Company Overview
The Onvansertib Opportunity

JANUARY 2024

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 a number of 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, our need for additional financing; our ability to continue as a going concern; 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 candidates; our clinical trials may encounter delays in initiation or enrollment that impact the cost and timing of the trial readout; risks related to business interruptions, including the outbreak of COVID-19 coronavirus, 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; regulatory, and risks related to failure to obtain FDA clearances or approvals and noncompliance with FDA regulations. There are no guarantees that any of our technology or products 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 any precision medicine therapeutics 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, 2022, 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: Positioned to improve 1st line RAS-mut mCRC treatment

First-in-Class PLK1 inhibitor	Robust clinical data in 2L KRAS-mut mCRC	FDA	Pfizer
• **Onvansertib**: first well-tolerated PLK1-selective inhibitor • PLK1 inhibition disrupts tumor growth several ways	• **73%** response rate vs **~25%** in SoC • **15 month** progression free survival vs **~8 month** in SoC	• **FDA**-agreed path to 1st line RAS-mut mCRC accelerated approval	• **Pfizer** is equity investor and has seat on SAB • **Pfizer** provides clinical execution of 1st line trial

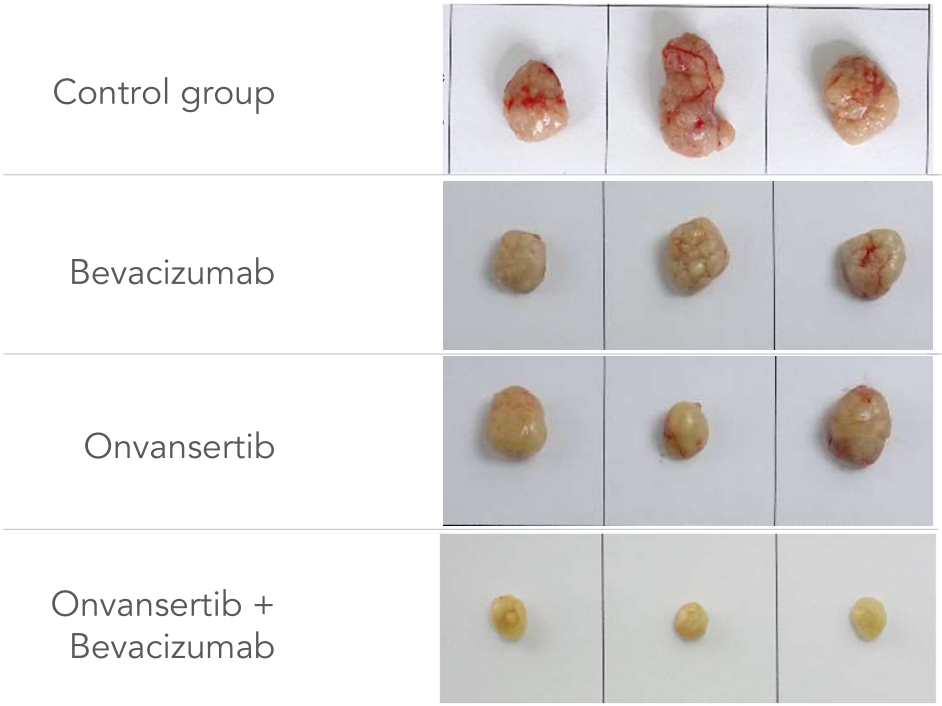
We expect clinical data from our 1st line RAS-mutated mCRC trial in mid-2024

Runway with current cash extends into 2025

Onvansertib combines powerfully with bevacizumab to inhibit tumor growth

Human metastatic colorectal cancer (mCRC) tumors grown in mice (KRAS G12V)

The combination of onvansertib and bevacizumab shows dramatically reduced tumor size and vascularization



- Roche drug Avastin®
- 8th largest global drug in 2019
  - $7.1B sales

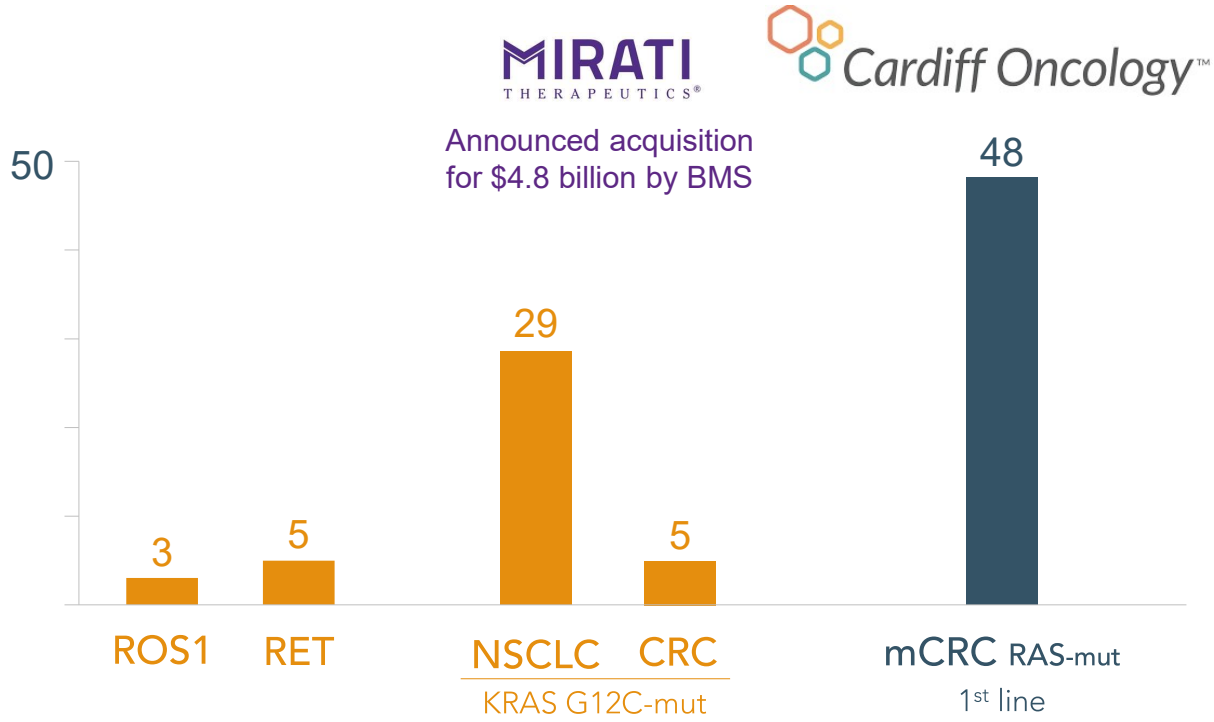
Cardiff Oncology™

* SW620 KRAS-G12V 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.

Onvansertib's targets large patient populations with unmet need

Targets with oncogenic alterations	Targets without oncogenic alterations
ROS1	**PLK1**
RET	PARP
KRAS G12C	CDK4/6
EGFR	PD1/PDL1
TRK	VEGF

Annual eligible U.S. patients ('000s)*



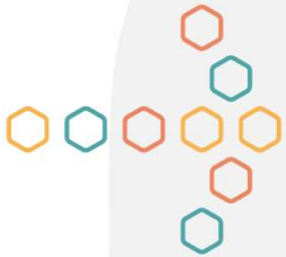
* ROS1 estimated eligible patients presented in Turning Point Therapeutics' corporate presentation May 2022 slide 6 (NSCLC disease incidence in the US of 140k of which 2% of patients harbor ROS1 translocation). RET estimated eligible patients presented in Loxo Oncology's corporate presentation January 2018 disclosed on Form 8-K (Jan 8, 2018).

KRAS G12C estimated eligible patients includes patient numbers from SEER website and G12C percentage from Mirati's corporate presentation. BMS announced its intention to acquire MRTX for $4.8B equity value on 10/8/2023. mCRC estimated population includes 1st line, KRAS- and NRAS-mutated cancers.

Our pipeline opens many attractive opportunities for onvansertib

	Line of Therapy	Trial	IIT*	Ph2	Ph3	Combination with:
mCRC (RAS-mut)	1st line	Ph 2 (w/Pfizer)		randomized		FOLFIRI/bev and FOLFOX/bev
	2nd line	Ph 1b/2		completed		FOLFIRI/bev
mPDAC	2nd line	Ph 2				Nal-IRI/leucovorin/ 5-FU
	1st line	Ph 2	OHSU Knight Cancer Institute			Gemzar®/Abraxane®
SCLC	2nd line	Ph 2	UPMC LIFE CHANGING MEDICINE			None (monotherapy)
TNBC	2nd line	Ph 2	Dana-Farber Cancer Institute			Paclitaxel

* For investigator-initiated trials (IITs) only, the investigator's institution is provided.
mPDAC = metastatic pancreatic ductal adenocarcinoma; SCLC = small-cell lung cancer; TNBC = triple-negative breast cancer; bev= bevacizumab, or Avastin®



Fighting mCRC through PLK1 inhibition

Robust data in lead mCRC program

Path forward to accelerated approval

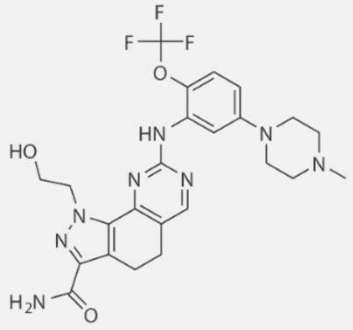
Onvansertib specifically targets PLK1, a well-established cancer target

Onvansertib

First oral, well-tolerated PLK1-selective inhibitor

PROPERTIES

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



SPECIFICITY

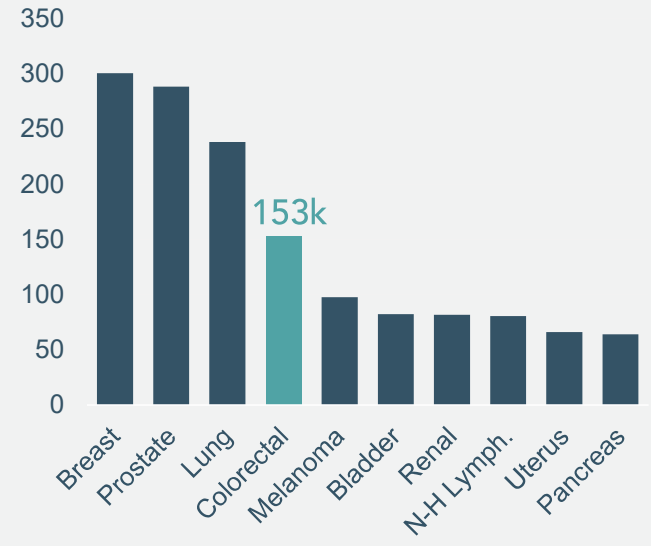
Exquisitely specific for PLK1

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

Our lead program targets RAS-mutated metastatic colorectal cancer

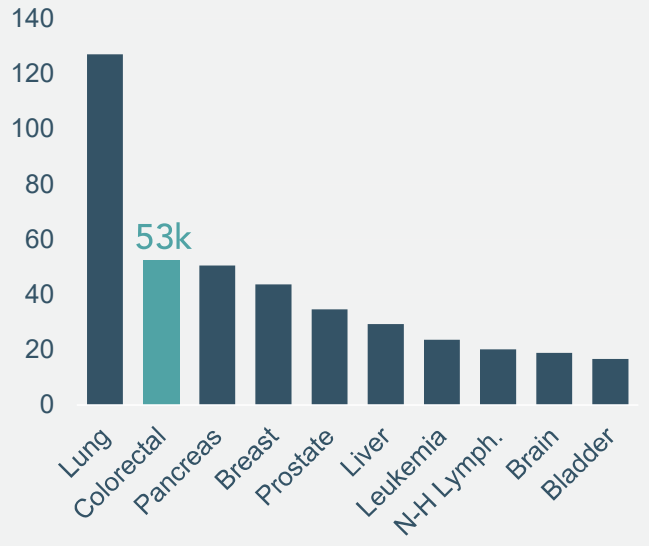
mCRC is BOTH common…

2023 new US cases ('000s)*



…and challenging to treat

2023 US deaths ('000s)*



* National cancer institute SEER data statistics.

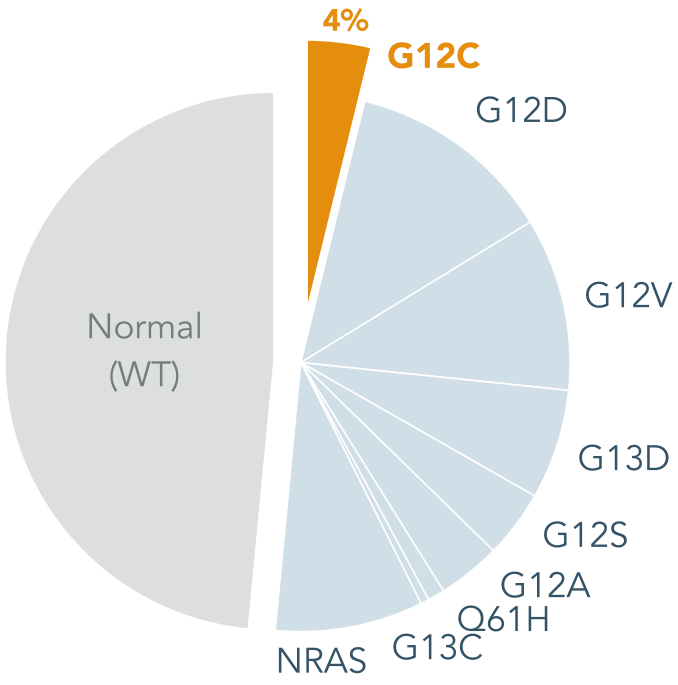
mCRC standard of care leaves a significant unmet need

Standard of Care for 1st / 2nd line RAS-mutated mCRC includes chemo + bevacizumab

