



Company Overview The Onvansertib Opportunity

SEPTEMBER 2025

Forward-looking statements

CERTAIN STATEMENTS IN THIS PRESENTATION ARE

FORWARD-LOOKING within the meaning of the Private Securities Litigation Reform Act of 1995. These statements may be identified by the use of words such as "anticipate," "believe," "forecast," "estimated" and "intend" or other similar terms or expressions that concern our expectations, strategy, plans or intentions. These forward-looking statements are based on our current expectations and actual results could differ materially. There are several factors that could cause actual events to differ materially from those indicated by such forward-looking statements. These factors include, but are not limited to, clinical trials involve a lengthy and expensive process with an uncertain outcome, and results of earlier studies and trials may not be predictive of future trial results; our clinical trials may be suspended or discontinued due to unexpected side effects or other safety risks that could preclude approval of our product candidate; results of preclinical studies or clinical trials for our product candidate could be unfavorable or delayed; our need for additional financing; risks related to business interruptions, including the outbreak of COVID-19 coronavirus and cyber-attacks on our information technology infrastructure, which could seriously harm our financial condition and increase our costs and expenses; uncertainties of government or third party payer reimbursement; dependence on key personnel; limited experience in marketing and sales; substantial competition; uncertainties of patent protection and litigation;

dependence upon third parties; and risks related to failure to obtain FDA clearances or approvals and noncompliance with FDA regulations. There are no guarantees that our product candidate will be utilized or prove to be commercially successful. Additionally, there are no guarantees that future clinical trials will be completed or successful or that our product candidate will receive regulatory approval for any indication or prove to be commercially successful. Investors should read the risk factors set forth in our Form 10-K for the year ended December 31, 2024, and other periodic reports filed with the Securities and Exchange Commission. While the list of factors presented here is considered representative, no such list should be considered to be a complete statement of all potential risks and uncertainties. Unlisted factors may present significant additional obstacles to the realization of forward-looking statements. Forward-looking statements included herein are made as of the date hereof, and we do not undertake any obligation to update publicly such statements to reflect subsequent events or circumstances.

Cardiff Oncology's lead development asset is onvansertib

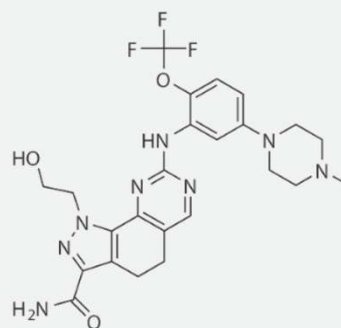
Onvansertib

First oral, well-tolerated
PLK1-selective inhibitor



PROPERTIES

- Small molecule
- Oral dosing
- 24-hour half-life

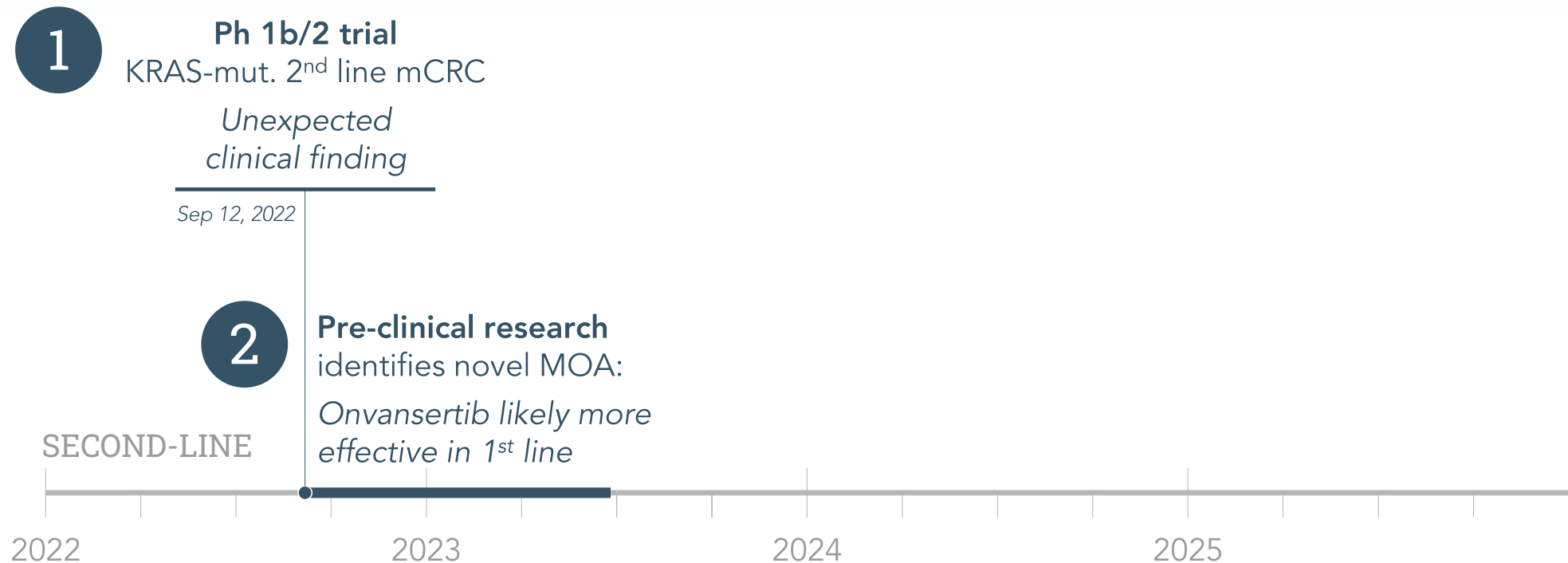


SPECIFICITY

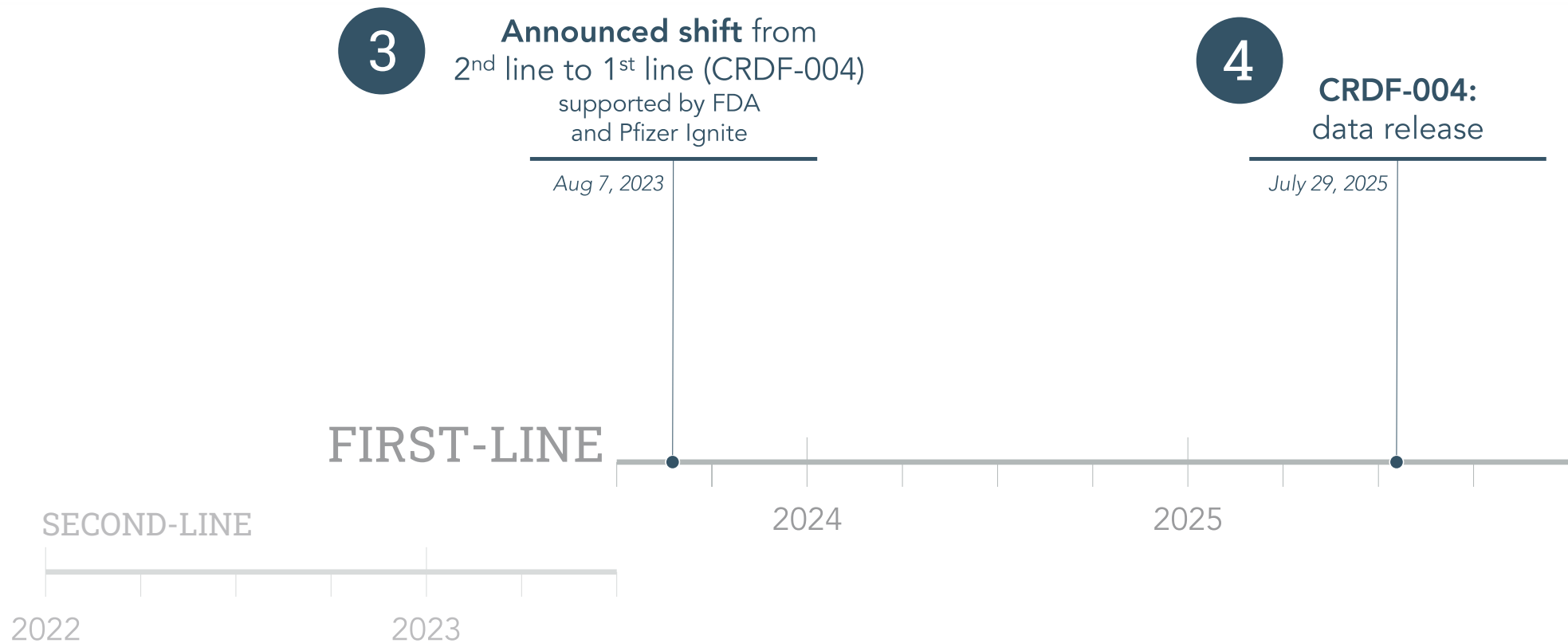
Exquisitely specific for PLK1

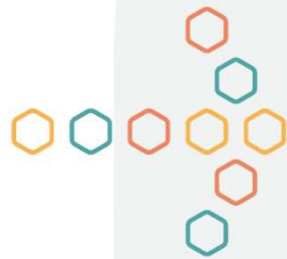
ENZYME	IC ₅₀ (μM)
PLK1	0.002
PLK2	>10
PLK3	>10
CK2	0.4
FLT3	0.4
CDK1/CycB	>10
42 other kinases and >140 in the Millipore panel	>10

We shifted our RAS-mutated mCRC program to the first-line



We are encouraged by the initial clinical data from CRDF-004





OUR SHIFT

TO FIRST-LINE RAS-MUTATED mCRC

The strength of our 1st-line program

The rationale for our shift from 2nd-line

The coming catalysts

CRC: High unmet need with limited therapies for RAS-mut mCRC

COLORECTAL CANCER

3rd

most common cancer worldwide

Annually in the United States

150,000

new cases

50,000

deaths

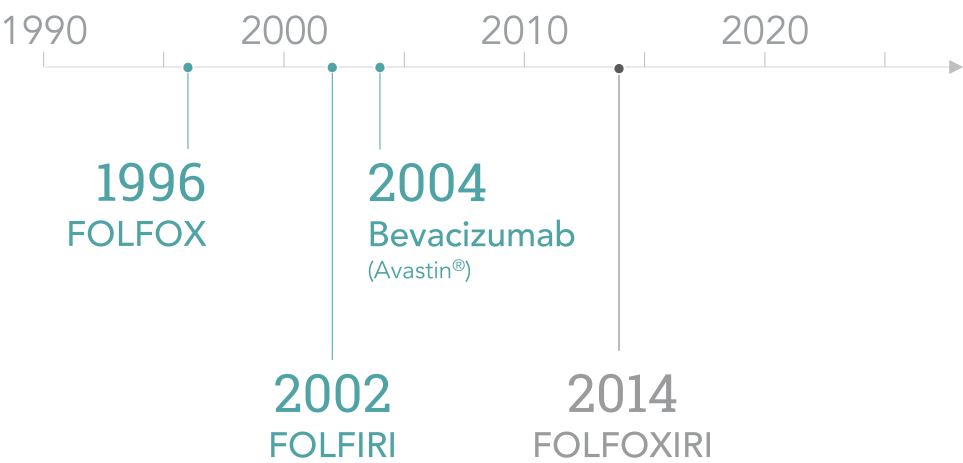
For patients with metastatic CRC

15%

5-year relative OS

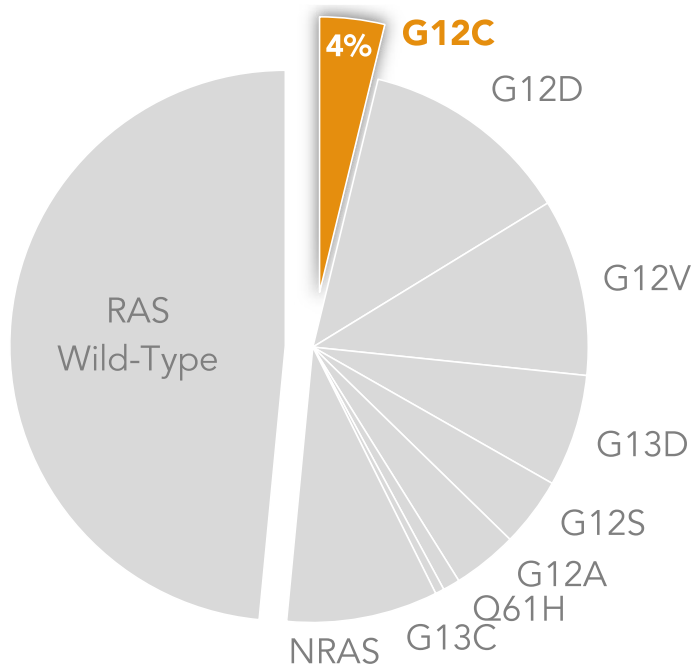
Less than 12 months
Median PFS

1st LINE STANDARD of CARE RAS-mutated mCRC

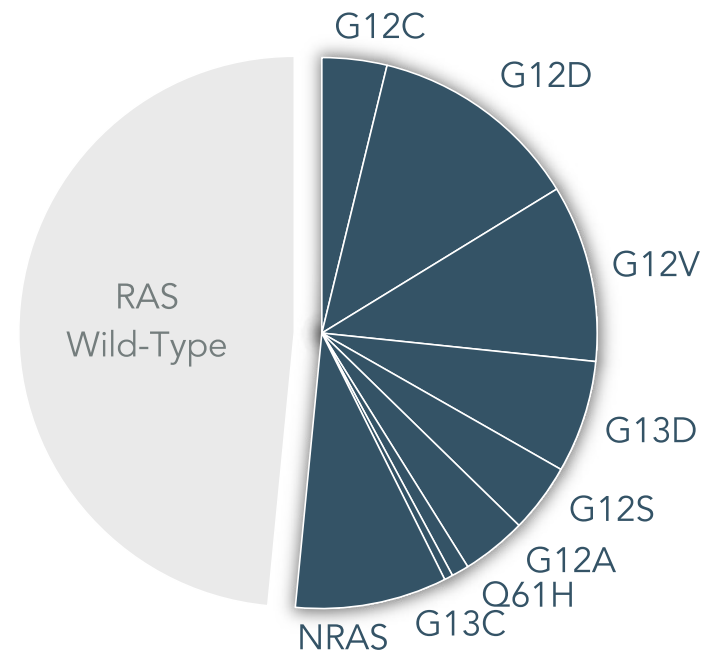


Onvansertib's MOA allows us to target ALL RAS-mutated mCRC

KRAS G12C therapies would address a small part of the need¹



ONVANSERTIB addresses 52% of mCRC cases are RAS-mutated¹



1. Jones R et al. Br J Cancer. 2017 Mar 28;116(7):923-929.

Prior 1st line Ph3 mCRC trials provide benchmarks for current SoC

Data from Positive 1st line mCRC Chemo/bev Phase 3 Clinical Trials by RAS-mut Status*

Targeted agent	Trial	Mechanism of action	Trial population		Sample size	ORR Exp. vs Ctrl.	ORR delta	PFS (months) Exp. vs Ctrl.	Hazard ratio
Bevacizumab	IFL/bev vs IFL	Antiangiogenic	KRAS WT or mutant	All ITT patients	813	45% vs 35%	10%	10.6 vs 6.2	0.54 p<0.0001
				Mutant only ¹	78	43% vs 41%	2%	9.3 vs 5.5	0.41
FOLFOXIRI/bev (TRIBE trial)	FOLFOXIRI/bev vs FOLFIRI/bev	Chemo	RAS WT or mutant	All ITT patients	508	65% vs 54%	11%	12.3 vs 9.7	0.77 p=0.006
				Mutant only ¹	236	66% vs 55%	11%	12.0 vs 9.5	0.78

* Source: Bevacizumab: USPI from accessdata.fda.gov, Hurwitz H, et al. The Oncologist 2009. FOLFOXIRI: Cremolini C, et al. Lancet Oncol 2015. 1. RAS mutation was evaluated retrospectively and tumor samples for RAS analysis were not available for all patients. mCRC, metastatic colorectal cancer; SoC, standard of care; ORR, objective response rate; ITT, intent-to-treat; Exp, experimental arm; Ctrl, control arm; PFS, progression free survival; WT, wild type; bev, bevacizumab; p, p-value

Trial design of CRDF-004: 1st line RAS-mutated mCRC Phase 2 trial

ENROLLMENT CRITERIA

First-line mCRC
KRAS+/NRAS+
Unresectable
No prior bev

R
ITT=110

6 RANDOMIZATION ARMS

SoC alone
1. FOLFIRI/bev
2. FOLFOX/bev

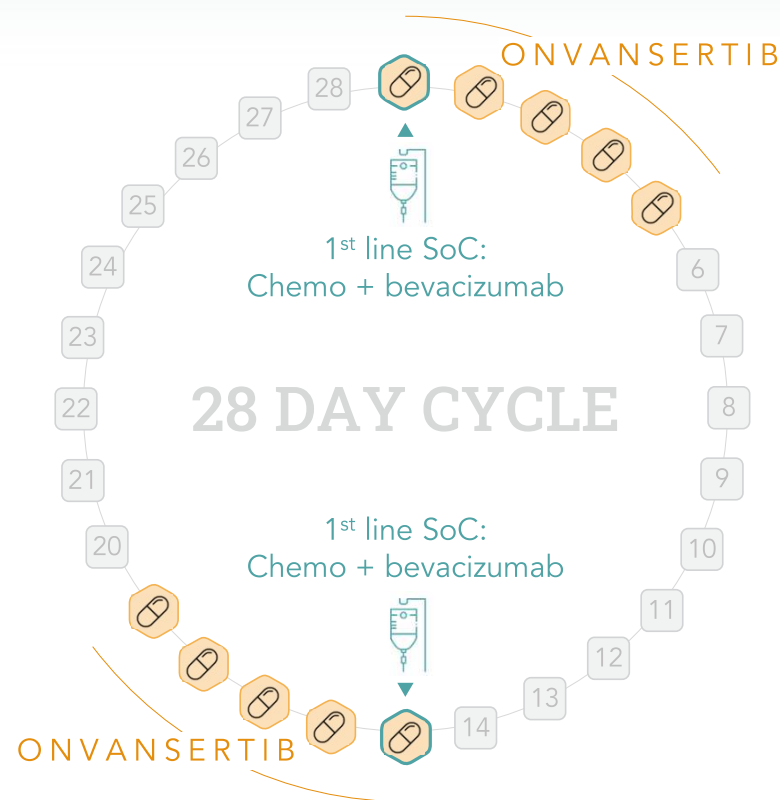
Onv 20mg +
3. FOLFIRI/bev
4. FOLFOX/bev

Onv 30mg +
5. FOLFIRI/bev
6. FOLFOX/bev

ENDPOINTS*

Primary: ORR
Secondary: DoR and PFS

* Assessed by blinded independent central review (BICR)



Patient's tumors are scanned every 8 weeks

As of July 8, 2025, a majority of CRDF-004 patients remain on treatment

Study Populations as of July 8, 2025*

Population, n	Control (SoC alone)	Onv 20mg + SoC	Onv 30mg + SoC	Total
Intent-to-treat (ITT)	37	36	37	110
Safety population (dosed)	34	34	36	104
Patients still on trial	18	19	23	60
Patients with only a 2-month scan and remain on trial	3	2	1	6
Median follow up time for all patients is ~6 months				

* CRDF-004 population data as of July 8, 2025 from an ongoing trial and unlocked database. SoC, standard of care; onv, onvansertib

Dose-dependent increase in objective response rates observed with onvansertib+SoC

Objective Response Rates per RECIST 1.1*

Intent-to-treat (ITT) (N=110)	Control (SoC alone) (n=37)	Onv 20mg + SoC (n=36)	Onv 30mg + SoC (n=37)	Onv 30mg vs. Control
Confirmed ORR ¹ n, [95% CI]	30% n=11 [16-47]	42% n=15 [26-59]	49% n=18 [32-66]	19% p=0.018 ²
Confirmed ORR at 6 months	22% n=8	33% n=12	46% n=17	

* Radiographic response determined per RECIST 1.1 by blinded independent central review as of July 8, 2025 from an ongoing trial and unlocked database. 1. Confirmed ORR includes positively confirmed CRs and PRs per RECIST 1.1. 2. To facilitate dose selection, the 2-sided p-values were computed using the exact binomial test with the response rate from the control group treated as a fixed value to establish a statistical basis to compare each of the 20mg and 30mg arms to control. SoC, standard of care; ORR, objective response rate; CI, confidence interval; p, p-value; onv, onvansertib

Dose-dependent increase in objective response rates observed with onvansertib+SoC

