



Company Overview The Onvansertib Opportunity

MAY 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 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, 2023, 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

- **Onvansertib**: first well-tolerated PLK1-selective inhibitor
- PLK1 inhibition disrupts tumor growth several ways

Robust clinical data in 2L KRAS-mut mCRC

- **73%** response rate vs **~25%** in SoC
- **15 month** progression free survival vs **~8 month** in SoC
- ONSEMBLE **validates** strong data signal

FDA

- **FDA**-agreed path to 1st line RAS-mut mCRC accelerated approval

Pfizer

- **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 H2 2024
Runway with current cash extends into Q3 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



 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 targets large patient populations with unmet need

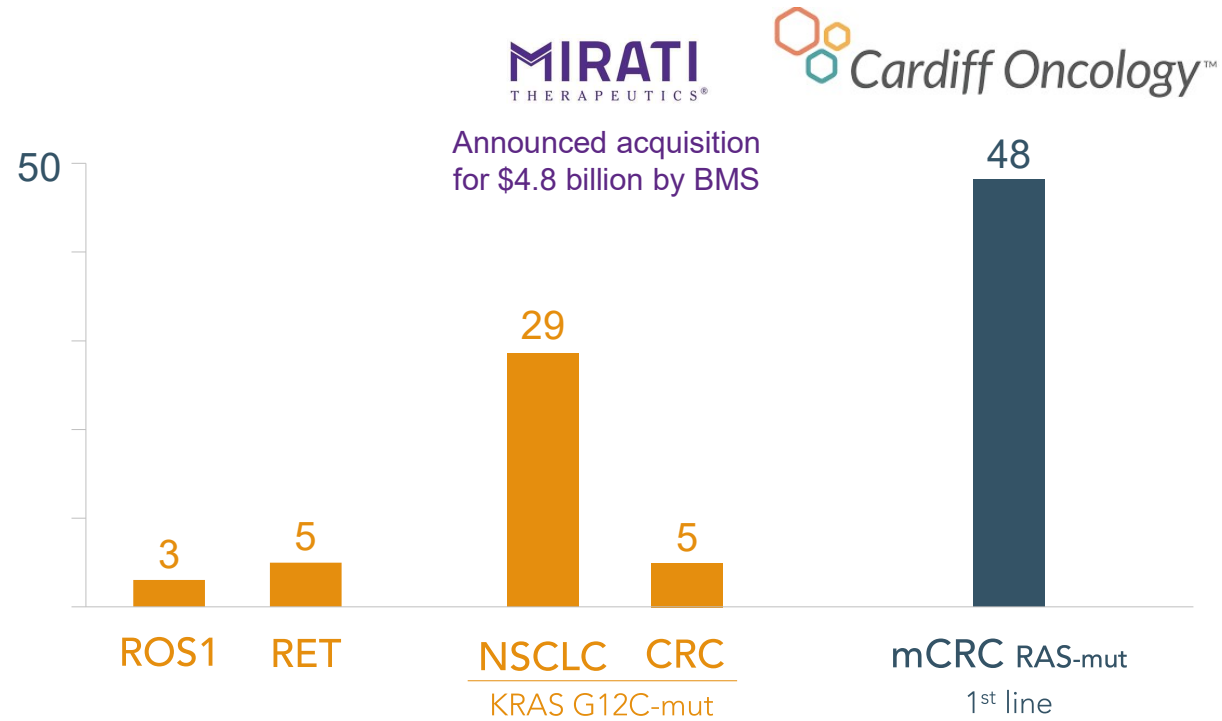
Targets with oncogenic alterations

ROS1
RET
KRAS G12C
EGFR
TRK

Targets without oncogenic alterations

PLK1
PARP
CDK4/6
PD1/PDL1
VEGF










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



* 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) | 1 st line | CRDF-004 (w/Pfizer) | |  <i>randomized</i> | | FOLFIRI/bev and FOLFOX/bev |
| | 2 nd line | Ph 1b/2 | |  <i>completed</i> | | FOLFIRI/bev |
| | 2 nd line | CRDF-003 (ONSEMBLE) | |  <i>randomized</i> | | FOLFIRI/bev |
| mPDAC | 2 nd line | Ph 2 | |  | | Nal-IRI/leucovorin/ 5-FU |
| | 1 st line | Ph 2 |  OHSU Knight Cancer Institute | | | Gemzar®/Abraxane® |
| SCLC | 2 nd line | Ph 2 |  |  | | None (monotherapy) |
| TNBC | 2 nd line | Ph 2 |  |  | | Paclitaxel |

* For investigator-initiated trials (IITs) only, the investigator's institution is provided.

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

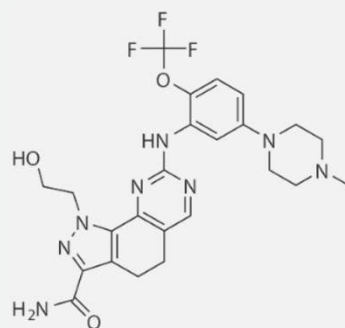
Onvansertib

First oral, well-tolerated
PLK1-selective inhibitor



PROPERTIES

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



SPECIFICITY

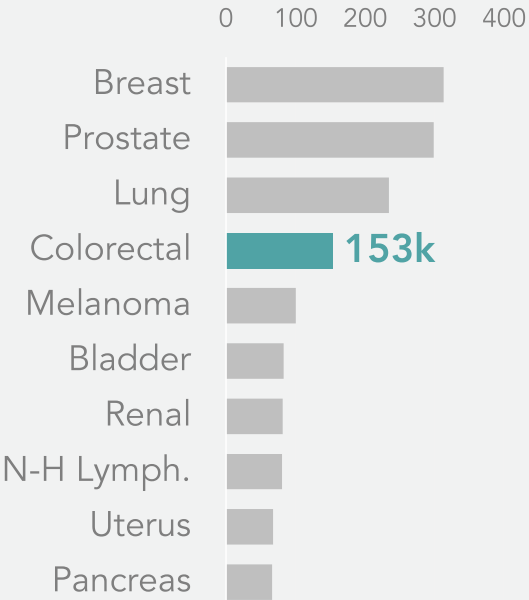
Exquisitely specific for PLK1

| 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

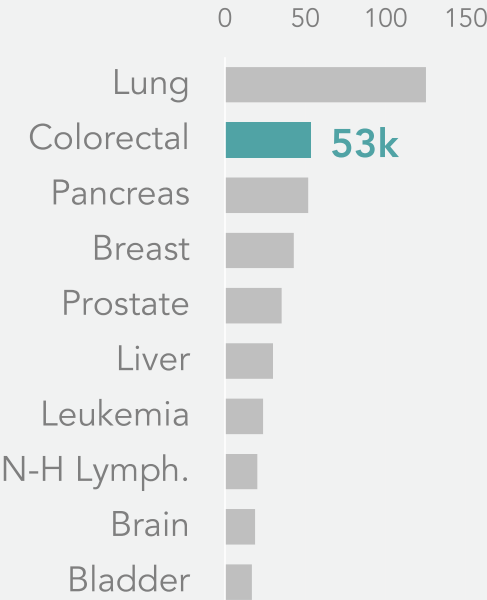
mCRC is BOTH common...

2023 new US cases ('000s)*



...and challenging to treat

2023 US deaths ('000s)*



* American Cancer Society Cancer Facts and Figures 2024.

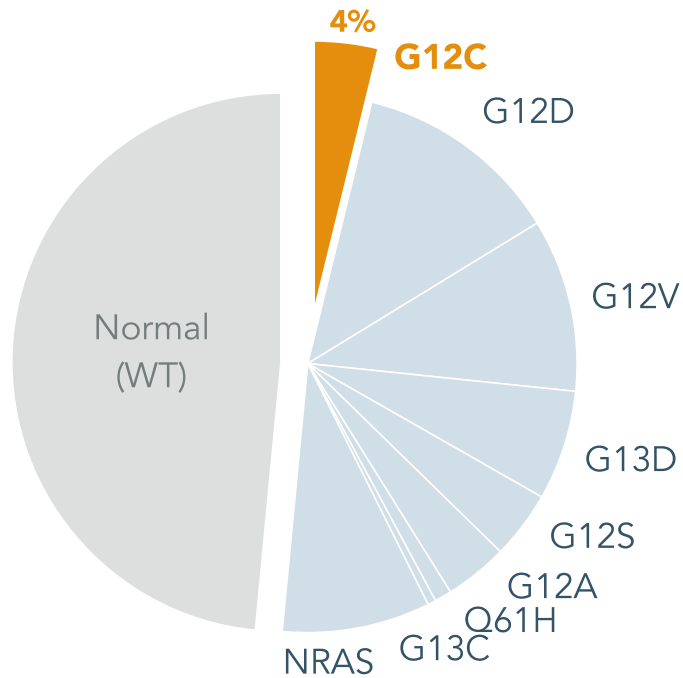
mCRC standard of care leaves a significant unmet need

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

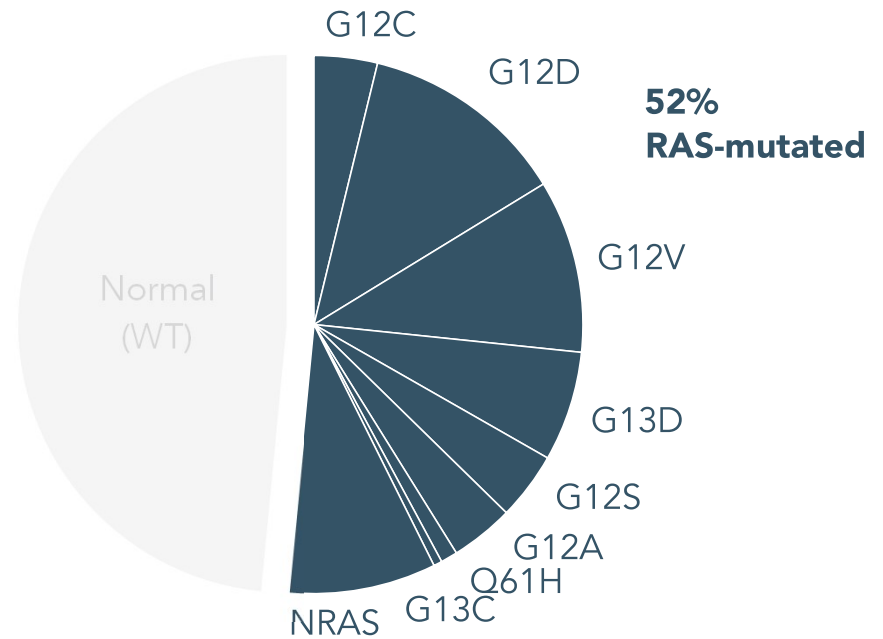
| | |
|------------------|---|
| Chemotherapy | FOLFOX (approved 1996) FOLFIRI (approved 2002) |
| + | |
| Antiangiogenic | Bevacizumab (Avastin®) (approved 2004) |
| Targeted therapy | None |

Other mCRC development programs leave a significant unmet need

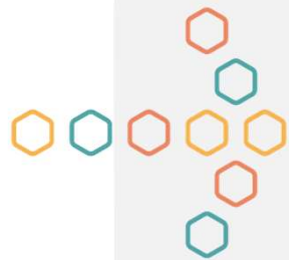
KRAS G12C therapies would address a small part of the need¹



Onvansertib is targeting all RAS-mutated mCRC¹



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



Fighting mCRC through PLK1 inhibition

Robust data in lead mCRC program

Path forward to accelerated approval

Our mCRC journey of discovery led us from second-line to first-line

FIRST LINE

CRDF-004

ENROLLING

RAS-mutated mCRC
90 patients,
randomized,
3 arms (2 doses +
control),
Pfizer Ignite

SECOND LINE

Ph 1b/2
(TROV-054)

COMPLETED

KRAS-mutated mCRC
66 evaluable patients,
single arm

CRDF-003
 **ONSEMBLE**
mCRC Clinical Trial

DISCONTINUED

RAS-mutated mCRC
23 patients*,
randomized,
blinded,
3 arms (2 doses +
control)

* ONSEMBLE enrolled 23 patients, and 2 patients were not evaluable for efficacy because one withdrew consent prior to their first dose and one withdrew consent before their first post-baseline scan. Both patients were “bev exposed” and randomized to the control arm.

Our mCRC journey of discovery led us from second-line to first-line

FIRST LINE

Provided initial signal of efficacy in second-line RAS-mutated mCRC

CRDF-004

ENROLLING

RAS-mutated mCRC
90 patients, randomized,
3 arms (2 doses + control)
Pfizer Ignite

SECOND LINE

Ph 1b/2
(TROV-054)

COMPLETED

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66 evaluable patients,
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Our mCRC journey of discovery led us from second-line to first-line

FIRST LINE

Randomized second-line trial designed to show onvansertib's contribution to SoC that was discontinued

CRDF-004

ENROLLING

RAS-mutated mCRC
90 patients, randomized,
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Pfizer Ignite

SECOND LINE

Ph 1b/2
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Our mCRC journey of discovery led us from second-line to first-line

FIRST LINE

Shift to 1st-line setting based on:

1. Phase 1b/2 clinical data
2. New mechanism of action
3. FDA recommendation
4. ONSEMBLE validation

CRDF-004

ENROLLING

RAS-mutated mCRC
90 patients,
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3 arms (2 doses +
control)
Pfizer Ignite

SECOND LINE

Ph 1b/2
(TROV-054)

COMPLETED

KRAS-mutated mCRC
66 evaluable patients,
single arm

CRDF-003

ONSEMBLE
mCRC Clinical Trial

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Our mCRC journey of discovery led us from second-line to first-line

FIRST LINE

CRDF-004

ENROLLING

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90 patients,
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3 arms (2 doses +
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Pfizer Ignite

SECOND LINE

Ph 1b/2
(TROV-054)

COMPLETED

KRAS-mutated mCRC
66 evaluable patients,
single arm

CRDF-003



DISCONTINUED

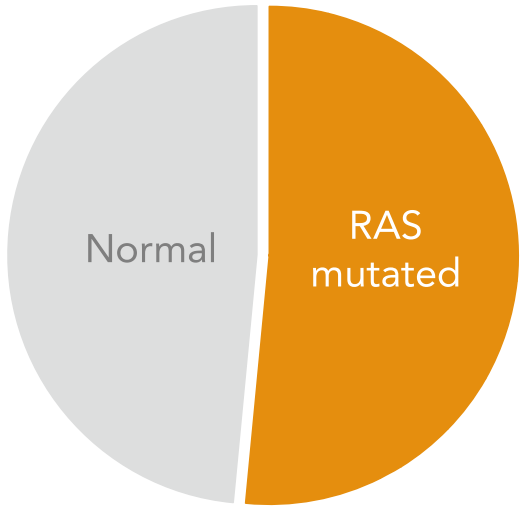
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Our focus is RAS-mutated tumors where there are no targeted therapies

| | Normal | 1 st LINE | 2 nd LINE |
|--------------------|--------|----------------------|----------------------|
| Standard* | | Chemo + bevacizumab | Chemo + bevacizumab |
| Targeted | | + EGFR inhibitor | NONE |
| RAS Mutated | | | |
| Standard* | | Chemo + bevacizumab | Chemo + bevacizumab |
| Targeted | | NONE | NONE |

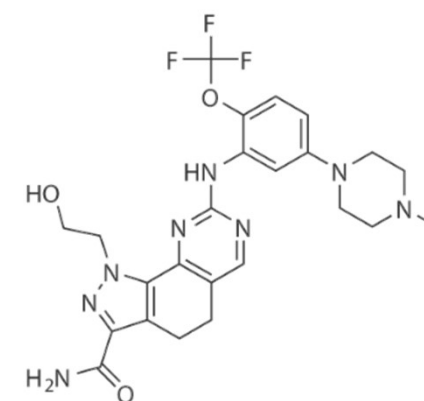
RAS-mut mCRC is approx. half the mCRC population¹



* 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

| | 1 st LINE | 2 nd LINE |
|--------------------|----------------------|-----------------------|
| Normal | | |
| 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

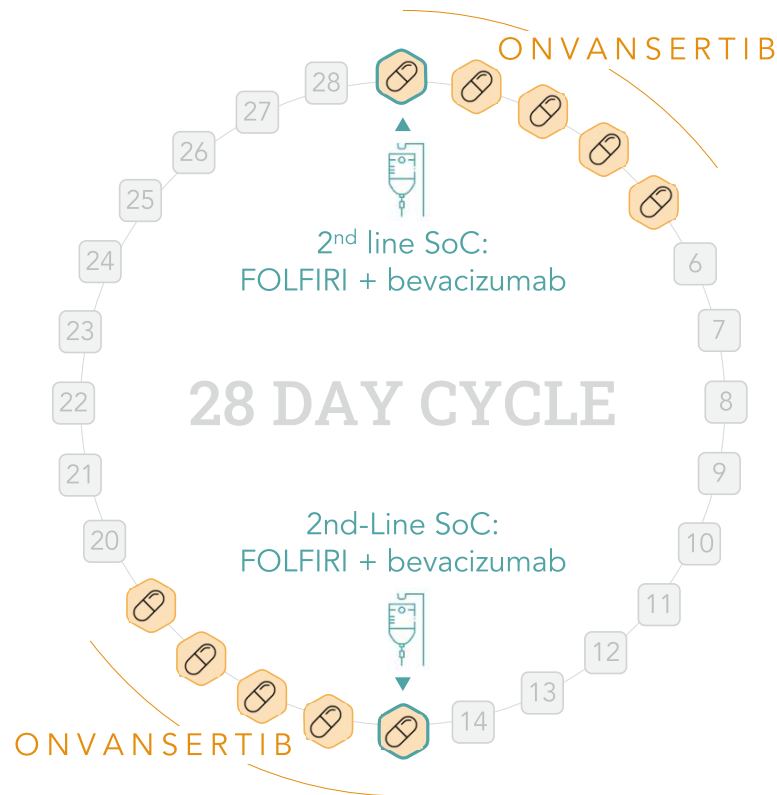
ENROLLMENT CRITERIA

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

Ph 1b/2 trial patients may or may not have received bev in 1st line

Bev exposed vs bev naïve patients

“Bev naïve” patients who did not receive prior bev in 1st line

or

“Bev exposed” patients who received bev in 1st line

1st LINE

FOLFOX

23% (15 of 66)

