Cardiff Oncology™

Turning the Tide on Cancer

April 2021

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; 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; our ability to develop tests, kits and systems and the success of those products; regulatory, financial and business risks related to our international expansion 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, 2020, 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 Strategy – Transforming to Lead the Way

Undergoing Corporate Transformation to Position Cardiff for Long-term Success

- Accelerating corporate governance best practices, starting with new CEO leadership, board evolution and updated policies
- Seeking leading talent for key roles, including CFO, CMO and CSO
- Committed to investor communication transparency and disclosure

Maximizing Our Clinical Development Capabilities

- Cultivating the most advanced PLK1 inhibitor
- Developing strategies to enable the most rapid path to approval
- Focusing on opportunities to lead the “drugability” enablement of KRAS mutated cancers

Leading with Research and Data

- PLK1 is at a unique nexus within the convergence of many tumor-promoting pathways
- Leveraging deep expertise in translational biomarker integration within clinical programs
- Focusing on pipeline expansion through synergistic combinations

Fully Leverage Onvansertib in Combination with Targeted Therapeutics and Chemotherapies Across Multiple Cancer Indications

Experienced Management Team With Drug Development and Biomarker Technology Expertise

Mark Erlander, PhD
Chief Executive Officer

Vicki Kelemen
Chief Operating Officer

Brigitte Lindsay
Vice President of Finance

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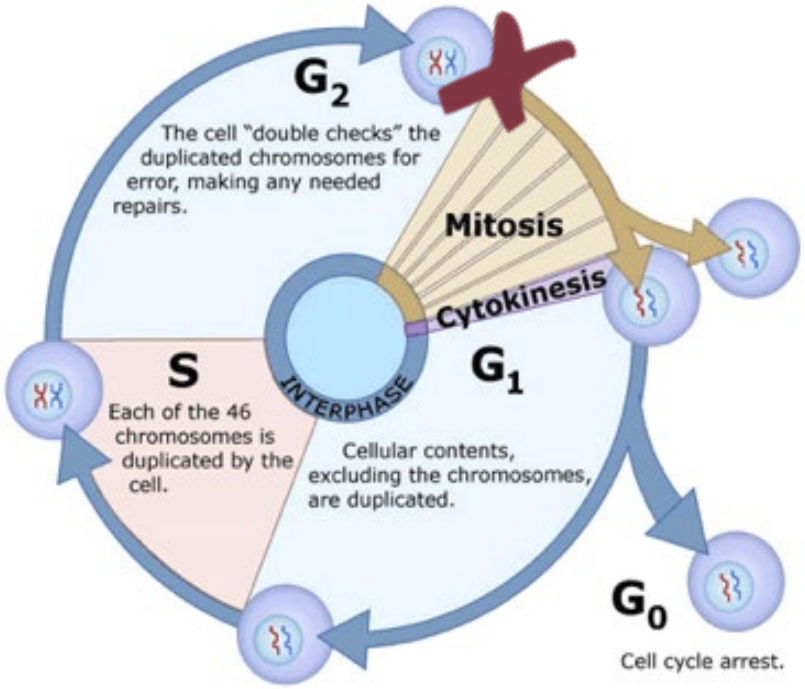
Onvansertib

3rd generation, 1st in class, oral and highly selective PLK1 inhibitor addressing unmet needs across a broad range of cancer indications

PLK1 is a Proven Therapeutic Target that is Overexpressed in Most Cancers

- PLK1 is a serine/threonine kinase and master regulator of cell-cycle progression
- PLK1 controls G2/mitosis (G2/M) checkpoint
- Inhibition of PLK1 causes mitotic arrest and subsequent cell death
- Emerging data demonstrate that PLK1 is also a key regulator of cellular functions beyond mitosis that are essential for tumor growth:
  - Biosynthesis of DNA
  - DNA Damage Response



Inhibition of PLK1 causes mitotic arrest and subsequent cell death[1]

[1]Zitouni et al., Nat Rev Mol Cell Biol. 2014 Jul;15(7):433-52; PLK1: Polo-like kinase 1

PLK1-Specific ATP Competitive Inhibitor[1]

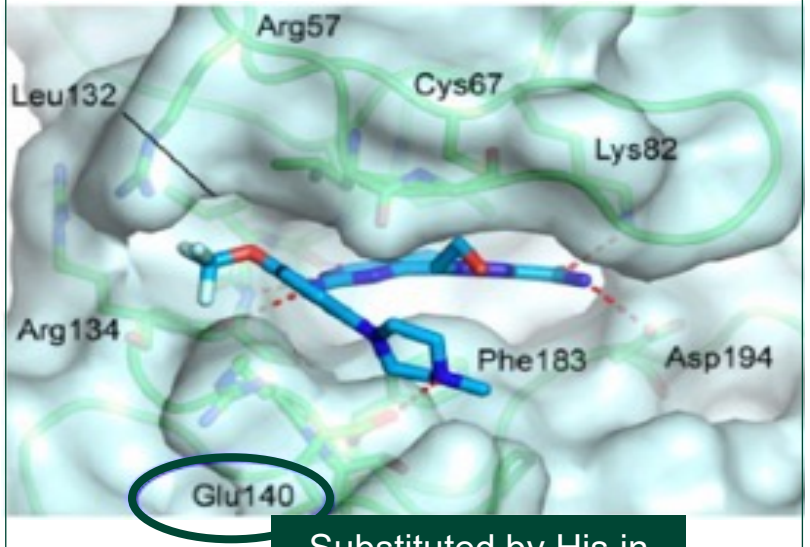
Biochemical Profile

Enzyme	IC_{50} (μM)
PLK1	**0.002**
PLK2	>10
PLK3	>10
CK2	0.4
FLT3	0.4
CDK1/CycB	3.8
42 additional kinases in house	>10
>190 additional kinases in the Millipore panel	>10

Profile Characteristics

Small Molecule	MW 648.60 Daltons
Formulation	5mg and 20mg oral gelcaps
Plasma Protein Binding	95% at 10μM and 91% at 50μM
Metabolic Overview	Moderate intrinsic clearance (9.3 mL/min/kg)[1] 2 metabolites identified in metabolic profiling in low quantities (parent drug accounted for 93% of total drug-related material)[1] No Cytochrome P450 inhibition at therapeutic concentrations[2]
Pharmacokinetics[3]	Systemic exposure of drug increased with dose, as shown by an increase in C_{max} and AUC_{0-24} T_{max} is approximatively 3h Half-life is approximately 24h

Co-crystal of Onvansertib with PLK1



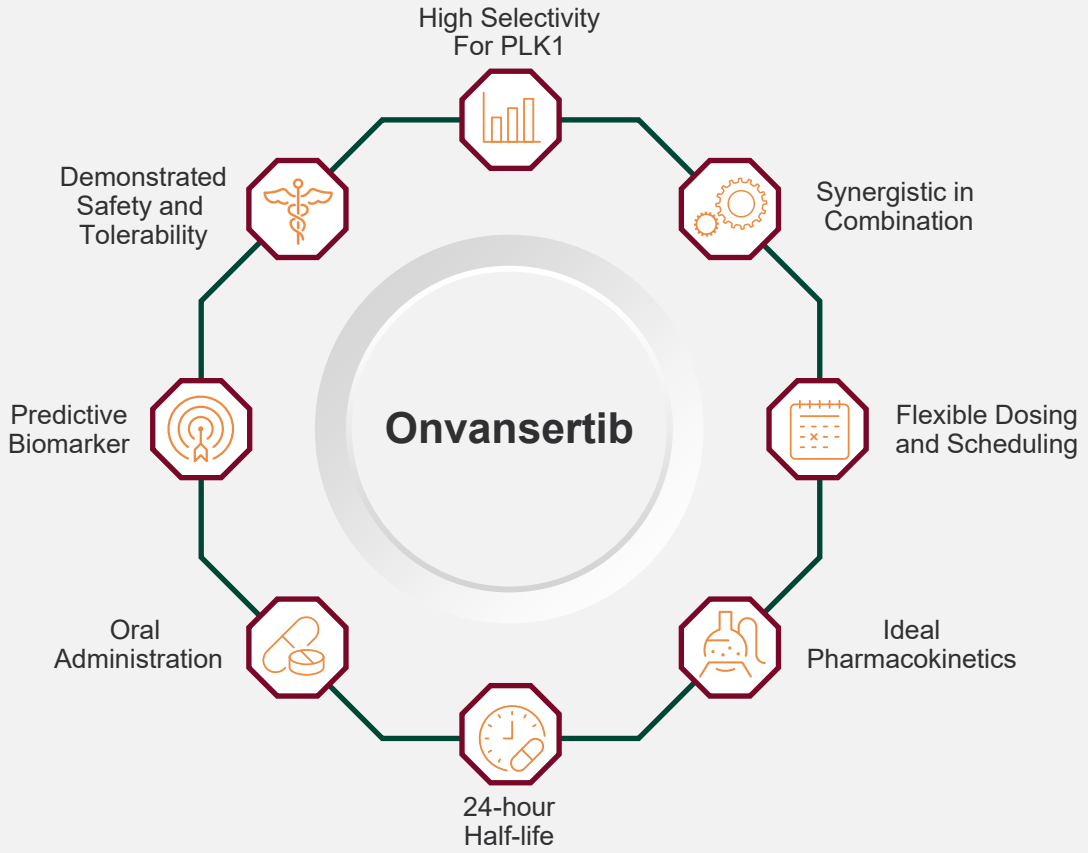
Onvansertib

- A selective, ATP competitive PLK1 inhibitor
- Selectivity is driven by polar interaction with the side chain of Glu140 of PLK1
- Interaction is hampered in both PLK2 and PLK3 where Glu140 is replaced by histidine

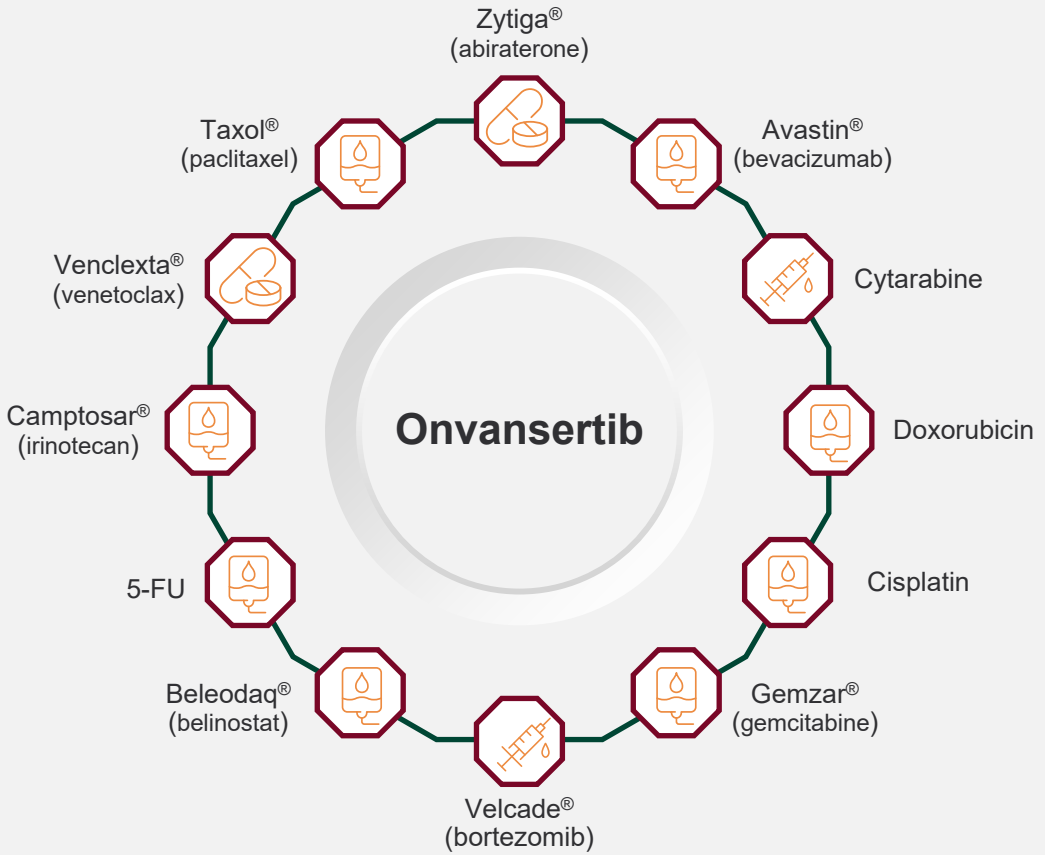
[1]Valsasina Mol Cancer Ther 2012

Onvansertib has Optimal Drug Properties and Synergistically Combines with Standard-of-Care Therapies

Optimal Drug Properties



Synergistic in Combination with Standard-of-Care Chemo and Targeted Therapies



Second-Line Treatment of KRAS-Mutated mCRC

Phase 1b/2 open-label trial of onvansertib + FOLFIRI/bevacizumab

Trial Sites: USC Norris Comprehensive Cancer Center; Mayo Clinics (Arizona, Minnesota, Florida), Kansas University Medical Center, CARTI Cancer Center, Inova Schar Cancer Institute

Principal Investigator: Dr. Heinz-Josef Lenz

Benchmarking for Second Line Treatment of mCRC

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Second-Line mCRC Treatment is an Unmet Need

Standard-of-Care Second Line mCRC Benchmarks for Median ORR, PFS and OS

	Objective Response Rate (ORR)	Progression-Free Survival (PFS)	Overall Survival (OS)
Systematic Literature-Based Analysis of 23 Randomized Trials (10,800 Patients) in Second-Line mCRC[1] (2000 – 2013)	11.4%	4.5 months	11.5 months
TRIBE2 Randomized Phase 3 Trial: SOC arm FOLFIRI + bev in Second-line following FOLFOX + bev First-line[2,3] (2015 – 2017)	13%	5.6 months	Not Reported for Second-line
ML18147 Phase 3 Registrational Trial of FOLFIRI + bev in Second-Line[4] (2006 – 2008)	5%	5.7 months	11.2 months

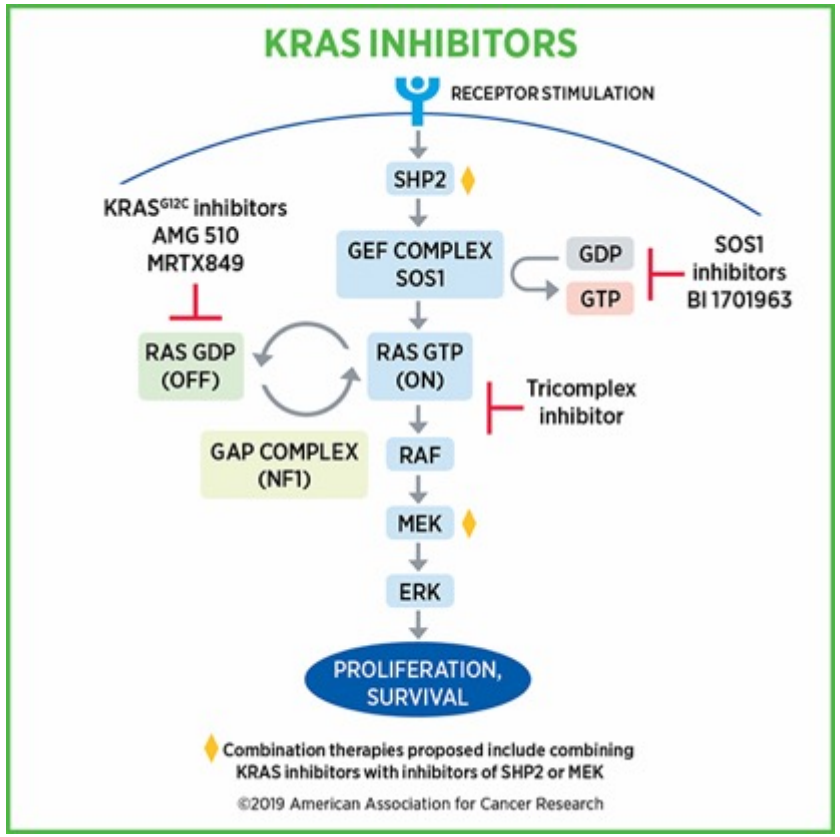
- Prognosis is poor with a five-year survival rate of 10%
- Other drugs currently in development do not address the most prevalent KRAS mutations in mCRC