Objective Response Rates per RECIST 1.1*

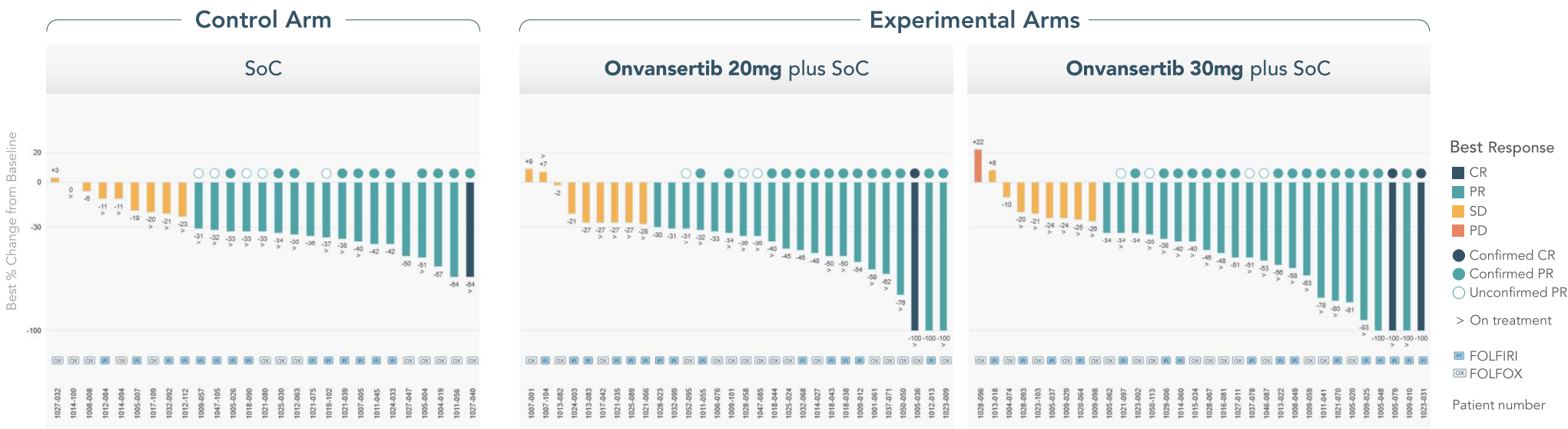
Intent-to-treat (ITT) (N=110)	Control (SoC alone) (n=37)	Onv 20mg + SoC (n=36)	Onv 30mg + SoC (n=37)	Onv 30mg vs. Control
Confirmed ORR ¹ n, [95% CI]	30% n=11 [16-47]	42% n=15 [26-59]	49% n=18 [32-66]	19% p=0.018 ²
Confirmed ORR at 6 months	22% n=8	33% n=12	46% n=17	
ORR ³ n, [95% CI]	43% n=16 [27-61]	50% n=18 [33-67]	59% n=22 [42-75]	
Best response on trial				
Complete Response (CR)	1 (3%)	1 (3%)	2 (5%)	
Partial Response (PR)	15 (41%)	17 (47%)	20 (54%)	
Unconfirmed (will not confirm) PR/CR	3 (8%)	3 (8%)	1 (3%)	
Stable Disease (SD)	9 (24%)	10 (28%)	8 (22%)	
Progressive Disease (PD)	0	0	1 (3%)	
Death	1 (3%)	0	1 (3%)	
Not evaluable	8 (22%)	5 (14%)	4 (11%)	

* Radiographic response determined per RECIST 1.1 by blinded independent central review as of July 8, 2025 from an ongoing trial and unlocked database. 1. Confirmed ORR includes positively confirmed CRs and PRs per RECIST 1.1. 2. To facilitate dose selection, the 2-sided p-values were computed using the exact binomial test with the response rate from the control group treated as a fixed value to establish a statistical basis to compare each of the 20mg and 30mg arms to control. 3. ORR includes positively confirmed CRs and PRs and unconfirmed PRs who were still on treatment and may yet be confirmed. SoC, standard of care; ORR, objective response rate; CI, confidence interval; p, p-value; onv, onvansertib

Deeper tumor regression observed with onvansertib+SoC

Best Radiographic Response BY ONVANSERTIB DOSE*

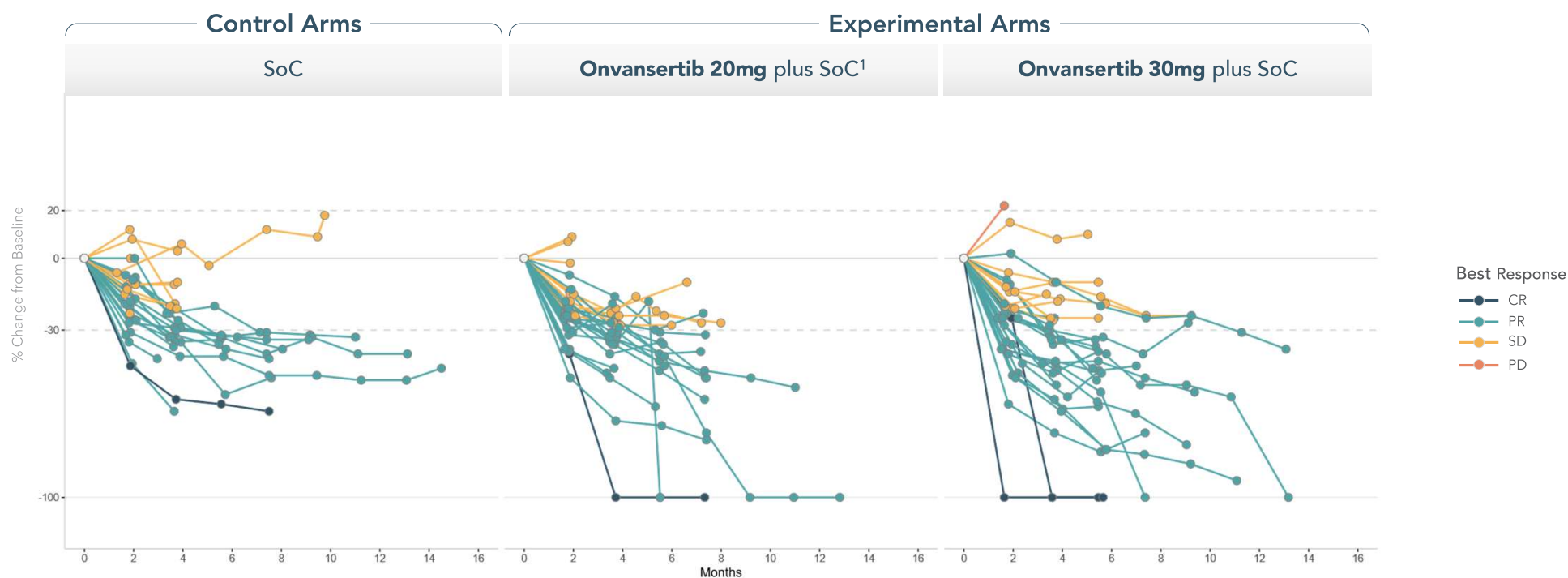
Intent-to-treat (ITT)	Control (SoC alone)	Onv 20mg + SoC	Onv 30mg + SoC
Confirmed ORR ¹	30%	42%	49%
ORR ²	43%	50%	59%



* Radiographic response determined per RECIST 1.1 by blinded independent central review as of July 8, 2025 from an ongoing trial and unlocked database for all patients with measurable disease. A PR with no circle above is an unconfirmed PR with treatment discontinued (will never confirm) and is not considered a responder for ORR calculation. Patients 1003-065 (unconfirmed PR) and 1011-106 (Non-CR/Non-PD) do not appear on the waterfall plot as they had no target lesions per BICR assessment. 1. Confirmed ORR includes positively confirmed CRs and PRs per RECIST 1.1. 2. ORR includes positively confirmed CRs and PRs and unconfirmed PRs who were still on treatment and may yet be confirmed. Patient 1027-040 achieved a CR with 67% reduction because a lymph node was selected as the target lesion. SoC, standard of care; ORR, objective response rate; onv, onvansertib; CR, complete response; PR, partial response; SD, stable disease; PD, progressive disease

Deeper tumor regression over time observed with onvansertib+SoC

Radiographic Response over Time*

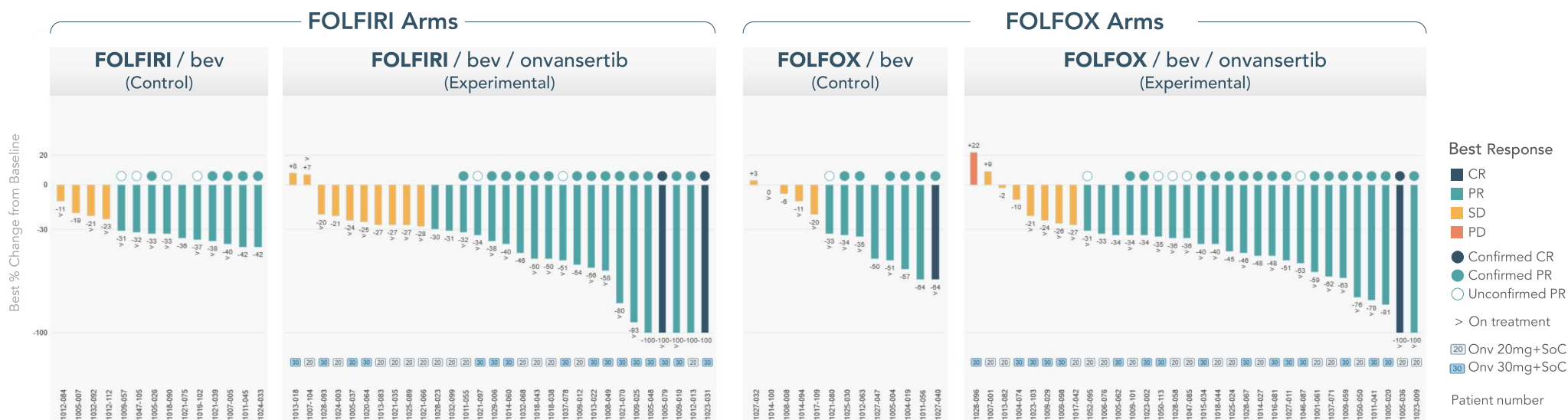


* Radiographic response determined per RECIST 1.1 by blinded independent central review as of July 8, 2025 from an ongoing trial and unlocked database for all patients with measurable disease. 1. Per protocol, patients' tumors are assessed by CT scan every 2 months, and Patient 1012-013 in the 20mg onv arm had an off-protocol MRI (different modality) of their tumors in preparation for their curative surgery (which occurred after their 6-month, -100% scan), which showed a spike (increase) in the size of the patient's tumor. SoC, standard of care; CR, complete response; PR, partial response; SD, stable disease; PD, progressive disease

Deeper tumor regression observed when adding onvansertib to either chemo backbone vs SoC alone

Best Radiographic Response BY CHEMO BACKBONE*

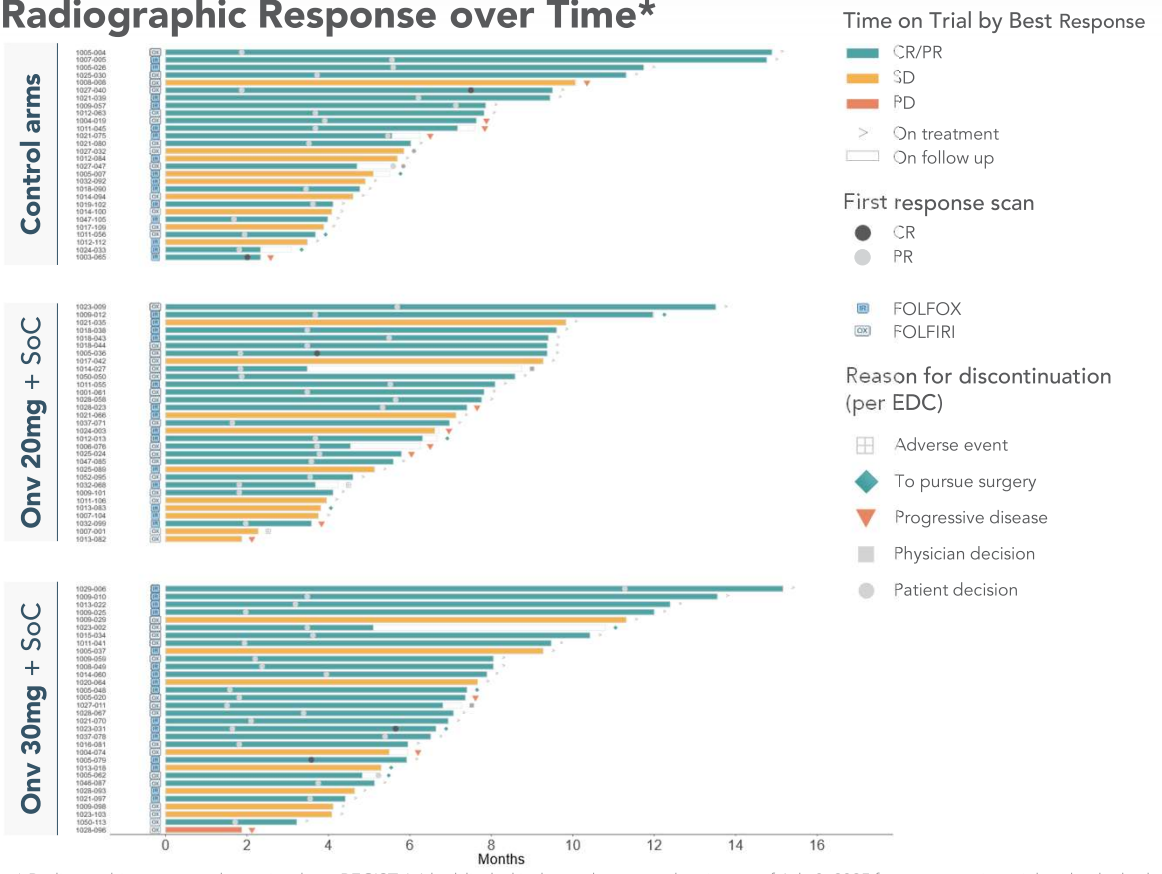
Intent-to-treat (ITT)	FOLFIRI		FOLFOX	
	Control	SoC + Onv	Control	SoC + Onv
Confirmed ORR ¹	26%	44%	33%	46%
ORR ²	47%	50%	39%	59%



* Radiographic response determined per RECIST 1.1 by blinded independent central review as of July 8, 2025 from an ongoing trial and unlocked database for all patients with measurable disease. A PR with no circle above is an unconfirmed PR with treatment discontinued (will never confirm) and is not considered a responder for ORR calculation. Patients 1003-065 (unconfirmed PR) and 1011-106 (Non-CR/Non-PD) do not appear on the waterfall plot as they had no target lesions. 1. Confirmed ORR includes positively confirmed CRs and PRs per RECIST 1.1. 2. ORR includes positively confirmed CRs and PRs and unconfirmed PRs who were still on treatment and may yet be confirmed. SoC, standard of care; ORR, objective response rate; onv, onvansertib; CR, complete response; PR, partial response; SD, stable disease; PD, progressive disease

Higher number of 30mg onvansertib patients remain on trial vs. control

Radiographic Response over Time*



Safety Population (Dosed)	Control (SoC alone)	Onv 20mg + SoC	Onv 30mg + SoC
Patients on treatment	18 (53%)	19 (56%)	23 (64%)
Patients discontinued treatment:	16 (47%)	15 (44%)	13 (36%)
To pursue surgery	3	3	5
Progressive disease	5	6	3
Adverse events/toxicity ¹	1	3	2
Median follow up time for all patients is ~6 months			

* Radiographic response determined per RECIST 1.1 by blinded independent central review as of July 8, 2025 from an ongoing trial and unlocked database for all patients with at least one post-baseline scan. 1. One control, one 20mg and two 30mg patients discontinued due to adverse events / toxicity prior to their first post-baseline scan and are not included in the swimmer plot. SoC, standard of care; CR, complete response; PR, partial response; SD, stable disease; PD, progressive disease; onv, onvansertib; EDC, electronic data capture system

Several patients in onvansertib arms achieved deep responses, CR, and surgery referrals*

47-year-old female

Metastatic disease on enrollment.
Right sided colon cancer.

Target lesions in peritoneum (SLD 27mm) with non-target lesions throughout peritoneum.

Achieved CR and went to curative surgery after 6 cycles of treatment.

30mg onv + FOLFIRI/bev

69-year-old male

Adjuvant FOLFOX for stage 3 colon cancer 1 year prior to study.
Right sided colon cancer.

Target lesions paracolic gutter and peritoneum (SLD 39 mm) with non-target lesions peritoneal nodules throughout abdomen.

Achieved CR of target lesions and confirmed 100% PR. Continues on treatment.

20mg onv + FOLFOX/bev

49-year-old male

Neoadjuvant CAPOX for stage 3 colon cancer 1 year prior to study.
Bilateral disease (right and left) colon cancer.

Target lesions in lung and seminal vesicles (SLD 50 mm) with non-target lesions in retroperitoneum and liver.

Achieved CR after 4 cycles of treatment. Continues on treatment.

20mg onv + FOLFOX/bev

62-year-old male

Metastatic disease. Right sided colon cancer.

Target lesions in liver (SLD 32mm), non-target lesions in liver and adrenal gland.

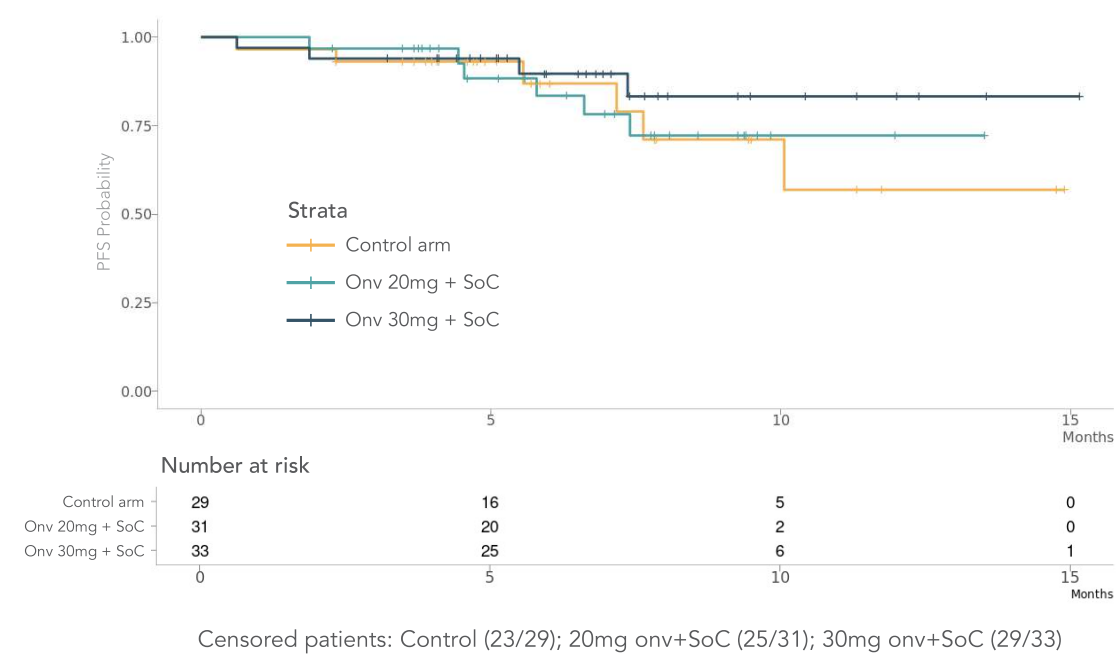
Achieved CR after 6 cycles. Referred for curative surgery.

30mg onv + FOLFIRI/bev

* Radiographic response determined per RECIST 1.1 by blinded independent central review as of July 8, 2025 from an ongoing trial and unlocked database. SLD, sum of the longest diameters; onv, onvansertib; bev, bevacizumab; CR, complete response; PR, partial response

PFS as of July 8, 2025 data cutoff shows initial separation between 30mg onv and control arms

Progression Free Survival – Median PFS Not Reached*



Hazard Ratio (HR)	HR	95% CI
Control vs. all onv arms	0.69	0.25, 1.90
Control vs. onv 20mg + SoC	0.89	0.28, 2.77
Control vs. onv 30mg + SoC	0.52	0.15,1.83

Median follow up is ~6 months

* Progression determined per electronic data capture system as of July 8, 2025 from an ongoing trial and unlocked database. SoC, standard of care; PFS, progression free survival; HR, hazard ratio; CI, confidence interval; onv, onvansertib

In 1st line mCRC, two response metrics predict PFS and OS

Early
Tumor Shrinkage (ETS)
≥20% reduction in tumor size at 2-month scan

Depth
of Response (DpR)
Deepest reduction in tumor size while on therapy on trial

Proof-of-Principle

ANNALS OF ONCOLOGY
Cremolini, et. al.
Feb, 2015

Early Tumor Shrinkage and Depth of Response Predict Long-term Outcome in mCRC Patients Treated with 1st-line Chemo+bev

Journal of Clinical Oncology®
Piessevaux, et. al.
Oct, 2013

Use of Early Tumor Shrinkage to Predict Long-Term Outcome in mCRC Treated With Cetuximab

Meta Analysis Validation



Bando, et. al.
Apr, 2025

Associations Between Early Tumor Shrinkage/Depth of Response and Survival from the ARCAD Database

Ph3 TRIAL DATA*

TRIBE
FOLFOXIRI+bev
vs. FOLFIRI+bev

CRYSTAL
FOLFIRI+cetux.
vs FOLFIRI

OPUS
FOLFOX-4+cetux.
vs. FOLFOX-4

8 randomized trials

* First-line mCRC trials in which ETS and/or DpR were evaluated as predictors of PFS and OS comparing a control arm of chemo alone vs. an experimental arm of chemo + an active agent including bevacizumab (TRIBE) and cetuximab (CRYSTAL and OPUS). mCRC, metastatic colorectal cancer; PFS, progression free survival; OS, overall survival; bev, bevacizumab; cetux, cetuximab.