FOLFOX +
bevacizumab

77% (51 of 66)

2nd LINE

FOLFIRI +

bevacizumab

+

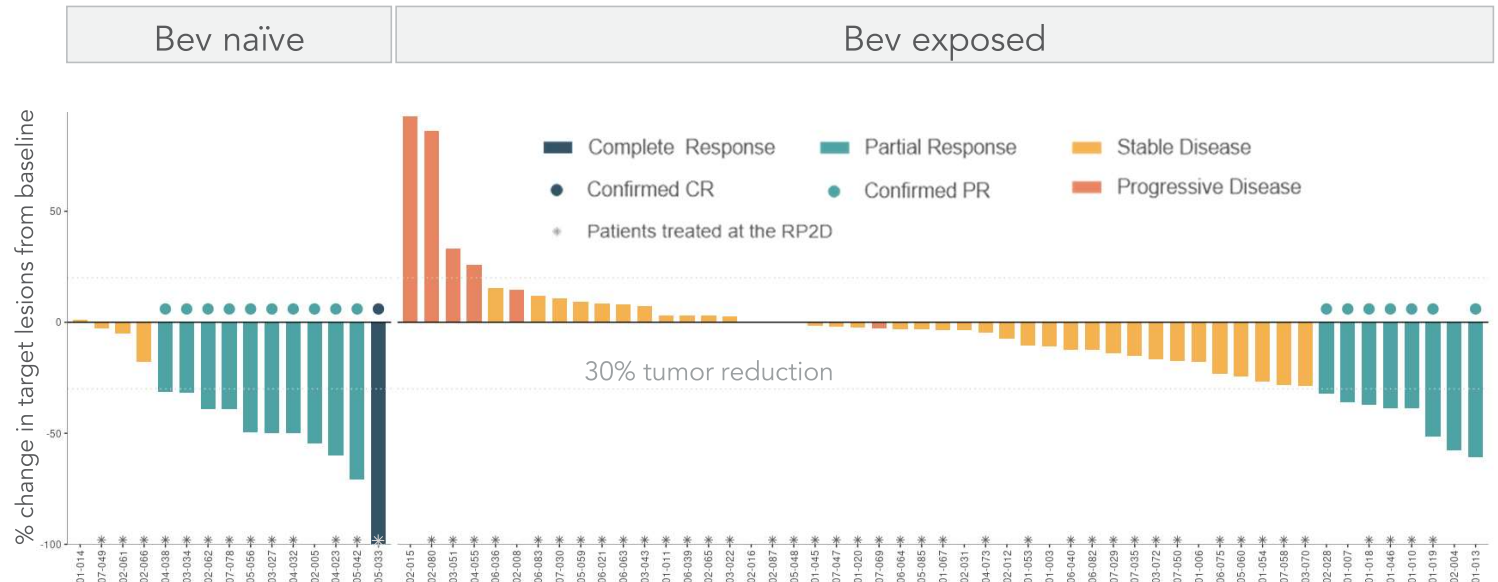
ONVANSERTIB

All patients received FOLFIRI + bev + onv in our trial

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)

| | 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. mDoR CI: “-” means not reached.

** 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 patients achieved responses across KRAS mutations

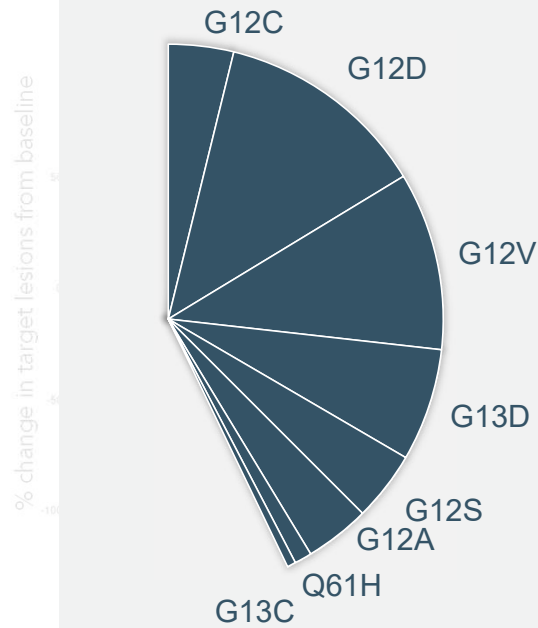
Best Radiographic Response a

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Historical controls**

| | | |
|-----|--------|-------|
| ORR | 23-26% | 5-13% |
|-----|--------|-------|

Frequency of Common KRAS Mutations in mCRC¹



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 |

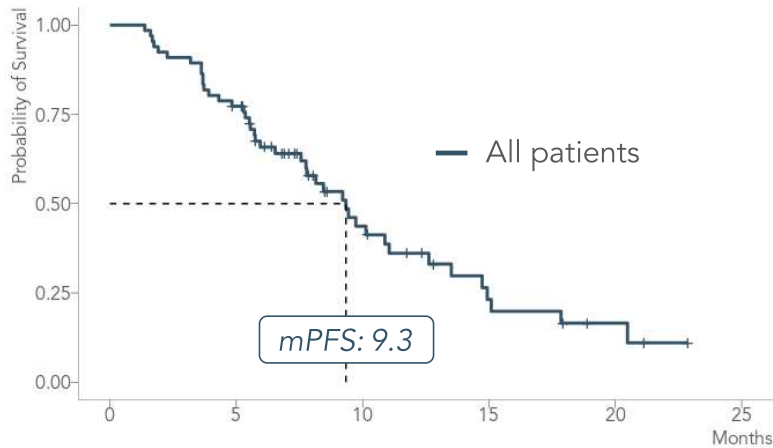
* Radiographic response determined per RECIST 1.1. Waterfall plot and table re Patients 02006 and 07429 were categorized as bev naïve in the July 25, 2023 update. Patients 03-025 and 04-038 were confirmed PRs.

** Benouna et al., Lancet Oncol 2013; 14: 29-37, Giesen et al., Acta Oncologica 2015; 54: 187-194, Gramelin et al., Lancet Oncol 2020; 21: 497-507, Antonietti et al., Correspondence Lancet Oncol June 2020, Giannico et al., 2007, J Clin Oncol 25: 1539-1544, Morwak et al., Med Oncol 2012; 29: 2842-2848, Beretta et al., Med Oncol 2013; 30:485

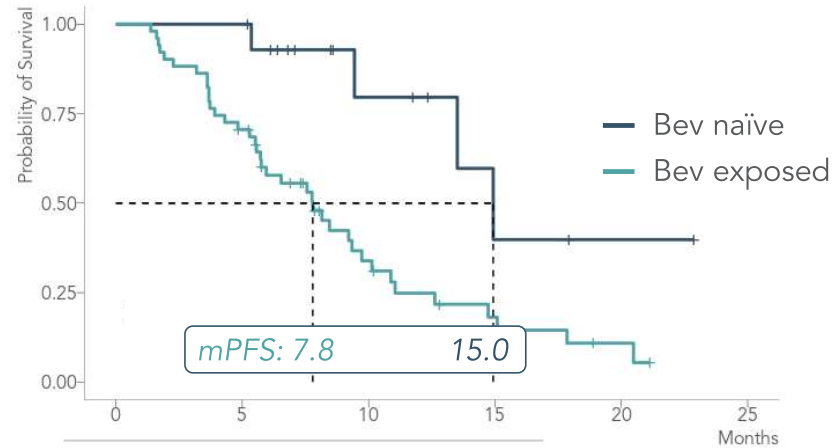
1. Jones R et al. Br J Cancer. 2017 Mar 28;116(7):923-929

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

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 |
|------|--------------|--------------|
| mPFS | 4.5 - 6.7mos | 6.9 - 8.5mos |

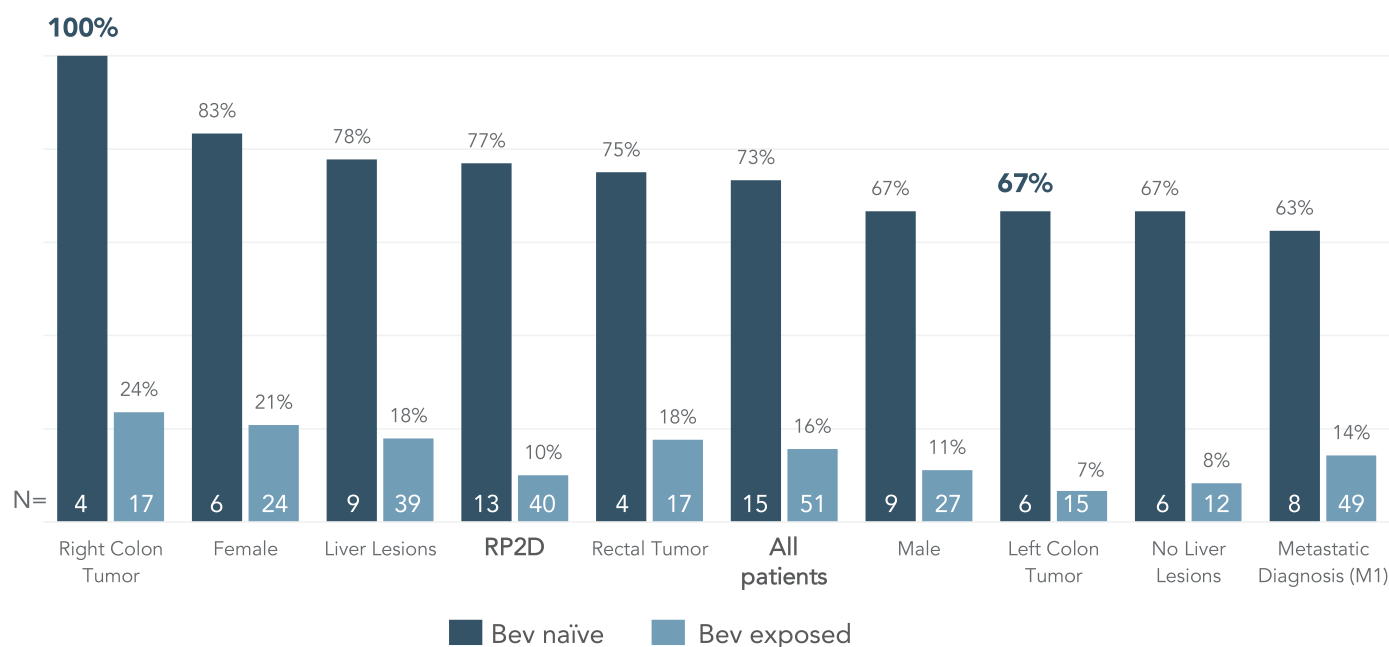
* Onvansertib mPFS are interim data as of June 16, 2023 from an ongoing trial and unlocked database

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Ph 1b/2 trial 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

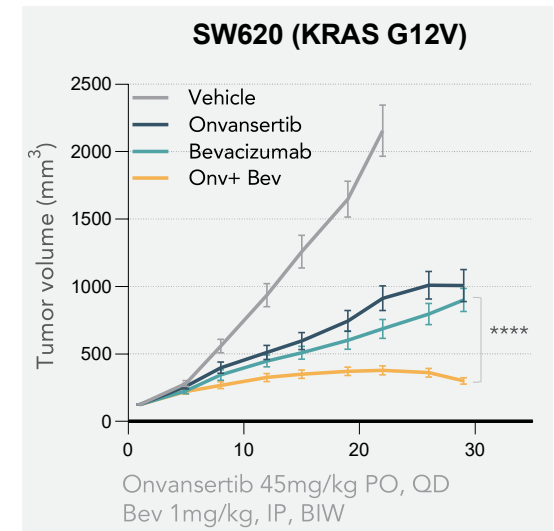
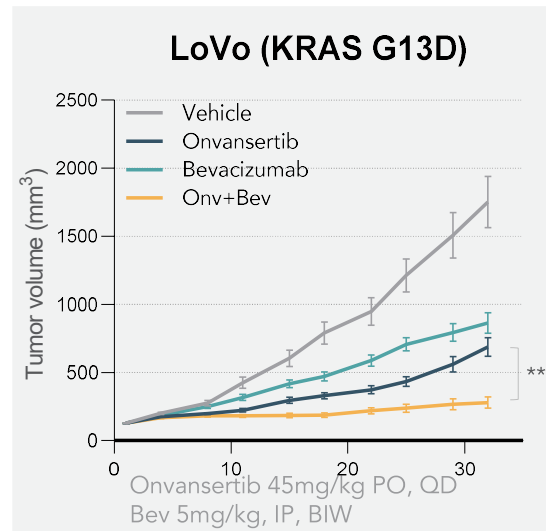
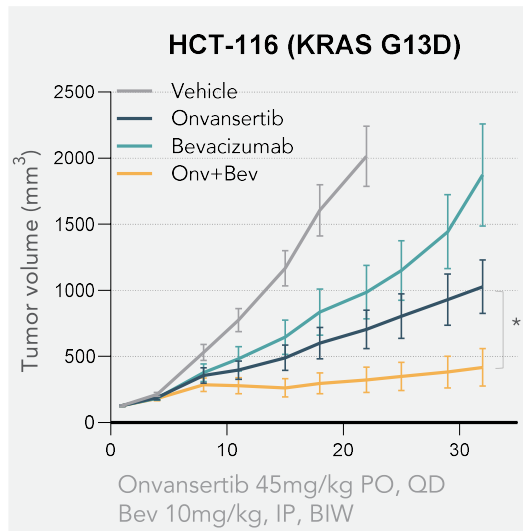


* Onvansertib ORR is interim data as of June 16, 2023 from an ongoing trial and unlocked database.

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 \pm SEM are represented on graphs. An unpaired t-test was used to test the difference in tumor volume change on the last day of treatment between the combination treatment and the most effective control arm. * $p < 0.05$, *** $p < 0.001$, **** $p < 0.0001$

Onvansertib plays an independent role in antiangiogenesis that complements bev

| | LoVo (KRAS G13D)* | | | SW620 (KRAS G12V)* | | | |
|-------------------|---|---|---|--|---|---|---|
| Control (vehicle) |  |  |  |  |  |  | |
| Bevacizumab |  |  |  |  |  |  | <ul style="list-style-type: none"> • Roche drug Avastin® • 8th largest global drug in 2019 • \$7.1B sales |
| Onvansertib |  |  |  |  |  |  | |
| Onv+Bev |  |  |  |  |  |  | |



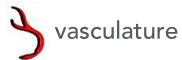
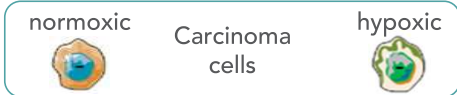
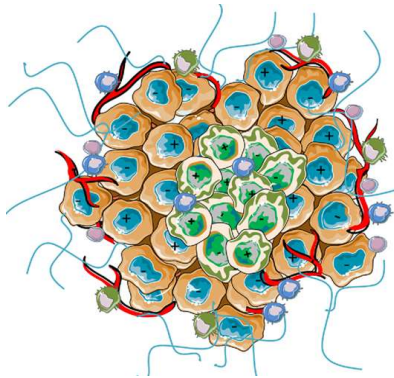
KRAS-mut mCRC tumors from mice treated with onv + bev appear smaller and pale (less vascularized)