[1]Giessen et al., Acta Oncologica, 2015, 54: 187-193; [2]Cremolini et al., Lancet Oncol 2020, 21: 497–507; [3]Antoniotti et al., Correspondence Lancet Oncol June 2020; [4]Bennouna et al., Lancet Oncol 2013; 14: 29–37

11 2020 Corporate Presentation 11

Targeted Therapies for KRAS Mutant Patients is an Unmet Need

- KRAS Targeted Drugs in Development:
  - Two KRAS G12C inhibitors are currently in clinical development
    - Sotorasib (AMG510, Amgen) and Adagrasib (MRTX849, Miriati Therapeutics)
- KRAS G12C inhibitors have limited efficacy in mCRC patients
  - At the last data update, Sotorasib has an ORR of 7% (3 of 42 patients)[1] and Adagrasib of 17% (3 of 18 patients)[2]
  - KRAS G12C represents only 8% of KRAS mutations in CRC
- SHP2 Inhibitor in combination with MEK inhibitor has had limited activity in mCRC[3]
- SOS1 inhibitor BI 1701963, is the only pan-KRAS inhibitor currently in clinical development. It is being evaluated in a Phase 1 as a single agent and in combination with the MEK inhibitor trametinib
- Onvansertib provides new potential treatment option in mCRC
  - Downstream target with synthetic lethality across KRAS mutations

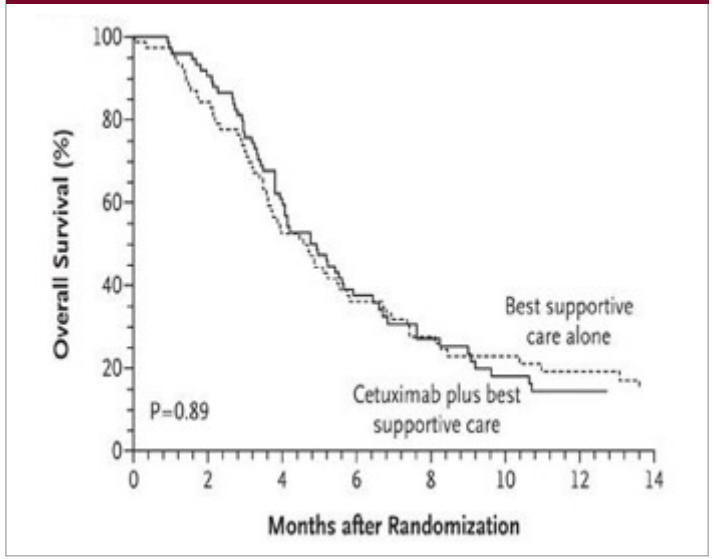


[1]Hong et al., NEJM 2020; [2]Johnson et al., ENA 2020, #LBA-04; [3]https://www.revmed.com/pipeline/rmc-4630

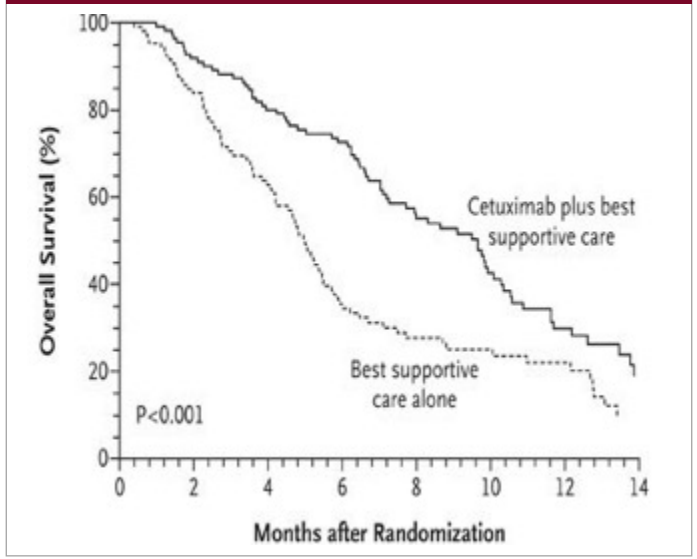
KRAS is a Pivotal Diagnostic Biomarker in the CRC Treatment Paradigm

- KRAS-mutated patients do not benefit from anti-EGFR agents:
  - No increase in OS, PFS and ORR was observed in KRAS mutant patients treated with EGFR inhibitors vs control arm[1,2]
  - The use of anti-EGFRs is therefore limited to KRAS wild-type patients
- Mutations in KRAS represent also the most frequent mechanism of resistance to anti-EGFRs (i.e. cetuximab)

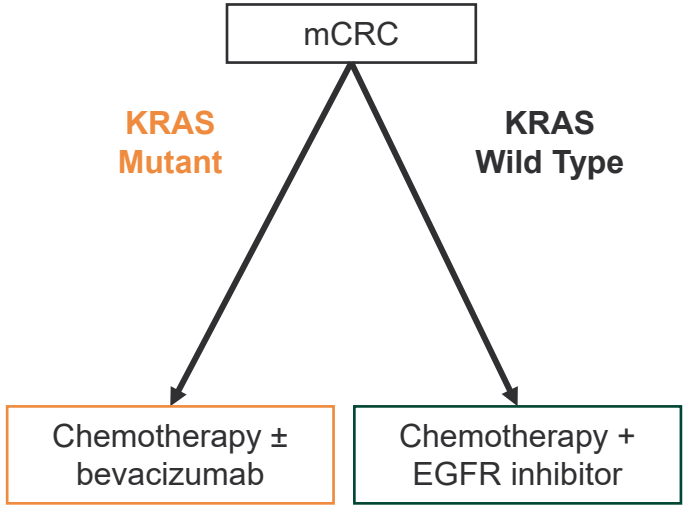
KRAS Mutant



KRAS Wild-type



Treatment Paradigm



[1]Karapetis et al., NEJM 2008;359:1757-1765; [2]Amado et al., JCO 2008, 26:1626-1634

Flatiron Health Data: Second-line Treatment

- FOLFIRI/Bev is the most utilized second-line regimen following first-line FOLFOX/Bev; other anti-angiogenic therapies are much less commonly used

255
Cancer clinics representing
1.7 million active cancer patients

14,315
Colorectal cancer patients

7,034
Colorectal cancer patients who receive second line therapy

	Number	Percent
Second-line regimens after first-line FOLFOX + bevacizumab ($N = 2470$)		
FOLFIRI + bevacizumab	1176	47.6
FOLFIRI	262	10.6
FOLFIRI + cetuximab	159	6.4
FOLFIRI + Ziv-aflibercept	114	4.6
FOLFIRI + panitumumab	91	3.7
Irinotecan + cetuximab	85	3.4
FOLFIRI + ramucirumab	74	3.0
Irinotecan + bevacizumab	53	2.1
Regorafenib	33	1.3
Irinotecan	30	1.2
Panitumumab	27	1.1
Second-line regimens after first-line FOLFOX ($N = 1249$)		
FOLFOX + bevacizumab	373	29.9
FOLFIRI	235	18.8
FOLFIRI + bevacizumab	210	16.8
Fluoropyrimidine + bevacizumab	85	6.8
FOLFIRI + cetuximab	43	3.4
FOLFOX + panitumumab	37	3.0
Irinotecan + cetuximab	24	1.9
FOLFIRI + panitumumab	23	1.8
FOLFOX + cetuximab	22	1.8
Bevacizumab	17	1.4
Irinotecan	15	1.2
Panitumumab	15	1.2
FOLFOXIRI + bevacizumab	14	1.1

Denotes combination with bevacizumab

Denotes combination with other antiangiogenics

Source: Hess, L. International Journal of Colorectal Disease; 2019. Data is limited to limited to second-line regimens used in >1% of the cohort. FOLFOX: fluoropyrimidine, leucovorin, oxaliplatin. FOLFIRI: fluoropyrimidine, leucovorin, irinotecan, FOLFOXIRI: fluoropyrimidine, leucovorin, irinotecan, oxaliplatin

Scientific Rationale: Synthetic Lethality and Synergy

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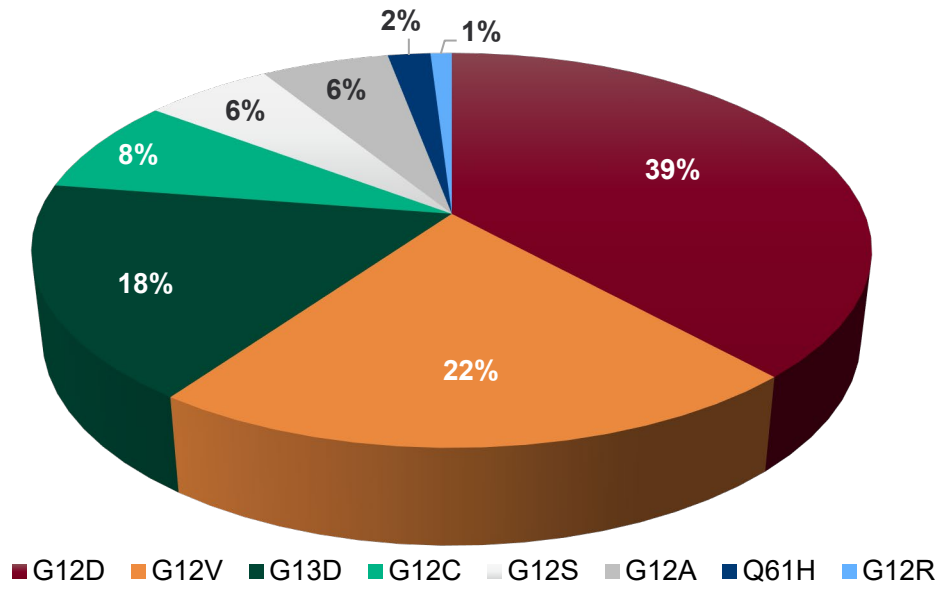
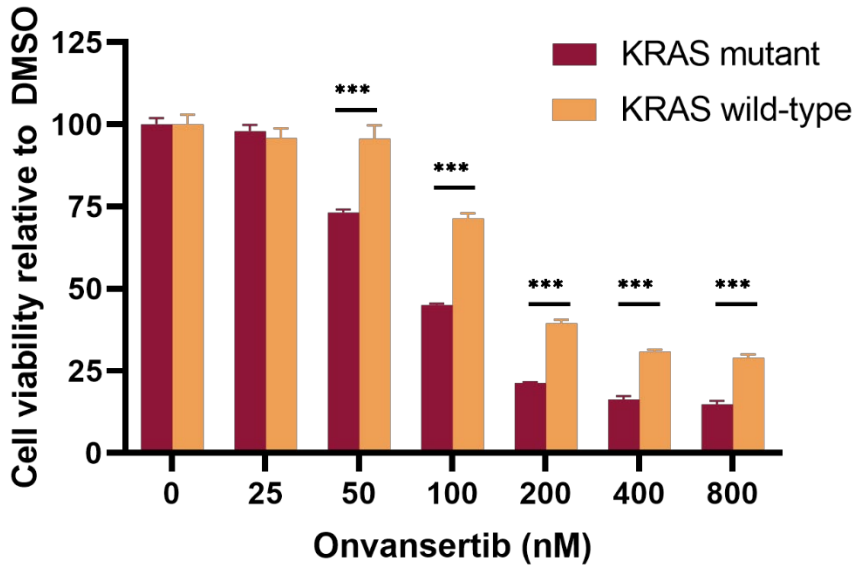
Synthetic Lethality: Cells with KRAS Mutations are Hypersensitive to Inhibition of PLK1

The output of the RAS-mutated pathway activates PLK1, which is inhibited by onvansertib

Onvansertib Addresses KRAS Mutation Subtypes in mCRC



Cell Viability in Onvansertib-Treated KRAS Mutant and Wild Type Isogenic CRC Cells



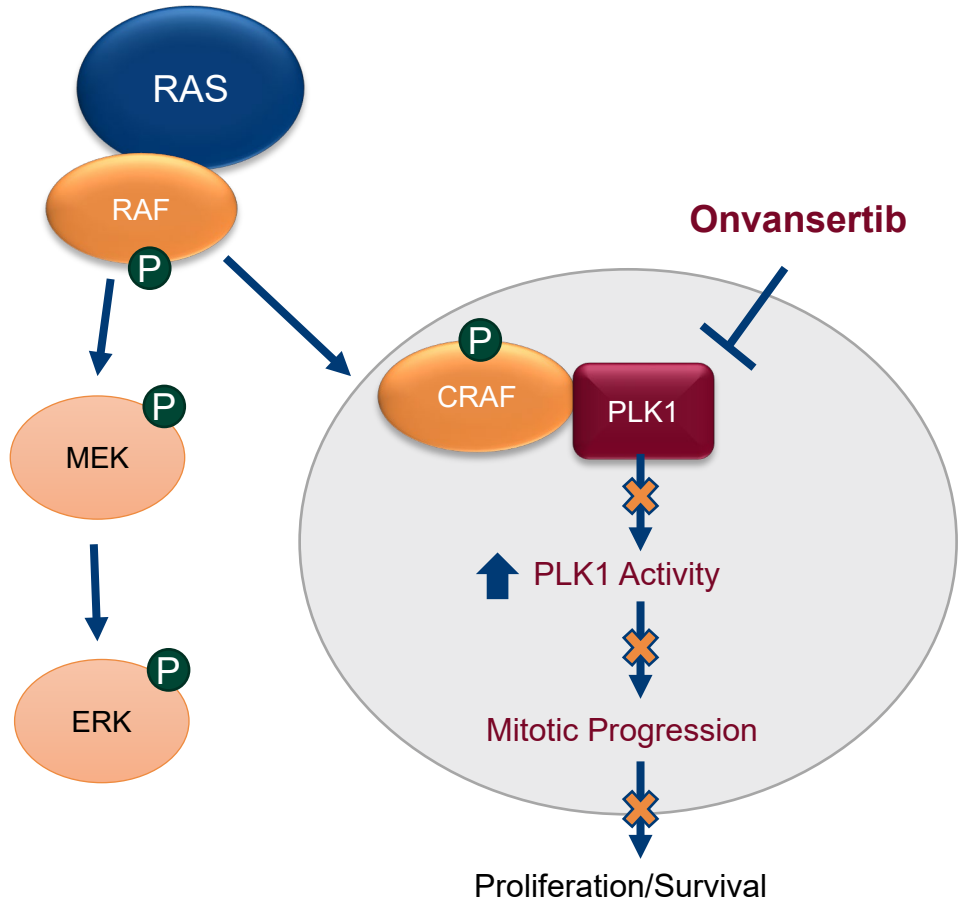
PLK1: Polo-like Kinase 1; mCRC: Metastatic colorectal cancer

