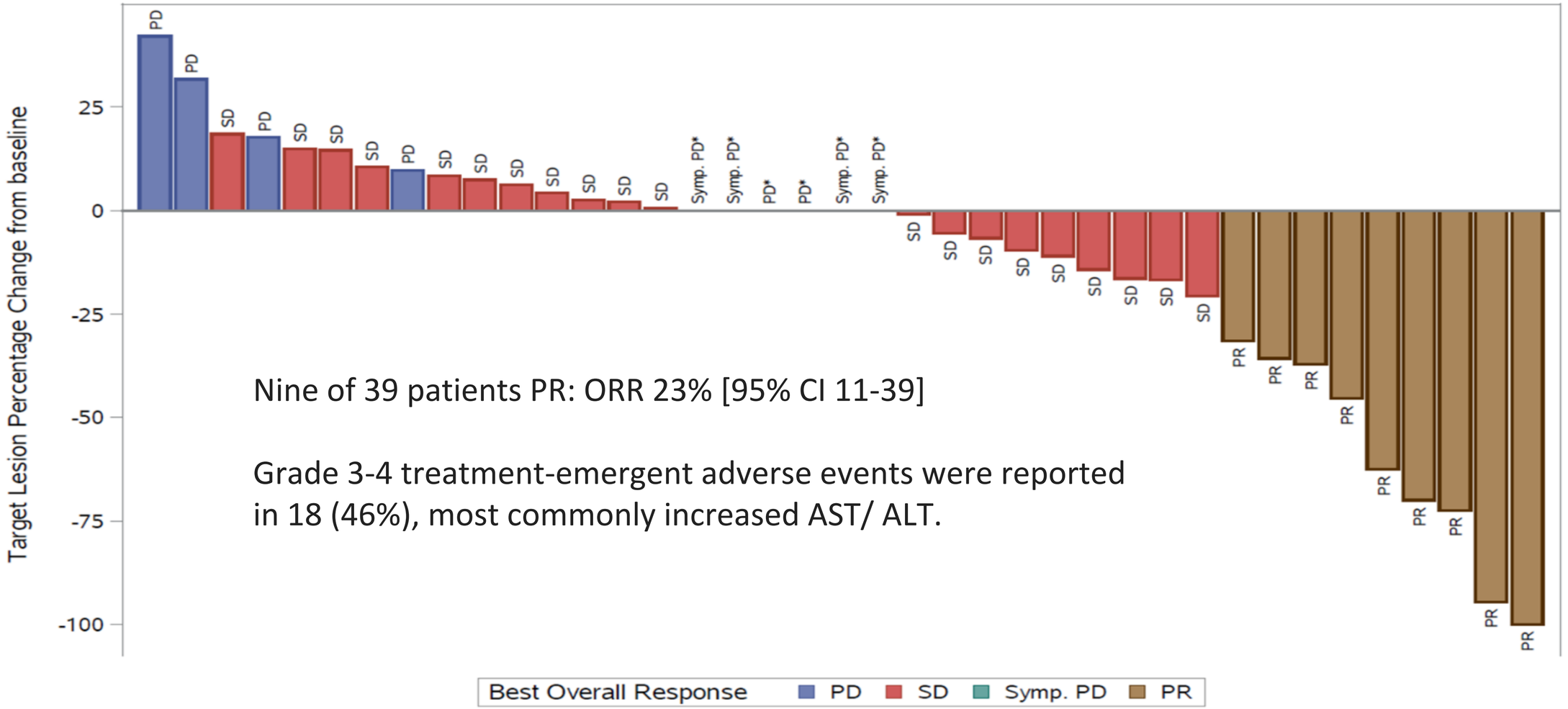
BRAF V600E mutated cholangiocarcinoma

Efficacy of Dabrafenib + Trametinib



Subbiah V, et al. *Lancet Oncol* 2020;21:1234–1243

Trastuzumab plus pertuzumab for HER2/neu-amplified BTC



Nine of 39 patients PR: ORR 23% [95% CI 11-39]

Grade 3-4 treatment-emergent adverse events were reported in 18 (46%), most commonly increased AST/ ALT.

Javle M, et al. Lancet Oncol 2021 Sep;22(9):1290-1300.

09:06 - 09:07

61P - Clinical and molecular characterisation of IDH1/2 mutant cholangiocarcinoma

F. Castet[1], Q. Serra Camprubí[2], C. Fabregat-Franco[1], H. Verdaguer[1], G. Castillo[1], T. Tian[2], T. Macarulla Mercade[1], [1]Vall d'Hebron University Hospital, Barcelona, ES, [2]Vall d'Hebron Institute of Oncology (VHIO)-Cellex Center, Barcelona, ES

09:07 - 09:08

62P - Proteomic and single-cell landscape reveals novel pathogenic mechanisms of HBV-infected intrahepatic cholangiocarcinoma

X. Shuaishuai, W. Wu, R. Chen, C. Ye, Q. Li, J. Chen, Q. Jiang, J. Ruan, The First Affiliated Hospital, Zhejiang University School of Medicine, Hangzhou, CN

09:08 - 09:09

63P - Intrahepatic cholangiocarcinoma (iCCA) genomic findings with high versu low tumor mutational burdens

T.-Y. Tang[1], J. Ross[2], J. Rodon[1], M. Javle[1], [1]The University of Texas MD Anderson Cancer Center, Houston, US, [2]Foundation Medicine, Inc, Cambridge, US

