



# Summary of ARC-8 Final Overall Survival Analysis

Phase 1 / 1b Randomized Study of Quemliclustat + Gemcitabine / Nab-Paclitaxel ±  
Zimberelimab in Patients With Treatment-Naïve Metastatic Pancreatic Adenocarcinoma

**Data presented at ASCO GI, January 19, 2024, based on a data cutoff of June 19, 2023.**

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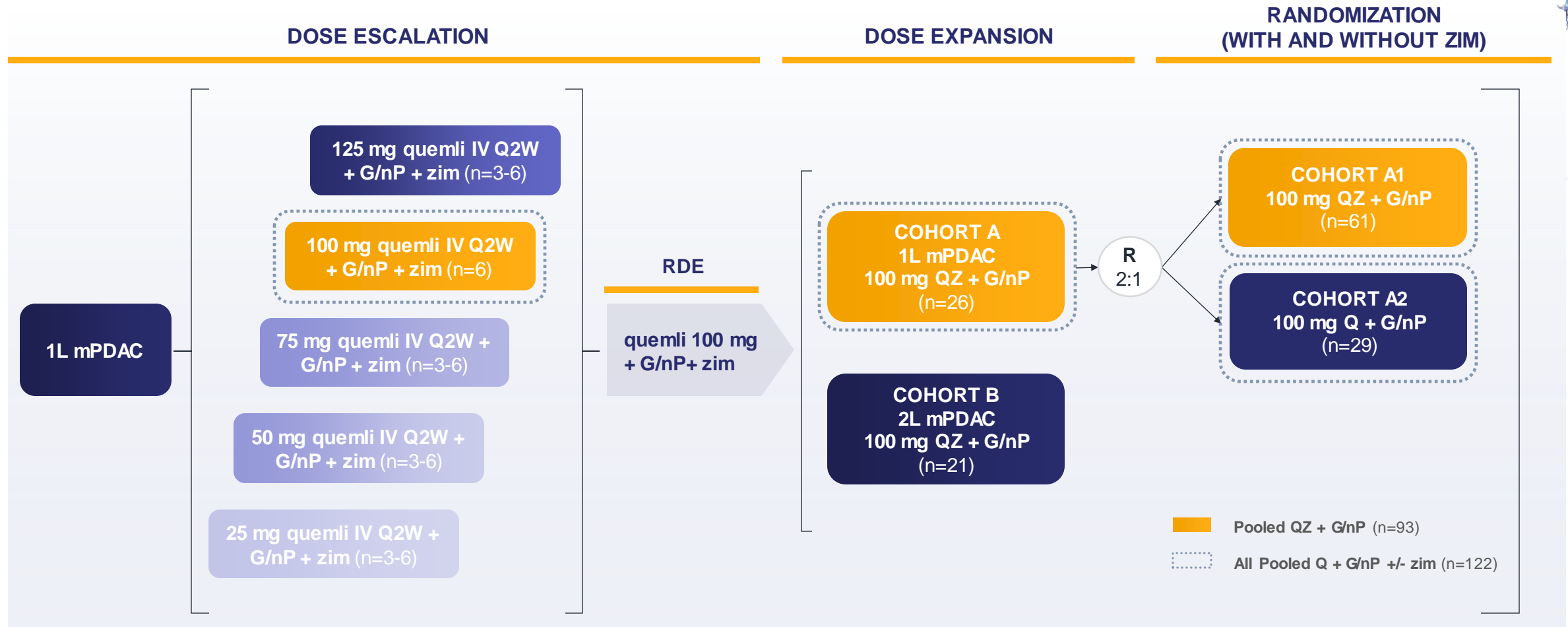
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# Key Takeaways From the ARC-8 Study in 1L PDAC

- Quemliclustat (quemli) is a first-in-class small molecule CD73 inhibitor
- ARC-8 is a Phase 1/1b study designed to determine if a quemli-based regimen can improve the efficacy of gem + nab-paclitaxel (G/nP) in 1L PDAC
  - The study included a dose escalation and expansion portion, followed by a randomized portion whereby 90 patients were randomized 2:1 to either quemli + G/nP + zim (anti-PD-1) or quemli + G/nP to determine whether zim was additive in this setting → results indicate that zim did not contribute to efficacy in this setting
- In an analysis of all patients treated with 100 mg quemli + G/nP +/- zim (n=122):
  - **Median Overall Survival (mOS) was 15.7 months for All Pooled patients, which exceeds the historical benchmark data for chemotherapy alone (approx. 9-11 mos)**
- Because ARC-8 did not include a control arm of G/nP, Arcus engaged Medidata to generate a Synthetic Control Arm® (SCA) where each ARC-8 patient was matched to a patient from Medidata's historical clinical trial database based on several baseline characteristics; the analysis showed:
  - 37% reduction in the risk of death, HR=0.63 (CI: 0.47 – 0.85, p=0.0030) for the ARC-8 patients vs. the SCA, and
  - 5.9-month increase in mOS (15.7 vs 9.8 months) for the ARC-8 patients vs. the SCA
- No new safety signals were observed in the study

# ARC-8 Study Design Included Dose Escalation, Expansion and Randomized Portions



**Safety monitoring throughout treatment period; radiographic disease evaluation every 8 weeks. Study treatment continued to disease progression, unacceptable toxicity, consent withdrawal, or investigator decision.**

1L: first-line; 2L: second-line; IV: intravenously; G/nP: gemcitabine/nab-paclitaxel; mPDAC: metastatic pancreatic ductal adenocarcinoma; PDAC: pancreatic ductal adenocarcinoma; Q2W: every 2 weeks; Q/quemli: quemliclustat; R: randomization; RDE: recommended dose for expansion; Z/zim: zimberelimab  
NCT #: NCT04104672

Wainberg ZA, et al. ASCO GI, Jan. 19, 2024, data cut off of June 19, 2023

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# Dataset Includes Four Groups of Patients Treated with 100 mg of Quemli

Cohort	Quemli Dose	Combination	Participants Dosed	>18m OS f/u?	Population
Dose escalation	25 mg	Q + Z + G/nP (quad)	4	Yes	1L mPDAC
Dose escalation	50 mg	Q + Z + G/nP (quad)	6	Yes	1L mPDAC
Dose escalation	75 mg	Q + Z + G/nP (quad)	3	Yes	1L mPDAC
<b>Dose escalation</b>	<b>100 mg</b>	<b>Q + Z + G/nP (quad)</b>	6	Yes	1L mPDAC
<b>Cohort A</b>	<b>100 mg</b>	<b>Q + Z + G/nP (quad)</b>	26*	Yes (except for 3)*	1L mPDAC
<b>Cohort A1 (randomized)</b>	<b>100 mg</b>	<b>Q + Z + G/nP (quad)</b>	<b>61</b>	Yes	1L mPDAC
<b>Cohort A2 (randomized)</b>	<b>100 mg</b>	<b>Q + G/nP (triplet)</b>	<b>29</b>	Yes	1L mPDAC
Dose escalation	125 mg	Q + Z + G/nP (quad)	3	Yes	1L mPDAC

**93**  
Pooled  
Q100 quad

**122**  
Pooled  
Q100 All

1L: first-line, f/u: follow up, G/nP: gemcitabine/nab-paclitaxel, mPDAC: metastatic pancreatic ductal adenocarcinoma, OS: overall survival, Q/quemli: quemliclustat, Z/zim: zimberelimab

3 additional patients enrolled as contemporaneous control for Cohort C

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# Demographics And Baseline Characteristics Are Well Balanced Across Arms & Efficacy-evaluated Populations

% ECOG 1 (65%-69%) Was Higher than Historical G/nP Studies (42-57%)

% (n)		A2: Q + G/nP (n=29)	A1: QZ + G/nP (n=61)	Pooled Q100 QZ + G/nP (n=93)	All Pooled Q100 Q ±Z)+G/nP (n=122)
Median Age (IQR)		65.0 (61, 70)	66.0 (58, 72)	66.0 (58, 72)	65.5 (59, 72)
Age ≥65		55 (16)	59 (36)	58.1 (54)	57.4 (70)
Female		48 (14)	49 (30)	47 (44)	48 (58)
Race	White	83 (24)	74 (45)	74 (69)	76 (93)
	Asian	6.9 (2)	8.2 (5)	8.6 (8)	8.2 (10)
	Black	3.4 (1)	6.6 (4)	5.4 (5)	4.9 (6)
	Other/NR	6.9 (2)	11 (7)	12 (11)	11 (13)
ECOG 0		31 (9)	30 (18)	34 (32)	34 (41)
ECOG 1		69 (20)	69 (42)	65 (60)	66 (80)
ECOG Missing		-	1.6 (1)	1.1 (1)	0.8 (1)

# Summary of Disease History

% Liver Mets (59%-69%) Was Slightly Lower than Historical G/nP Studies (78-85%) – See Slide 12 for OS Results for ARC-8 Patients With and Without Liver Mets

% (n)	A2: Q + G/nP (n=29)	A1: QZ + G/nP (n=61)	Pooled Q100 QZ + G/nP (n=93)	All Pooled Q100 Q ±Z)+G/nP (n=122)
<b>Liver Metastasis At Baseline<sup>1</sup></b>	58.6 (17)	68.9 (42)	66.7 (62)	64.8 (79)
<b>Prior Pancreatic Cancer Surgery<sup>2</sup></b>	27.6 (8)	11.5 (7)	14.0 (13)	17.2 (21)
<b>Any Prior Systemic Anti-cancer Therapy</b>	13.8 (4)	9.8 (6)	11.8 (11)	12.3 (15)
<b>Any Prior Radiotherapy</b>	3.4 (1)	6.6 (4)	9.7 (9)	8.2 (10)
<b>Months Since Initial Diagnosis, median (Min/Max)<sup>3</sup></b>	1.3 (0, 39)	0.9 (0, 55)	0.9 (0, 55)	1.1 (0, 55)

G/nP: gemcitabine/nab-paclitaxel, mets: metastasis, OS: overall survival, Q: quemiclustat, Z: zimberelimab

