Company Overview
The Onvansertib Opportunity

AUGUST 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.

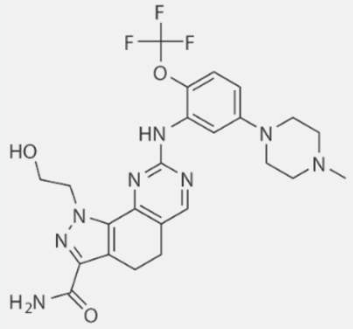
Cardiff Oncology's lead development asset is onvansertib

Onvansertib

First oral, well-tolerated PLK1-selective inhibitor

PROPERTIES

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

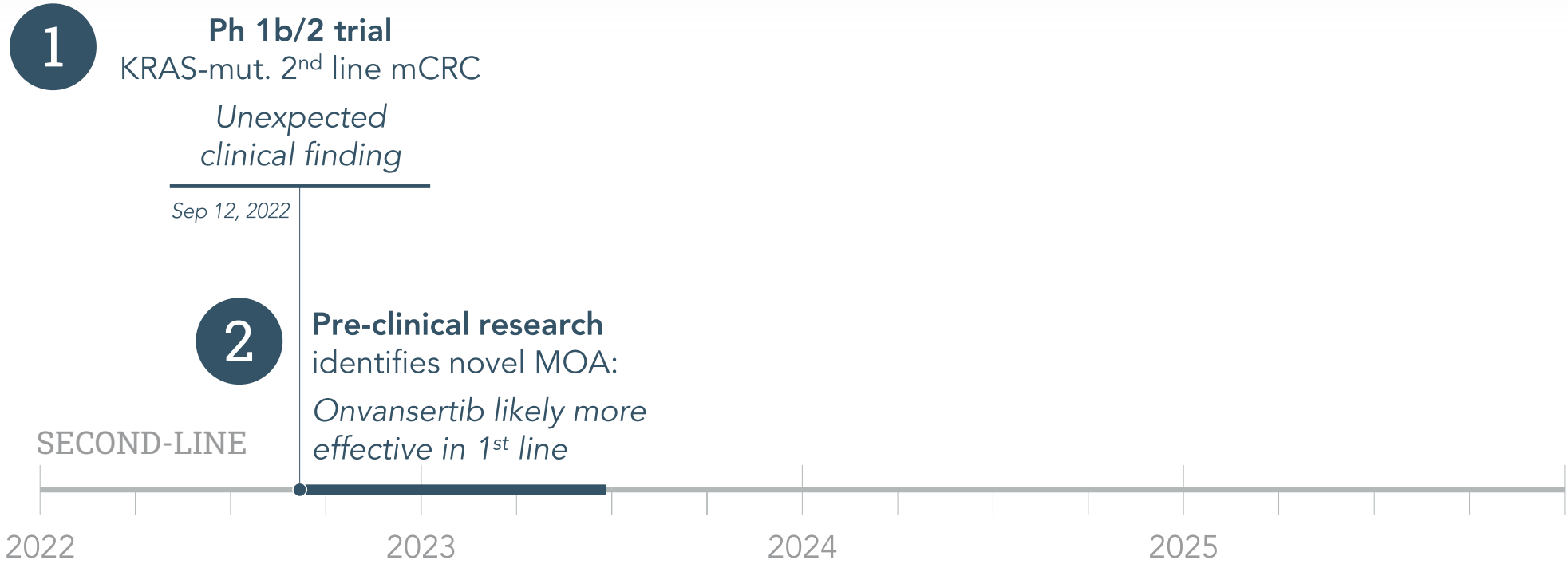


SPECIFICITY

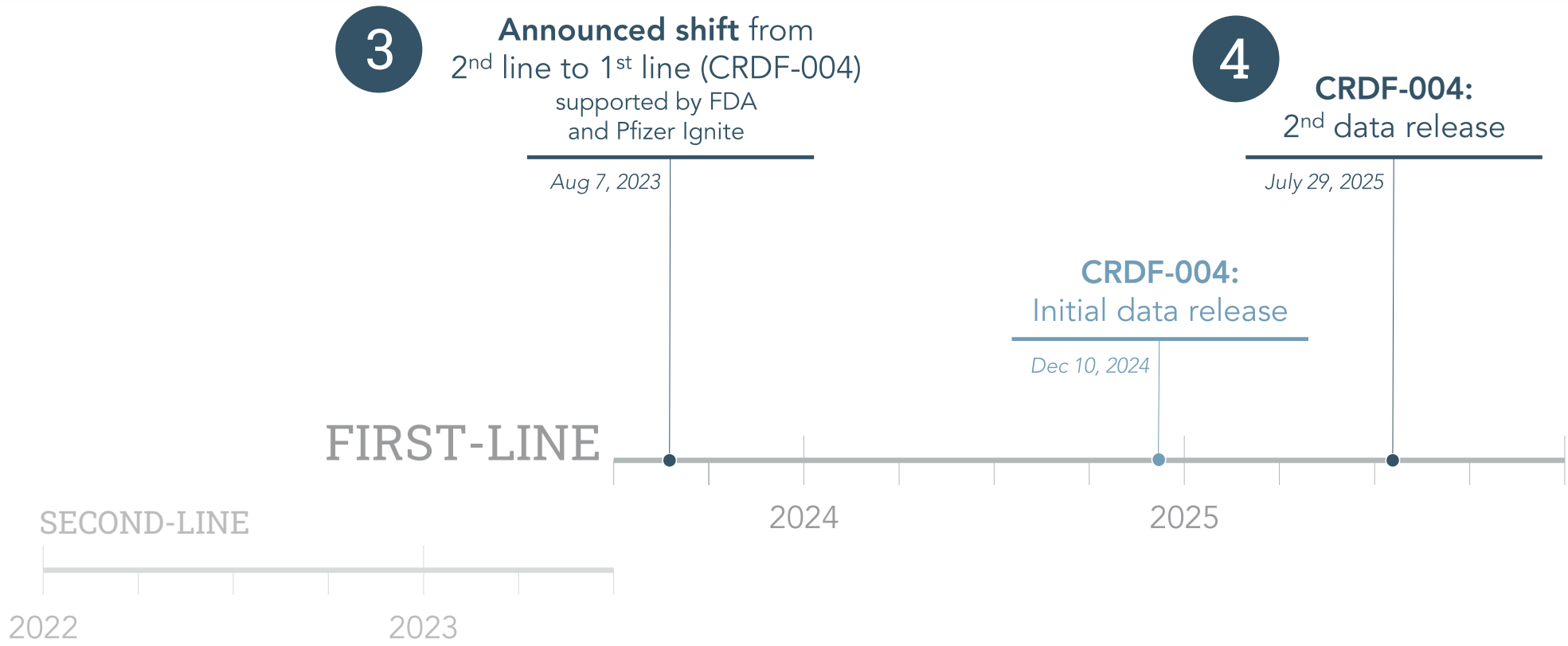
Exquisitely specific for PLK1

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

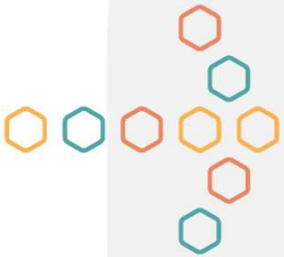


We are encouraged by the initial clinical data from CRDF-004



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

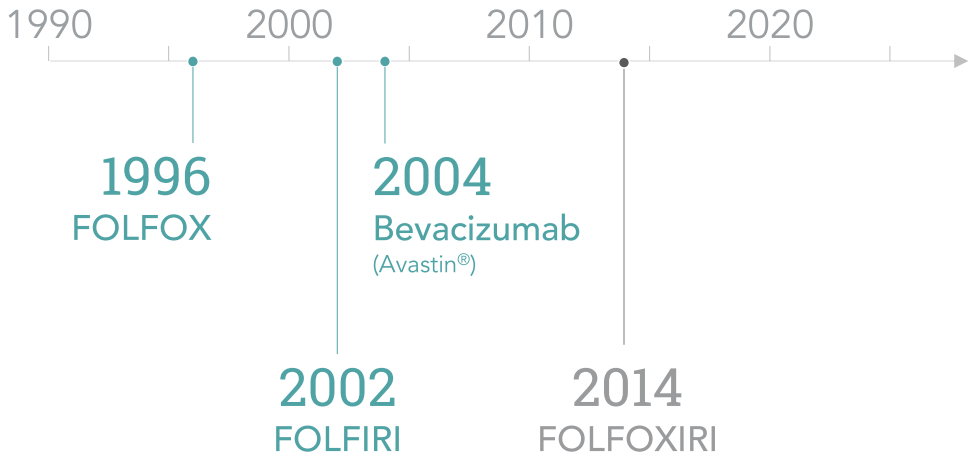
50,000
deaths

For patients with metastatic CRC

15%
5-year relative OS

Less than **12** months
Median PFS

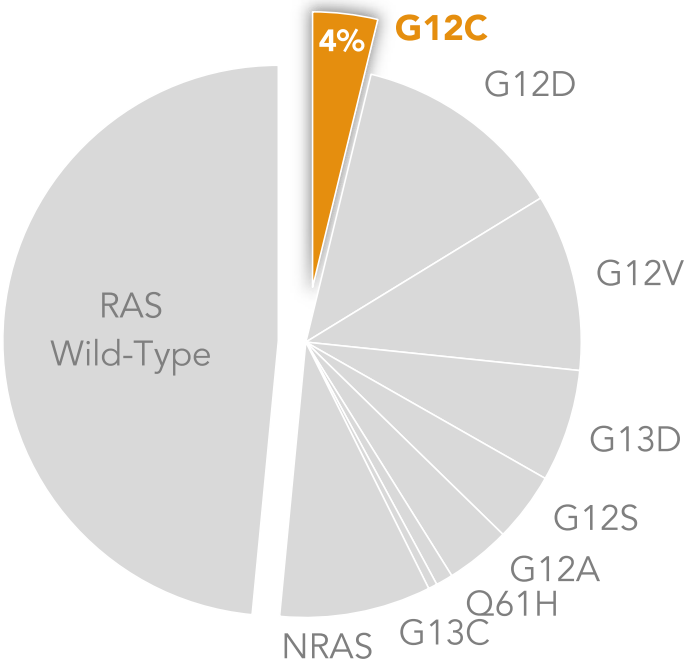
1st LINE STANDARD of CARE
RAS-mutated mCRC



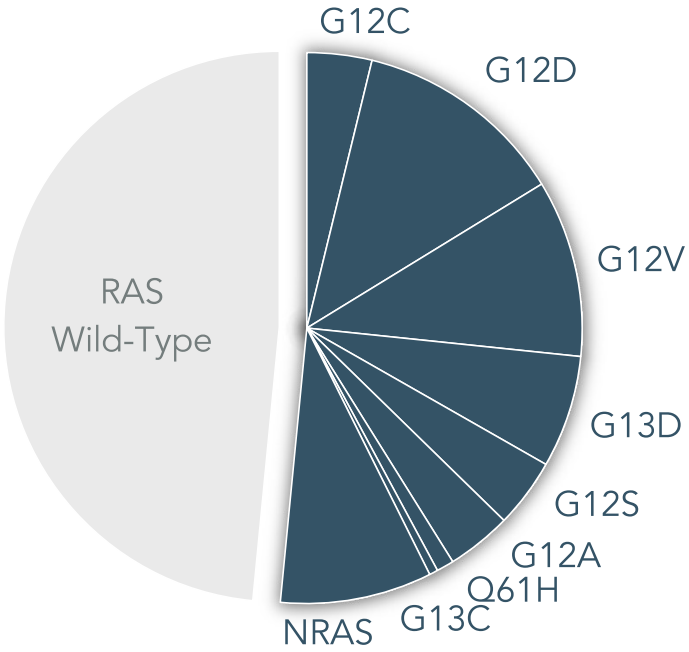
Morris et al., J Clin Oncol 2023, Shi et al., J Clin Oncol 2025. CRC, colorectal cancer; mCRC, metastatic colorectal cancer; mut, mutant; OS, overall survival; PFS, progression free survival

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

KRAS G12C therapies would address a small part of the need[1]



ONVANSERTIB addresses 52% of mCRC cases are RAS-mutated[1]



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

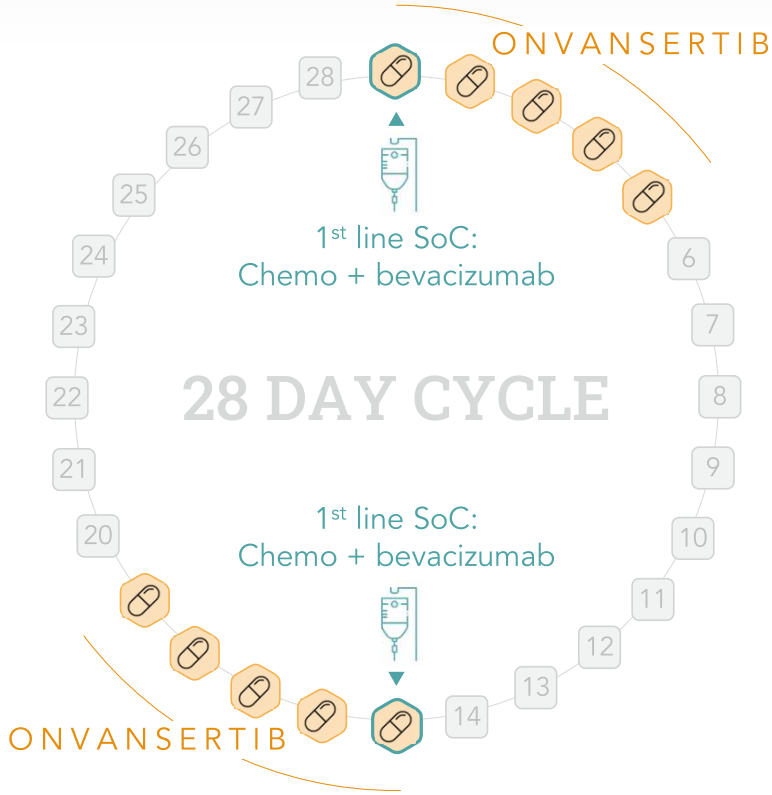
ENROLLMENT CRITERIA

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

R
N=90

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



Patient's tumors are scanned every 8 weeks

ENDPOINTS*

Primary:	ORR
Secondary:	DoR and PFS

* Assessed by blinded independent central review (BICR)

mCRC, metastatic colorectal cancer; ORR, objective response rate; DoR, duration of response; PFS, progression free survival; SoC, standard of care; onv, onvansertib; bev, bevacizumab

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

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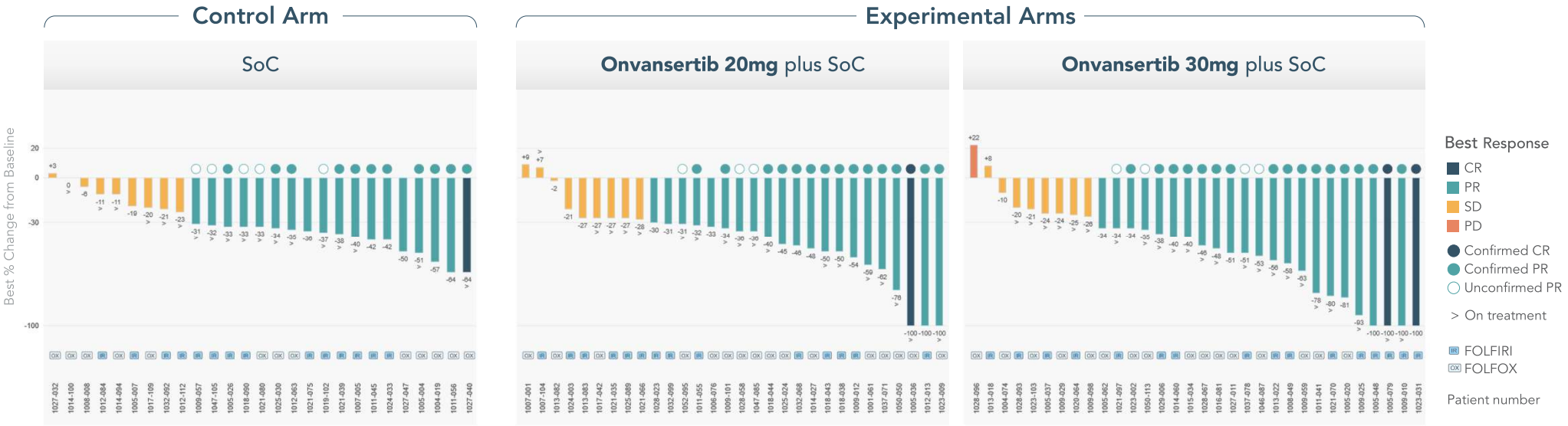
Confirmed ORR at 6 months	22% n=8	33% n=12	46% n=17	
ORR[3] n, [95% CI]	43% n=16 [27–61]	50% n=18 [33–67]	59% n=22 [42–75]	
Best response on trial				
Complete Response (CR)	1 (3%)	1 (3%)	2 (5%)	
Partial Response (PR)	15 (41%)	17 (47%)	20 (54%)	
Unconfirmed (will not confirm) PR/CR	3 (8%)	3 (8%)	1 (3%)	
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. 3. 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*

