Cardiff Oncology™

Turning the Tide on Cancer

February 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, 2019, 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.

Investment Highlights

3rd Generation, 1st-in-class, Oral PLK1 Inhibitor

Onvansertib overcomes the shortcomings of prior PLK inhibitors:

- Highly selective for PLK1
- Orally administered
- 24-hour half-life
- Flexible dose and schedule

Specifically targets a known mechanism of cell division that is required for tumor cell viability

Preliminary clinical data demonstrate the safety, tolerability and efficacy of onvansertib in combination with SOC across multiple indications

Strong Lead Program in KRAS-mutated mCRC

Supported by compelling preliminary clinical data from a Phase 1b/2 trial showing a ten-fold improvement in ORR compared to SOC

Preclinical data support:

- MOA of synthetic lethality between KRAS mutant mCRC and PLK1 inhibition
- Synergy with irinotecan and 5-FU

First Indication: 2nd line treatment in patients who have failed 1st line treatment with FOLFOX with/without bevacizumab

FDA Fast Track Designation

Diversified Pipeline Across Numerous Cancers

Clinical data from ongoing trials support the use of onvansertib in combination regimens across Numerous aggressive cancers:

- mCRC Phase 1b/2 trial
- mCRPC Phase 2 trial
- PDAC Phase 2 trial
- AML Phase 2 trial

Expansion opportunities:

- Chronic myelomonocytic leukemia
- Triple negative breast cancer
- Lung cancer
- Ovarian cancer

Integrated Biomarker Strategy

Circulating Tumor DNA: changes in KRAS mutational burden in blood are predictive of subsequent tumor shrinkage (mCRC)

Circulating Tumor Cells: changes are predictive of overcoming anti-androgen resistance (mCRPC)

Circulating Tumor DNA: changes are predictive of decreases in leukemic bone marrow cells (AML)

PLK: Polo-like Kinase; SOC: Standard-of-care; ORR: Overall response rate; MOA: Mechanism of action; mCRC: metastatic colorectal cancer; mCRPC: metastatic castration resistant prostate cancer; PDAC: Pancreatic ductal adenocarcinoma; AML: Acute myeloid leukemia

Experienced Management Team With Drug Development and Biomarker Technology Expertise

Mark Erlander, PhD

Chief Executive Officer

BIOMÉRIEUX

Johnson & Johnson PHARMACEUTICAL RESEARCH & DEVELOPMENT

Vicki Kelemen

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Bayer HealthCare Pharmaceuticals

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Maxim Pharmaceuticals

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Dura Pharmaceuticals

Brigitte Lindsay

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ZEISS

PHILIPS RESPIRONICS

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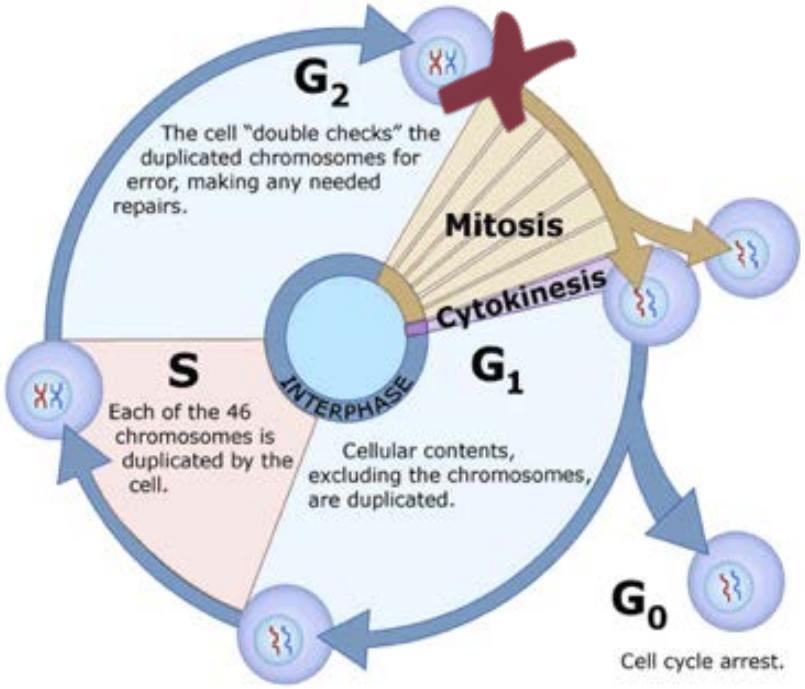
Onvansertib