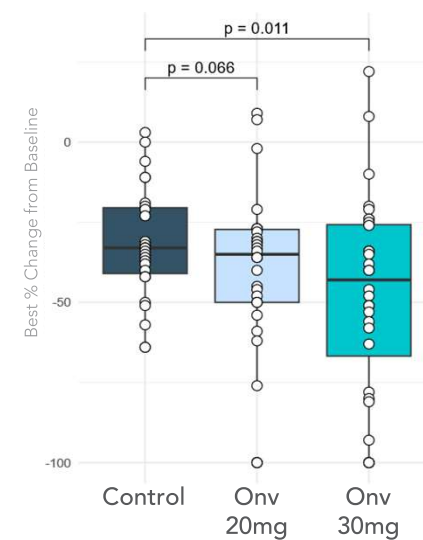
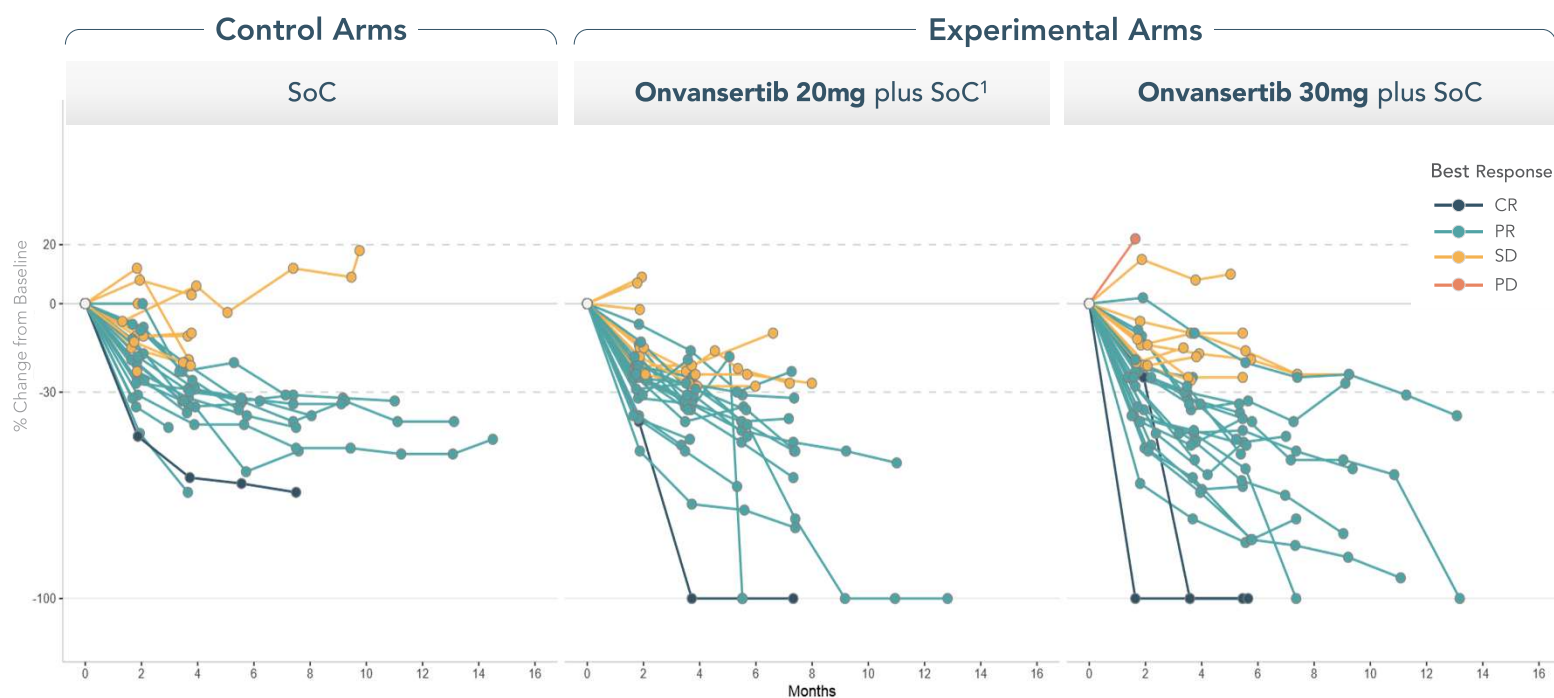
Greater number of onvansertib 30mg dose patients achieved Early Tumor Shrinkage

	% of patients with ETS	Previous Ph3 1 st Line mCRC Trials ¹			CRDF-004 RAS mut.	
		TRIBE RAS WT/mut.	CRYSTAL RAS WT	OPUS RAS WT		
Early Tumor Shrinkage (ETS) ≥20% reduction in tumor size at 2-month scan.	Control Arm	52%	49%	46%	41% (11/27)	
	Experimental Arm	63%	62%	69%	Onv 20mg 63% (19/30)	Onv 30mg 69% (22/32)
Final data: All patients on trial have had a 2-month scan.	ETS Delta <i>p-value</i>	11% 0.025	13% 0.02	23% 0.006	22% 0.114	28% 0.038
	Hazard Ratio	0.79	0.68	0.57		
Improvement in PFS		2.0 mo	4.4 mo	3.7 mo		

1. First-line mCRC trials in which ETS and/or DpR were evaluated as predictors of PFS and OS comparing a control arm of chemo alone vs. an experimental arm of chemo + an active agent including bevacizumab (TRIBE) and cetuximab (CRYSTAL and OPUS). Piessevaux, et al, J Clin Oncol 2013; Cremolini, et al, Ann Oncol 2015; Van Cutsem, et. al, N Engl J Med 2009 (HR for CRYSTAL); Bokemeyer et al, Ann Oncol 2011 (HR for OPUS). ETS, early tumor shrinkage; mCRC, metastatic colorectal cancer; WT, wild type; mut., mutated; PFS, progression free survival; bev, bevacizumab; onv, onvansertib.

Tumor regression vs. baseline is deeper over time with onv 30mg dose

Radiographic Response over Time*



* Radiographic response determined per RECIST 1.1 by blinded independent central review as of July 8, 2025 from an ongoing trial and unlocked database. 1. Per protocol, patients' tumors are assessed by CT scan every 2 months, and Patient 1012-013 in the 20mg onv arm had an off-protocol MRI (different modality) of their tumors in preparation for their curative surgery (which occurred after their 6-month, -100% scan), which showed a spike (increase) in the size of the patient's tumor. SoC, standard of care; CR, complete response; PR, partial response; SD, stable disease; PD, progressive disease; onv, onvansertib; p, p-value

Depth of Response is deeper for the onv 30mg dose arm

	% Tumor Shrinkage	Previous Ph3 1 st Line mCRC Trials ¹			CRDF-004 RAS mut.	
		TRIBE RAS WT/mut.	CRYSTAL RAS WT	OPUS RAS WT		
Depth of Response (DpR)	Control Arm	38%	33%	31%	32%	
Maximum tumor shrinkage at nadir on trial	Experimental Arm	43%	51%	58%	Onv 20mg 41%	Onv 30mg 48%
Interim data: Patients on trial may achieve deeper tumor regression	DpR Delta	5%	18%	27%	9% <i>p-value 0.066</i>	16% <i>0.011</i>
	Hazard Ratio	0.79	0.68	0.57		
	Improvement in PFS	2.0 mo	4.4 mo	3.7 mo		

1. First-line mCRC trials in which ETS and/or DpR were evaluated as predictors of PFS and OS comparing a control arm of chemo alone vs. an experimental arm of chemo + an active agent including bevacizumab (TRIBE) and cetuximab (CRYSTAL and OPUS). 1. Cremolini, et al, Ann Oncol 2015; Piessevaux, et al, J Clin Oncol 2013; Mansmann, et al, Ann Oncol 2013; Van Cutsem, et. al, N Engl J Med 2009 (HR for CRYSTAL); Bokemeyer et al, Ann Oncol 2011 (HR for OPUS). DpR, depth of response; mCRC, metastatic colorectal cancer; WT, wild type; mut., mutated; PFS, progression free survival; onv, onvansertib.

CRDF-004 demographics and baseline characteristics*

Safety Population (Dosed)	FOLFIRI/bev (n=17)	FOLFIRI/bev/onv 20 (n=17)	FOLFIRI/bev/onv 30 (n=18)	FOLFOX/bev (n=17)	FOLFOX/bev/onv 20 (n=17)	FOLFOX/bev/onv 30 (n=18)	Total (n=104)
Age (years)							
Median	53 (32, 81)	52 (30, 78)	60 (34, 81)	57 (34, 82)	66 (34, 79)	59.5 (39, 86)	57 (30, 86)
Gender, n (%)							
Male	10 (58.8)	10 (58.8)	10 (55.6)	11 (64.7)	7 (41.2)	11 (61.1)	59 (56.7)
Female	7 (41.2)	7 (41.2)	8 (44.4)	6 (35.3)	10 (58.8)	7 (38.9)	45 (43.3)
Race, n (%)							
White	13 (76.5)	15 (88.2)	15 (83.3)	12 (70.6)	13 (76.5)	13 (72.2)	81 (77.9)
Black or African American	2 (11.8)	0	1 (5.6)	1 (5.9)	0	2 (11.1)	6 (5.8)
Asian	1 (5.9)	0	1 (5.6)	1 (5.9)	2 (11.8)	1 (5.6)	6 (5.8)
Native Hawaiian or Other Pacific Islander	0	1 (5.9)	0	1 (5.9)	0	0	2 (1.9)
Not reported	0	1 (5.9)	0	2 (11.8)	1 (5.9)	1 (5.6)	5 (4.8)
Unknown	1 (5.9)	0	1 (5.6)	0	1 (5.9)	1 (5.6)	4 (3.8)
ECOG, n (%)							
0	6 (35.3)	14 (82.4)	11 (61.1)	7 (41.2)	10 (58.8)	11 (61.1)	59 (56.7)
1	11 (64.7)	3 (17.6)	7 (38.9)	10 (58.8)	7 (41.2)	7 (38.9)	45 (43.3)
Stage at Initial Diagnosis, n (%)							
STAGE I	0	1 (5.9)	0	0	1 (5.9)	1 (5.6)	3 (2.9)
STAGE II	3 (17.6)	2 (11.8)	2 (11.1)	2 (11.8)	3 (17.6)	1 (5.6)	13 (12.5)
STAGE III	4 (23.5)	4 (23.5)	2 (11.1)	6 (35.3)	2 (11.8)	3 (16.7)	21 (20.2)
STAGE IV	9 (52.9)	10 (58.8)	14 (77.8)	9 (52.9)	11 (64.7)	13 (72.2)	66 (63.5)
Missing	1 (5.9)	0	0	0	0	0	1 (1.0)
Side of Tumor, n (%)							
Bilateral	6 (35.3)	2 (11.8)	6 (33.3)	4 (23.5)	2 (11.8)	7 (38.9)	27 (26.0)
Left	6 (35.3)	7 (41.2)	6 (33.3)	5 (29.4)	8 (47.1)	4 (22.2)	36 (34.6)
Right	5 (29.4)	8 (47.1)	6 (33.3)	8 (47.1)	7 (41.2)	7 (38.9)	41 (39.4)
Liver metastasis at study entry, n (%)							
No	7 (41.2)	8 (47.1)	5 (27.8)	9 (52.9)	5 (29.4)	4 (22.2)	38 (36.5)
Yes	10 (58.8)	9 (52.9)	13 (72.2)	8 (47.1)	12 (70.6)	14 (77.8)	66 (63.5)
Liver only disease, n (%)							
No	15 (88.2)	15 (88.2)	11 (61.1)	14 (82.4)	16 (94.1)	15 (83.3)	86 (82.7)
Yes	2 (11.8)	2 (11.8)	7 (38.9)	3 (17.6)	1 (5.9)	3 (16.7)	18 (17.3)
Number of organs involved at baseline, n (%)							
<3 organs	13 (76.5)	9 (52.9)	10 (55.6)	12 (70.6)	11 (64.7)	8 (44.4)	63 (60.6)
≥3 organs	4 (23.5)	7 (41.2)	8 (44.4)	5 (29.4)	6 (35.3)	10 (55.6)	40 (38.5)
Missing	0	1 (5.9)	0	0	0	0	1 (1.0)
Prior adjuvant or neo-adjuvant chemotherapy, n (%)							
No	13 (76.5)	12 (70.6)	14 (77.8)	12 (70.6)	12 (70.6)	16 (88.9)	79 (76.0)
Yes	4 (23.5)	5 (29.4)	4 (22.2)	5 (29.4)	5 (29.4)	2 (11.1)	25 (24.0)

* Demographics and baseline characteristics are as of July 8, 2025 from an ongoing trial and unlocked database. Bev, bevacizumab; onv, onvansertib

CRDF-004 treatment emergent adverse events (TEAE) data*

Safety Population (Dosed) N (% of total)	All Control Arms (N=34)		Onv 20mg + SoC (N=34)		Onv 30mg + SoC (N=36)	
	All Grades	Gr ≥3	All Grades	Gr ≥3	All Grades	Gr ≥3
Any Adverse Events	33 (97.1)	21 (61.8)	34 (100.0)	24 (70.6)	36 (100.0)	28 (77.8)
Fatigue	16 (47.1)	2 (5.9)	24 (70.6)	1 (2.9)	21 (58.3)	0
Nausea	17 (50.0)	1 (2.9)	25 (73.5)	0	17 (47.2)	0
Diarrhoea	17 (50.0)	1 (2.9)	19 (55.9)	2 (5.9)	16 (44.4)	0
Neutrophil count decreased	18 (52.9)	11 (32.4)	13 (38.2)	6 (17.6)	17 (47.2)	11 (30.6)
Hypertension	7 (20.6)	1 (2.9)	12 (35.3)	4 (11.8)	12 (33.3)	3 (8.3)
Vomiting	8 (23.5)	1 (2.9)	13 (38.2)	0	8 (22.2)	0
Constipation	5 (14.7)	1 (2.9)	13 (38.2)	0	10 (27.8)	0
Epistaxis	7 (20.6)	0	11 (32.4)	0	9 (25.0)	0
Peripheral sensory neuropathy	8 (23.5)	0	10 (29.4)	2 (5.9)	9 (25.0)	1 (2.8)
Abdominal pain	5 (14.7)	2 (5.9)	10 (29.4)	1 (2.9)	11 (30.6)	1 (2.8)
Anaemia	7 (20.6)	1 (2.9)	8 (23.5)	0	11 (30.6)	4 (11.1)
Decreased appetite	9 (26.5)	0	11 (32.4)	0	6 (16.7)	0
Platelet count decreased	9 (26.5)	2 (5.9)	8 (23.5)	0	9 (25.0)	1 (2.8)
Alopecia	7 (20.6)	0	8 (23.5)	0	8 (22.2)	0
Headache	8 (23.5)	0	10 (29.4)	0	3 (8.3)	0
White blood cell count decreased	10 (29.4)	0	4 (11.8)	0	7 (19.4)	1 (2.8)
Dizziness	6 (17.6)	0	7 (20.6)	0	7 (19.4)	0
Dysgeusia	6 (17.6)	0	6 (17.6)	0	8 (22.2)	0
Weight decreased	8 (23.5)	1 (2.9)	4 (11.8)	0	8 (22.2)	0
Hypokalaemia	5 (14.7)	1 (2.9)	6 (17.6)	2 (5.9)	8 (22.2)	3 (8.3)
Stomatitis	8 (23.5)	0	8 (23.5)	0	2 (5.6)	0
Insomnia	1 (2.9)	0	9 (26.5)	0	7 (19.4)	0
Paraesthesia	3 (8.8)	0	7 (20.6)	0	6 (16.7)	0
Lymphocyte count decreased	5 (14.7)	0	3 (8.8)	0	7 (19.4)	2 (5.6)
Cough	5 (14.7)	0	4 (11.8)	0	5 (13.9)	0
Pyrexia	4 (11.8)	0	6 (17.6)	1 (2.9)	4 (11.1)	1 (2.8)
Blood alkaline phosphatase increased	7 (20.6)	0	1 (2.9)	0	4 (11.1)	0
Dyspepsia	2 (5.9)	0	5 (14.7)	0	5 (13.9)	0
Proteinuria	2 (5.9)	0	6 (17.6)	0	4 (11.1)	0

* Data consists of all adverse events entered into the electronic data capture (EDC) system as of July 8, 2025, from an ongoing trial and unlocked EDC database. N: number of patients; events shown occurred in ≥10% of total patients; numbers indicate number of patients experiencing the event, (regardless of causality); each patient is only counted once and only for the highest grade of a given event. Columns show the absolute # of patients and (%) of the population. Onv, onvansertib; SoC, standard of care

We believe CRDF-004 data positions onvansertib for registrational trial

1st line RAS-mutated mCRC clinical development program

Agreed with FDA June 2023 Type C meeting

CRDF-004

PHASE 2 DOSE-CONFIRMATION TRIAL

CRDF-005

PHASE 3 REGISTRATIONAL TRIAL

Designed for accelerated and full-approval

Endpoint for accelerated approval:

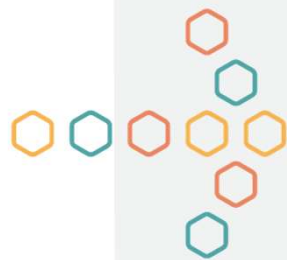
- ORR with DoR

Endpoint for full approval:

- PFS / lack of detriment on OS

OUR SHIFT

TO FIRST-LINE RAS-MUTATED mCRC



The strength of our 1st-line program

The rationale for our shift from 2nd-line

The coming catalysts

Our second-line phase 1b/2 trial generated a novel finding

1

Ph 1b/2 trial
KRAS-mut. 2nd line mCRC

*Unexpected
clinical finding*

Sep 12, 2022

SECOND-LINE

2022

2023

2024

2025

Our Ph1b/2 trial combined onvansertib with the current SoC in 2nd line

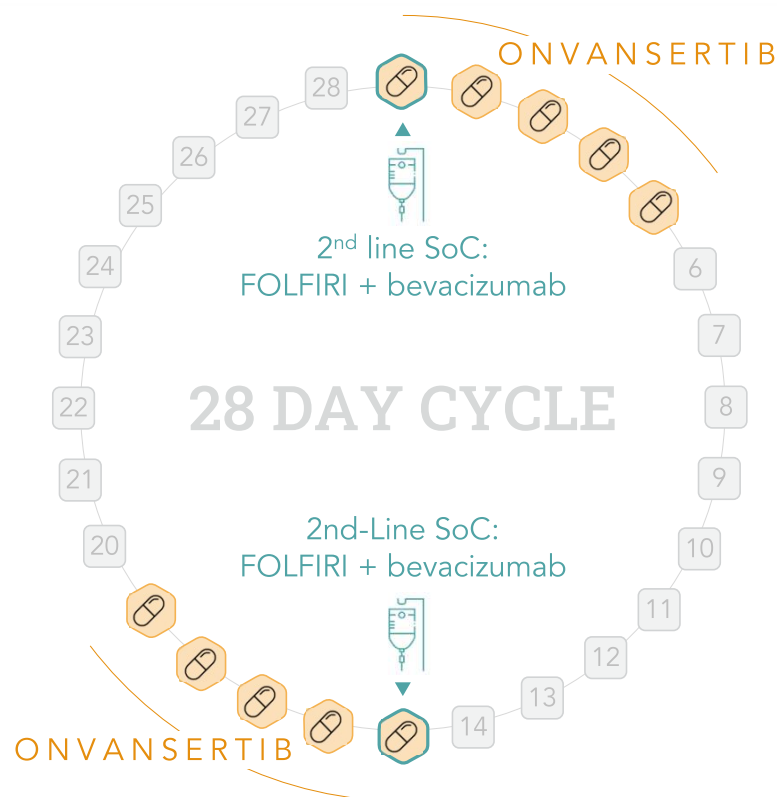
ENROLLMENT CRITERIA

2nd line mCRC

KRAS-mut

Unresectable

N=68 (66 evaluable)



EFFICACY ENDPOINTS

- 1** Primary:
Objective Response Rate (ORR)
per RECIST v1.1 in patients who
receive ≥ 1 cycle of treatment
- 2** Secondary:
Progression-Free Survival (PFS)
and Duration of Response (DoR)
- 3** Exploratory:
decrease in KRAS-mutational
burden and response to
treatment

Our Ph1b/2 trial added onvansertib to SoC in the 2nd line setting

Patients who came to our second-line trial not having received bev in first-line are called, "bev naïve"

1st LINE

Standard of Care

FOLFOX	<i>chemotherapy</i>
--------	---------------------

Bev (optional)	Yes	No
----------------	-----	----

"bev naïve"