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

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

Tumor growth

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



Hypoxia

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

HIF1 α

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

VEGF-A

Angiogenesis:
Vascularization
of the tumor

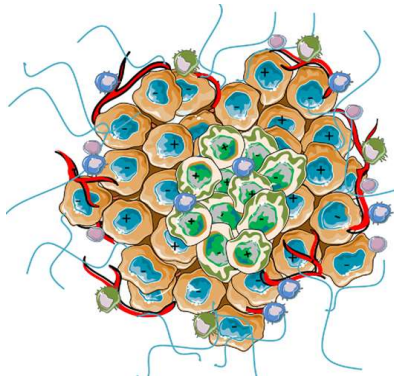
Tumor cell
survival

Proliferation

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

Tumor growth

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



Hypoxia

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

HIF1 α

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

onvansertib

inhibits HIF1 α expression

bevacizumab

neutralizes VEGF-A

VEGF-A

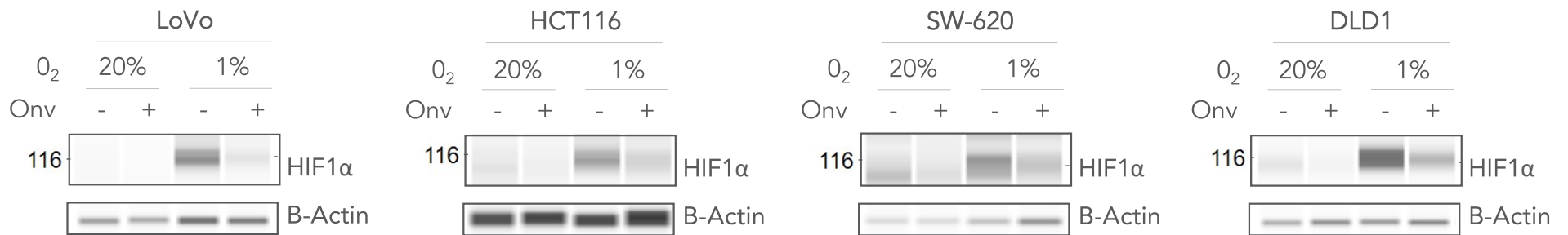
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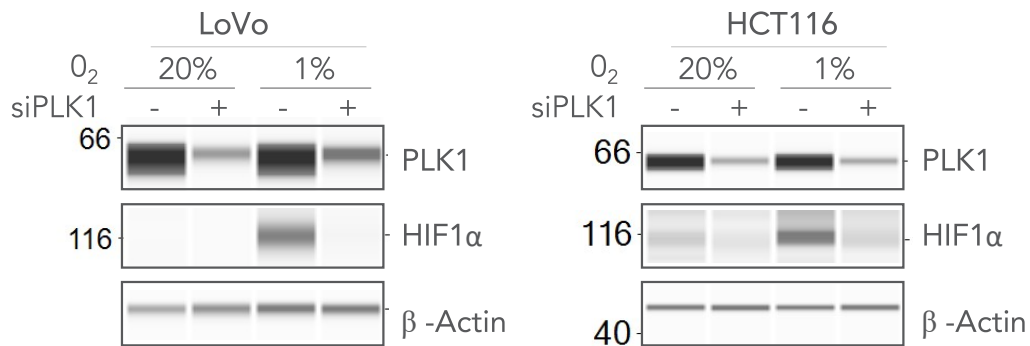
Proliferation

Onvansertib inhibits the hypoxia signaling pathway by downregulating HIF1 α expression

In 4 RAS-mutant CRC cell lines¹, onvansertib inhibited hypoxia-induced HIF1 α expression



PLK1 inhibition using siRNA against PLK1 (siPLK1)² prevented hypoxia-induced HIF1 α expression



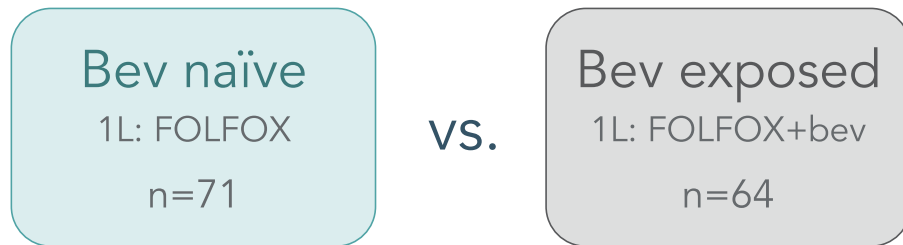
1. KRAS-mutant CRC cell lines were cultured under normoxia (20%O₂) or hypoxia (1%O₂), in the presence (+) or absence (-) of onvansertib. HIF1 α expression was induced under hypoxia.
2. LoVo and HCT116 cells were transfected with siRNA control (-) or siRNA targeting PLK1 (siPLK1) and then exposed to 20% or 1%O₂. Cells were collected 24h after transfection.

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

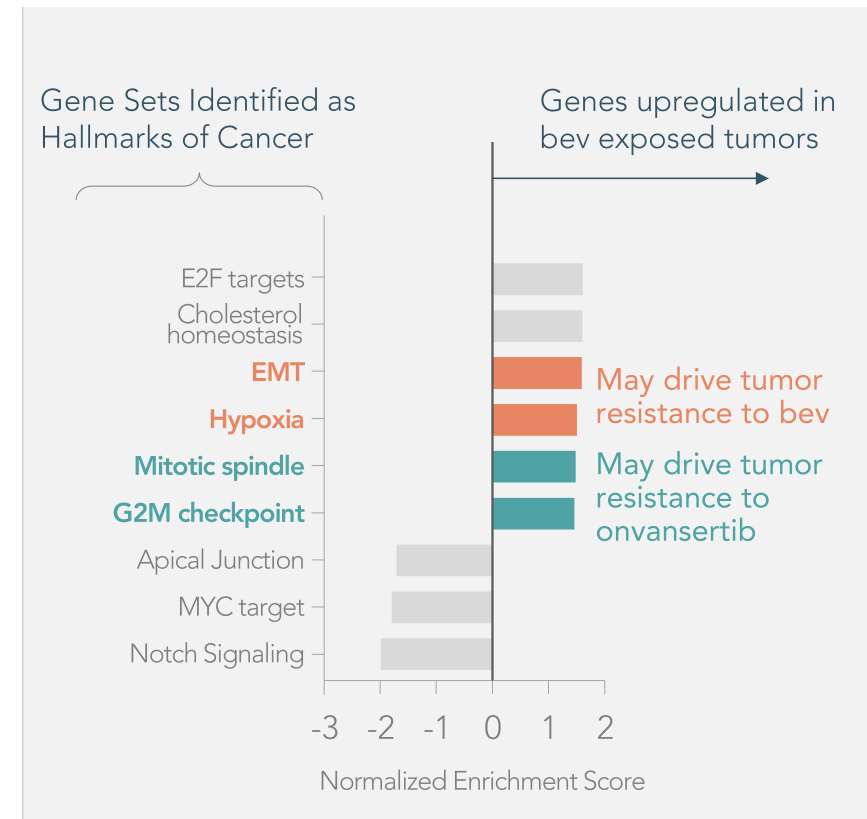
'TEMPUS Tumor Biopsy Library

135 tumor biopsy samples identified

- All from KRAS-mut mCRC patients
- After completing 1st line therapy (prior to 2nd line)



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



Our mCRC journey of discovery led us from second-line to first-line

FIRST LINE

CRDF-004

ENROLLING

RAS-mutated mCRC
90 patients,
randomized,
3 arms (2 doses +
control)
Pfizer Ignite

SECOND LINE

Ph 1b/2
(TROV-054)

COMPLETED

KRAS-mutated mCRC
66 evaluable patients,
single arm

CRDF-003



DISCONTINUED

RAS-mutated mCRC
23 patients*,
randomized,
blinded,
3 arms (2 doses +
control)

* ONSEMBLE enrolled 23 patients, and 2 patients were not evaluable because one withdrew consent prior to their first dose and one withdrew consent before their first post-baseline scan. Both patients were "bev exposed" and randomized to the control arm.

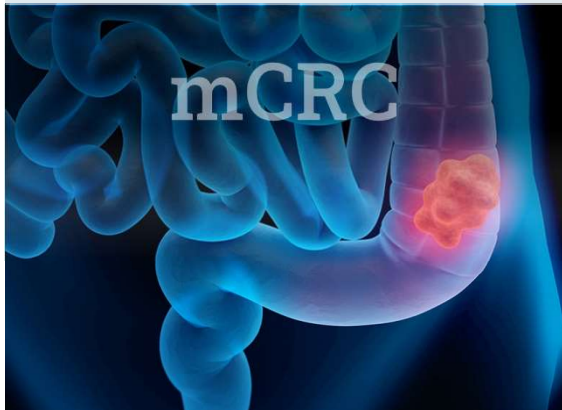
ONSEMBLE Ph 2 trial was designed to generate randomized data

ENROLLMENT CRITERIA

2nd line mCRC
KRAS+/NRAS+
Unresectable

R

N=23
1:1:1



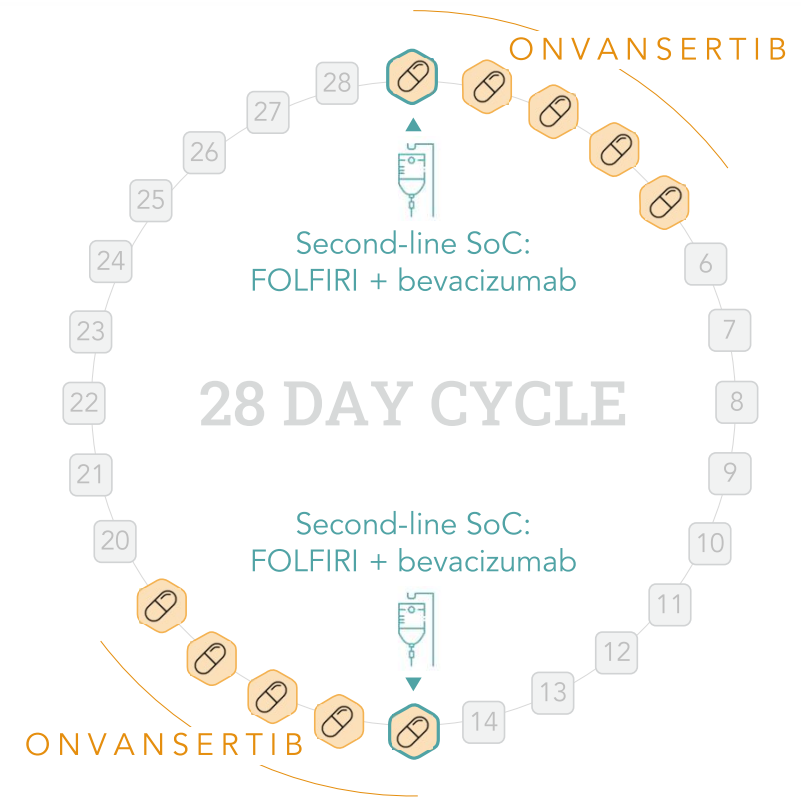
SoC: FOLFIRI/bev

Onv 20mg + FOLFIRI/bev

Onv 30mg + FOLFIRI/bev

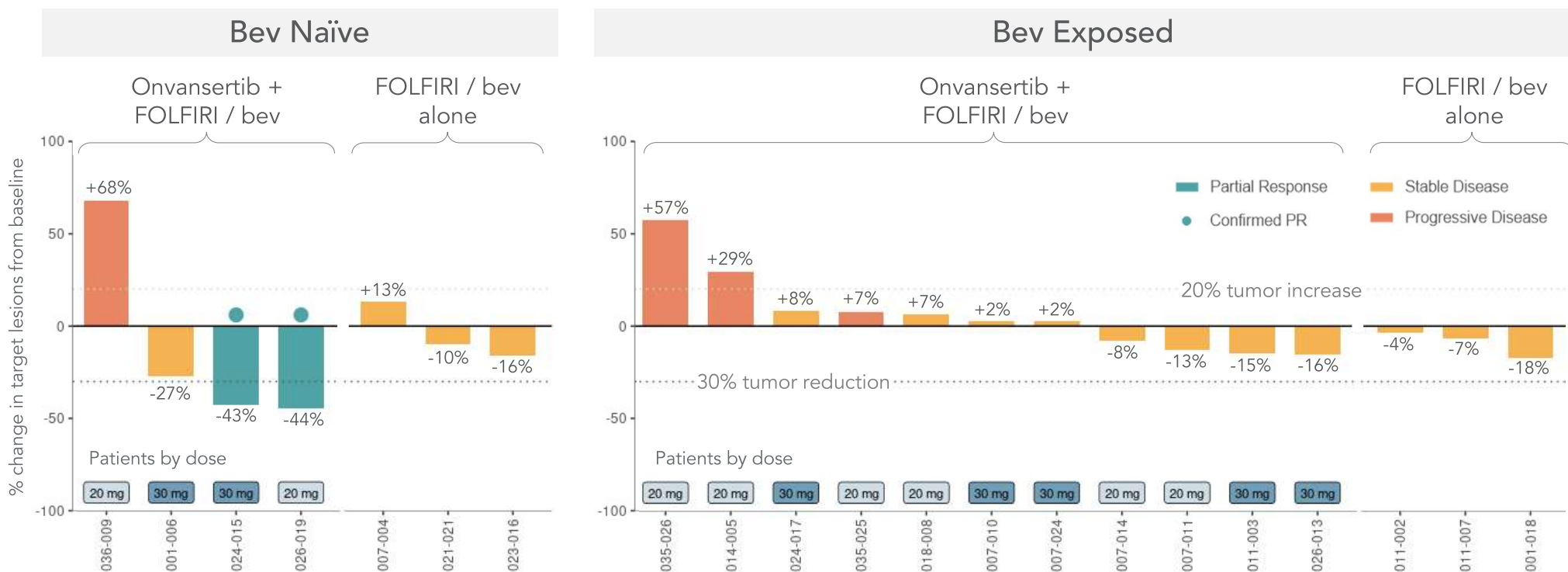
PRIMARY ENDPOINT

Objective Response Rate



ONSEMBLE bev naïve patients treated with onvansertib + SoC achieved deeper responses than SoC alone

Best Radiographic Response* –  ONSEMBLE patients (as of February 26, 2024)

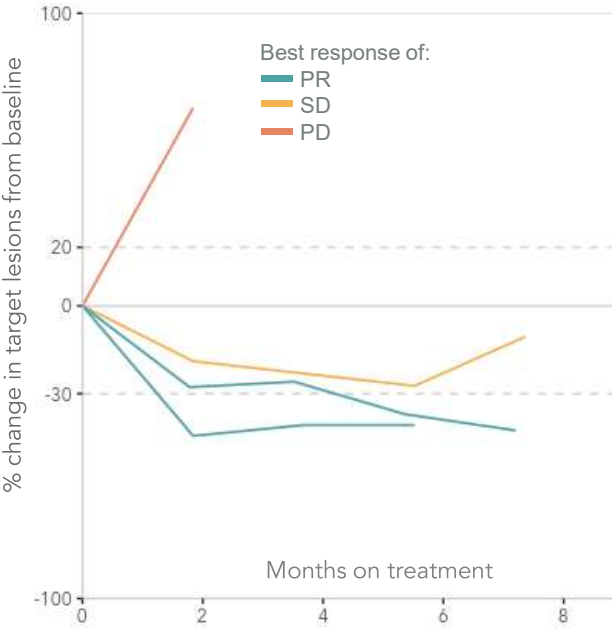


* Radiographic response determined per RECIST 1.1. Waterfall plot reflects interim data as of February 26, 2024 from an ongoing, discontinued trial and unlocked database.

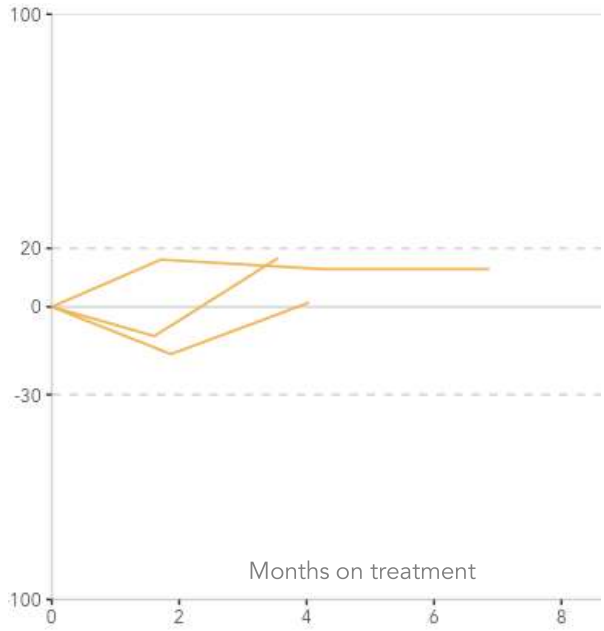
ONSEMBLE bev naïve patients treated with onvansertib + SoC achieved deeper responses than SoC alone

Change in tumor size from baseline* –  bev naïve patients (as of February 26, 2024)