09:09 - 09:10

64P - Phase I/II study of nivolumab plus lenvatinib for advanced biliary tract cancer (JCOG1808/NCCH1817, SNIPE)

M. Ueno[1], C. Morizane[2], M. Ikeda[3], M. Ozaka[4], F. Nagashima[5], T. Kataoka[2], J. Mizusawa[2], A. Ohba[2], S. Kobayashi[1], H. Imaoka[3], A. Kasuga[4], N. Okano[5], Y. Nagasaka[2],

09:03 - 09:04

58P - Spectrum of germline pathogenic mutations in 1087 Chinese patients with biliary tract cancer

J. Shen[1], R. Kong[2], D. Guo[2], S. Chen[2], T. Han[2], M. Wang[2], G. Lu[2], W. Deng[2], R. Ding[3], F. Bu[3], [1]Eastern Hepatobiliary Surgery Hospital, Second Military Medical University, Shanghai, Shanghai, CN, [2]Jiangsu Simcere Diagnostics Co., Ltd., Nanjing, CN, [3]Jiangsu Simcere Diagnostics Co., Ltd, Nanjing, CN

09:04 - 09:05

59P - Efficacy of derazantinib in intrahepatic cholangiocarcinoma (iCCA) patients with FGFR2 fusions, mutations or amplifications

M. Borad[1], M. Javle[2], W.L. Shaib[3], K. Mody[4], F. Bergamo[5], W. Harris[6], N. Damjanov[7], T. Macarulla Mercade[8], G. Brandi[9], G. Masi[10], M. Droz Dit Busset[11], A. Boncompagni[12], M.

57P - Immune-mediated adverse event (imAE) incidence, timing and association with efficacy in the phase III TOPAZ-1 study of durvalumab (D) or placebo (PBO) plus gemcitabine and cisplatin (+ GC) in advanced biliary tract cancer (BTC)

L. Antonuzzo[1], H. Takahashi[2], J.O. Park[3], A. Sookprasert[4], R. Gillmore[5], S.-S. Yang[6], J.

13:00 - 14:30	**Type: Industry Satellite Symposium** **Title: Incyte Biosciences International Sàrl - Targeting FGFR alterations in cholangiocarcinoma and other solid tumours: A new frontier in personalised medicine** Chair(s): David Malka, FR; Juan Valle, GB	**7.2.F - Fécamp Auditorium**

13:00 - 13:05 **Welcome and introduction**

J. Valle, The Christie NHS Foundation Trust, Manchester, GB

13:05 - 13:18 **Cholangiocarcinoma: The little-known, rare cancer of the biliary tract**

F.G.M. De Braud, Fondazione IRCCS - Istituto Nazionale dei Tumori, Milan, IT

13:18 - 13:31 **The challenges associated with diagnosing intrahepatic cholangiocarcinoma for targeted therapies**

J. Valle, The Christie NHS Foundation Trust, Manchester, GB

13:31 - 13:44 **Optimising molecular profiling and the multidisciplinary team approach in cholangiocarcinoma**

A. Lamarca, Hospital Universitario Fundacion Jimenez Diaz, Madrid, ES

13:44 - 13:58 **Clinical practice guidelines for biliary tract cancer: Updates for the management of patients with locally advanced or metastatic intrahepatic cholangiocarcinoma**

D. Malka, Institut Gustave Roussy, Villejuif, Cedex, FR

13:58 - 14:11 **Targeting FGFR alterations in cholangiocarcinoma and other solid tumours**

A. Hollebecque, Institut Gustave Roussy, Villejuif, Cedex, FR

14:11 - 14:29 **Panel discussion**

J. Valle[1], D. Malka[2], F.G.M. De Braud[3], A. Lamarca[4], A. Hollebecque[2], [1]The Christie NHS Foundation Trust, Manchester, GB, [2]Institut Gustave Roussy, Villejuif, Cedex, FR, [3]Fondazione IRCCS - Istituto Nazionale dei Tumori, Milan, IT, [4]Hospital Universitario Fundacion Jimenez Diaz, Madrid, ES

14:29 - 14:30 **Closing remarks**

D. Malka, Institut Gustave Roussy, Villejuif, Cedex, FR

Pancreatic Cancer

Several areas of major interest

Cytotoxic Combos

gBRACA 1/2

Many other targets but not yet successful

Pancreatic Cancer: Scope of the Problem

- About 60,430 people diagnosed with pancreatic cancer in US in 2021, 48,220 died of the disease
- Stage for stage, pancreatic cancer is associated with the lowest survival rates of any major cancer type[2]
- By 2030, pancreatic cancer is expected to rise to the second leading cause of cancer-related mortality in the United States (after lung cancer)[3]
- The vast majority of pts (> 80%) are inoperable at time of diagnosis[1]

1. American Cancer Society. Cancer facts & figures 2021.
2. Siegel RL, et al. CA Cancer J Clin. 2016;66:7-30.
3. Rahib L, et al. Cancer Res. 2014;74:2913-2921.