2nd LINE

Cardiff Oncology Phase 1b/2 trial

FOLFIRI	<i>chemotherapy</i>
---------	---------------------

Bev	<i>antiangiogenic</i>
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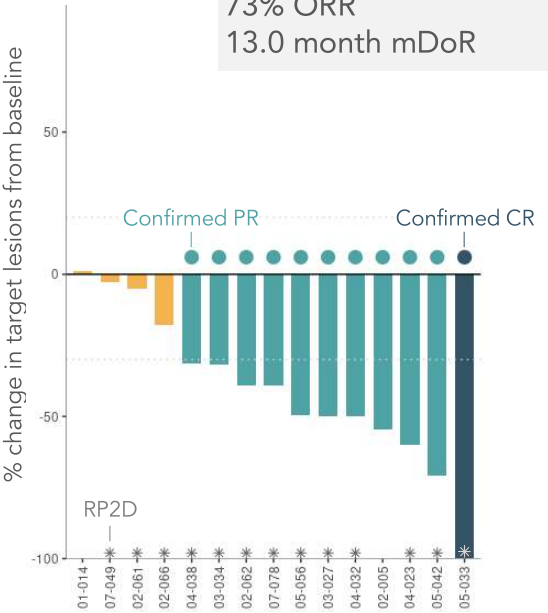
Onvansertib	<i>PLK1 inhibitor</i>
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Ph 1b/2 trial bev naïve patients achieved higher response rates

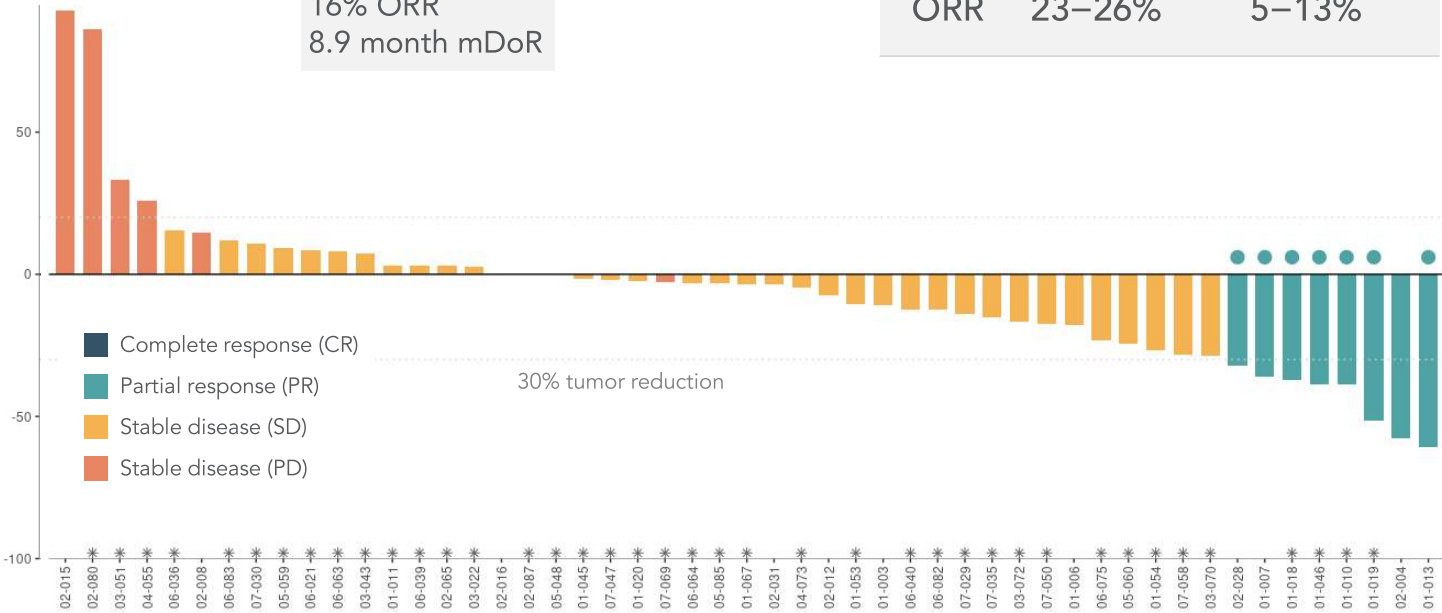
Best Radiographic Response and Duration of Response*

66 evaluable patients (as of June 16, 2023)

Bev naïve: 15 of 66 patients (23%)
73% ORR
13.0 month mDoR



Bev exposed: 51 of 66 (77%)
16% ORR
8.9 month mDoR



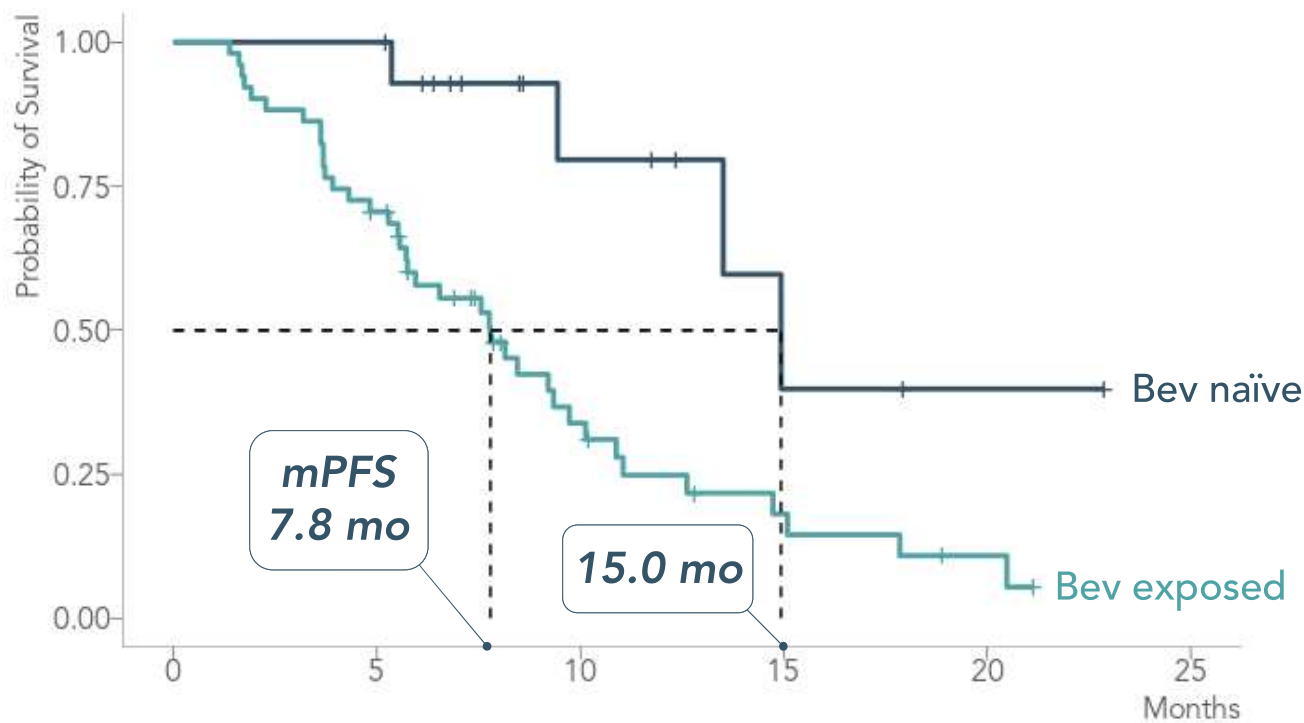
	Historical controls**	
	Bev naïve	Bev exposed
ORR	23–26%	5–13%

* Radiographic response determined per RECIST 1.1. Waterfall plot and table reflect interim data as of June 16, 2023 from an ongoing trial and unlocked EDC database.

** Bennouna et al., Lancet Oncol 2013; 14: 29–37; Giessen et al., Acta Oncologica, 2015, 54: 187–193; Cremolini et al., Lancet Oncol 2020, 21: 497–507; Antoniotti et al., Correspondence Lancet Oncol June 2020. Giantonio et al., 2007, J Clin Oncol 25:1539–1544; Moriwaki et al., Med Oncol, 2012, 29:2842–2848; Beretta et al., Med Oncol 2013, 30:486.

Ph 1b/2 trial mPFS exceeds historical controls for SoC

Progression-free survival*
66 evaluable patients (as of June 16, 2023)



	Historical controls**	
	Bev naïve	Bev exposed
mPFS (mo)	6.9–8.5	4.5–6.7

* Onvansertib mPFS are interim data as of June 16, 2023 from an ongoing trial and unlocked EDC database.

** Bennouna et al., Lancet Oncol 2013; 14: 29–37; Giessen et al., Acta Oncologica, 2015, 54: 187-193; Cremolini et al., Lancet Oncol 2020, 21: 497–507; Antoniotti et al., Correspondence Lancet Oncol June 2020. Giontonio et al., 2007, J Clin Oncol 25:1539-1544; Moriwaki et al., Med Oncol, 2012, 29:2842–2848; Beretta et al, Med Oncol 2013, 30:486.

32

Phase 1b/2 multivariable analysis shows prior exposure to bev is the only patient characteristic associated with greater ORR and PFS

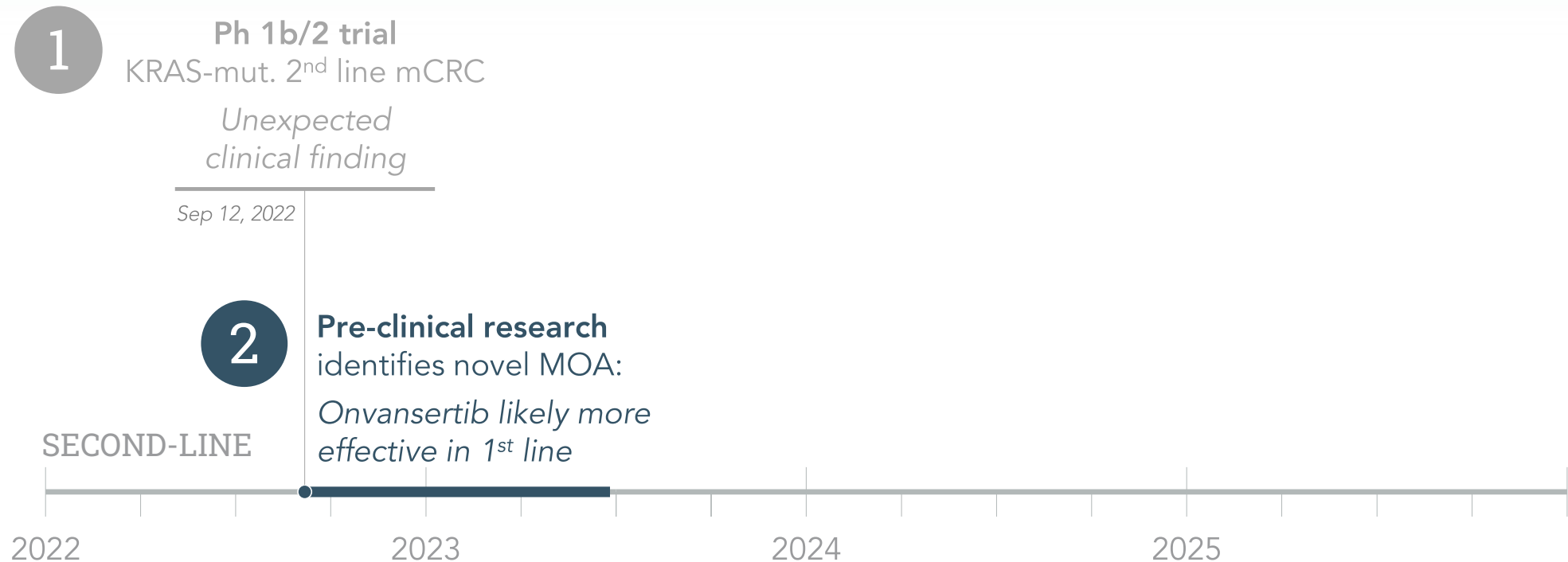
Univariable analysis of baseline characteristics for ORR and PFS indicate superior clinical benefit for bev naïve patients and for patients without metastatic disease at time of diagnosis

Multivariable Analysis was performed with these two characteristics, resulting in only prior bev exposure remaining independently associated with clinical benefit

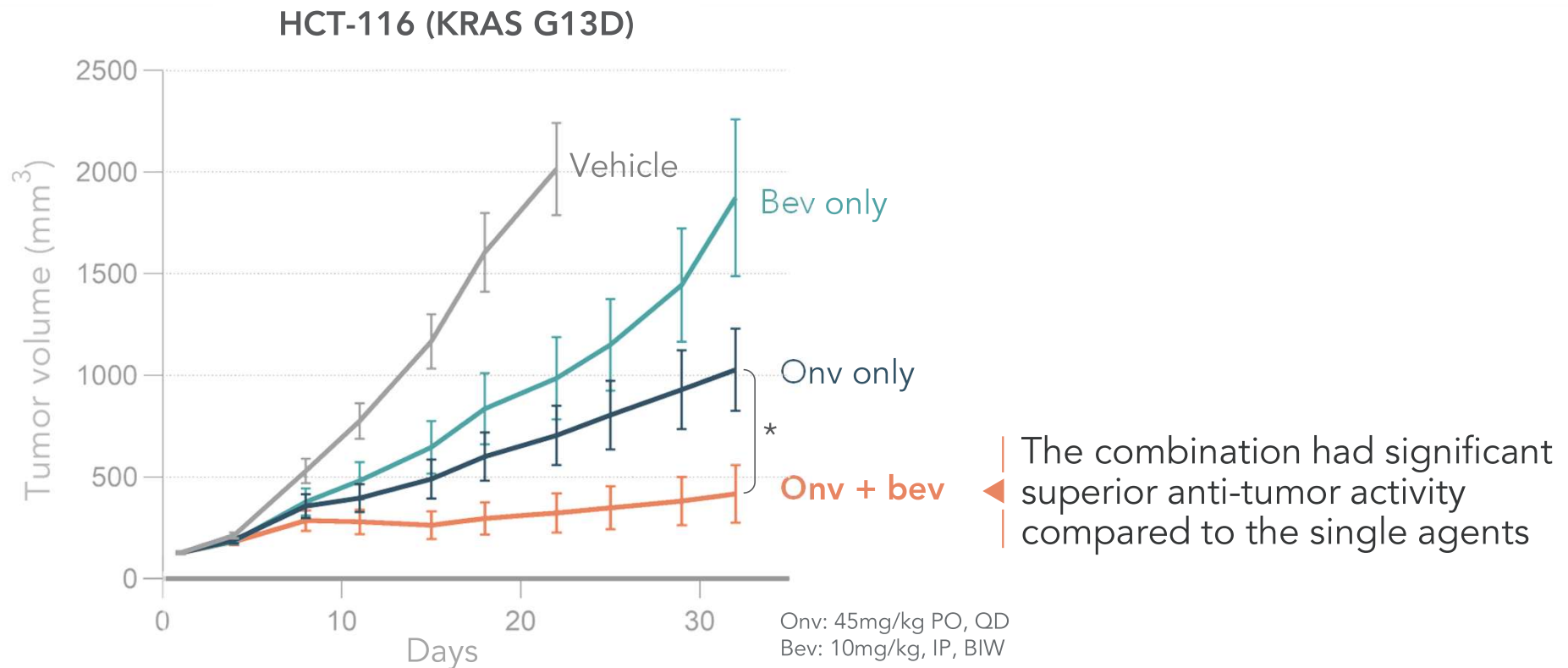
		n	ORR (Odds Ratio)	p-value	PFS (Hazard Ratio)	p-value
Bev Exposure	Bev Naive	15		<0.001		<0.001
	Prior Bev	51				
Age	>=70	9		0.281		0.459
	<70	57				
Sex	F	30		0.457		0.659
	M	36				
Race	Other	14		0.202		0.854
	White	52				
ECOG	0	36		0.369		0.741
	1	30				
Primary Tumor	Right Colon/Other	24		0.54		0.181
	Left Colon/Rectum	42				
Metastatic at Diagnosis*	No	10		0.00298		0.066
	Yes	56				
Liver Mets	Liver mets	48		0.911		0.156
	No liver mets	18				
# of Metastases	Multiple	62		0.861		0.659
	Single	4				
			0.01 1 5 15 30 60 90		0.01 1 2.5 5 15	
Bev Exposure	Bev Naive	15		0.00128		0.00131
	Prior Bev	51				
Metastatic at Diagnosis*	No	10		0.196		0.741
	Yes	56				
			0.01 1 5 15 30 60 90		0.01 1 10 20 30	

* Metastatic at Diagnosis: "Yes" means the patient's cancer had already metastasized when first diagnosed. "No" means the patient's initial diagnosis was non-metastatic CRC, but developed metastatic disease prior to enrolling in our Ph 1b/2 trial.

Unexpected clinical findings prompted new pre-clinical research



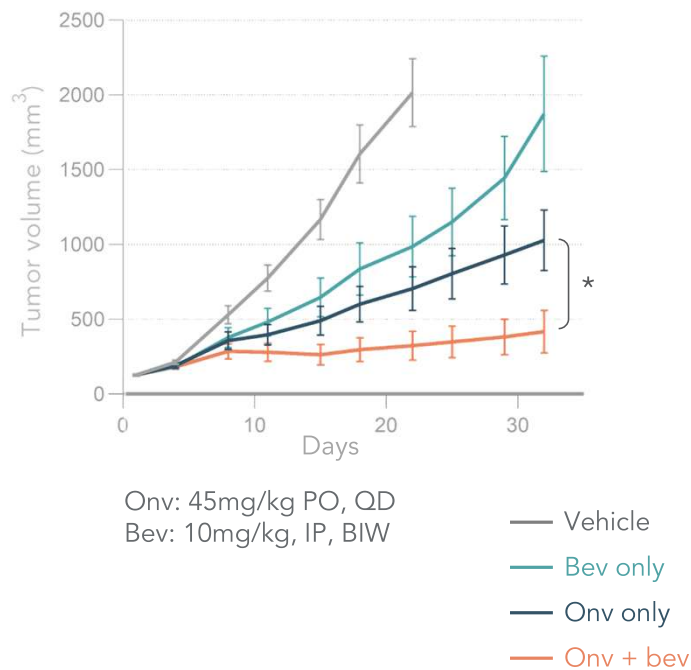
Onvansertib + bev inhibits tumor growth greater than either agent alone



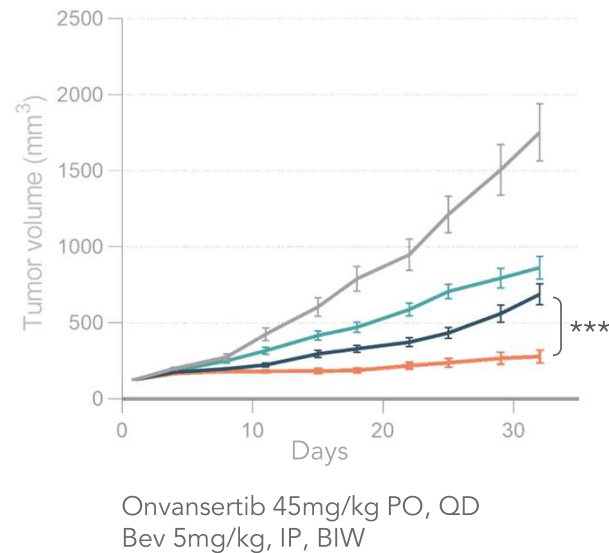
Three KRAS-mutant mCRC xenograft models were treated with vehicle (control), onvansertib, bevacizumab or the combination of onvansertib and bev. 8-9mice/ group. Mean $\pm$ SEM are represented on graphs. An unpaired t-test was used to test the difference in tumor volume change on the last day of treatment between the combination treatment and the most effective control arm. * $p < 0.05$, *** $p < 0.001$, **** $p < 0.0001$.