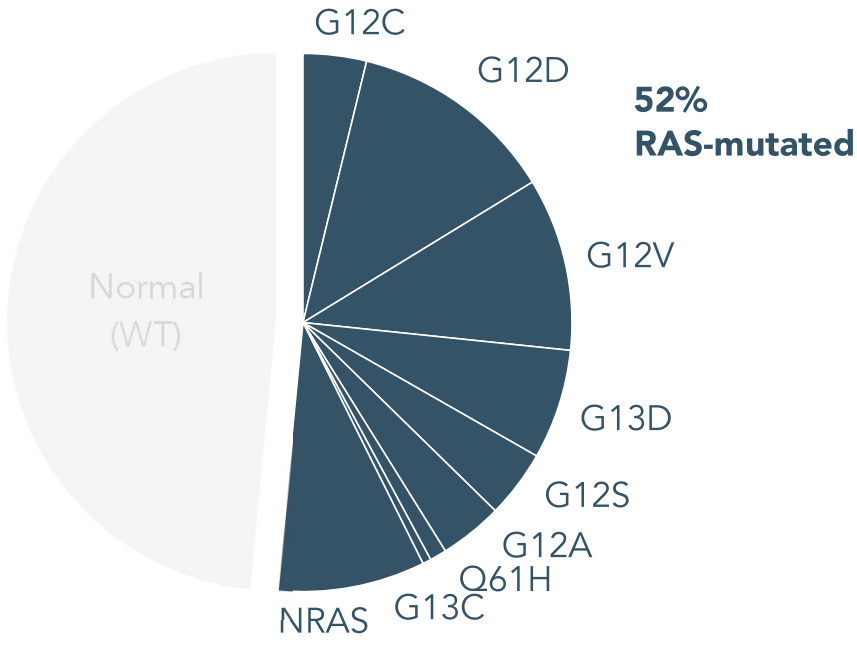
Chemotherapy	FOLFOX FOLFIRI	(approved 1996) (approved 2002)
✚		
Antiangiogenic	Bevacizumab (Avastin®)	(approved 2004)
Targeted therapy	None	

Other mCRC development programs leave a significant unmet need

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



Onvansertib is targeting all RAS-mutated mCRC[1]



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

Multiple onvansertib MOAs underlie our focus on RAS-mutated mCRC

Onvansertib attacks RAS-mutated mCRC in three ways

1	Synthetic lethality	RAS-mut mCRC tumor cells are hypersensitive to onvansertib
2	Inhibit DNA repair	Onvansertib inhibits repair of chemo-induced DNA damage
3	Inhibit tumor vasculature	Onvansertib inhibits creation of new blood vessels

Onvansertib is targeting all RAS-mutated mCRC[1]

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

Onvansertib's MOA targets large patient populations with unmet need

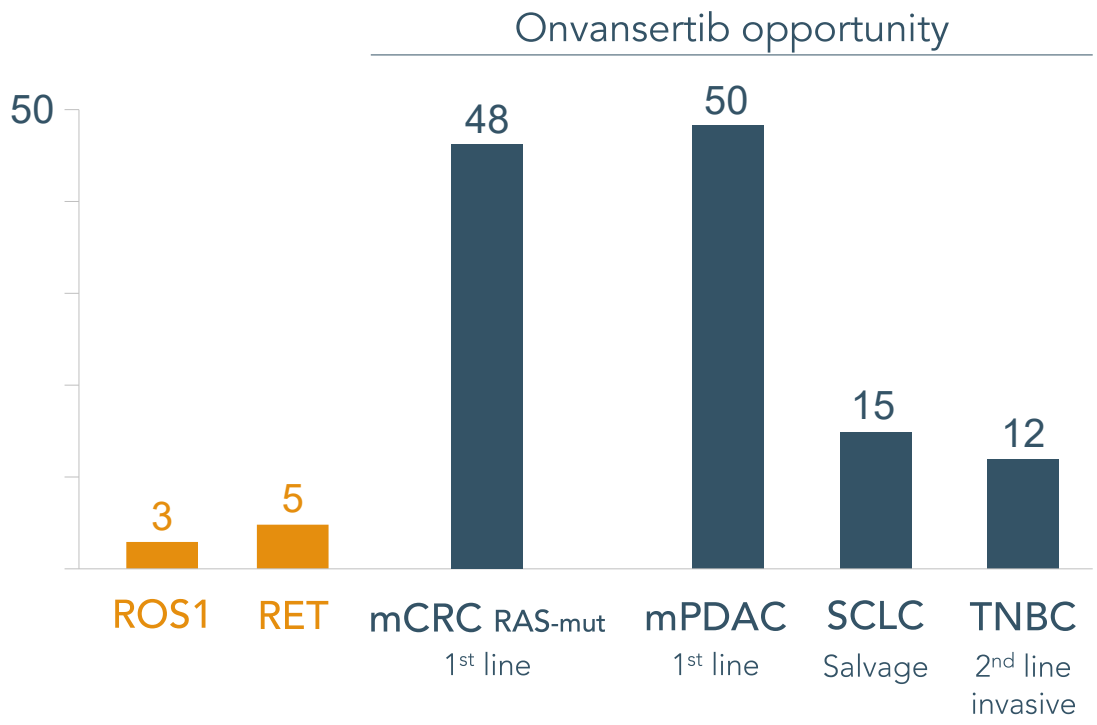
Targets with oncogenic alterations

- ROS1
- RET
- KRAS G12C
- EGFR
- TRK

Targets without oncogenic alterations

- **PLK1**
- PARP
- CDK4/6
- PD1/PDL1
- VEGF

Annual eligible U.S. patients ('000s)*



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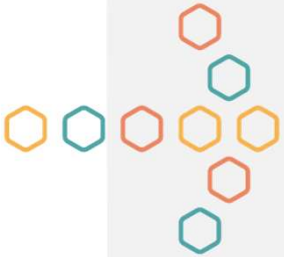
mCRC estimated population includes 1st line, KRAS- and NRAS-mutated cancers. mPDAC estimated population includes 1st line PDAC patients. SCLC estimated population includes SCLC salvage patients. TNBC estimated population includes invasive, 2nd line TNBC patients.



Fighting mCRC through PLK1 inhibition

Robust data in lead mCRC program

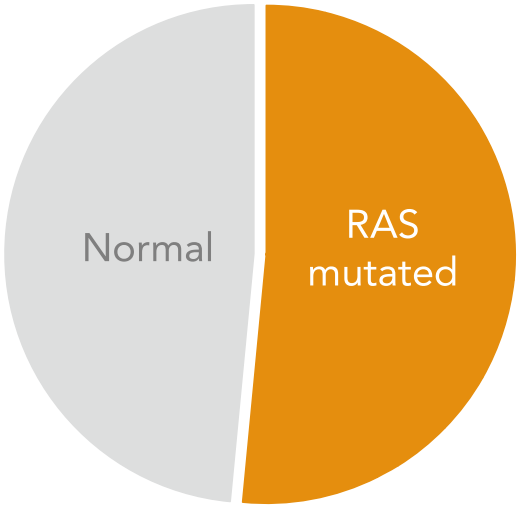
Path forward to accelerated approval

Our focus is RAS-mutated tumors where there are no targeted therapies

Normal	1st LINE	2nd LINE
Standard*	Chemo + bevacizumab	Chemo + bevacizumab
Targeted	+ EGFR inhibitor	NONE

RAS Mutated		
Standard*	Chemo + bevacizumab	Chemo + bevacizumab
Targeted	**NONE**	**NONE**

RAS-mut mCRC is approx. half the mCRC population[1]



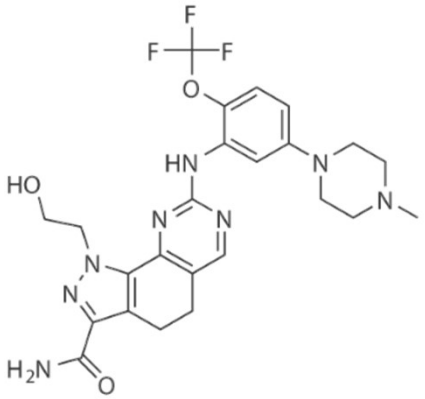
* FOLFOX and FOLFIRI are interchangeable as SoC chemo for 1st and 2nd line.

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

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

Normal	1st LINE	2nd LINE
Standard	Chemo + bevacizumab	Chemo + bevacizumab
Targeted	+ EGFR inhibitor	NONE

RAS Mutated		
Standard	FOLFOX + bevacizumab	FOLFIRI + bevacizumab
Targeted	NONE	ONVANSERTIB

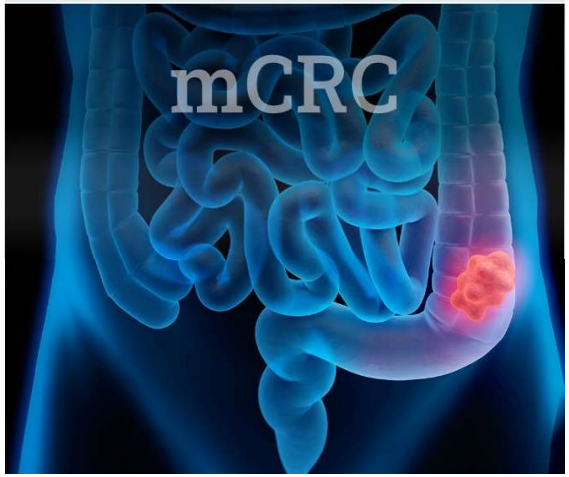


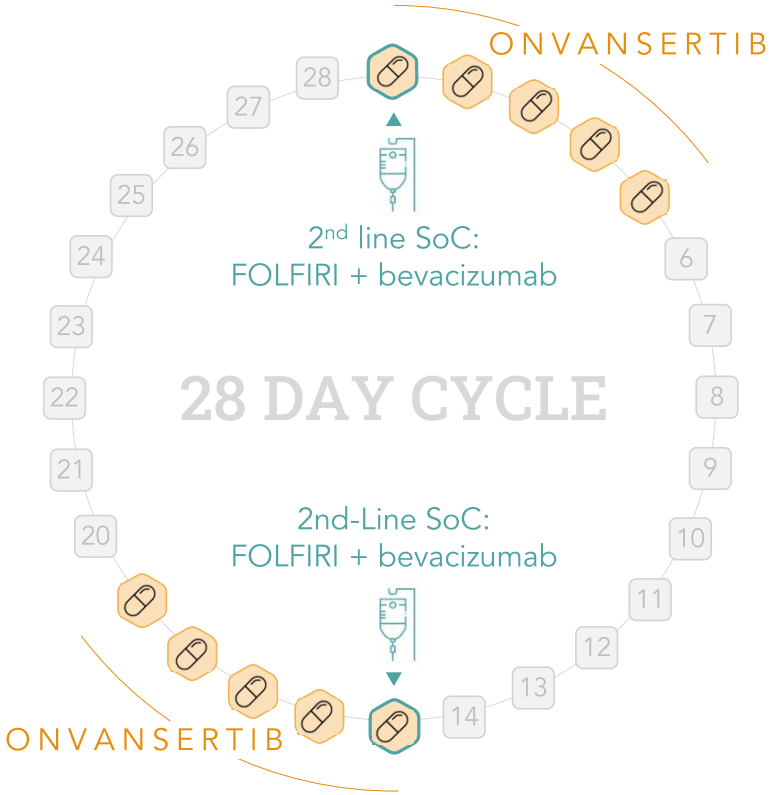
Our trial explored adding onvansertib to FOLFIRI + bev (SoC)

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 2nd line trial patients may or may not have received bev in 1st line

Bev exposed vs bev naïve patients

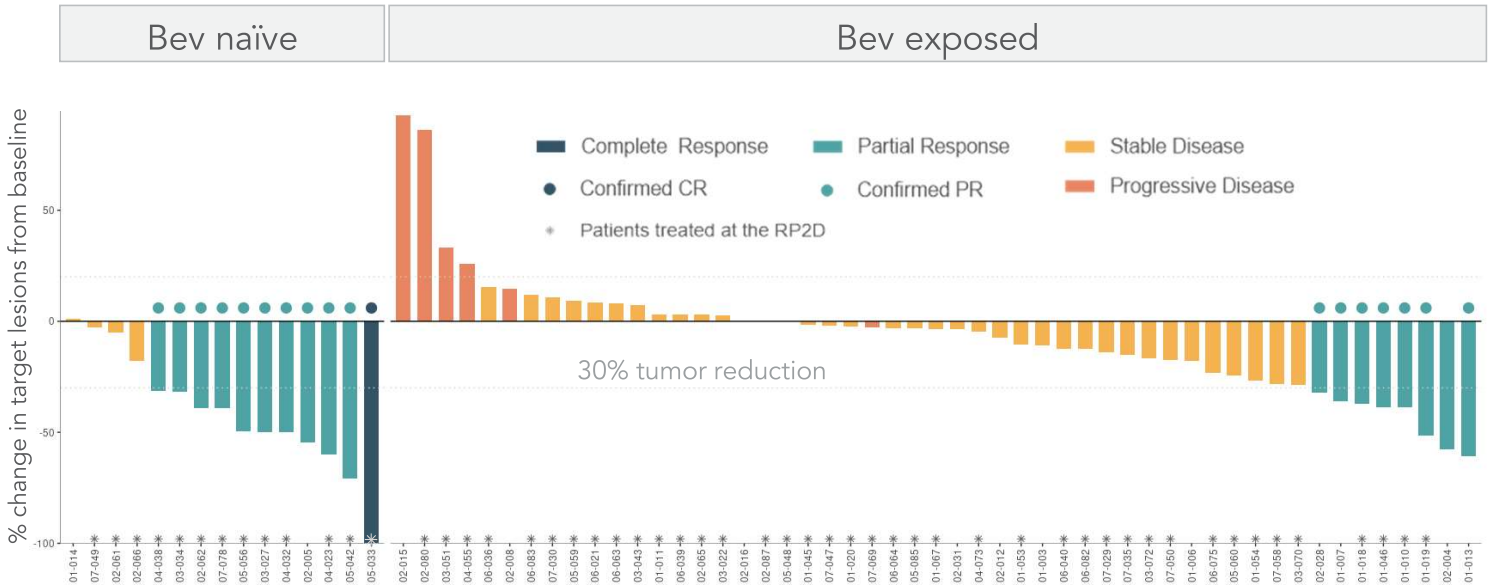
		1st LINE	2nd LINE
"Bev naïve"	patients who did not receive prior bev in 1st line	FOLFOX 23% (15 of 66)	FOLFIRI + **bevacizumab** + ONVANSERTIB
or			
"Bev exposed"	patients who received bev in 1st line	FOLFOX + **bevacizumab** 77% (51 of 66)	

All patients received FOLFIRI + bev + onv in our trial

Bev naïve patients achieved higher response rate with onvansertib+SoC

Best Radiographic Response and Duration of Response* – 66 evaluable patients (as of June 16, 2023)

	All patients	Bev naïve	Bev exposed
N	66	15	51
ORR	**29%** (19)	**73%** (11)	**16%** (8)
95% CI	(18-41%)	(45-92%)	(7-29%)
mDoR	12.0mo	13.0mo	8.9mo
95% CI	(8.9, –)	(12.0, –)	(3.9, –)
Disease Control Rate	91%	100%	88%
Historical controls**			
ORR		23-26%	5-13%

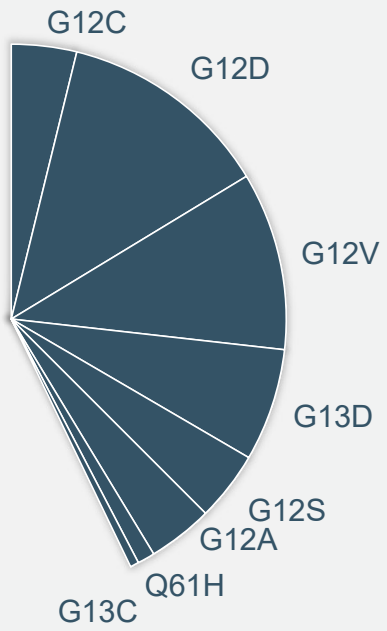


* Radiographic response determined per RECIST 1.1. Waterfall plot and table reflect interim data as of June 16, 2023 from an ongoing trial and unlocked database. Patients 02-008 and 07-029 were categorized as bev naïve in the July 25, 2022 data, but are now determined to have been bev exposed. mDoR CI: "–" means not reached. After external review of the tumor measurements completed May 12, 2023, it was determined that patients 02-028 and 04-038 were confirmed PRs.

