CRDF-004 Trial Update

1st Line RAS-mutated mCRC

JULY 29, 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.

Mark Erlander, PhD

Chief Executive Officer

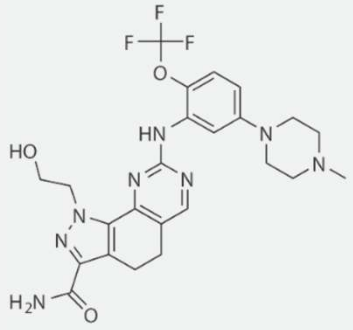
Onvansertib specifically targets PLK1, a well-established cancer target

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 designed the CRDF-004 trial to address four objectives

CRDF-004 Ph2 trial
RAS-mut mCRC

shift from
2nd line to 1st line

Aug 7, 2023

INTENT

1. Select a Ph3 dose – per FDA's Project Optimus
2. Assess efficacy signal
3. Characterize safety profile in 1st line setting
4. Basis for meeting with FDA to agree Ph3 trial

mCRC, metastatic colorectal cancer; mut, mutated

Dr. Sidhu brings a wealth of clinical development experience

Deep Expertise in mCRC and Drug Development

PRACTICAL EXPERIENCE AT AMGEN

- Advanced multiple therapeutic candidates in oncology and hematology
- Led multiple Ph3 clinical trials of panitumumab (Vectibix®, approved US and globally)

A LEADER IN mCRC RAS BIOLOGY

Dr. Sidhu is a leader in advancing RAS biology and therapeutics in mCRC, with publications in peer-reviewed journals, including the *New England Journal of Medicine.*

CAREER

Dr. Sidhu served as Executive Vice President and Chief Medical Officer at Roivant Sciences. He was also the Chief Medical Officer at Eterna Therapeutics, Inc. and Cell Design Labs, up until its acquisition by the Gilead subsidiary Kite, where he subsequently served as VP, Clinical Development. He was most recently the Chief Medical Officer and acting CEO at Treadwell Therapeutics.

Dr. Sidhu is a Fellow of the Royal College of Physicians and Surgeons of Canada in both internal medicine and medical oncology. He earned his medical degree from Queen's University in Kingston, Ontario Canada and his bachelor's degree in biochemistry from the University of Alberta in Edmonton, Alberta. Dr. Sidhu trained in internal medicine at Queen's University and medical oncology at the British Columbia Cancer Agency in Vancouver, British Columbia and the Cross Cancer Institute in Edmonton, Alberta.

Roger Sidhu, MD

Chief Medical Officer

AGENDA

1st line RAS-mut mCRC program update

1. ORR efficacy and safety
2. PFS analyses
3. Registrational program path forward

mCRC, metastatic colorectal cancer; Mut, mutant; ORR, objective response rate; PFS, progression free survival

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

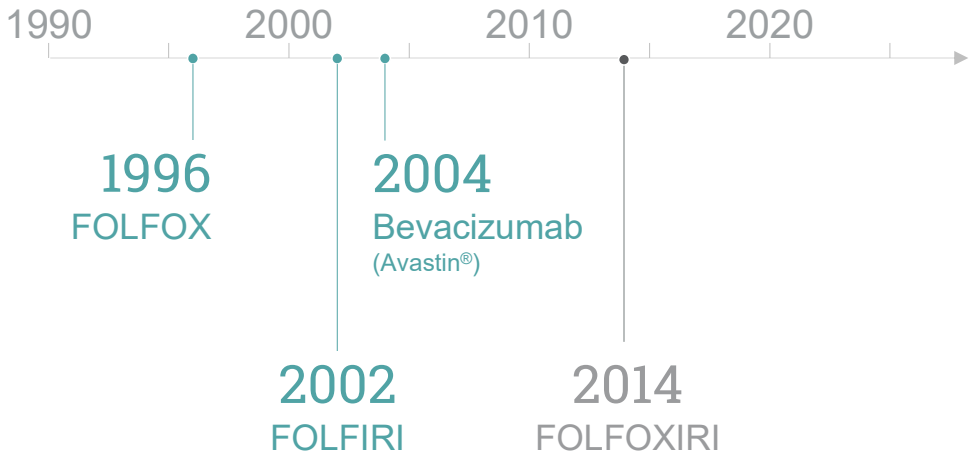
50,000
deaths

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

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

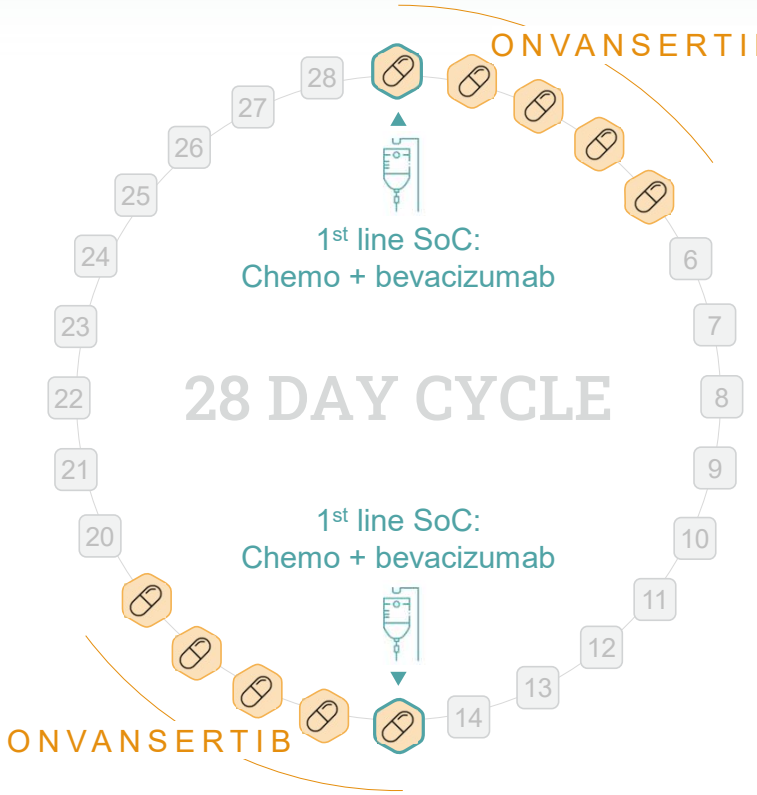
No prior bev

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
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. 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*