TIMELINE FOR DRUG APPROVALS IN PDAC

Pre-1996	The dark ages. Nothing works
1996	Gemcitabine improves survival compared with 5-FU. Gemcitabine is approved for PC
1996-2005	Many agents tested. No drug or drug combination is better than Gemcitabine
2005	Erlotinib + Gemcitabine modestly improves survival compared with Gemcitabine. Erlotinib is approved for PC
2005-2009	More drugs tested. Many more negative trials
2010	FOLFIRINOX improves survival compared with Gemcitabine
2012	*nab*-Paclitaxel + Gemcitabine improves survival compared with Gemcitabine
2016	Nal-IRI + 5FU/ LVF approved for 2nd line therapy for PC
2017	Pembrolizumab approved for MSI-H cancers including pancreatic cancer
2019	**Olaparib approved for gBRCA PDAC**

FOLFIRINOX vs. Gemcitabine
Advanced Pancreatic Cancer PS 0-1

Patients with stage IV pancreatic cancer

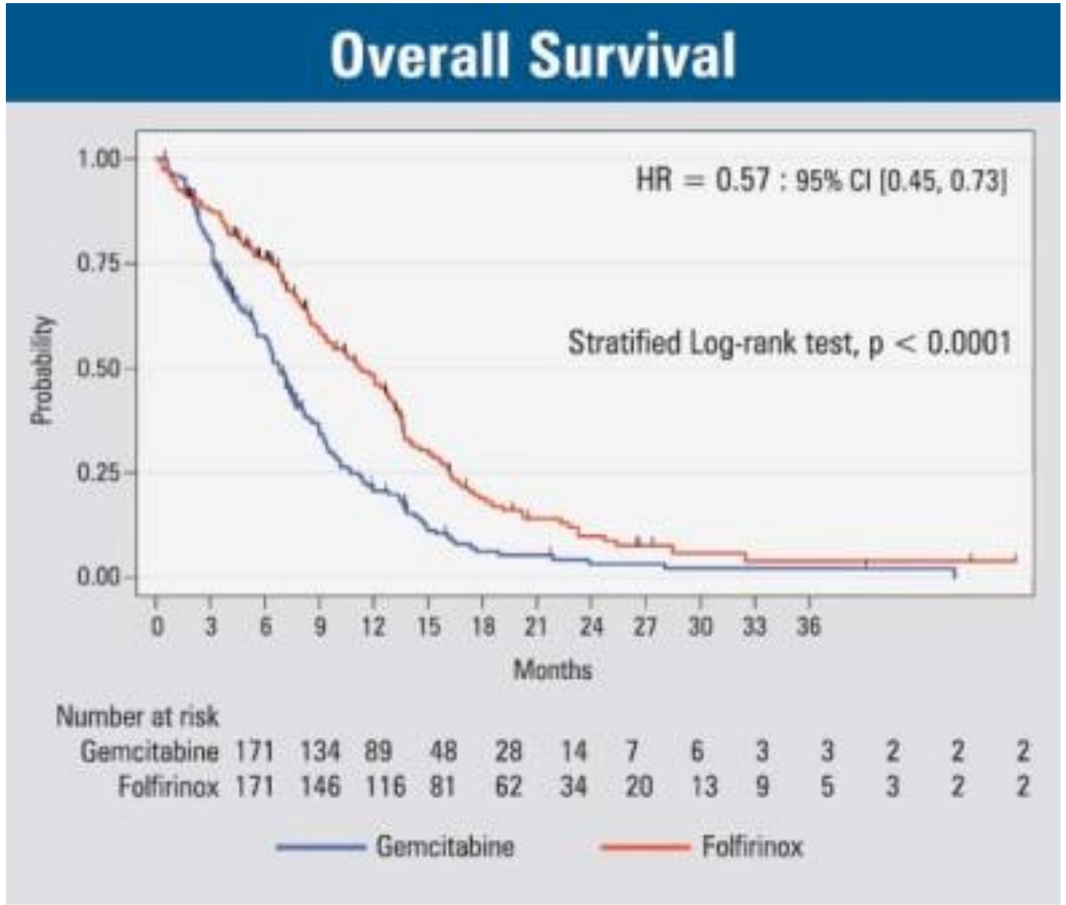
No prior chemotherapy

Excellent performance status

Normal liver function

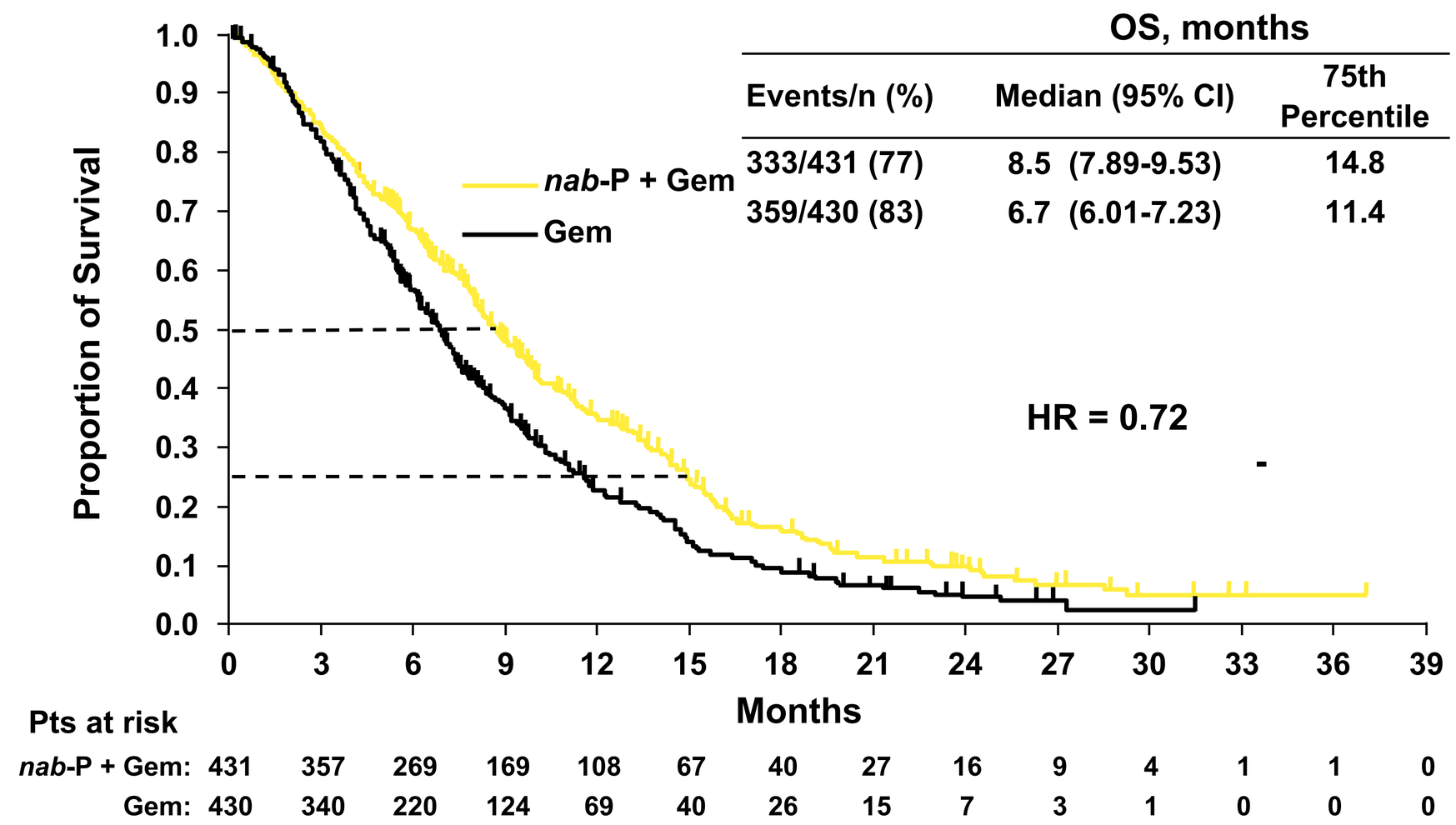
342 enrolled: 5FU, irinotecan, oxaliplatin vs.gemcitabine