** 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.

Patients on our trial achieved responses across KRAS mutations

Frequency of Common KRAS Mutations in mCRC[1]



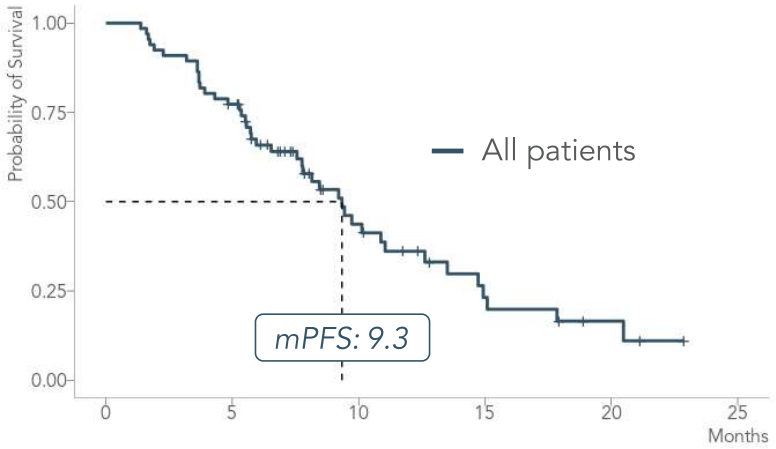
Onvansertib responses across KRAS mutations (as of June 16, 2023)

KRAS Variant	CR+PR	SD	PD	Total
G12D	7	13	1	21
G12V	1	10	2	13
G12A	4	4		8
G13D	4	4		8
G12C	1	2	1	4
G12S		3	1	4
A146T	1	2		3
Q61H	1	2		3
K117N		1	1	2
Total	19	41	6	66

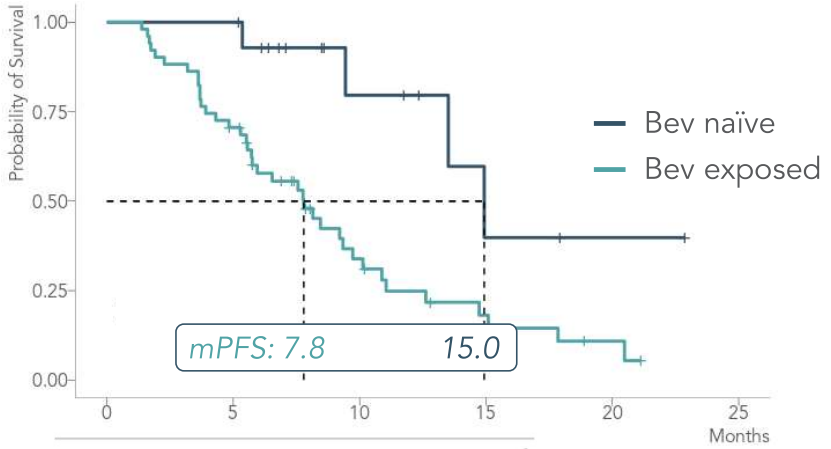
1. Jones R et al. Br J Cancer. 2017 Mar 28;116(7):923-929

PFS exceeds historical controls for SoC, particularly in bev naïve patients

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



Characteristic	N	Event N	mPFS (95%CI)
Overall	66	42	9.3 (7.8, 14)



Characteristic	N	Event N	mPFS (95%CI)	p-value[†]
prior_chemo	66	42		0.003
Bev Naive			15 (14, —)	
Prior Bev			7.8 (5.8, 10)	

[†] Log-rank test

CI of "–" means not reached

Historical controls**

	Bev exposed	Bev naïve
PFS	4.5 - 6.7mos	6.9 - 8.5mos

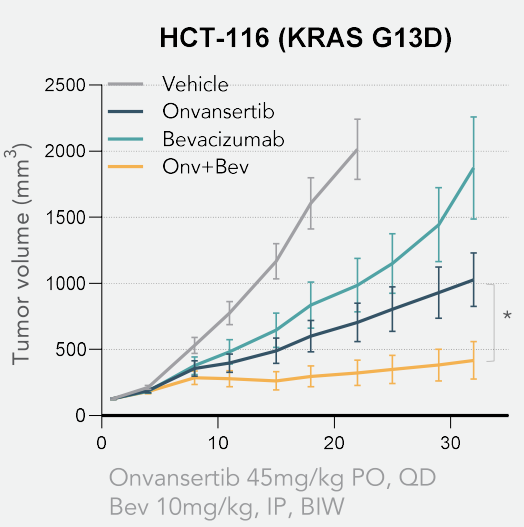
* Onvansertib mPFS are interim data as of June 16, 2023 from an ongoing trial and unlocked database

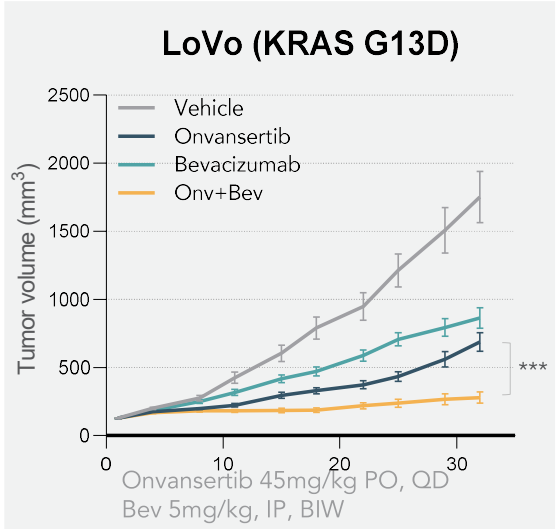
** Bennouna et al., Lancet Oncol 2013; 14: 29–37; Giessen et al., Acta Oncologica, 2015, 54: 187-193; Cremolini et al., Lancet Oncol 2020, 21: 497–507; Antoniotti et al., Correspondence Lancet Oncol June 2020. Giantonio et al., 2007, J Clin Oncol 25:1539-1544; Moriwaki et al., Med Oncol, 2012, 29:2842–2848;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

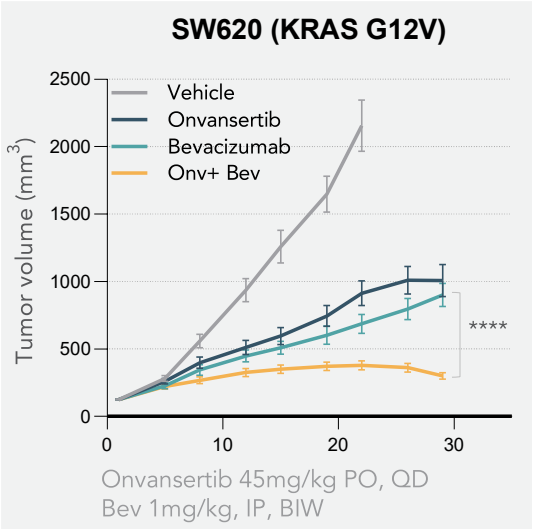
Scientific basis for clinical findings

Onvansertib + bev inhibits tumor growth greater than either agent alone

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

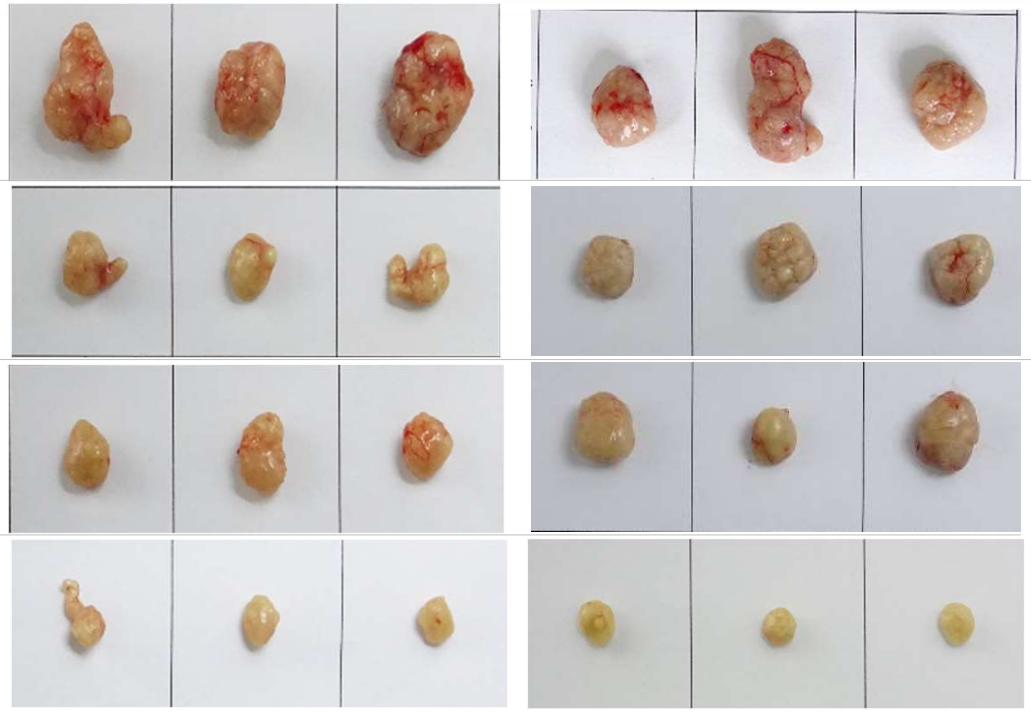






Three KRAS-mutant mCRC xenograft models were treated with vehicle (control), onvansertib, bevacizumab or the combination of onvansertib and bev. 8-9mice/ group. Mean ± SEM are represented on graphs. An unpaired t-test was used to test the difference in tumor volume change on the last day of treatment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

Onvansertib plays an independent role in antiangiogenesis that complements bev



- Roche drug Avastin®
- 8th largest global drug in 2019
  - $7.1B sales

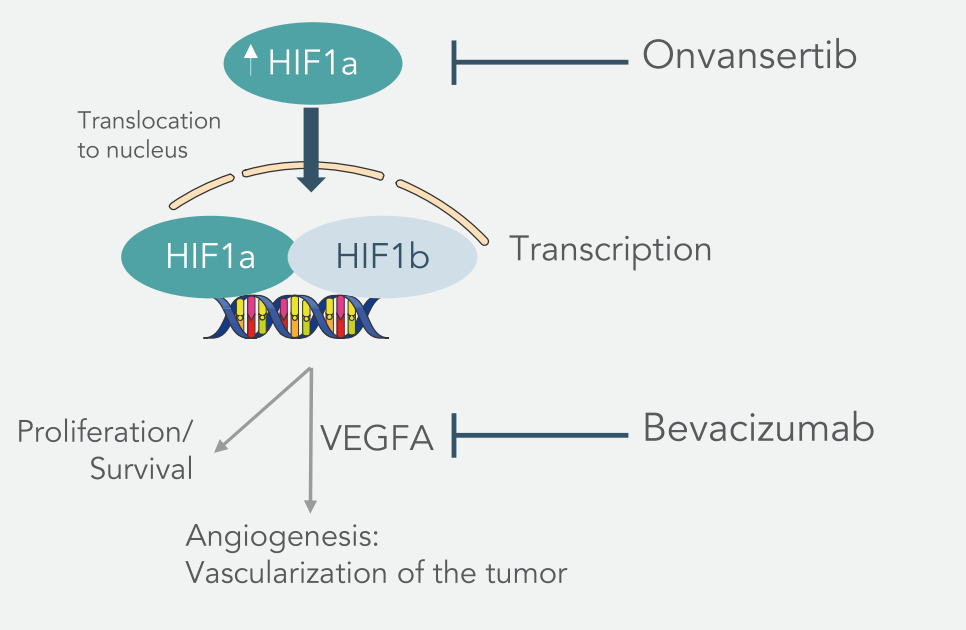
Cardiff Oncology™

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.