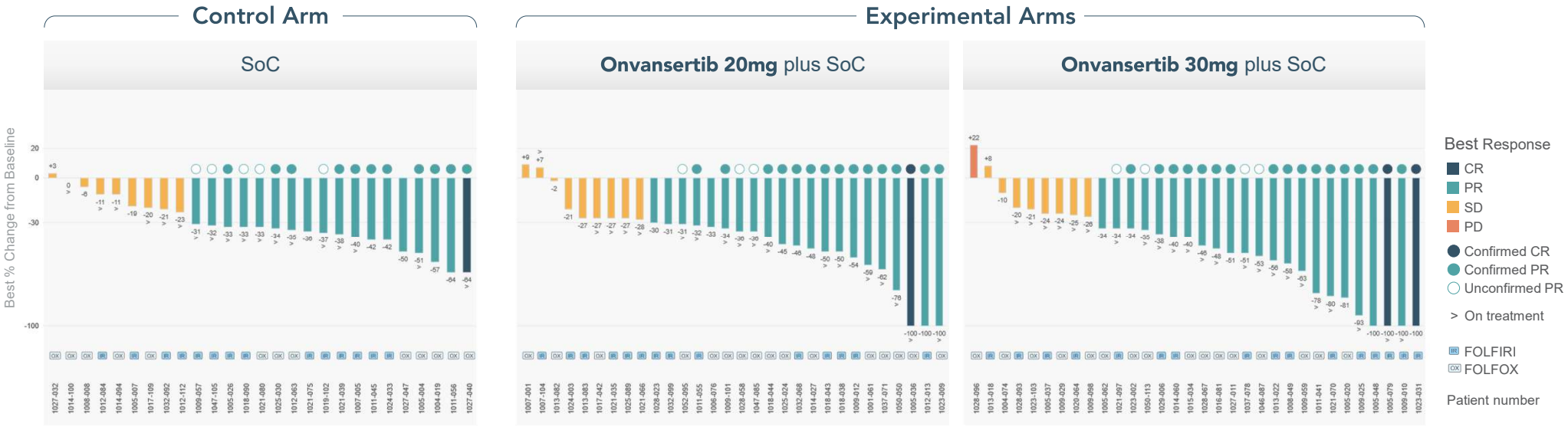
Intent-to-treat (ITT) (N=110)	Control (SoC alone) (n=37)	Onv 20mg + SoC (n=36)	Onv 30mg + SoC (n=37)	Onv 30mg vs. Control
Confirmed ORR[1] n, [95% CI]	30% n=11 [16-47]	42% n=15 [26–59]	49% n=18 [32–66]	19% p=0.018
Confirmed ORR at 6 months	22% n=8	33% n=12	46% n=17	
ORR[2] n, [95% CI]	43% n=16 [27–61]	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. 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*

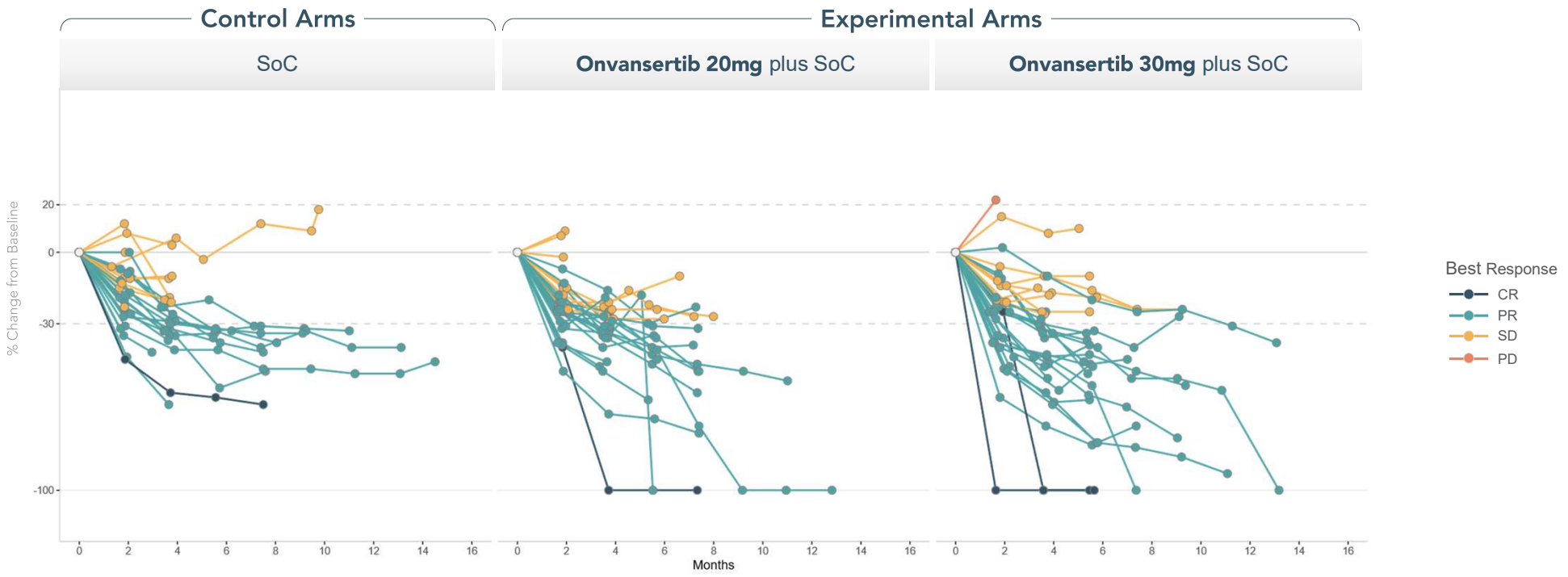
Intent-to-treat (ITT)	Control (SoC alone)	Onv 20mg + SoC	Onv 30mg + SoC
Confirmed ORR[1]	30%	42%	49%
ORR[2]	43%	50%	59%