1. Derived from baseline tumor assessment data

2. Derived from prior procedures data

3. Stage not specified

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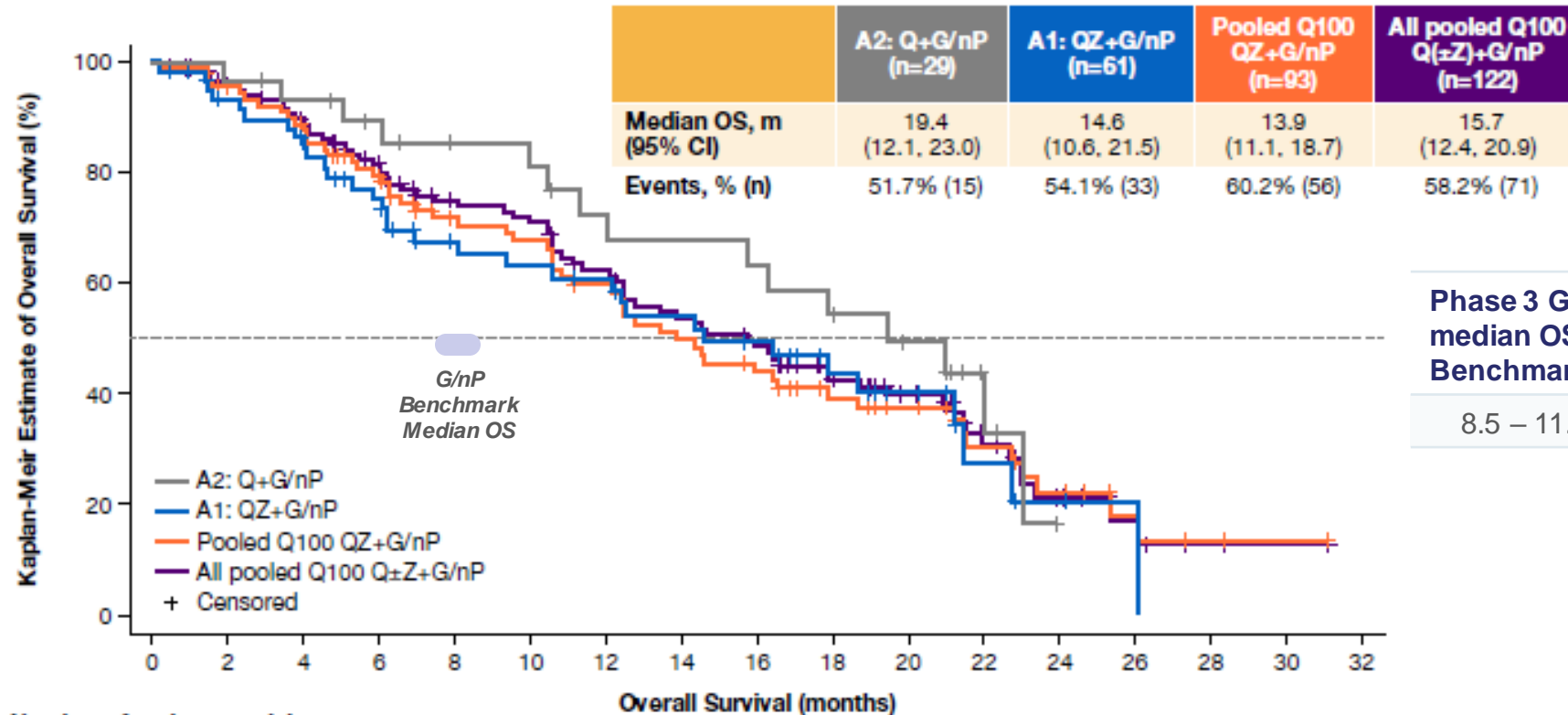


# With 21-month Median Follow-up, Overall Survival (OS) Results Exceed Phase 3 Benchmarks for G/nP

% (n)	A2: Q + G/nP (n=29)	A1: QZ + G/nP (n=61)	Pooled Q100 QZ + G/nP (n=93)	All Pooled Q100 Q ±Z)+G/nP (n=122)
OS Events (%)	15 (51.7)	33 (54.1)	56 (60.2)	71 (58.2)
Median OS, months	19.4	14.6	13.9	15.7
95% CI	12.1, 23.0	10.6, 21.5	11.1, 18.7	12.4, 20.9
12m OS Rate, %	72.3	60.9	59.6	62.7
18m OS Rate, %	54.2	43.5	39.3	42.8
Median Follow-up, months	21.1	17.6	20.3	21.0
95% CI	19.8, 22.3	16.6, 20.3	17.1, 24.6	19.0, 22.8



# With 21-month Median Follow-up, OS Results Exceed Ph3 Benchmarks for G/nP



Phase 3 G/nP  
median OS  
Benchmarks<sup>1,2</sup>

8.5 – 11.1 months

Number of patients at risk		Overall Survival (months)															
A2: Q+G/nP	29	28	26	23	20	19	16	15	14	12	9	3	0	0	0	0	0
A1: QZ+G/nP	61	53	48	40	31	29	27	23	20	13	9	4	2	1	0	0	0
Pooled Q100 QZ+G/nP	93	84	77	66	53	50	43	35	30	22	18	12	8	4	2	1	0
All pooled Q100 Q(±Z)+G/nP	122	112	103	89	73	69	59	50	44	34	27	15	8	4	2	1	0

NE, not estimable; OS, overall survival; Q, quercetin; Z, zirconium.

CI: confidence interval; G/nP: gemcitabine/nab-paclitaxel; Ph3: Phase 3

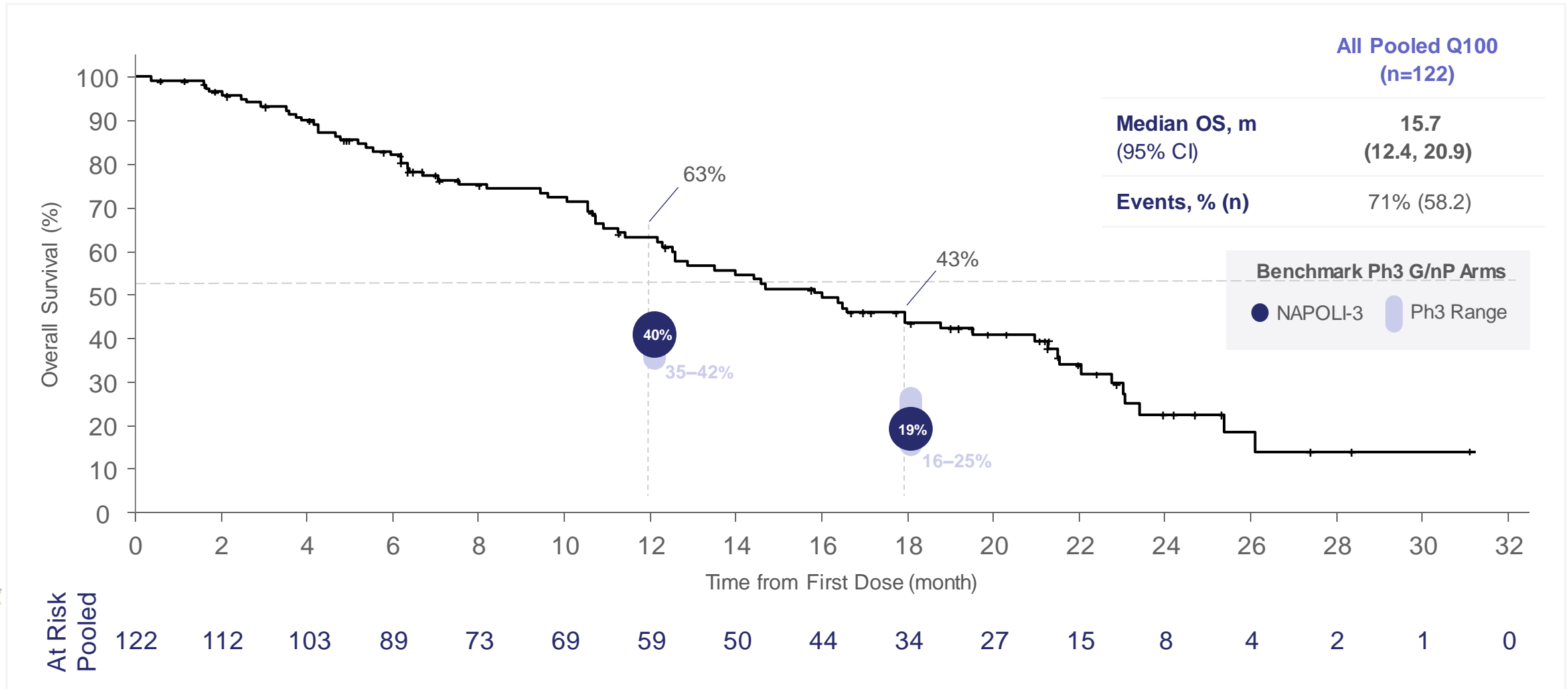
1. Abraxane USPI, 2020 and Wainberg ZA, Melisi D, Macarulla T, et al. NALIRIFOX versus nab-paclitaxel and gemcitabine in treatment-naïve patients with metastatic pancreatic ductal adenocarcinoma (NAPOLI 3): a randomised, open-label, phase 3 trial. Lancet. 2023;402(10409):1272-1281. doi:10.1016/S0140-6736(23)01366-1

2. Von Hoff et al. N Engl J Med. 2013;369:1691-703.

Wainberg ZA, et al. ASCO GI, Jan. 19, 2024, data cut off of June 19, 2023

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# OS for All Pooled Quemli 100 mg Exceeds Ph3 Benchmarks Including NAPOLI-3; CI Lower Bound Exceeds 12 Months



CI: confidence interval; G/nP: gemcitabine/nab-paclitaxel; OS: overall survival; Q/quemli: quemliclustat; Ph3: Phase 3  
Wainberg, et al. *The Lancet*. Sept 2023. [https://doi.org/10.1016/S0140-6736\(23\)01366-1](https://doi.org/10.1016/S0140-6736(23)01366-1)  
Wainberg ZA, et al. *ASCO GI*, Jan. 19, 2024, data cut off of June 19, 2023  
NAPOLI-3: Wainberg, et al. *The Lancet*. Sept 2023. [https://doi.org/10.1016/S0140-6736\(23\)01366-1](https://doi.org/10.1016/S0140-6736(23)01366-1).  
Data shown is for the G/nP arm only