Pancreatic cancer patients can tolerate aggressive chemotherapy



N Engl J Med 2011; 364:1817-1825

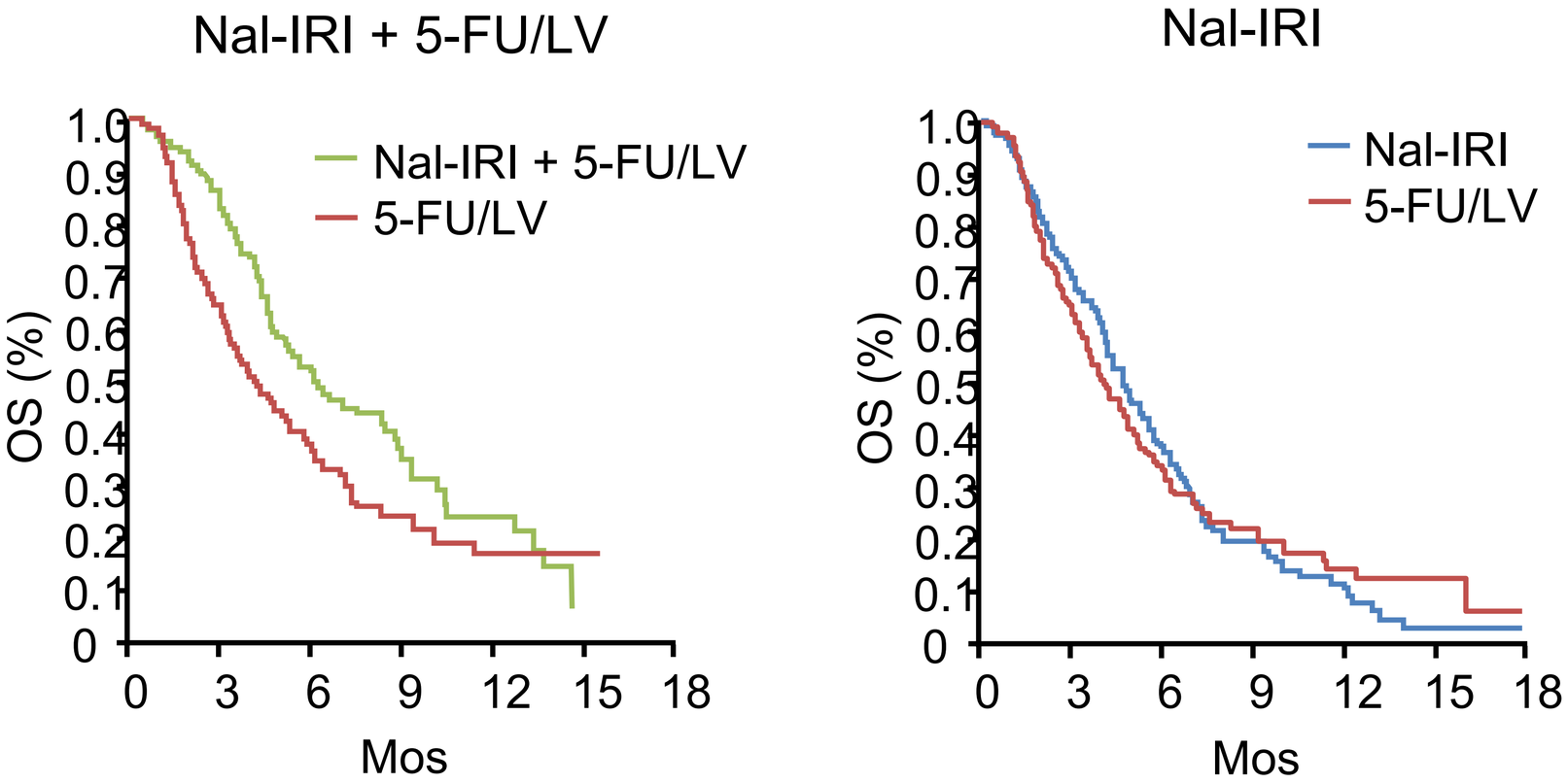
Overall Survival



- Multi-agent chemotherapy is feasible in community setting with PS 0-2

Von Hoff et al. ASCO 2013.