* Radiographic response determined per RECIST 1.1 by blinded independent central review as of July 8, 2025 from an ongoing trial and unlocked database. 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

Deeper tumor regression over time observed with onvansertib+SoC

Radiographic Response over Time*

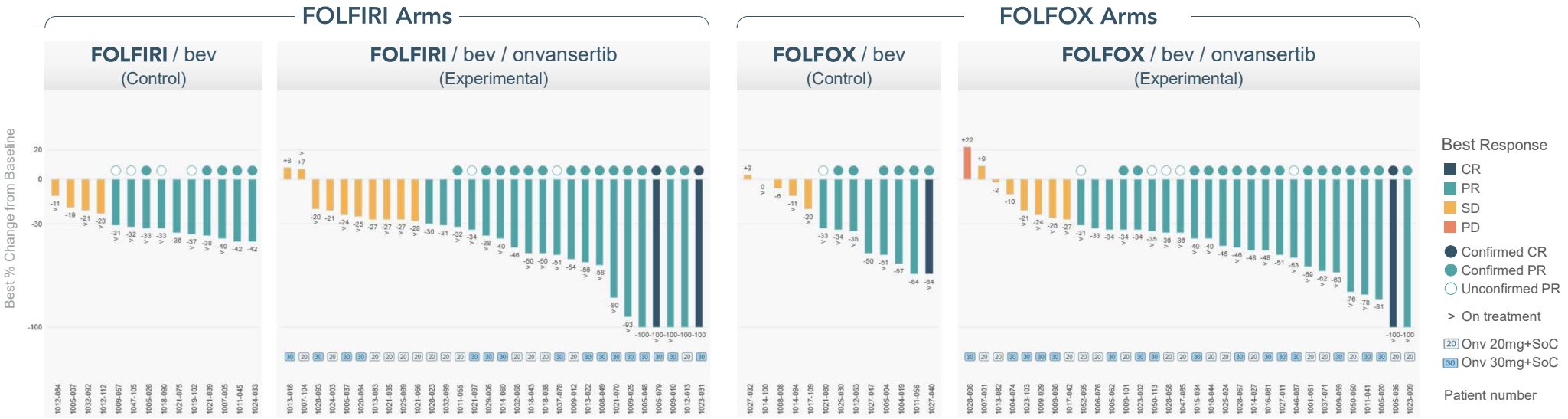


* Radiographic response determined per RECIST 1.1 by blinded independent central review as of July 8, 2025 from an ongoing trial and unlocked database. SoC, standard of care; CR, complete response; PR, partial response; SD, stable disease; PD, progressive disease

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

Best Radiographic Response BY CHEMO BACKBONE*

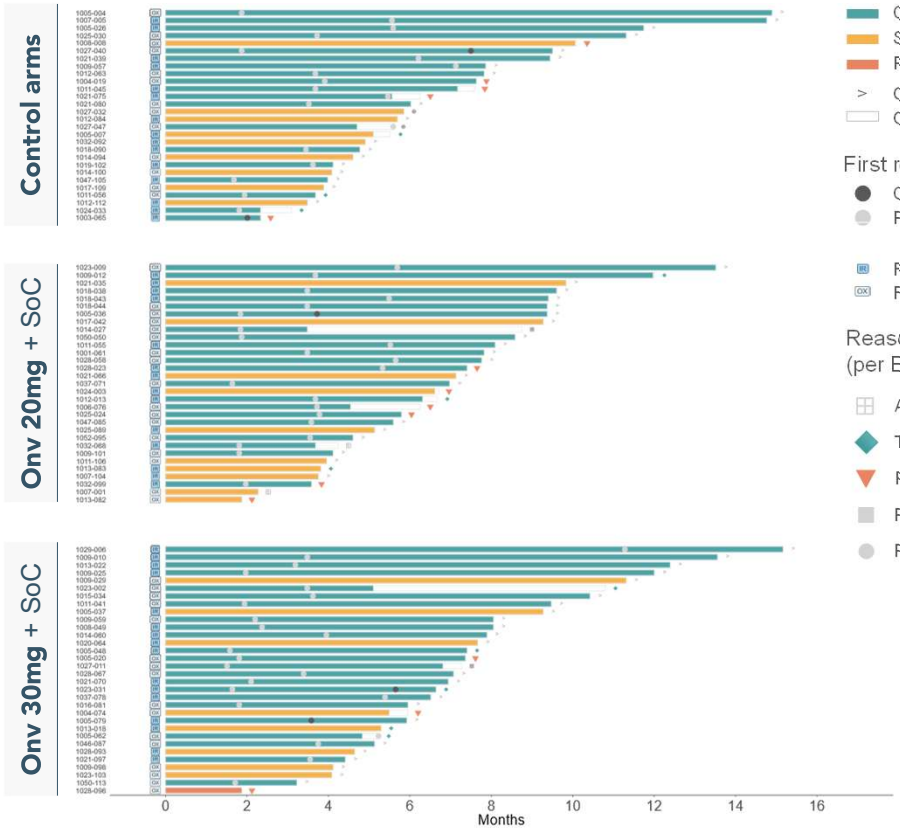
Intent-to-treat (ITT)	FOLFIRI		FOLFOX	
	Control	SoC + Onv	Control	SoC + Onv
Confirmed ORR[1]	26%	44%	33%	46%
ORR[2]	47%	50%	39%	59%