# OS Data Compares Very Favorably to Historical Benchmarks, Including at the 12- & 18-month Landmarks

Randomized Trial	Regimen	N	ORR <sup>a</sup>	mPFS	Landmark PFS		mOS	Landmark OS		Key Baseline Characteristics
					6m	12m		12m	18m	
<b>ARC-8 All Pooled Q100</b>	Q + G/nP ± Z	122	39%	6.3m [5.4-7.7]	53%	22%	15.7m [12.4-20.9]	63%	43%	Liver mets: 65% ECOG PS1: 66% Prior surgery: 17% Asian: 8%
<b>MPACT</b> <i>Phase 3: Von Hoff, NEJM 2013</i>	G/nP	431	29%	5.5m [4.5-5.9]	44%	16%	8.5m [7.9-9.5]	35%	16%	Liver mets: 85% ECOG PS1: 42% Prior surgery: 7% Asian: 2%
<b>NAPOLI-3</b> <i>Phase 3: Wainberg, ASCO 2023</i>	G/nP	387	36%	5.6m [5.3-5.8]	43%	14%	9.2m [8.3-10.6]	40%	19%	Liver mets: 80% ECOG PS1: 57% Prior surgery: 5% Asian: 3%
<b>RESOLVE</b> <i>Phase 3: Tempero, AnnOnc 2021</i>	G/nP	213	42%	6.0m	~50%	~17%	10.8m	~41%	~18%	Liver mets: 81% KPS 70-80: 31% Prior surgery: 14% Asian: 28%
<b>CanStem111P</b> <i>Phase 3: Bekaii-Saab, eClinMed 2023*</i>	G/nP	569	43%	6.1m [5.6-7.1]	~50%	~17%	11.7m [10.7-12.7]	~42%	~25%	Liver mets: 78% ECOG PS1: 55% Prior surgery: 4% Asian: 34%
<b>NAPOLI-3</b> <i>Phase 3: Wainberg, ASCO 2023</i>	NALIRIFOX	383	42%	7.4m [6.0-7.7]	~55%	27%	11.1m [10-12.1]	46%	26%	Liver mets: 80% ECOG PS1: 58% Prior surgery: 5% Asian: 3%
<b>PRODIGE</b> <i>Phase 2/3: Conroy, NEJM 2011</i>	FOLFIRINOX	167	31%	6.4m [5.5-7.2]	53%	12%	11.1m [9.0-13.1]	48%	19%	Liver mets: 88% ECOG PS1: 62% Prior surgery: N/A

ECOG PS: Eastern Cooperative Oncology Group performance status; G/nP: gemcitabine/nab-paclitaxel; m: month; mets: metastasis; mOS: median overall survival; mPFS: median progression-free survival; ORR: overall response rate; PFS: progression-free survival; Q: quercetin; Z: zidovudine  
<sup>a</sup> ORR = Best Overall Response per RECIST v1.1  
*Bekaii-Saab et al. eClinMed 2023:* "In CanStem111P [vs MPACT], there were proportionally fewer patients reporting as white (62.1% vs 88%) and proportionally more reporting as Asian (33.7% vs 2%). CanStem111P included patients from Japan and South Korea, and these patients had the longest OS in both the nab-paclitaxel and control treatment arms."  
Wainberg ZA, et al. ASCO GI, Jan. 19, 2024, data cut off of June 19, 2023

# Favorable OS for Patients With & Without Liver Metastasis

- Because ARC-8 had a lower incidence of liver mets than historical studies, we also analyzed separately the OS for ARC-8 patients with and without liver mets as shown below
- When adjusting for the lower incidence of liver mets in the triplet arm as shown below, the mOS for the triplet and quad arms looked almost identical at approx. 12 months
- When evaluating just those patients with liver mets, median OS still exceeded historical benchmarks AND outperformed the OS for patients with liver mets in NAPOLI-3 (the most contemporary phase 3 in 1L pancreatic) -- 12.1 mos for ARC-8 vs. 8.6 mos for NAPOLI-3 as shown below**

Liver Mets at Baseline	A2: Q + G/nP (n=17)	A1: QZ + G/nP (n=42)	Pooled Q100 QZ + G/nP (n=62)	All Pooled Q100 Q(±Z) + G/nP (n=79)	NAPOLI-3 (n=309)
Events (%)	11 (64.7)	26 (61.9)	40 (64.5)	51 (64.6)	242 (78.3)
Median OS, months	12.1	12.2	11.1	12.1	8.6
95% CI	10.0, 20.9	6.2, 17.9	8.1, 14.5	10.0, 15.7	

No Liver Mets at Baseline	A2: Q + G/nP (n=12)	A1: QZ + G/nP (n=19)	Pooled Q100 QZ + G/nP (n=31)	All Pooled Q100 Q(±Z) + G/nP (n=43)	NAPOLI-3 (n=78)
Events (%)	4 (33.3)	7 (36.8)	16 (51.6)	20 (46.5)	43 (55.1)
Median OS, months	22.0	21.2	21.2	21.5	13.8
95% CI	17.9, NE	14.6, NE	13.9, 25.4	17.9, 25.4	

BL: Baseline; CI: confidence interval; G/nP: gemcitabine/nab-paclitaxel; mets: metastasis; mos: months;  
 NE: not estimable; OS: overall survival; Q: quercetin  
 NAPOLI-3: Wainberg, et al. *The Lancet*. Sept 2023. [https://doi.org/10.1016/S0140-6736\(23\)01366-1](https://doi.org/10.1016/S0140-6736(23)01366-1).  
 Data shown is for the G/nP arm only

Wainberg ZA, et al. ASCO GI, Jan. 19, 2024, data cut off of June 19, 2023

# While PFS is More in Line with Historical Benchmarks, It Also Appears Slightly Improved Relative to Historical Data

%, (n)	A2: Q + G/nP (n=29)	A1: QZ + G/nP (n=61)	Pooled Q100 QZ + G/nP (n=93)	All Pooled Q100 Q ±Z) + G/nP (n=122)	Phase 3 G/nP Benchmarks (n= 387 – 431) <sup>1,2</sup>
<b>Events (%)</b>	20 (69.0)	49 (80.3)	72 (77.4)	92 (75.4)	
<b>Median PFS, m (95% CI)</b>	<b>8.8 (6.4, 12.6)</b>	<b>4.9 (3.7, 6.0)</b>	<b>5.4 (4.9, 7.3)</b>	<b>6.3 (5.4, 7.7)</b>	<b>5.5 – 5.6</b>
<b>6m PFS Rate, %</b>	75.2	38.3	45.3	52.8	43.2 - 44
<b>12m PFS Rate, %</b>	32.0	17.9	18.3	21.8	13.9-16
<b>18m PFS Rate, %</b>	18.3	6.0	7.1	9.8	3.6
<b>Median Follow-up, m</b>	19.2 (16.4, NE)	20.2 (14.6, NE)	18.3 (14.6, NE)	19.2 (16.4, 20.5)	

CI: confidence interval; G/nP: gemcitabine/nab-paclitaxel; m: month; NE: not estimable; PFS: progression-free survival; Q: quermiclustat; Z: zimberelimab

Wainberg ZA, et al. ASCO GI, Jan. 19, 2024, data cut off of June 19, 2023

1. Wainberg, et al. The Lancet. Sept 2023. [https://doi.org/10.1016/S0140-6736\(23\)01366-1](https://doi.org/10.1016/S0140-6736(23)01366-1)

2. Von Hoff et al. N Engl J Med 2013;369:1691-703

# Disease Control Rates Are Improved Compared to the NAPOLI-3 G/nP Arm

%, (n)	A2: Q + G/nP (n=29)	A1: QZ + G/nP (n=61)	Pooled Q100 QZ + G/nP (n=93)	All Pooled Q100 Q ±Z)+G/nP (n=122)	NAPOLI-3 G/nP (n=387)
<b>Best Overall Response (95% CI)</b>	41.4 (23.5, 61.1)	34.4 (22.7, 47.7)	37.6 (27.8, 48.3)	38.5 (29.9, 47.8)	36.2 (31.4, 41.2)
<b>CR</b>	0	0	0	0	0.3
<b>PR</b>	41.4 (12)	34.4 (21)	37.6 (35)	38.5 (47)	35.9
<b>SD</b>	44.8 (13)	37.7 (23)	37.6 (35)	39.3 (48)	26.1
<b>PD</b>	10.3 (3)	11.5 (7)	11.8 (11)	11.5 (14)	14.5
<b>NA</b>	3.4 (1)	16.4 (10)	12.9 (12)	10.7 (13)	23.3
<b>Disease Control Rate</b>	86.2	72.1	75.2	77.8	62.3
<b>Median DOR (months)</b>	5.5 (4.1, 11.2)	3.7 (2.6, 10.5)	4.7 (3.3, 9.3)	5.4 (3.7, 9.3)	5.0 (3.8, 5.6)

**Median OS for patients with stable disease performed above historical benchmarks, demonstrating the potential for the quemli-based regimen to benefit patients regardless of RECIST response**

# Safety Profile Similar to G/nP with Regards to Overall TEAEs

%	A2: Q + G/nP (n=29)	Pooled Q100 QZ + G/nP (n=93)	All Pooled Q100 Q ±Z)+G/nP (n=122)	NAPOLI-3 G/nP Benchmark <sup>4</sup> (n=379)
Any TEAE	100	100	100	99
Any TRAE	100	98.9	99.2	93
Grade 3-5 TEAE	89.7	83.9	85.2	86
Grade 3-5 TRAE	75.9	72.0	73.0	68
Serious TEAE	51.7	53.8	53.3	52
Serious TRAE	34.5	25.8	27.9	19
Grade 5 TEAE	0	5.4	4.1	6
Grade 5 TRAE	0	0	0	2
AE leading to mod <sup>1</sup>	58.6	51.6	53.3	54
AE leading to dose delay	75.9	75.3	75.4	NR
AE leading to discon <sup>2</sup>	24.1	22.6	23.0	23
IRR <sup>2</sup>	10.3	6.5	7.4	N/A
Immune related AE <sup>3</sup>	6.9	10.8	9.8	N/A

AE: adverse event; G/nP: gemcitabine/nab-paclitaxel; IRR: infusion-related reaction; NA: not applicable; NR: not reported; TEAE: treatment-emergent adverse event; TRAE: treatment-related adverse event

1. AE leading to dose reduction; 2. Discontinuation of any study drug; 3. As reported by investigator;

4. Wainberg, et al. The Lancet. Sept 2023. [https://doi.org/10.1016/S0140-6736\(23\)01366-1](https://doi.org/10.1016/S0140-6736(23)01366-1)

Wainberg ZA, et al. ASCO GI, Jan. 19, 2024, data cut off of June 19, 2023





# Summary of Synthetic Control Arm Analysis

Data presented at ASCO GI, January 19, 2024, based on a data cutoff of June 19, 2023.