Onvansertib + bev inhibits tumor growth greater than either agent alone

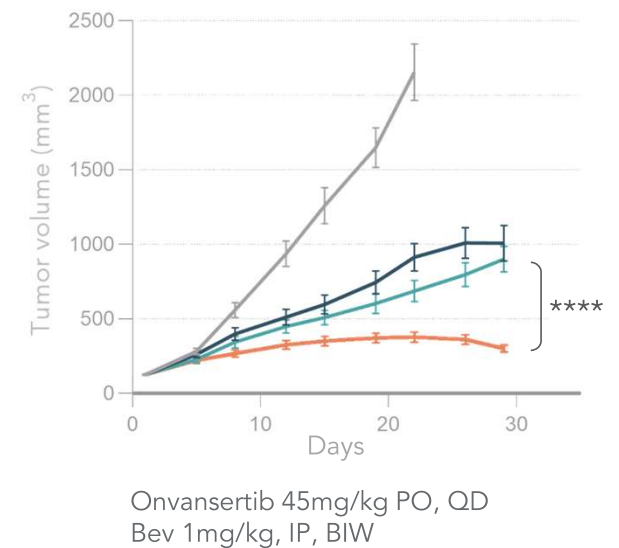
HCT-116 (KRAS G13D)



LoVo (KRAS G13D)

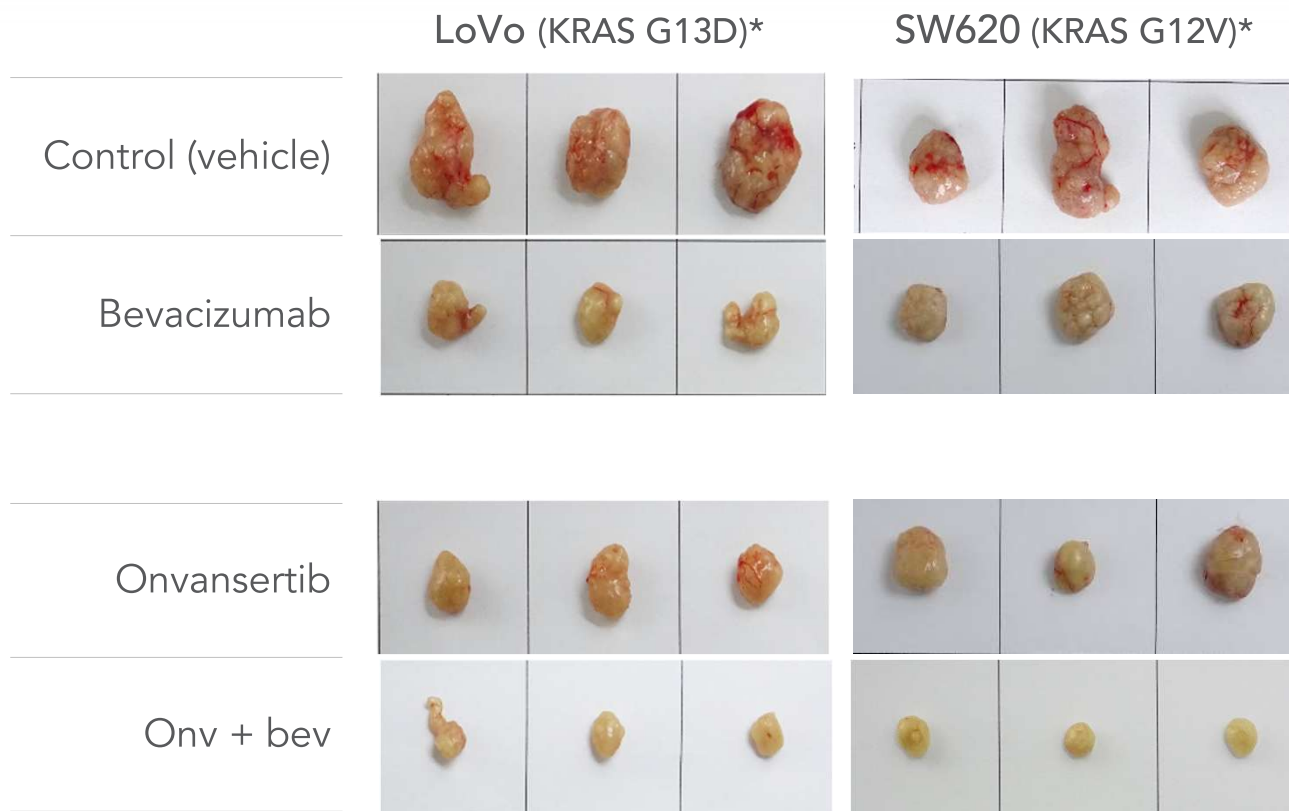


SW620 (KRAS G12V)



Three KRAS-mutant mCRC xenograft models were treated with vehicle (control), onvansertib, bevacizumab or the combination of onvansertib and bev. 8-9 mice/group. Mean $\pm$ SEM are represented on graphs. An unpaired t-test was used to test the difference in tumor volume change on the last day of treatment between the combination treatment and the most effective control arm. * $p < 0.05$, *** $p < 0.001$, **** $p < 0.0001$.

Onvansertib's independent role in antiangiogenesis complements bev



◀ Roche drug Avastin[®]
8th largest global drug in 2019
(\$7.1B sales)

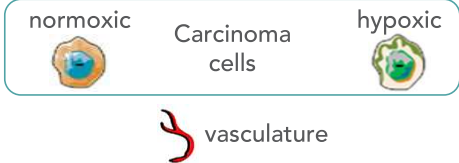
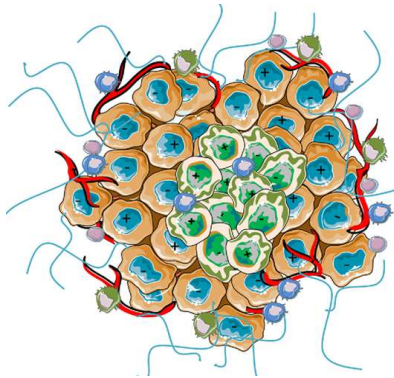
◀ KRAS-mut mCRC tumors from mice
treated with onv + bev appear
smaller and pale (less vascularized)

* Two KRAS-mutant mCRC xenograft models were treated with control (vehicle), onvansertib, bevacizumab or the combination of onvansertib and bev 8-9mice / group. Tumors were removed and photographed at the end of the study. Representative photographs from three mice from each group are shown.

HIF1 α plays a critical role in a tumor's response to hypoxia

Tumor growth

The tumor cells outgrow the blood supply and become starved of oxygen and nutrients...



Hypoxia

... low oxygen levels lead to elevated HIF1 α protein expression

HIF1 α

... turns on VEGF-A expression and secretion to recruit new vasculature as well as turning on a multitude of downstream survival genes

VEGF-A

Angiogenesis:
Vascularization
of the tumor

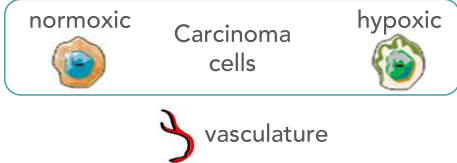
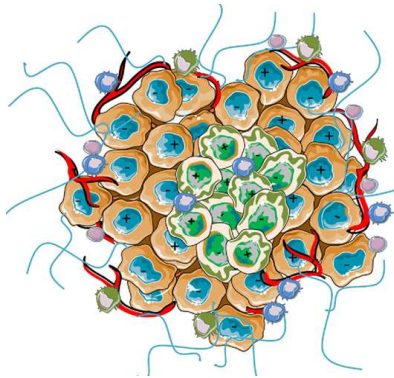
Tumor cell
survival

Proliferation

Bev inhibits tumor angiogenesis by neutralizing VEGF-A

Tumor growth

The tumor cells outgrow the blood supply and become starved of oxygen and nutrients...



Hypoxia

... low oxygen levels lead to elevated HIF1 α protein expression

HIF1 α

... turns on VEGF-A expression and secretion to recruit new vasculature as well as turning on a multitude of downstream survival genes

bevacizumab —| VEGF-A
neutralizes VEGF-A

Angiogenesis:
Vascularization
of the tumor

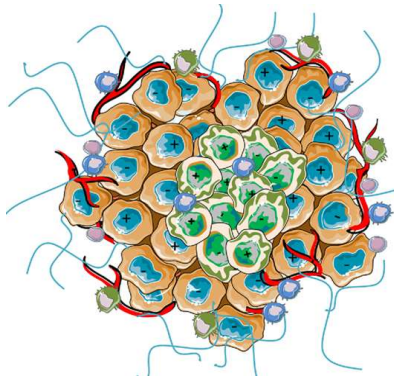
Tumor cell
survival

Proliferation

Onvansertib restricts tumor's broader ability to adapt to hypoxia

Tumor growth

The tumor cells outgrow the blood supply and become starved of oxygen and nutrients...



Hypoxia

... low oxygen levels lead to elevated HIF1 α protein expression

HIF1 α

... turns on VEGF-A expression and secretion to recruit new vasculature as well as turning on a multitude of downstream survival genes

onvansertib

inhibits HIF1 α expression

bevacizumab

neutralizes VEGF-A

VEGF-A

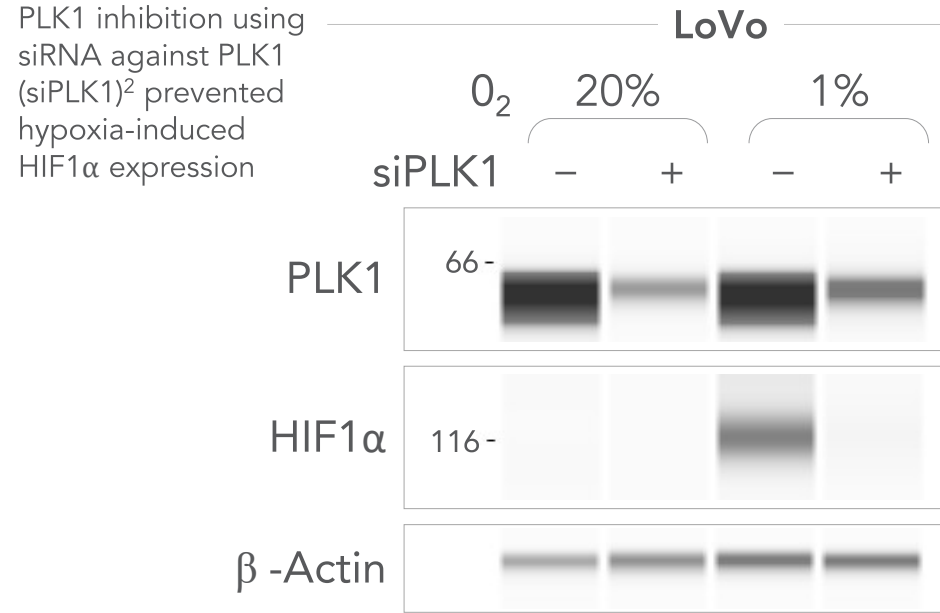
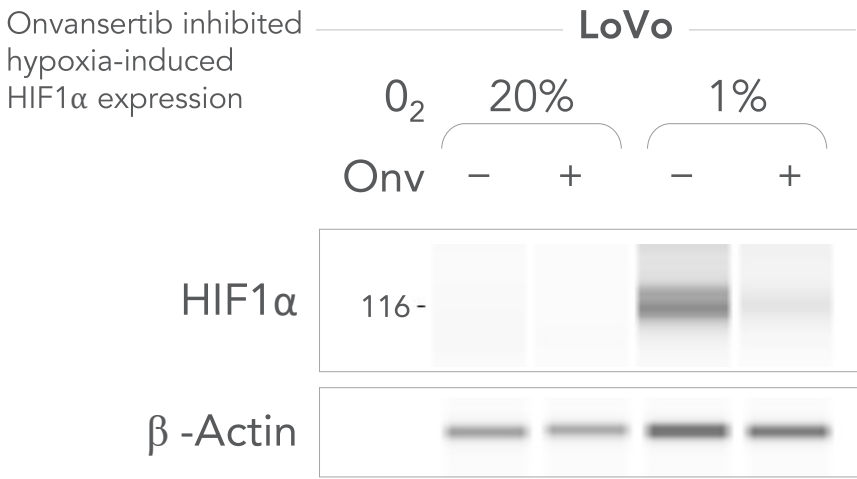
Angiogenesis:
Vascularization
of the tumor

Tumor cell
survival

Proliferation

Onvansertib inhibits the hypoxia signaling pathway by downregulating HIF1α expression

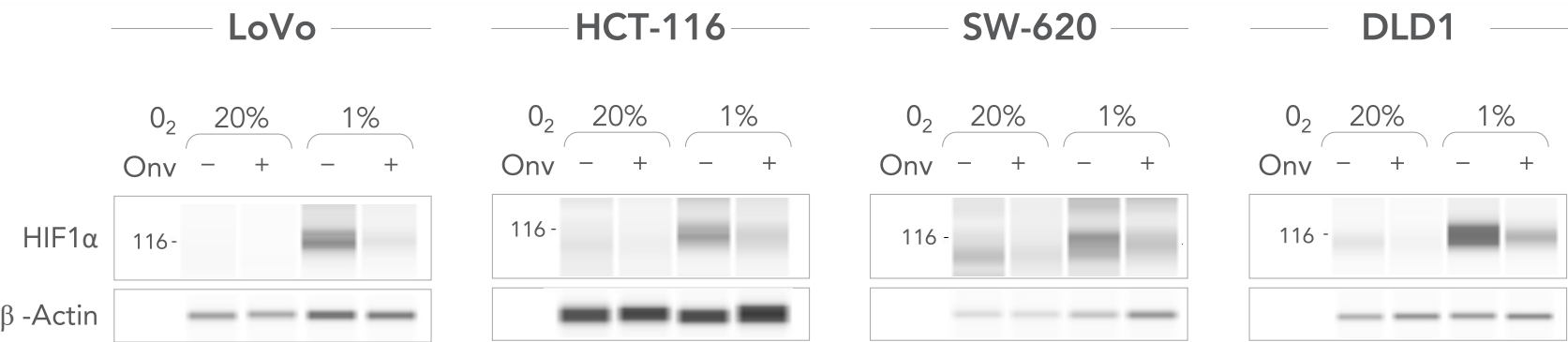
PLK1 inhibition in LoVo RAS-mutant CRC cell lines¹



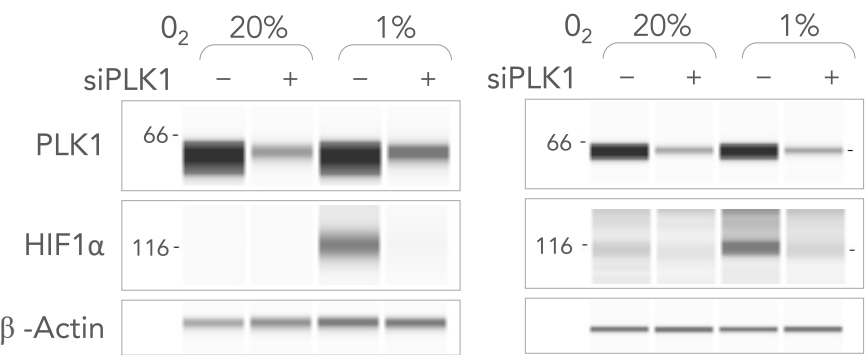
1. KRAS-mutant CRC cell lines were cultured under normoxia (20%O₂) or hypoxia (1%O₂), in the presence (+) or absence (-) of onvansertib. HIF1α expression was induced under hypoxia.
2. LoVo and HCT116 cells were transfected with siRNA control (-) or siRNA targeting PLK1 (siPLK1) and then exposed to 20% or 1%O₂. Cells were collected 24h after transfection.

Onvansertib inhibits the hypoxia signaling pathway by downregulating HIF1α expression

In 4 RAS-mutant CRC cell lines¹, onvansertib inhibited hypoxia-induced HIF1α expression

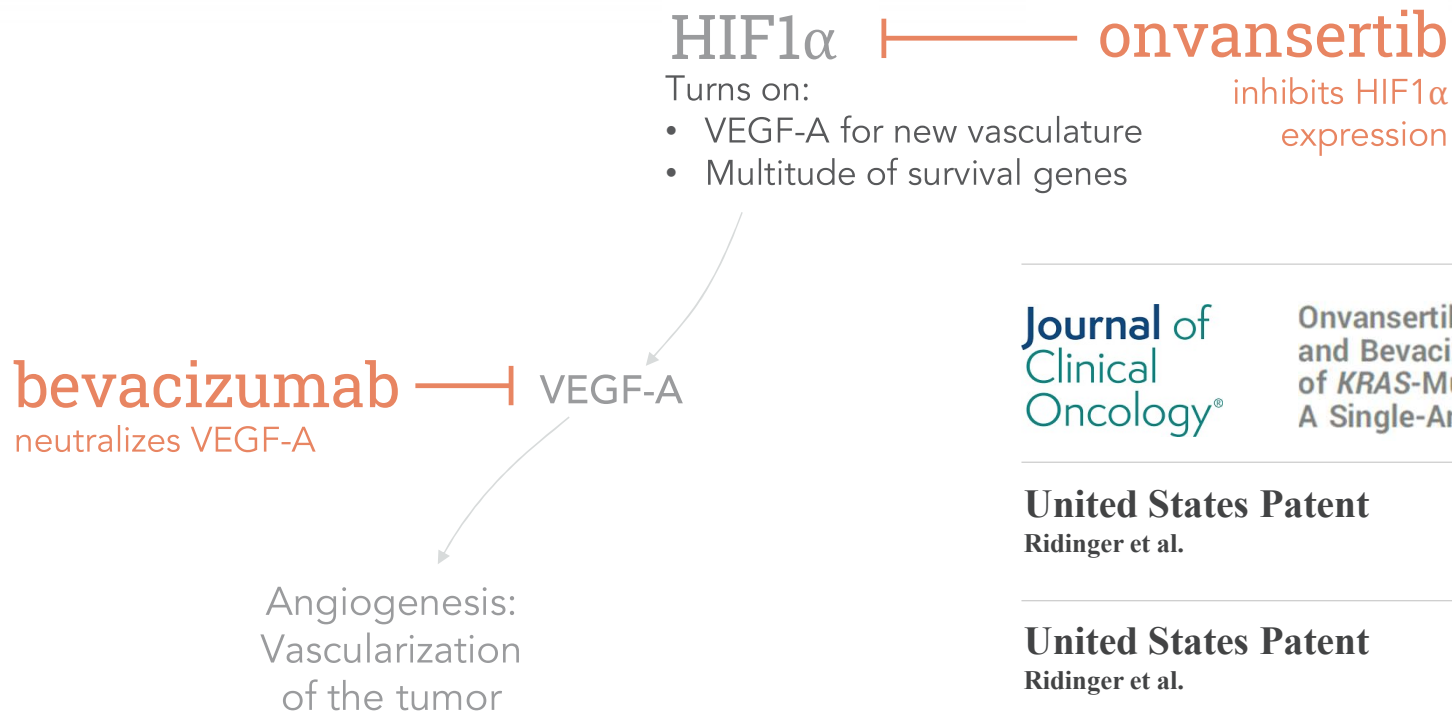


PLK1 inhibition using siRNA against PLK1 (siPLK1)² prevented hypoxia-induced HIF1α expression



1. KRAS-mutant CRC cell lines were cultured under normoxia (20%O₂) or hypoxia (1%O₂), in the presence (+) or absence (-) of onvansertib. HIF1α expression was induced under hypoxia.
2. LoVo and HCT116 cells were transfected with siRNA control (-) or siRNA targeting PLK1 (siPLK1) and then exposed to 20% or 1%O₂. Cells were collected 24h after transfection.

Novel mechanism of action strengthened our intellectual property



**Journal of
Clinical
Oncology®**

Onvansertib in Combination With Chemotherapy and Bevacizumab in Second-Line Treatment of *KRAS*-Mutant Metastatic Colorectal Cancer: A Single-Arm, Phase II Trial

United States Patent

Ridinger et al.

Patent No.:	US 12,144,813 B2
Date of Patent:	Nov. 19, 2024
Expiration:	Not before 2043

United States Patent

Ridinger et al.

Patent No.:	US 12,263,173 B2
Date of Patent:	Apr. 1, 2025
Expiration:	Not before 2043

Proposed MOA of onv+bev therapy in bev naïve / bev exposed tumors

Journal of
Clinical
Oncology®

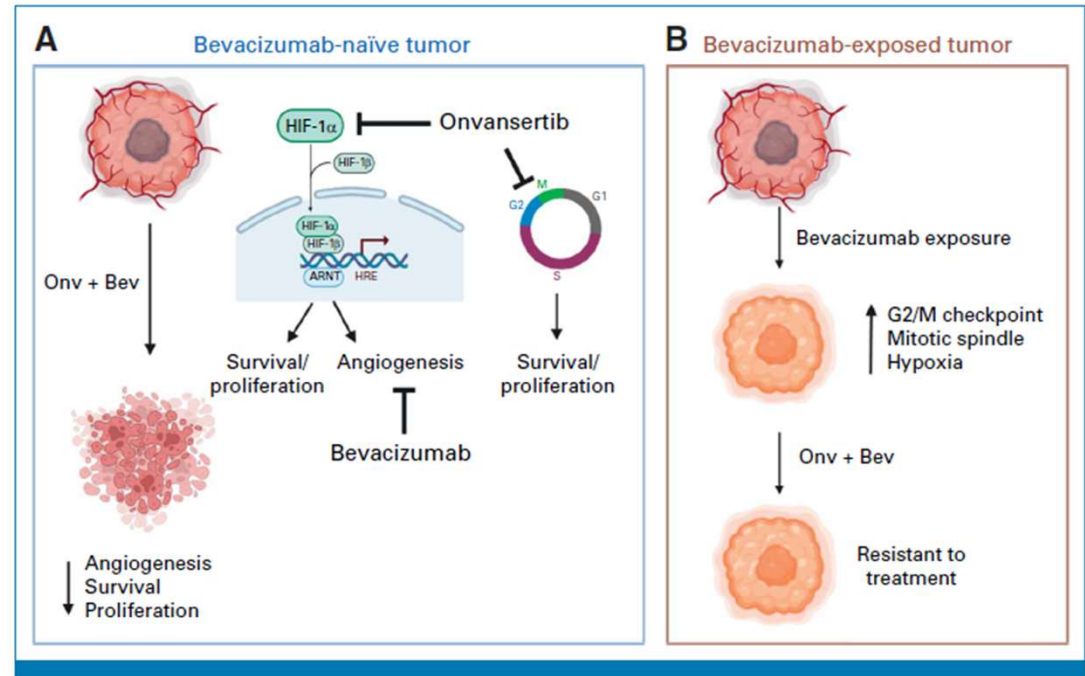
MOA

Onvansertib's inhibition of the hypoxia response pathway

(A) In bev naïve tumors, the combination of onvansertib and bev effectively inhibits cell survival, proliferation, and angiogenesis

(B) In bev exposed tumors, bev exposure leads to upregulation of mitotic and hypoxia pathways resulting in resistance to both onvansertib and bev

Proposed mechanisms of onvansertib and bev combination therapy in bev naïve and bev exposed tumors



Prior bev therapy in 1st line can confer resistance to bev, and onvansertib

"TEMPUS

Tumor Biopsy Library

135 biopsies:

All from KRAS-mut
mCRC patients after
completing first-line
therapy (prior to
second-line)

Bev naïve

1st line: FOLFOX

n=71

vs.