PLK1 and RAS Cooperative Relationship

RAS activates PLK1 through a MEK/ERK-independent mechanism

The downstream target of KRAS, pCRAF, localizes to the mitotic spindle poles at mitosis where it interacts with PLK1 and promotes PLK1 activation, leading to mitosis and tumor progression[1]

Data suggest that KRAS-activated cells are dependent on PLK1 for their proliferation and survival and inhibition of PLK1 by onvansertib could inhibit tumor growth

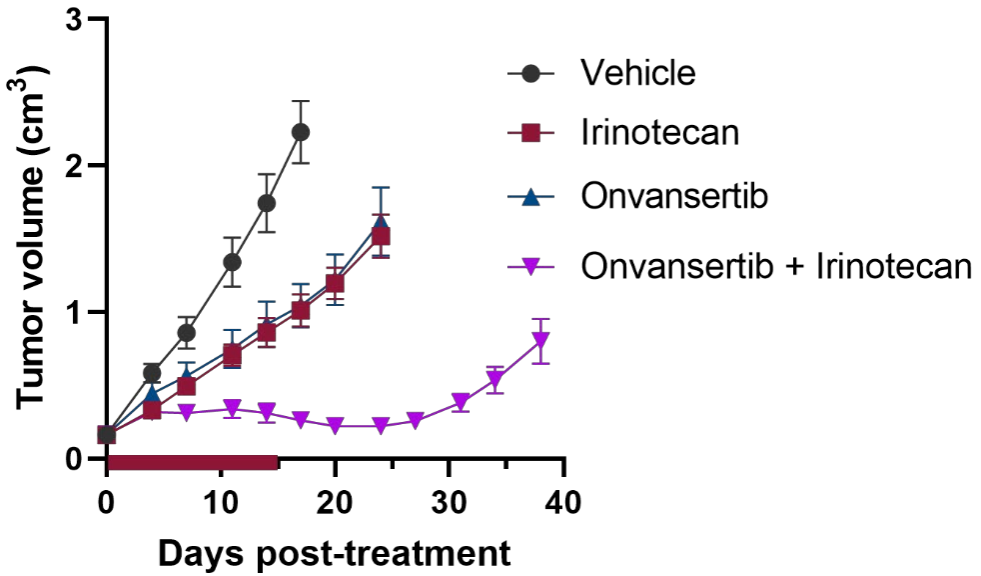


[1]Mielgo et al., Nat. Med. 2011; 17(12):1641-5

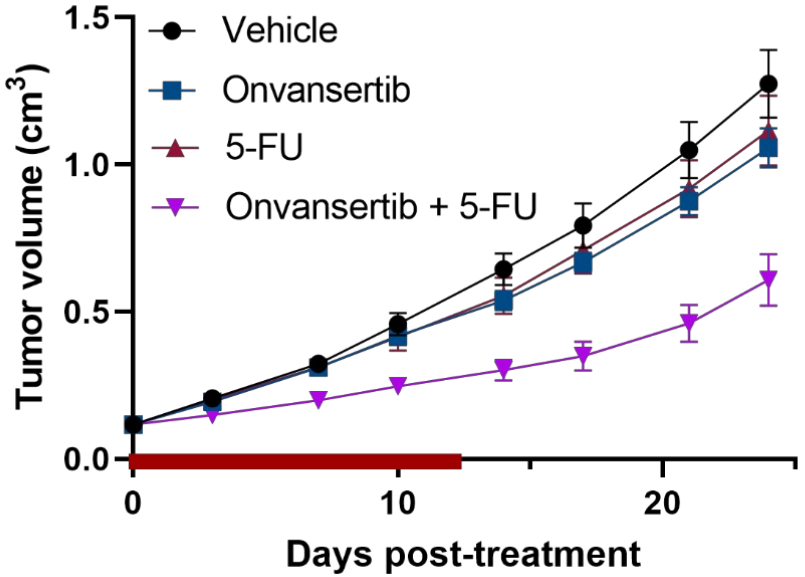
Synergy: Onvansertib in Combination with SOC Irinotecan and 5-FU

Onvansertib works synergistically in combination with standard-of-care FOLFIRI (irinotecan and 5-FU)
HCT-116 (with G13D KRAS mutation)

Synergy in Combination with Irinotecan

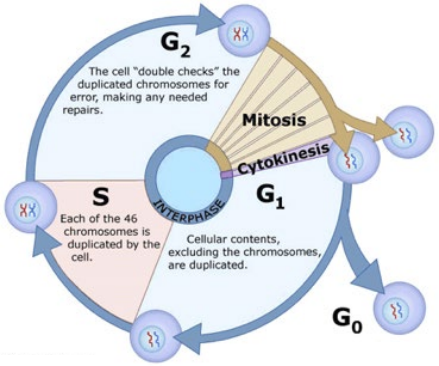


Synergy in Combination with 5-FU



PLK1 Regulates DNA Damage Response[1,2]

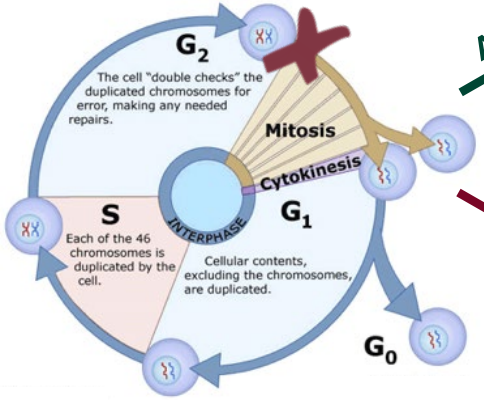
DNA Damaging Agents



- Irinotecan
- 5-FU

DNA Damage Response (DDR) arrests cells at G2/M checkpoint

G2/M Arrest



Active PLK1

PLK1 Inhibited

Mitosis

1. Checkpoint adaptation
2. PLK1 inhibits DDR, induces mitotic entry for tumor cells & cell division

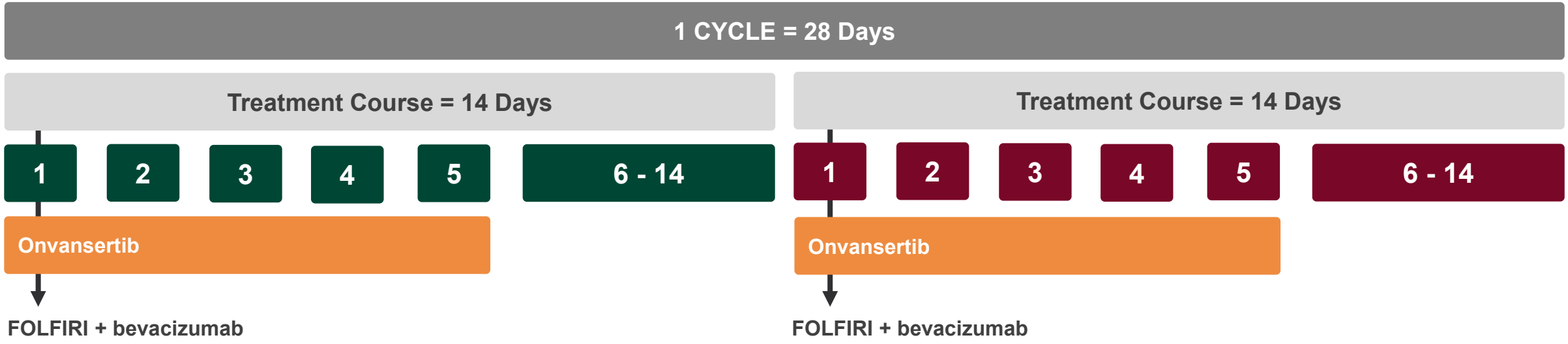
Cell Death

1. Keeps tumor cells in G2/M arrest leading to apoptosis
2. For cells that escape, mitosis is blocked, also leading to apoptosis

[1]van Vugt & Yaffe, Cell Cycle 2010 9:2097-2101; [2]van Vugt et al., 2010, PLoS 8:1-19

Phase 1b/2 Open Label Trial of Onvansertib + FOLFIRI/bevacizumab

Trial Design



Efficacy Endpoints

- Overall response in patients who receive ≥1 cycle (2 courses) of treatment
- Progression-free survival (PFS) and duration of response (DOR)
- Decreases in KRAS mutation burden and response to treatment

Clinically Meaningful Outcome

- ≥5 of 26 (~20%) patients achieve clinical response confirmed by radiographic scan (per protocol)
- Achieve median progression-free survival of ≥ 6 months

Phase 1b/2 Enrollment and Patient Baseline Characteristics

Enrollment (as of 04-Apr-2021)

Number of Patients (N)	Phase 1b Dose Level 0 Onvansertib 12 mg/m²	Phase 1b Dose Level +1 Onvansertib 15 mg/m²	Phase 1b Dose level +2 Onvansertib 18 mg/m²	Phase 2 RP2D Onvansertib 15 mg/m²
Treated	6	6	6	11
Completed Cycle 1	5	6	5	6
Currently on Treatment	0	3	2	11

Total Patients N=29	Median [range] or n (%)
Age (years)	56 [36-83]
Sex	
Male	16 (55%)
Female	13 (45%)
ECOG	
0	17 (59%)
1	11 (38%)
Primary tumor site	
Colon	13 (45%)
Rectum	10 (34%)
Unknown/Not provided	6 (21%)
Liver metastasis	
None	8 (28%)
Liver and other	14 (48%)
Liver only	5 (17%)
Number of metastatic organs	
1	10 (34%)
≥2	17 (59%)
Prior Bevacizumab treatment	
Yes	16 (55%)
No	8 (28%)

Phase 1b/2 Safety Assessment

Most Common Treatment-Emergent AEs (as of 04-Apr-2021)

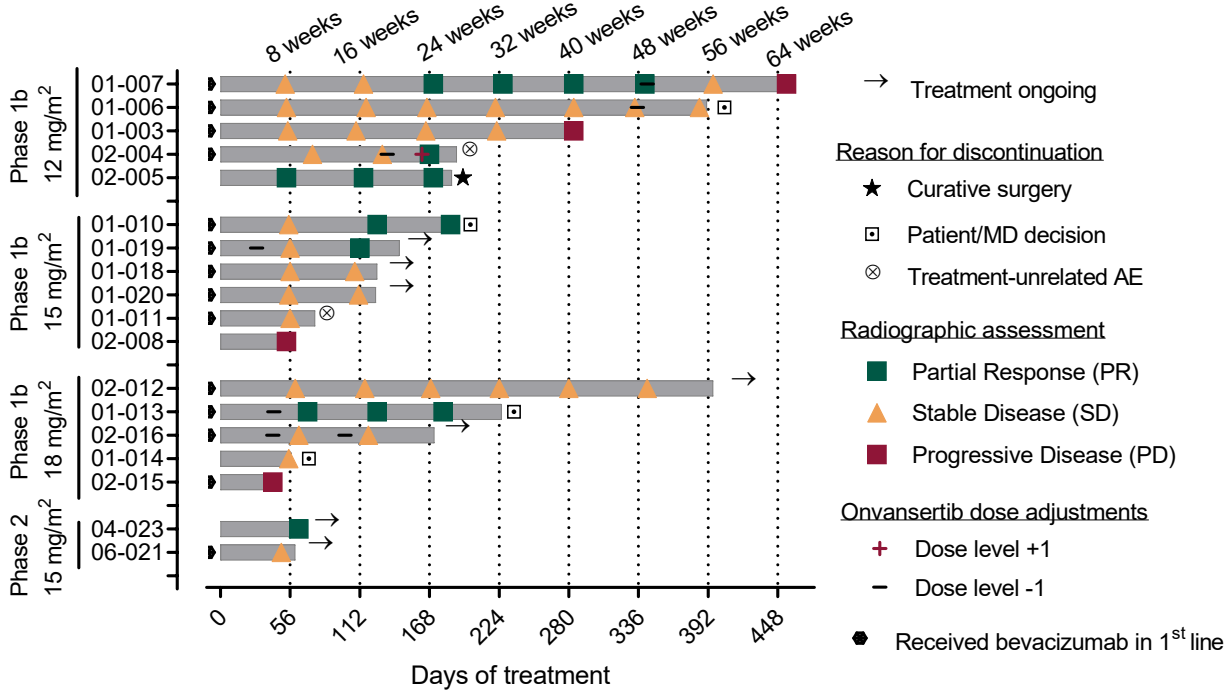
Adverse Events (AEs)	Grade 1	Grade 2	Grade 3	Grade 4	All Grades
Nausea	13	5	2	0	20
Fatigue	10	8	1	0	19
Neutropenia	3	4	5	4	16
Abdominal pain	8	5	1	0	14
Diarrhea	7	5	0	0	12
Alopecia	8	2	0	0	10
WBC Decreased	3	5	1	1	10
Vomiting	4	4	1	0	9
Anemia	6	2	0	0	8
Platelet count decreased	5	2	0	0	7
Stomatitis	5	1	0	0	6
Headache	5	0	0	0	5
Neuropathy	4	0	0	0	4
Epistaxis	4	0	0	0	4
ALT increase	3	0	1	0	4
Hypertension	1	1	1	0	3
Dehydration	0	2	1	0	3

- 5 patients had G4 adverse events:
  - G4 neutropenic fever (n=1); G4 neutropenia (n=4); Decreased WBC (n=1); Hyperphosphatemia (n=1) - also neutropenia and WBC deceased noted above
- Onvansertib RP2D was confirmed at 15 mg/m^2
- Combination regimen was well tolerated:
  - Of all AEs only 11.3% (28/247) were G3/G4
  - The only G3/G4 AE reported in ≥2 patients were neutropenia (n=8); which was managed by dose delay, growth factor and/or discontinuation of the 5-FU bolus; WBC decease (n=2); Nausea (n=2)
- 5-FU bolus was discontinued in 16 of 18 patients in Phase 1b due to hematological toxicities; which led to resolution of associated toxicities
- No major or unexpected toxicities were attributed to onvansertib

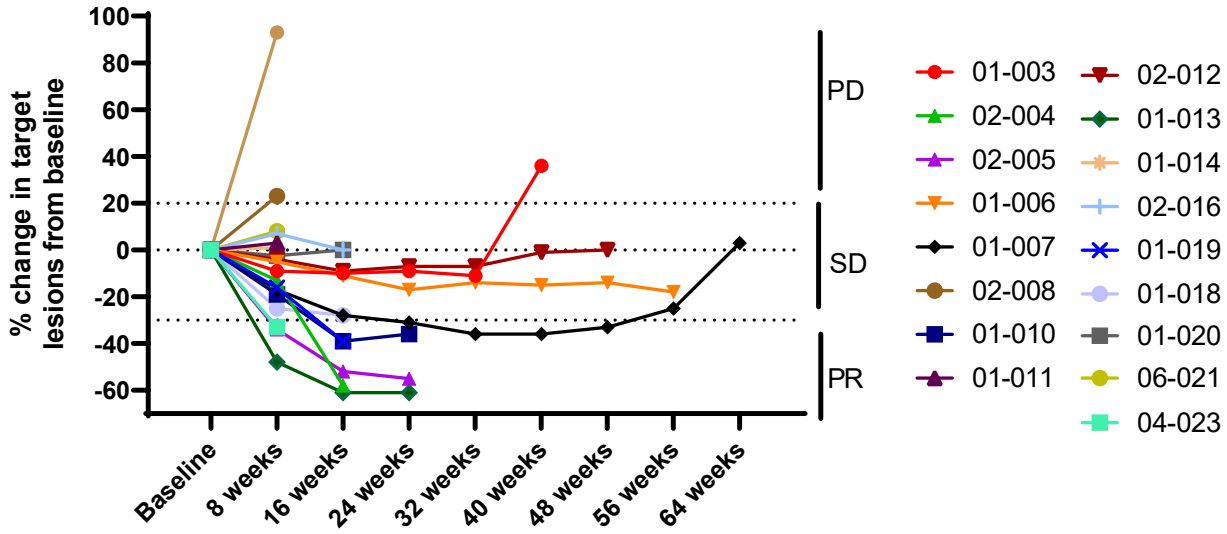
n=number of patients (total N=30); WBC=white blood cells; ALT= alanine aminotransferase