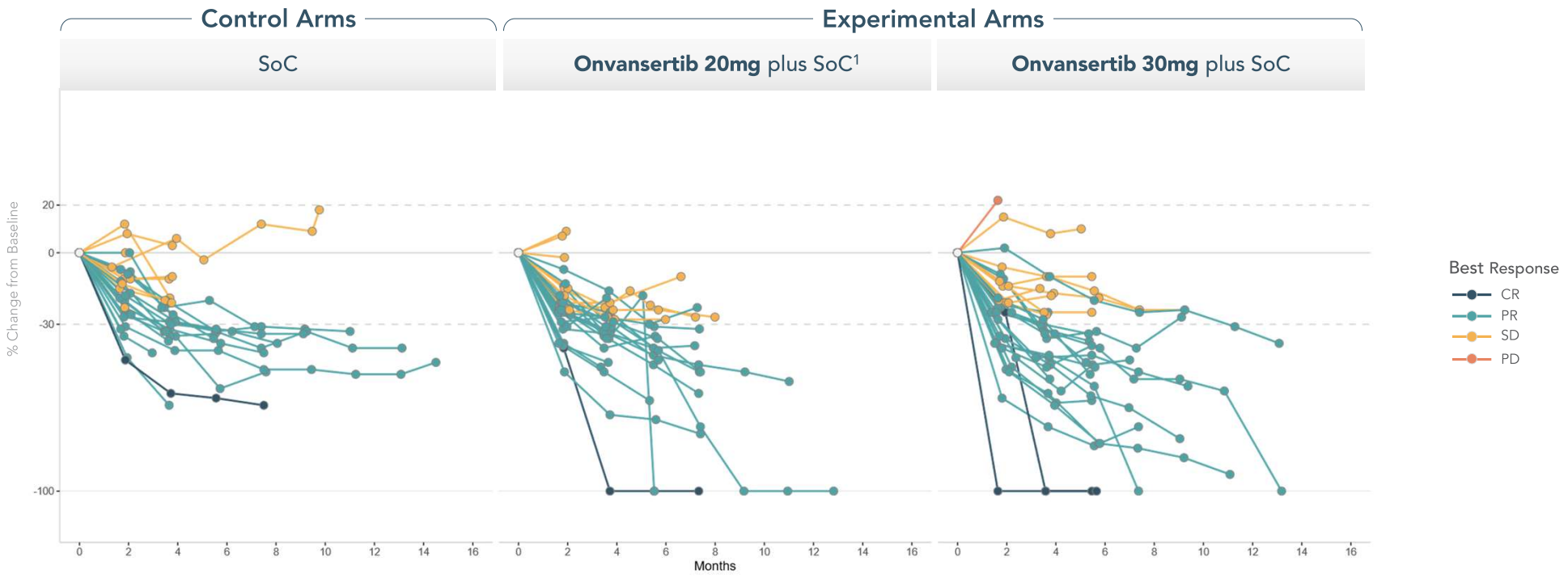
Intent-to-treat (ITT)	Control (SoC alone)	Onv 20mg + SoC	Onv 30mg + SoC
Confirmed ORR[1]	30%	42%	49%
ORR[2]	43%	50%	59%



* 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*

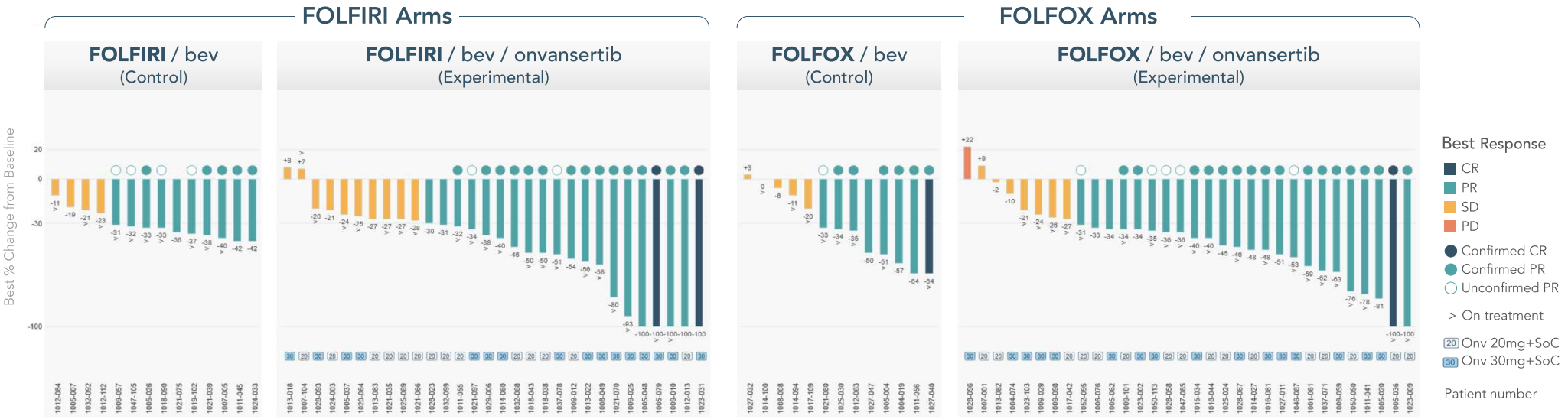


* Radiographic response determined per RECIST 1.1 by blinded independent central review as of July 8, 2025 from an ongoing trial and unlocked database for all patients with measurable disease. 1. Per protocol, patients' tumors are assessed by CT scan every 2 months, and Patient 1012-013 in the 20mg onv 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*

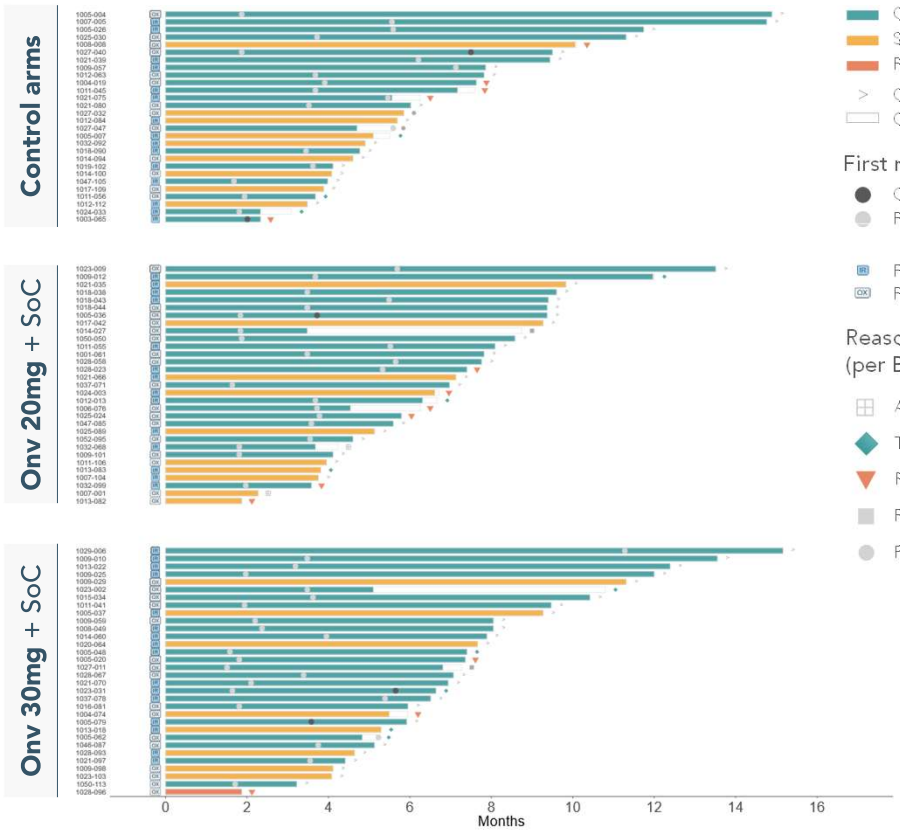
Intent-to-treat (ITT)	FOLFIRI		FOLFOX	
	Control	SoC + Onv	Control	SoC + Onv
Confirmed ORR[1]	26%	44%	33%	46%
ORR[2]	47%	50%	39%	59%



* 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.

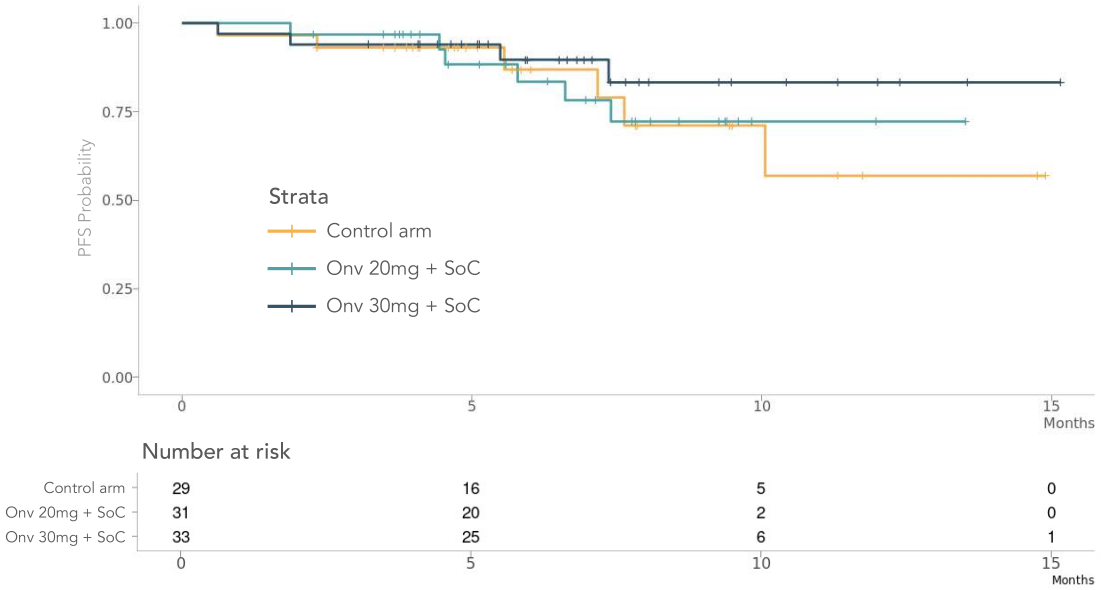
Achieved CR after 6 cycles. Referred for curative surgery.

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*



Censored patients: Control (23/29); 20mg onv+SoC (25/31); 30mg onv+SoC (29/33)

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

OXFORD

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

Early Tumor Shrinkage (ETS)

≥20% reduction in tumor size at 2-month scan.

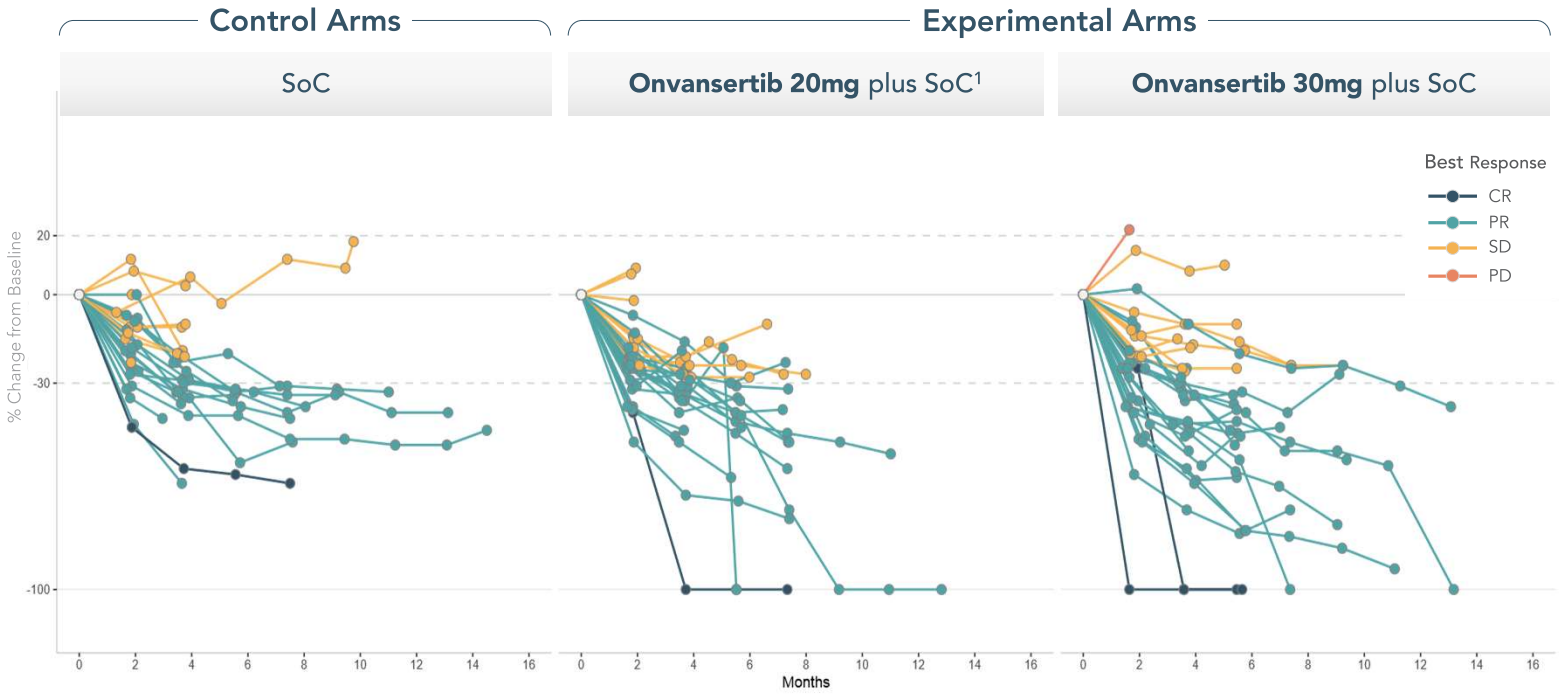
Final data: All patients on trial have had a 2-month scan.