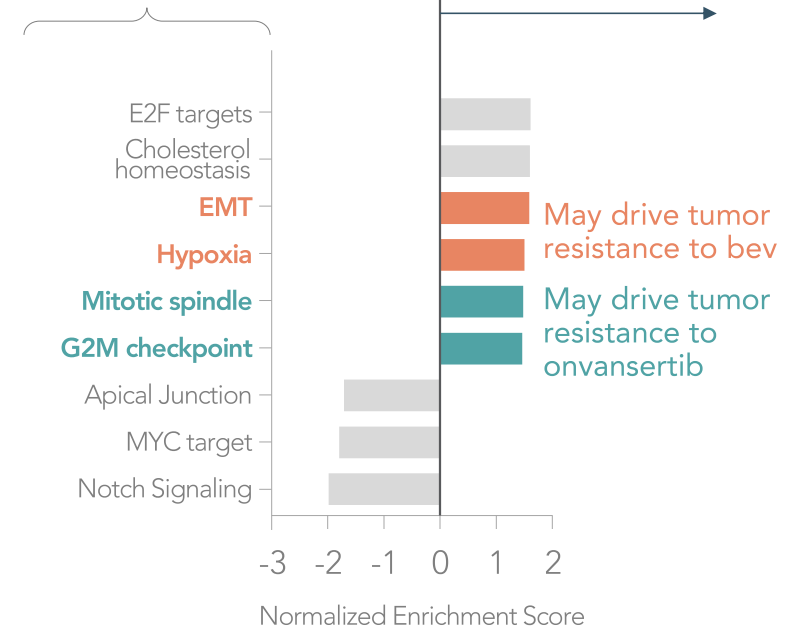
Bev exposed

1st line: FOLFOX+bev

n=64

Performed RNA sequencing to see
changes in tumor biology after 1st line
treatment +/- bev

Gene Sets Identified as
Hallmarks of Cancer



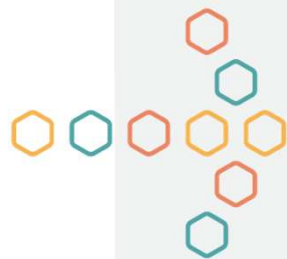
OUR SHIFT

TO FIRST-LINE RAS-MUTATED mCRC

The strength of our 1st-line program

The rationale for our shift from 2nd-line

The coming catalysts



Cardiff Oncology: Positioned to improve 1st line RAS-mut mCRC treatment

First-in-Class PLK1 inhibitor	2 nd line KRAS-mut. mCRC program	Shift to 1 st line	Clinical signal from CRDF-004 1 st trial	
Onvansertib First well-tolerated PLK1-selective inhibitor	Ph 1b/2 data High efficacy in bev naïve patients	Strong support • 2nd line data • FDA agreed path to 1st line accelerated approval • Pfizer: clinical execution in 1st line	Encouraging data • 49% confirmed response rate for 30 mg onv + SoC • 30% confirmed response rate for SoC alone	Additional clinical data from our 1 st line RAS-mutated mCRC trial is expected by Q1 2026
June 30, 2025 cash and investments*				\$71.0M
6-month net cash used in Operating Activities* (Two-quarter period ending June 30, 2025)				\$22.1M

* Financial information above is derived from our unaudited financials in Form 10-Q filed on 7/29/2025.

Our pipeline opens many attractive opportunities for onvansertib

	Line of Therapy	Trial	IIT*	Ph2	Ph3	Combination with:
mCRC (RAS-mut)	1 st line	CRDF-004 (w/Pfizer)		 randomized		FOLFIRI/bev and FOLFOX/bev
	2 nd line	Ph 1b/2		 completed		FOLFIRI/bev
mPDAC	1 st line	Ph 2				NALIRIFOX
	2 nd line	Ph 2		 completed		Nal-IRI/leucovorin/ 5-FU
SCLC	2 nd line	Ph 2				None (monotherapy)
TNBC	2 nd line	Ph 2				Paclitaxel

* For investigator-initiated trials (IITs) only, the investigator's institution is provided. The planned first-line mPDAC trial will be conducted by an investigator to be named. mPDAC, metastatic pancreatic ductal adenocarcinoma; SCLC, small-cell lung cancer; TNBC, triple-negative breast cancer; bev, bevacizumab.

Pfizer supports clinical execution of CRDF-004, our first-line mCRC trial

PFIZER BREAKTHROUGH GROWTH INITIATIVE

November 2021

- \$15M investment
- Nicholas Choong, MD (Vice President of Clinical Development and Therapeutic Area Head for GI cancers, Gynecologic cancers and Melanoma at Pfizer) serves on Scientific Advisory Board
- Right of first access to data

PFIZER Ignite

August 2023

- Pfizer Ignite is responsible for the clinical execution of 1st line mCRC trial (CRDF-004), including development capabilities, scale and expertise
- Cardiff Oncology retains full economic ownership and control of onvansertib

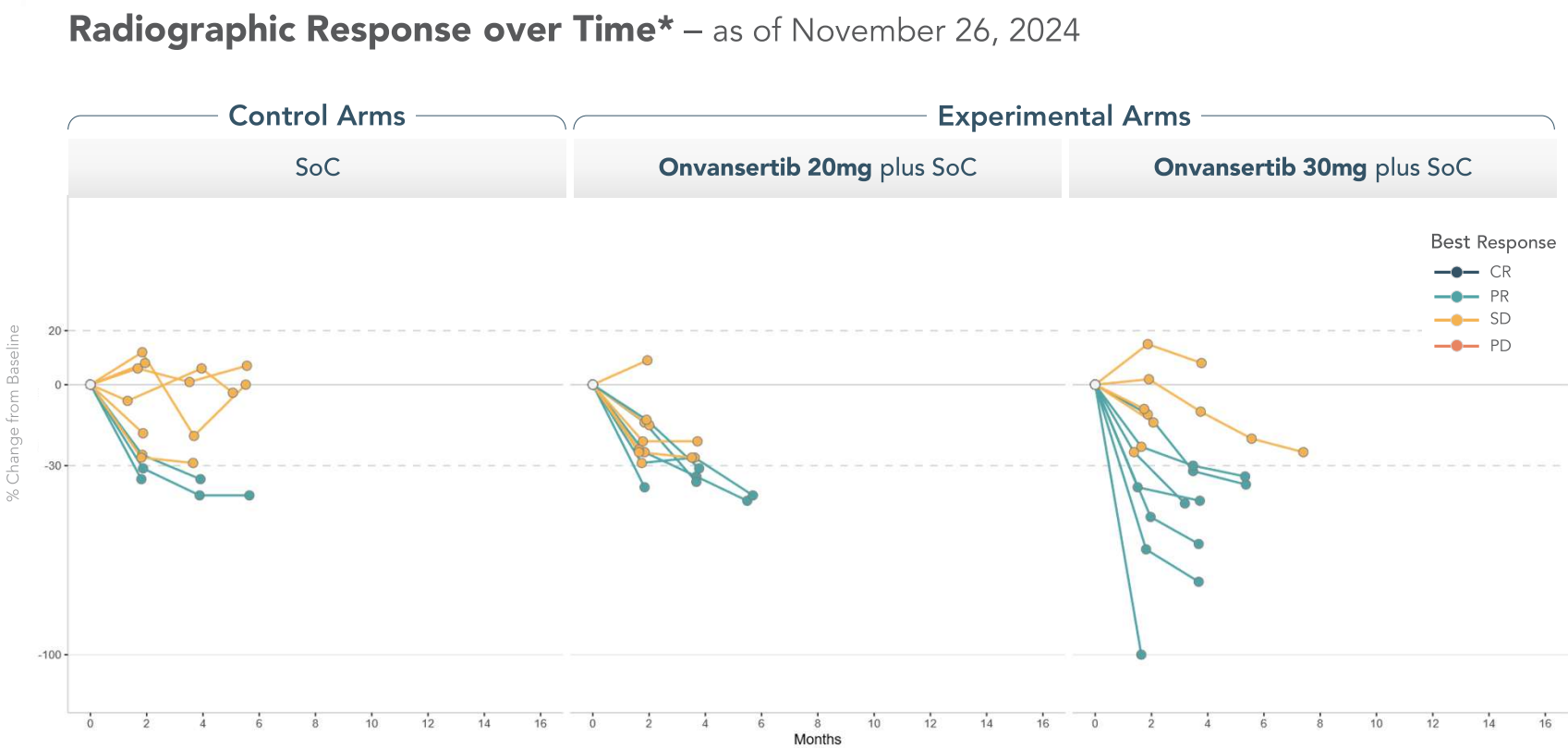


Appendix

Additional mCRC Data

CRDF-004 Dec 2024: Initial data showed deeper tumor shrinkage with onvansertib that appeared dose-dependent

Initial
30 patients
data disclosed
Dec 10, 2024

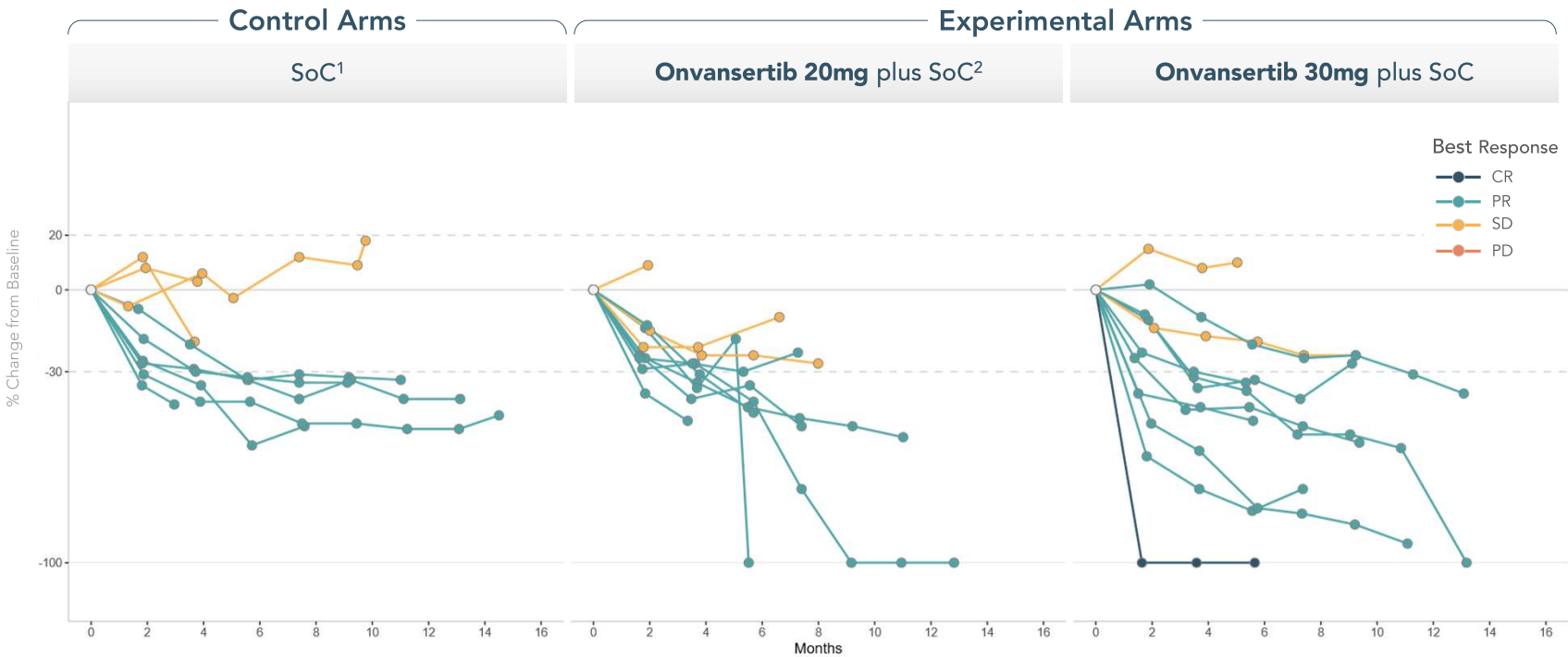


* Radiographic response determined per RECIST 1.1 by blinded independent central review as of November 26, 2024 from an ongoing trial and unlocked database. Response data for one control arm patient changed from the November 26, 2024 data cut as a result of the radiologist at the blinded independent central review modifying the target lesions. SoC, standard of care; CR, complete response; PR, partial response; SD, stable disease; PD, progressive disease

CRDF-004 July 2025: Data for same 30 patients continued to show deeper dose-dependent responses in onvansertib arms

Initial
30 patients
data disclosed
July 29, 2025

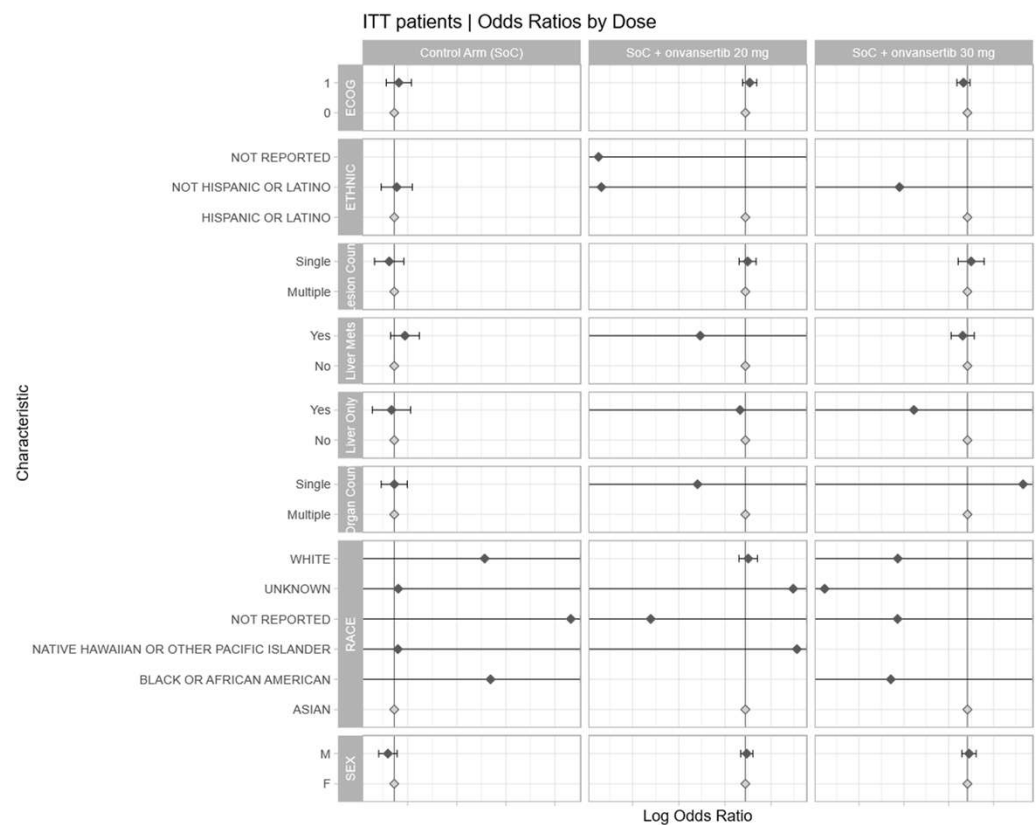
Radiographic Response over Time* – as of July 8, 2025



* Radiographic response determined per RECIST 1.1 by blinded independent central review as of July 8, 2025 from an ongoing trial and unlocked database. 1. For control arm patient 1007-005, after the Dec 10, 2024 data release, the BICR removed one target lesion for all scans on trial due to previous radiation treatment, changing the percent change from baseline for all scans. 2. Per protocol, patients' tumors are assessed by CT scan every 2 months, and Patient 1012-013 in the 20mg onv arm had an off-protocol MRI (different modality) of their tumors in preparation for their curative surgery (which occurred after their 6-month, -100% scan), which showed a spike (increase) in the size of the patient's tumor. SoC, standard of care; CR, complete response; PR, partial response; SD, stable disease; PD, progressive disease

CRDF-004 No baseline characteristic has a significant impact on ORR

Forest Plot of the Treatment Effect on ORR by Baseline Characteristic*



* Radiographic response determined per RECIST 1.1 by blinded independent central review as of July 8, 2025 from an ongoing trial and unlocked database. SoC, standard of care; ECOG, Eastern Cooperative Oncology Group