Phase 1b/2 Preliminary Efficacy Assessment (as of 04-Apr-2021)

Treatment Response and Duration



Changes in Tumor Size From Baseline



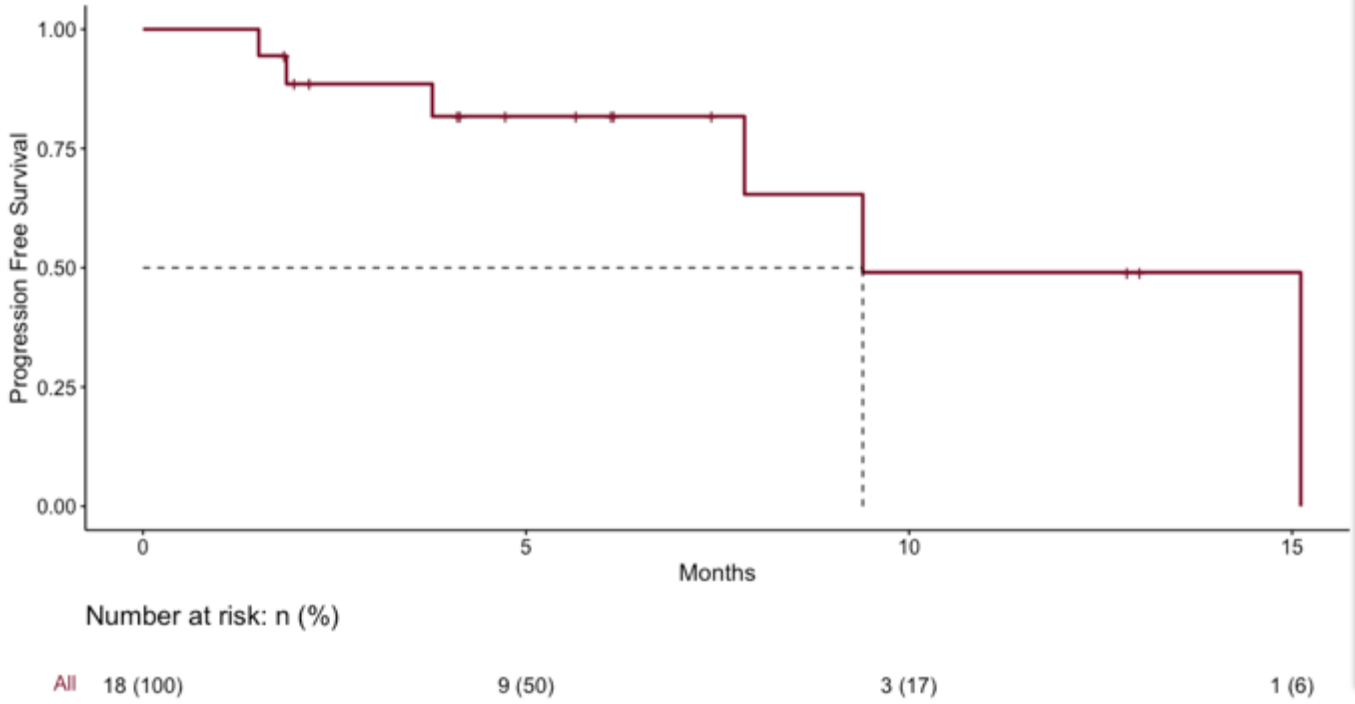
- Of the 18 patients evaluable for efficacy*, 7 (39%) achieved a partial response (PR) representing KRAS mutations G12D (n=2), G13D (n=1), G12V (n=1), G12A (n=2) and A146T (n=1)
  - 4 patients had a confirmed PR; 1 patient went on to have curative surgery
  - 1 patient (02-004) with non-confirmed PR went off study following PR due to treatment-unrelated AE
  - 2 patients (01-019; 04-023) with non-confirmed PR await results from next scans

*completed at least 1 cycle of treatment and had radiographic scan or progressed within 8 weeks while on treatment

Median Progression-free Survival (PFS)

Median Progression-Free Survival (mPFS)

Median PFS (95% CI) = 9.40 months (7.85, not reached)

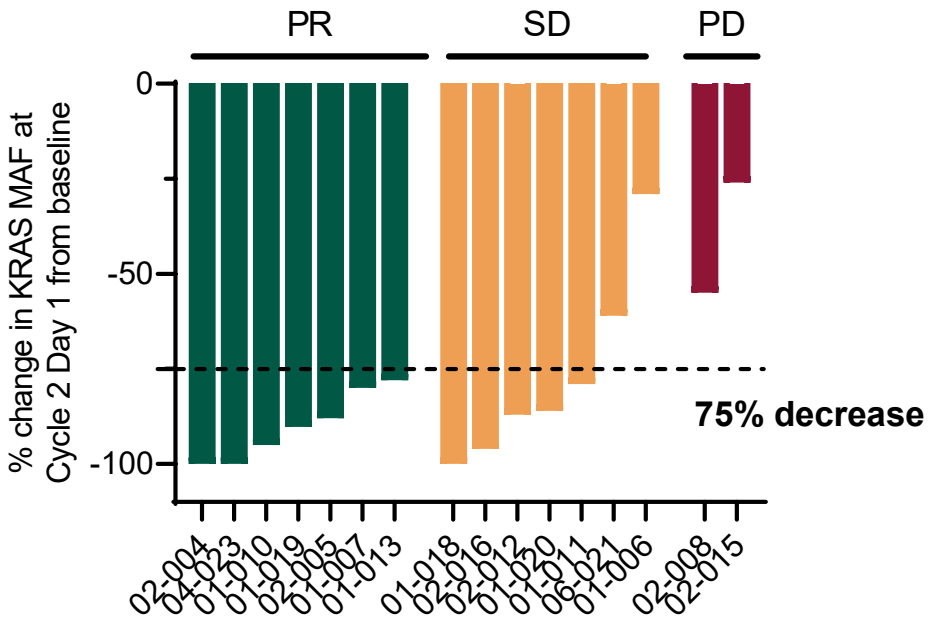


- mPFS for patients treated to-date with onvansertib + standard-of-care = 9.4 months
- Comparatively, mPFS = 4.5 months for standard-of-care benchmark second line treatment mCRC (from systematic literature-based analysis of 23 randomized trials - 10,800 patients)[1]
- Pivotal trial for FDA approval of FOLFIRI + Bev for second line mCRC[2]
  - Median PFS = 5.7 months (95% CI 5.2–6.2 months)
- mPFS is favorable compared to current standard-of-care

[1]Giessen et al, Acta Oncologica, 2015; 54:187-193; [2]Bennouna et al., Lancet Oncol. 2013; 14(1):29-37

KRAS Mutant Allelic Frequency (MAF) Biomarker Analyses

% KRAS MAF Decrease Following 1 Cycle of Treatment



- KRAS MAF was measured by digital droplet PCR (ddPCR) at baseline (Cycle 1 Day 1, pre-dose) and on-treatment (Day 1 of Cycles 2 to 9)
- 16 of 18 patients had a KRAS mutation detected by ddPCR at baseline (all had a KRAS mutation detected by NGS)
- Clinical responses were observed across patients with different KRAS mutations, including the 3 most prevalent in CRC (G12D, G12V, G13D)
- The greatest decreases in KRAS MAF after 1 cycle of treatment were observed in patients achieving a PR
  - All 7 patients with a PR had >75% decrease
  - 5 of the 7 patients with SD had reductions >75%
  - the 2 patients who progressed showed a more modest decrease in KRAS MAF (-55% and -26%)

PR: partial response, SD: stable disease, PD: progressive disease

Conclusions

- **Safety Assessment:**
  - The combination of onvansertib and FOLFIRI/bev is well-tolerated
  - In patients experiencing hematologic toxicities, eliminating the 5-FU bolus from the regimen led to resolution of associated AEs
  - Onvansertib MTD was established at 15 mg/m^2
- **Preliminary Efficacy:**
  - 7 (39%) of the 18 evaluable patients achieved a partial response (PR), including 4 confirmed PRs and 2 patients with upcoming confirmatory scans
  - 1 patient proceeded to curative surgery
  - Median PFS is 9.4 months, which is approximately two-fold greater than current SOC mPFS of 4.5 – 5.7 months
  - 7 of the 18 patients remain on treatment to-date
- **KRAS Mutant Allelic Frequency (MAF) Biomarker:**
  - Clinical responses were observed across different KRAS variants, including the 3 most common in CRC
  - Patients achieving a PR or SD showed the greatest decreases in plasma mutant KRAS after the first cycle of therapy

Patient Case Report

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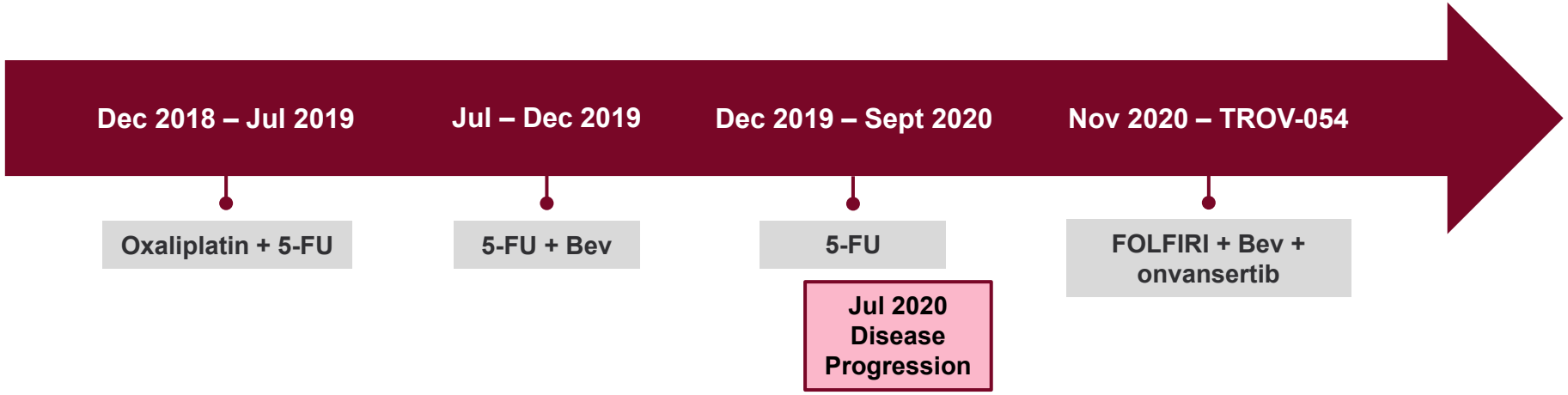
Case Report – Patient 01-019 **Background**

Patient Overview

- 83-year-old woman with KRAS G12D metastatic colon cancer

Treatment History



Additional Details

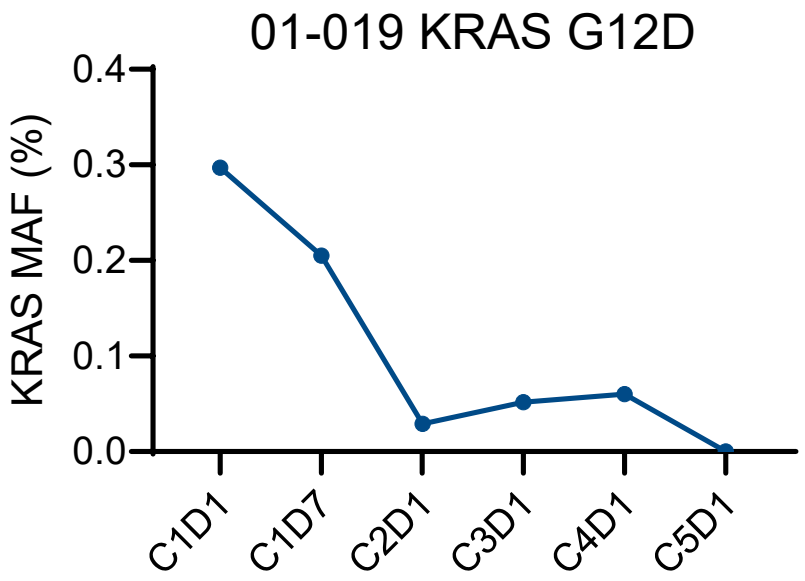
- *C1D15* – G4 neutropenia (DLT); treatment was held
- *C2D1* – 5-FU bolus eliminated
- *C3D1* – G3 neutropenia; treatment was held
- *C3D15* – Dose reduction (-1) for irinotecan and 5-FU

Case Report – Patient 01-019 **Response**

Summary

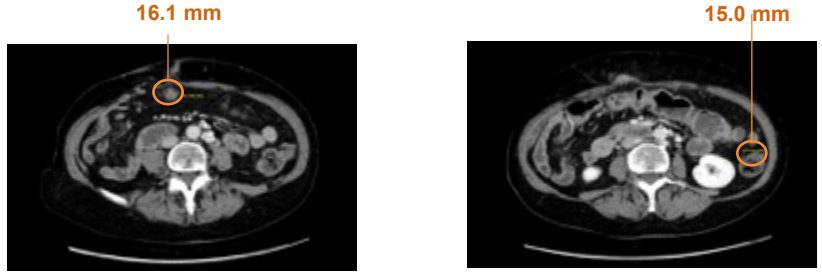
- *January 2021 (8-week scan):* stable disease (-16%) with decrease in size of metastatic lesions
- *March 2021 (16-week scan): partial response (-39%)* with further decrease in size of metastatic lesions

Changes in MAF

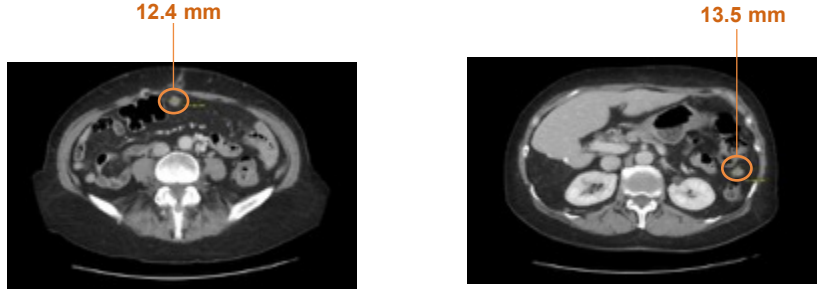


KRAS mutant allelic frequency decreased to non-detectable at C5D1 – March 5, 2021

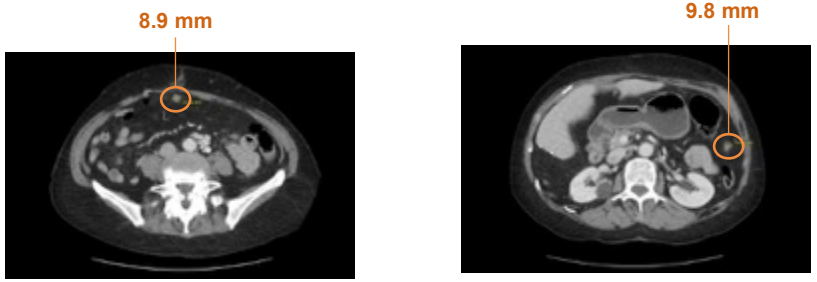
Baseline Scan
05-Nov-2020



8-week Scan
08-Jan-2021
-16% stable disease (SD)