# Synthetic Control Arm Background

- Historical external clinical trials are selected according to their treatment intervention (eg, G/nP) and comparability to the investigational study (eg, ARC-8)
- Patient level data from the external clinical trial patients are further matched 1:1 to the patients in the investigational study for key baseline characteristics
- The resulting Synthetic Control Arm (SCA) consist of external patient level data
  - Treated with a select treatment intervention (eg, G/nP)
  - Baseline characteristics comparable and balanced to the patients of the investigational study (eg, ARC-8)

# Arcus & Medidata AI Synthetic Control Arm (SCA) Project

- Developed in collaboration with Medidata, the industry's leading provider of electronic data capture used in clinical trials:
  - Patient level data from over 30,000 trials and 9 million patients over past 22 years
- Constructed SCA using historical clinical trial data from patients treated with G/nP alone and balanced to the patient baseline characteristics of ARC-8
  - Contemporaneous global Phase 2 and 3 clinical trials that meet key ARC-8 entry criteria
  - 515 eligible external patients identified for further matching
  - SCA matched to All Pooled Q100 Q±Z+G/nP (n=122) using propensity score statistical method including exact matching on baseline liver metastasis
  - Refer to ASCO GI poster for additional details
- Assess treatment effects on OS, PFS, and objective response rate in the SCA patients
- Compare the treatment effects and clinical activity between matched SCA and ARC-8
- SCA analyses were conducted versus all four analysis groups and showed consistent results; for simplicity, only the SCA for the All Pooled Q100 group is reported

# SCA Study Level Features

Study Attributes	ARC-8	Historical Data
<b>Trial Phase</b>	Phase I/Ib	Phase II & III (~50% each)
<b>Target Intervention</b>	Quemli + G/nP +/- Zim	G/nP
<b>Intervention Assignment</b>	Sequential/Randomized Assignment	Randomized Assignment
<b>Masking</b>	Open Label	Open Label
<b>Study Start Year</b>	2019	2013 - 2019
<b>Study Primary Completion Year</b>	2024	2018 - 2023
<b>Key Endpoints</b>	OS, PFS, ORR	OS, PFS, ORR
<b>Planned Follow-up Duration (Primary Endpoints)</b>	18 months	1 to 2.5 years
<b>Region</b>	United States	Global
<b>Number of Potential Historical Clinical Trials (HCTs)</b>	N/A	<5
<b>Number of Potential HCT Patients</b>	N/A	515

# SCA-Eligible Pool from Historical 1L PDAC Trials (n=515)

Baseline Characteristics		SCA-Eligible (n = 515)	Efficacy Endpoints		SCA-Eligible (n = 515)
Age Mean (SD)		64.4 (8.44)	Median Overall Survival (OS) (95% CI)		9.5 (8.8, 10.5)
Sex (F/M) n (%)		223 (43%); 292 (57%)	Median follow-up		26.3m
Race n (%)	White	428 (83%)	12 month OS Rate, % (95% CI)		39.7 (35.4, 44.0)
	Asian	28 (5.4%)	18 month OS Rate, % (95% CI)		20.1 (16.5, 23.6)
	Black	19 (3.7%)	Median PFS (95% CI)		5.6 (5.4, 6.0)
	Others/NR	40 (8%)	Median follow-up		11.4m
ECOG 0 n (%)		245 (47.6%)	6 month OS Rate, % (95% CI)		45.4 (40.6, 50.1)
ECOG 1		270 (52.4%)	12 month OS Rate, % (95% CI)		12.4 (8.8, 16.1)
Prior Surgery n (%)		46 (8.9%)	Objective Response Rate, % (95% CI)		37.3 (33.1, 41.6)
Duration since Diagnosis, months Mean (SD)		3.8m (10.8)	Disease Control Rate, % (95% CI)		71.7 (67.5, 75.5)
Liver Mets at baseline n (%)		415 (80.6%)			

# SCA Population Baseline Demographics & Disease Characteristics Before and After Matching

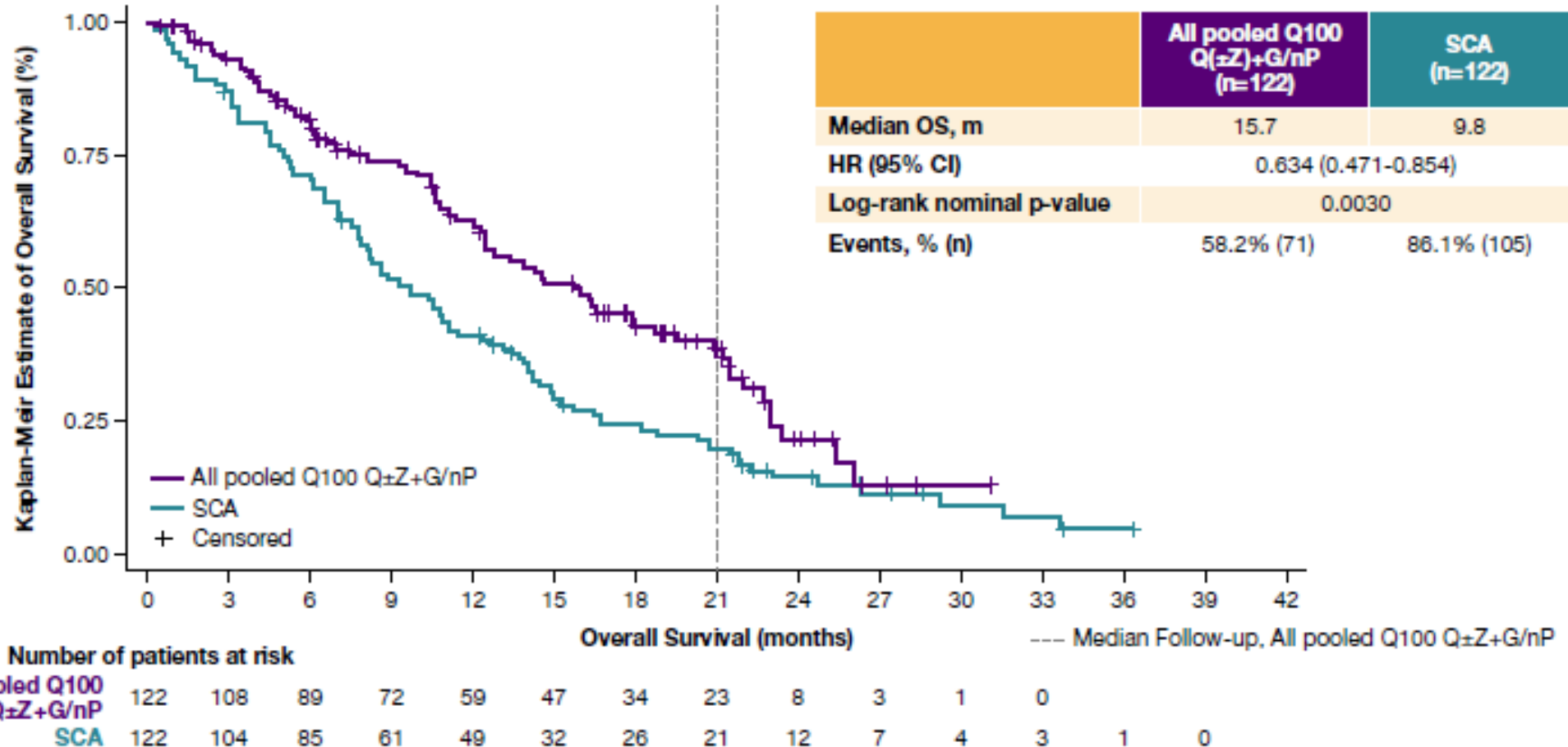
% (n)		Before Matching		After Matching	
		All pooled Q100 Q(±Z)+G/nP (n=122)	SCA Eligible (n=515)	All pooled Q100 Q(±Z)+G/nP (n=122)	SCA (n=122)
Median Age		65.5 (59, 72)	65.0 (60, 71)	65.5 (59, 72)	64.0 (60, 72)
Female		48 (58)	43 (223)	48 (58)	47 (57)
Race	White/NR	85 (104)	88 (454)	85 (104)	83 (101)
	Other	15 (18)	12 (61)	15 (18)	17 (21)
ECOG 0		34 (42)	48 (245)	34 (42)	38 (46)
ECOG 1		66 (80)	52 (270)	66 (80)	62 (76)
Liver Metastases at BL		65 (79)	81 (415)	65 (79)	65 (79)
Time to Dx, mean mos (SD)		4.7 (10.0)	3.8 (10.8)	4.7 (10.0)	4.5 (11.4)
Prior Surgery for PDAC		17 (21)	9 (46)	17 (21)	16 (19)

BL: baseline; Dx: diagnosis; ECOG: Eastern Cooperative Oncology Group; IQR: interquartile range; mets: metastasis; mos: months, NR: not reported; PDAC: pancreatic ductal adenocarcinoma; quemi: quemiclustat; SCA: synthetic control arm; SD: standard deviation