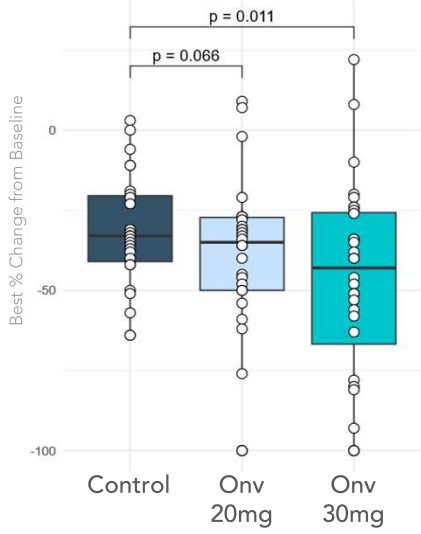
	Previous Ph3 1st Line mCRC Trials[1]				
% of patients with ETS	**TRIBE** RAS WT/mut.	**CRYSTAL** RAS WT	**OPUS** RAS WT	**CRDF-004** RAS mut.	
Control Arm	52%	49%	46%	41% (11/27)	
Experimental Arm	63%	62%	69%	**Onv 20mg** 63% (19/30)	**Onv 30mg** 69% (22/32)
ETS Delta *p-value*	**11%** *0.025*	**13%** *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

Depth of Response (DpR)

Maximum tumor shrinkage at nadir on trial

Interim data: Patients on trial may achieve deeper tumor regression

	Previous Ph3 1st Line mCRC Trials[1]				
% Tumor Shrinkage	**TRIBE** RAS WT/mut.	**CRYSTAL** RAS WT	**OPUS** RAS WT	**CRDF-004** RAS mut.	
Control Arm	38%	33%	31%	32%	
Experimental Arm	43%	51%	58%	**Onv 20mg** 41%	**Onv 30mg** 48%
DpR Delta	**5%**	**18%**	**27%**	**9%** *p-value 0.066*	**16%** *0.011*
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	FOLFIRI/bev/onv 20	FOLFIRI/bev/onv 30	FOLFOX/bev	FOLFOX/bev/onv 20	FOLFOX/bev/onv 30	Total
	(n=17)	(n=17)	(n=18)	(n=17)	(n=17)	(n=18)	(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)	All Control Arms (N=34)		Onv 20mg + SoC (N=34)		Onv 30mg + SoC (N=36)	
N (% of total)	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

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

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

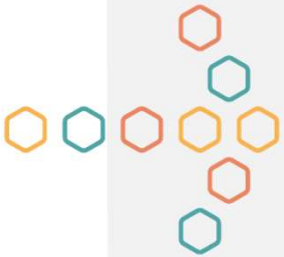
Endpoint for accelerated approval:
- ORR with DoR

Endpoint for full approval:
- PFS / lack of detriment on OS

mCRC, metastatic colorectal cancer; ORR, objective response rate; DoR, duration of response; PFS, progression free survival; OS, overall survival

OUR SHIFT

TO FIRST-LINE RAS-MUTATED mCRC

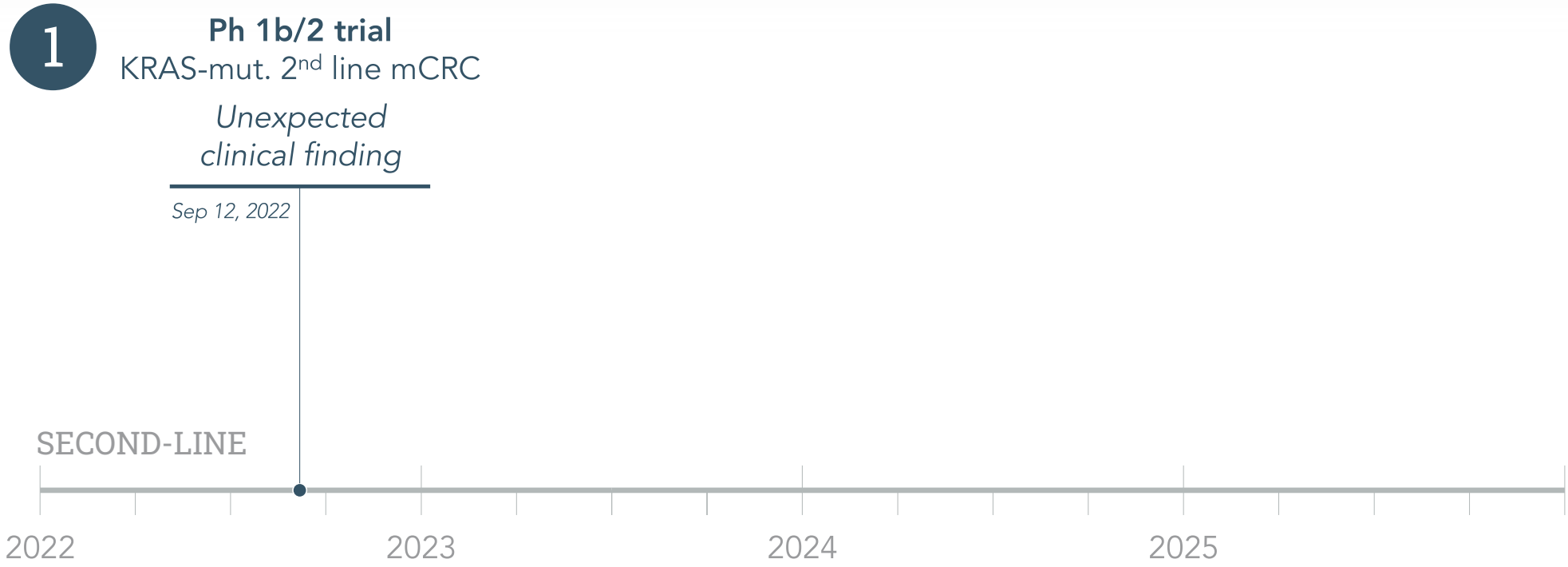


The strength of our 1st-line program

The rationale for our shift from 2nd-line

The coming catalysts

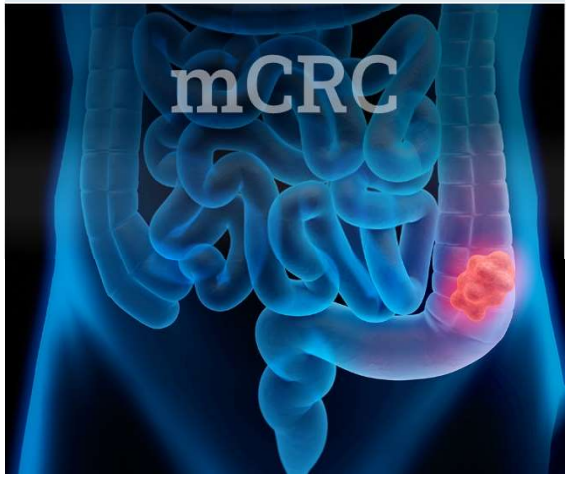
Our second-line phase 1b/2 trial generated a novel finding

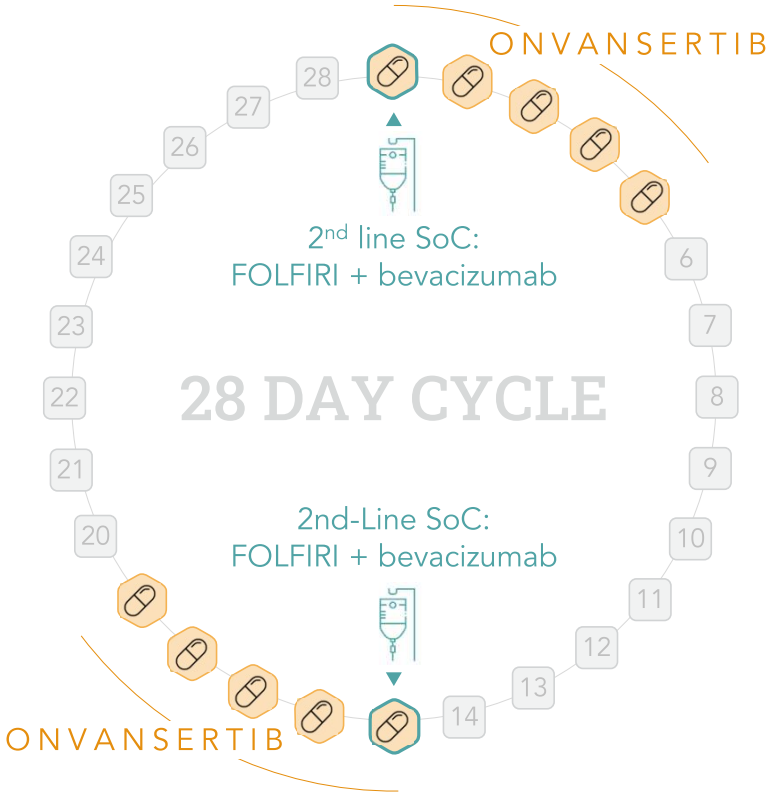


Our Ph1b/2 trial combined onvansertib with the current SoC in 2nd line

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	*chemotherapy*	
Bev (optional)	Yes	No

“bev naïve"

2nd LINE

Cardiff Oncology Phase 1b/2 trial

FOLFIRI	*chemotherapy*
Bev	*antiangiogenic*
Onvansertib	*PLK1 inhibitor*

Ph 1b/2 trial bev naïve patients achieved higher response rates

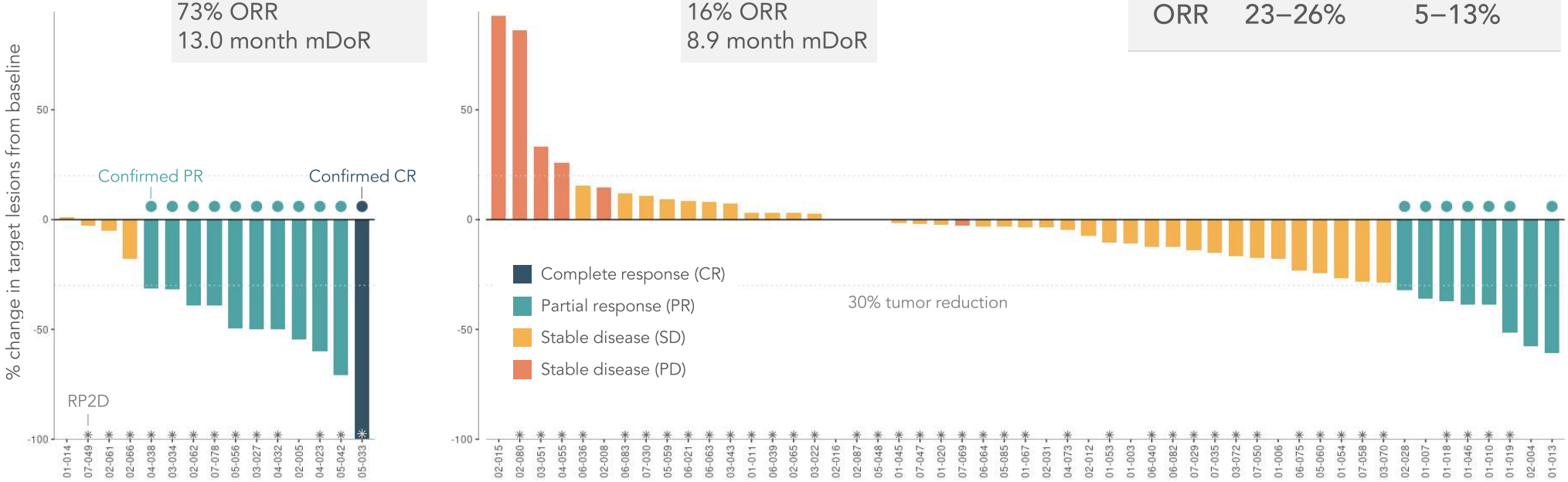
Best Radiographic Response and Duration of Response*

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%

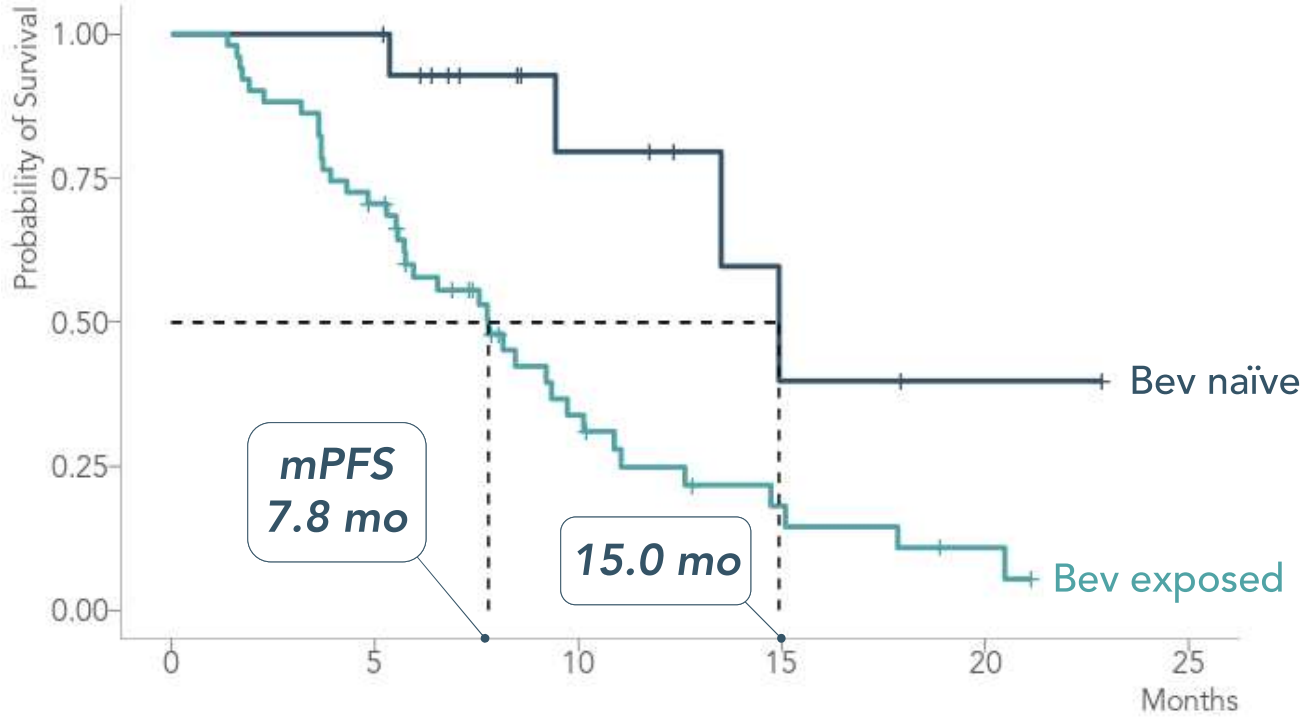


* Radiographic response determined per RECIST 1.1. Waterfall plot and table reflect interim data as of June 16, 2023 from an ongoing trial and unlocked EDC database.

** 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

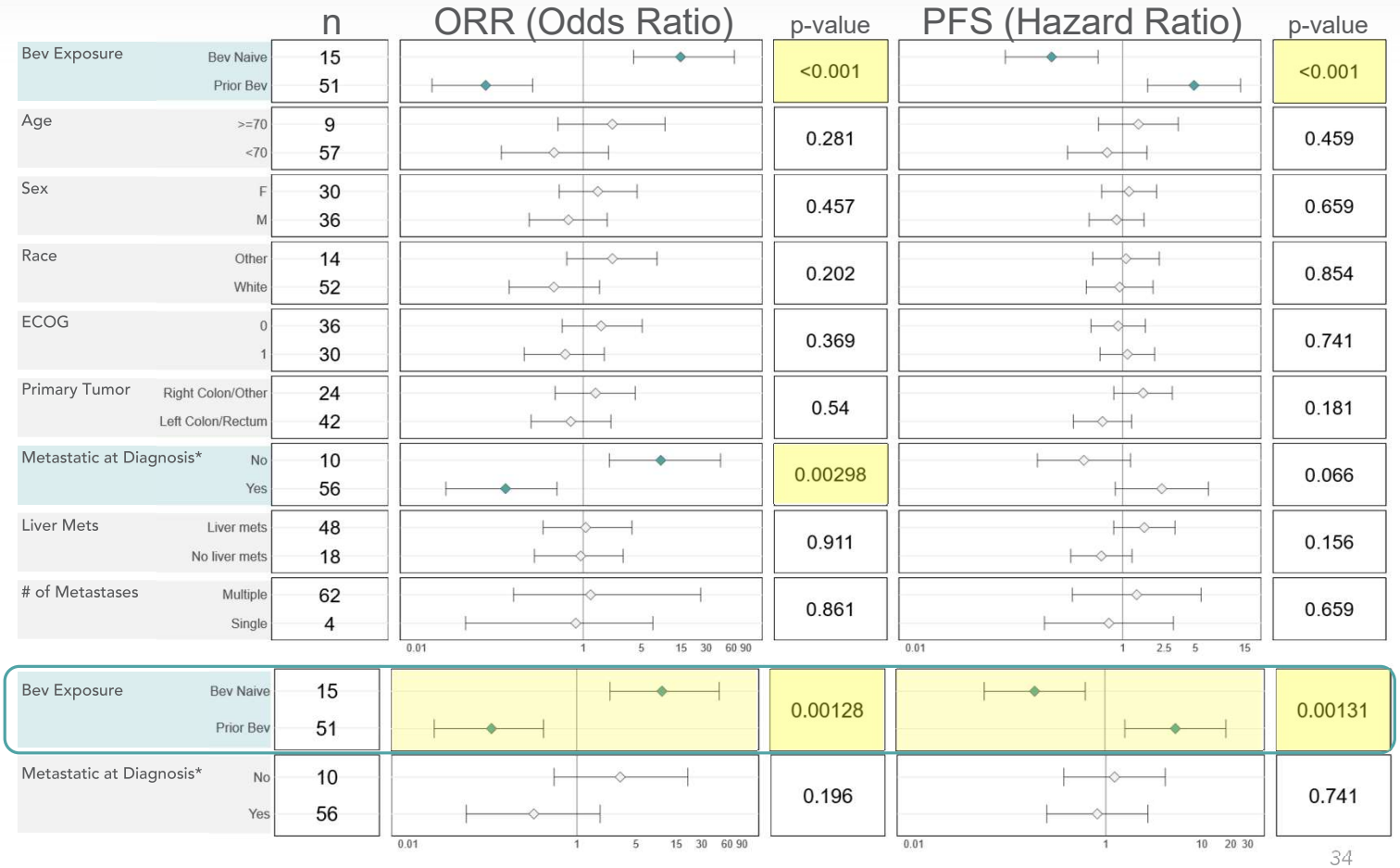
* Onvansertib mPFS are interim data as of June 16, 2023 from an ongoing trial and unlocked EDC database.