NAPOLI-1: Nanoliposomal Irinotecan ± 5-FU/LV vs 5-FU/LV—OS

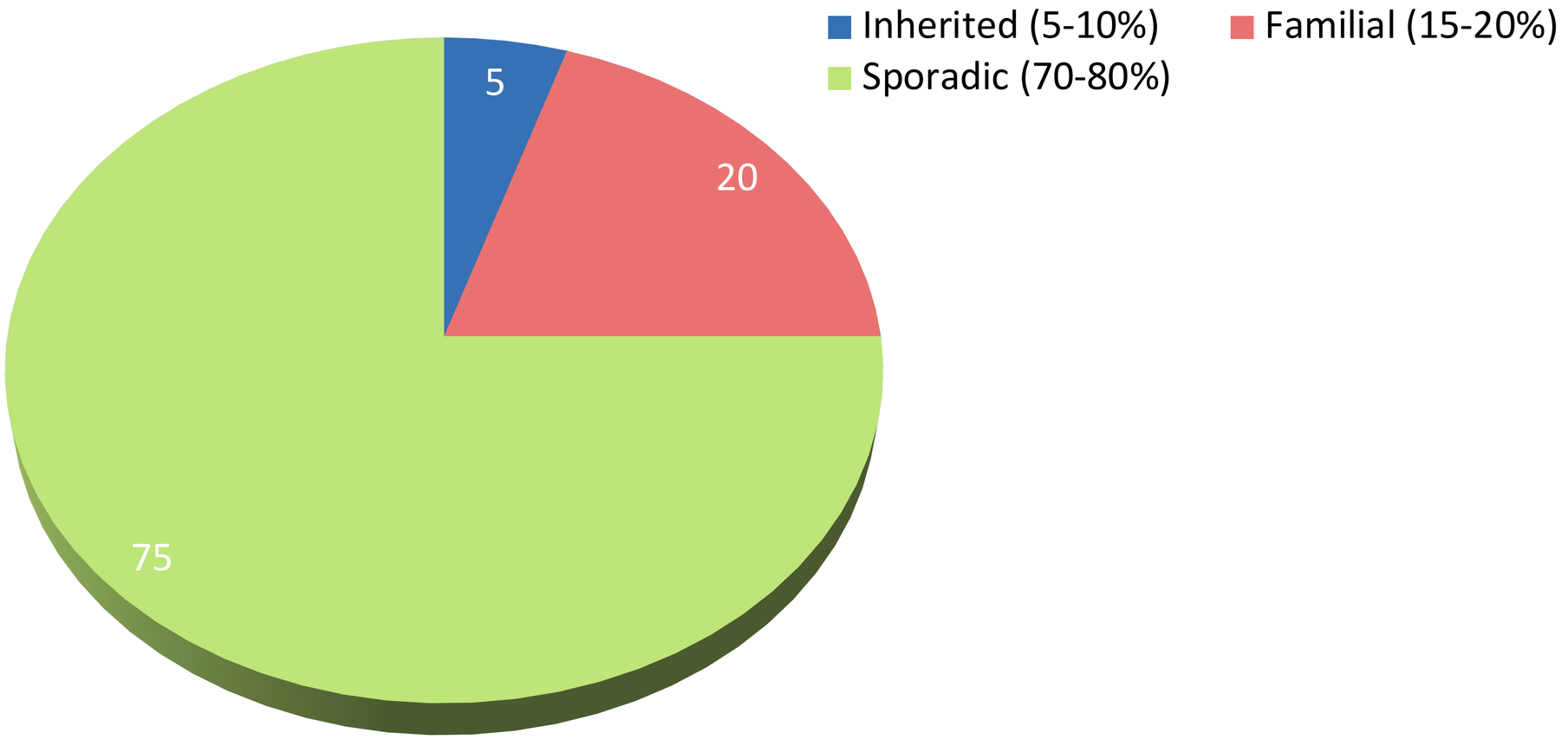


Median OS: 6.1 vs 4.2 mos
HR: 0.57 (95% CI: 0.41-0.80; *P* = .0009)

Median OS: 4.9 vs 4.2 mos
HR: 0.93 (95% CI: 0.71-1.21; *P* = .5545)

Wang-Gillam A, et al. Lancet. 2016;387:545-557.