Wainberg ZA, et al. ASCO GI, Jan. 19, 2024, data cut off of June 19, 2023

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# Quemli-based Regimen Significantly Reduced Risk of Death by 37% and increased mOS by 5.9 months

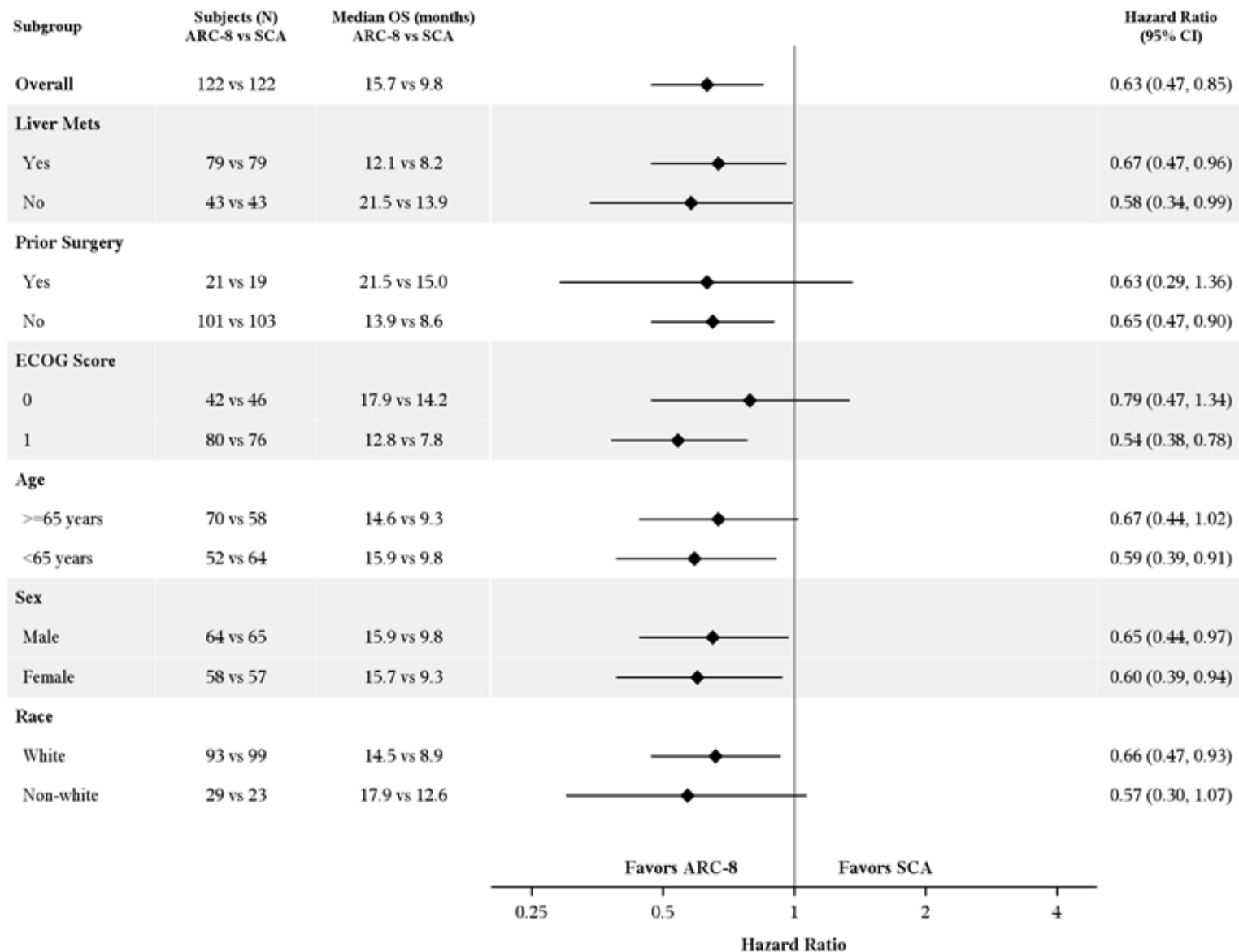


G/nP, gemcitabine/nab-paclitaxel; OS, overall survival; Q, quemliclustat; SCA, synthetic control arm; Z, zimberelimab.



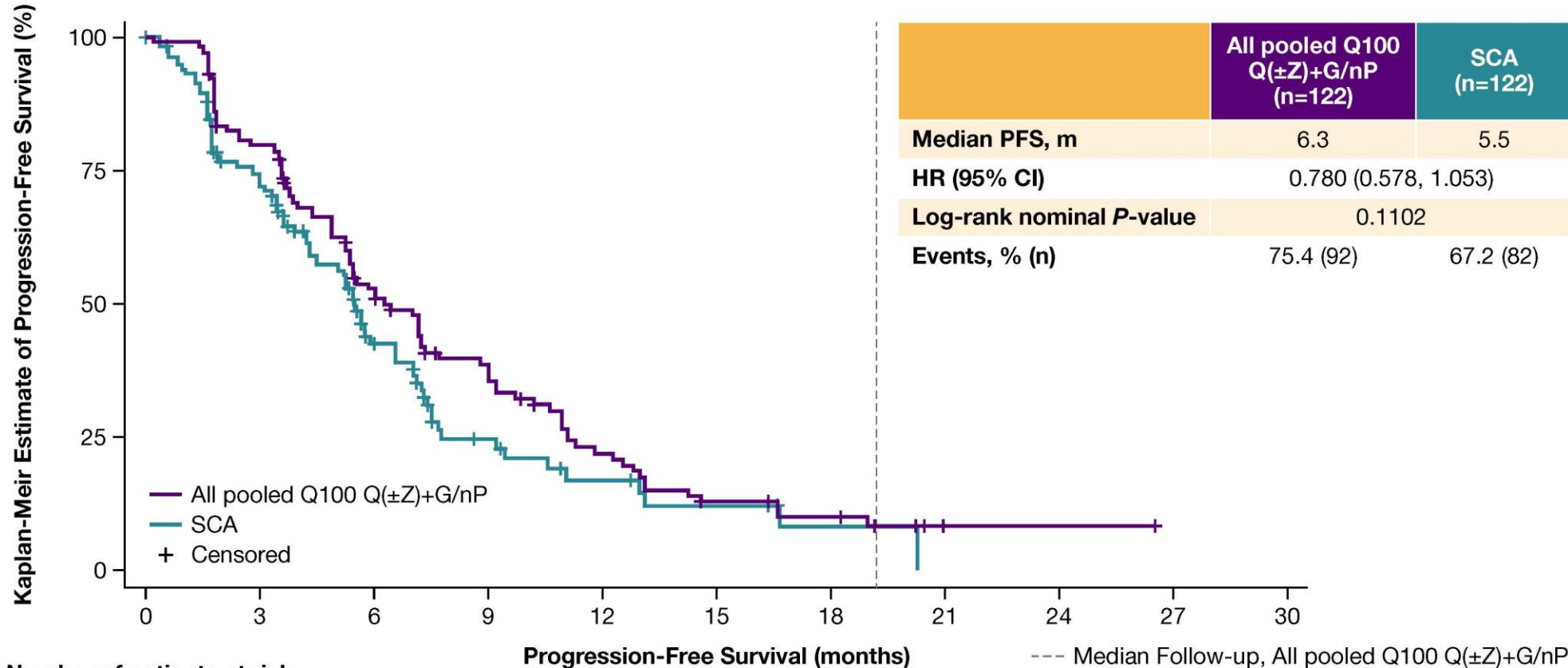
# Every Subgroup in ARC-8 Demonstrated Improved OS Over the SCA

Forest Plot of Overall Survival for ARC-8 Quemli 100 mg Pooled Patients (ARC-8) versus Corresponding Synthetic Control Arm (SCA)



# The Quemli-based Regimen Reduced Risk of Progression or Death by 22%

Progression-Free Survival: Pooled Q( $\pm$ Z)+G/nP vs SCA



Number of patients at risk										
All pooled Q100 Q( $\pm$ Z)+G/nP	122	90	54	35	19	10	7	1	1	0
	SCA	122	81	35	14	8	5	2	0	

# ARC-8 ORR and DCR Were Consistent with the SCA

	ARC-8 All Pooled Q100 (n=122)		SCA (n=122)	
	n	% (95% CI)	n	% (95% CI)
<b>Objective Response Rate</b>	47	38.5 (29.9, 47.8)	50	41.0 (32.2, 50.3)
<b>Best Overall Response</b>				
CR	0		0	
PR	47	38.5 (29.9, 47.8)	50	41.0 (32.2, 50.3)
SD	48	39.3 (30.6, 48.6)	39	32.0 (23.8, 41.0)
PD	14	11.5 (6.4, 18.5)	14	11.5 (6.4, 18.5)
NE	0		1	0.8 (0.0, 4.5)
NA#	13	10.7 (5.8, 17.5)	18*	14.8 (9.0, 22.3)
<b>Disease Control Rate (DCR)</b>	95	77.9 (69.5, 84.9)	89	73.0 (64.2, 80.6)

CI: confidence interval; CR: complete response; NA: not available (no post-baseline tumor assessments recorded); NE: not estimable; ORR: overall response rate; PD: progressive disease; PR: partial response; Q: quercetin; SCA: synthetic control arm

\*\*Reason for treatment discontinuation: Death = 5, Progressive Disease = 3, Withdrawal from Treatment by Subject = 8, Adverse Event = 2

Wainberg ZA, et al. ASCO GI, Jan. 19, 2024, data cut off of June 19, 2023

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# Subsequent Therapy Incidence in the SCA was Consistent with ARC-8

The number of patients receiving subsequent treatment in the SCA is slightly higher than in ARC-8; Types of subsequent therapy between SCA and ARC-8 are comparable

Subsequent Therapies Category 1 %, (n)	SCA (n=122)	ARC-8 All Pooled Q100 (n=122)
<b>Systemic Therapy</b>	70 (57.4)	47
<b>FOLFIRINOX</b>	19 (15.6)	26 (21)
<b>FOLFIRI</b>	18 (14.8)	23 (19)
<b>FOLFOX</b>	12 (9.8)	9 (7)
<b>Cisplatin</b>	0	7 (6)
<b>G, G/nP, or GP</b>	29 (23.8)	11 (9)
<b>Investigational agents</b>	8 (6.6)	10 (8)
<b>Other</b>	16 (13.1)	11 (9)