Onvansertib and bev are complementary inhibitors of the hypoxia signaling pathway

This new MOA, which inhibits a "survival switch" of tumorigenesis, may underlie the increased efficacy observed clinically



In the low oxygen tumor microenvironment (hypoxia), HIF1a is induced by tumors to increase vascularization by secreting VEGF, and to promote proliferation and survival

Fighting mCRC through PLK1 inhibition

Robust data in lead mCRC program

Path forward to accelerated approval

mCRC program positions onvansertib for accelerated and full-approval

mCRC clinical development program agreed with FDA at June 2023 Type C meeting

CRDF-004

1st line RAS-mutated mCRC trial
90 patients, randomized, 2 doses of onvansertib

Highlights of **CRDF-004** exploratory trial

- Provide randomized clinical safety / efficacy data
- Confirm optimal dose in 1st line
- Expect to provide interim data readout in mid-2024
- Pfizer Ignite will provide clinical execution

CRDF-005

1st line RAS-mutated mCRC registrational trial
320 patients, randomized

Highlights of **CRDF-005** registrational trial

- Seamless registrational trial for accelerated and full approval, as agreed with FDA
- ORR endpoint: For accelerated approval
- PFS / OS trend endpoint: For full approval

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

ENROLLMENT CRITERIA

1st line mCRC

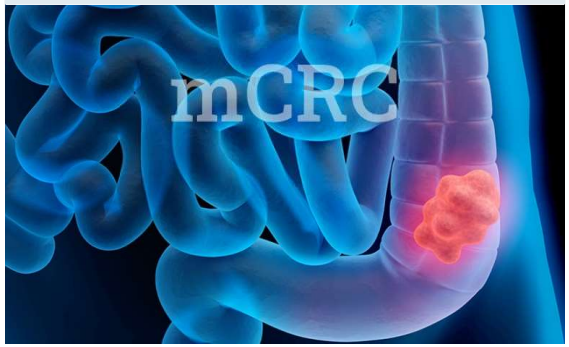
KRAS+/NRAS+

Unresectable

No prior bev, FOLFIRI or FOLFOX treatment

R

N=90
1:1:1



- Onv 20mg + FOLFIRI/bev or FOLFOX/bev (n=30)
- Onv 30mg + FOLFIRI/bev or FOLFOX/bev (n=30)
- SoC: FOLFIRI/bev or FOLFOX/bev (n=30)

ENDPOINTS

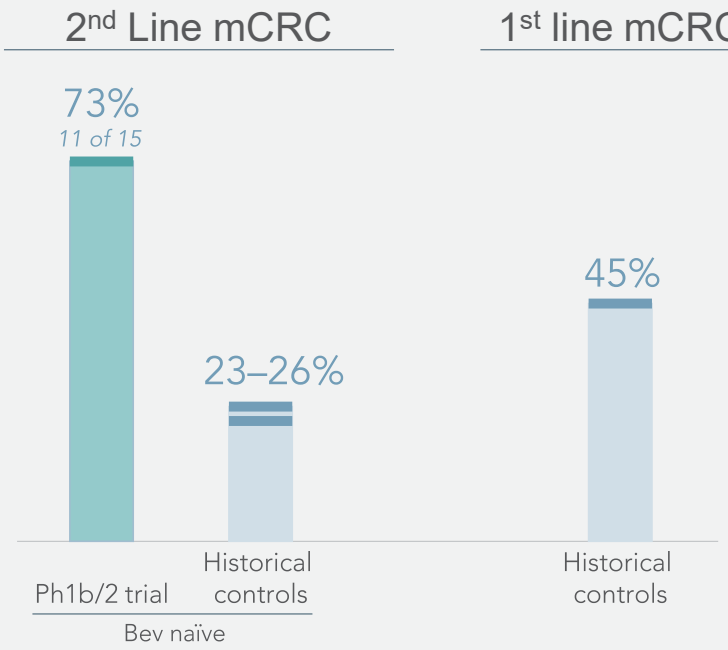
Primary	ORR
Secondary	DoR and PFS
Benchmark of success	ORR ≥65%

PFIZER IGNITE will provide clinical execution for CRDF-004

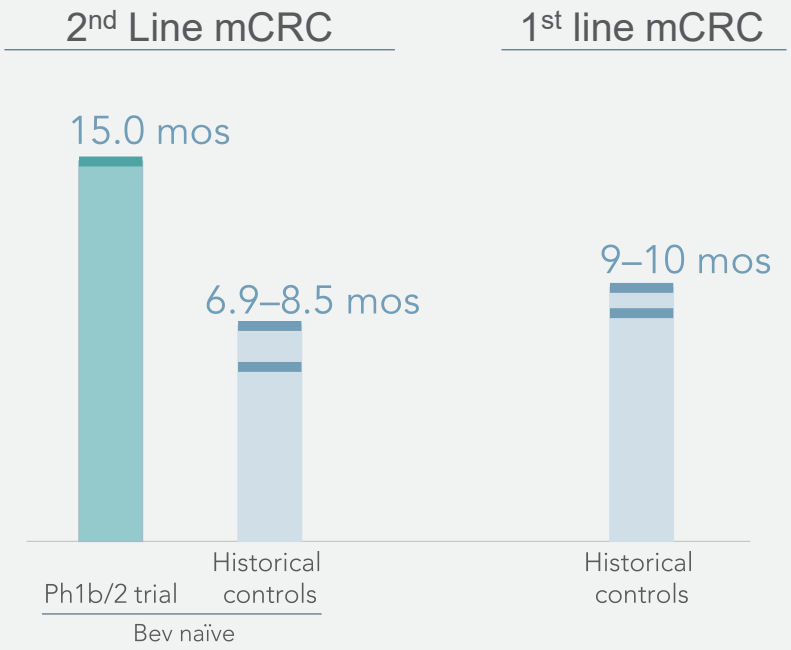
In CRDF-004, each arm will have an equal number of FOLFIRI/bev and FOLFOX/bev patients.

ORR/PFS for bev naïve patients exceeds 1st and 2nd line historical controls

ORR: Onvansertib+SoC vs historical controls*



mPFS: Onvansertib+SoC vs historical controls*



Given the design of prior trials, historical controls include RAS-mut and RAS wild-type cancers

* 2008: Bennouna et al., Lancet Oncol 2013; 14: 29–37; 2013: Giessen et al., Acta Oncologica, 2015, 54: 187-193; 2017: Cremolini et al., Lancet Oncol 2020, 21: 497–507; and Antoniotti et al., Correspondence Lancet Oncol June 2020. J. Clin. Med. 2020, 9, 3889; doi:10.3390/jcm9123889. ORR ad PFS data are interim data from an ongoing trial and unlocked database. Historical controls are from studies in similar anti-angiogenic drugs and restricted geographical areas, and do not all represent purely comparable 2nd line mCRC patient populations.

Pfizer will support clinical execution of 1st line mCRC trial

PFIZER BREAKTHROUGH GROWTH INITIATIVE

November 2021

- $15M investment
- Adam Schayowitz, Ph.D., MBA, Vice President & Medicine Team Group Lead for Breast Cancer, Colorectal Cancer and Melanoma at Pfizer joins Scientific Advisory Board
- Right of first access to data

PFIZER Ignite

August 2023

- Pfizer Ignite will be 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: Positioned to improve 1st line mCRC treatment

First-in-Class PLK1 inhibitor	Robust clinical data in 2L KRAS-mut mCRC	FDA	Pfizer
• **Onvansertib**: first well-tolerated PLK1-selective inhibitor • PLK1 inhibition disrupts tumor growth several ways	• **73%** response rate vs **~25%** in SoC • **15 month** progression free survival vs **~8 month** in SoC	• **FDA**-agreed path to 1st line accelerated approval	• **Pfizer** is equity investor and has seat on SAB • **Pfizer** provides clinical execution of 1st line trial

We expect clinical data from our 1st line RAS-mutated mCRC trial in mid-2024

September 30, 2023 cash and investments*	$81.4M
Net cash used in Operating Activities* (Rolling two-quarter period ending September 30, 2023)	$15.1M
Runway with current cash extends into 2025	

* Financial information above is derived from our unaudited financials in Form 10Q filed on 11/2/23.

Cardiff Oncology™

Appendix

Additional mCRC Data

The trial's patient demographics reflects 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	
1	5 (7%)
≥2	63 (93%)
Prior bevacizumab treatment[5]	
Yes	51 (75%)
No	17 (25%)

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

Bev naïve patients experienced more durable responses

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

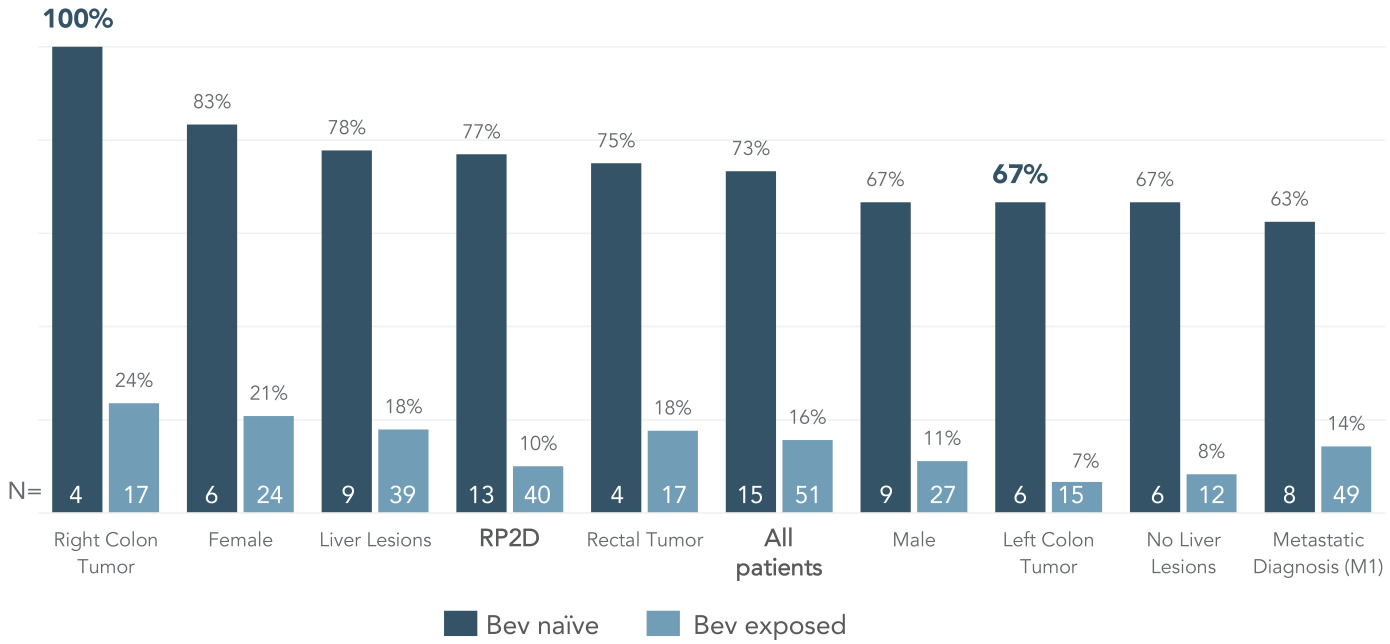
	All patients	Bev naïve	Bev exposed
Pursued surgery / ablation	18% (12/66)	53% (8/15)	8% (4/51)
Initial PR at 8 week scan	9	8	1
Initial PR at 16+ week scan	10	3	7

* Swimmer plot / table reflect interim data as of June 16, 2023 from an ongoing trial and unlocked 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.

ORR is consistently greater for bev naïve patients across characteristics

No single patient characteristic explains the difference in response rates by prior bev status

ORR (%) for Bevacizumab Naïve vs. Exposed Patients* – as of June 16, 2023



* Onvansertib ORR is interim data as of June 16, 2023 from an ongoing trial and unlocked database.

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

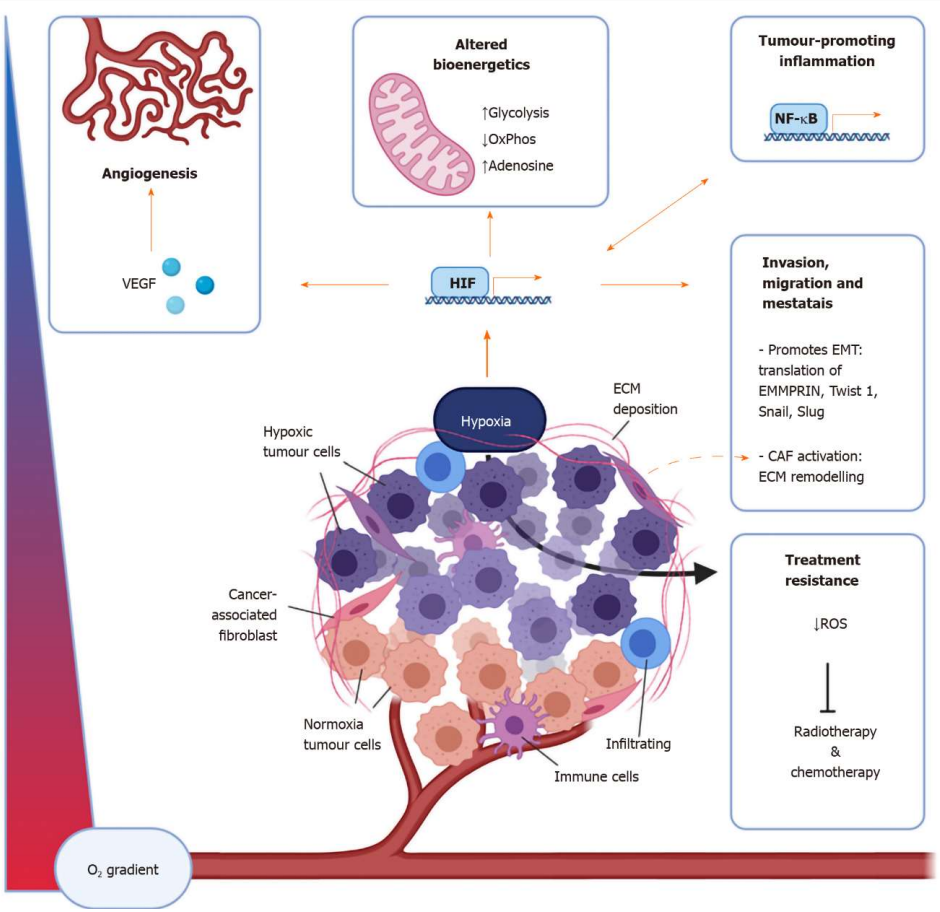
TEAE	GR1	GR2	GR3	GR4	TOTAL		TEAE	GR1	GR2	GR3	GR4	TOTAL	
Fatigue	24	22	7	0	53	78%	Cough	11	0	0	0	11	16%
Neutropenia	1	18	23	7	49	72%	Pyrexia	8	1	1	0	10	15%
Nausea	29	13	4	0	46	68%	Dyspnea	7	3	0	0	10	15%
Diarrhea	21	13	4	0	38	56%	AST Increase	7	2	1	0	10	15%
Leukopenia	9	14	5	1	29	43%	Lymphocytopenia	2	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 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.