* Radiographic response determined per RECIST 1.1 by blinded independent central review as of July 8, 2025 from an ongoing trial and unlocked database. 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*



Time on Trial by Best Response
- CR/PR
- SD
- PD
- On treatment
- On follow up

First response scan
- CR
- PR

- FOLFOX
- FOLFIRI

Reason for discontinuation (per EDC)
- Adverse event
- To pursue surgery
- Progressive disease
- Physician decision
- Patient decision

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. 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

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)	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

AGENDA

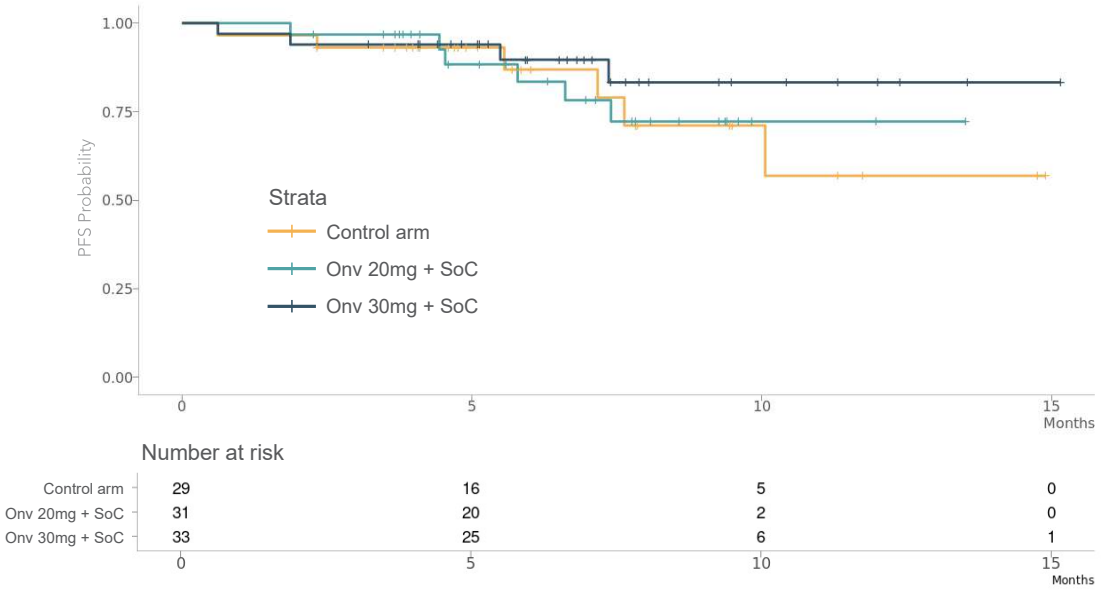
1st line RAS-mut mCRC program update

1. ORR efficacy and safety
2. PFS analyses
3. Registrational program path forward

mCRC, metastatic colorectal cancer; mut, mutant; ORR, objective response rate; PFS, progression free survival

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.

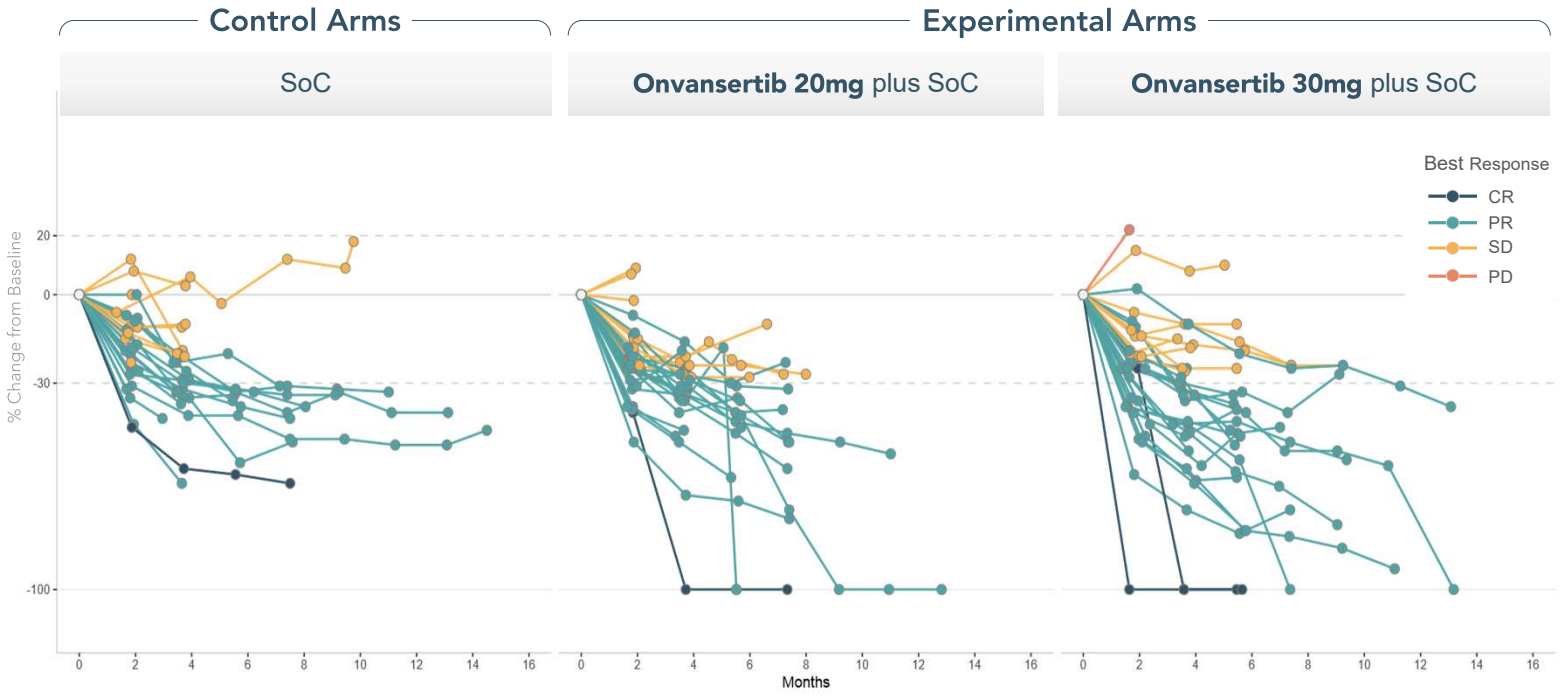
Final data: All patients on trial have had a 2-month scan.