16-week Scan
04-Mar-21
-39% partial response (PR)



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Expanded Access Program (EAP) of Onvansertib in Combination with FOLFIRI/Bevacizumab for Treatment of Patients with KRAS-mutated Metastatic Colorectal Cancer

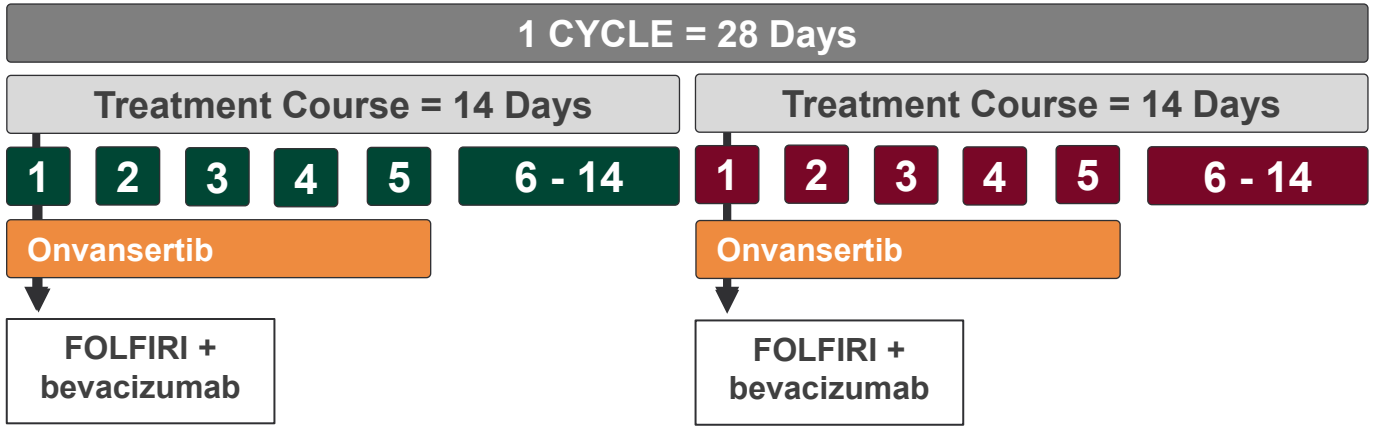
Effective Treatment Options for Heavily Pre-Treated Patients are Needed

- Third- or later-lines of treatment have poor outcomes:
  - Approved therapies for KRAS mutant patients are Stivarga® (regorafenib) and Lonsurf® [trifluridine/tipiracil (TAS-102)]
- These agents have a median progression-free survival (PFS) of 2-3 months and median overall survival of 6-9 months[1]
- Although most patients had previously received FOLFIRI; the Expanded Access Program provided the opportunity to evaluate the potential clinical benefit with the addition of onvansertib to FOLFIRI/bev regimen

EAP Provides Access to Onvansertib in Combination with FOLFIRI/bevacizumab for Patients with KRAS-mutant mCRC

Eligibility:

- Metastatic and unresectable CRC with a confirmed KRAS mutation
- Participants have failed or progressed on multiple lines of standard-of-care systemic therapy, including prior FOLFIRI
- Participants are not eligible for ongoing Phase 1b/2 clinical trial



Treatment:

- Participants receive onvansertib (15 mg/m^2) + FOLFIRI + Bevacizumab
- Option to eliminate 5-FU bolus

Aims:

- Primary: evaluate safety of the combination
- Exploratory: progression-free survival (PFS); changes in plasma KRAS mutant allelic frequency (MAF)

Enrollment as of 12-Apr-21:

# of Participants Treated	45
# Reaching First On-Treatment CT Scan and with Results Provided (11 of 20 remain on treatment)	20
# Discontinuing Prior to First CT Scan	2

Safety and Clinical Benefit Assessed in EAP Participants

Safety:

- Onvansertib in combination with FOLFIRI + Bevacizumab has been well-tolerated with no serious adverse events (SAEs) reported to-date in any of the treated participants (N=43)

Clinical Benefit:

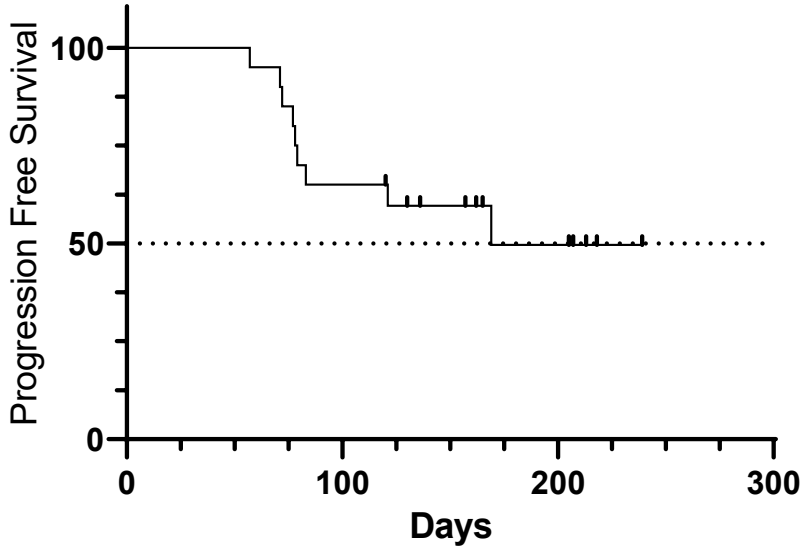
- 20 participants were evaluated for clinical benefit*
  - Participants had median number of 3 prior lines of treatment
  - 65% were progressing prior to enrolling in EAP

Baseline Characteristics (n=20)	Median [range] or N (%)
Participant age	50 [35-74]
Prior lines of therapy	3 [1-6]
Participants who received irinotecan-based regimen as last therapy	15 (75%)
Participants progressing prior to EAP	13 (65%)

*Participants who had at least one on-treatment CT scan and results were provided

- Participants had a median PFS on EAP of 5.6 months (95% CI: 2.7 – not-reached) and 11 of 20 remain on treatment to-date

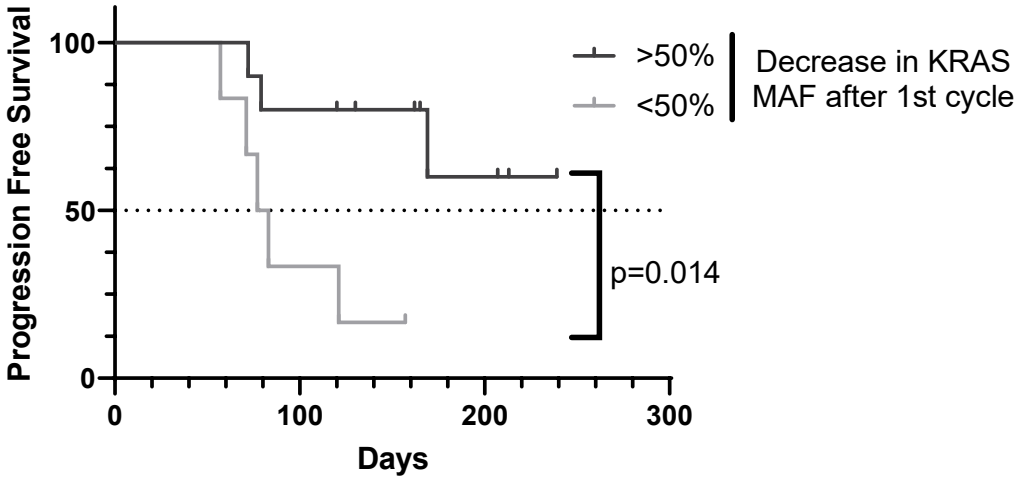
PFS of participants evaluable for clinical benefit*



Changes in Plasma KRAS-mutant Stratify Participant Outcomes

- KRAS mutant allelic frequency (MAF) was measured by digital droplet PCR (ddPCR) at baseline and end of Cycle 1 in all participants evaluable for clinical benefit*
- 16 of 20 participants had a KRAS variant detected by ddPCR at baseline
- Participants with greater than 50% decrease in KRAS MAF (n=10) had a significant increase in PFS compared with participants who had less than 50% decrease (n=6), supporting that early changes in KRAS MAF are predictive of clinical benefit

PFS of participants with detectable plasma KRAS mutant at baseline



Decrease in KRAS MAF	Median PFS (95% CI)
≥50%	Not-reached [NR] (5.5 – NR)
<50%	2.6 months (2.3 – NR)

*Participants who had at least one on-treatment CT scan and results were provided

Patient Case Report

Cardiff Oncology™

Participant Case Report

Participant 101-032: 61-year-old female with KRAS G12V metastatic sigmoid colon cancer

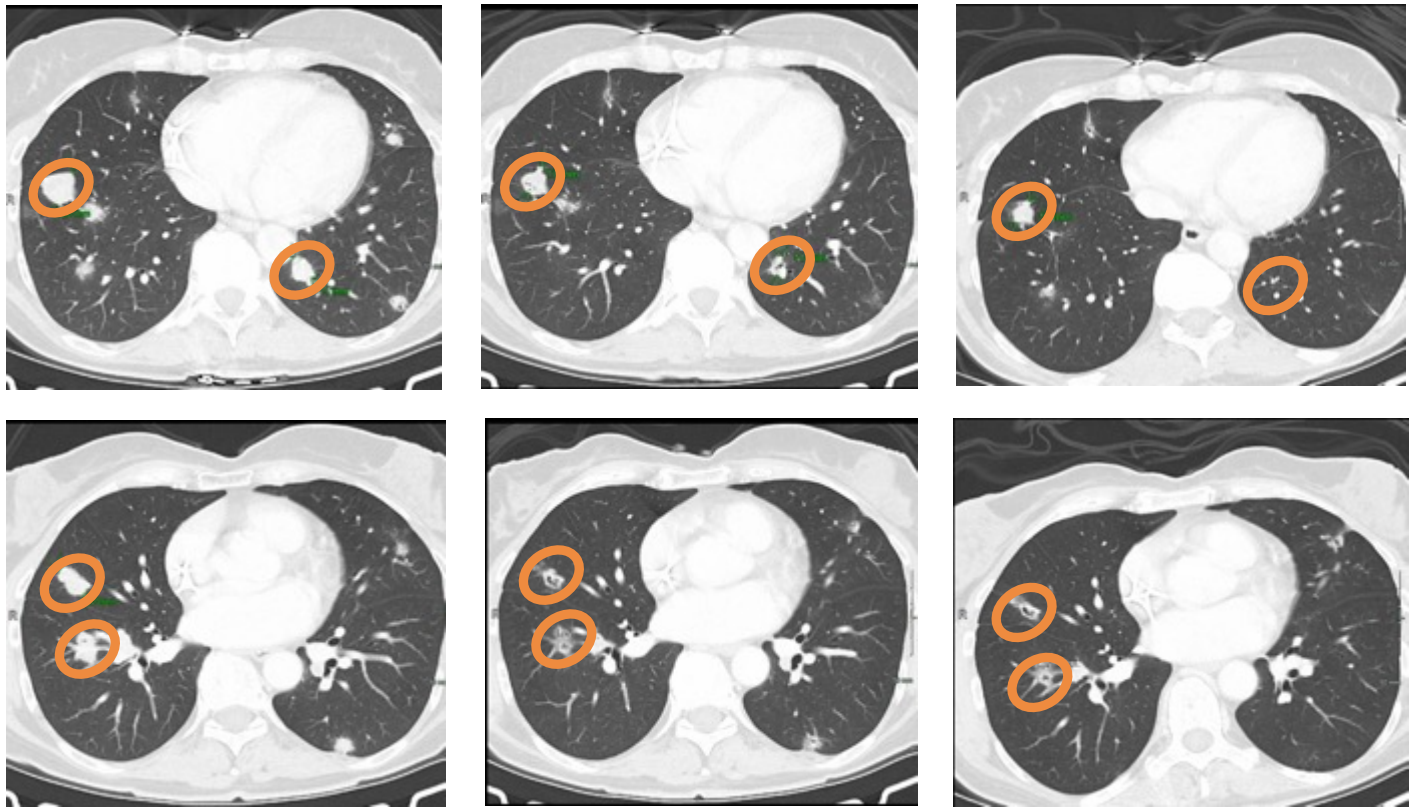
- Participant received several prior lines of treatment including FOLFIRI + Bev
- Oct 2020 – progressed on investigational drug and had increase in size of lung metastases
- Nov 2020 – enrolled in EAP and received onvansertib 15 mg/m^2 + FOLFIRI + Bevacizumab

Clinical Benefit Demonstrated

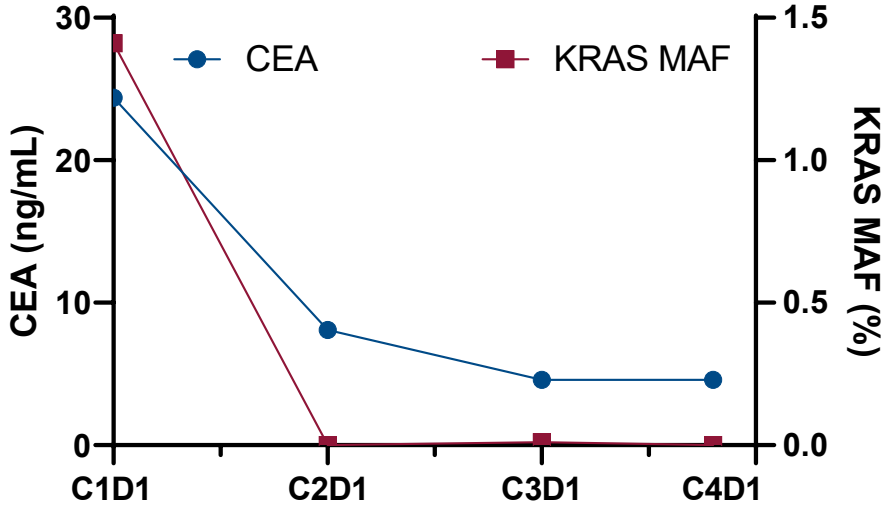
Clinical Benefit / Response to Onvansertib + FOLFIRI + Bev Combination

- 8-week CT scan: decrease in size of numerous lung metastases; many appearing necrotic
- 16-week CT scan: further decrease in size of lung metastases; many continuing to appear necrotic

Baseline CT | **8-week CT** | **16-week CT**



Decreases in tumor lesions were accompanied by a decrease in KRAS MAF from 1.4% to 0% (undetectable) and a decrease in CEA from 24.4 to 4.6 ng/mL



Summary

- Treatment with onvansertib + FOLFIRI + Bevacizumab in the EAP has been well tolerated with no SAEs reported to-date

- At the AACR cutoff date of March 10, 2021, 20 participants with a median of 3 or more prior therapies, were evaluated for clinical benefit
  - Median progression-free survival (PFS) is 5.6 months, and 11 of 20 participants remain on treatment to-date (representing a significant contrast vs historical control of 2-3 months[1])

- Changes in plasma KRAS-mutant allelic frequency (MAF) correlates with clinical benefit
  - Participants with a greater than 50% decrease in KRAS MAF had a significant increase in PFS (PFS not-reached) compared with those who had a decrease of less than 50% (PFS of 2.6 months)