Inherited Pancreatic Cancer Syndromes

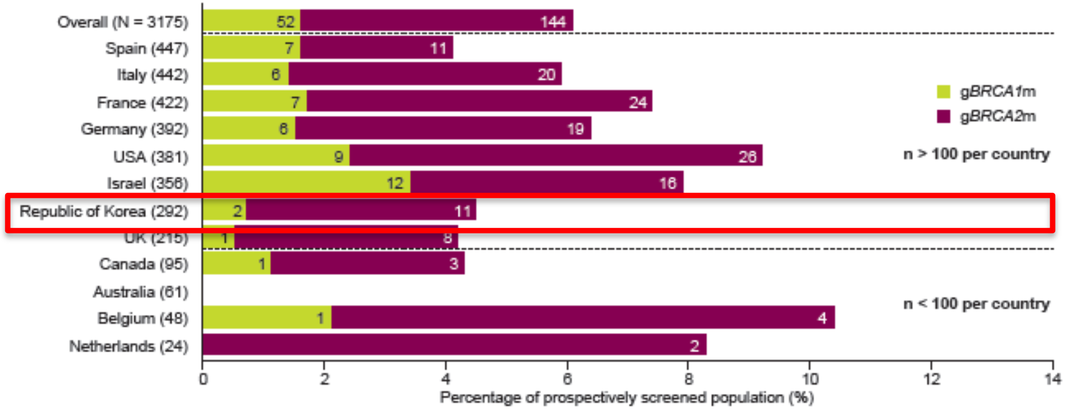


Genetic Syndrome	Gene	Pancreatic cancer risk	Histology
Hereditary breast and ovarian cancer	BRCA1, BRCA2	3.5-10	Ductal adenocarcinoma
Peutz Jegher	STK11/LKB1	132	IPMN
Hereditary pancreatitis	PRSS1, SPINK1	53	Ductal adenocarcinoma
HNPCC	MMR genes	?	Medullary carcinoma
FAMMM	CDKN2	13-22	Ductal adenocarcinoma
Familial pancreatic cancer	?	9-32	

DNA repair defects common in hereditary pancreatic cancers

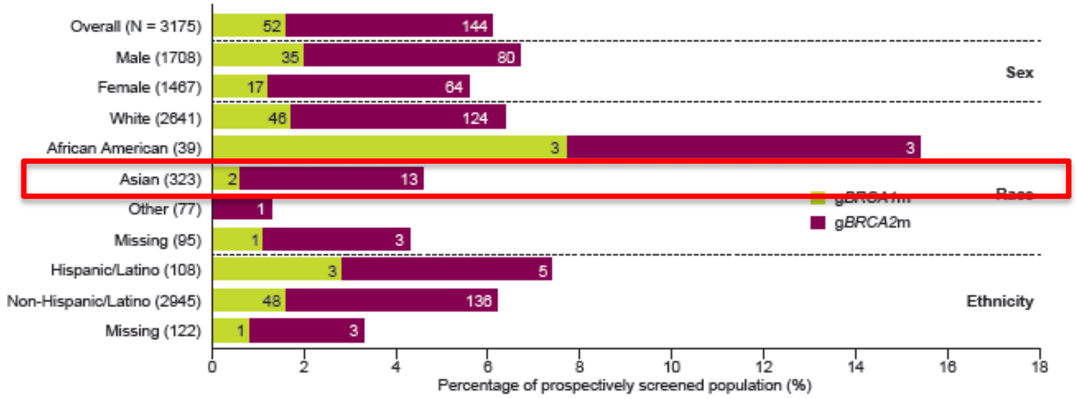
Overall prevalence of gBRCA1/2: 6.2% (196/3175)

Figure 2. Prevalence of g*BRCA1*m and g*BRCA2*m per country.