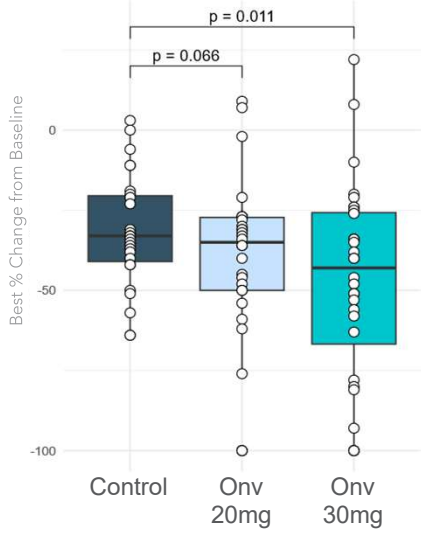
	Previous Ph3 1st Line mCRC Trials[1]				
% of patients with ETS	**TRIBE** RAS WT/mut.	**CRYSTAL** RAS WT	**OPUS** RAS WT	**CRDF-004** RAS mut.	
Control Arm	52%	49%	46%	41% (11/27)	
				Onv 20mg	**Onv 30mg**
Experimental Arm	63%	62%	69%	63% (19/30)	69% (22/32)
ETS Delta *p-value*	**11%** *0.025*	**13%**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

AGENDA

1st line RAS-mut mCRC program update

1. ORR efficacy and safety
2. PFS analyses
3. Registrational program path forward

mCRC, metastatic colorectal cancer; Mut, mutant; ORR, objective response rate; PFS, progression free survival

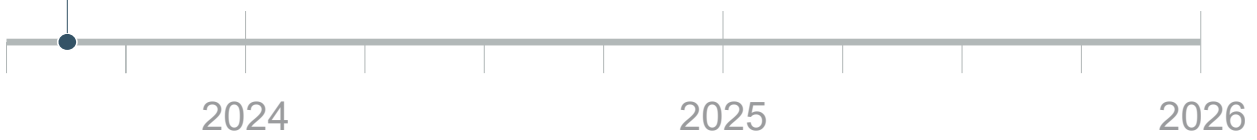
Current CRDF-004 trial data are supportive of a 30mg dose

CRDF-004 Ph2 trial

1st line RAS-mut mCRC

INTENT

1. **Select a Ph3 dose – per FDA's Project Optimus**
2. Assess efficacy signal
3. Characterize safety profile in first-line setting
4. Basis for meeting with FDA to agree Ph3 trial



Progress to date

Data supports focus on onvansertib 30mg dose

mCRC, metastatic colorectal cancer; mut., mutated

Dose response observed across ORR, ETS and DpR efficacy signals and may predict longer PFS

CRDF-004 Ph2 trial

1st line RAS-mut mCRC

INTENT

1. Select a Ph3 dose – per FDA's Project Optimus
2. **Assess efficacy signal**
3. Characterize safety profile in first-line setting
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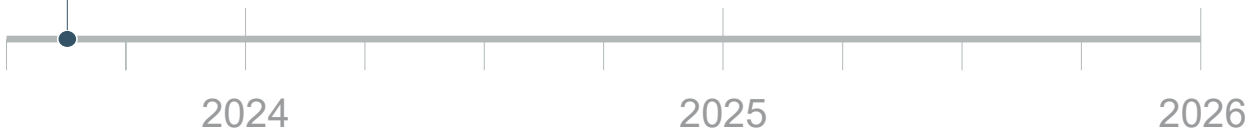


Progress to date

ORR: meaningful deltas in context of 1st line mCRC

PFS: early PFS separation and correlative response signals

Dose-dependent response

mCRC, metastatic colorectal cancer; mut., mutated; ORR, objective response rate; PFS, progression free survival

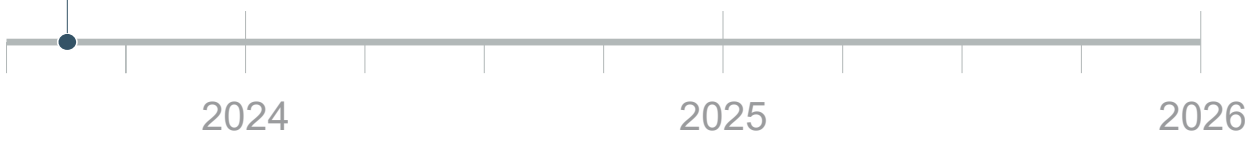
Onvansertib in combination with SoC is generally well-tolerated