Hypoxia: a hallmark of cancer

In response to hypoxia, cancer cells activate the hypoxia-inducible factor (HIF) pathway, which can promote tumorigenesis through multiple means:

- Angiogenesis
- Cell proliferation and survival
- Highly immunosuppressive and invasive tumor microenvironment
- Hypoxia-induced EMT and acquisition of cancer cell stemness in turn driving metastasis
- Reprogrammed cancer cell metabolism and increased glycolysis
- Delivery of anti-cancer agents rendered more intractable

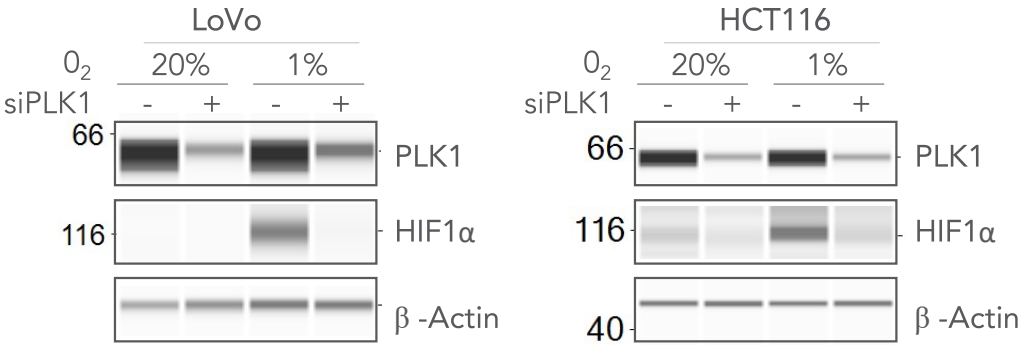


From: King et al., World J Gastrointest Oncol. 2021

Onvansertib inhibits the hypoxia signaling pathway by downregulating HIF1α expression

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

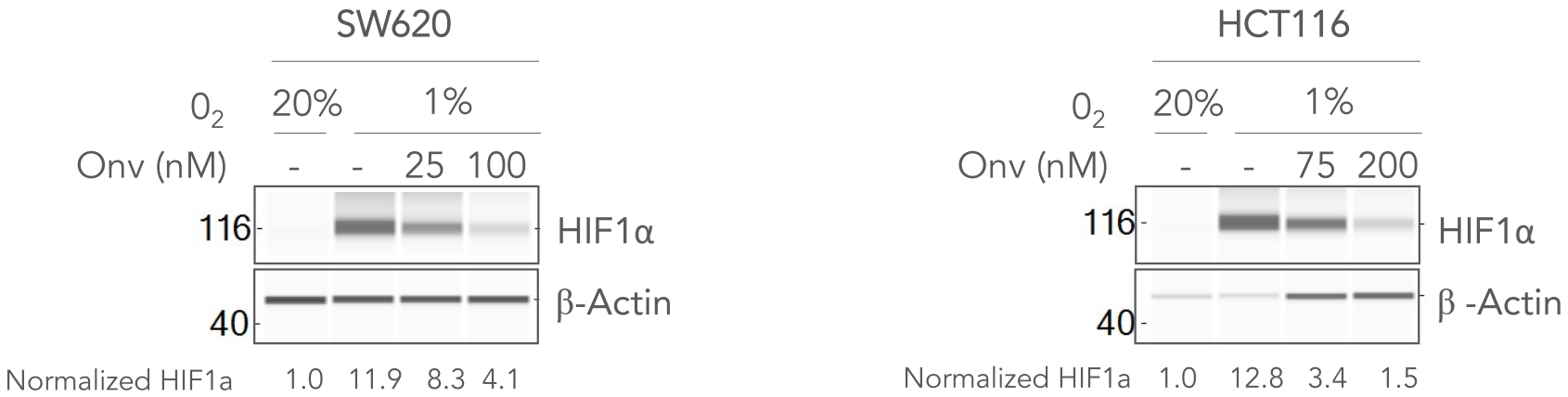
PLK1 inhibition using siRNA against PLK1 (siPLK1)[2] prevented hypoxia-induced HIF1α expression



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

PLK1 inhibition blocks hypoxia-induced HIF1α protein expression in a dose dependent manner in KRAS-mutant mCRC cells

- KRAS-mutant CRC cell lines were cultured under normoxia (20%0_2) or hypoxia (1%0_2), in the presence or absence (-) of onvansertib
- HIF1α protein was induced by hypoxia in SW620 and HCT116 cells
- Onvansertib inhibited in a dose-dependent manner HIF1α induction under hypoxia in both cell lines



SW620 and HCT116 cell lines were treated for 20h with or without onvansertib (Onv) and then cultured for an additional 4h in 20%02 or 1%02.

Prior bev treatment modulates gene pathways that can confer resistance to bev and onvansertib

Aim: to identify potential mechanisms of treatment resistance in bev exposed KRAS-mutant mCRC patients
Method:

KRAS-mutant mCRC patients
1st line treatment

FOLFOX (n=71)

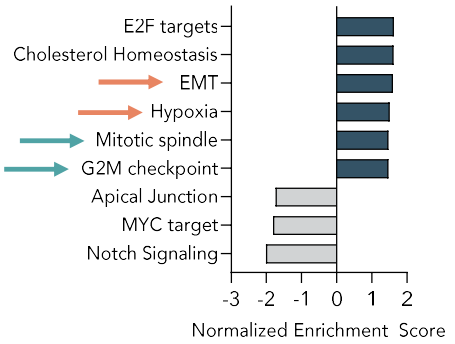
FOLFOX + bev (n=64)

RNA-sequencing of post-treatment biopsies

Analysis of genes and pathways differentially expressed in Bev-exposed vs Bev-naïve patients

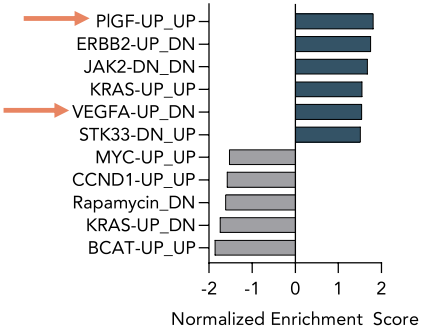
- Bev exposed tumors showed up-regulation of pathways associated with:
  - Hypoxia
  - G2/M checkpoint and mitosis
- Up-regulation of these pathways may drive resistance to onvansertib and bev
- Additionally, modulation of oncogenic signatures associated with angiogenic factors (PlGF, VEGFA) were observed in bev exposed tumors and may drive treatment resistance

GSEA Hallmarks of Cancer
Enriched in Bev-exposed Tumors



FDR p-value≤0.05

Oncogenic Signatures
Enriched in Bev-exposed Tumors



UP: up-regulated, DN: down-regulated

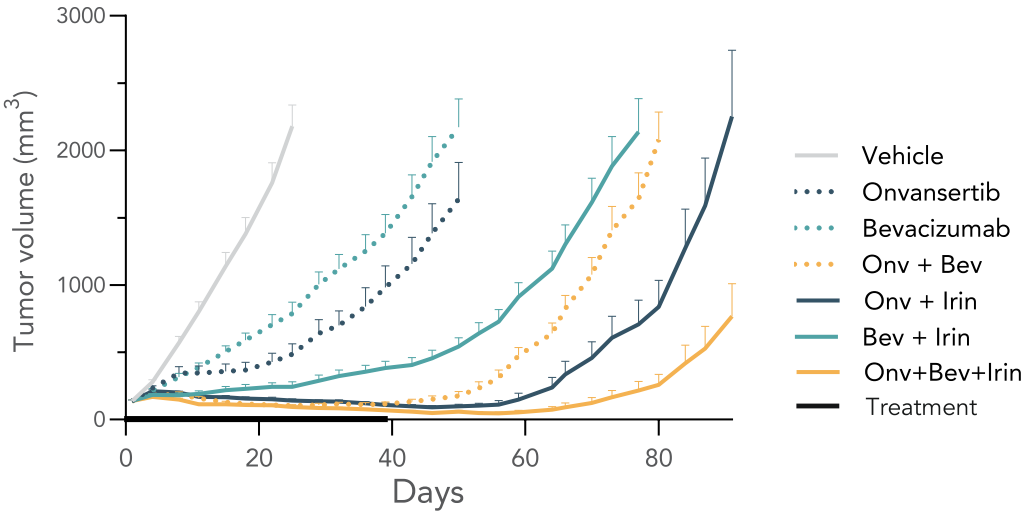
In collaboration with Tempus

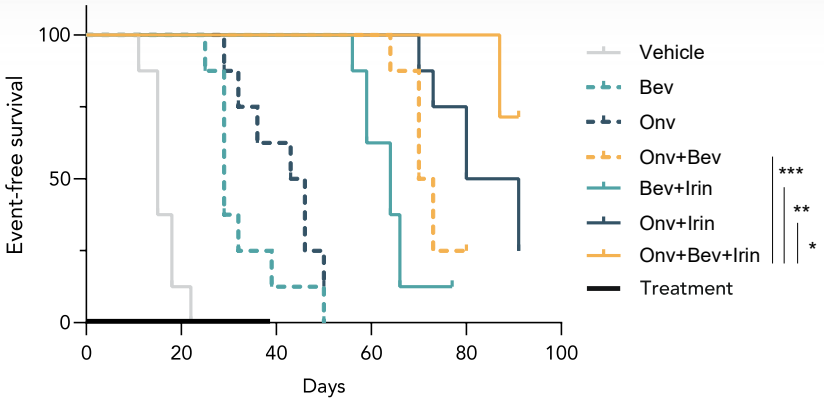
The combination of onvansertib, bevacizumab and irinotecan showed greater potency than each individual or doublet therapy

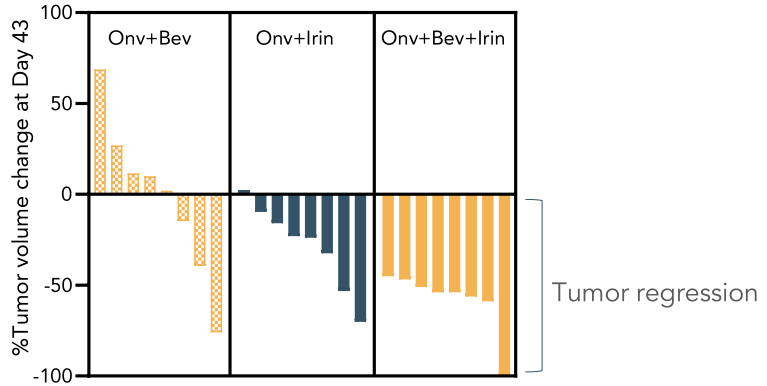
The combination of onvansertib, bevacizumab and irinotecan was potent in the HCT116 xenograft model, resulting in:

- 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.

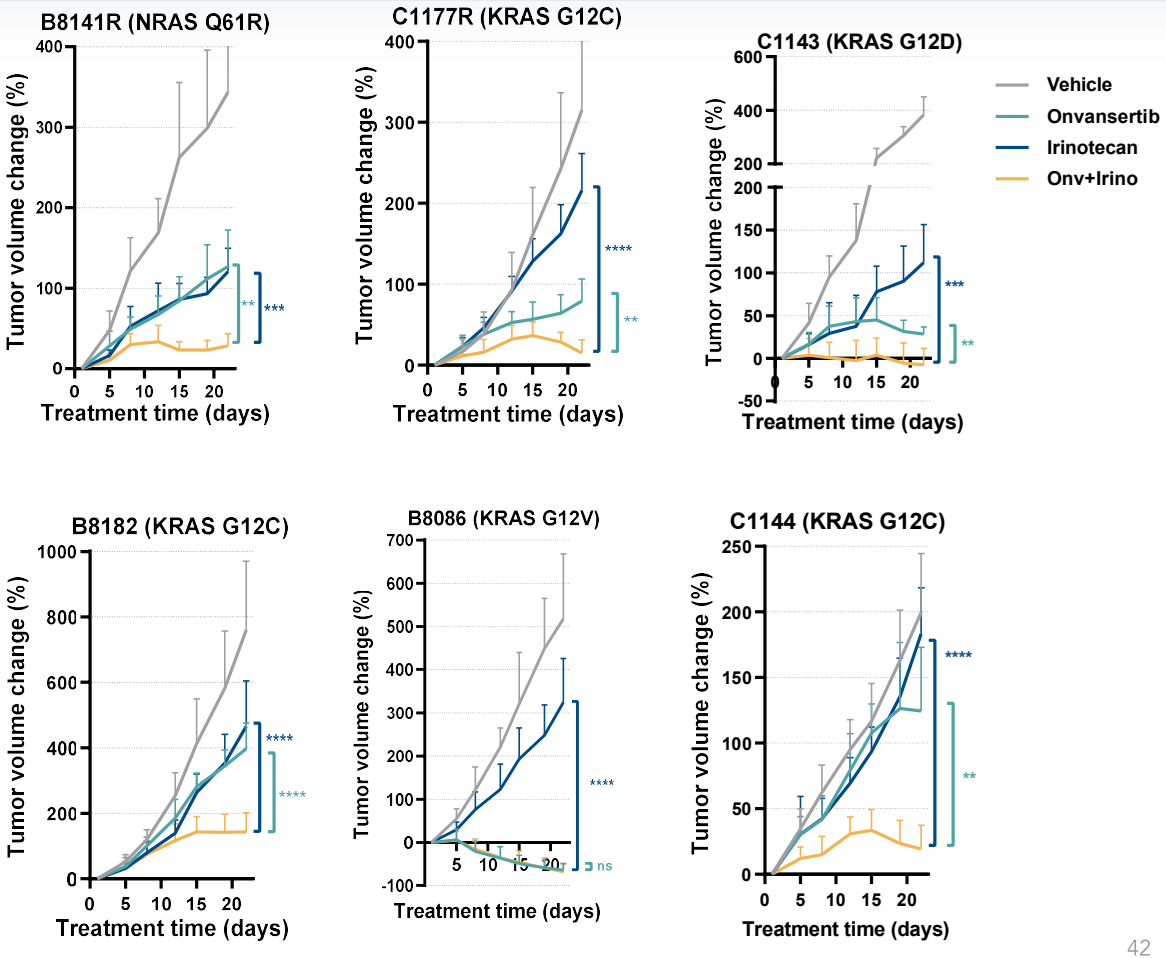
Onvansertib in combination with irinotecan in RAS-mutant CRC PDXs