Second-Line Treatment of Metastatic PDAC

Phase 2 open label trial of onvansertib + nanoliposomal irinotecan, 5-FU and leucovorin

Trial Sites: Mayo Clinics (Arizona, Minnesota, Florida), Emory University, Kansas University Medical Center and Inova Schar Cancer Institute

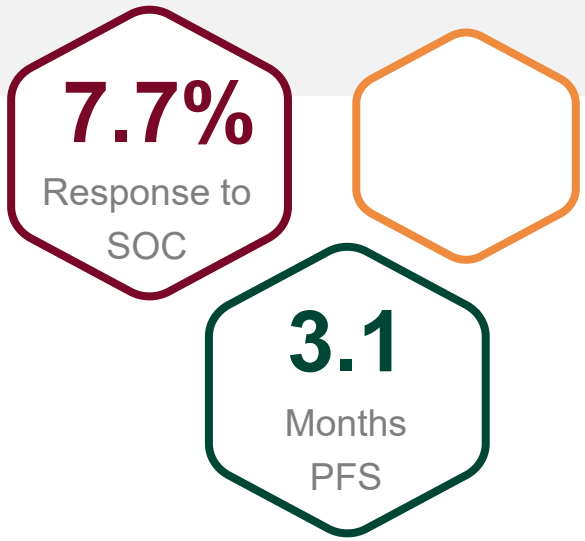
Principal Investigator: Dr. Daniel H. Ahn

New Second-Line Therapies are Needed for Metastatic Pancreatic Ductal Adenocarcinoma (PDAC) Patients

Second-line treatment with SOC irinotecan + 5-FU/leucovorin has a response rate of **only 7.7%**[1]

Second-line treatment with SOC irinotecan + 5-FU/leucovorin offers a mOS benefit of **only 6.1 months**[2]

- **Mutant KRAS** contributes to treatment resistance and metastases and is essential for PDAC growth[3]



- Leveraging the synergy between onvansertib and irinotecan + 5-FU

- The promising response rates and impressive durability seen in KRAS-mutated mCRC with the combination of onvansertib + irinotecan + 5-FU, support onvansertib's potential in PDAC, where ~95% of patients have a KRAS mutation

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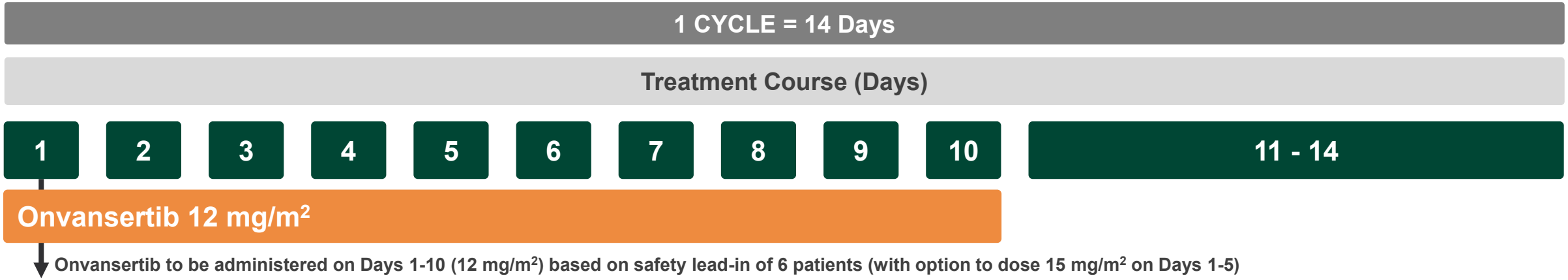
[1]Onyvide Package Insert: https://www.accessdata.fda.gov/drugsatfda_docs/label/2015/207793lbl.pdf; [2]Wang-Gillam A, Li C-P, Bodoky G, et al. Lancet 2016;387:545-57. [3]Waters AM, Der CJ. Cold Spring Harb Perspect Med 2018;8(9). SOC: Standard-of-care; PFS: Progression free survival

Phase 2 Open Label Trial of Onvansertib + Nanoliposomal Irinotecan + 5-FU in Metastatic PDAC



Eligibility Criteria

- Prior abraxane/gemcitabine and no prior irinotecan, nanoliposomal irinotecan or investigational PLK1 inhibitor

Primary Efficacy Endpoint

- Overall response rate (ORR)

Clinically Meaningful Outcome

- 8 of 39 (≥20%) patients achieve ORR

Trial Design (~45 patients):

Metastatic Castration-Resistant Prostate Cancer

Phase 2 open-label trial of onvansertib + abiraterone

Trial Sites: Beth Israel Deaconess, Dana Farber, Mass General Hospital

Principal Investigator: Dr. David Einstein

New Therapeutic Options are Needed to Overcome Resistance to SOC Androgen Receptor Signaling Inhibitors (ARSi)

Resistance develops to treatment with standard of care ARSi's within 9-15 months[1]

ARSi's offer a median overall survival (mOS) benefit of **only ~4 months**[1]

No effective treatment options are available for the up to 40% of mCRPC patients with an AR-V7 mutation[2]

9-15
Months until ARSi resistance

~4
Month mOS benefit

Limited options for patients once resistant to abiraterone

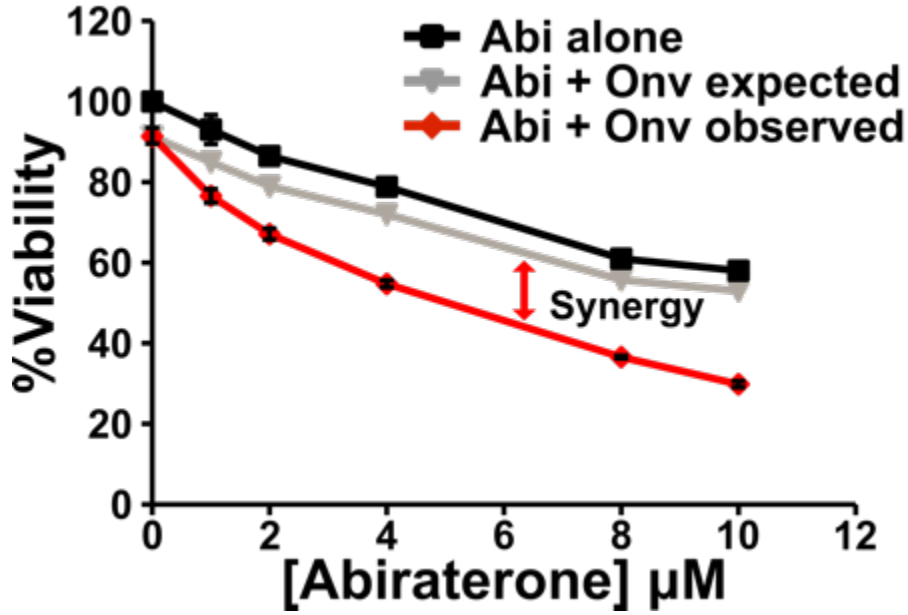
New treatment options are needed to extend the duration of response to ARSi's and increase overall survival

[1]Antonarakis, Emmannel – Current Understanding of Resistance to Abiraterone and Enzalutamide in Advanced Prostate Cancer; Clinical Advances in Hematology & Oncology – May 2016 – Volume 14, Issue 5; [2]Armstrong et al., 2019, JCO 37: 1120-1129; SOC: Standard-of-care; mCRPC: Metastatic castration resistant prostate cancer

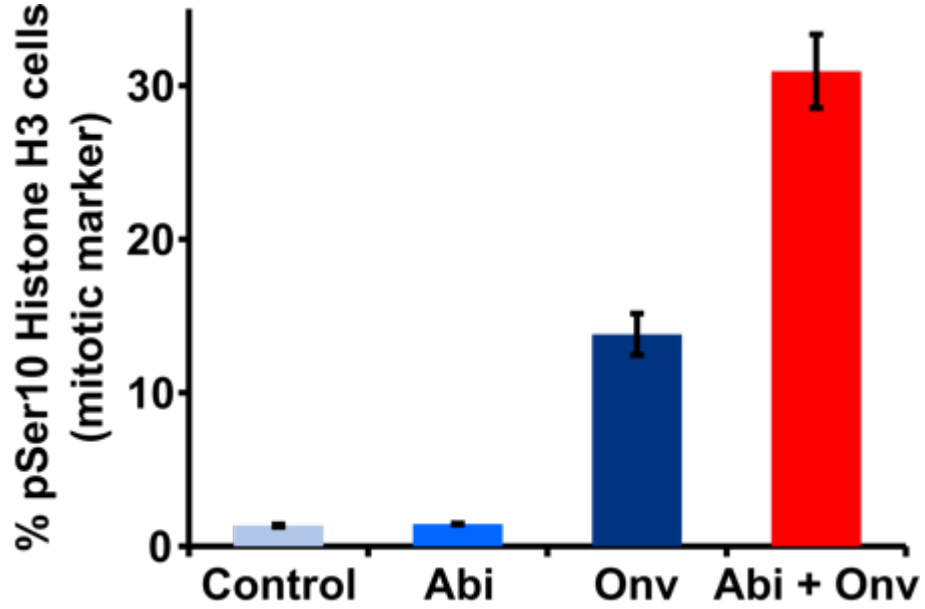
Onvansertib Extends the Response to Androgen Receptor Signaling Inhibitors

Onvansertib works synergistically in combination with abiraterone (Zytiga®) and significantly increases mitotic arrest

Onvansertib + Abiraterone (Zytiga®) Demonstrate Synergy in mCRPC model (C4-2)[1]



Onvansertib + Abiraterone (Zytiga®) Significantly Increase Mitotic Arrest[1]

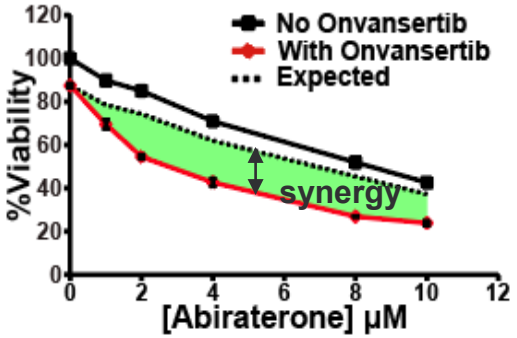


[1]Patterson & Yaffe, 2019, MIT; mCRPC: Metastatic castration resistant prostate cancer

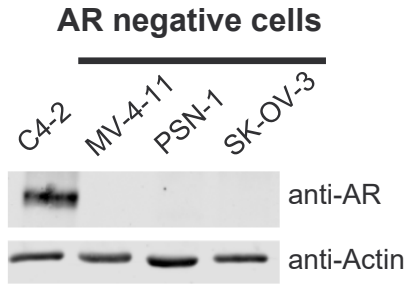
Clinical Trial Background and Rationale

- PLK1 - a promising target for prostate cancer:
  - PLK1 is overexpressed in prostate cancer and linked to higher tumor grades[1]
  - PLK1 inhibition and abiraterone demonstrated synergy in CRPC in vitro and in vivo models: the combination induced increased mitotic arrest and apoptosis in comparison with single agents
- Onvansertib synergizes with abiraterone through an AR-independent pathway
  - Onvansertib synergizes with abiraterone, but not with the AR antagonist enzalutamide
  - Onvansertib synergizes with abiraterone in AR-negative non-prostate models
  - Ongoing preclinical studies suggest that abiraterone sensitizes cells to onvansertib through regulation of mitotic processes

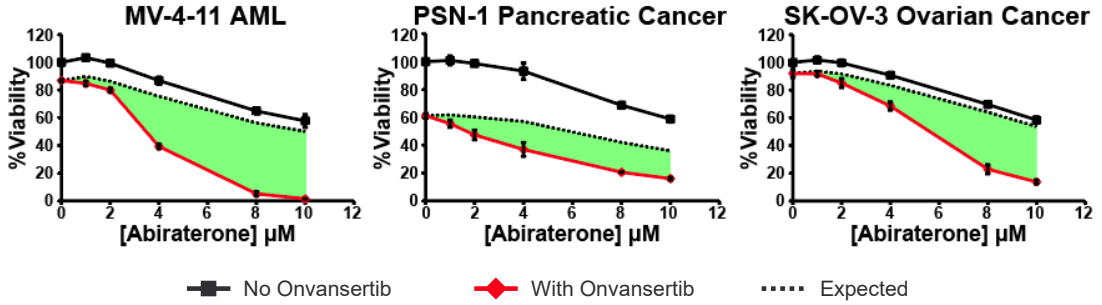
Synergy In Vitro in C4-2 Cells



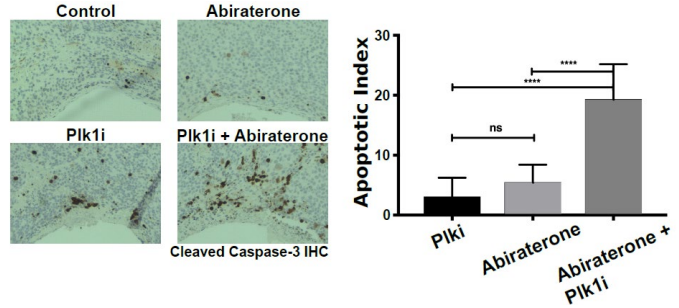
AR Expression



Synergy In Vitro in AR Negative Models



Synergy In Vivo in C4-2 Xenograft Model



[1]Weichert et al., Prostate 2004;60(3):240-5

Phase 2 Trial Design, Objectives and Enrollment (NCT03414034)

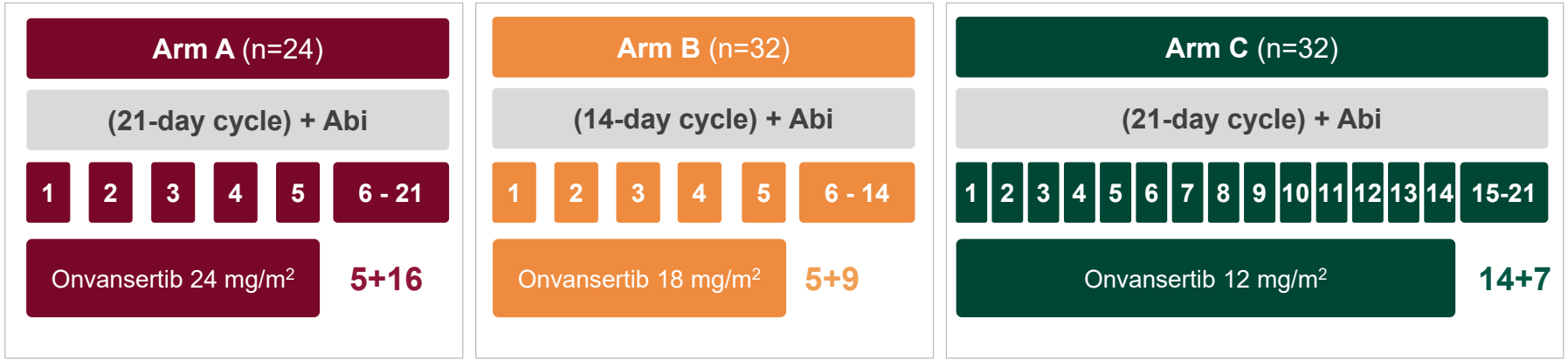
Key Eligibility Criteria:

- Initial signs of abiraterone resistance defined as 2 rising PSAs; one rise of ≥0.3 ng/mL separated by one week

Key Exclusion Criteria:

- Prior treatment with either enzalutamide or apalutamide
- Rapidly progressing disease or significant symptoms related to disease progression