CRDF-004 Ph2 trial

1st line RAS-mut mCRC

INTENT

1. Select a Ph3 dose – per FDA's Project Optimus
2. Assess efficacy signal
3. **Characterize safety profile in first-line setting**
4. Basis for meeting with FDA to agree Ph3 trial



Progress to date

Onvansertib is generally well-tolerated in combination with both chemo backbones and bev

SoC, standard of care; mCRC, metastatic colorectal cancer; mut., mutated; bev, bevacizumab

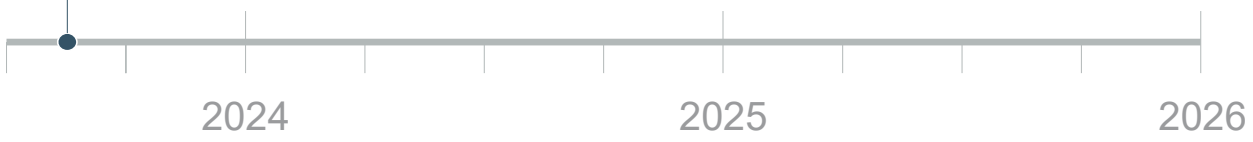
We intend to discuss our registrational trial protocol with FDA

CRDF-004 Ph2 trial

1st line RAS-mut mCRC

INTENT

1. Select a Ph3 dose – per FDA's Project Optimus
2. Assess efficacy signal
3. Characterize safety profile in first-line setting
4. **Basis for meeting with FDA to agree Ph3 trial**



Progress to date

Totality of data supports moving forward with FDA interactions on the registrational program

mCRC, metastatic colorectal cancer; mut., mutated

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

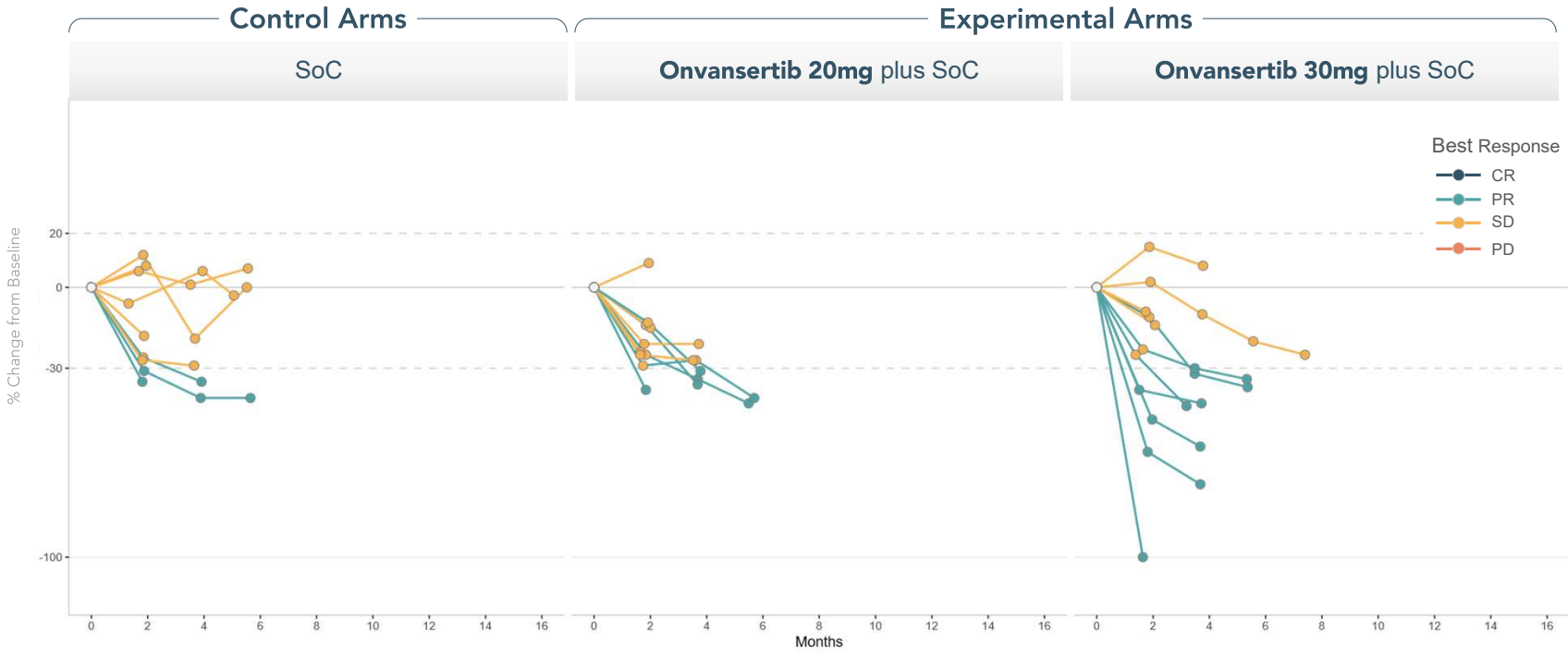
mCRC, metastatic colorectal cancer; ORR, objective response rate; DoR, duration of response; PFS, progression free survival; OS, overall survival