Bev naïve: onvansertib + FOLFIRI/bev arm



Bev naïve: FOLFIRI/bev (control) arm



Progressive disease
Stable disease
Partial response

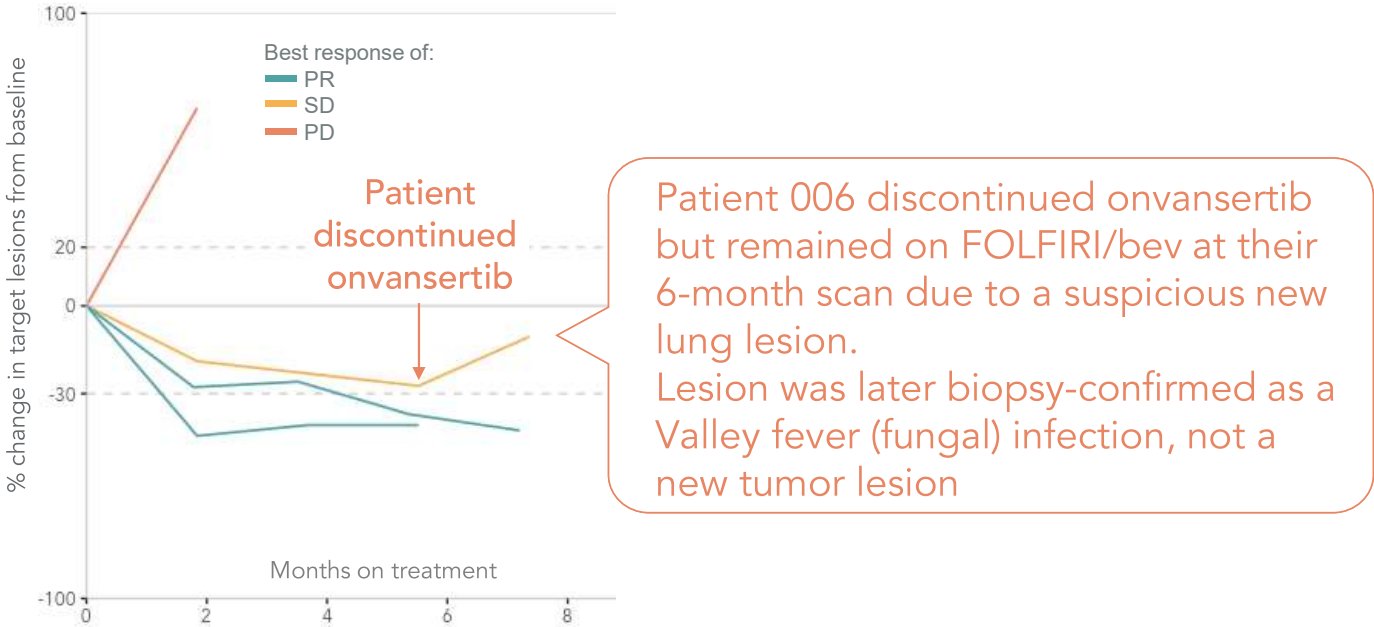
← -30% tumor reduction →

* Spider plots reflect interim data as of February 26, 2024 from an ongoing, discontinued trial and unlocked database

ONSEMBLE bev naïve patients treated with onvansertib + SoC achieved deeper responses than SoC alone


Change in tumor size from baseline* –  bev naïve patients (as of February 26, 2024)

Bev naïve: onvansertib + FOLFIRI/bev arm



* Spider plots reflect interim data as of February 26, 2024 from an ongoing, discontinued trial and unlocked database

Two independent clinical trials demonstrate the bev naïve finding

| | | Objective Response Rate (ORR) by Cohort* | | |
|--|---------------------|--|-------------------|------------------|
| | | N | Bev Naïve | Bev Exposed |
|  | Onvansertib + SoC | 15 | 50% (2 of 4) | 0% (0 of 11) |
| | Control (SoC alone) | 6 | 0% (0 of 3) | 0% (0 of 3) |
| Phase 1b/2 Single-arm | Onvansertib + SoC | 66 | 73% (11 of 15) | 16% (8 of 51) |

* Radiographic response determined per RECIST 1.1. ONSEMBLE data reflects interim data as of February 26, 2024 from an ongoing, discontinued trial and unlocked database. Onvansertib + SoC includes patients at both the 20mg and 30mg dose of onvansertib. Phase 1b/2 data reflects interim data as of June 16, 2023 from an ongoing trial and unlocked database.

ONSEMBLE second-line data support our CRDF-004 first-line strategy

 Results from
ONSEMBLE
Second-line RAS-mut mCRC

Implications for
CRDF-004
First-line RAS-mut mCRC

Efficacy signal in
bev naïve patients

Objective responses observed
only in bev naïve patients that
received onvansertib with SoC

All first-line mCRC patients
are bev naïve

No SoC signal in
the control arm

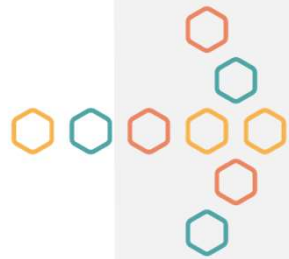
No objective responses observed
in bev naïve patients randomized
to the control arm (SoC only)

Addition of onvansertib may
improve efficacy of SoC chemo/bev

Signal in both
20mg & 30mg dose

1 partial response observed in
each dose of onvansertib
(20mg and 30mg)

Data from 20mg and 30mg
arms could be combined for
earlier efficacy evaluation



Fighting mCRC through PLK1 inhibition

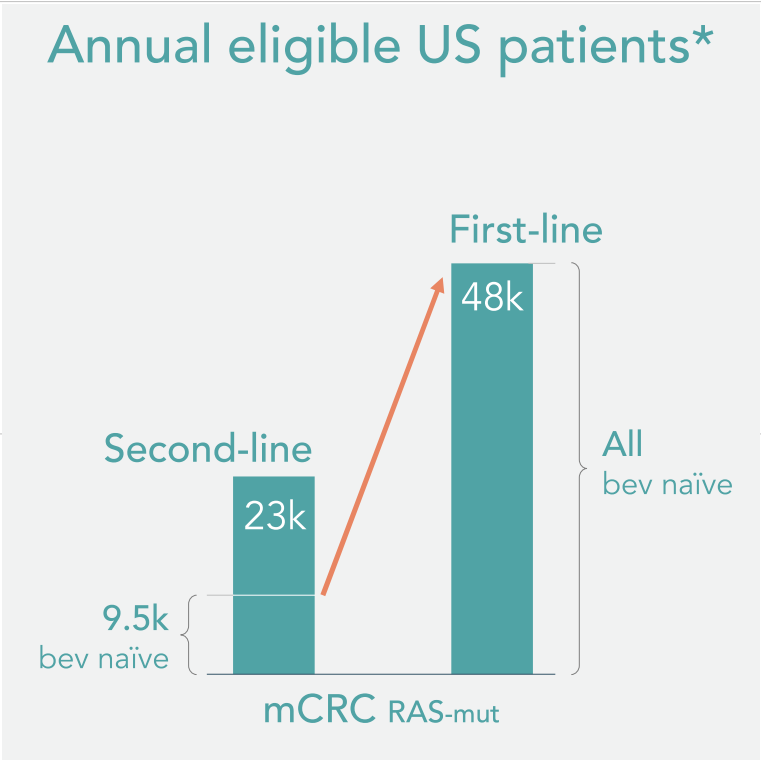
Robust data in lead mCRC program

Path forward to accelerated approval

Our mCRC journey of discovery led us from second-line to first-line

FIRST LINE

SECOND LINE



CRDF-004

ENROLLING

RAS-mutated mCRC
90 patients, randomized,
3 arms (2 doses + control)
Pfizer Ignite

CRDF-003

ONSEMBLE
mCRC Clinical Trial

DISCONTINUED

RAS-mutated mCRC
23 patients, randomized,
blinded,
3 arms (2 doses + control)

* Company estimates of first-line and second-line mCRC population with KRAS- and NRAS-mutated cancers.

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 initial 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: first-line RAS-mutated mCRC Phase 2 trial

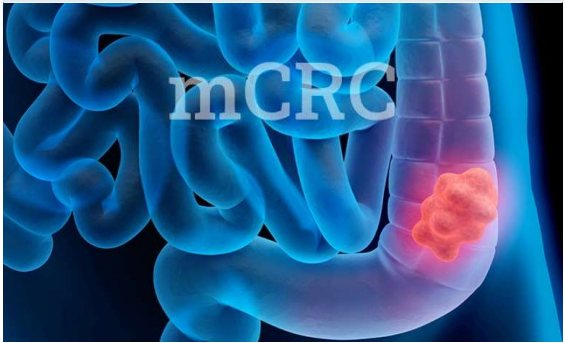
ENROLLMENT CRITERIA

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

R
 N=90
 1:1:1



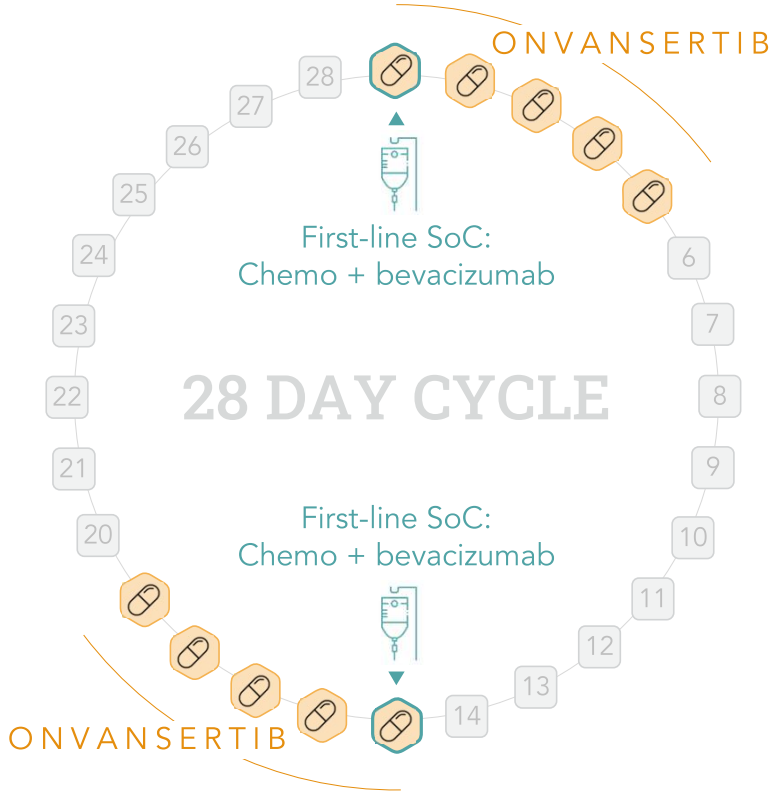
- SoC: FOLFIRI/bev or FOLFOX/bev (n=30)
- Onv 20mg + FOLFIRI/bev or FOLFOX/bev (n=30)
- Onv 30mg + FOLFIRI/bev or FOLFOX/bev (n=30)



ENDPOINTS

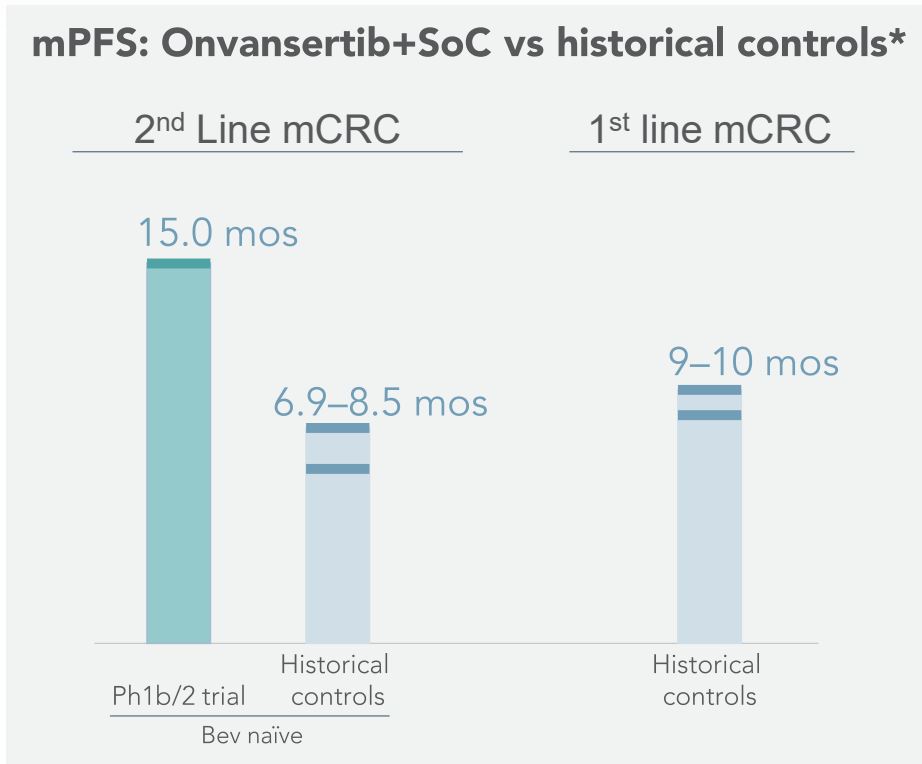
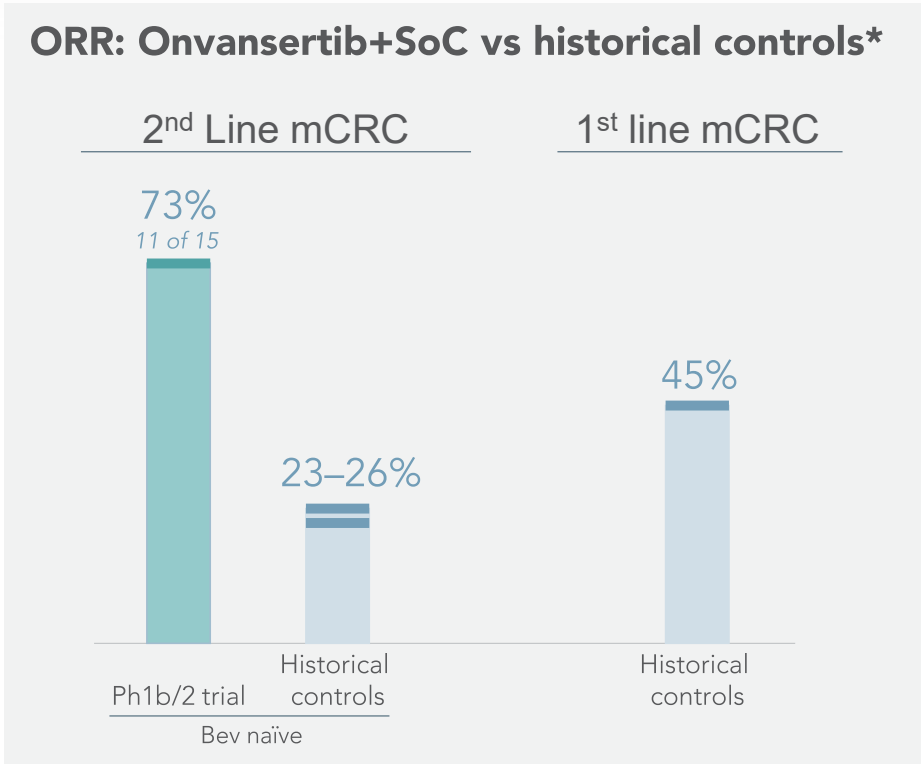
Primary: ORR
 Secondary: DoR and PFS

PFIZER IGNITE is providing 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



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 |
|---|--|---|--|
| <ul style="list-style-type: none"> • Onvansertib: first well-tolerated PLK1-selective inhibitor • PLK1 inhibition disrupts tumor growth several ways | <ul style="list-style-type: none"> • 73% response rate vs ~25% in SoC • 15 month mPFS vs ~8 month in SoC • ONSEMBLE data | <ul style="list-style-type: none"> • FDA-agreed path to 1st line accelerated approval | <ul style="list-style-type: none"> • 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 H2 2024

March 31, 2024 cash and investments* \$67.2M

Net cash used in Operating Activities*
(Rolling two-quarter period ending March 31, 2024) \$14.9M

Runway with current cash extends into Q3 2025

* Financial information above is derived from our audited financials in Form 10K filed on 2/29/24 and unaudited financials in Form 10Q filed on 5/2/24.



Appendix

Additional mCRC Data

Ph 1b/2 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%) |

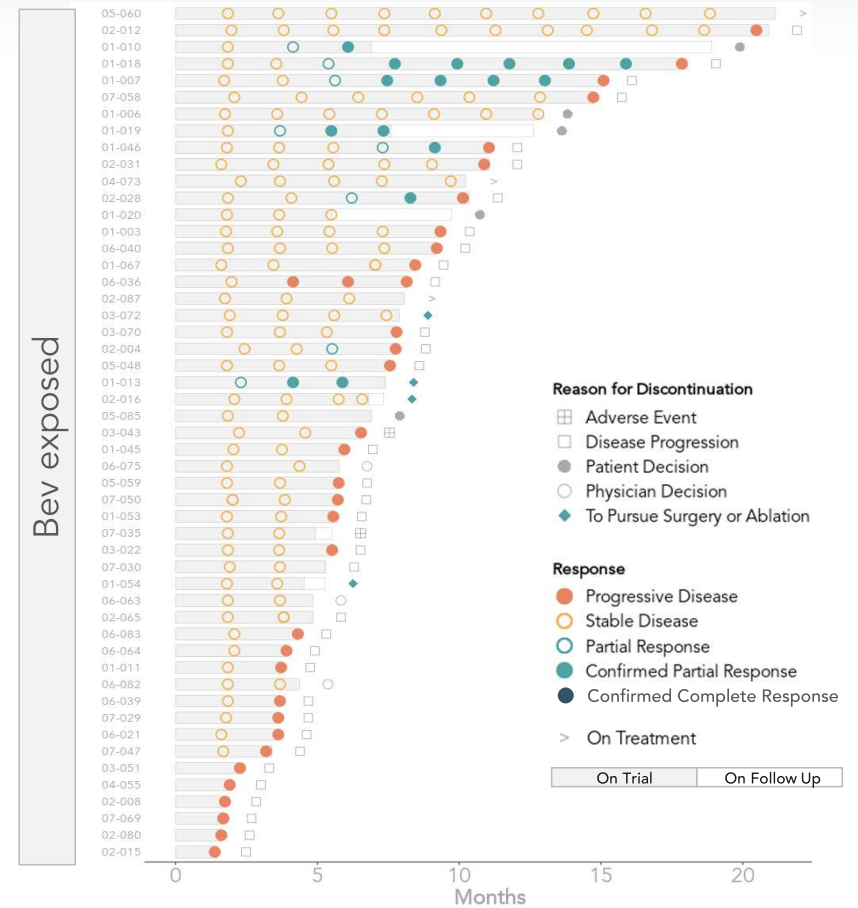
| Total Patients N=68 | Median n (%) |
|-----------------------------|--------------|
| Liver metastasis | |
| None | 20 (29%) |
| Liver and other | 36 (53%) |
| Liver only | 12 (18%) |
| Number of metastatic organs | |
| None | 1 (1.5%) |
| 1 | 4 (6%) |
| ≥2 | 63 (92.5%) |
| Prior bevacizumab treatment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

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

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 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/m², 15mg/m², 18mg/m²)
- 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.