Treatment Schedules for Each Study Arm



Enrollment as of January 11th, 2021

Number of patients (N)	Arm A (5+16)	Arm B (5+9)	Arm C (14+7)
Treated	24	17	10
Completing 12-weeks	14	8	6
Currently on Treatment	0	4	7

Efficacy Endpoints

- Primary: Disease control evaluated as PSA decline or stabilization (PSA rise <25% over baseline) after 12 weeks of treatment
- Secondary: Radiographic response per RECIST v1.1 criteria, time to PSA progression, and time to radiographic response

Correlative Studies

- Analysis of circulating tumor cells (CTC), archival tissue, and circulating tumor DNA (ctDNA) to identify response biomarkers

Baseline Characteristics and Safety

Baseline Characteristics

Total patients N=51	Median [range] or n (%)
Age, years	72 [51-87]
Nonwhite ethnicity	7 (14%)
ECOG	
0	43 (84%)
1	7 (14%)
Years since diagnosis	4 [1-28]
Grade groups 4 and 5	29 (57%)
De novo metastatic disease	19 (37%)
Presence of bone metastasis	42 (82%)
Presence of visceral metastasis	18 (35%)
Baseline PSA, ng/mL	11.4 [0.6-515]
AR-V7+ at baseline*	10 (20%)
Baseline CTC/7.5 mL of blood**	15.8 [0-653]

*AR-V7 status was evaluated using the EPIC and Johns Hopkins University testing platforms **CTC count was performed by EPIC

Safety Assessment

- Most frequent Grade 3 and 4 adverse events (AEs) were expected, on-target, reversible hematological (anemia, neutropenia, thrombocytopenia and WBC decrease), associated with the mechanism of action of onvansertib
- Hematological AEs were reversible and effectively managed by dose delay, dose reduction and/or growth factor support

Most Common Treatment-Emergent Adverse Events in Treated Patients (≥10% of patients)

Adverse Events	Grade 1	Grade 2	Grade 3	Grade 4	All Grades
Anemia	10 (20%)	6 (12%)	1 (2%)		17 (33%)
Fatigue	10 (20%)	3 (6%)			13 (25%)
Thrombocytopenia	11 (22%)	1 (2%)			13 (25%)
Neutropenia	1 (2%)	1 (2%)	7 (14%)		12 (24%)
Hypophosphatemia	3 (6%)	3 (6%)	4 (8%)		10 (20%)
WBC decrease	3 (6%)	2 (4%)	3 (6%)	2 (4%)	10 (20%)
Back pain	4 (8%)	3 (6%)			7 (14%)
Hypokalemia	3 (6%)	1 (2%)	1 (2%)		5 (10%)

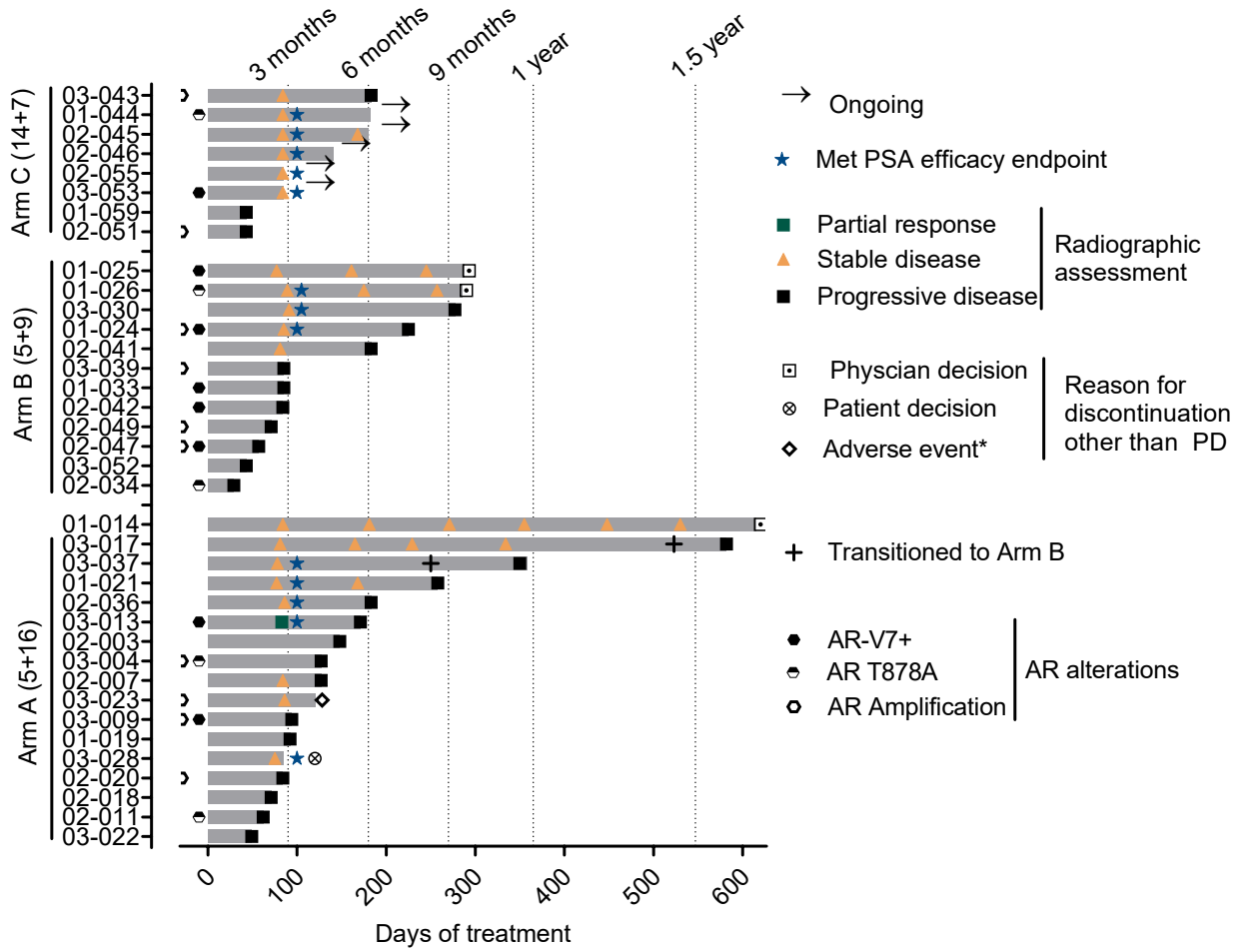
n= number of patients (total N=51)

Efficacy Assessment

	Arm A (5+16)	Arm B (5+9)	Arm C (14+7)
Evaluable for efficacy*	17	12	8
Completed at least 12 weeks of treatment	14	8	6
Had radiographic or clinical progression within 12 weeks	3	4	2
Disease control at 12 weeks**	5 (29%)	3 (25%)	**5 (63%)**
Radiographic stable disease at 12 weeks	9 (53%)	5 (42%)	**6 (75%)**
Durable response (≥6 months)	5 (29%)	5 (42%)	3 (37%)

* Completed at least 12 weeks of treatment or had radiographic/clinical progression within 12 weeks
** Defined as PSA stabilization or decline (PSA rise <25% over baseline)

- Nineteen (53%) patients had at least 1 AR alteration associated with abiraterone-resistance (AR-V7 expression, AR mutation T878A and/or amplification of AR)[1]:
  - 5 (26%) patients had disease control at 12 weeks
  - 8 (42%) patients had radiographic stable disease at 12 weeks



[1]Watson et al., Nat Rev Cancer, 15(12):701-711, 2015

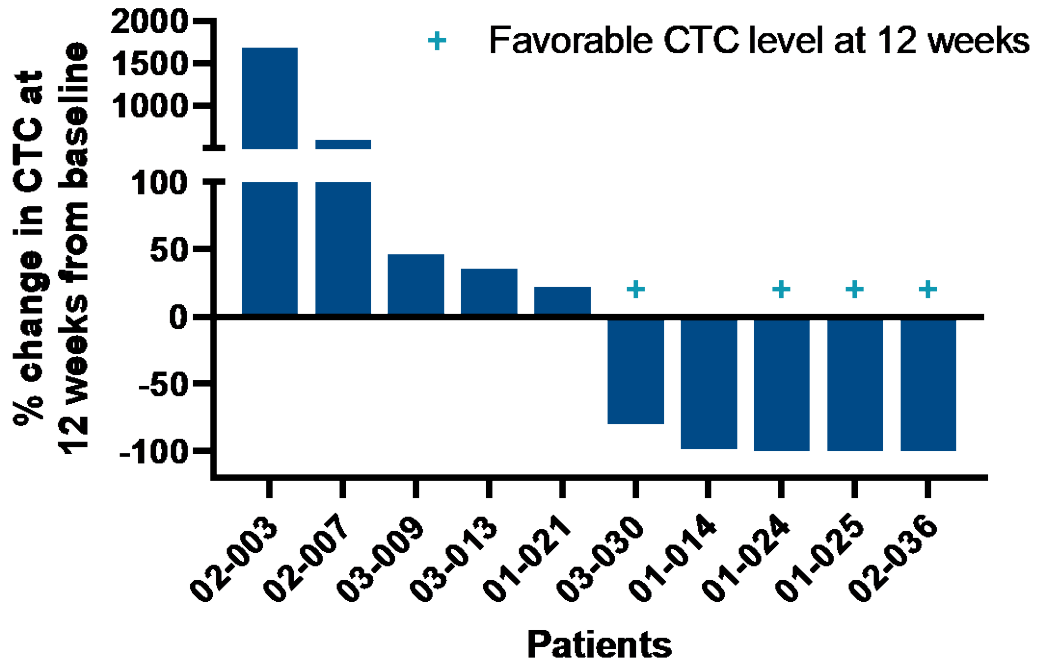
Onvansertib-Induced Circulating Tumor Cell Decrease is Associated with Progression-Free Survival

Circulating tumor cell (CTC) count, reported as favorable or unfavorable (<5 versus ≥5 CTC/7.5mL of blood, respectively) is a prognostic factor for survival in CRPC – conversion from unfavorable to favorable is associated with improved survival[1]

10 patients with unfavorable CTC at baseline were re-analyzed after 12 weeks of treatment:

- 5 (50%) patients had an ≥80% CTC decrease, including 2 AR-V7+ patients (01-024 and 01-025)
- 4 (40%) patients converted from unfavorable to favorable CTC level, including 3 patients with no detectable CTC
- Median time on treatment was 9.2 months for patients with CTC decrease (n=5) vs 4.9 months for patients with CTC increase (n=5)

Percent Change in CTC: 12-Weeks vs Baseline in Patients with Unfavorable CTC Level at Baseline



[1]Pantel et al., Clin Chem, 65(1):87-99, 2019 ; CRPC: Castration resistant prostate cancer

Biomarker Analyses

ctDNA Genomic Profiling

Mutation profiling of circulating tumor DNA (ctDNA) isolated from baseline liquid biopsy was performed using Guardant platform

33 Patients Analyzed

A total of 379 somatic variants were identified in 154 genes, with a median number of variants of 9 [1-54] per patient

- A gene list enrichment analysis tool (Enrichr) was used to compare lists of genes exclusively mutated in either SD or PD patients with the hallmark gene sets from the Molecular Signatures Database (MSigDB)[1-3]
- Analysis showed enrichment for G2/M checkpoint, E2F target and DNA repair in SD, but not PD patients, consistent with the role of PLK1 in cell cycle regulation and DNA damage response pathways
- Based on these data, we hypothesize that a subset of patients with early resistance to abiraterone may be more dependent on PLK1-related pathways and consequently more vulnerable to PLK1 inhibition

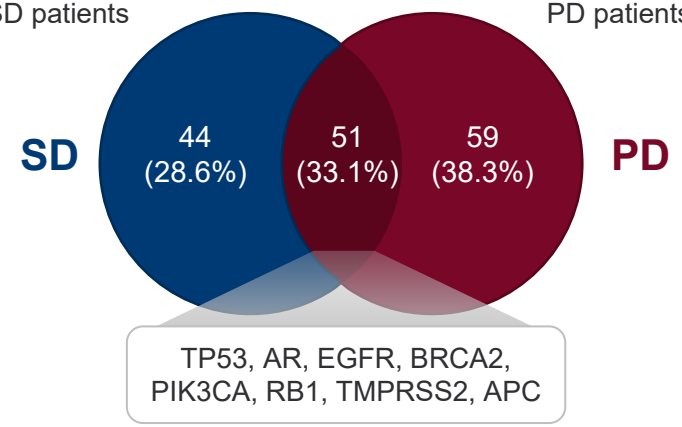
Analysis of Genes Differentially Mutated in SD and PD Patients

18 patients had SD at 12 weeks

44 genes were exclusively mutated in SD patients

15 patients had PD at or before 12 weeks

59 genes were exclusively mutated in PD patients



Pathways enriched in SD patients
Wnt-beta Catenin Signaling
PI3K/AKT/mTOR Signaling
G2-M Checkpoint
E2F Targets
IL-2/STAT5 Signaling
KRAS Signaling Up
IL-6/JAK/STAT3 Signaling
UV Response
DNA Repair
Apoptosis

P-values < 0.05

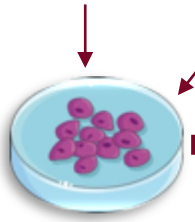
Pathways enriched in PD patients
UV Response
Wnt-beta Catenin Signaling
KRAS Signaling Up
Apoptosis
Myogenesis
PI3K/AKT/mTOR Signaling
Notch Signaling
TNF-alpha Signaling via NF-kB
Apical Junction
IL-6/JAK/STAT3 Signaling

P-values < 0.03

[1]Chen et al. BMC Bioinformatics 2013:128(4); [2]Kuleshov et al., NAR 2016:qkw377; [3]Liberzon et al., Cell Syst. 2015:1(6)

Identifying an Onvansertib-Abiraterone Response Gene Signature

Onvansertib/Abiraterone



- Synergy study
- RNA-sequencing

Abiraterone induces expression of mitotic genes in prostate cancer cells synergistic for Onv+Abi

Identification of an Abi/Onv synergy gene signature

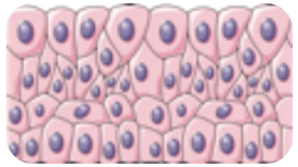
DECIPHER BIOSCIENCES

Transcriptome analysis of 32,000 prostate cancer specimens

Identified 4 molecular subtypes:
- Luminal A
- Luminal Proliferating
- Basal
- Basal Immune

Abi/Onv synergy gene signature is enriched in the Basal subtype, a subtype representing ~30% of CRPC patients and associated with lower response to androgen deprivation therapy (ADT)

Currently analyzing archived tissue from patients enrolled in the trial



Transcriptome analysis with Decipher Biosciences

Correlate clinical response with Basal molecular subtype

Conclusions

- **Safety:**
  - Onvansertib + abiraterone demonstrated safety across 3 different dosing schedules: Arm A (5 days ON, 16 days OFF), Arm B (5 days ON, 9 days OFF), Arm C (14 days ON, 7 days OFF)

- **Efficacy:**
  - Arms A (n=17) and B (n=12) showed similar efficacy with 29% and 25% of patients achieving the primary endpoint and 53% and 42% of patients with SD at 12 weeks, respectively
  - The more continuous dosing schedule of Arm C (n=8) has shown so far higher response rate with 63% of patients achieving the primary endpoint and 75% with SD at 12 weeks
  - Efficacy was observed in patients harboring AR alterations across all 3 arms
  - Onvansertib + abiraterone induced unfavorable-to-favorable CTC conversion, and this conversion was correlated with durable response