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]

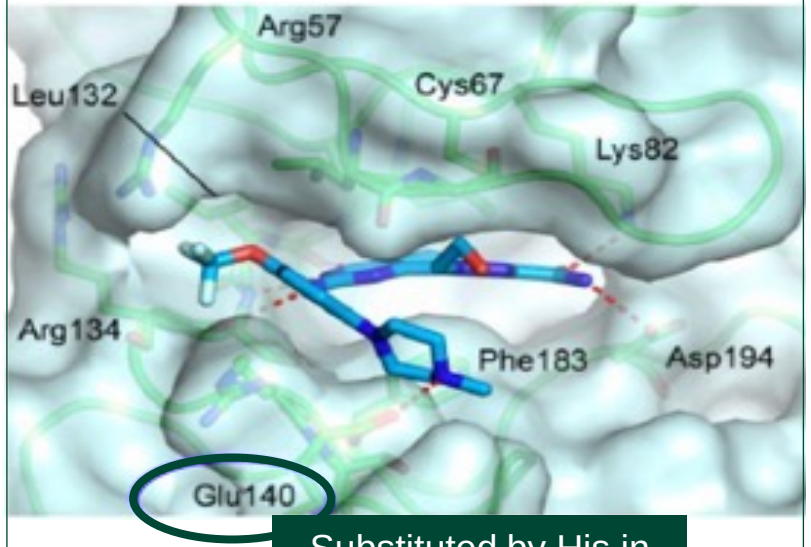
Biochemical Profile

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



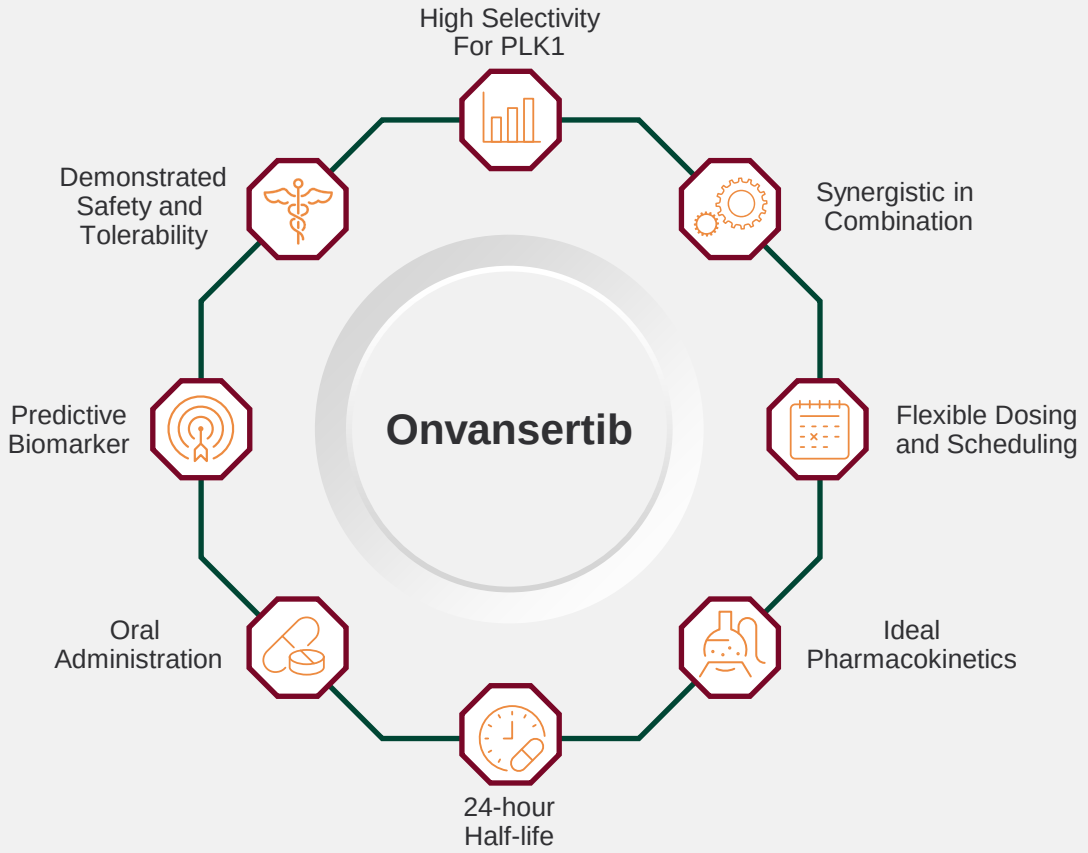