ONSEMBLE's patient demographics reflect second-line mCRC population

Enrollment*

| Number of Patients (N) | FOLFIRI and bev | FOLFIRI-bev and Onvansertib - 20mg | FOLFIRI-bev and Onvansertib - 30mg | Total Patients All Doses |
|---|-----------------|------------------------------------|------------------------------------|--------------------------|
| Intent to Treat | 8 | 8 | 7 | 23 |
| Treated (included in safety evaluable patients) | 7 | 8 | 7 | 22 |
| Evaluable for efficacy | 6 | 8 | 7 | 21 |

| Total Patients N=22 | Median [range] or n (%) |
|---------------------|-------------------------|
| Age (years) | 53 [35-81] |
| Sex | |
| Male | 12 (54%) |
| Female | 10 (46%) |
| ECOG ¹ | |
| 0 | 9 (41%) |
| 1 | 12 (55%) |

| Total Patients N=22 | Median n (%) |
|-----------------------------|--------------|
| Liver metastasis | |
| None | 5 (23%) |
| Liver and other | 13 (59%) |
| Liver only | 4 (18%) |
| Number of metastatic organs | |
| 1 | 7 (32%) |
| ≥2 | 15 (68%) |
| Prior bevacizumab treatment | |
| Yes | 15 (68%) |
| No | 7 (32%) |

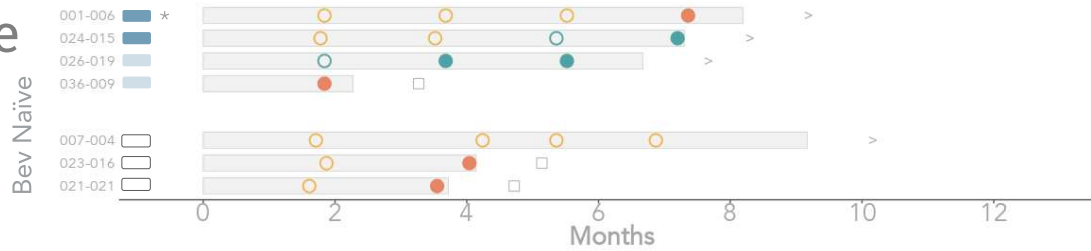
* Data are interim as of January 3, 2024 from an ongoing trial and unlocked database. ONSEMBLE enrolled 23 patients, and 2 patients were not evaluable because one withdrew consent prior to their first dose and one withdrew consent before their first post-baseline scan. Both patients were "bev exposed" and randomized to the control arm.

¹ ECOG was not recorded for one patient

ONSEMBLE swimmer plot

Swimmer plot* –  patients (as of February 26, 2024)

Bev Naïve



Treatment Arm

- Control
- Onvansertib 20 mg
- Onvansertib 30 mg

Response

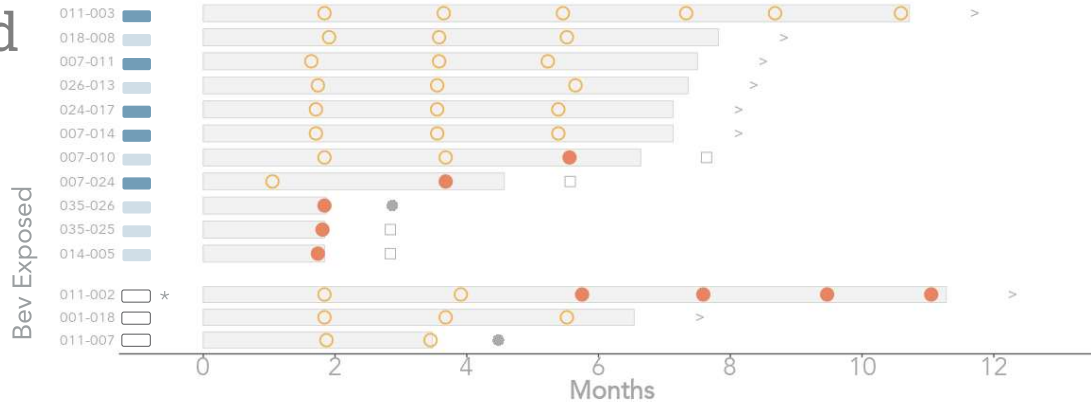
- Progressive Disease
- Stable Disease
- Partial Response
- Confirmed Partial Response

Reason for Discontinuation

- Disease Progression
- Patient Decision

> On Treatment

Bev Exposed

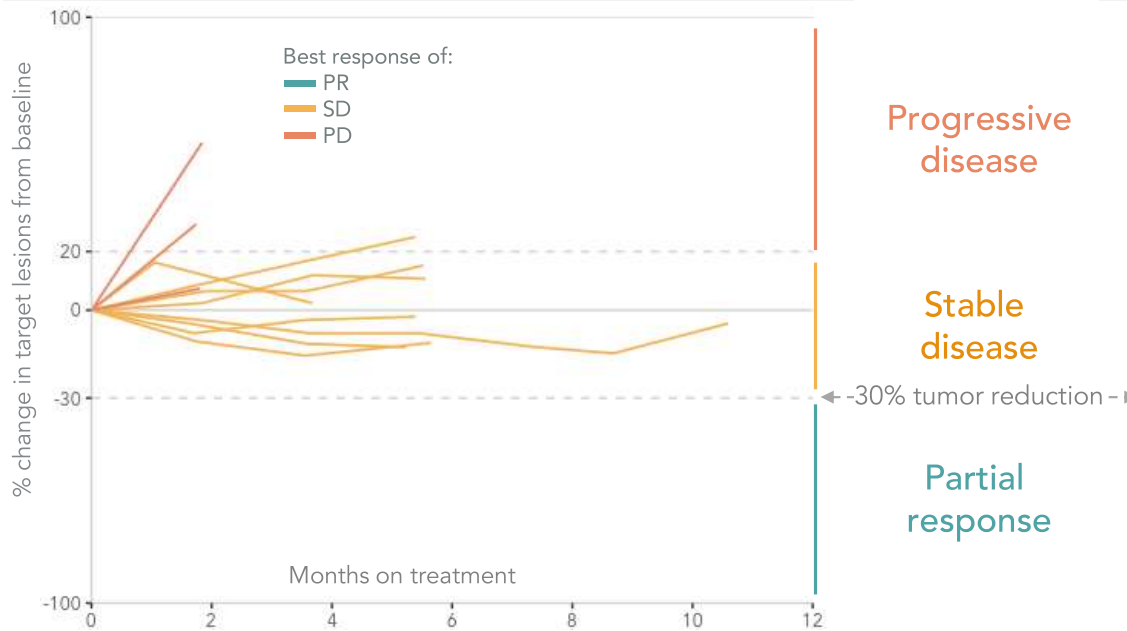


* Swimmer plot reflects interim data as of February 26, 2024 from an ongoing, discontinued trial and unlocked database. Patient 001-006 discontinued onvansertib at their 6-month scan due to a suspicious new lung lesion, which was later biopsy-confirmed as a Valley fever (fungal) infection. Patient 011-002 continues on trial in the control arm despite progressive disease, as the treating physician believes the patient continues to have clinical benefit from second-line standard of care treatment..

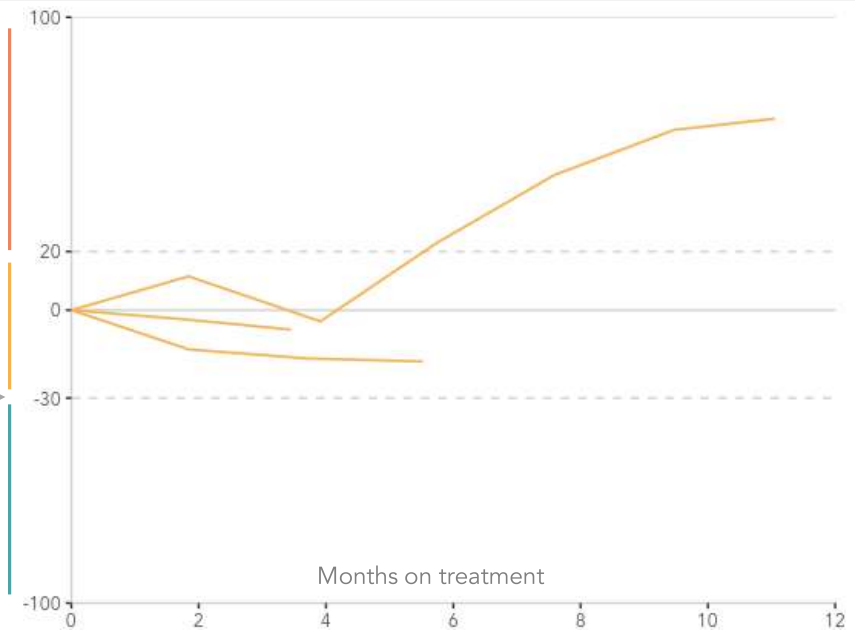
ONSEMBLE bev exposed patients, with or without onvansertib, showed no responses

Change in tumor size from baseline* –  ONSEMBLE bev exposed patients (as of February 26, 2024)

Bev exposed: onvansertib + FOLFIRI/bev arm



Bev exposed: FOLFIRI/bev (control) arm



* Spider plots reflect interim data as of February 26, 2024 from an ongoing, discontinued trial and unlocked database

ONSEMBLE Control Arm: Treatment Emergent Adverse Effects (TEAEs)

| | N (% of total) | Grade 1 | Grade 2 | Grade 3 | Grade 4 | Total |
|-----------------------------------|----------------|-----------|-----------|-----------|----------|-----------|
| Control arm | | | | | | |
| (N=7) | | | | | | |
| Patients received FOLFIRI+bev | | | | | | |
| No major/unexpected toxicity seen | | | | | | |
| Any Adverse Events | 6 (85.7) | 6 (85.7) | 6 (85.7) | 3 (42.9) | 0 (0.0) | 6 (85.7) |
| Diarrhea | 3 (42.9) | 1 (14.3) | 1 (14.3) | 0 (0.0) | 0 (0.0) | 4 (57.1) |
| Nausea | 2 (28.6) | 1 (14.3) | 1 (14.3) | 1 (14.3) | 0 (0.0) | 4 (57.1) |
| Fatigue | 3 (42.9) | 0 (0.0) | 0 (0.0) | 1 (14.3) | 0 (0.0) | 4 (57.1) |
| Neutropenia | 0 (0.0) | 3 (42.9) | 3 (42.9) | 0 (0.0) | 0 (0.0) | 3 (42.9) |
| Stomatitis | 1 (14.3) | 1 (14.3) | 1 (14.3) | 1 (14.3) | 0 (0.0) | 3 (42.9) |
| Vomiting | 1 (14.3) | 0 (0.0) | 0 (0.0) | 1 (14.3) | 0 (0.0) | 2 (28.6) |
| Alopecia | 1 (14.3) | 2 (28.6) | 2 (28.6) | 0 (0.0) | 0 (0.0) | 3 (42.9) |
| Constipation | 2 (28.6) | 1 (14.3) | 1 (14.3) | 0 (0.0) | 0 (0.0) | 3 (42.9) |
| Decreased appetite | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Insomnia | 0 (0.0) | 1 (14.3) | 1 (14.3) | 0 (0.0) | 0 (0.0) | 1 (14.3) |
| Hypokalaemia | 1 (14.3) | 1 (14.3) | 1 (14.3) | 0 (0.0) | 0 (0.0) | 2 (28.6) |
| Anaemia | 0 (0.0) | 1 (14.3) | 1 (14.3) | 0 (0.0) | 0 (0.0) | 1 (14.3) |
| Cough | 1 (14.3) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (14.3) |
| Dysgeusia | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Dyspepsia | 0 (0.0) | 1 (14.3) | 1 (14.3) | 0 (0.0) | 0 (0.0) | 1 (14.3) |
| Hypertension | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (14.3) | 0 (0.0) | 1 (14.3) |
| Lymphopenia | 0 (0.0) | 1 (14.3) | 1 (14.3) | 0 (0.0) | 0 (0.0) | 1 (14.3) |
| Pyrexia | 0 (0.0) | 1 (14.3) | 1 (14.3) | 0 (0.0) | 0 (0.0) | 1 (14.3) |

* Data consists of all adverse events entered into the EDC as of January 3, 2024, from an ongoing trial and unlocked database. N: number of patients; 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; Columns show the absolute # of patients and (%) of the population.

ONSEMBLE onvansertib 30mg Arm TEAEs: Onvansertib in combination with FOLFIRI+bev is well-tolerated

| | N (% of total) | Grade 1 | Grade 2 | Grade 3 | Grade 4 | Total |
|--|--------------------|-----------|-----------|-----------|----------|-----------|
| Experimental arm | | | | | | |
| Onv 30mg (N=7) | | | | | | |
| Patients received FOLFIRI+bev +30 mg dose of onvansertib | | | | | | |
| No major/unexpected toxicity seen | | | | | | |
| | Any Adverse Events | 7 (100.0) | 7 (100.0) | 4 (57.1) | 0 (0.0) | 7 (100.0) |
| | Diarrhea | 1 (14.3) | 1 (14.3) | 2 (28.6) | 0 (0.0) | 4 (57.1) |
| | Nausea | 2 (28.6) | 1 (14.3) | 0 (0.0) | 0 (0.0) | 3 (42.9) |
| | Fatigue | 3 (42.9) | 1 (14.3) | 0 (0.0) | 0 (0.0) | 4 (57.1) |
| | Neutropenia | 0 (0.0) | 1 (14.3) | 2 (28.6) | 0 (0.0) | 3 (42.9) |
| | Stomatitis | 2 (28.6) | 1 (14.3) | 0 (0.0) | 0 (0.0) | 3 (42.9) |
| | Vomiting | 2 (28.6) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 2 (28.6) |
| | Alopecia | 1 (14.3) | 1 (14.3) | 0 (0.0) | 0 (0.0) | 2 (28.6) |
| | Constipation | 1 (14.3) | 1 (14.3) | 0 (0.0) | 0 (0.0) | 2 (28.6) |
| | Decreased appetite | 0 (0.0) | 2 (28.6) | 0 (0.0) | 0 (0.0) | 2 (28.6) |
| | Insomnia | 3 (42.9) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 3 (42.9) |
| | Hypokalaemia | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| | Anaemia | 1 (14.3) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (14.3) |
| | Cough | 2 (28.6) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 2 (28.6) |
| | Dysgeusia | 0 (0.0) | 1 (14.3) | 0 (0.0) | 0 (0.0) | 1 (14.3) |
| | Dyspepsia | 0 (0.0) | 1 (14.3) | 0 (0.0) | 0 (0.0) | 1 (14.3) |
| | Hypertension | 0 (0.0) | 1 (14.3) | 1 (14.3) | 0 (0.0) | 2 (28.6) |
| | Lymphopenia | 2 (28.6) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 2 (28.6) |
| | Pyrexia | 0 (0.0) | 0 (0.0) | 1 (14.3) | 0 (0.0) | 1 (14.3) |
| | Thrombocytopenia | 0 (0.0) | 2 (28.6) | 0 (0.0) | 0 (0.0) | 2 (28.6) |

* Data consists of all adverse events entered into the EDC as of January 3, 2024, from an ongoing trial and unlocked database. N: number of patients; 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; Columns show the absolute # of patients and (%) of the population.