CRDF-004 treatment emergent adverse events (TEAE) data*

Safety Population (Dosed) N (% of total)	FOLFIRI/bev (n=17)		FOLFIRI/bev/onv 20mg (n=17)		FOLFIRI/bev/onv 30mg (n=18)		FOLFOX/bev (n=17)		FOLFOX/bev/onv 20mg (n=17)		FOLFOX/bev/onv 30mg (n=18)		All Control Arms (n=34)		All Experimental Arms (n=70)	
	All Grades	Gr ≥3	All Grades	Gr ≥3	All Grades	Gr ≥3	All Grades	Gr ≥3	All Grades	Gr ≥3	All Grades	Gr ≥3	All Grades	Gr ≥3	All Grades	Gr ≥3
Any Adverse Events	17 (100.0)	12 (70.6)	17 (100.0)	14 (82.4)	18 (100.0)	15 (83.3)	16 (94.1)	9 (52.9)	17 (100.0)	10 (58.8)	18 (100.0)	13 (72.2)	33 (97.1)	21 (61.8)	70 (100.0)	52 (74.3)
Fatigue	7 (41.2)	0	12 (70.6)	0	11 (61.1)	0	9 (52.9)	2 (11.8)	12 (70.6)	1 (5.9)	10 (55.6)	0	16 (47.1)	2 (5.9)	45 (64.3)	1 (1.4)
Nausea	6 (35.3)	1 (5.9)	13 (76.5)	0	9 (50.0)	0	11 (64.7)	0	12 (70.6)	0	8 (44.4)	0	17 (50.0)	1 (2.9)	42 (60.0)	0
Diarrhea	10 (58.8)	1 (5.9)	12 (70.6)	1 (5.9)	9 (50.0)	0	7 (41.2)	0	7 (41.2)	1 (5.9)	7 (38.9)	0	17 (50.0)	1 (2.9)	35 (50.0)	2 (2.9)
Neutrophil count decreased	8 (47.1)	4 (23.5)	4 (23.5)	1 (5.9)	6 (33.3)	3 (16.7)	5 (29.4)	5 (29.4)	6 (35.3)	3 (17.6)	7 (38.9)	4 (22.2)	13 (38.2)	9 (26.5)	23 (32.9)	11 (15.7)
Neutropenia	2 (11.8)	1 (5.9)	1 (5.9)	0	4 (22.2)	4 (22.2)	3 (17.6)	1 (5.9)	2 (11.8)	2 (11.8)	0	0	5 (14.7)	2 (5.9)	7 (10.0)	6 (8.6)
Hypertension	4 (23.5)	1 (5.9)	8 (47.1)	3 (17.6)	6 (33.3)	1 (5.6)	3 (17.6)	0	4 (23.5)	1 (5.9)	6 (33.3)	2 (11.1)	7 (20.6)	1 (2.9)	24 (34.3)	7 (10.0)
Vomiting	5 (29.4)	1 (5.9)	7 (41.2)	0	6 (33.3)	0	3 (17.6)	0	6 (35.3)	0	2 (11.1)	0	8 (23.5)	1 (2.9)	21 (30.0)	0
Constipation	3 (17.6)	1 (5.9)	5 (29.4)	0	5 (27.8)	0	2 (11.8)	0	8 (47.1)	0	5 (27.8)	0	5 (14.7)	1 (2.9)	23 (32.9)	0
Epistaxis	4 (23.5)	0	8 (47.1)	0	6 (33.3)	0	3 (17.6)	0	3 (17.6)	0	3 (16.7)	0	7 (20.6)	0	20 (28.6)	0
Peripheral sensory neuropathy	4 (23.5)	0	2 (11.8)	0	1 (5.6)	0	4 (23.5)	0	8 (47.1)	2 (11.8)	8 (44.4)	1 (5.6)	8 (23.5)	0	19 (27.1)	3 (4.3)
Abdominal pain	3 (17.6)	2 (11.8)	4 (23.5)	1 (5.9)	6 (33.3)	1 (5.6)	2 (11.8)	0	6 (35.3)	0	5 (27.8)	0	5 (14.7)	2 (5.9)	21 (30.0)	2 (2.9)
Anaemia	4 (23.5)	1 (5.9)	6 (35.3)	0	4 (22.2)	1 (5.6)	3 (17.6)	0	2 (11.8)	0	7 (38.9)	3 (16.7)	7 (20.6)	1 (2.9)	19 (27.1)	4 (5.7)
Decreased appetite	6 (35.3)	0	5 (29.4)	0	4 (22.2)	0	3 (17.6)	0	6 (35.3)	0	2 (11.1)	0	9 (26.5)	0	17 (24.3)	0
Platelet count decreased	2 (11.8)	1 (5.9)	1 (5.9)	0	2 (11.1)	0	7 (41.2)	1 (5.9)	7 (41.2)	0	7 (38.9)	1 (5.6)	9 (26.5)	2 (5.9)	17 (24.3)	1 (1.4)
Alopecia	5 (29.4)	0	4 (23.5)	0	6 (33.3)	0	2 (11.8)	0	4 (23.5)	0	2 (11.1)	0	7 (20.6)	0	16 (22.9)	0
Headache	4 (23.5)	0	6 (35.3)	0	2 (11.1)	0	4 (23.5)	0	4 (23.5)	0	1 (5.6)	0	8 (23.5)	0	13 (18.6)	0
White blood cell count decreased	4 (23.5)	0	4 (23.5)	0	5 (27.8)	0	6 (35.3)	0	0	0	2 (11.1)	1 (5.6)	10 (29.4)	0	11 (15.7)	1 (1.4)
Dizziness	3 (17.6)	0	3 (17.6)	0	2 (11.1)	0	3 (17.6)	0	4 (23.5)	0	5 (27.8)	0	6 (17.6)	0	14 (20.0)	0
Dysgeusia	2 (11.8)	0	1 (5.9)	0	3 (16.7)	0	4 (23.5)	0	5 (29.4)	0	5 (27.8)	0	6 (17.6)	0	14 (20.0)	0
Weight decreased	6 (35.3)	1 (5.9)	2 (11.8)	0	5 (27.8)	0	2 (11.8)	0	2 (11.8)	0	3 (16.7)	0	8 (23.5)	1 (2.9)	12 (17.1)	0
Hypokalaemia	3 (17.6)	0	3 (17.6)	2 (11.8)	4 (22.2)	2 (11.1)	2 (11.8)	1 (5.9)	3 (17.6)	0	4 (22.2)	1 (5.6)	5 (14.7)	1 (2.9)	14 (20.0)	5 (7.1)
Stomatitis	3 (17.6)	0	6 (35.3)	0	1 (5.6)	0	5 (29.4)	0	2 (11.8)	0	1 (5.6)	0	8 (23.5)	0	10 (14.3)	0
Insomnia	0 (0.0)	0	4 (23.5)	0	3 (16.7)	0	1 (5.9)	0	5 (29.4)	0	4 (22.2)	0	1 (2.9)	0	16 (22.9)	0
Paraesthesia	1 (5.9)	0	2 (11.8)	0	0	0	2 (11.8)	0	5 (29.4)	0	6 (33.3)	0	3 (8.8)	0	13 (18.6)	0
Lymphocyte count decreased	3 (17.6)	0	2 (11.8)	0	4 (22.2)	0	2 (11.8)	0	1 (5.9)	0	3 (16.7)	2 (11.1)	5 (14.7)	0	10 (14.3)	2 (2.9)
Cough	4 (23.5)	0	4 (23.5)	0	2 (11.1)	0	1 (5.9)	0	0	0	3 (16.7)	0	5 (14.7)	0	9 (12.9)	0
Pyrexia	2 (11.8)	0	3 (17.6)	1 (5.9)	3 (16.7)	1 (5.6)	2 (11.8)	0	3 (17.6)	0	1 (5.6)	0	4 (11.8)	0	10 (14.3)	2 (2.9)
Blood alkaline phosphatase increased	3 (17.6)	0	1 (5.9)	0	1 (5.6)	0	4 (23.5)	0	0	0	3 (16.7)	0	7 (20.6)	0	5 (7.1)	0
Dyspepsia	1 (5.9)	0	4 (23.5)	0	2 (11.1)	0	1 (5.9)	0	1 (5.9)	0	3 (16.7)	0	2 (5.9)	0	10 (14.3)	0
Proteinuria	2 (11.8)	0	3 (17.6)	0	2 (11.1)	0	0	0	3 (17.6)	0	2 (11.1)	0	2 (5.9)	0	10 (14.3)	0

* Data consists of all adverse events entered into the electronic data capture (EDC) system as of July 8, 2025, from an ongoing trial and unlocked EDC database. N: number of patients; events shown occurred in ≥10% of total patients; numbers indicate number of patients experiencing the event, (regardless of causality); each patient is only counted once and only for the highest grade of a given event. Columns show the absolute # of patients and (%) of the population. Bev, bevacizumab; onv, onvansertib

CRDF-004 dose intensity is similar and high across all trial arms

Relative Dose Intensity: actual amount of study drug a patient receives over time compared to the planned dose and schedule*

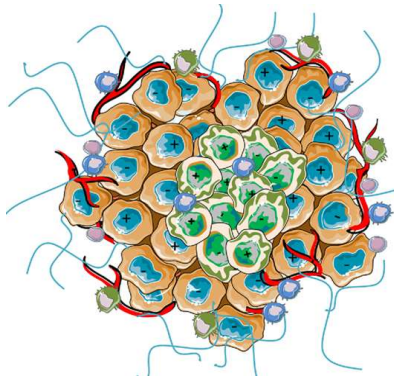
Safety Population (Dosed)	FOLFIRI/bev (n=17)	FOLFIRI/bev/onv 20 (n=17)	FOLFIRI/bev/onv 30 (n=18)	FOLFOX/bev (n=17)	FOLFOX/bev/onv 20 (n=17)	FOLFOX/bev/onv 30 (n=18)
Relative dose intensity (%)						
Mean (Std)	91.84 (12.8)	90.37 (12.6)	91.39 (9.8)	91.34 (11.0)	93.34 (9.1)	86.89 (15.1)
Median	96.93	96.32	93.24	93.24	96.5	91.22

* Data as of July 8, 2025 from an ongoing trial and unlocked database. Bev, bevacizumab; onv, onvansertib; Std, standard deviation

Onvansertib and bev independently inhibit tumor response to hypoxia in bev naïve tumors

Tumor growth

The tumor cells outgrow the blood supply and become starved of oxygen and nutrients...



Hypoxia

... low oxygen levels lead to elevated HIF1 α protein expression

HIF1 α

... turns on VEGF-A expression and secretion to recruit new vasculature as well as turning on a multitude of downstream survival genes

onvansertib
inhibits HIF1 α expression

bevacizumab
neutralizes VEGF-A

VEGF-A

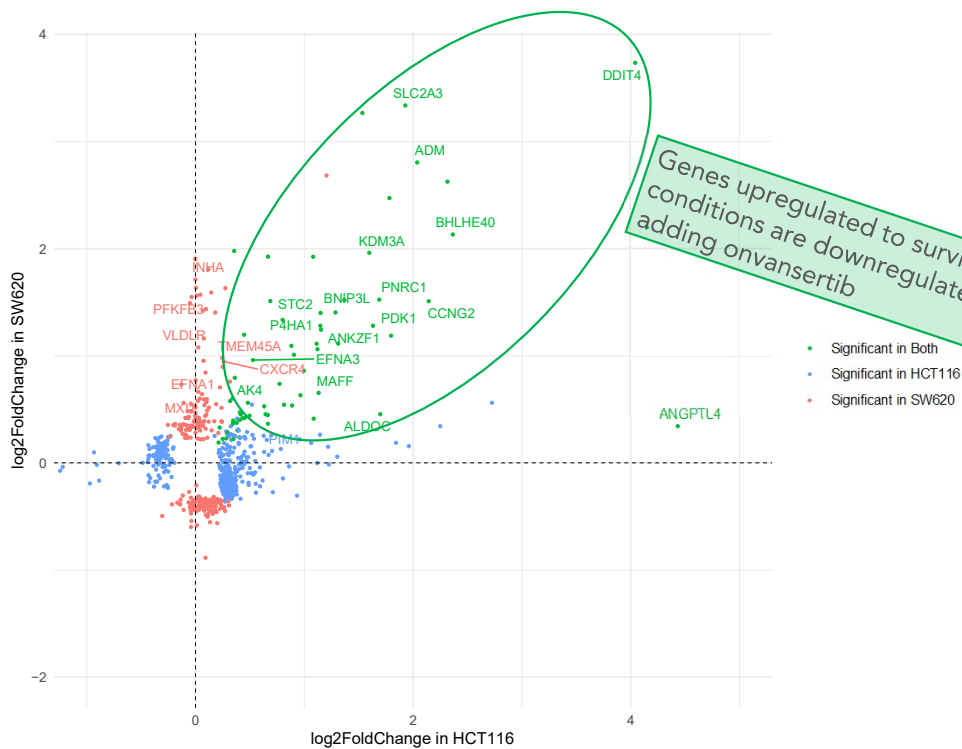
Angiogenesis:
Vascularization
of the tumor

Tumor cell
survival

Proliferation

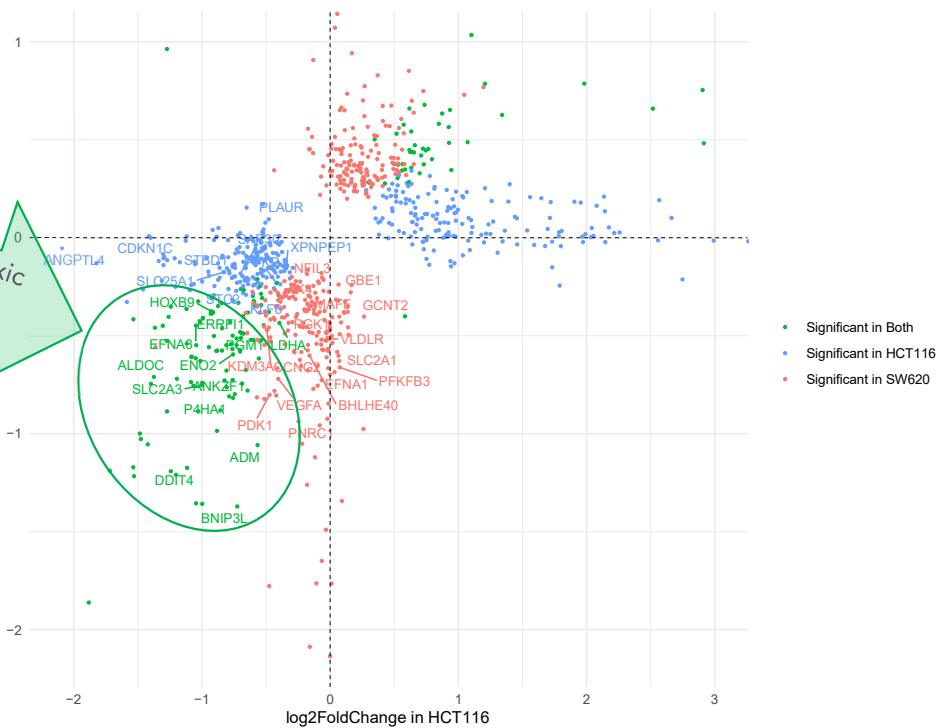
Onvansertib down-regulates genes induced by tumors in hypoxic conditions

Genes induced by hypoxia in two mCRC cell lines



Hypoxia vs normoxia gene expression in HCT116 and SW620 cells

Adding onvansertib inhibits adaptation to hypoxia



With vs without onvansertib gene expression in hypoxic HCT116 and SW620 cells

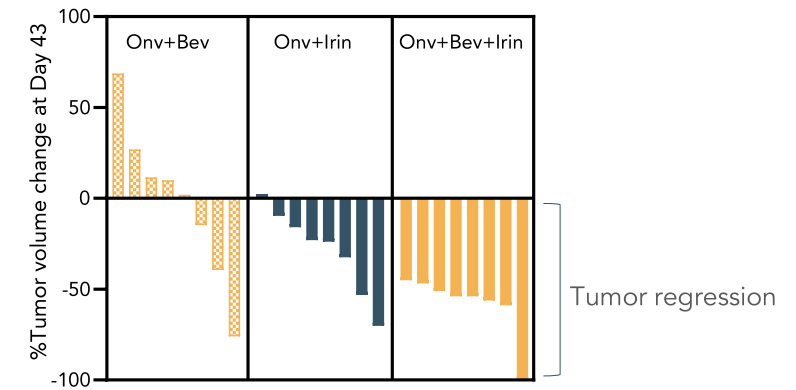
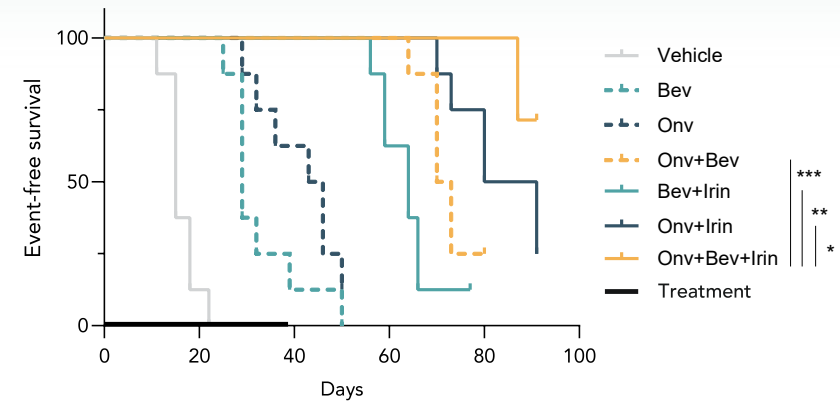
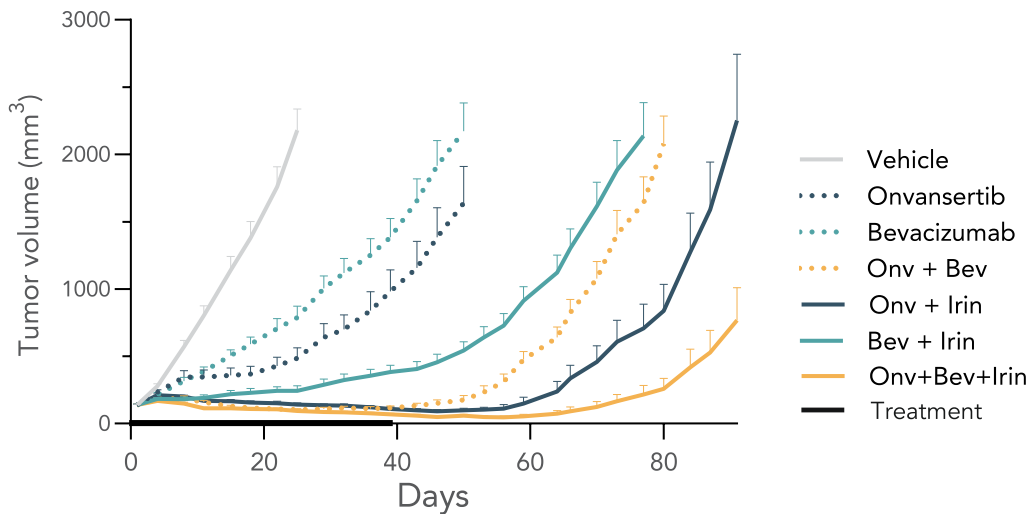
* Genes in the Hallmarks Hypoxia gene set are labeled. Top 250 genes with P-adjusted < 0.05 shown.

The combination of onvansertib, bevacizumab and irinotecan showed greater potency than each individual or doublet therapy

The combination of onvansertib, bevacizumab and irinotecan was potent in the HCT116 xenograft model, resulting in:

- tumor regression in all treated mice (8/8), including 1 CR
- prolonged event-free survival

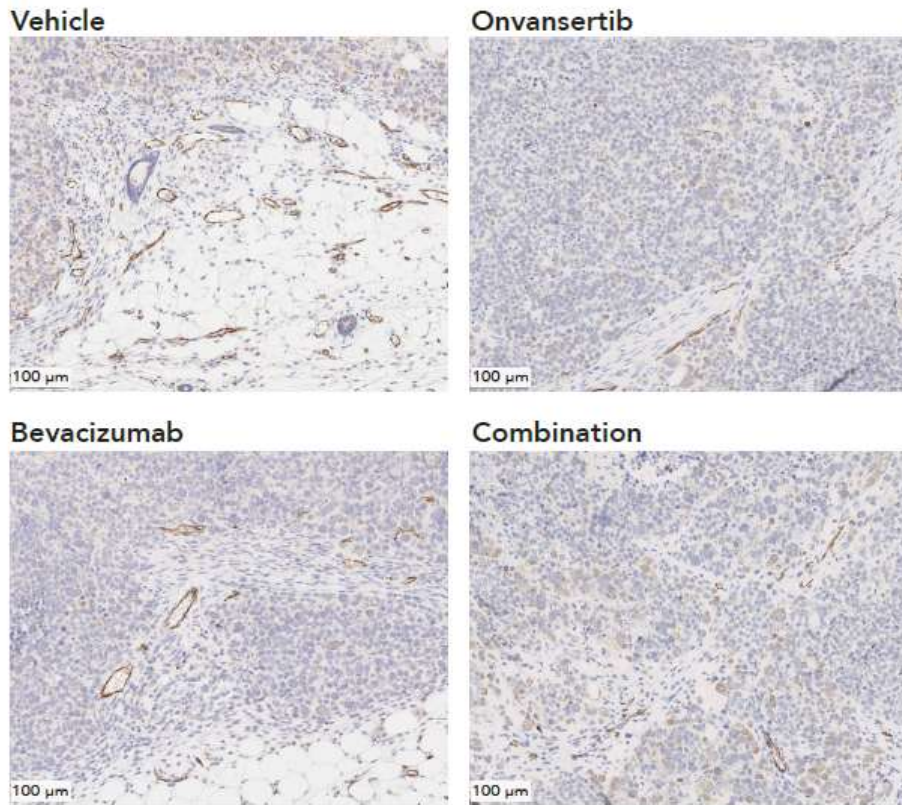
At the end of the study (Day 91), 6 of the 8 mice treated with the triplet combination had tumors $<1000\text{mm}^3$



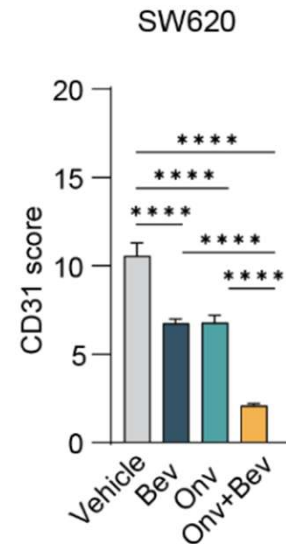
HCT116 xenografts were treated with the indicated drugs for 39 days and tumor volumes were measured (8mice/group, mean + SEM are represented on graph). Kaplan-Meier survival curve for event-free survival (time to reach tumor volume 1000mm^3) was calculated. Log-rank Mantel Cox test was used for survival analyses, * $p<0.05$, ** $p<0.01$, *** $p<0.001$.

The combination of onvansertib and bev reduces tumor vascularization

CD31



- Vascularization was quantified using the endothelial marker CD31
- Onvansertib and bev monotherapies reduced tumor vascularization
- The combination treatment of onvansertib and bev resulted in further decrease in vascularization



SW620 xenograft model is shown. CD31 scoring: for each sample 5 fields of view at 100 μ m magnification were randomly selected in the tumor area. CD31 positive vessels were manually counted in these fields. Mean score $\pm$ SEM for each treatment group (n=6/group) are plotted. One-way ANOVA was used to test differences between treatment arms. * p <0.05, ** p <0.01, *** p <0.001, **** p <0.0001.