Subsequent Therapies Category 2 %, (n)	SCA (n=122)	ARC-8 All Pooled Q100 (n=122)
<b>Systemic Therapy</b>	70 (57.4)	47
<b>Cytotoxic/chemotherapy</b>	69 (56.6)	5 (4)
<b>Investigational</b>	8 (6.6)	1 (1)

G: gemcitabine; G/nP: gemcitabine/nab-paclitaxel; GP: gemcitabine/paclitaxel; Q: quemiclustat;  
SCA: synthetic control arm

Output Date: December 22, 2023

Wainberg ZA, et al. ASCO GI, Jan. 19, 2024, data cut off of June 19, 2023

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# Summary

**Quemliclustat (quemli) is an investigational, first-in-class, small-molecule CD73 inhibitor**

**Median overall survival (mOS) was 15.7 months for patients treated with a quemliclustat-based regimen, which exceeds the historical benchmark data for chemotherapy alone (8.5 – 11.7 months)<sup>1,2</sup>**

**A 37% reduction in risk of death and a 5.9-month improvement in mOS was observed for patients treated with the quemli-based regimen when compared to a synthetic control arm of patients treated with G/nP alone<sup>1</sup>**

**The quemli-based regimen was well-tolerated, with no new safety signals or significant added toxicity compared to chemotherapy alone<sup>1</sup>**

CI: confidence interval; G/nP: gemcitabine/nab-paclitaxel; HR: hazard ratio; OS: overall survival

1. Wainberg ZA, et al. ASCO GI, Jan. 19, 2024, data cut off of June 19, 2023

2. Abraxane USPI, 2020 and Wainberg ZA, Melisi D, Macarulla T, et al. NALIRIFOX versus nab-paclitaxel and gemcitabine in treatment-naïve patients with metastatic pancreatic ductal adenocarcinoma (NAPOLI 3): a randomised, open-label, phase 3 trial. Lancet. 2023;402(10409):1272-1281. doi:10.1016/S0140-6736(23)01366-1

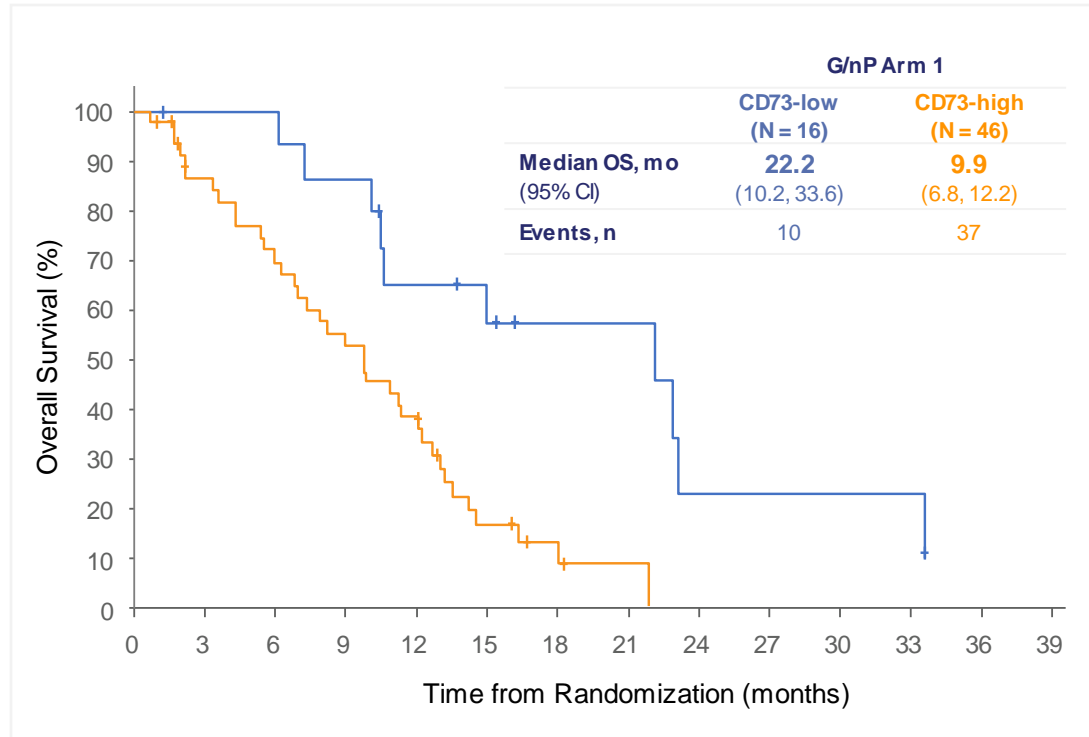
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# Appendix

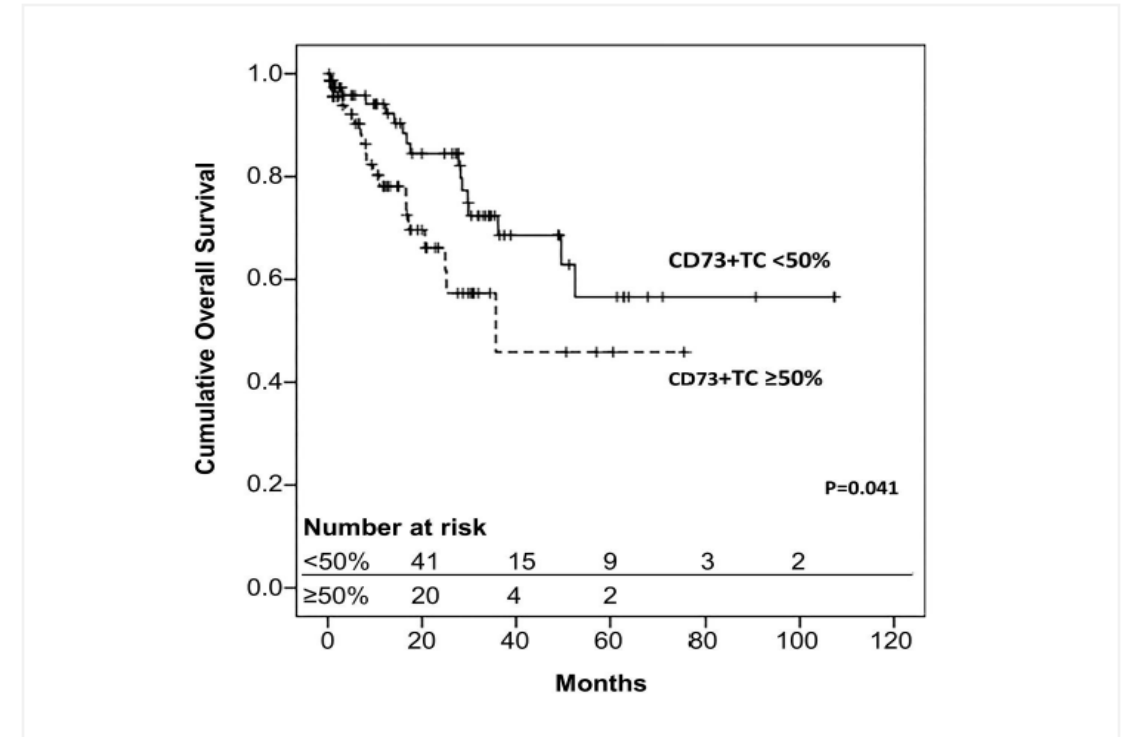
# High Levels of CD73 Are Associated with Shorter Survival in Multiple Tumor Types, including PDAC<sup>1-3</sup>, NSCLC<sup>4,5</sup>, CRC<sup>6,7</sup>, GC<sup>8</sup>

CD73 is a strong negative predictor of OS with G/nP in the AZ Ph2 study of G/nP ± Oleclumab ± Durva

Figure S6. Cumulative overall survival rates for hepatobilio-pancreatic malignancies, based on CD73 expression (Kaplan-Meier plot)



Visual recreation by Arcus of G/nP control arm by CD73 expression, from Covelev et al., ASCO2023, #4136.