APPENDIX

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

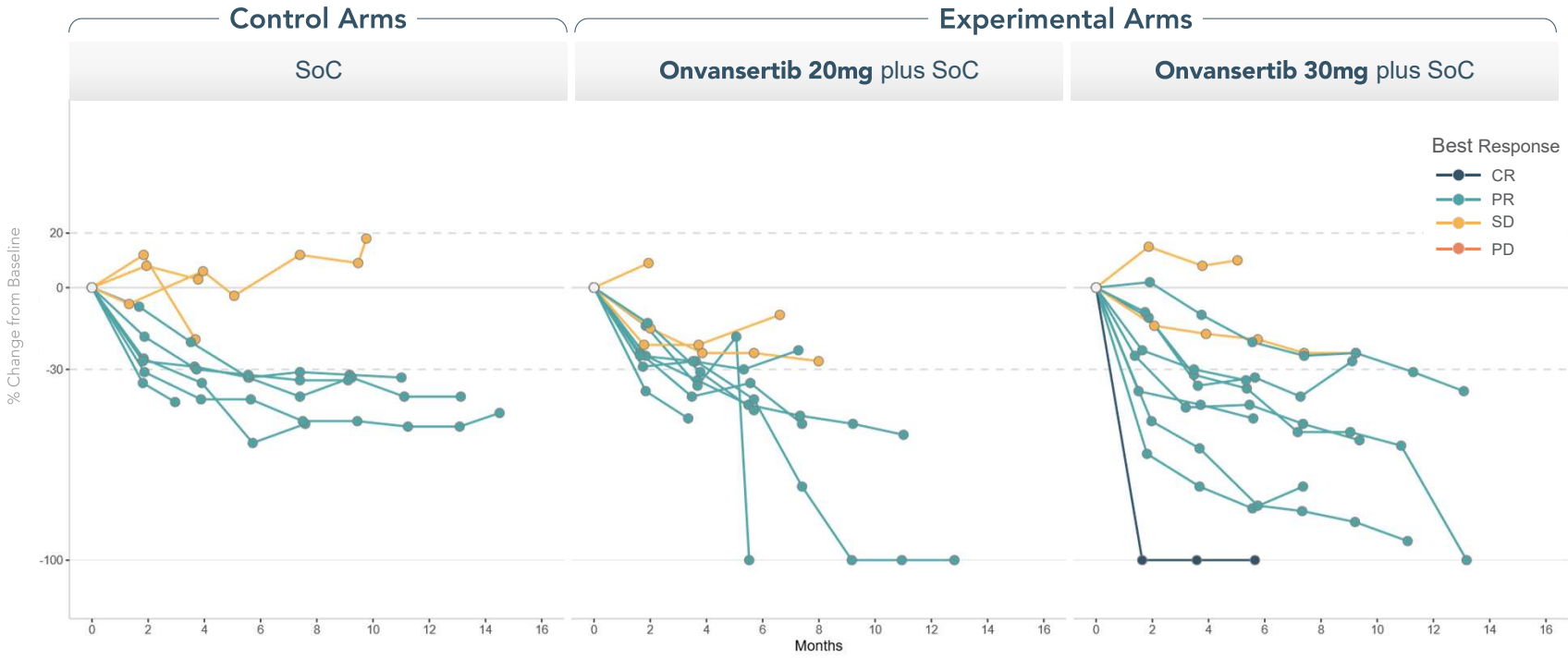


* Radiographic response determined per RECIST 1.1 by blinded independent central review as of November 26, 2024 from an ongoing trial and unlocked database. Response data for one control arm patient changed from the November 26, 2024 data cut as a result of the radiologist at the blinded independent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

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

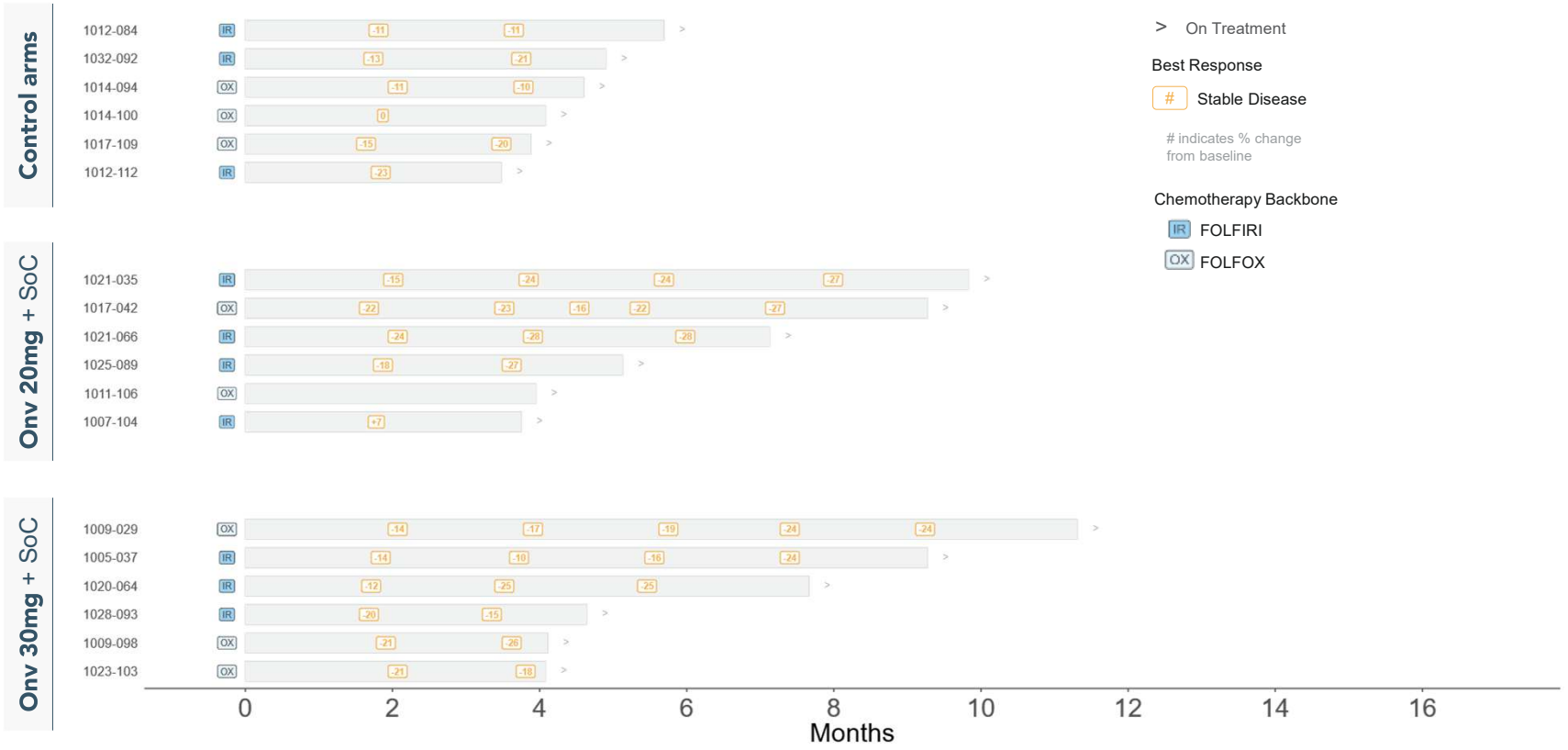
Radiographic Response over Time* – as of July 8, 2025