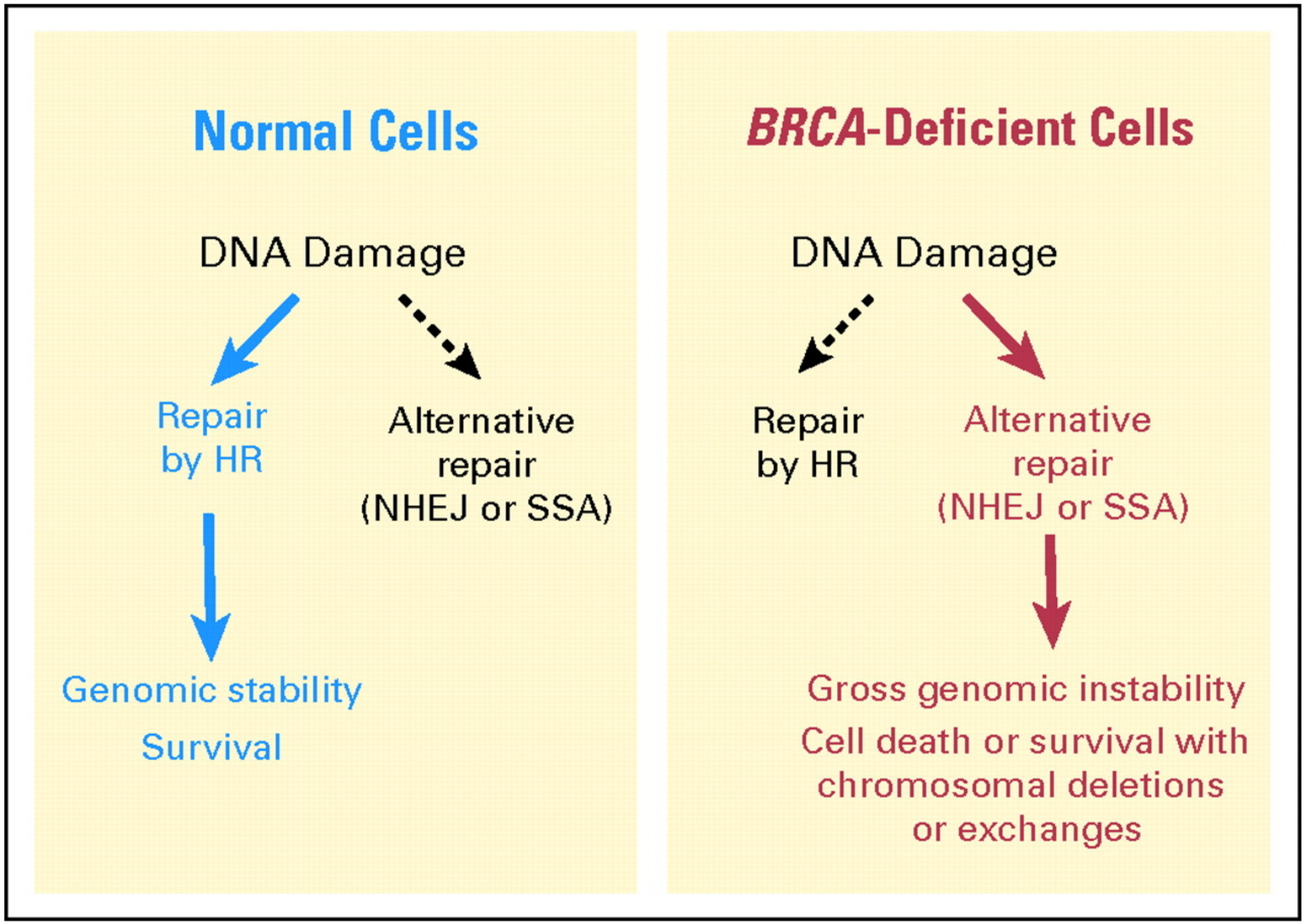
Number of patients with g*BRCA1*m or g*BRCA2*m per country is shown on each bar.
g*BRCA1*m, germline *BRCA1* mutations; g*BRCA2*m, germline *BRCA2* mutations.

Figure 3. Prevalence of g*BRCA1*m and g*BRCA2*m by sex, race and ethnicity.



T Golan et al.
NEJM 2019

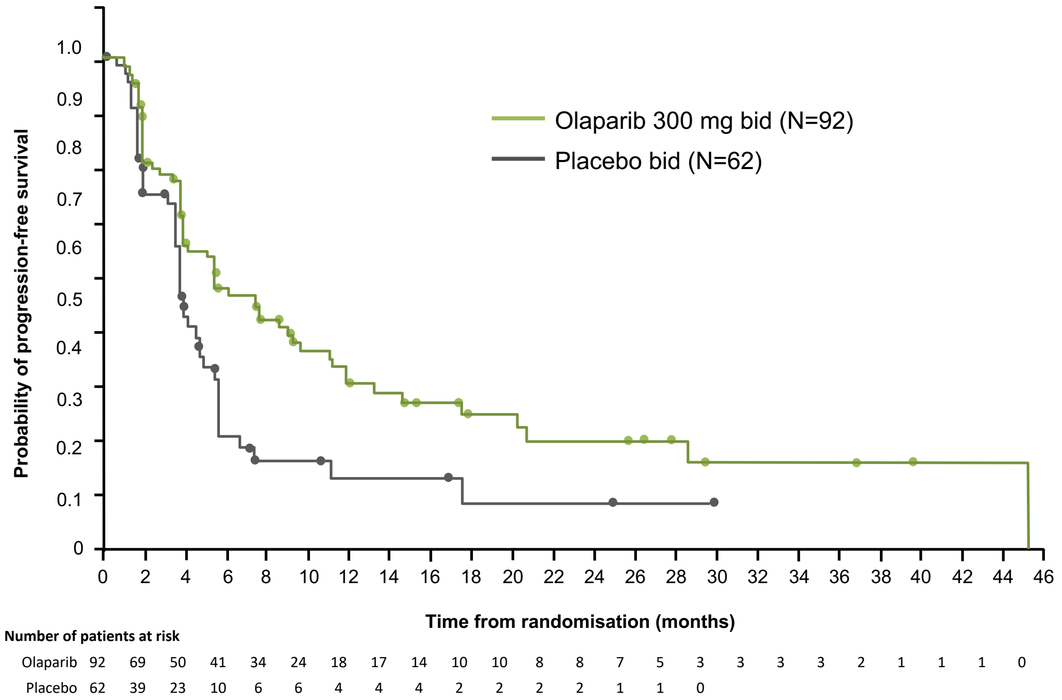
DNA Repair as Target



Ashworth, A. J Clin Oncol; 26:3785-3790 2008

Olaparib maintenance reduced the risk of disease progression or death by 47% in patients with gBRCAm mPDAC who have disease control following PBC