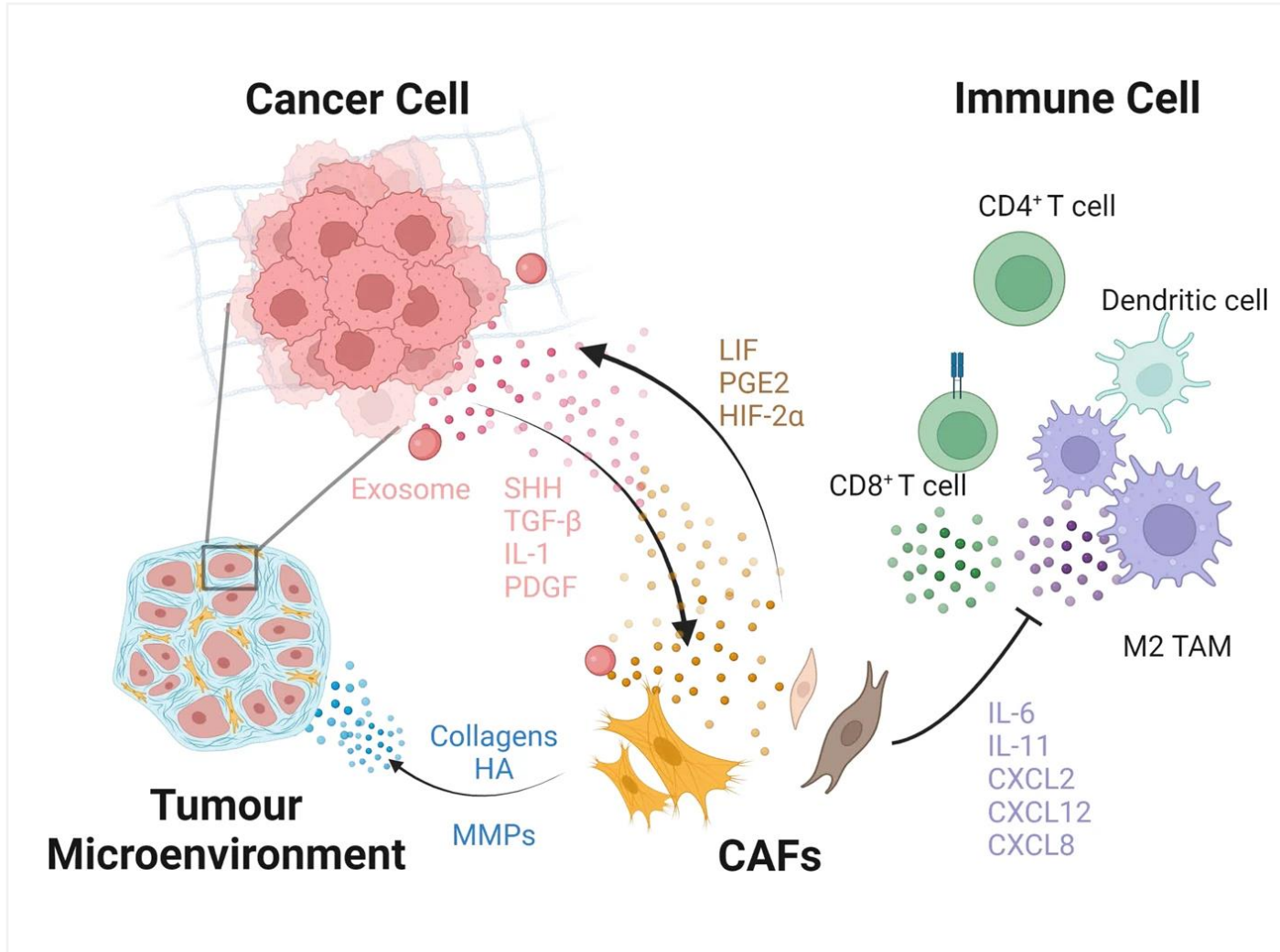
- n=202 surgical specimens representative of various hepatobiliopancreatic conditions: PDAC (n=42), HCC (n=24); etc.
- CD73 expressed in all cases of invasive PDAC; median 80% positive TC
- In PDAC, CD73 expression is inversely correlated with differentiation
- High CD73 associated with reduced OS and loss of E-cadherin

Sciarra A et al (2019) PMID: 30607549

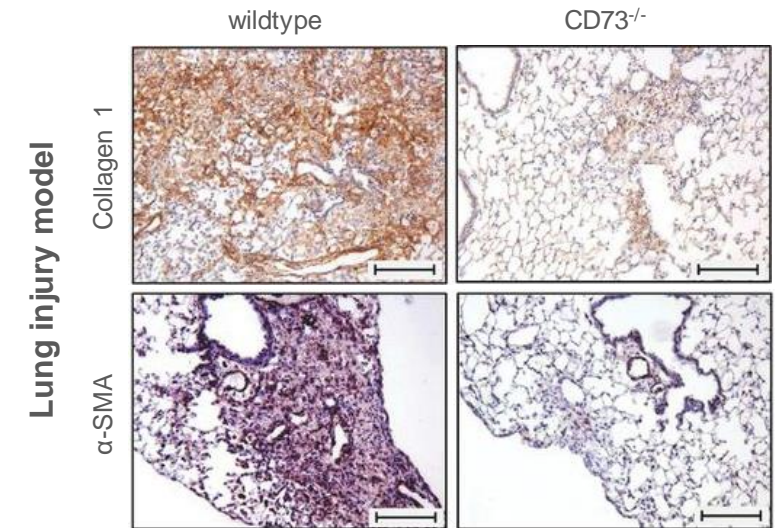
AZ: AstraZeneca; CI: confidence interval; CRC: colorectal cancer; durva: durvalumab; GC: gastric carcinoma; G/nP: gemcitabine/nab-paclitaxel; HCC: hepatocellular carcinoma; NSCLC: non-small cell lung cancer; OS: overall survival; PDAC: pancreatic ductal adenocarcinoma; TC: tumor cells  
 1. Zhao, J et al (2021) PMID: 333832821; 2. Tahkola K et al (2021) PMID: 32676968; 3. Sciarra A et al (2019) PMID: 30607549; 4. Inoue, Y et. al. (2017) PMID: 28060732; 5. Ishii H (2020) PMID: 32061060; 6. Wu et. al (2012) PMID: 22287455; 7. Messaoudi N et. al (2020) PMID: 32363113; 8. Lu WJ et. al. (2013) PMID: 23569336



# Cancer-Associated Fibroblasts (CAFs) are Central to Modulating the Pancreatic Tumor Microenvironment



**CAFs respond to CD73-generated adenosine, leading to enhanced desmoplasia and fibrosis**

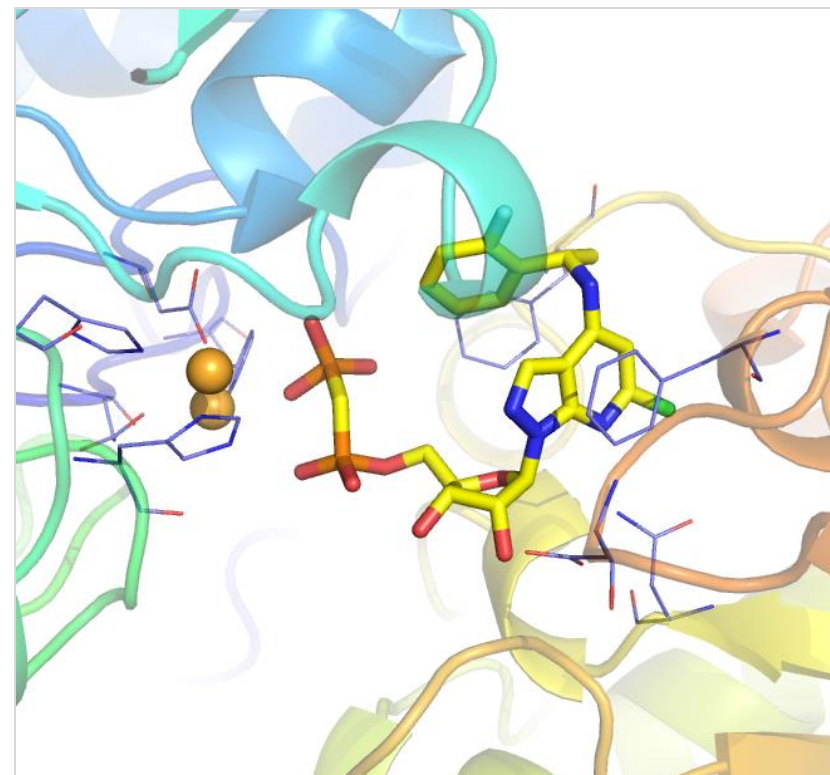


Wirsdorfer et al. *Cancer Res.* 2016

# Quemli Binds to CD73 Catalytic Site with Affinity $10^7$ Times Greater than the Natural Substrate AMP

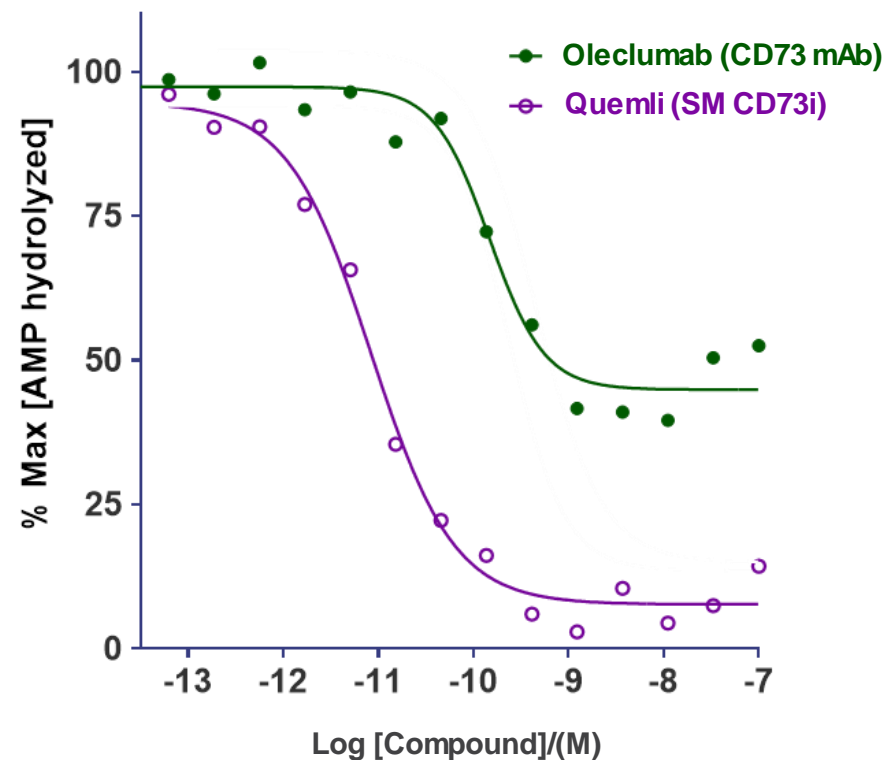
Quemli is a tight-binding, reversible inhibitor ( $K_i$  hCD73 = 4.9 pM)

CD73 Potency	
Target	IC <sub>50</sub> (nM)
hCD73-CHO	0.070
hCD73 (soluble)	0.043
Human CD8 <sup>+</sup> T Cells	0.008
hPBMC	0.011