** 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. 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.

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

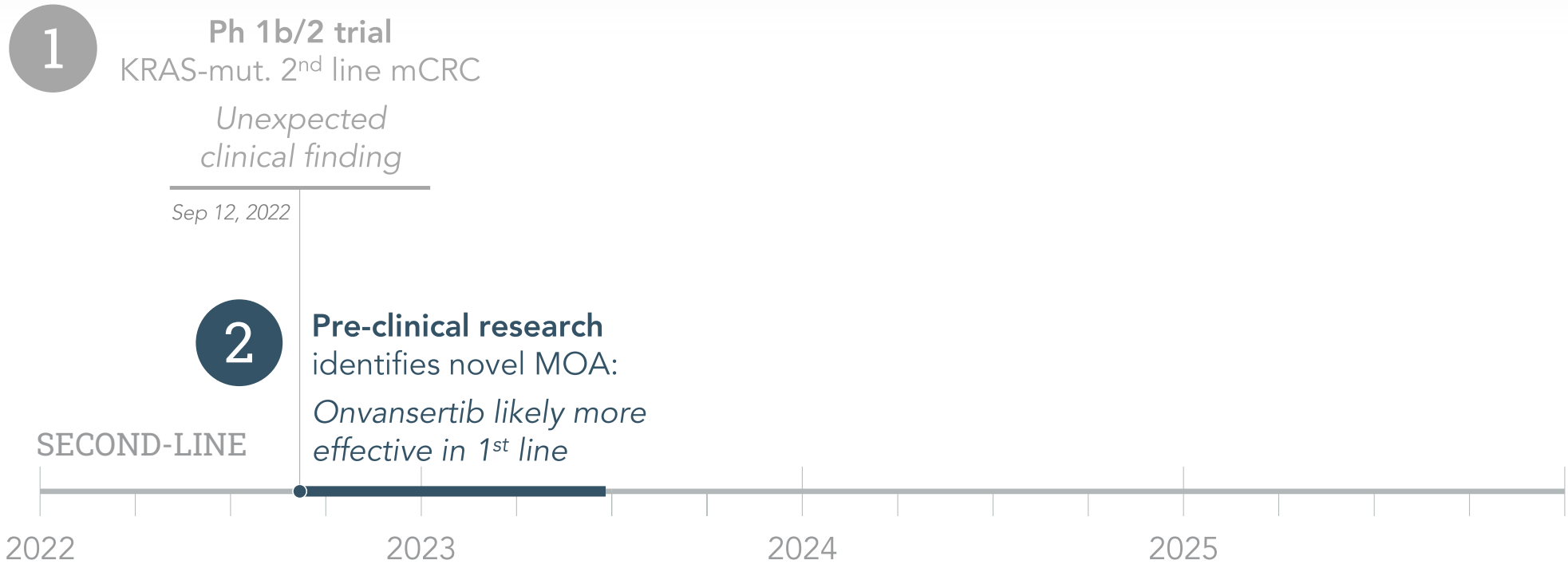
Univariable analysis of baseline characteristics for ORR and PFS indicate superior clinical benefit for bev naïve patients and for patients without metastatic disease at time of diagnosis

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

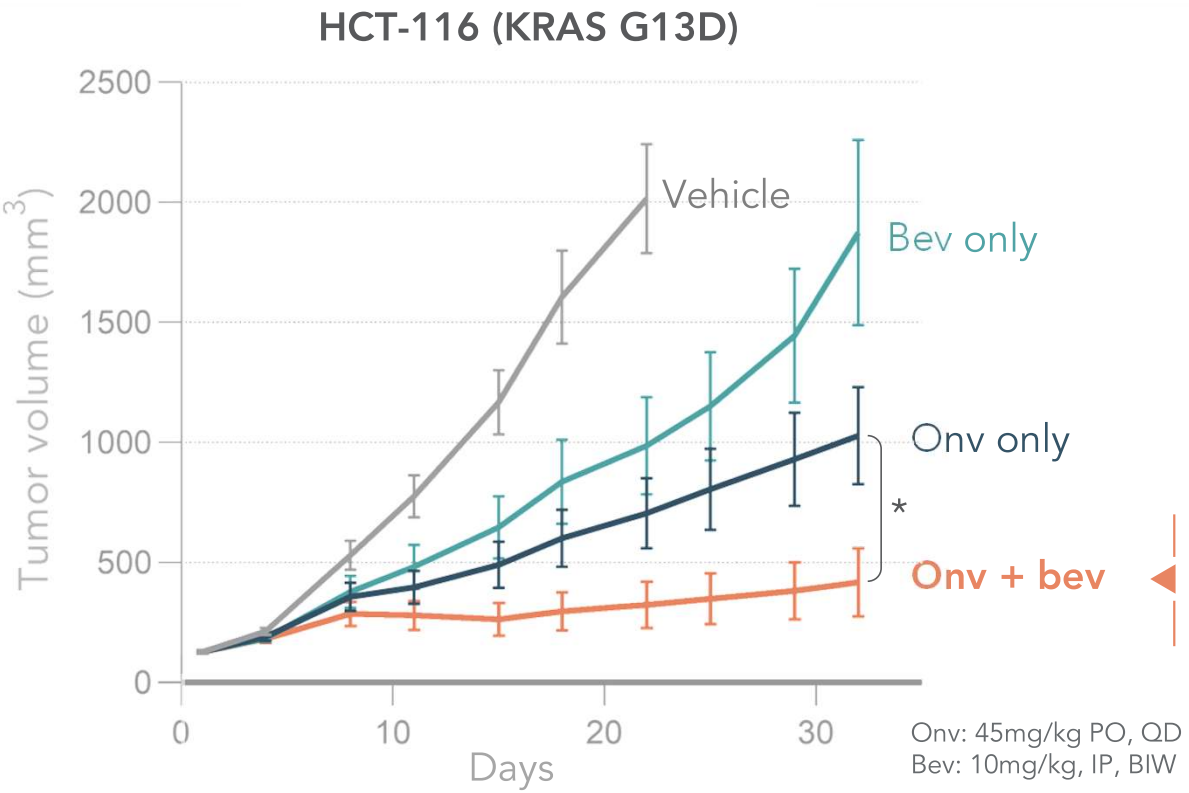


* Metastatic at Diagnosis: "Yes" means the patient's cancer had already metastasized when first diagnosed. "No" means the patient's initial diagnosis was non-metastatic CRC, but developed metastatic disease prior to enrolling in our Ph 1b/2 trial.

Unexpected clinical findings prompted new pre-clinical research



Onvansertib + bev inhibits tumor growth greater than either agent alone

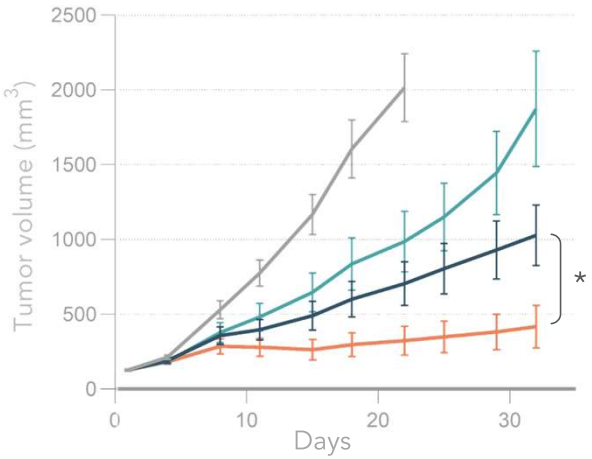


The combination had significant superior anti-tumor activity compared to the single agents

Three KRAS-mutant mCRC xenograft models were treated with vehicle (control), onvansertib, bevacizumab or the combination of onvansertib and bev 8-9mice/ group. Mean ± 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.

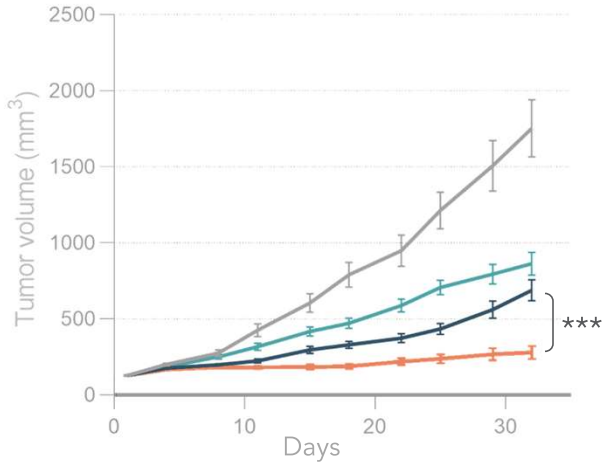
Onvansertib + bev inhibits tumor growth greater than either agent alone

HCT-116 (KRAS G13D)



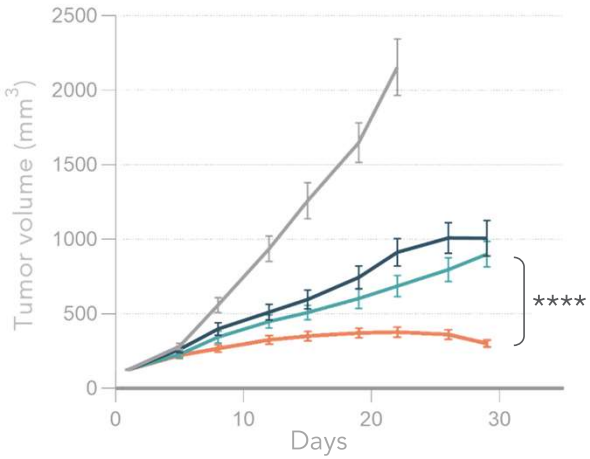
Onv: 45mg/kg PO, QD
Bev: 10mg/kg, IP, BIW

LoVo (KRAS G13D)



Onvansertib 45mg/kg PO, QD
Bev 5mg/kg, IP, BIW

SW620 (KRAS G12V)

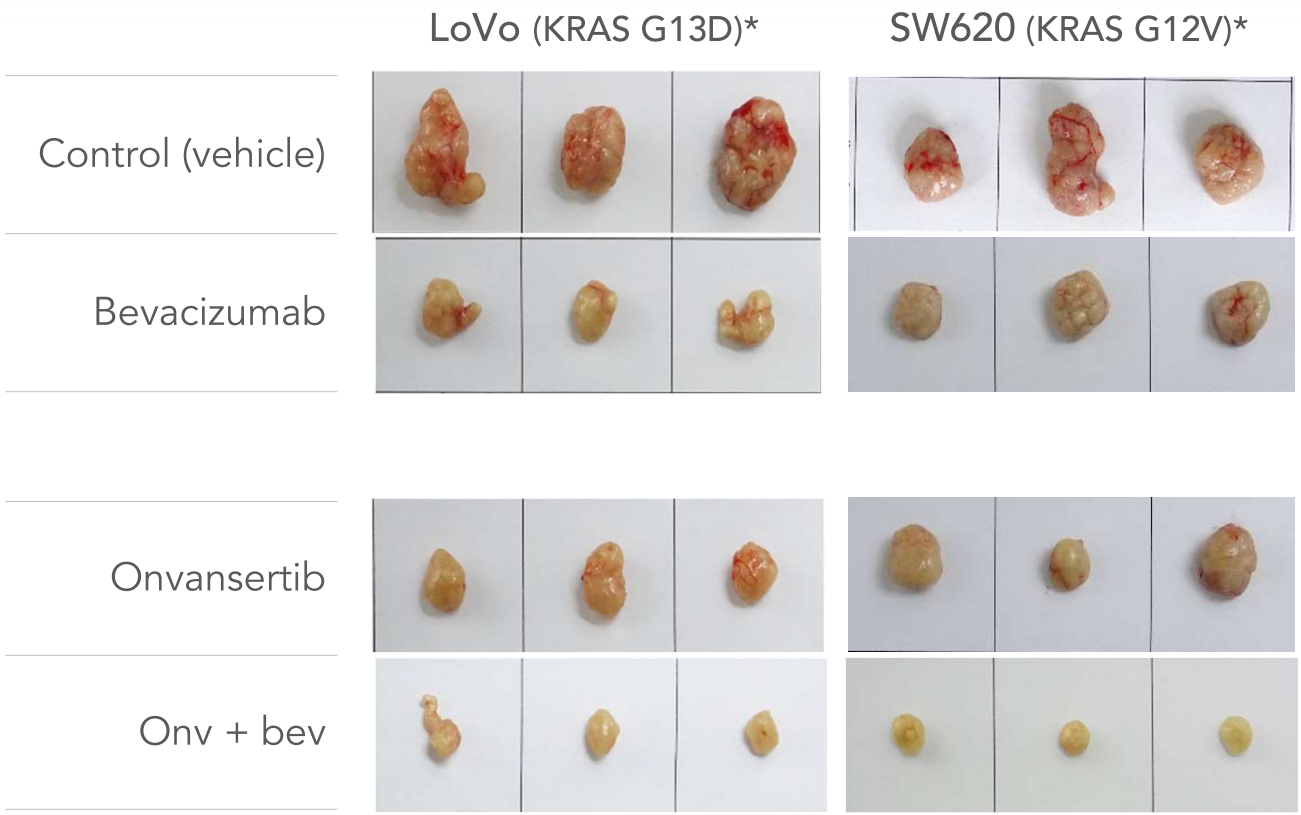


Onvansertib 45mg/kg PO, QD
Bev 1mg/kg, IP, BIW

Vehicle
Bev only
Onv only
Onv + bev

Three KRAS-mutant mCRC xenograft models were treated with vehicle (control), onvansertib, bevacizumab or the combination of onvansertib and bev 8-9mice/ group. Mean ± 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.

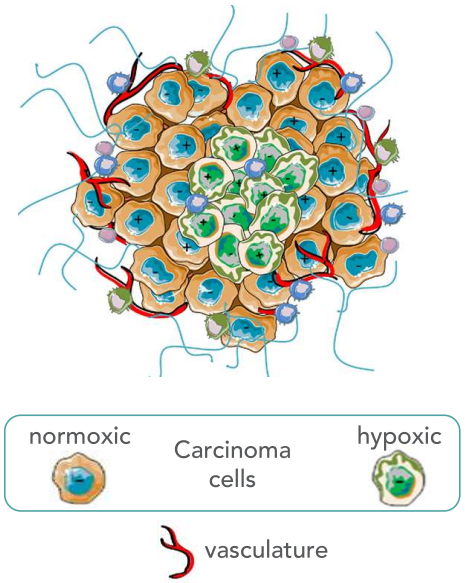
HIF1α plays a critical role in a tumor's response to hypoxia

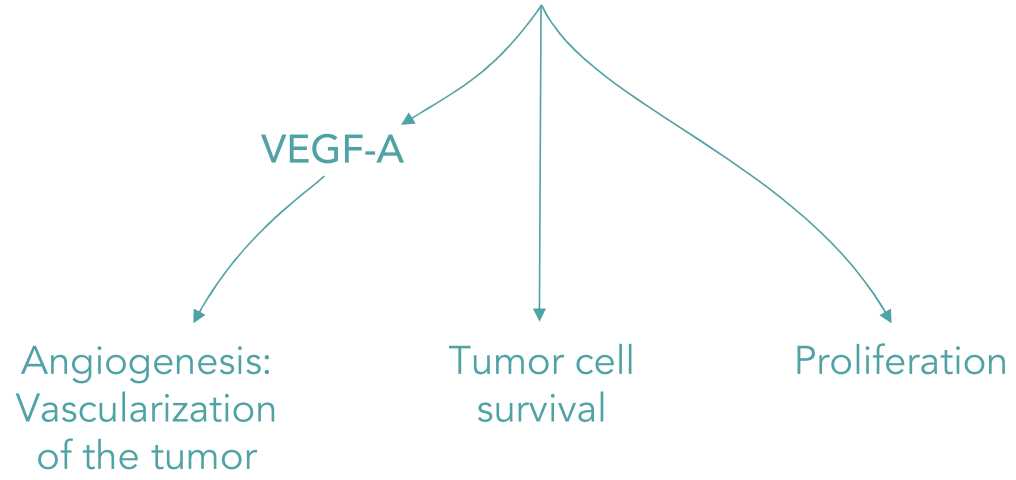
Tumor growth → Hypoxia → HIF1α

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

… low oxygen levels lead to elevated HIF1α protein expression

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





https://www.frontiersin.org/journals/immunology/articles/10.3389/fimmu.2017.01625/full