* Radiographic response determined per RECIST 1.1 by blinded independent central review as of July 8, 2025 from an ongoing trial and unlocked database. SoC, standard of care; CR, complete response; PR, partial response; SD, stable disease; PD, progressive disease

Swimmer Plot for Stable Disease patients still on trial

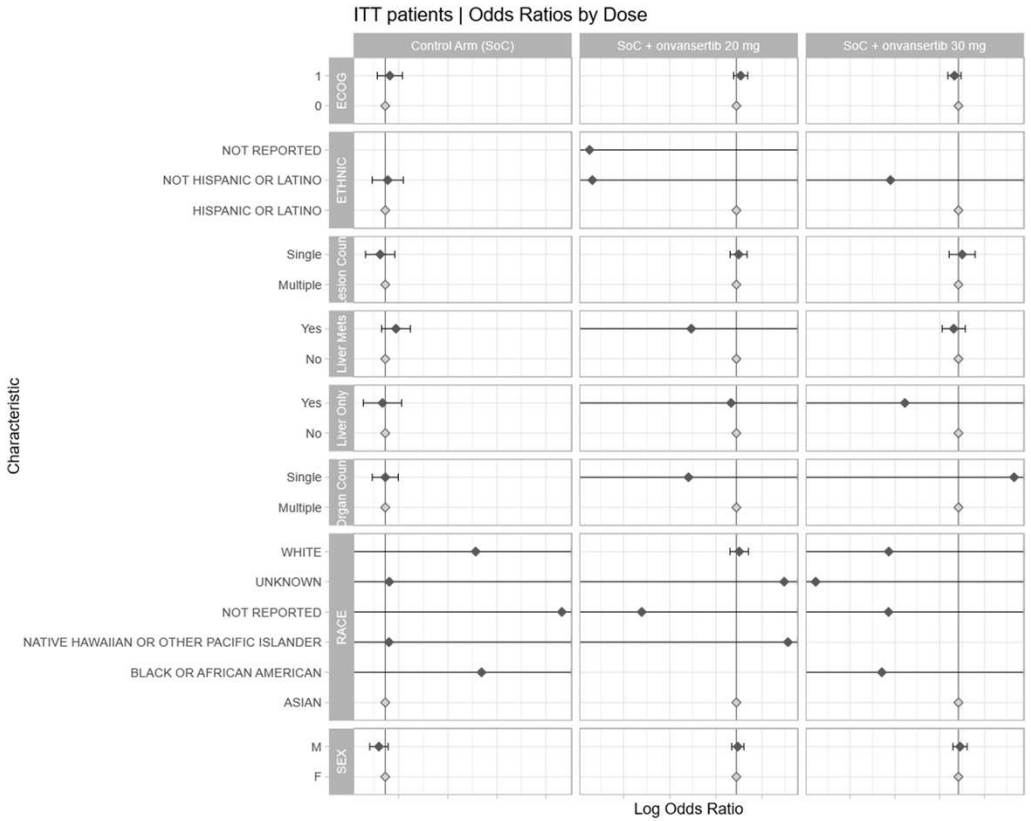
Radiographic Response over Time*



* Radiographic response determined per RECIST 1.1 by blinded independent central review as of July 8, 2025 from an ongoing trial and unlocked database. Patient 1011-106 in the onvansertib 20mg arm has only non-target lesions. SoC, standard of care; onv, onvansertib

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

Baseline measures of tumor burden (by sum of longest diameters)

The mean and median sum of the longest diameters was similar (not significantly different) for control, onvansertib 20mg and onvansertib 30mg arms

Safety population - Baseline Sum of Longest Dimensions* (SLD)

Characteristic	Control Arm (SoC) N = 34	SoC + onvansertib 20 mg N = 34	SoC + onvansertib 30 mg N = 36	p-value[1]
Baseline sum of longest dimensions:				
Mean (Min, Max)	91 (15, 281)	90 (10, 298)	83 (16, 270)	0.921
Median (Q1,Q3)	75 (39,121)	67 (28,134)	74 (43,114)	
Unknown	6	4	3	

* 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. Kruskal-Wallis rank sum test; Pearson's Chi-squared test; Fisher's exact test. SLD, sum of longest diameters; SoC, standard of care

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

Safety Population (Dosed)	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)	
N (% of total)	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