Median PFS (BICR) was improved by 3.6 months with olaparib treatment vs. placebo



Number of patients 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								

	Olaparib (n=92)	Placebo (n=62)
Events, n (%)	60 (65.2)	44 (71.0)
Median PFS, months (BICR)	**7.4**	**3.8**
Median difference, months	**+3.6**	
	HR=0.53 95% CI (0.35-0.82) p=0.004	

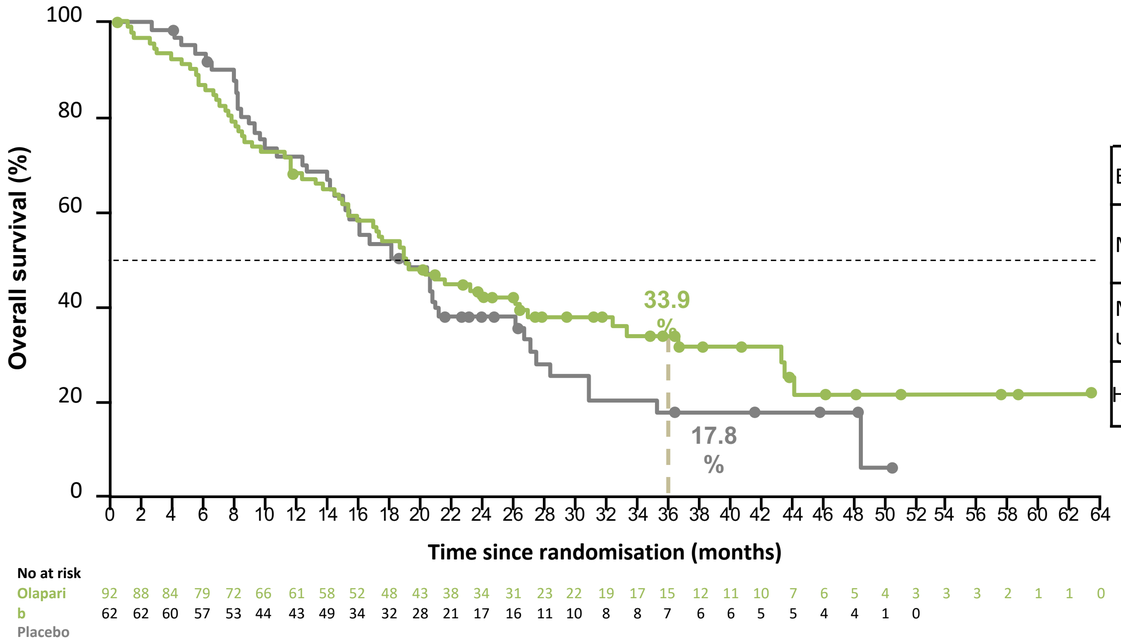
Median PFS by BICR was almost doubled with olaparib maintenance, with a 95% improvement over placebo

Note: PFS by BICR assessment
Data cut-off: 15 January 2019
Progression-free survival (PFS) measures the time from randomisation to objective disease progression or death
BICR=blinded independent central review; bid=twice daily; CI=confidence interval; HR=hazard ratio; mPDAC=metastatic pancreatic ductal adenocarcinoma; PBC=platinum-based chemotherapy; PFS=progression-free survival

1. Golan T *et al. N Engl J Med* 2019;381:317–327.

Nearly twice as many patients treated with olaparib were alive vs. those on placebo after 3 years (33.9% vs. 17.8%)

Although final OS did not demonstrate a statistically significant difference between treatment arms, the HR numerically favoured olaparib compared with placebo (HR 0.831; p=0.3487)



	Olaparib (n=92)	Placebo (n=62)
Events, n (%)	61 (66.3)	47 (75.8)
Median OS, months	19.0	19.2
Median survival follow-up, months (range)[a]	31.3 (0.3 –63.5)	23.9 (3.9 –50.6)
Hazard ratio (95% CI)	0.83 (0.56, 1.22); p=0.3487	

Data cut-off: 21 July 2020

[a]Censored patients

Overall survival is defined as the time from the date of randomisation until death due to any cause

bid=twice daily; CI=confidence interval; PARP=poly(ADP-ribose) polymerase; OS=overall survival.

Golan T, *et al.* Oral presentation presented at: ASCO Gastrointestinal Cancers Symposium 2021. Virtual Meeting. 15–17 January, 2021. Abstract 378

9:12

1298P - Extended overall survival results from the POLO study of active maintenance olaparib in patients with metastatic pancreatic cancer and a germline BRCA mutation

P. Hammel[1], T. Golan[2], M. Reni[3], E. Van Cutsem[4], T. Macarulla Mercade[5], M. Hall[6], J.O. Park[7], D. Hochhauser[8], D. Arnold[9], D.-Y. Oh[10], A. Reinacher-Schick[11], G. Tortora[12], H.