Bev inhibits tumor angiogenesis by neutralizing VEGF-A

Tumor growth → Hypoxia → HIF1α

Tumor growth

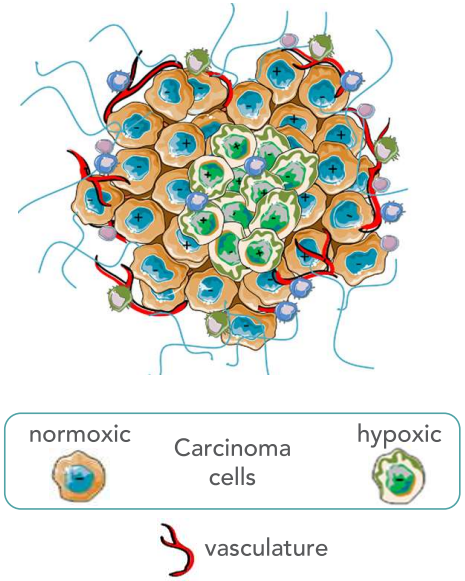
The tumor cells outgrow the blood supply and become starved of oxygen and nutrients…

Hypoxia

… low oxygen levels lead to elevated HIF1α protein expression

HIF1α

… 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

https://www.frontiersin.org/journals/immunology/articles/10.3389/fimmu.2017.01625/full

Onvansertib restricts tumor's broader ability to adapt to hypoxia

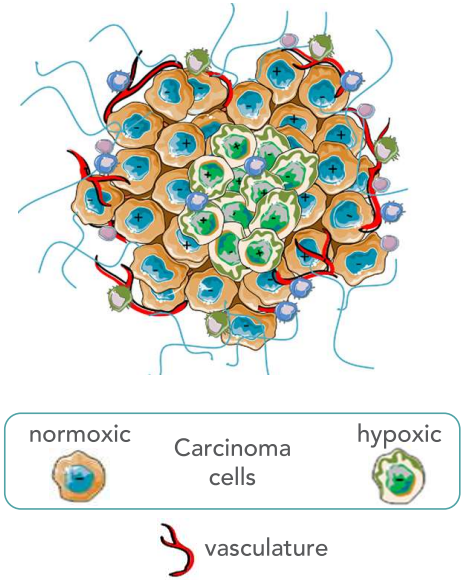
Tumor growth → **Hypoxia** → **HIF1α** ⊣ **onvansertib**

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

… low oxygen levels lead to elevated HIF1α protein expression

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

onvansertib inhibits HIF1α expression



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- Angiogenesis: Vascularization of the tumor
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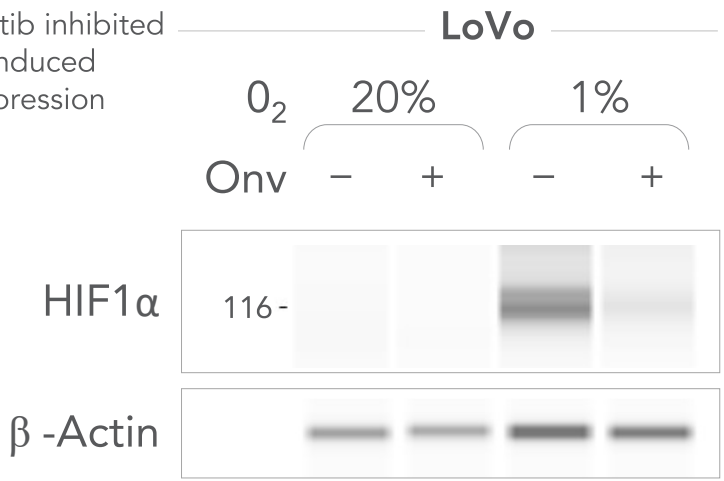
Onvansertib inhibits the hypoxia signaling pathway by downregulating HIF1α expression

PLK1 inhibition in LoVo RAS-mutant CRC cell lines[1]

Onvansertib inhibited hypoxia-induced HIF1α expression

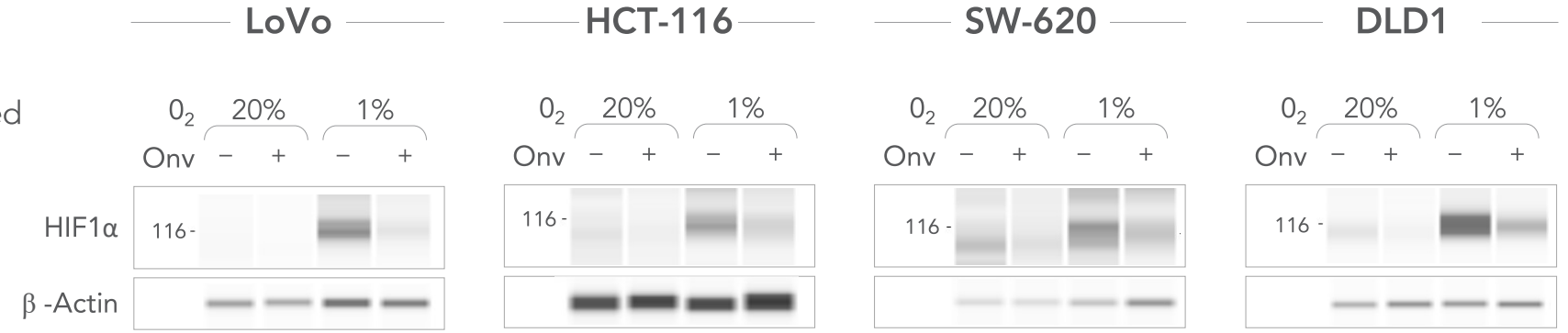


PLK1 inhibition using siRNA against PLK1 (siPLK1)[2] prevented hypoxia-induced HIF1α expression

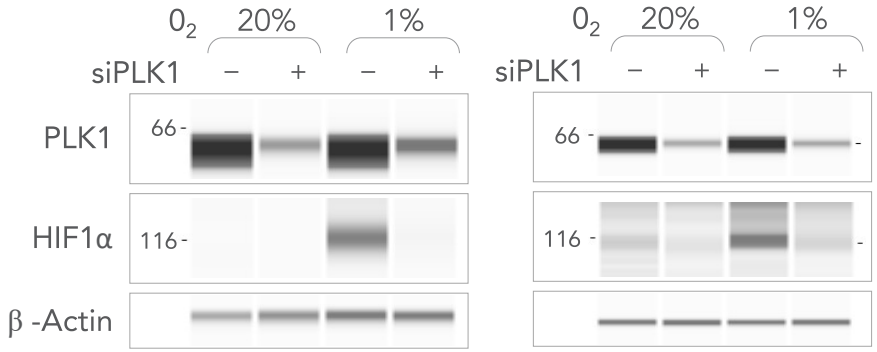
1. KRAS-mutant CRC cell lines were cultured under normoxia (20%O_2) or hypoxia (1%O_2), in the presence (+) or absence (-) of onvansertib. HIF1α expression was induced under hypoxia.
2. LoVo and HCT116 cells were transfected with siRNA control (-) or siRNA targeting PLK1 (siPLK1) and then exposed to 20% or 1%O_2. Cells were collected 24h after transfection.

Onvansertib inhibits the hypoxia signaling pathway by downregulating HIF1α expression

In 4 RAS-mutant CRC cell lines[1], onvansertib inhibited hypoxia-induced HIF1α expression

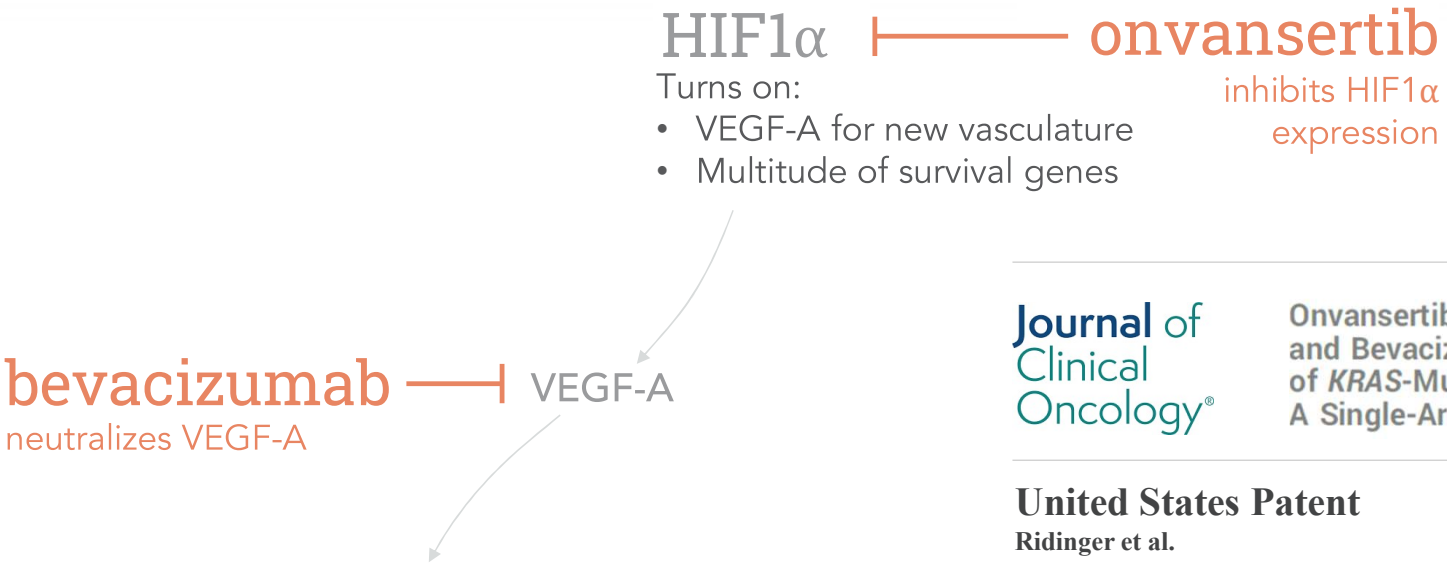


PLK1 inhibition using siRNA against PLK1 (siPLK1)[2] prevented hypoxia-induced HIF1α expression



1. KRAS-mutant CRC cell lines were cultured under normoxia (20%O_2) or hypoxia (1%O_2), 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%O_2. Cells were collected 24h after transfection.

Novel mechanism of action strengthened our intellectual property



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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.:** **Date of Patent:** **Expiration:**	**US 12,144,813 B2** **Nov. 19, 2024** **Not before 2043**
United States Patent **Ridinger et al.**	**Patent No.:** **Date of Patent:** **Expiration:**	**US 12,263,173 B2** **Apr. 1, 2025** **Not before 2043**

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

Journal of Clinical Oncology®

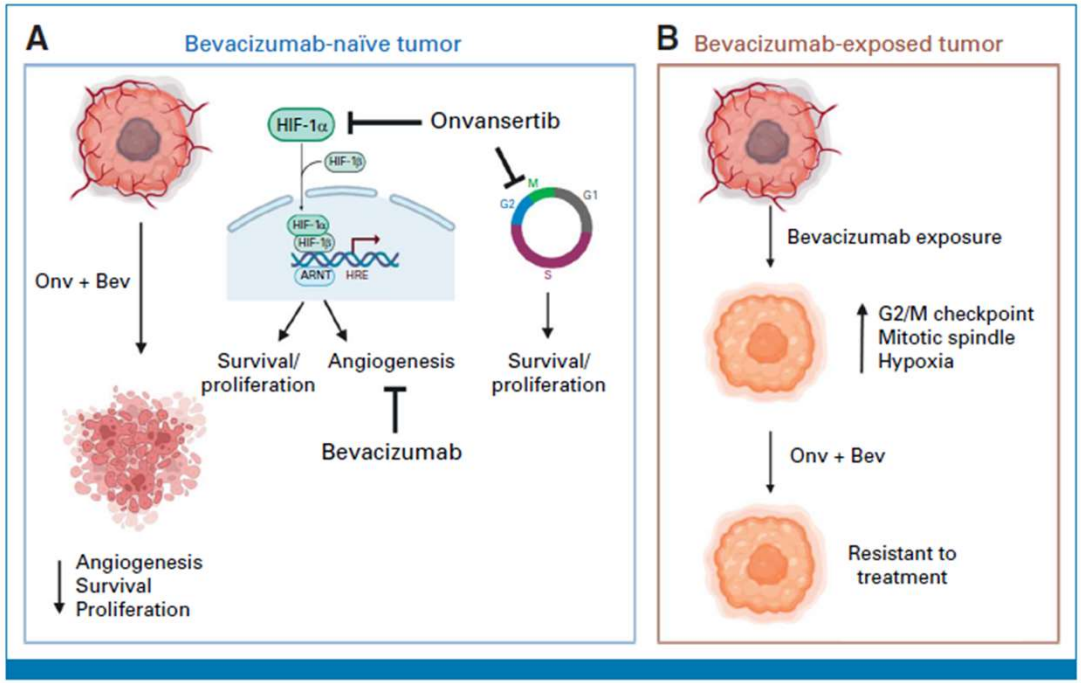
MOA

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

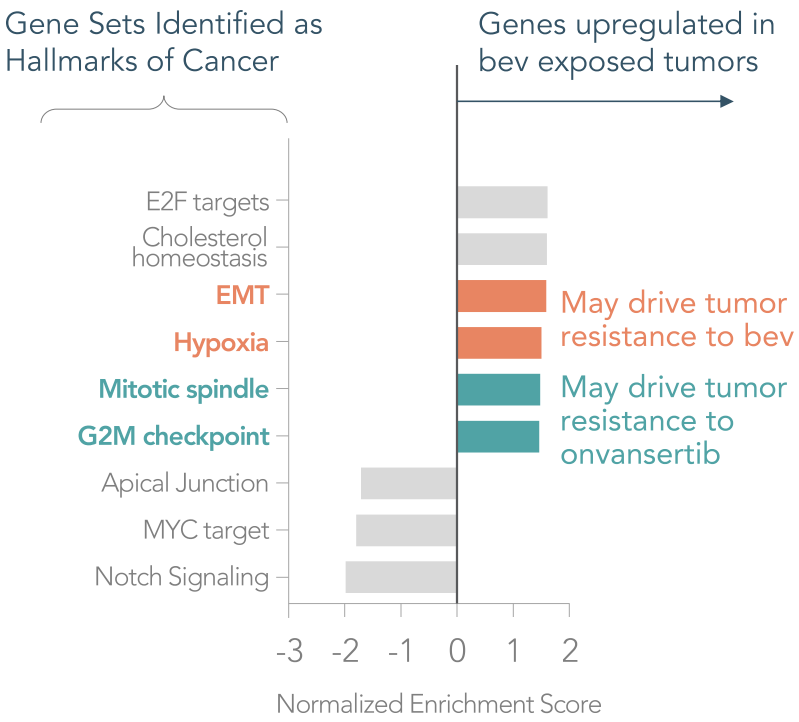
TEMPUS
Tumor Biopsy Library

135 biopsies:

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

Bev naïve	vs.	Bev exposed
1st line: FOLFOX n=71		1st line: FOLFOX+bev n=64

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



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

Onvansertib

First well-tolerated PLK1-selective inhibitor

2nd line KRAS-mut. mCRC program

Ph 1b/2 data

High efficacy in bev naïve patients

Shift to 1st line

Strong support

- 2nd line data
- FDA agreed path to 1st line accelerated approval
- Pfizer: clinical execution in 1st line

Clinical signal from CRDF-004 1st trial

Encouraging data

- 49% confirmed response rate for 30 mg onv + SoC
- 30% confirmed response rate for SoC alone

Additional clinical data

from our 1st 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)	1st line	CRDF-004 (w/Pfizer)		randomized		FOLFIRI/bev and FOLFOX/bev
	2nd line	Ph 1b/2		completed		FOLFIRI/bev
	2nd line	CRDF-003 (ONSEMBLE)		completed		FOLFIRI/bev
mPDAC	1st line	Ph 2	KU Medical Center, The University of Kansas			NALIRIFOX
	2nd line	Ph 2		completed		Nal-IRI/leucovorin/ 5-FU
SCLC	2nd line	Ph 2	University of Maryland Marlene and Stewart Greenebaum Comprehensive Cancer Center			None (monotherapy)
TNBC	2nd line	Ph 2	Dana-Farber Cancer Institute			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