Onvansertib in combination with irinotecan in RAS-mutant CRC PDXs

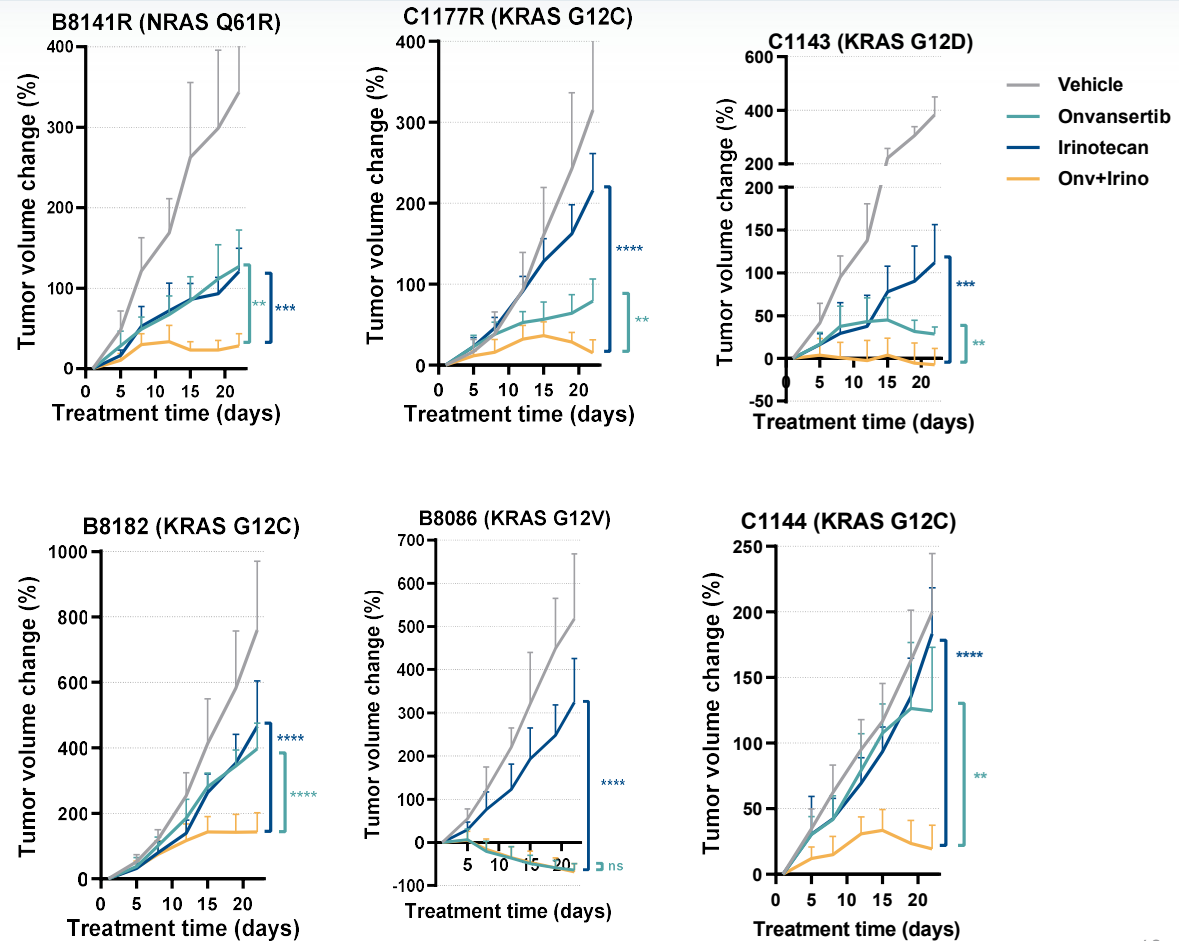
The combination of onvansertib and irinotecan showed anti-tumor activity in 6 RAS-mutated PDX models with either acquired or intrinsic resistance to irinotecan.

The combination showed significant increased anti-tumor activity compared to onvansertib single agent in 5 of the 6 models.

These data support that onvansertib + irinotecan is an active combination in RAS-mutated PDX models and that Onvansertib can sensitize tumors to irinotecan.

In collaboration with Dr. Kopetz (MD Anderson)

Dosing schedule: onvansertib 60 mg/kg daily; irinotecan 40mg/kg weekly, for up to 21 days. Mean + SD are represented. Unpaired t-test, **p<0.01, ***p<0.001, ****p<0.0001.



Onvansertib in combination with FOLFOX in RAS-mutant CRC PDXs

The chemotherapeutics oxaliplatin+5FU had no or modest activity in the 6 RAS-mutant PDX models tested.

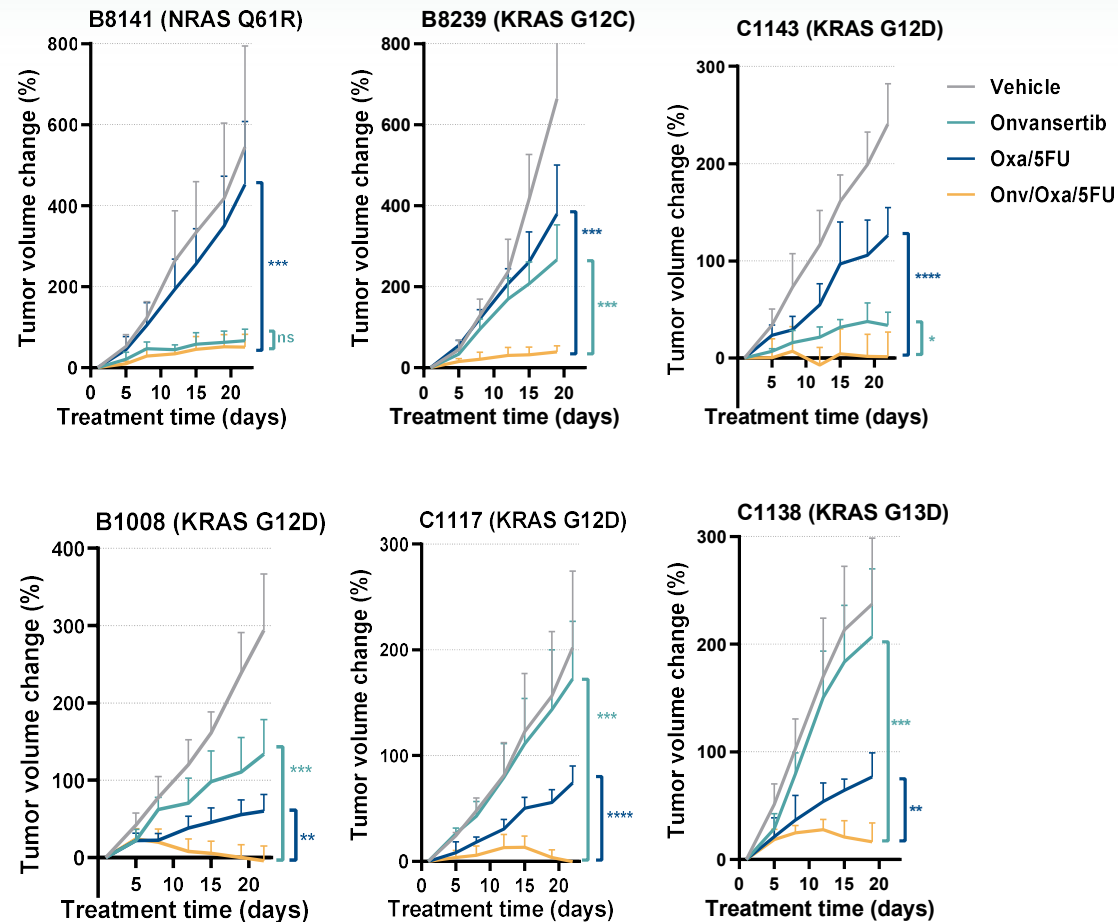
Conversely, the combination of onvansertib with oxaliplatin+5FU was efficacious in all 6 models, resulting in tumor stasis or tumor regression.

In 5 of the 6 models, the combination had significantly superior activity than the single agent treatments.

These data support the efficacy of onvansertib in combination with oxaliplatin+5FU in RAS-mutant CRC PDXs resistant or partially sensitive to oxaliplatin+5FU.

In collaboration with Dr. Kopetz (MD Anderson)

Dosing schedule: onvansertib 45 mg/kg daily; oxaliplatin 10mg/kg weekly; 5-FU 25mg/kg 5times/week for up to 21days. Mean + SD are represented. Unpaired t-test, *p<0.05, **p<0.01, ***p<0.001, ****p<0.0001.





Appendix:
Investigator-Initiated Trial
Small Cell Lung Cancer (SCLC)

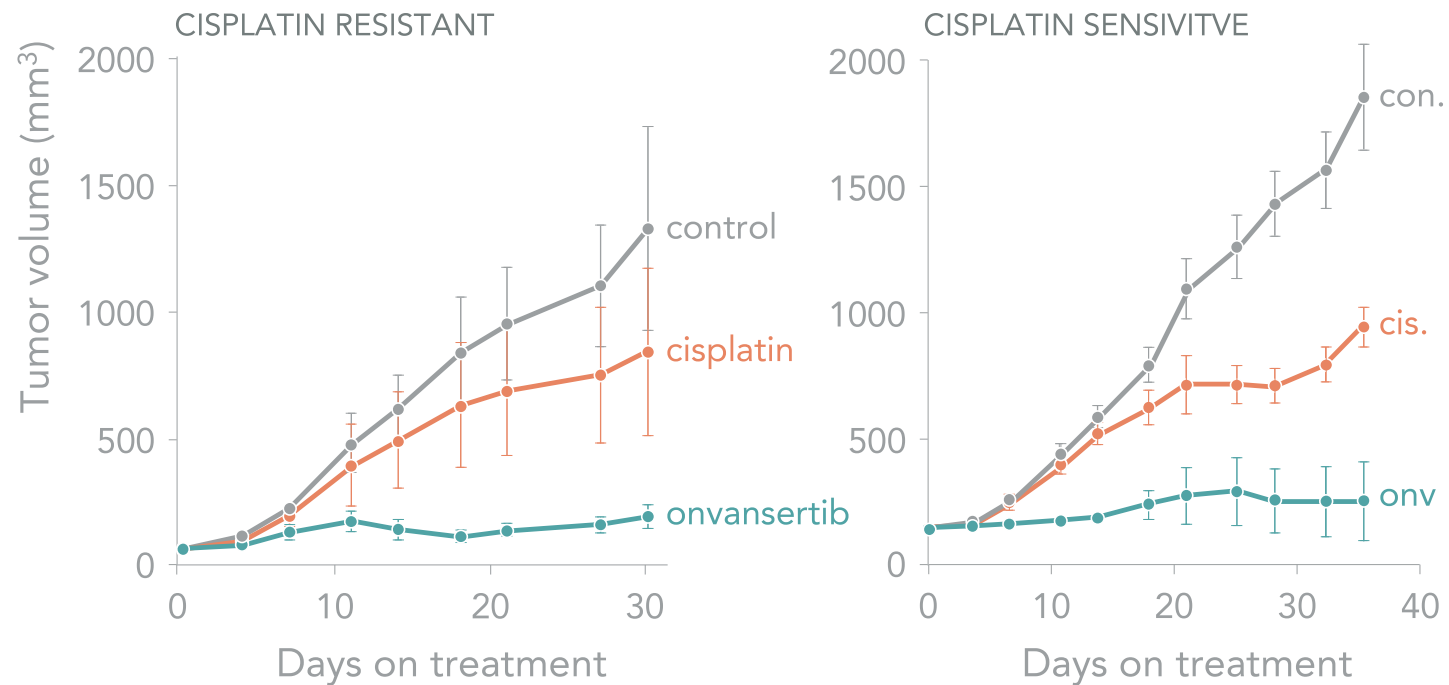
Onvansertib demonstrates single-agent activity in SCLC

TRIAL RATIONALE

Onvansertib monotherapy showed significant tumor growth inhibition against platinum-sensitive and -resistant models

SCLC

In vivo efficacy of onvansertib monotherapy (SCLC xenografts)*



* Mice were implanted with SCLC PDX and treated with vehicle, cisplatin 3mg/kg IP weekly, or onvansertib oral 60mg/kg 10 ON / 4 OFF.

Trial design for onvansertib monotherapy in extensive stage SCLC

ENROLLMENT CRITERIA

- Relapsed who have received ≤ 2 prior therapies
- Single-arm trial
- Stage 1: N=15
- Stage 2: N=20

SCLC



OBJECTIVE

To determine the efficacy and safety of onvansertib monotherapy

PRIMARY ENDPOINT

ORR (RECIST 1.1)

SECONDARY ENDPOINTS

Progression-Free Survival (PFS)
Overall Survival (OS)



Additional preliminary data for the small cell lung cancer investigator-initiated trial are available in our [investor presentation](#) filed on Form 8-K on September 26, 2023 (page 22 – 26).

Preliminary safety and efficacy for onvansertib monotherapy in SCLC

ENROLLMENT CRITERIA

Relapsed who have
received ≤ 2 prior therapies

Single-arm trial
Stage 1: N=15
Stage 2: N=20

PRELIMINARY SAFETY (N=6)

IRB reviewed safety data for the first 6 patients. Post IRB review, the trial continues to enroll with no conditions.

PRELIMINARY EFFICACY (N=7)

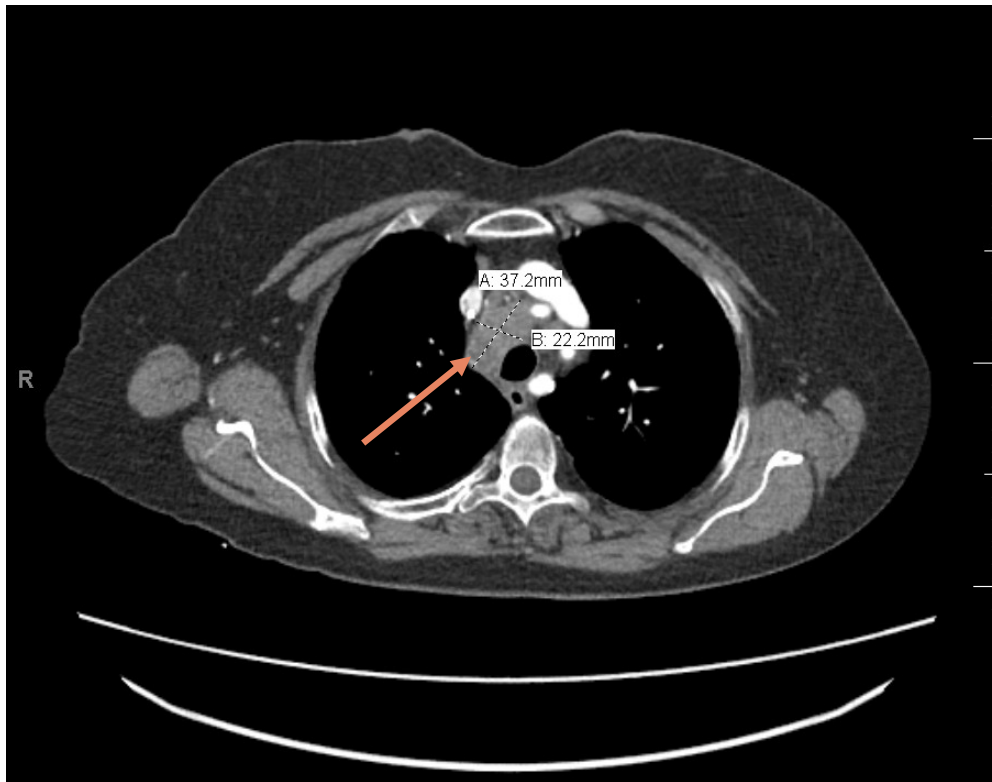
Best response	PR	SD	PD
# of patients	1 (confirmed)	3	3

Disease control rate = 57% (4/7)

SCLC

Radiographic scans for patient with a confirmed PR in SCLC

Baseline Scan



Restaging after Cycle 2





Appendix:
Investigator-Initiated Trial
Triple Negative Breast Cancer (TNBC)

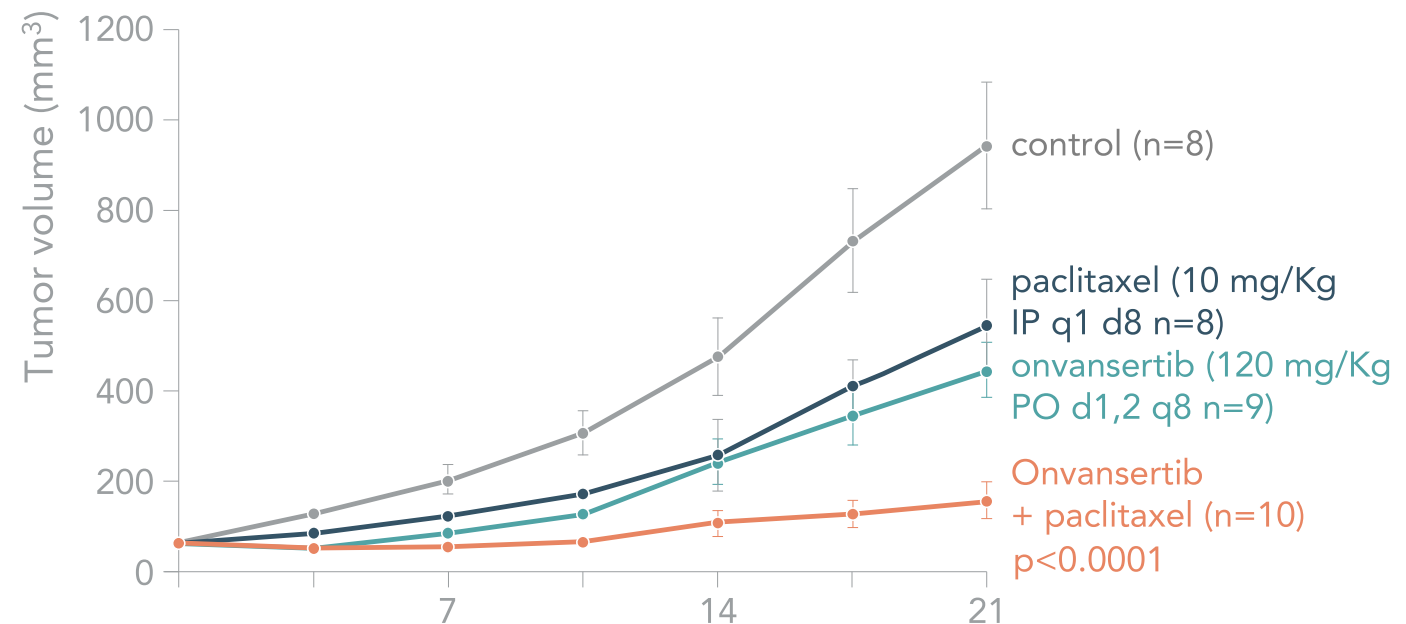
Preclinical: Onvansertib + paclitaxel is superior to single agent therapy

TRIAL RATIONALE

The combination of onvansertib + paclitaxel showed significant synergy

TNBC

In vivo efficacy of onvansertib in combination with paclitaxel
Tp53-Mutant SUM159 xenografts*



* SUM159 cells were implanted in the mammary fat pad of NOD-scid-IL2 receptor gamma null female mice, and treatments began as follows when tumor volume reached 40 mm³: vehicle, onvansertib oral (PO) twice per week (days 1-2), paclitaxel intraperitoneally (IP) weekly (day 1), or the combination.

This is the first trial to explore onvansertib + paclitaxel combination

ENROLLMENT CRITERIA

Metastatic TNBC relapsed or progressed

Single arm trial
Ph 1b: N=14–16
Ph 2: N=34



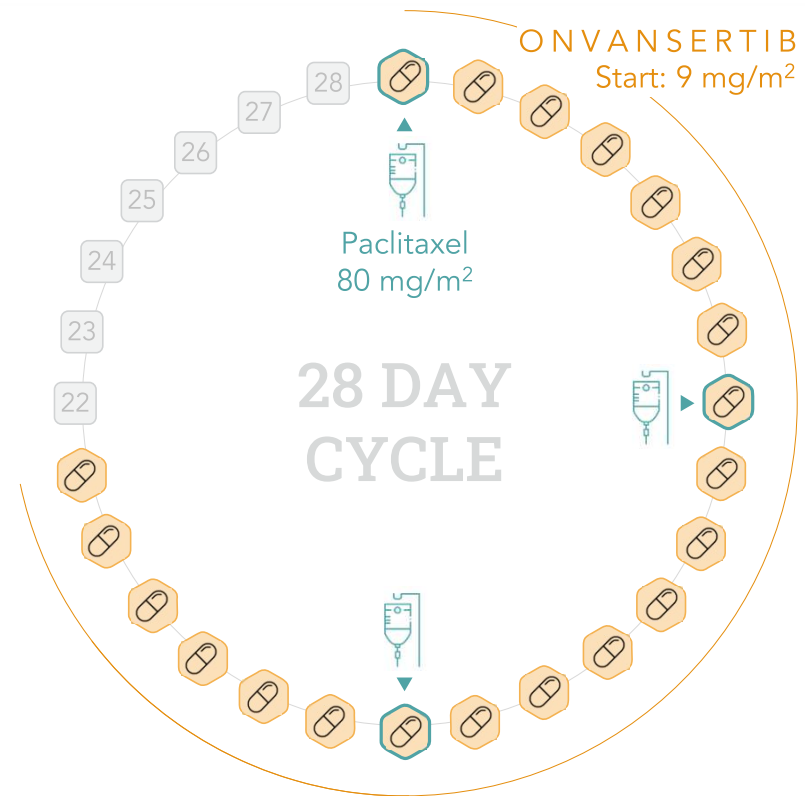
PRIMARY ENDPOINTS

Phase 1b
Safety, characterization of DLTs
Determination of RP2D

Phase 2
ORR (RECIST 1.1)

ONVANSERTIB DOSING

Escalation: 12 mg/m², 18 mg/m²
Starting: 9 mg/m²
De-escalation: 6 mg/m²



This is the first trial to explore onvansertib + paclitaxel combination

ENROLLMENT CRITERIA

Metastatic TNBC relapsed or progressed

Single arm trial
Ph 1b: N=14–16
Ph 2: N=34

TNBC

PRIMARY ENDPOINTS

Phase 1b
Safety, characterization of DLTs
Determination of RP2D

Phase 2
ORR (RECIST 1.1)

SECONDARY ENDPOINT

Phase 2
Progression-Free Survival (PFS)