Onvansertib 20mg Arm TEAEs: Onvansertib in combination with FOLFIRI+bev is well-tolerated

| | N (% of total) | Grade 1 | Grade 2 | Grade 3 | Grade 4 | Total |
|--|--------------------|-----------|-----------|-----------|-----------|-----------|
| Experimental arm | | | | | | |
| Onv 20mg (N=8) | | | | | | |
| Patients received FOLFIRI+bev +20 mg dose of onvansertib | | | | | | |
| No major/unexpected toxicity seen | | | | | | |
| 2 Grade 4 TEAEs of neutropenia seen in patients (008 and 019) receiving 20mg onvansertib+SoC | | | | | | |
| <ul style="list-style-type: none"> Both patients recovered after delaying their next cycle of treatment for 7 and 10 days, respectively Both patients are still on-trial | | | | | | |
| | Any Adverse Events | 8 (100.0) | 7 (87.5) | 2 (25.0) | 2 (25.0) | 8 (100.0) |
| | Diarrhea | 4 (50.0) | 3 (37.5) | 0 (0.0) | 0 (0.0) | 7 (87.5) |
| | Nausea | 3 (37.5) | 3 (37.5) | 0 (0.0) | 0 (0.0) | 6 (75.0) |
| | Fatigue | 2 (25.0) | 0 (0.0) | 1 (12.5) | 0 (0.0) | 3 (37.5) |
| | Neutropenia | 1 (12.5) | 0 (0.0) | 1 (12.5) | 2 (25.0) | 3 (37.5) |
| | Stomatitis | 1 (12.5) | 1 (12.5) | 0 (0.0) | 0 (0.0) | 2 (25.0) |
| | Vomiting | 2 (25.0) | 2 (25.0) | 0 (0.0) | 0 (0.0) | 4 (50.0) |
| | Alopecia | 2 (25.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 2 (25.0) |
| | Constipation | 1 (12.5) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (12.5) |
| | Decreased appetite | 2 (25.0) | 2 (25.0) | 0 (0.0) | 0 (0.0) | 4 (50.0) |
| | Insomnia | 1 (12.5) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (12.5) |
| | Hypokalaemia | 1 (12.5) | 0 (0.0) | 1 (12.5) | 0 (0.0) | 2 (25.0) |
| | Anaemia | 1 (12.5) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (12.5) |
| | Cough | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| | Dysgeusia | 2 (25.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 2 (25.0) |
| | Dyspepsia | 0 (0.0) | 1 (12.5) | 0 (0.0) | 0 (0.0) | 1 (12.5) |
| | Hypertension | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| | Lymphopenia | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| | Pyrexia | 1 (12.5) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (12.5) |
| | Thrombocytopenia | 0 (0.0) | 1 (12.5) | 0 (0.0) | 0 (0.0) | 1 (12.5) |

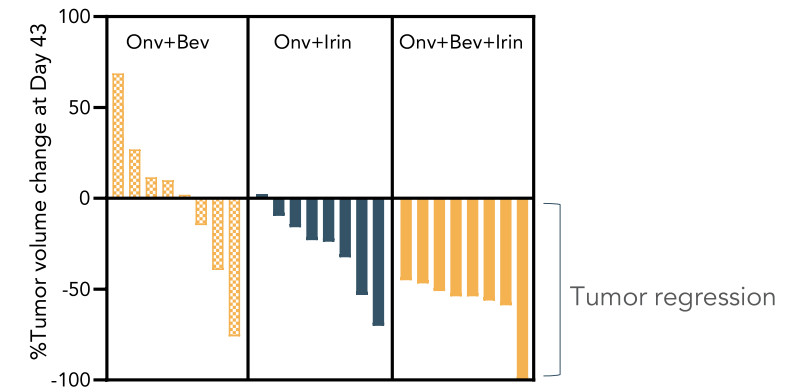
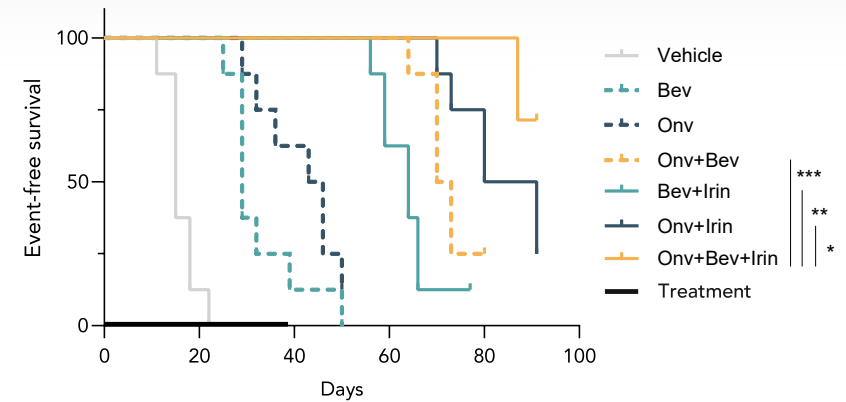
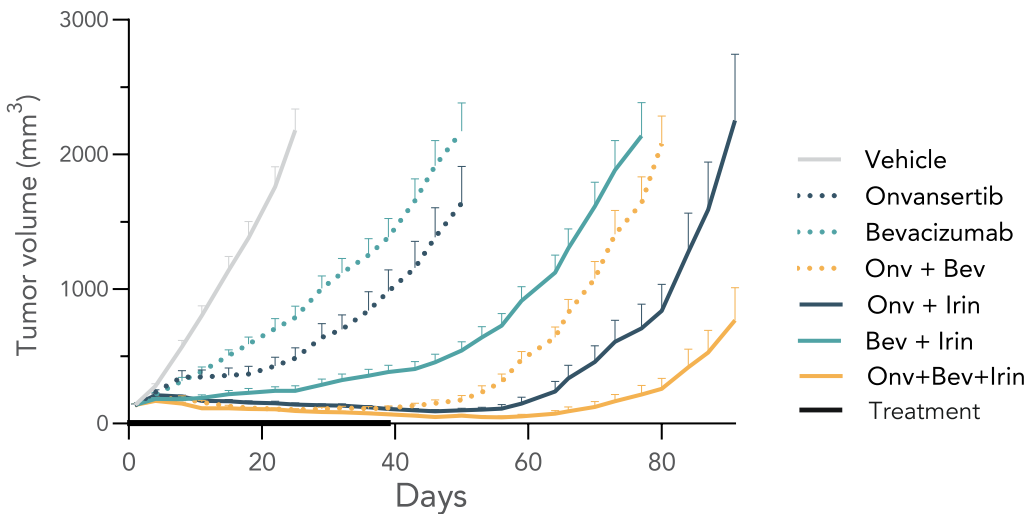
* Data consists of all adverse events entered into the EDC as of January 3, 2024, from an ongoing trial and unlocked database. N: number of patients; events shown occurred in ≥10% of patients; numbers indicate number of patients experiencing the event, (regardless of causality); each patient is only counted once and only for the highest grade of a given event. TEAEs: Treatment Emergent Adverse Events; Columns show the absolute # of patients and (%) of the population.

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

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

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

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



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

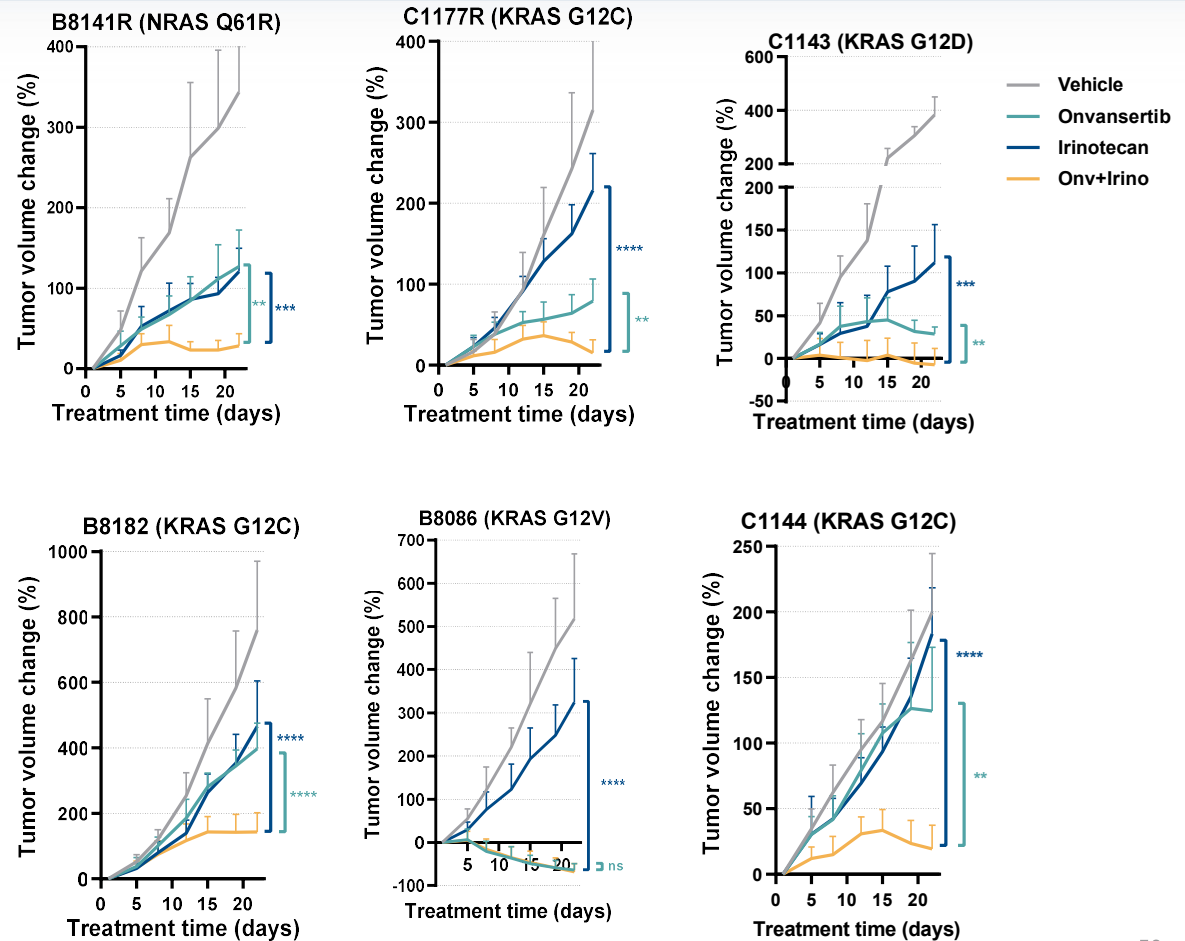
Onvansertib in combination with irinotecan in RAS-mutant CRC PDXs

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

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

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

In collaboration with Dr. Kopetz (MD Anderson)



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

Onvansertib in combination with FOLFOX in RAS-mutant CRC PDXs

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

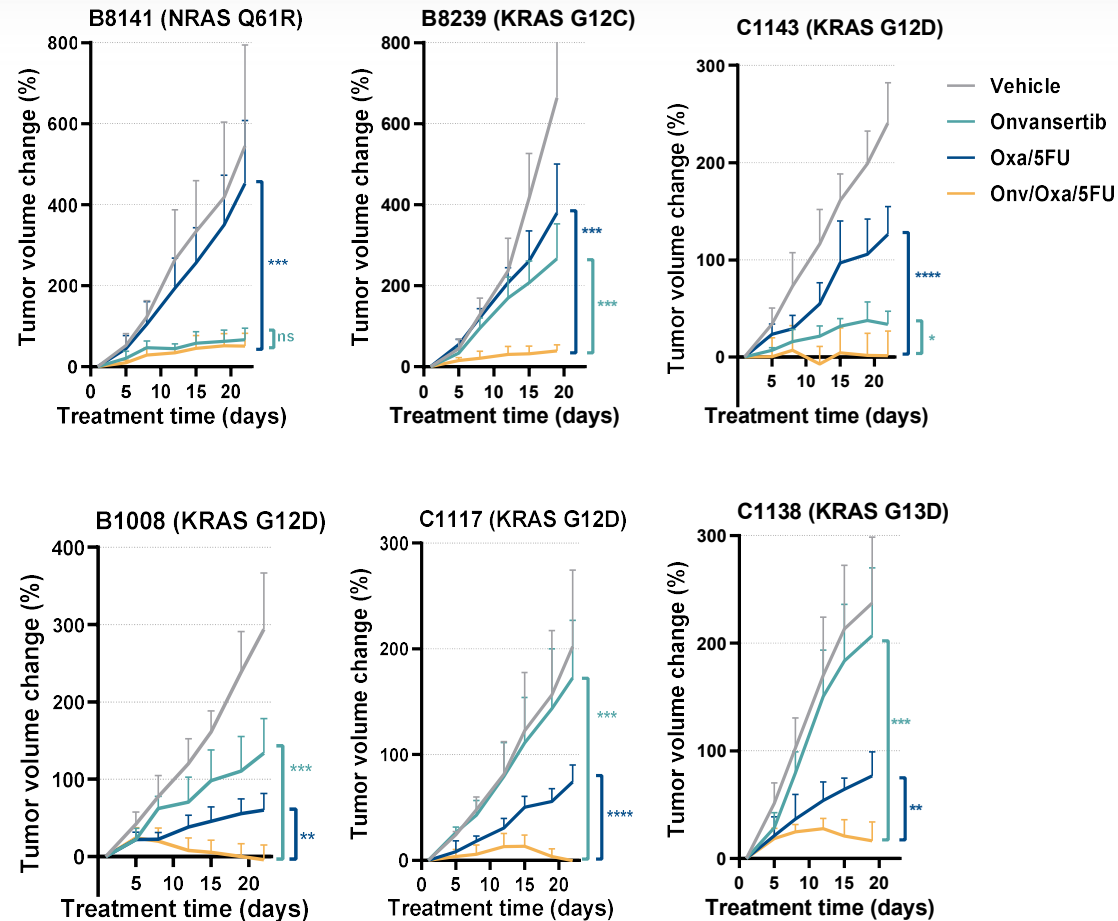
Conversely, the combination of onvansertib with oxaliplatin+5FU was efficacious in all 6 models, resulting in tumor stasis or tumor regression.

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

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

In collaboration with Dr. Kopetz (MD Anderson)

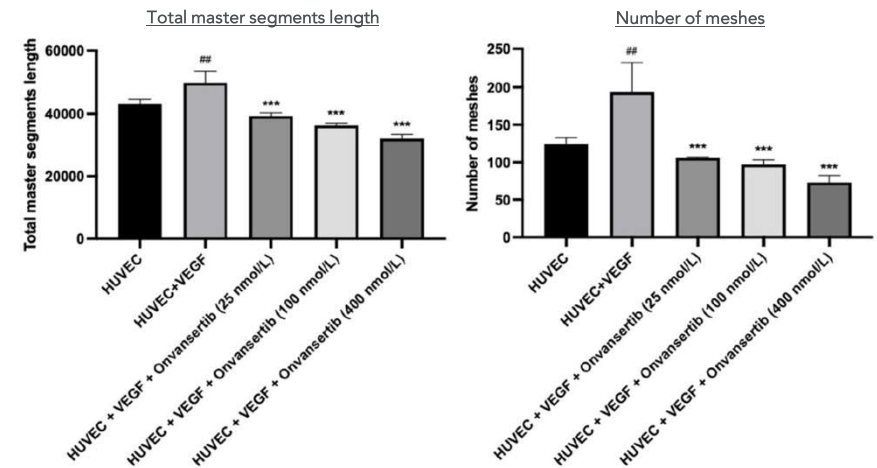
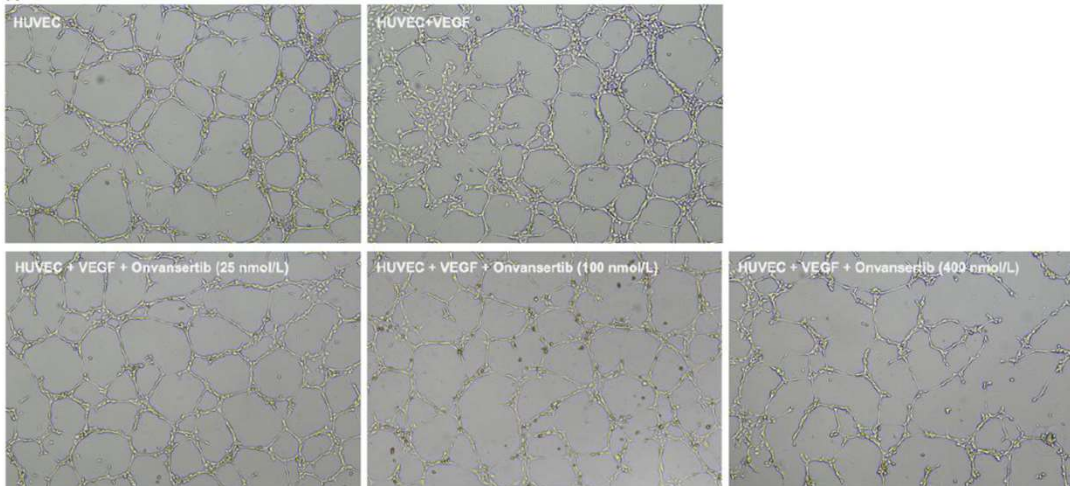
Dosing schedule: onvansertib 45 mg/kg daily; oxaliplatin 10mg/kg weekly; 5-FU 25mg/kg 5times/week for up to 21days. Mean + SD are represented. Unpaired t-test, *p<0.05, **p<0.01, ***p<0.001, ****p<0.0001