Cardiff Oncology™

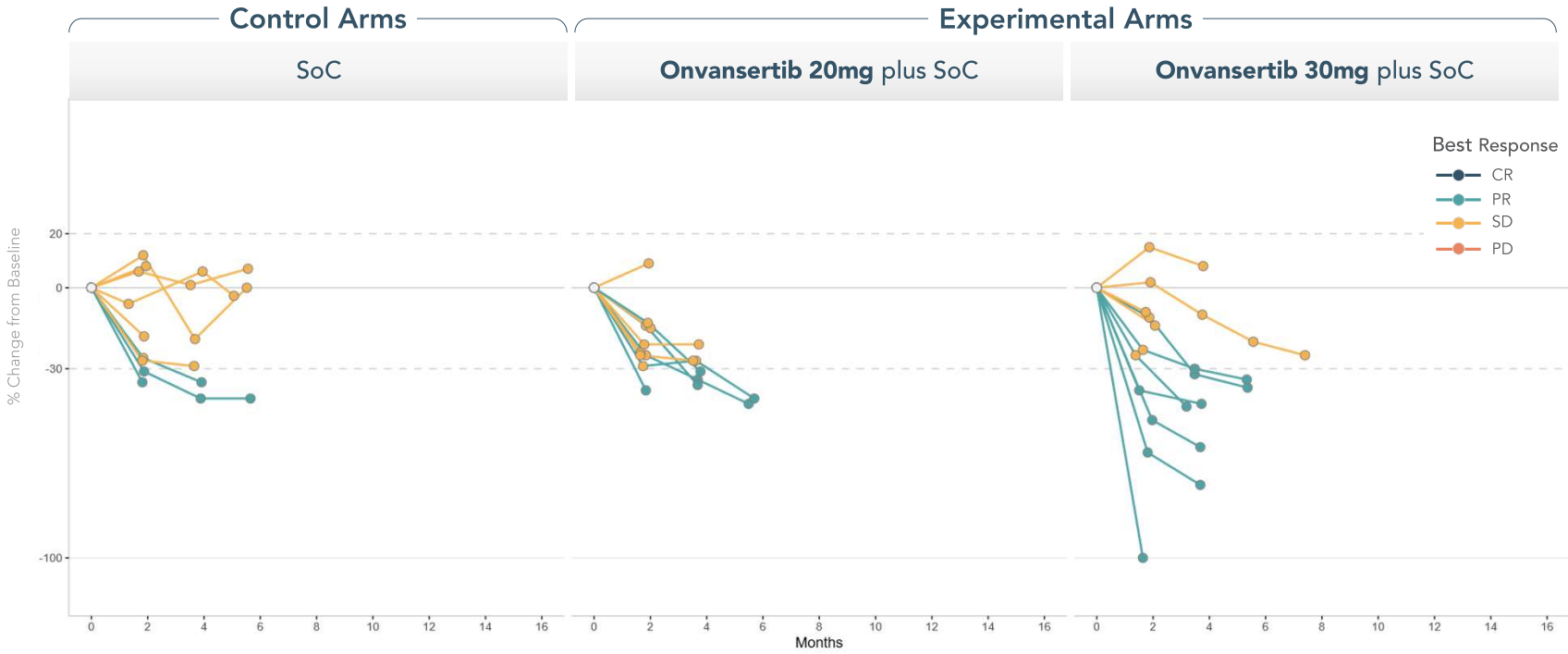
Appendix

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 over Time* – as of November 26, 2024

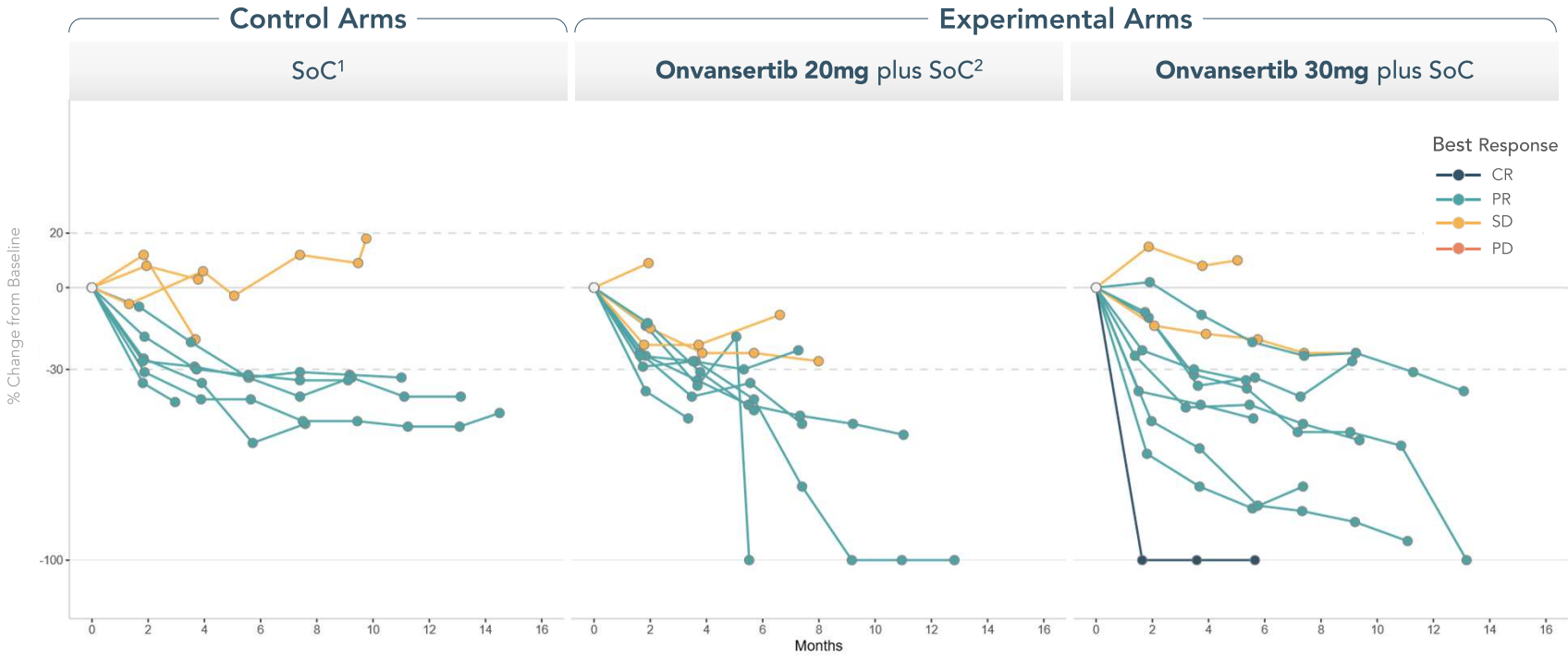


* Radiographic response determined per RECIST 1.1 by blinded independent central review as of November 26, 2024 from an ongoing trial and unlocked database. Response data for one control arm patient changed from the November 26, 2024 data cut as a result of the radiologist at the blinded independent 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

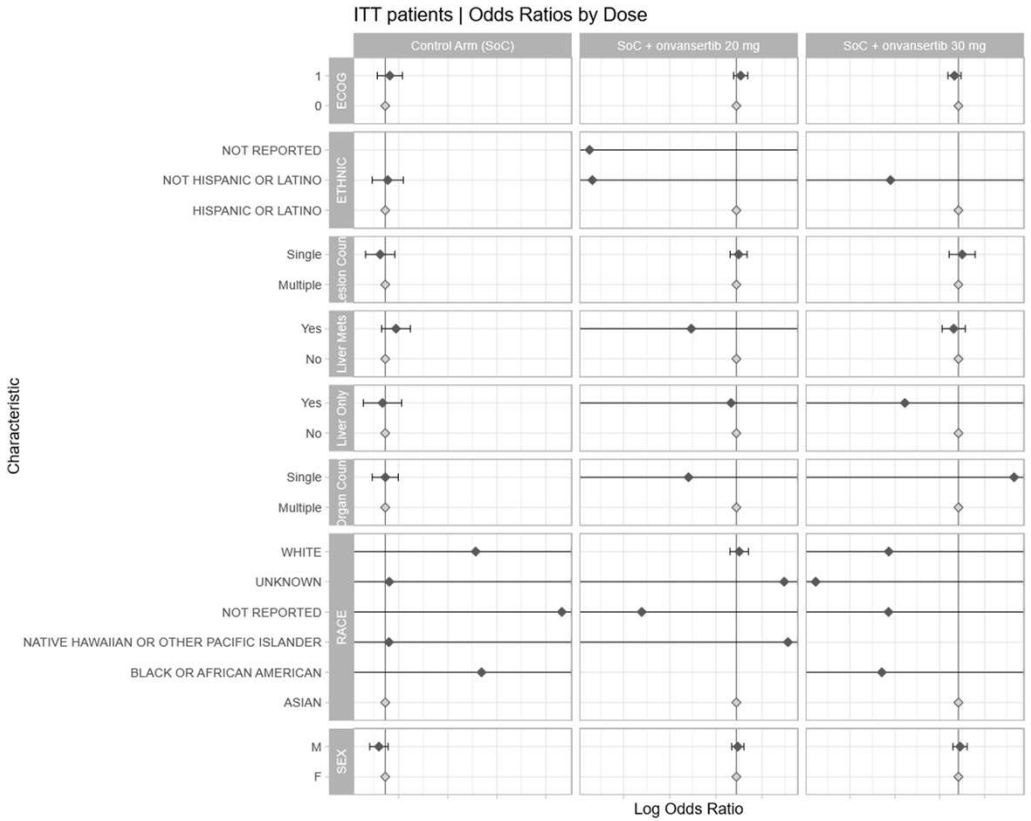
Radiographic Response over Time* – as of July 8, 2025



* 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

Ph 1b/2 trial's patient demographics reflect 2nd line mCRC population

Enrollment*

Number of Patients (N)	Phase 1b, Dose Level 0 Onvansertib 12 mg/m^2	Phase 1b, Dose Level +1 Onvansertib 15 mg/m^2	Phase 1b, Dose Level +2 Onvansertib 18 mg/m^2	Phase 2 RP2D Onvansertib 15 mg/m^2	Total Patients All Doses
Treated	6	6	6	50	68

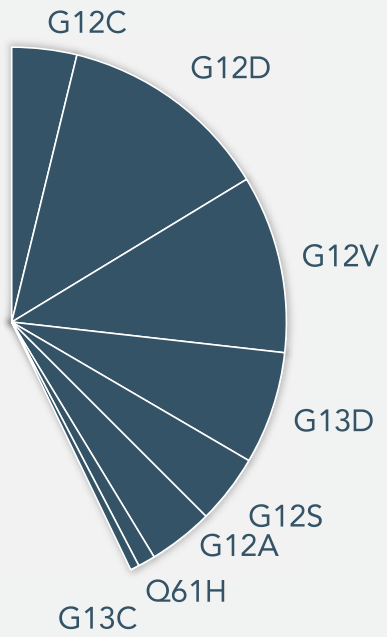
Total Patients N=68	Median [range] or n (%)
Age (years)	56 [34-83]
Sex	
Male	37 (54%)
Female	31 (46%)
ECOG	
0	36 (53%)
1	32 (47%)
Primary tumor site	
Colon	44 (65%)
Rectum	22 (32%)
Other	2 (3%)

Total Patients N=68	Median n (%)
Liver metastasis	
None	20 (29%)
Liver and other	36 (53%)
Liver only	12 (18%)
Number of metastatic organs	
None	1 (1.5%)
1	4 (6%)
≥2	63 (92.5%)
Prior bevacizumab treatment	
Yes	51 (75%)
No	17 (25%)

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

Ph 1b/2 trial patients achieved responses across KRAS mutations

Frequency of Common KRAS Mutations in mCRC[1]



Onvansertib responses across KRAS mutations (as of June 16, 2023)[2]

KRAS Variant	Bev naïve			Bev exposed			
	CR+PR	SD	PD	PR	SD	PD	Total
G12D	3	1		4	12	1	21
G12V	1				10	2	13
G13D	2			2	4		8
G12A	3	1		1	2		7
G12C	1				2	1	4
G12S		1			2	1	4
A146T				1	2		3
Q61H	1	1			1		3
K117N					1	1	2
G12R					1		1
Total	11	4	0	8	37	6	66

1. Jones R et al. Br J Cancer. 2017 Mar 28;116(7):923-929.
2. One patient that was categorized as G12A in the August 2023 data release has now been updated as G12R.

Ph 1b/2 trial bev naïve patients experienced more durable responses

Swimmer plot* – 66 evaluable patients (as of June 16, 2023)

	All patients	Bev naïve	Bev exposed
Pursued surgery / ablation	18% (12/66)	53% (8/15)	8% (4/51)
Initial PR at 8 week scan	9	8	1
Initial PR at 16+ week scan	10	3	7

* Swimmer plot / table reflect interim data as of June 16, 2023 from an ongoing trial and unlocked EDC database. After external review of the tumor measurements completed May 12, 2023, it was determined that patients 02-028 and 04-038 were confirmed PRs.

Ph 1b/2 trial: onvansertib in combination with FOLFIRI-bev is well-tolerated*

- All treated patients (N=68)
  - All dose levels (12mg/m^2, 15mg/m^2, 18mg/m^2)
- No major / unexpected toxicities are seen as compared to FOLFIRI / bev
- 8 G4 hematologic AEs occurred
  - All resolved without issue through dose holds, including the removal of the 5-FU bolus (as per NCCN Guidelines), and/or growth factor support
  - None of the 8 patients discontinued treatment due to these AEs

TEAE	GR1	GR2	GR3	GR4	TOTAL		TEAE	GR1	GR2	GR3	GR4	TOTAL	
Fatigue	24	22	7	0	53	78%	Cough	11	0	0	0	11	16%
Neutropenia	1	18	23	7	49	72%	Pyrexia	8	1	1	0	10	15%
Nausea	29	13	4	0	46	68%	Dyspnea	7	3	0	0	10	15%
Diarrhea	21	13	4	0	38	56%	AST Increase	7	2	1	0	10	15%
Leukopenia	9	14	5	1	29	43%	Lymphocytopenia	2	7	0	0	9	13%
Anemia	22	5	2	0	29	43%	Dyspepsia	9	0	0	0	9	13%
Alopecia	20	5	0	0	25	37%	ALT Increase	8	0	1	0	9	13%
Abdominal Pain	14	8	3	0	25	37%	Hypocalcemia	9	0	0	0	9	13%
Stomatitis	15	6	3	0	24	35%	Insomnia	9	0	0	0	9	13%
Hypertension	4	10	9	0	23	34%	Dehydration	1	5	2	0	8	12%
Thrombocytopenia	17	5	1	0	23	34%	Hypokalemia	6	2	0	0	8	12%
Constipation	17	2	1	0	20	29%	Arthralgia	6	2	0	0	8	12%
Vomiting	11	6	3	0	20	29%	Hand / Foot Syndrome	5	2	0	0	7	10%
Epistaxis	15	0	0	0	15	22%	Hemorrhoids	5	2	0	0	7	10%
Headache	13	0	0	0	13	19%	Non-Cardiac Chest Pain	6	1	0	0	7	10%
Decreased Appetite	4	6	2	0	12	18%	ALP Increase	5	1	1	0	7	10%
Back Pain	10	2	0	0	12	18%							

* Data consists of all adverse events entered into the EDC as of June 13, 2023, from an ongoing trial and unlocked EDC database. N: number of patients (total N=68); events shown occurred in ≥10% of 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. TEAEs: Treatment Emergent Adverse Events; TOTAL shows the absolute # of patients and (%) of the population. COVID, as an AE, is not included as that data is still under review and being tabulated.