- **Biomarker:**
  - ctDNA analysis revealed differences in baseline genomic profiles of patients achieving SD at 12 weeks vs patients progressing before or at 12 weeks: mutations exclusively present in SD patients were associated with cell cycle and DNA repair pathways that may result in increased sensitivity to onvansertib and efficacy of the combination
  - We identified a gene signature associated with onvansertib and abiraterone synergy in prostate cancer cells that is significantly enriched in the basal molecular subtype of prostate cancer patients. The utility of primary tumor transcriptomic profiling to predict clinical response will be further explored

Cardiff Oncology™

Leading with Research and Data

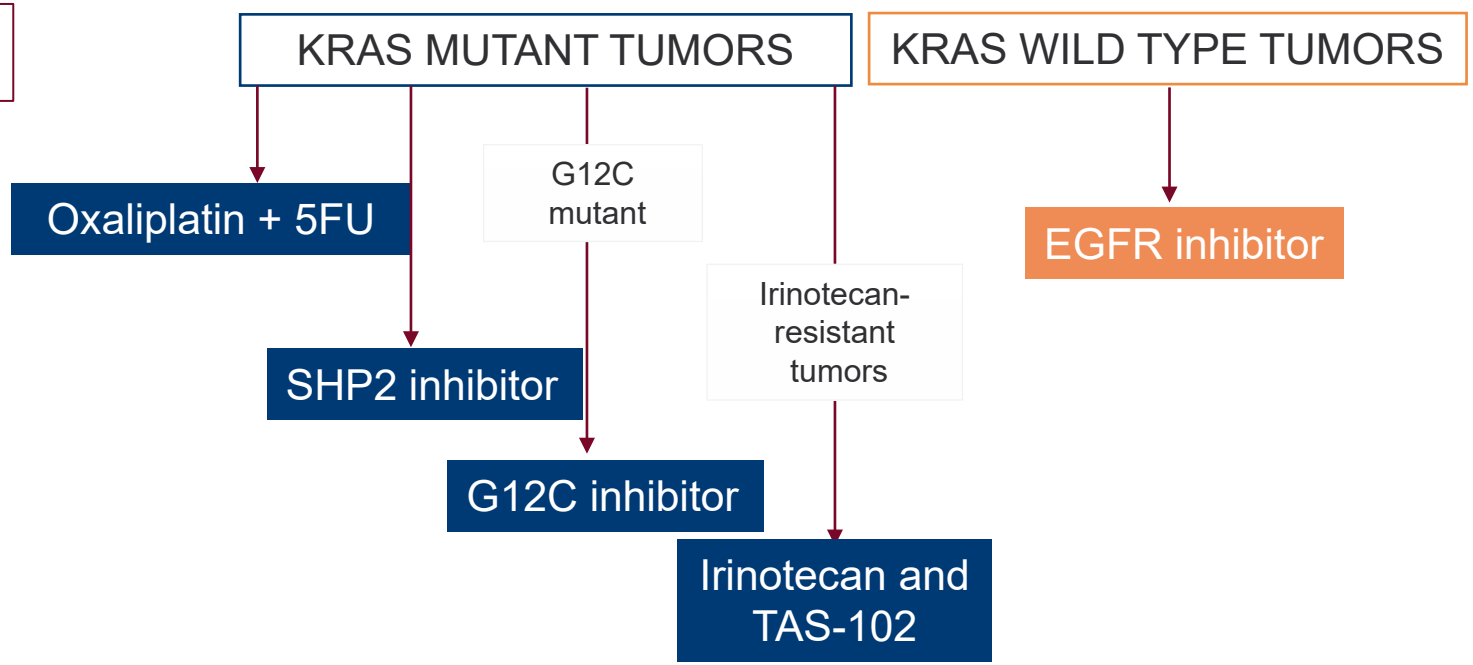
Identifying Novel Effective Combinations of Onvansertib in CRC

Research

PDX models

- PDX models from CRC patient biopsies with clinical and molecular features available

Proposed Combinations



Combining Onvansertib and PARP Inhibitors

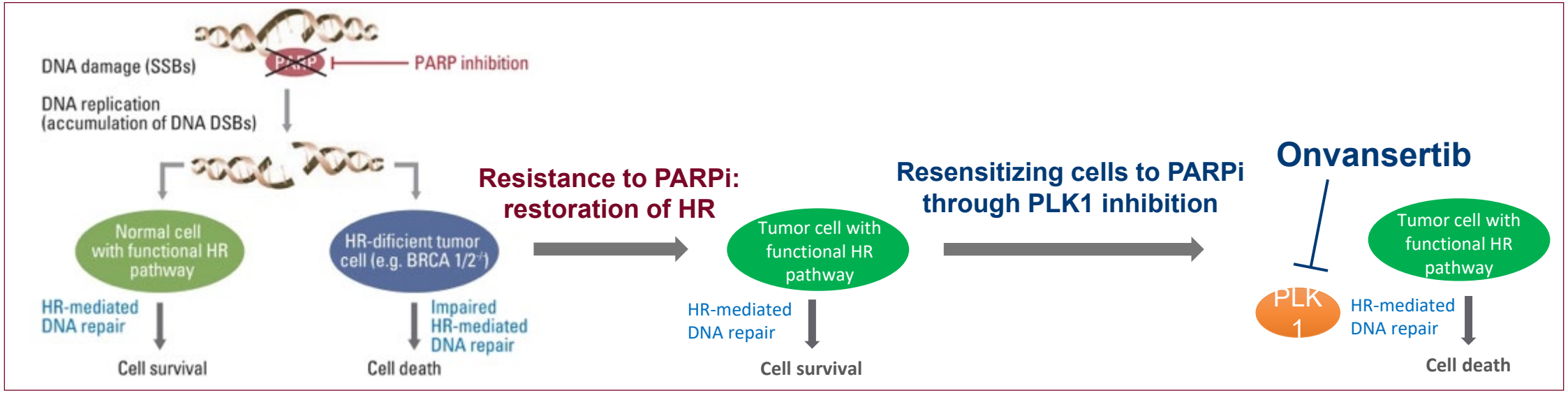
PARP Inhibitors

- PARP inhibitors are approved for BRCA1/2 mutant ovarian, breast, prostate and pancreatic cancer patients
- Although initial response to PARP inhibitors is high, patients will eventually develop resistance
- Mechanisms of resistance to PARP inhibitors include restoration of homologous recombination (HR)

Research

PLK1 Facilitates HR during Double Strand DNA Break (DSB) Repair

- PLK1 phosphorylates Rad51 and BRCA1, facilitating their recruitment to DSB sites and thereby HR-mediated DNA repair[1,2]



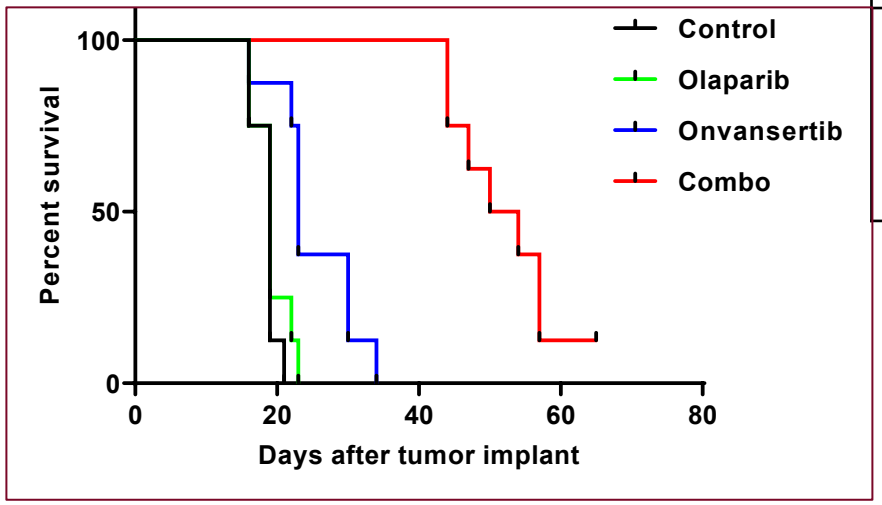
PARP is essential for repair of single strand DNA breaks (SSBs). Failure to repair SSBs through PARP inhibition results in double strand DNA breaks (DSBs). In cells with functional homologous recombination (HR) pathway, the DSB are repaired. In cells with a dysfunctional HR pathway, such as BRCA 1/2 mutant cells, the lesions cannot be adequately repaired resulting in cell death.

[1]Yata et al. Mol. Cell 45, 371-383, 2012; [2]Chabalier-Taste et al., Oncotarget 2016 Jan 19; 7(3): 2269-83

PLK1 Inhibition Sensitizes Cancer Cells to PARP Inhibitors

- In vitro preclinical studies showed that PLK1 inhibition sensitized cells to genotoxic stresses (i.e, radiation) and to PARP inhibitors through impairment of HR[1,2]
- Onvansertib sensitizes tumor cells to PARP inhibition **in vivo**:
  - In an ovarian BRCA1-mutant PDX model resistant to olaparib, the combination of onvansertib and the PARP inhibitor olaparib significantly increased the survival of mice (2.7-fold vs control or olaparib single agent)[3]
- Onvansertib has the potential to sensitize tumors resistant to PARP inhibitors and thereby expand the use of PARP inhibitors in the clinic

Ovarian BRCA1-mutant PARP-Resistant PDX model



Median survival (days)	Fold-increase in survival vs control
19	
19	0
23	1.2
52	**2.7**

Research

[1]Yata et al. Mol. Cell 45, 371-383, 2012; [2]Chabalier-Taste et al., Oncotarget 2016 Jan 19; 7(3): 2269-83; [3]Data on file

Corporate

Strong Patent Portfolio

Core Technology: 3 Issued Patents to 2030 in US, Europe and Asia, with anticipated extension to 2035

Compound (onvansertib): US 8614220

Salt forms of onvansertib: US 8648078

Combinations with anti-neoplastic compounds: US 8927530

Evergreening: Combination Therapy

Exclusive license from MIT for 2 US issued patents with broad method claims for combination of PLK inhibitor + anti-androgen compounds to treat any cancer

US 9566280; US 10155006; Expiration 2035

Evergreening: Biomarkers

Method for assessing PLK1 target phosphorylation status for identifying patients to be treated with PLK1 inhibitors

PCT US1948044, Expiration 2039

Method for treating patient with a PLK inhibitor when there is a PSA rise

Provisional, Expiration 2040

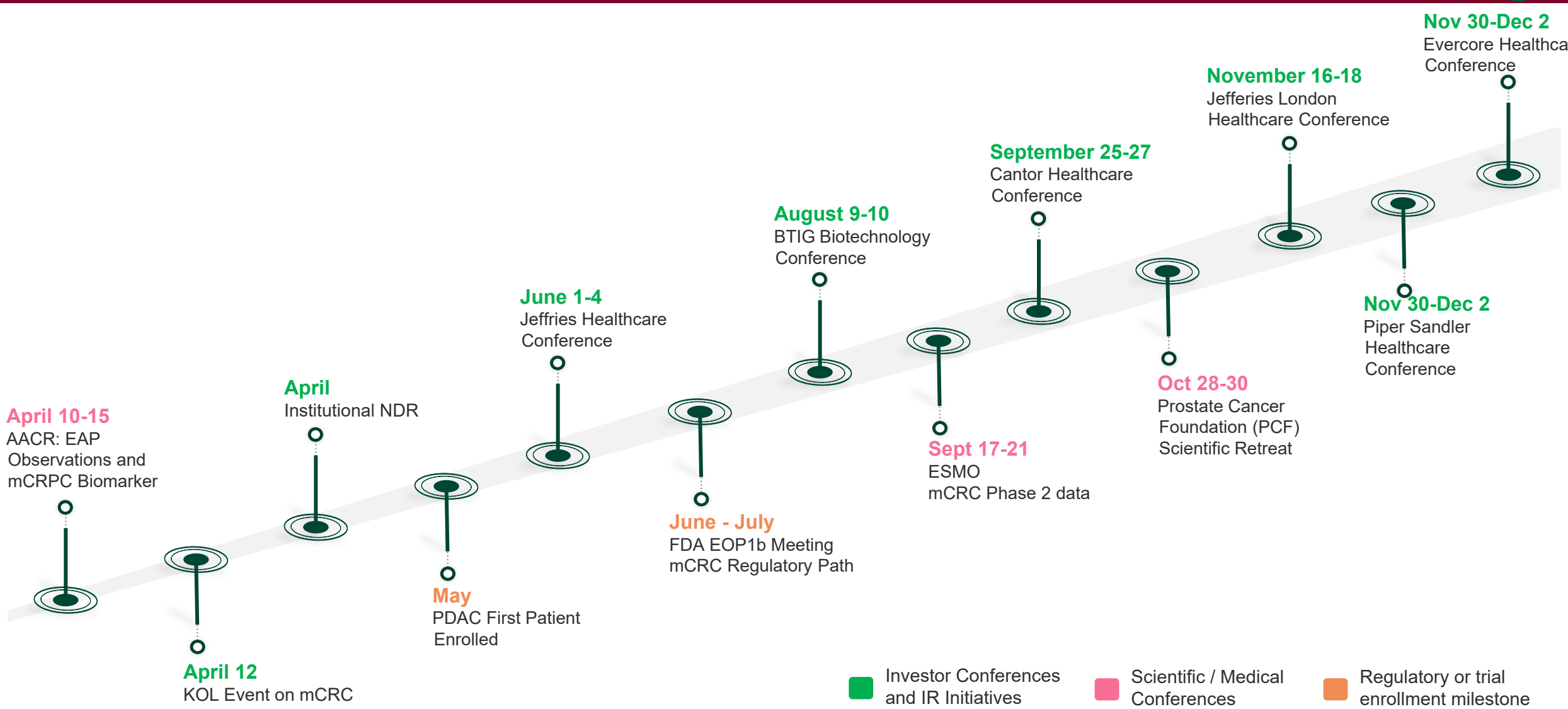
Cardiff Oncology At-A-Glance

Clinical-stage biotech company, developing **onvansertib,** an oral, highly-selective Polo-like Kinase 1 (PLK1) inhibitor, to treat cancers with the greatest medical need for new effective therapies

Exchange	Nasdaq: CRDF
Cash & Cash Equivalents as of 12/31/20	$131.0M
Net Cash used in Operating Activates FY 2020	$16.3M
Headquarters	San Diego, CA

The above financial information is derived from audited financials in CRDF Form 10K filed on 02/25/21

Timeline of Key Anticipated Catalysts for the Balance of 2021



Cardiff Oncology Strategy – Transforming to Lead the Way

Undergoing Corporate Transformation to Position Cardiff for Long-term Success

- Accelerating corporate governance best practices, starting with new CEO leadership, board evolution and updated policies
- Seeking leading talent for key roles, including CFO, CMO and CSO
- Committed to investor communication transparency and disclosure

Maximizing Our Clinical Development Capabilities

- Cultivating the most advanced PLK1 inhibitor
- Developing strategies to enable the most rapid path to approval
- Focusing on opportunities to lead the “drugability” enablement of KRAS mutated cancers

Leading with Research and Data

- PLK1 is at a unique nexus within the convergence of many tumor-promoting pathways
- Leveraging deep expertise in translational biomarker integration within clinical programs
- Focusing on pipeline expansion through synergistic combinations

Fully Leverage Onvansertib in Combination with Targeted Therapeutics and Chemotherapies Across Multiple Cancer Indications

Thank You

for more information contact:

ir@cardiffoncology.com