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*





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



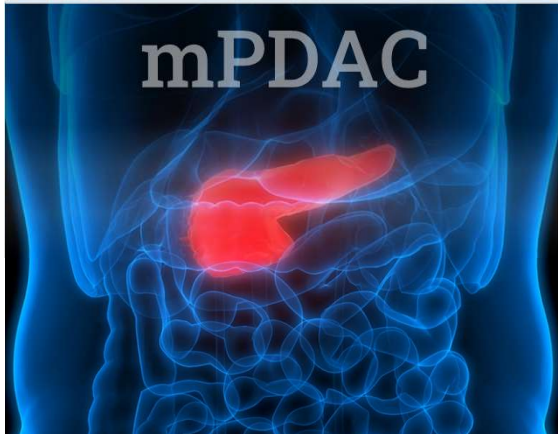
Path forward: Move to 1st line mPDAC

- 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

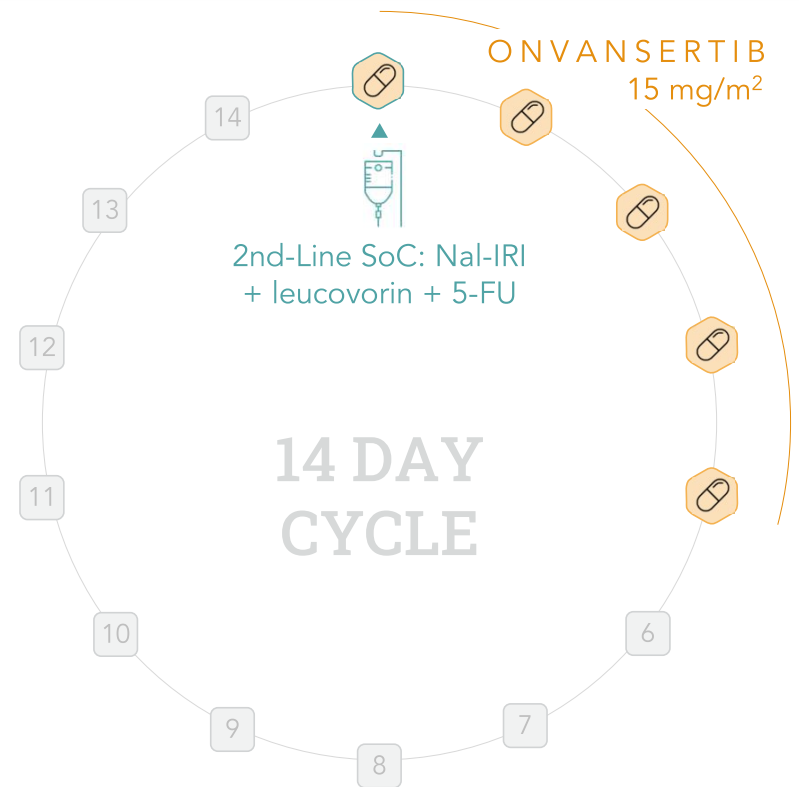
To determine the efficacy and safety of onvansertib when added to standard of care

PRIMARY ENDPOINT

ORR (RECIST 1.1)

SECONDARY ENDPOINT

Disease Control Rate (DCR)

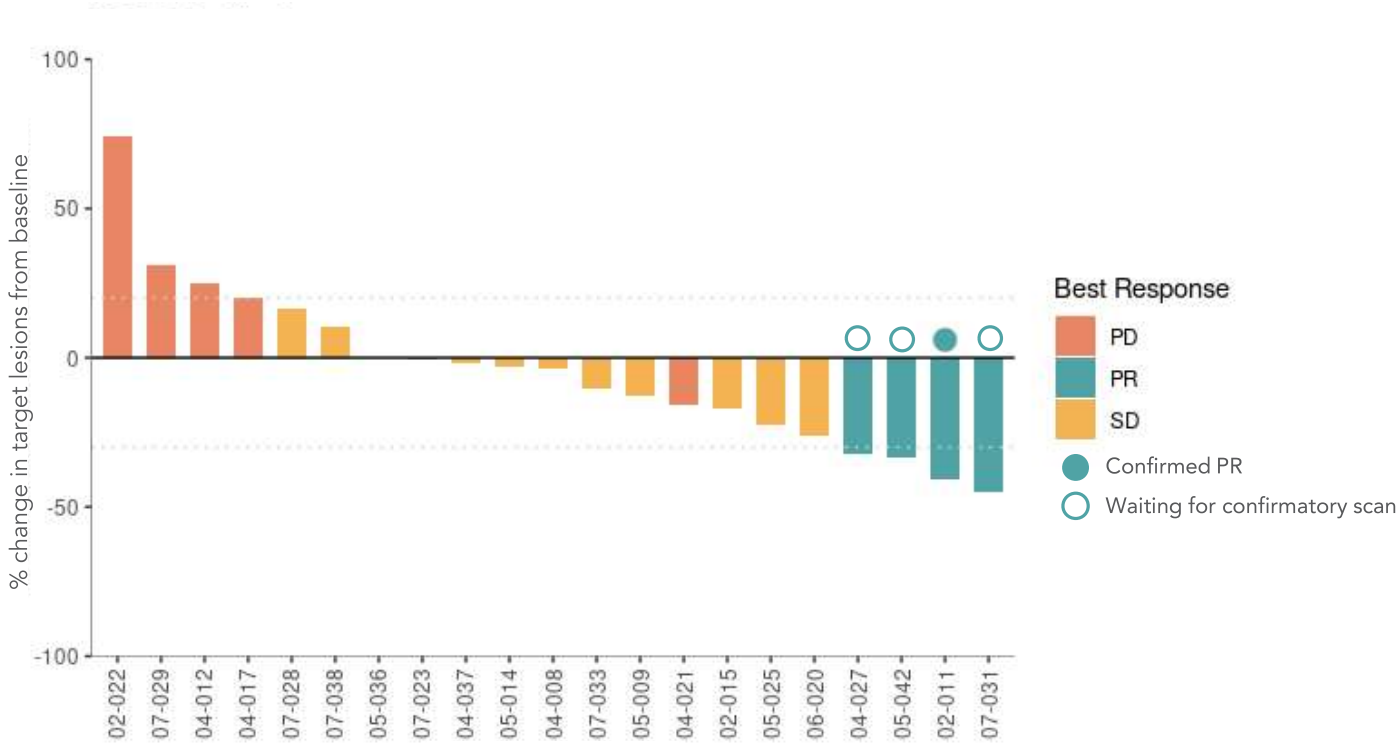


Onvansertib+SoC has higher efficacy than 2nd line historical controls

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

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

Subsequent disclosure on Feb 29, 2024: Three of the four initial partial responses confirmed on their subsequent scan, and one initial partial response did not confirm

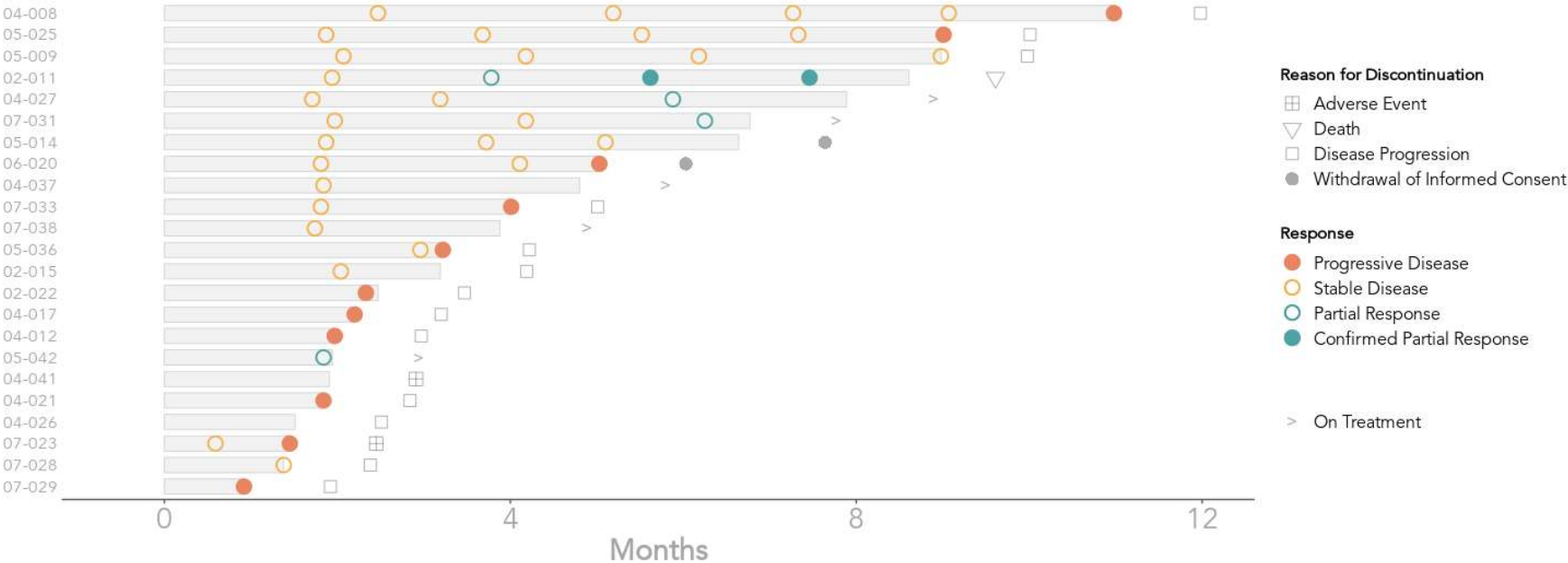


* Radiographic response determined per RECIST 1.1. Waterfall plot and table reflect interim data as of September 13, 2023 from an ongoing trial and unlocked database. For ORR analysis, there are two patients excluded (04-026 and 04-041) that had two cycles of treatment but left the trial before their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

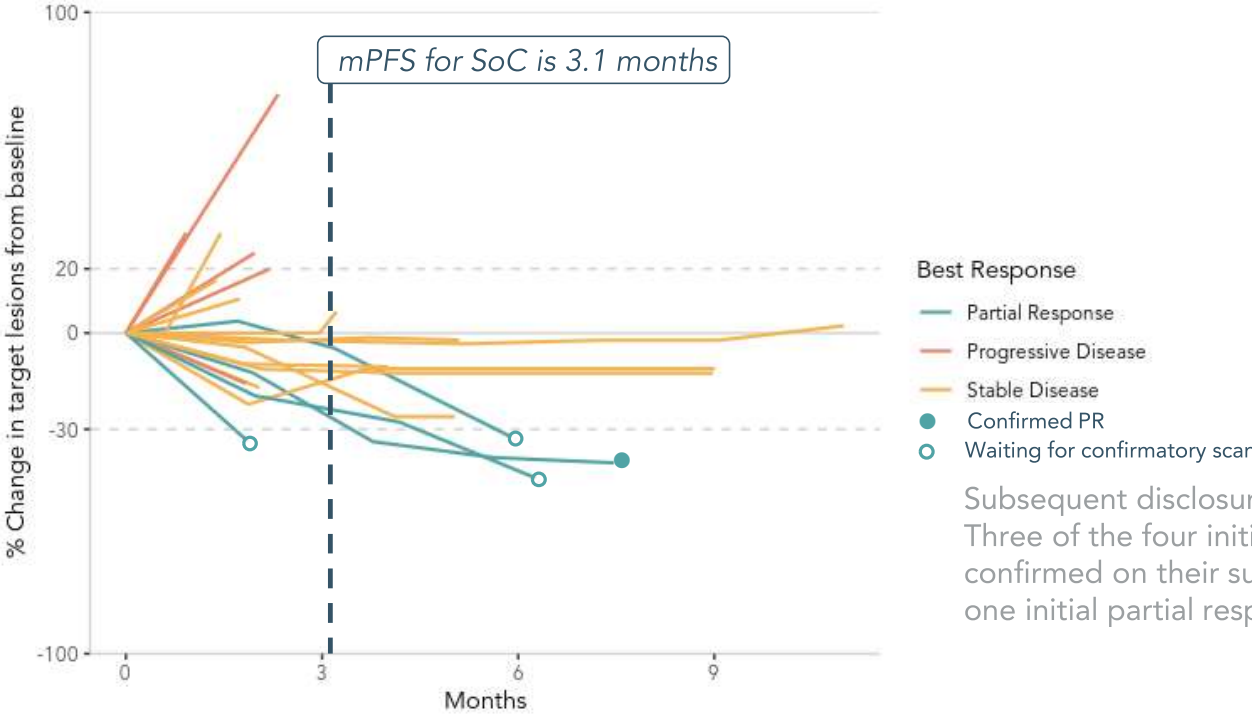
Swimmer plot – 23 evaluable patients (as of September 13, 2023)*



* 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)*



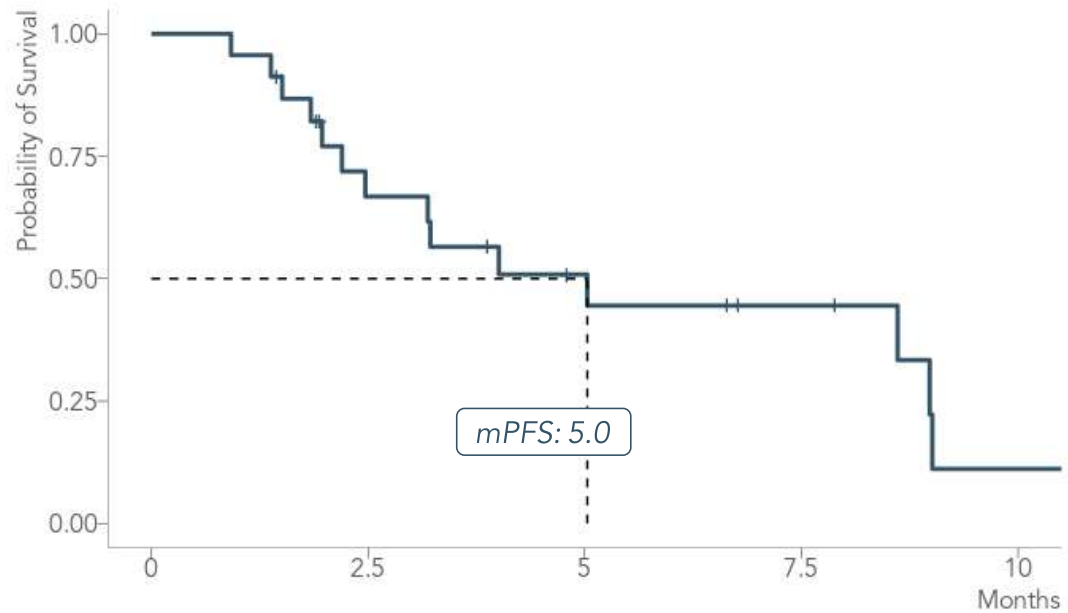
Subsequent disclosure on Feb 29, 2024:
 Three of the four initial partial responses confirmed on their subsequent scan, and one initial partial response did not confirm

* 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 | |
|---------------------------------------|----------|----------------------------------|----------------------------|
| | | 2 nd line mPDAC | 1 st 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

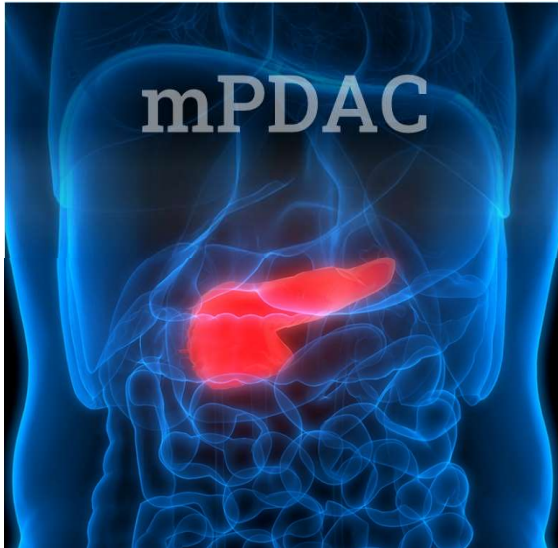
- New IIT combining onvansertib with SoC (Gemzar/Abraxane)

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

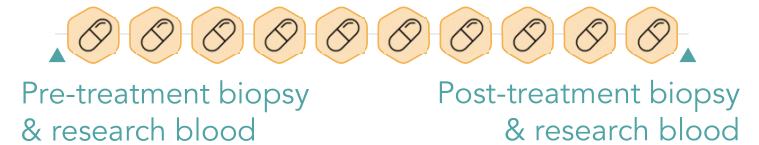
- To demonstrate pancreatic tumor response to onvansertib monotherapy by measuring Ki67 and CA 19-9

Predictive biomarkers

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

ONVANSERTIB MONOTHERAPY

(12mg/m² QD, 10 days)



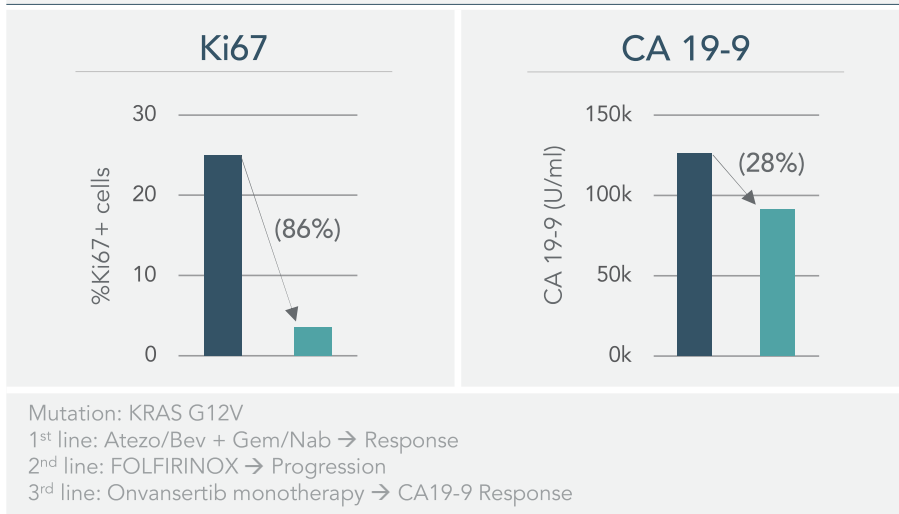
Obtain biopsies / bloodwork before and after 10 days of onvansertib monotherapy to conduct extensive multi-omic analyses