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

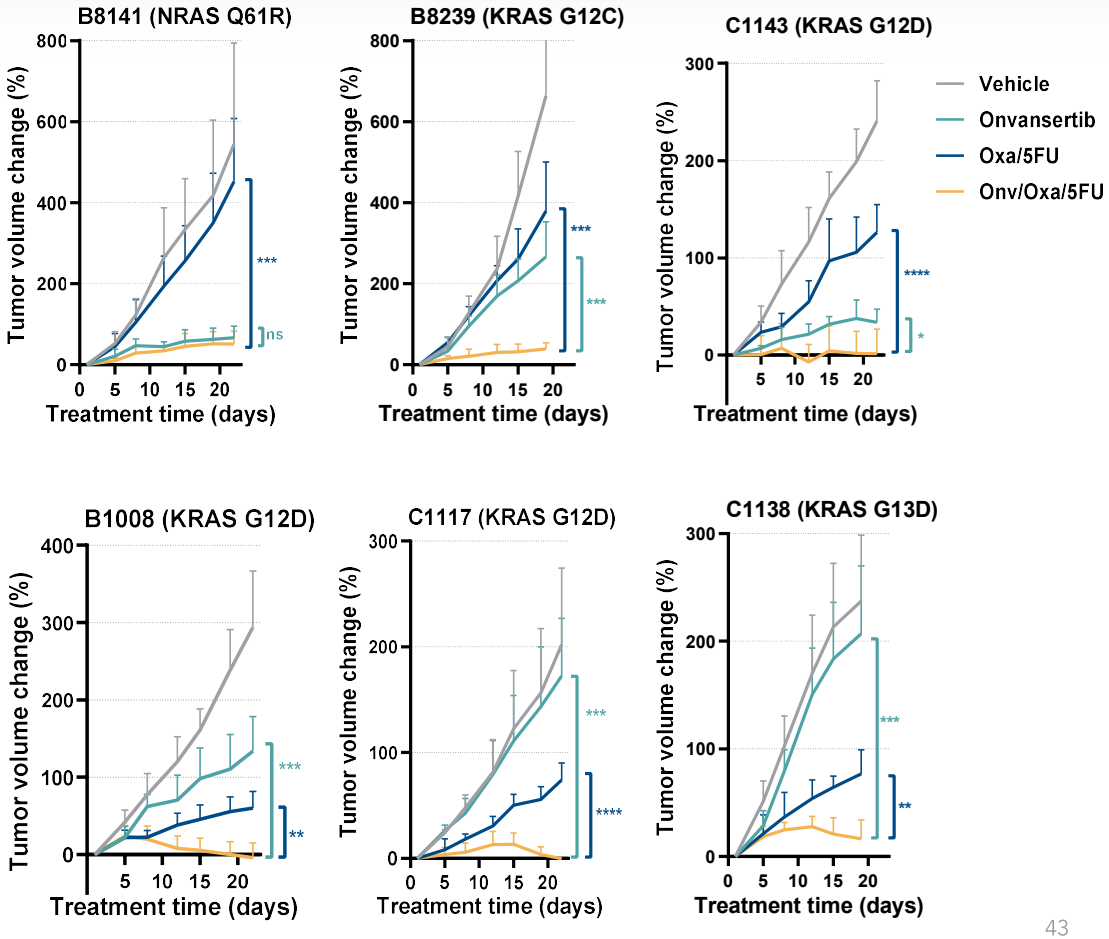
The chemotherapeutics oxaliplatin+5FU had no or modest activity in the 6 RAS-mutant PDX models tested.

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)

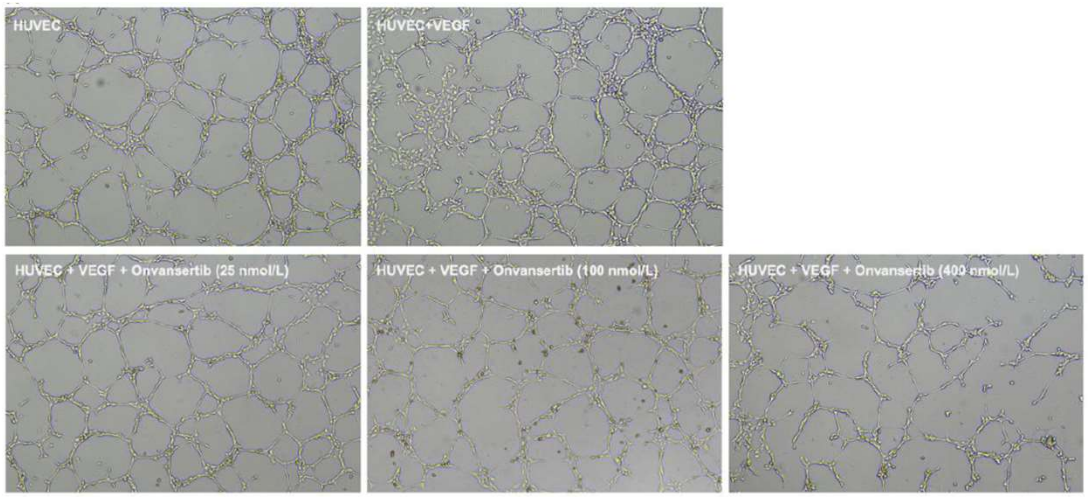


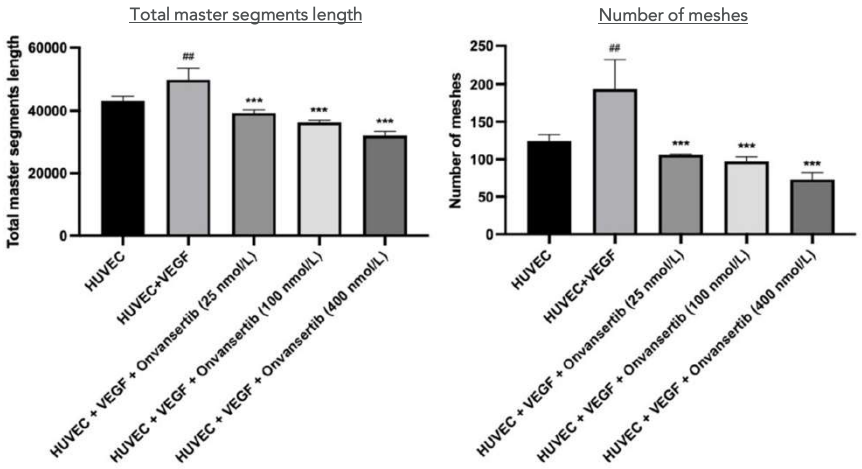
Dosing schedule: onvansertib 45 mg/kg daily; oxaliplatin 10mg/kg weekly; 5-FU 25mg/kg 5times/week for up to 21days. Mean + SD are represented. Unpaired t-test, *p<0.05, **p<0.01, ***p<0.001, ****p<0.0001

Onvansertib inhibits vascularization *in vitro*

Tube formation assay: HUVEC endothelial cells seeded onto a 3D extracellular matrix form tube-like structures upon stimulation with the angiogenic factor VEGFA, simulating the formation of new blood vessels

Treatment with onvansertib (25, 100 and 400nM) for 24h significantly reduced VEGFA-stimulated HUVECs tube formation in a dose-dependent manner, demonstrating that onvansertib inhibits angiogenesis *in vitro*





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Appendix:

Metastatic Pancreatic Adenocarcinoma (mPDAC)

Data from two mPDAC trials provides a path forward in 1st line setting

mPDAC
CRDF-001 Ph 2 Second-Line Trial

- Combination with Nal-irinotecan/leucovorin/5-FU

mPDAC
Biomarker Discovery Trial (IIT)

- Patients have 10 days of onvansertib monotherapy with pre- and post-therapy biopsies and bloodwork

Path forward: Move to 1st line mPDAC

- New IIT combining onvansertib with SoC (Gemzar/Abraxane)

Data from two mPDAC trials provides a path forward in 1st line setting

mPDAC
CRDF-001 Ph 2 Second-Line Trial

- Combination with Nal-irinotecan/leucovorin/5-FU

mPDAC
Biomarker Discovery Trial (IIT)

- Patients have 10 days of onvansertib monotherapy with pre- and post-therapy biopsies and bloodwork

Path forward: Move to 1st line mPDAC

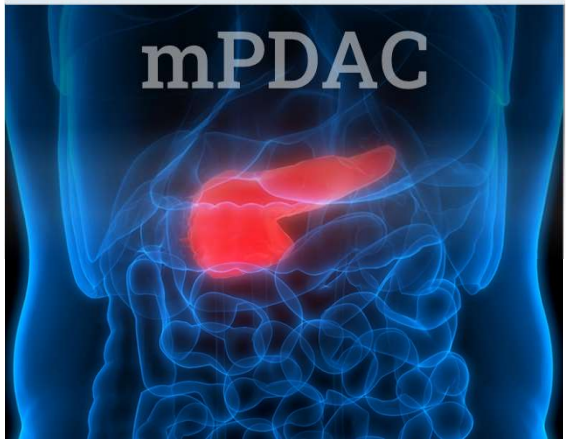
- New IIT combining onvansertib with SoC (Gemzar/Abraxane)

CRDF-001 mPDAC 2nd line Ph2 trial combines onvansertib with SoC

ENROLLMENT CRITERIA

2nd line refractory patients

Measurable tumor by RECIST 1.1



OBJECTIVE

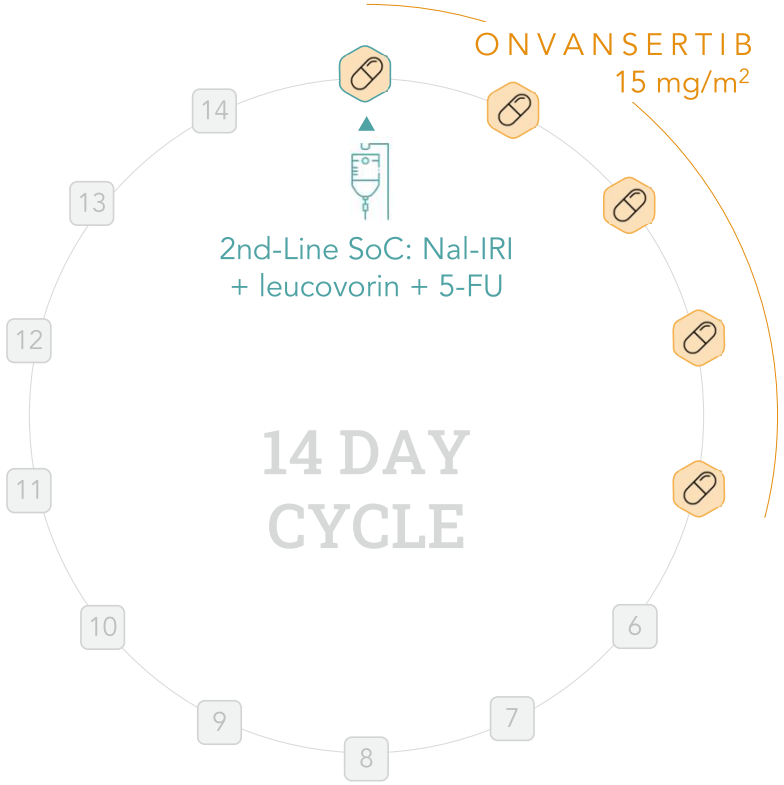
To determine the efficacy and safety of onvansertib when added to standard of care

PRIMARY ENDPOINT

ORR (RECIST 1.1)

SECONDARY ENDPOINT

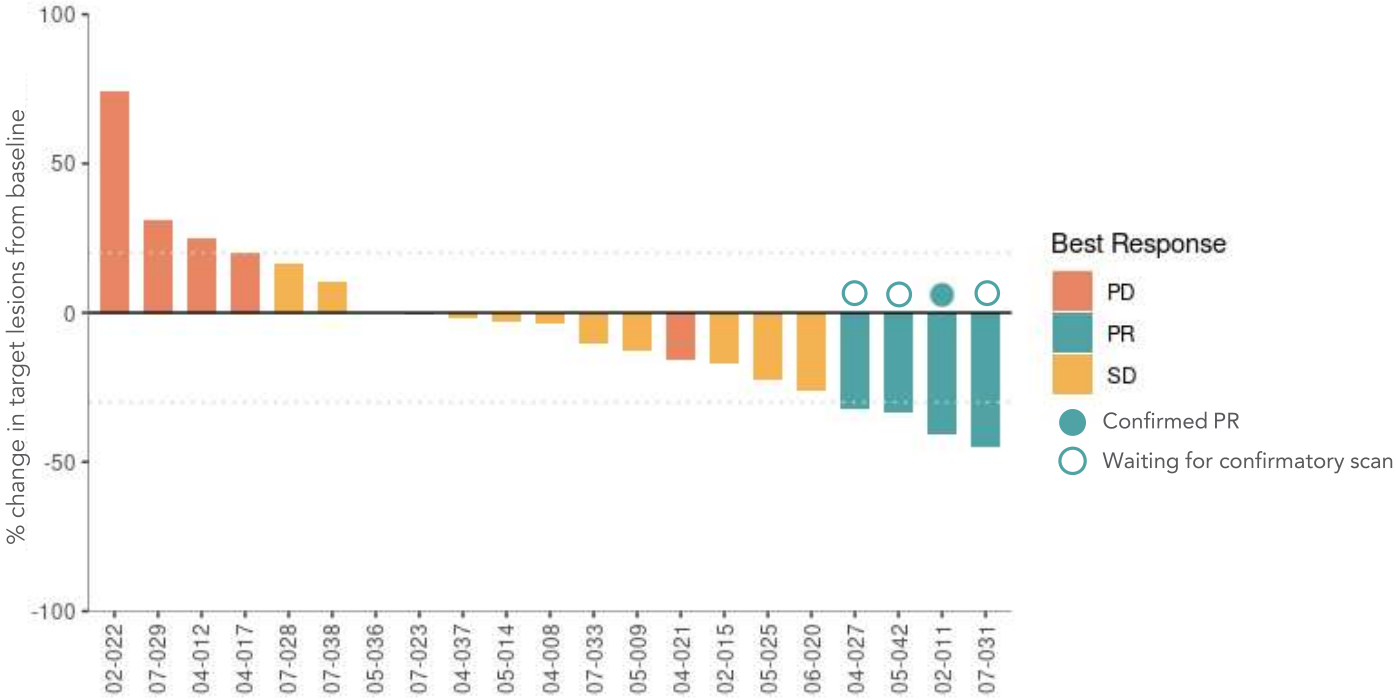
Disease Control Rate (DCR)



Onvansertib+SoC has higher efficacy than 2nd line historical controls

Best Radiographic Response – 21 evaluable patients (as of September 13, 2023)*

	CRDF-001	Historical controls[1] 2nd line mPDAC	Historical controls[1] 1st line mPDAC
ORR	19% (4/21)	7.7%	23%