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

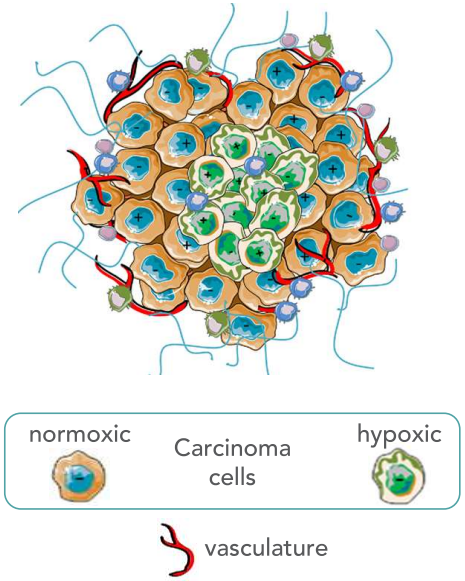
Tumor growth → **Hypoxia** → **HIF1α** ⊣ **onvansertib**

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

… low oxygen levels lead to elevated HIF1α protein expression

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

onvansertib: inhibits HIF1α expression



bevacizumab ⊣ VEGF-A

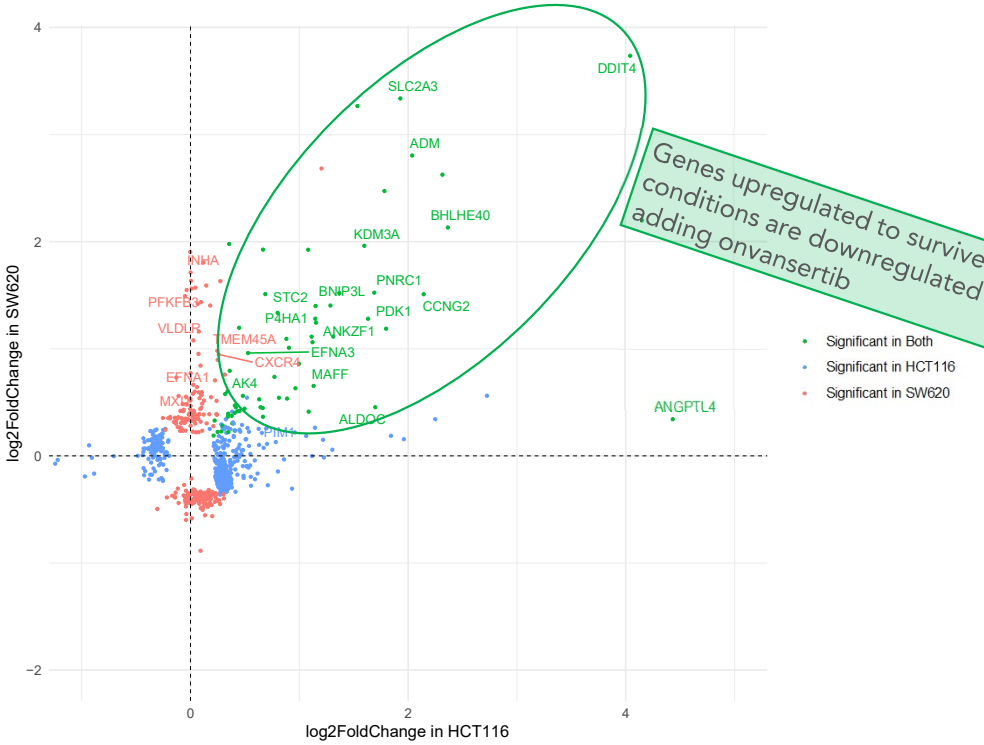
neutralizes VEGF-A

- Angiogenesis: Vascularization of the tumor
- Tumor cell survival
- Proliferation

https://www.frontiersin.org/journals/immunology/articles/10.3389/fimmu.2017.01625/full

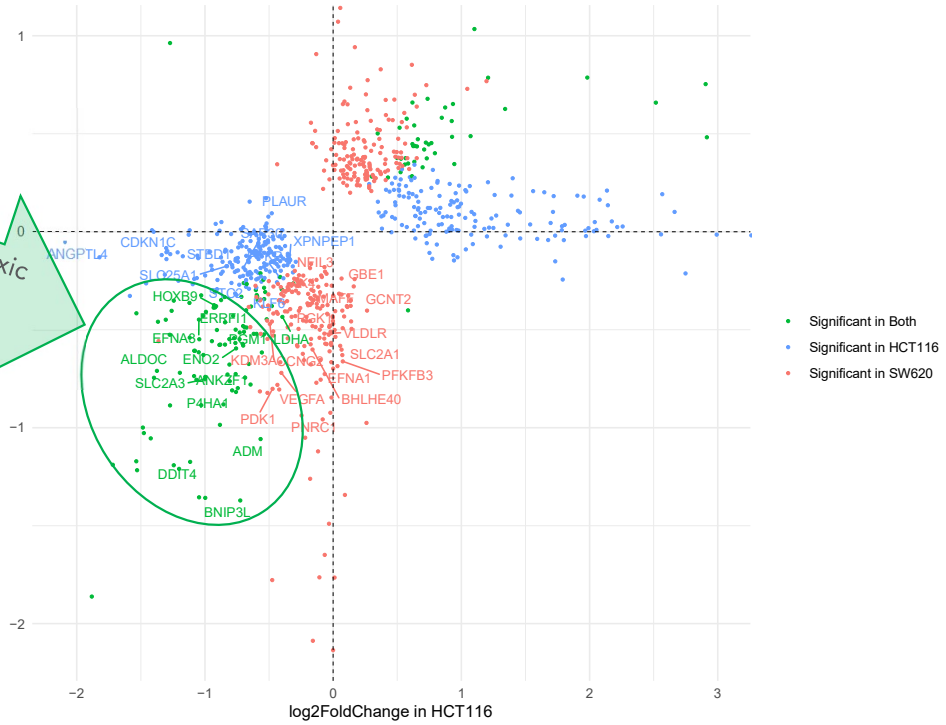
Onvansertib down-regulates genes induced by tumors in hypoxic conditions

Genes induced by hypoxia in two mCRC cell lines



Genes upregulated to survive hypoxic conditions are downregulated by adding onvansertib

Adding onvansertib inhibits adaptation to hypoxia



Hypoxia vs normoxia gene expression in HCT116 and SW620 cells

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

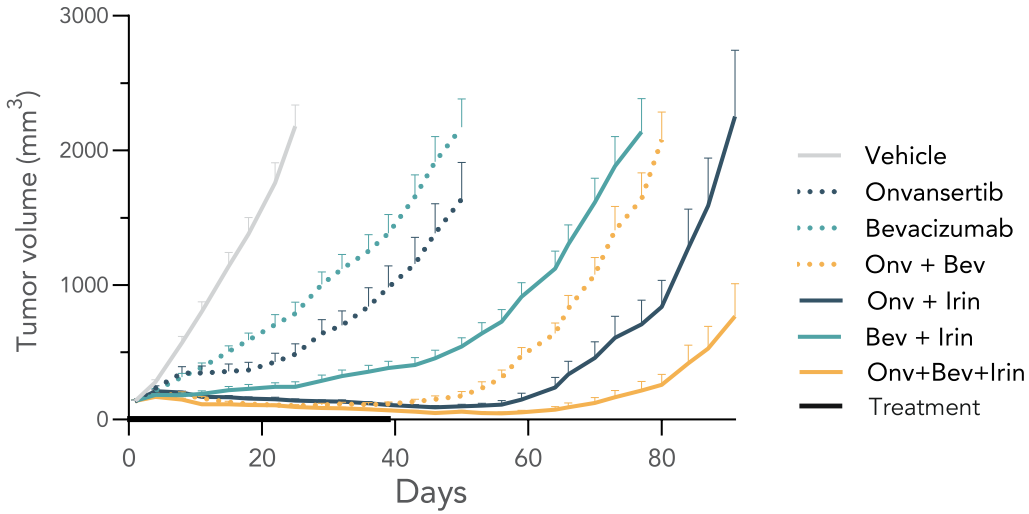
* Genes in the Hallmarks Hypoxia gene set are labeled. Top 250 genes with P-adjusted < 0.05 shown.

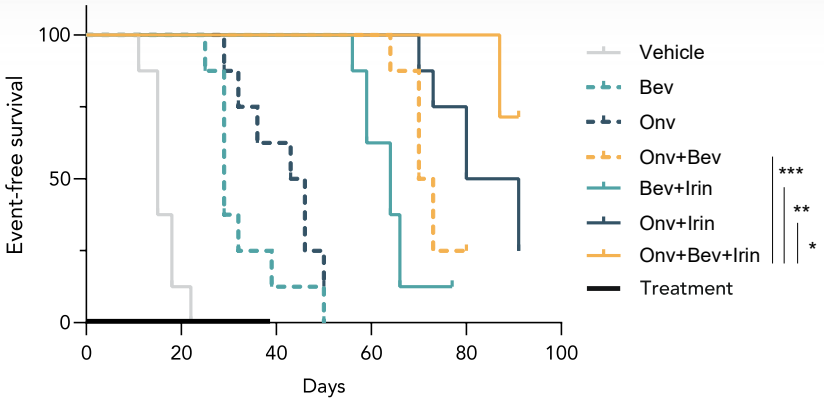
The combination of onvansertib, bevacizumab and irinotecan showed greater potency than each individual or doublet therapy

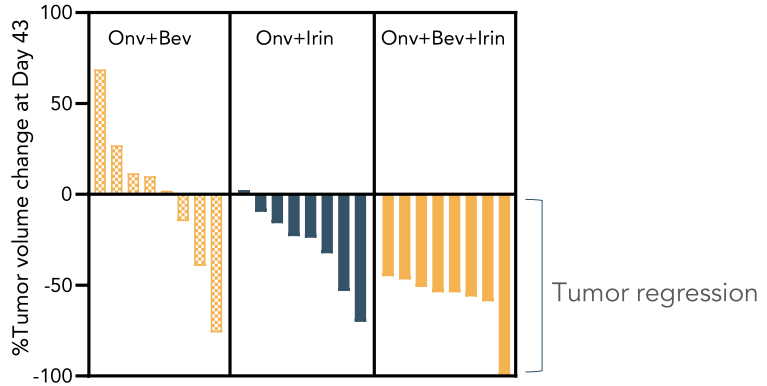
The combination of onvansertib, bevacizumab and irinotecan was potent in the HCT116 xenograft model, resulting in:

- 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<1000mm^3



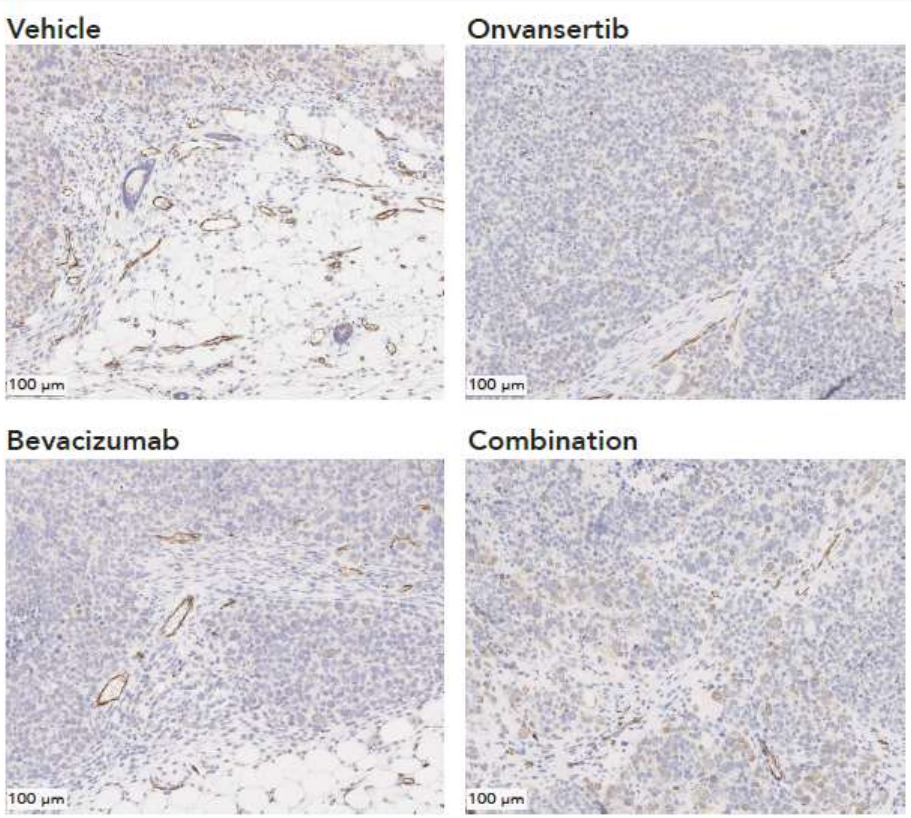




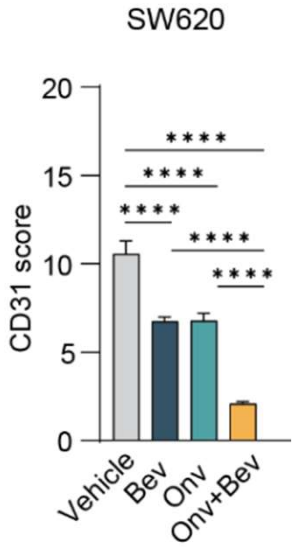
HCT116 xenografts were treated with the indicated drugs for 39 days and tumor volumes were measured (8mice/group, mean + SEM are represented on graph).
Kaplan-Meier survival curve for event-free survival (time to reach tumor volume 1000mm^3) was calculated. Log-rank Mantel Cox test was used for survival 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 µm magnification were randomly selected in the tumor area. CD31 positive vessels were manually counted in these fields. Mean score ± 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.

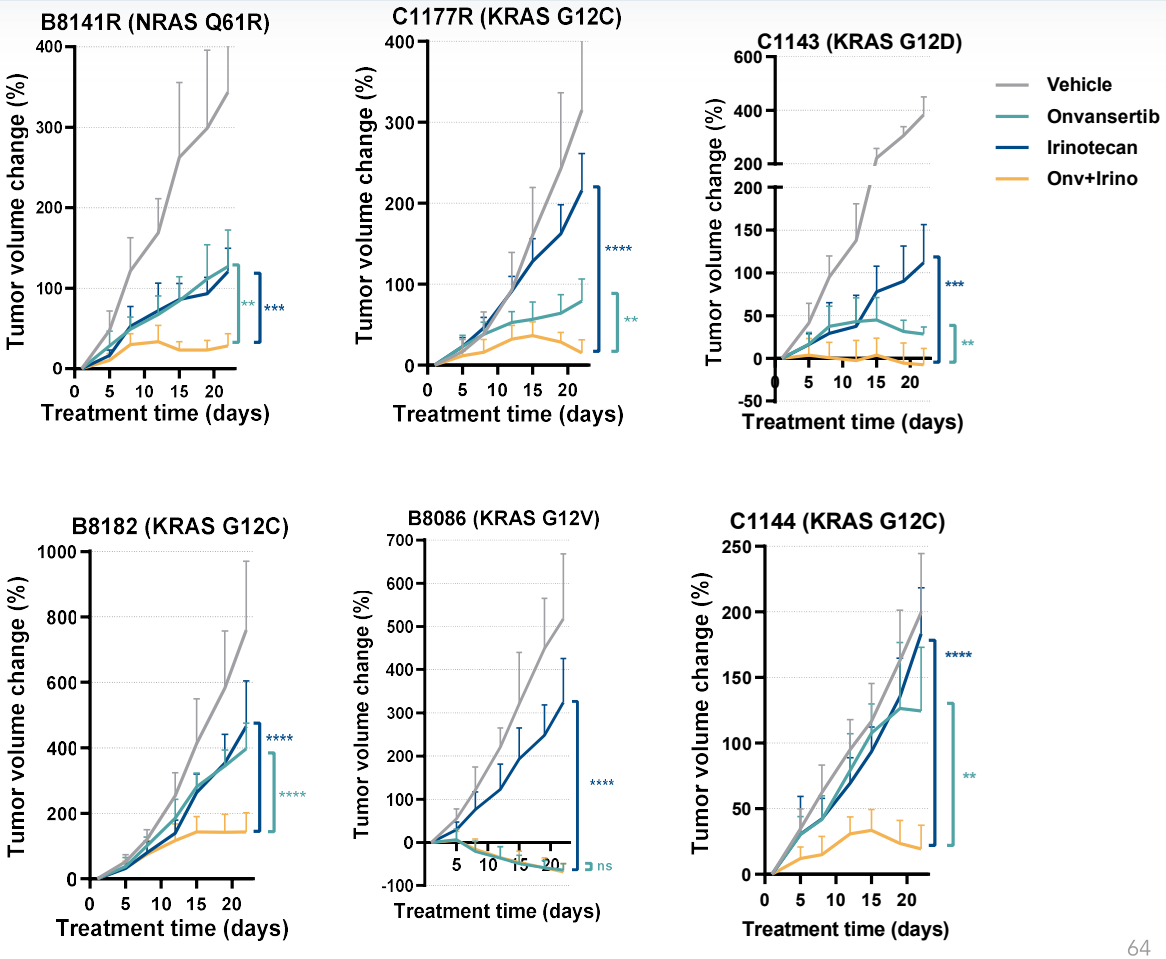
Onvansertib in combination with irinotecan in RAS-mutant CRC PDXs

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 21days. 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

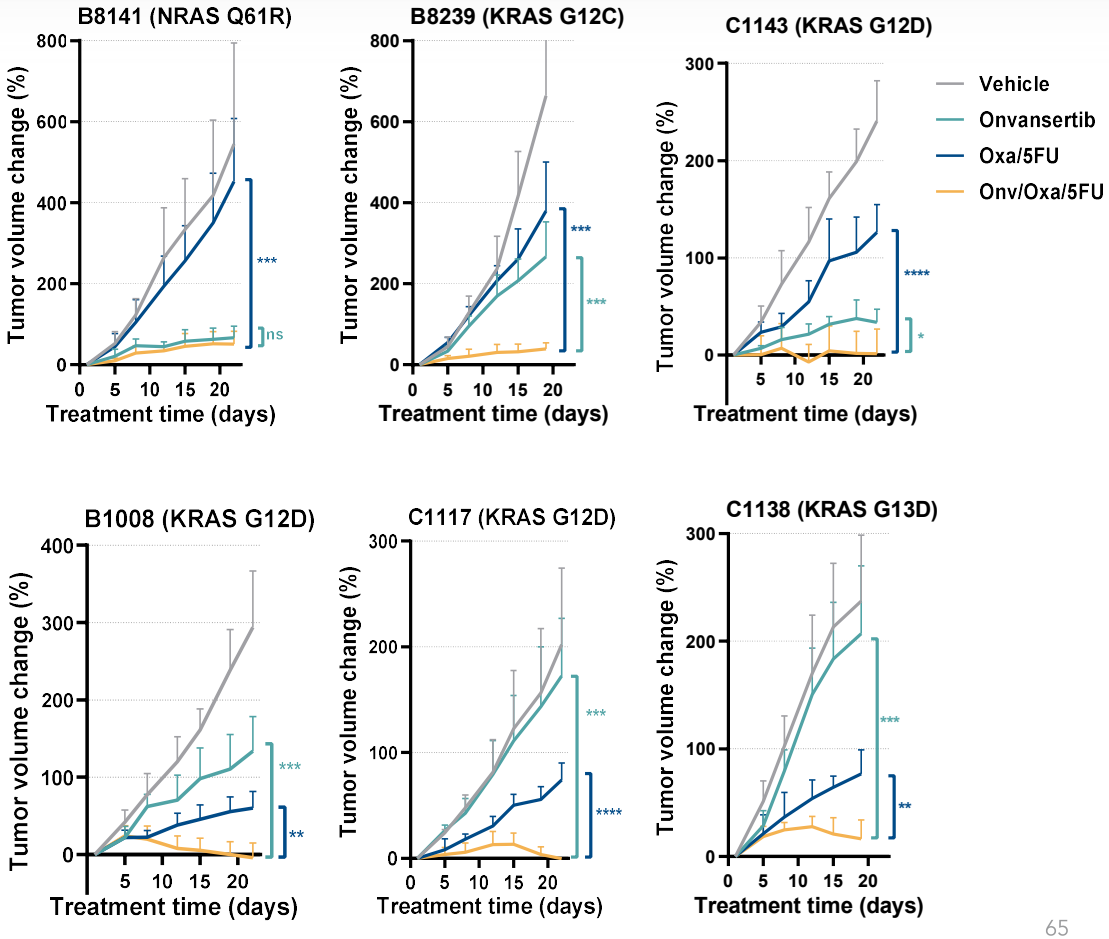
The chemotherapeutics oxaliplatin+5FU had no or modest activity in the 6 RAS-mutant PDX models tested.