Onvansertib monotherapy decreased tumor proliferation and CA19-9

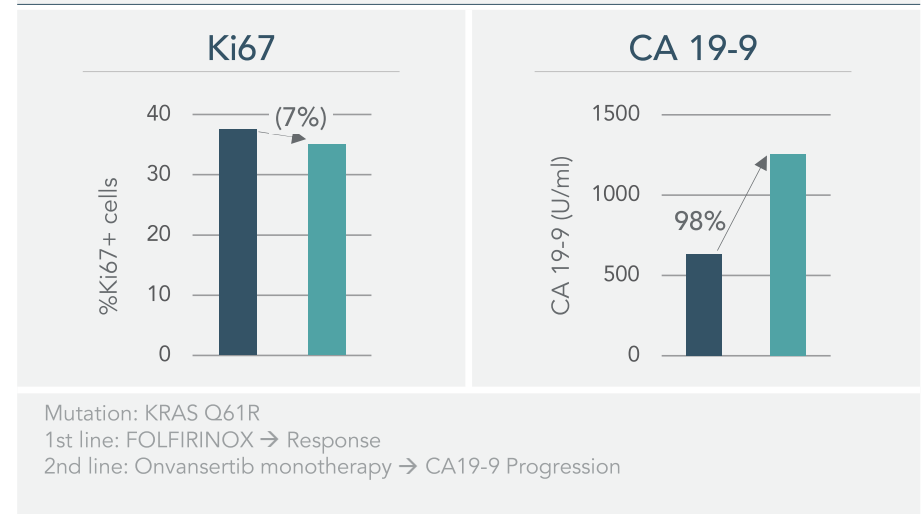
Biomarker Discovery Trial: Biomarker Response* – 2 patients (as of September 13, 2023)

- 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)



Patient 33 (tumor non-responder)



■ Pre-treatment ■ Post-treatment

* Patient 28 and patient 33 had liver metastases 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

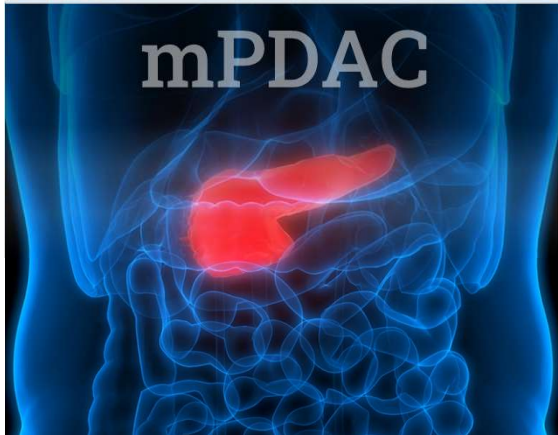
- New IIT combining onvansertib with SoC (Gemzar/Abraxane)

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

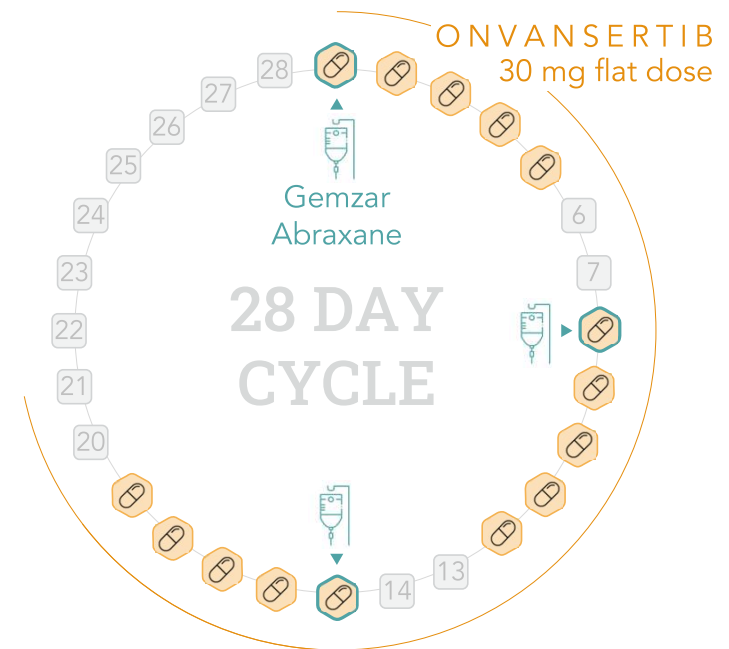
ORR, DCR at 16 weeks

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



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

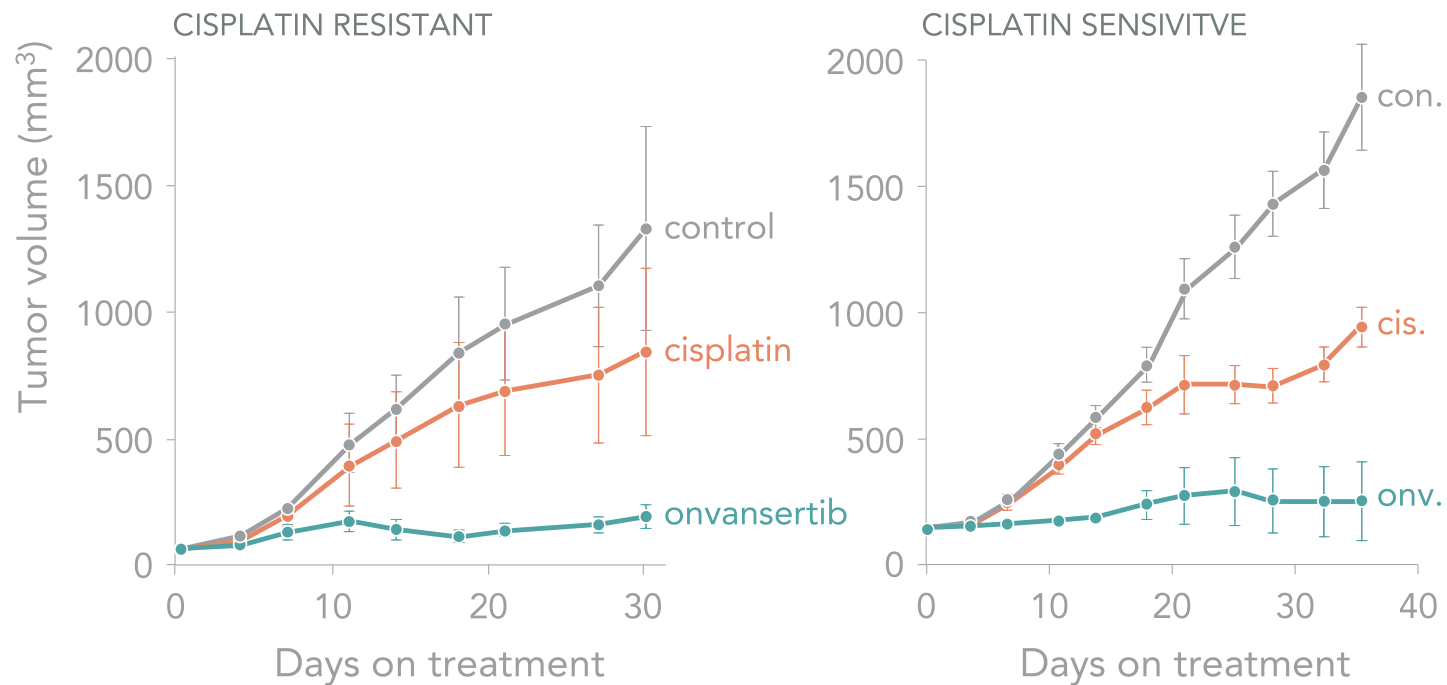
Onvansertib demonstrates single-agent activity in SCLC

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

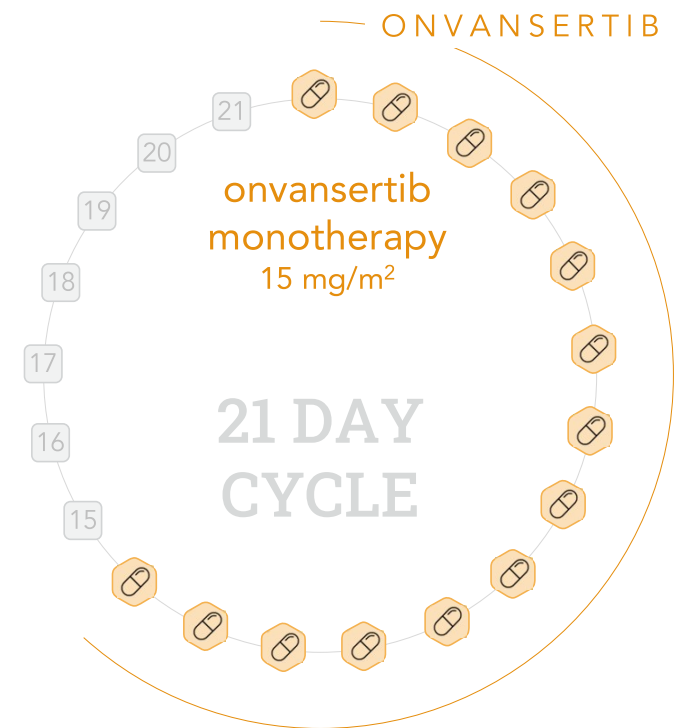
To determine the efficacy and safety of onvansertib monotherapy

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).

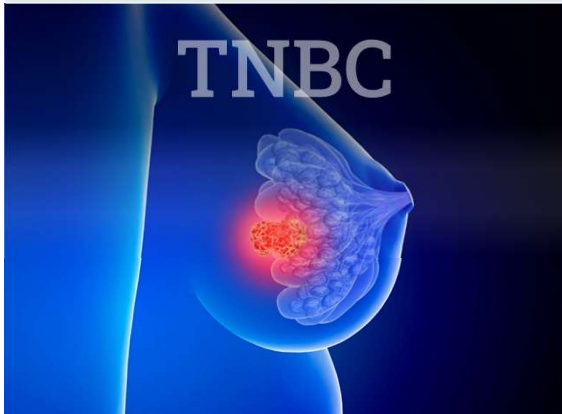


Appendix:
Investigator-Initiated Trial
Triple Negative Breast Cancer (TNBC)

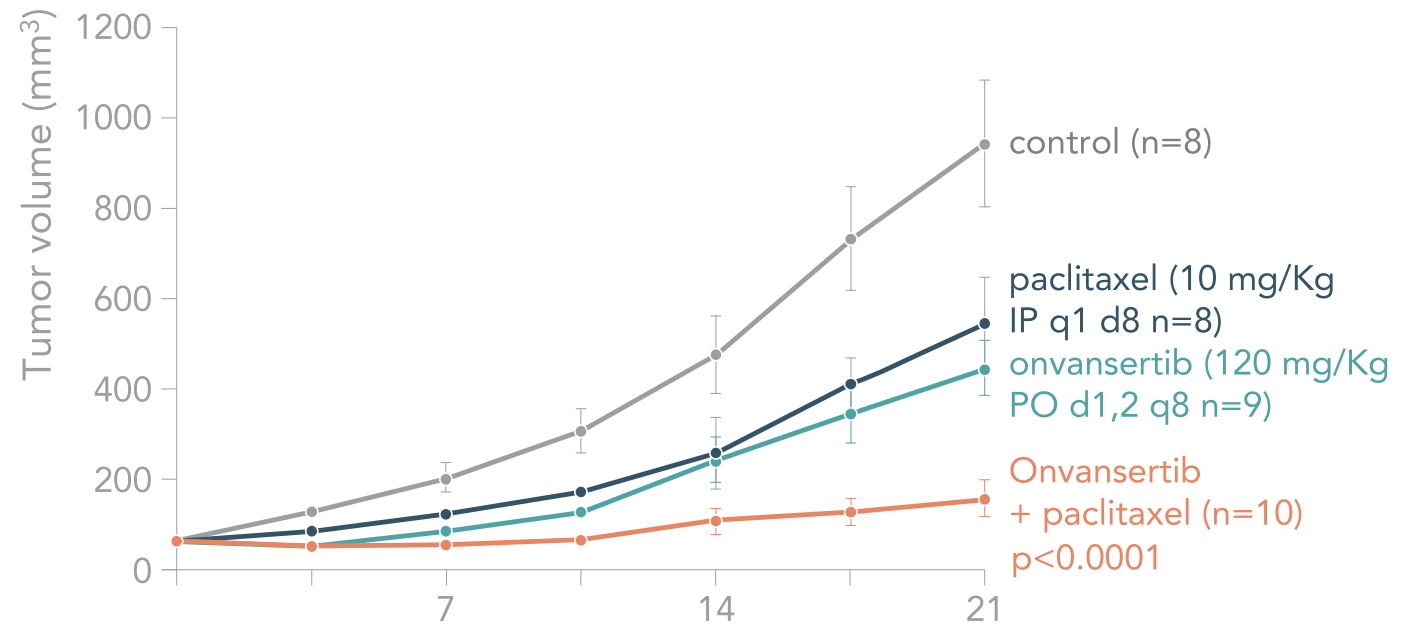
Onvansertib + paclitaxel is superior to single agent therapy

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 mm³: vehicle, onvansertib oral (PO) twice per week (days 1-2), paclitaxel intraperitoneally (IP) weekly (day 1), or the combination.

This is the first trial to explore onvansertib + paclitaxel combination

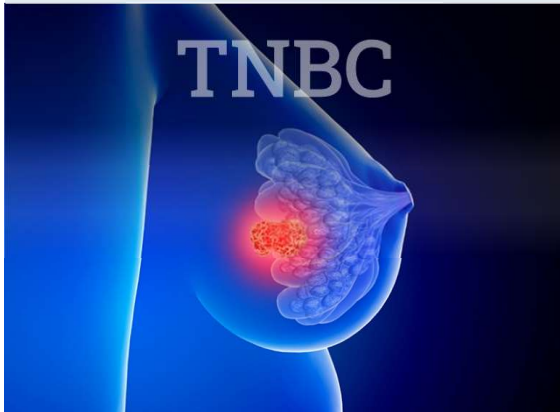
ENROLLMENT CRITERIA

Metastatic TNBC relapsed or progressed

Single arm trial

Ph 1b: N=14-16

Ph 2: N=34



PRIMARY ENDPOINTS

Phase 1b

Safety, characterization of DLTs

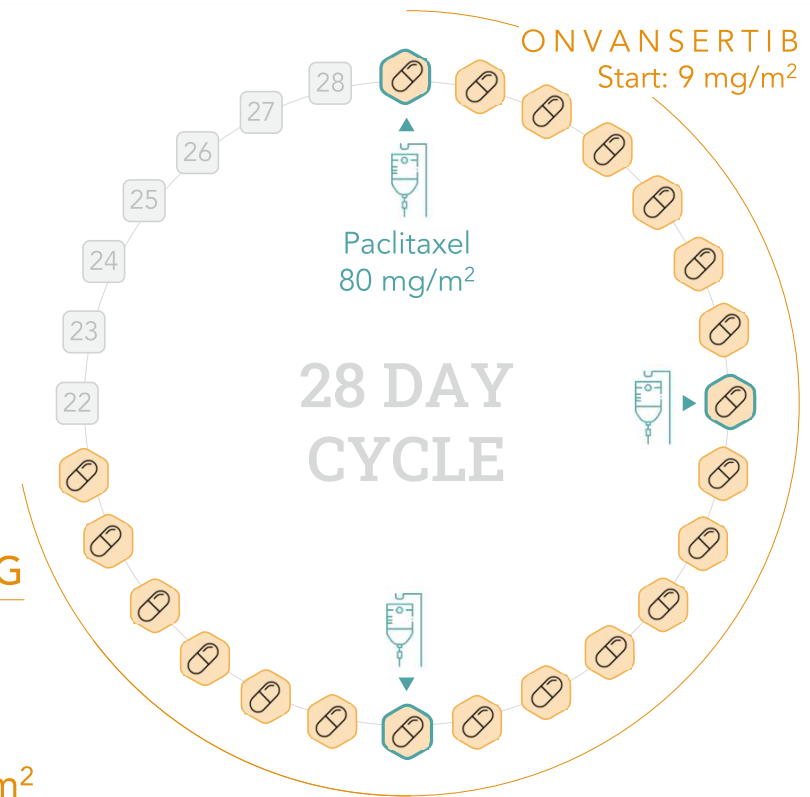
Determination of RP2D

Phase 2

ORR (RECIST 1.1)

ONVANSERTIB DOSING

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

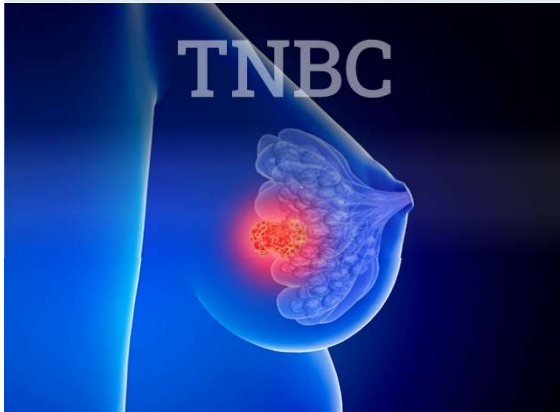


This is the first trial to explore onvansertib + paclitaxel combination

ENROLLMENT CRITERIA

Metastatic TNBC relapsed or progressed

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



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)