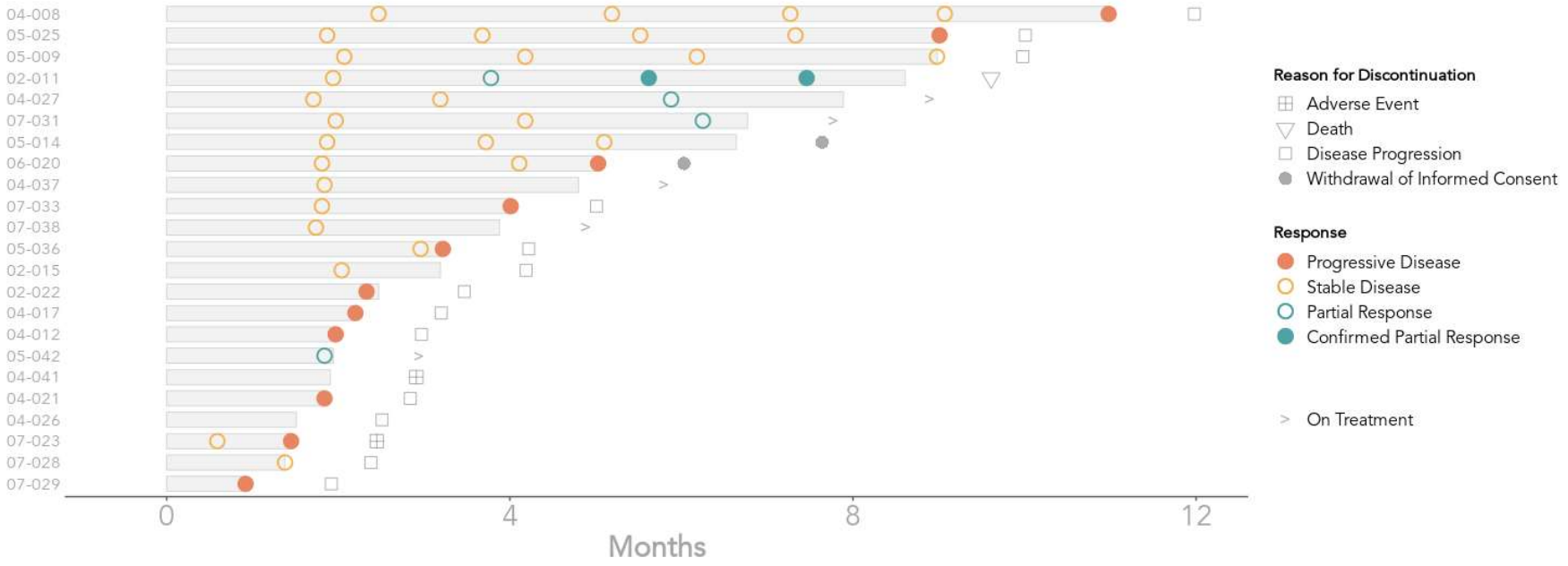


* Radiographic response determined per RECIST 1.1. Waterfall plot and table reflect interim data as of September 13, 2023 from an ongoing trial and unlocked database. For ORR analysis, there are two patients excluded (04-026 and 04-041) that had two cycles of treatment but left the trial before their first post-baseline scan.

1. FDA insert for Onivyde (Nal-IRI): https://www.accessdata.fda.gov/drugsatfda_docs/label/2015/207793lbl.pdf; 387: 545–57. Von Hoff et al., N Engl J Med 2013; 369:1691-703.

Stable disease patients have converted to partial responses over time

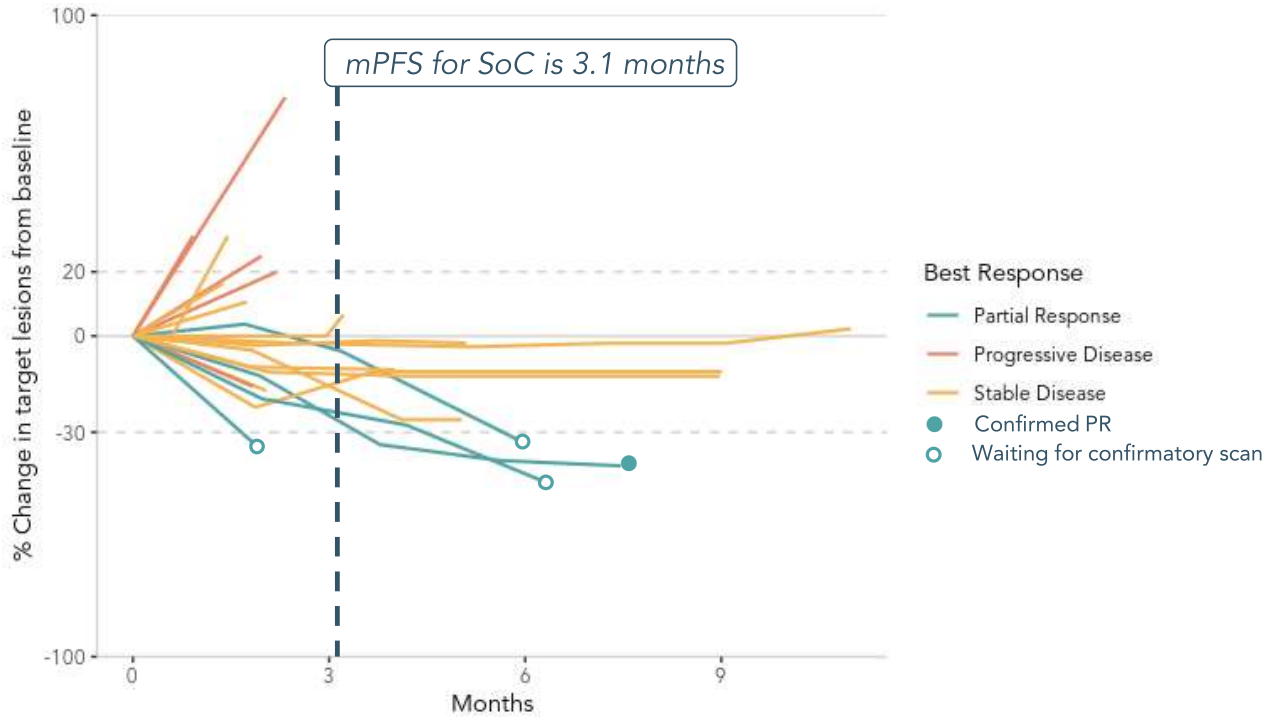
Swimmer plot – 23 evaluable patients (as of September 13, 2023)*



* Swimmer plot reflects interim data as of September 13, 2023 from an ongoing trial and unlocked database. For the swimmer plot, there are two patients included (04-026 and 04-041) that had two cycles of treatment but left the trial before their first post-baseline scan.

Patient responses to onvansertib+SoC can deepen over time

Spider plot – 21 evaluable patients (as of September 13, 2023)*

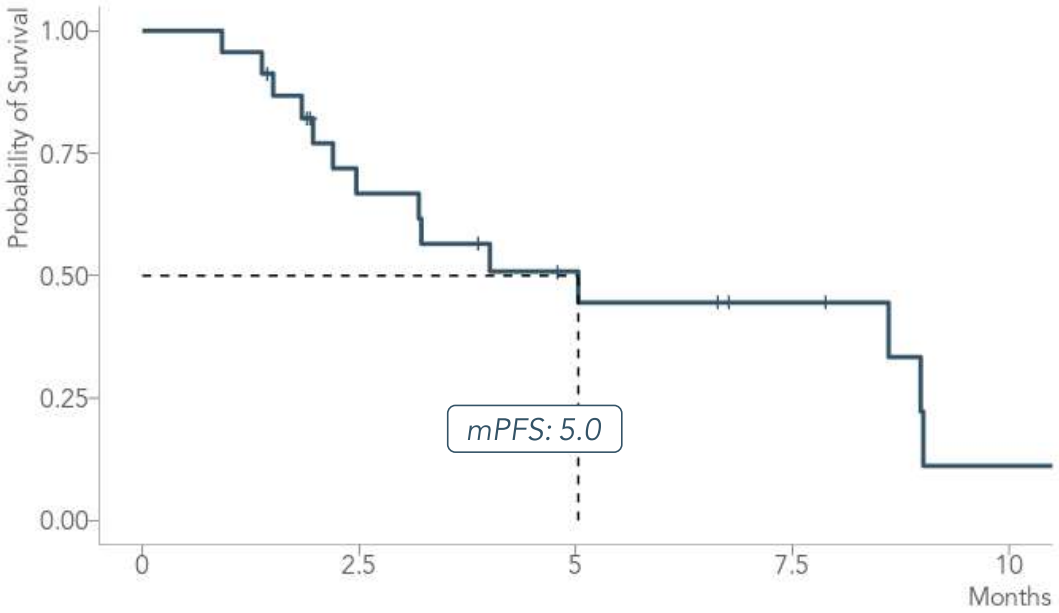


* Spider plot reflect interim data as of September 13, 2023 from an ongoing trial and unlocked database. For ORR analysis, there are two patients excluded (04-026 and 04-041) that had two cycles of treatment but left the trial before their first post-baseline scan.

Onvansertib+SoC has longer median PFS than 2nd line historical controls

Progression-free survival – 23 evaluable patients (as of September 13, 2023)*

	CRDF-001	Historical controls[1]	
		2nd line mPDAC	1st line mPDAC
mPFS	5.0 mos	3.1 mos	5.5 mos
16 week progression-free[2]	56%	Not available	48%



* Onvansertib mPFS are interim data as of September 13, 2023 from an ongoing trial and unlocked database. For PFS analysis, there are two patients included (04-026 and 04-041) that had two cycles of treatment but left the trial before their first post-baseline scan.

1. FDA insert for Onivyde (Nal-IRI): https://www.accessdata.fda.gov/drugsatfda_docs/label/2015/207793lbl.pdf ; 387: 545–57. Von Hoff et al., N Engl J Med 2013; 369:1691-703.
2. Probability of being progression-free at 16 weeks using KM survival analysis. Data not available for 2nd line

Data from two mPDAC trials provides a path forward in 1st line setting

mPDAC
CRDF-001 Ph 2 Second-Line Trial

- Combination with Nal-irinotecan/leucovorin/5-FU

mPDAC
Biomarker Discovery Trial (IIT)

- Patients have 10 days of onvansertib monotherapy with pre- and post-therapy biopsies and bloodwork

Path forward: Move to 1st line mPDAC

- New IIT combining onvansertib with SoC (Gemzar/Abraxane)

mPDAC Biomarker Discovery trial evaluates onvansertib monotherapy

Investigator-initiated trial at OHSU Knight Cancer Institute

ENROLLMENT CRITERIA

Patients with metastatic pancreatic cancer (any line)

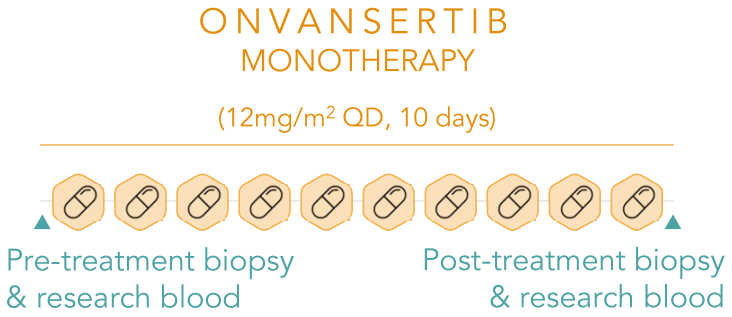
OBJECTIVES

Responsive biomarkers

- To demonstrate pancreatic tumor response to onvansertib monotherapy by measuring Ki67 and CA 19-9

Predictive biomarkers

- Use multi-omic analyses to identify predictive biomarkers of pancreatic tumor response to onvansertib



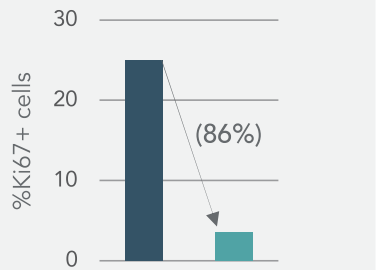
Obtain biopsies / bloodwork before and after 10 days of onvansertib monotherapy to conduct extensive multi-omic analyses

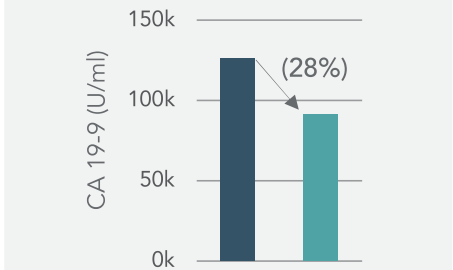
Onvansertib monotherapy decreased tumor proliferation and CA19-9

Biomarker Discovery Trial: Biomarker Response* – 2 patients (as of September 13, 2023)

- Ki67 is a well-established marker of tumor proliferation
- CA 19-9 is a clinically-used biomarker to monitor treatment response

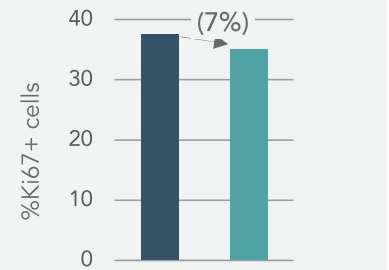
Patient 28 (tumor responder)

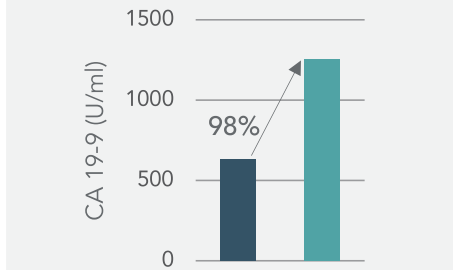




Mutation: KRAS G12V
1st line: Atezo/Bev + Gem/Nab → Response
2nd line: FOLFIRINOX → Progression
3rd line: Onvansertib monotherapy → CA19-9 Response

Patient 33 (tumor non-responder)





Mutation: KRAS Q61R
1st line: FOLFIRINOX → Response
2nd line: Onvansertib monotherapy → CA19-9 Progression

Pre-treatment Post-treatment

* Patient 28 and patient 33 had liver matastases and biopsies were taken pre- and post-onvansertib monotherapy treatment for ten days.