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

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

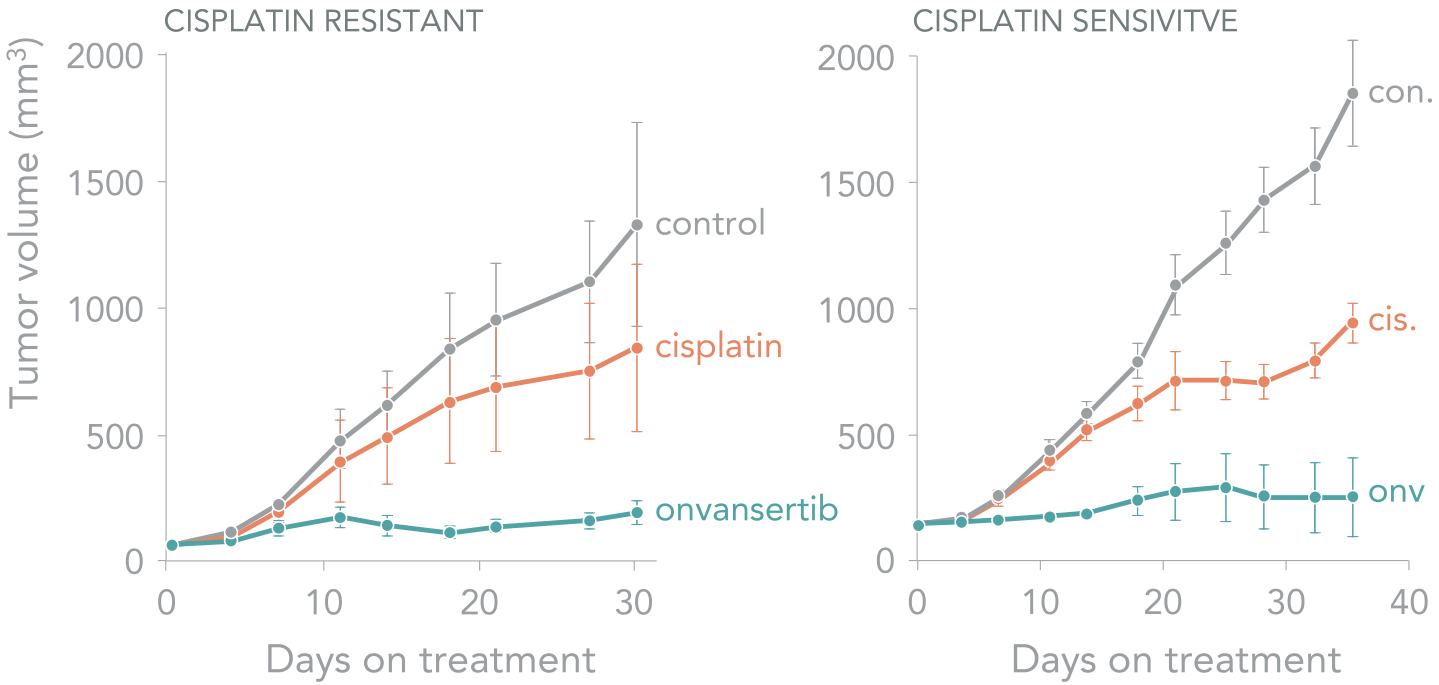
Onvansertib demonstrates single-agent activity in SCLC

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

UNIVERSITY of MARYLAND
MARLENE AND STEWART GREENEBAUM COMPREHENSIVE CANCER CENTER

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

SCLC

UNIVERSITY of MARYLAND
MARLENE AND STEWART GREENEBAUM
COMPREHENSIVE CANCER CENTER

PRELIMINARY SAFETY (N=6)

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

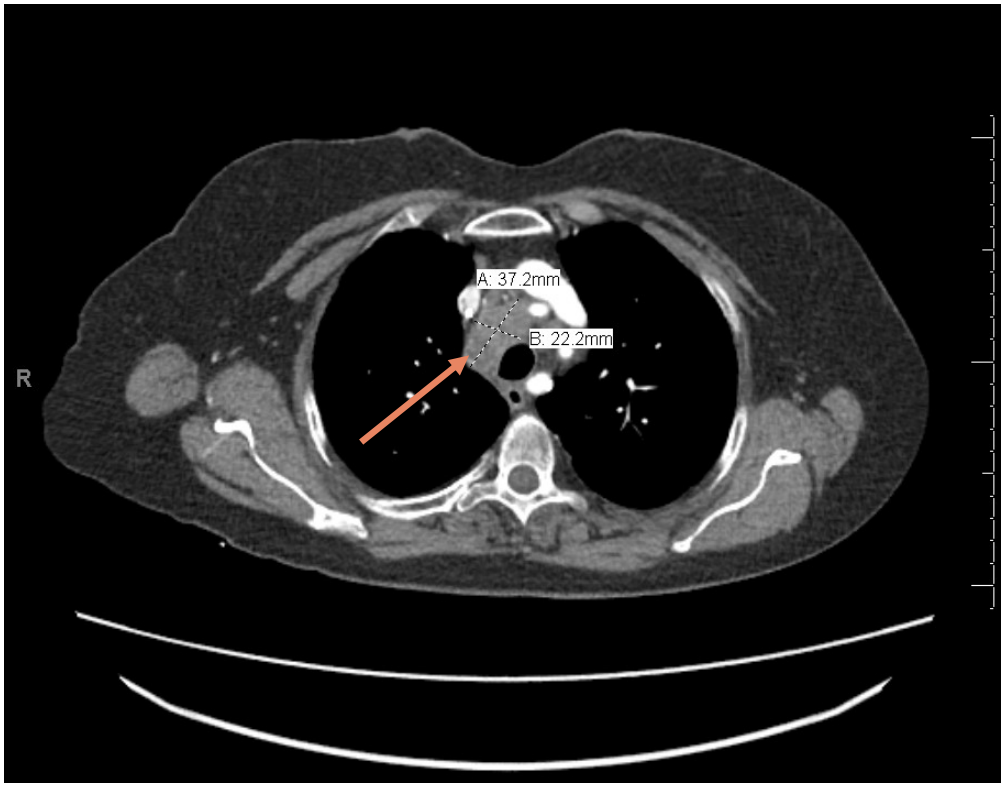
PRELIMINARY EFFICACY (N=7)

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

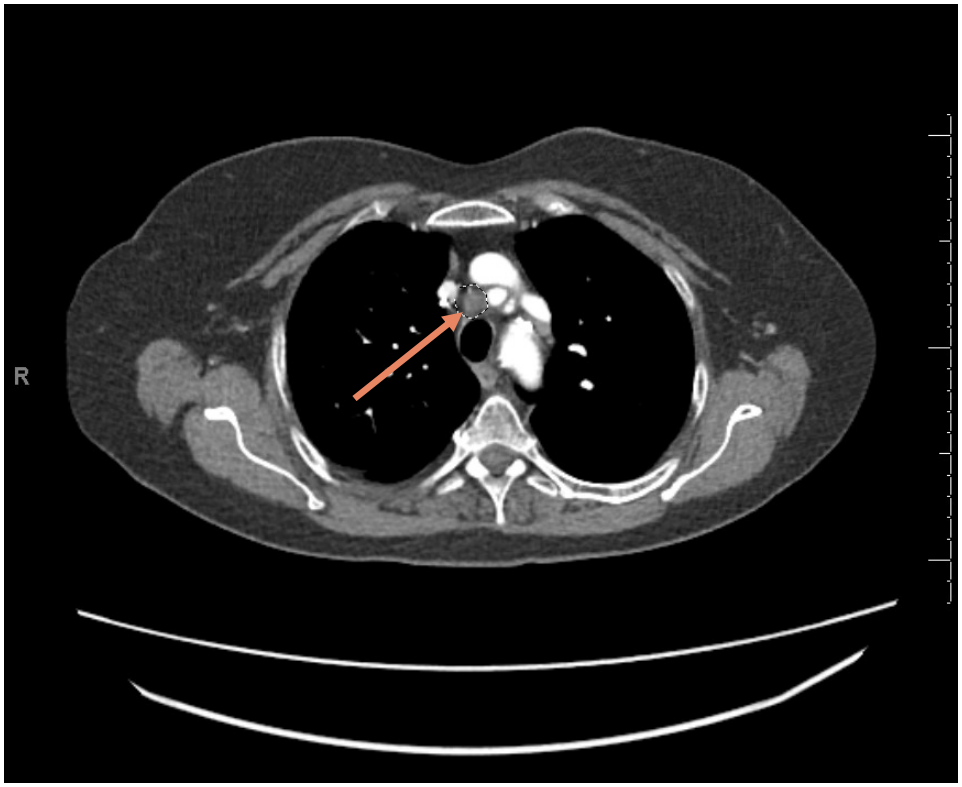
Disease control rate = 57% (4/7)

Radiographic scans for patient with a confirmed PR in SCLC

Baseline Scan



Restaging after Cycle 2



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Appendix:

Investigator-Initiated Trial

Triple Negative Breast Cancer (TNBC)

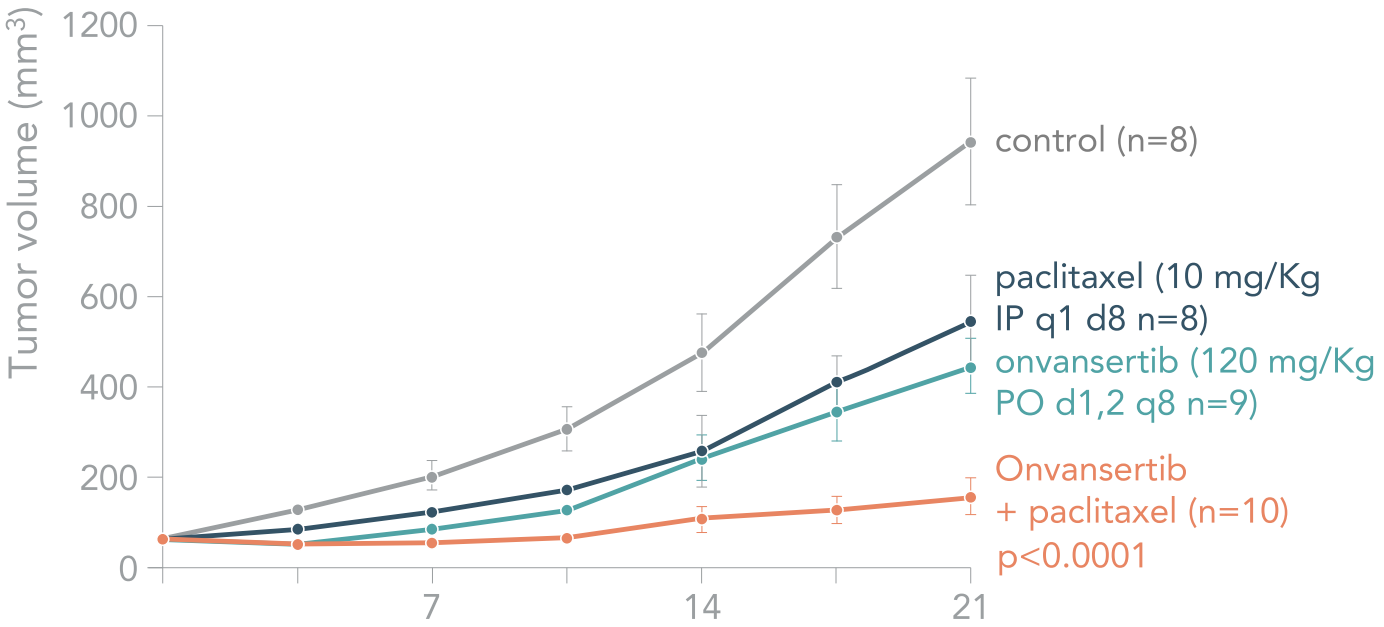
Preclinical: Onvansertib + paclitaxel is superior to single agent therapy

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 mm^3: 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

Dana-Farber Cancer Institute

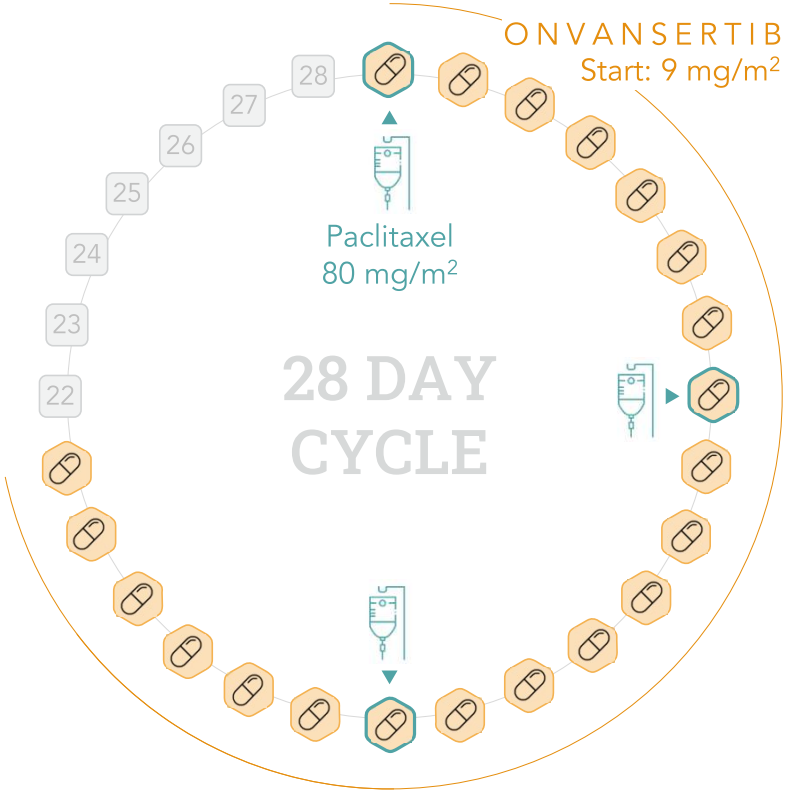
PRIMARY ENDPOINTS

Phase 1b
Safety, characterization of DLTs
Determination of RP2D

Phase 2
ORR (RECIST 1.1)

ONVANSERTIB DOSING

Starting: 9 mg/m^2
- Escalation: 12 mg/m^2, 18 mg/m^2
- De-escalation: 6 mg/m^2



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)