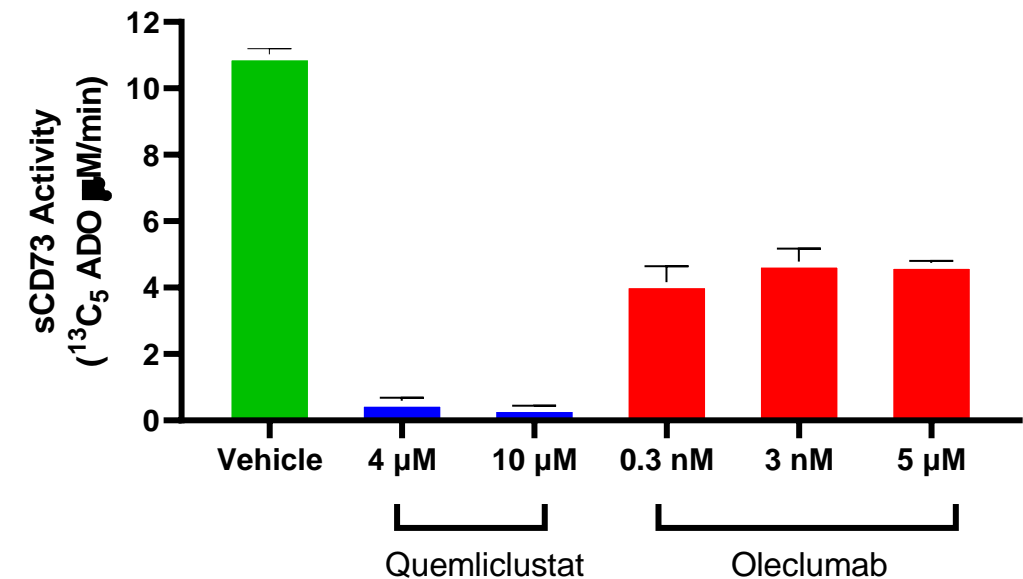


# Quemli Fully Inhibits CD73 Enzymatic Activity While Oleclumab Inhibits Adenosine Production By Only ~50%

Quemli (AB680) potently inhibits CD73 enzymatic activity on CD8<sup>+</sup> T Cells



Quemli (AB680) completely inhibits CD73 enzymatic activity in serum from PDAC patients (ARC-8) with highest sCD73 levels



Concentrations of quemli and oleclumab selected from dose-response curves to achieve maximal level of CD73 inhibition. Concentrations consistent with clinical levels of the respective drugs.

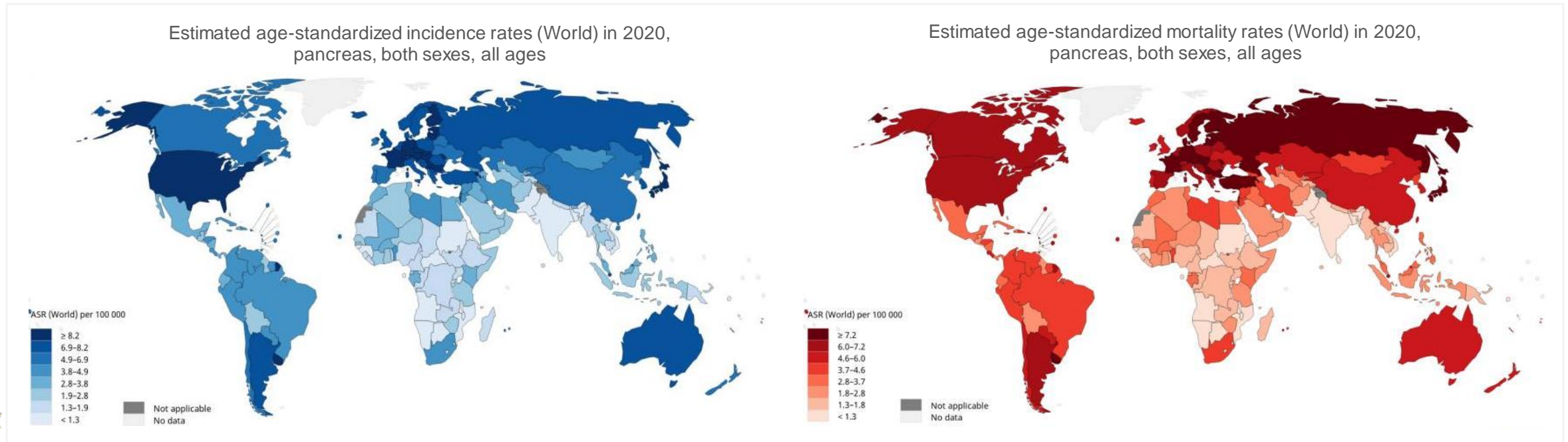
AMP: adenosine monophosphate; mAb: monoclonal antibody; PDAC: pancreatic ductal adenocarcinoma; quemli: quemliclustat

Oleclumab synthesized by Arcus based on the following reports: Hay et al., *Oncol Immunology* (2016) 5, e1208875; Patent Appl. US 2016/0129108Wainberg ZA, et al. ASCO GI, Jan. 19, 2024, data cut off of June 19, 2023



# Pancreatic Cancer is One of the Deadliest Cancers Globally

- **Enormous unmet need, with high incidence in the Americas and Europe<sup>1</sup>**
  - ~37k incident 1L metastatic pancreatic cancer patients each year in the US <sup>2</sup>
  - An additional ~70k annual 1L incidence across Europe and Japan<sup>2</sup>
  - **Estimated ~\$3b addressable market opportunity in the U.S. alone for 1L chemotherapy<sup>3</sup>**



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Data source: GLOBOCAN 2020  
Graph production: IARC  
(<http://gco.iarc.fr/today>)  
World Health Organization

World Health Organization  
© International Agency for Research on Cancer 2021

1L: first-line

1. Ilic I, Ilic M. International patterns in incidence and mortality trends of pancreatic cancer in the last three decades: a joinpoint regression analysis. World J Gastroenterol. 2022;28(32):4698-4715. doi:10.3748/wjg.v28.i32.4698

2. Decision Resources Group

3. Projection based on expected drug treatable US patient population and novel regimen pricing

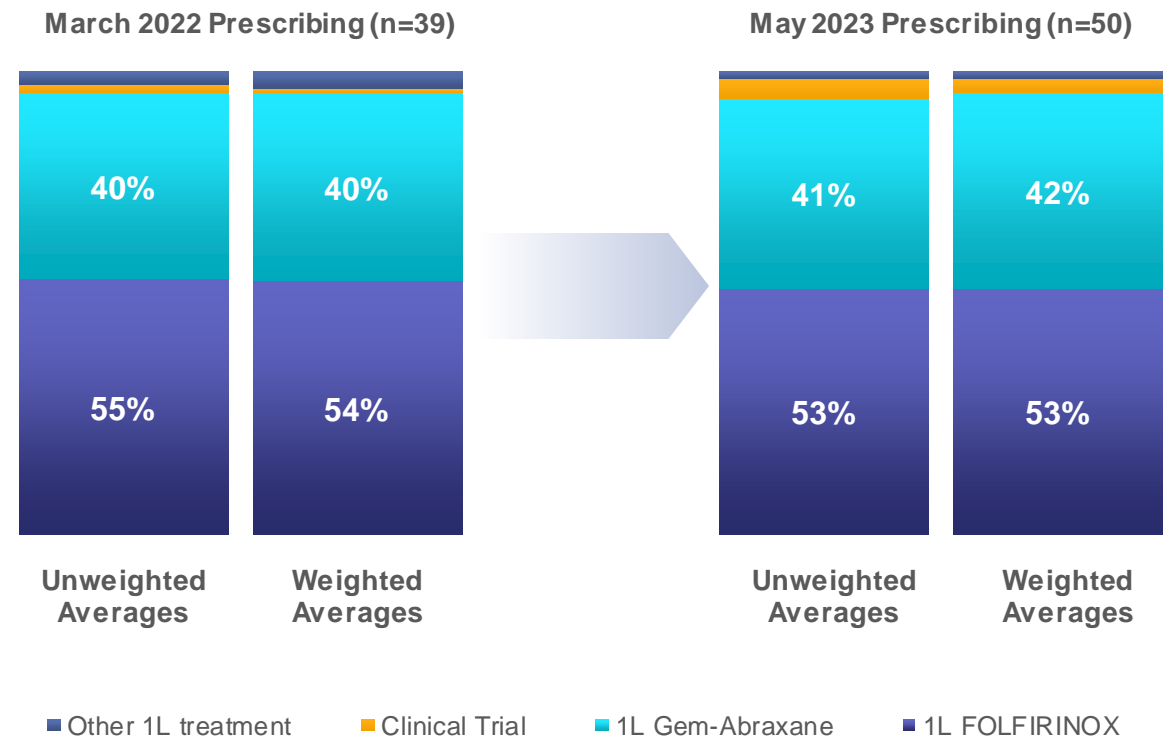
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# Chemotherapy Has Been the SOC for More Than 30 Years

- NCCN and ESMO guidelines recommend treatment with gemcitabine + nab-paclitaxel (G/nP) or FOLFIRINOX (oxaliplatin, fluoropyrimidine and irinotecan) for first-line metastatic PDAC
  - G/nP: 8.5 – 9.2 mOS and ~5.5 months mPFS<sup>1</sup>
  - FOLFIRINOX: 11.1 mOS and 6.4 months mPFS<sup>2</sup>
- FOLFIRINOX is typically reserved for the fittest pts due to its toxicity profile whereas G/nP can be used in patients with performance status up to ECOG 2 -- **prescribing mix between G/nP and FOLFIRINOX has been very stable at approx. 50/50**

## Stated Prescribing of 1L mPDAC Patients in the US

(Among Total Responders, Unweighted and Patient Weighted Average\*, 2022 n=39, 2023 n=50)



Source: Arcus primary research survey

\*Weighting based on self-reported PDAC patient volume

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1L: first-line; ECOG: Eastern Cooperative Oncology Group; ESMO: European Society for Medical Oncology; mOS: median overall survival; mPDAC: metastatic pancreatic ductal adenocarcinoma; mPFS: median progression-free survival; open-label, phase 3 trial. Lancet. 2023;402(10409):1272-1281. doi:10.1016/S0140-6736(23)01366-1

2. Conroy T, Desseigne F, Ychou M, et al. FOLFIRINOX versus gemcitabine for metastatic pancreatic cancer. *N Engl J Med*. 2011;364(19):1817-1825. doi:10.1056/NEJMoa1011923