Data from two mPDAC trials provides a path forward in 1st line setting

mPDAC
CRDF-001 Ph 2 Second-Line Trial

- Combination with Nal-irinotecan/leucovorin/5-FU

mPDAC
Biomarker Discovery Trial (IIT)

- Patients have 10 days of onvansertib monotherapy with pre- and post-therapy biopsies and bloodwork

Path forward: Move to 1st line mPDAC

- New IIT combining onvansertib with SoC (Gemzar/Abraxane)

Proposed mPDAC 1st line Ph2 trial combines onvansertib with SoC

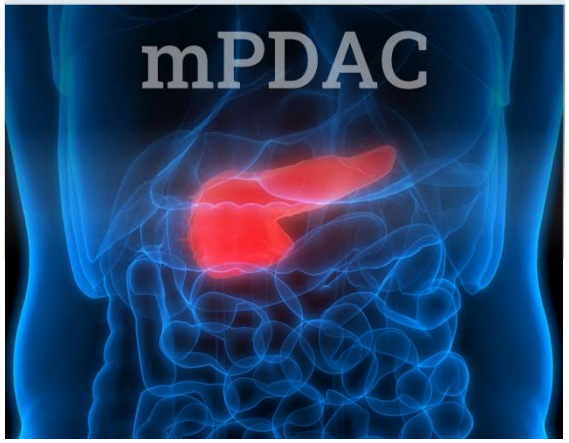
Proposed investigator-initiated trial with the OHSU Knight Cancer Institute

ENROLLMENT CRITERIA

First-line patients

Unresectable

Locally advanced or metastatic



TWO LEAD-IN COHORTS

Cohort 1

- 10-day lead-in with onvansertib monotherapy (30mg po daily)

Cohort 2

- No lead-in therapy

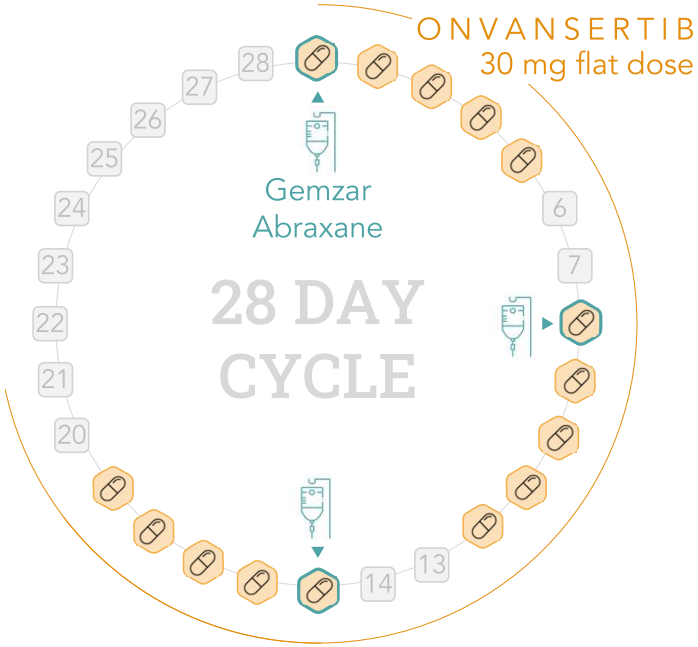
PRIMARY ENDPOINT

ORR, DCR at 16 weeks

SECONDARY ENDPOINTS

DoR, PFS, Safety

SUBSEQUENT CHEMO + ONVANSERTIB TREATMENT*



* If a DLT occurs at dose level 1; then omit day 8 chemo only, and continue with onvansertib 30mg dose; but if toxicity persists at day 15, then decrease onvansertib dose to 20mg daily

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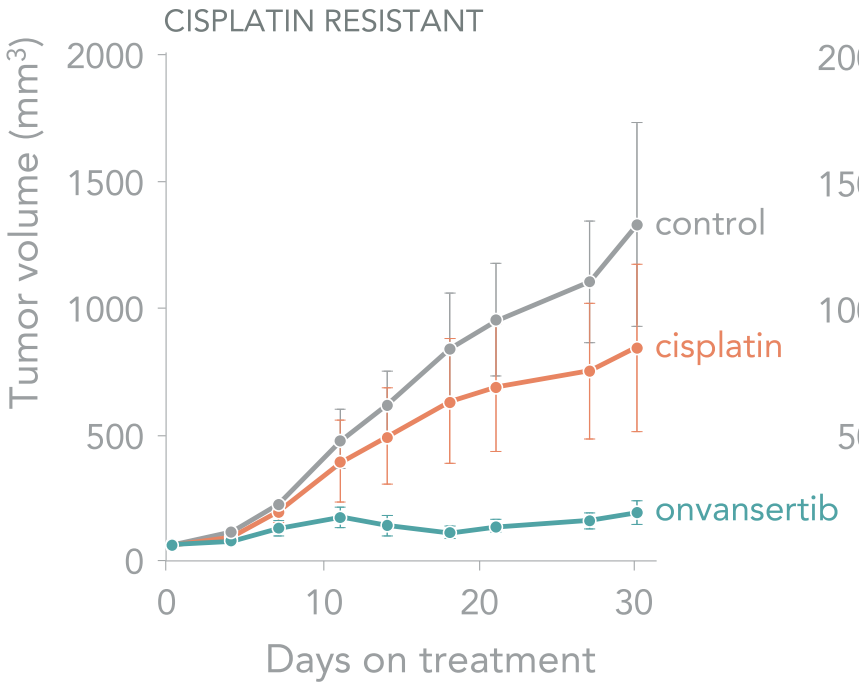
Appendix:
Investigator-Initiated Trial
Small Cell Lung Cancer (SCLC)

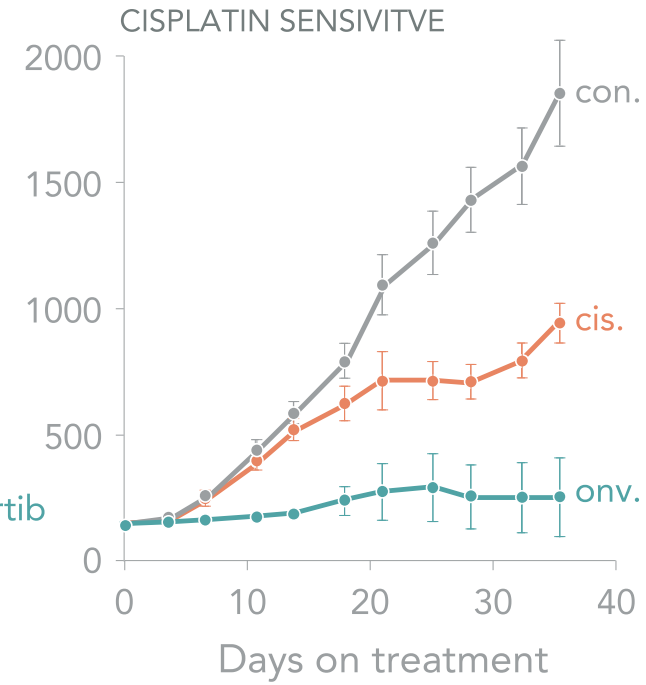
Onvansertib demonstrates single-agent activity in SCLC

TRIAL RATIONALE

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

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

UPMC LIFE CHANGING MEDICINE

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).

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Appendix:

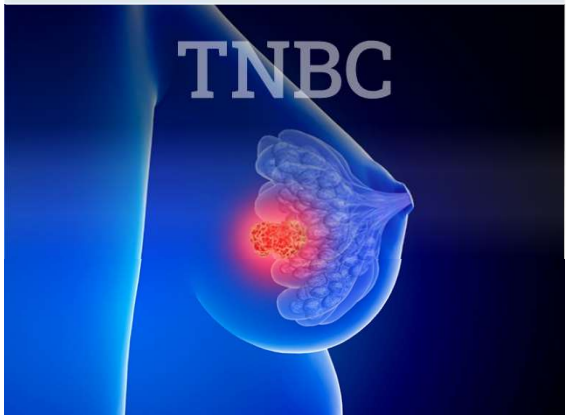
Investigator-Initiated Trial

Triple Negative Breast Cancer (TNBC)

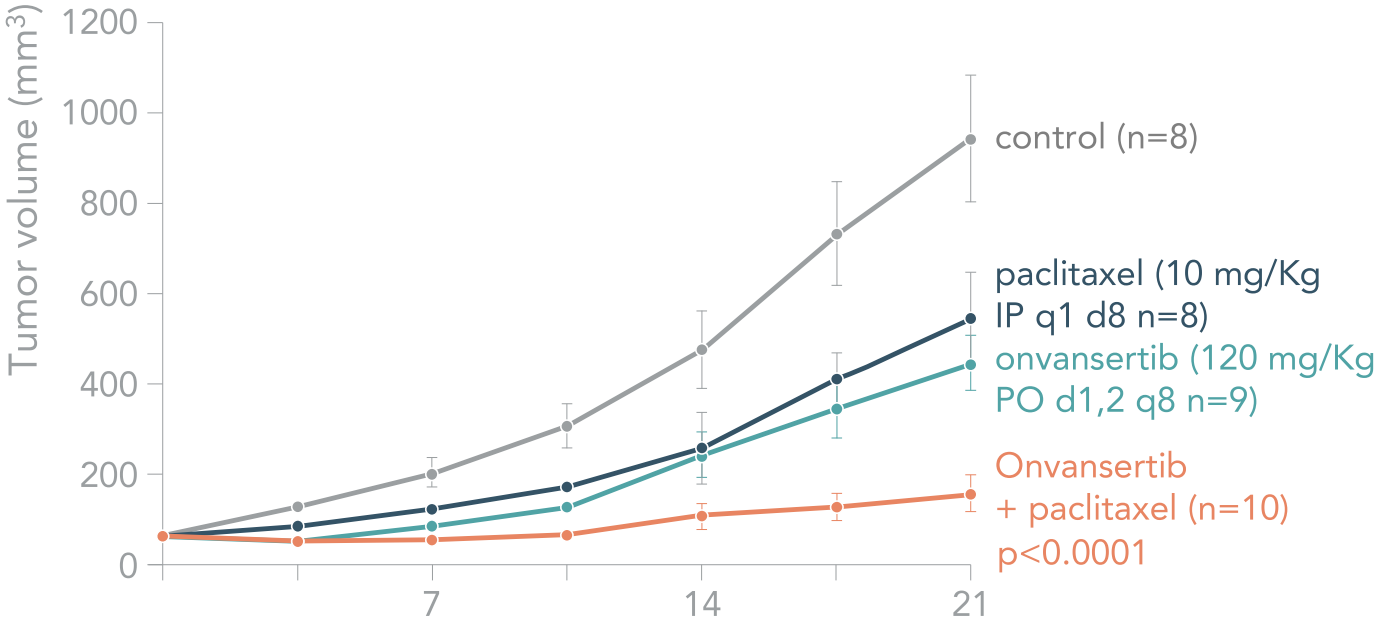
Onvansertib + paclitaxel is superior to single agent therapy

TRIAL RATIONALE

The combination of onvansertib + paclitaxel showed significant synergy



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.

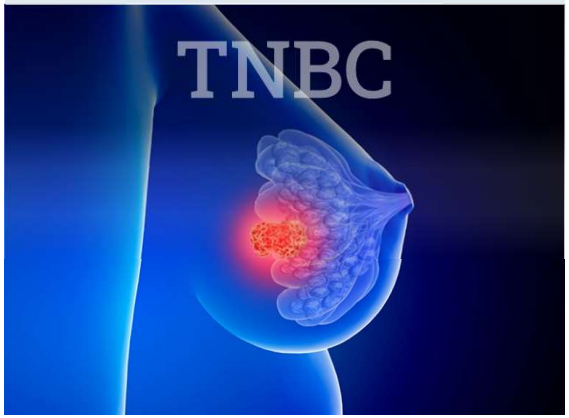
This is the first trial to explore onvansertib + paclitaxel combination

ENROLLMENT CRITERIA

Metastatic TNBC relapsed or progressed

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

Dana-Farber Cancer Institute



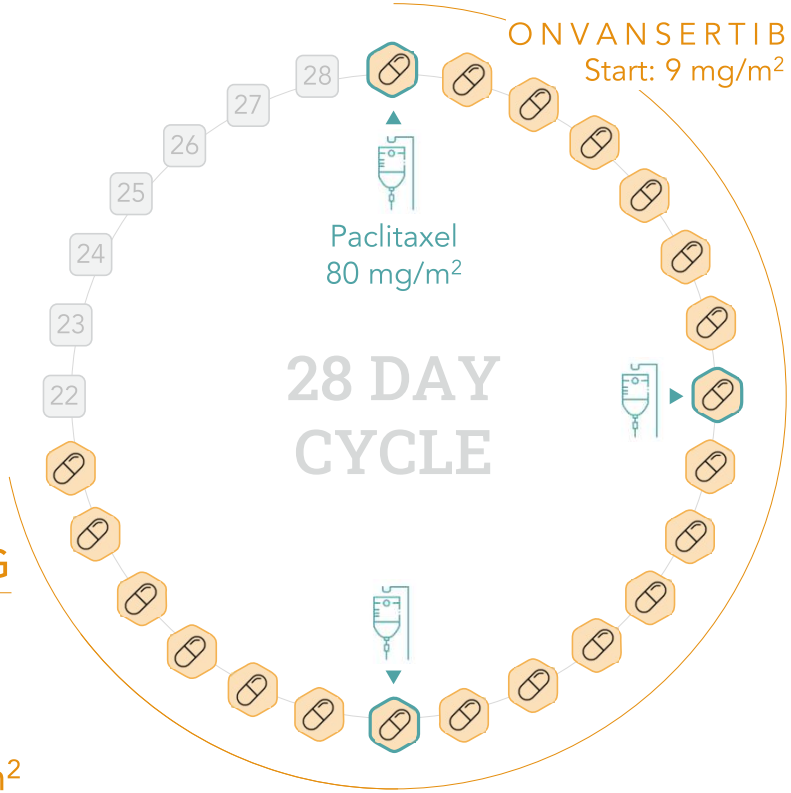
PRIMARY ENDPOINTS

Phase 1b
Safety, characterization of DLTs
Determination of RP2D

Phase 2
ORR (RECIST 1.1)

ONVANSERTIB DOSING

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

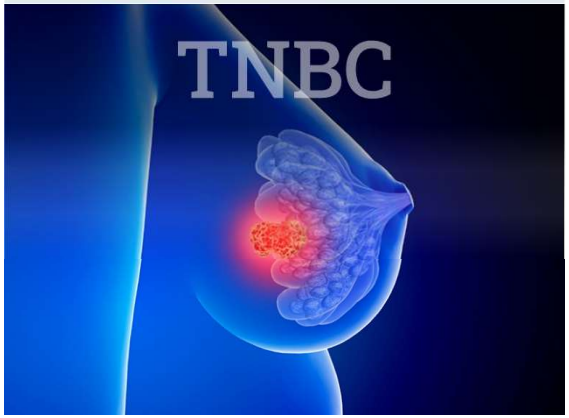


This is the first trial to explore onvansertib + paclitaxel combination

ENROLLMENT CRITERIA

Metastatic TNBC relapsed or progressed

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



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)