Onvansertib

- 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

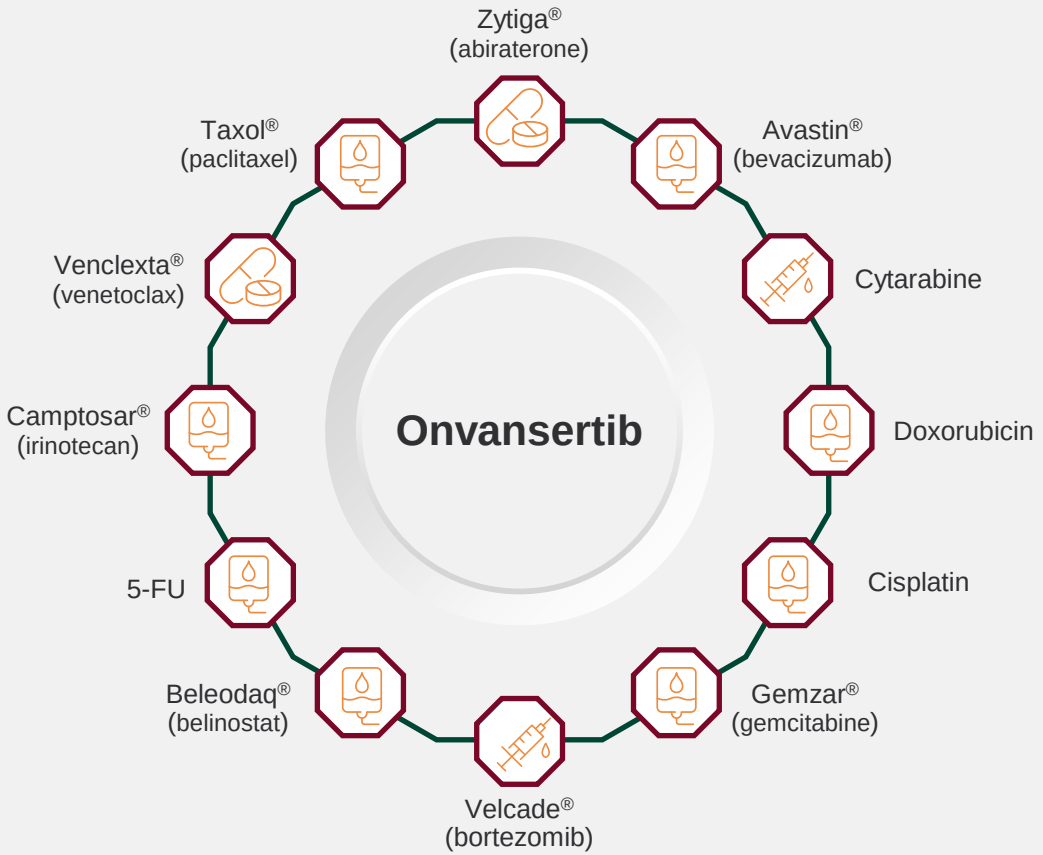
Cardiff Oncology™ [1]Valsasina Mol Cancer Ther 2012

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

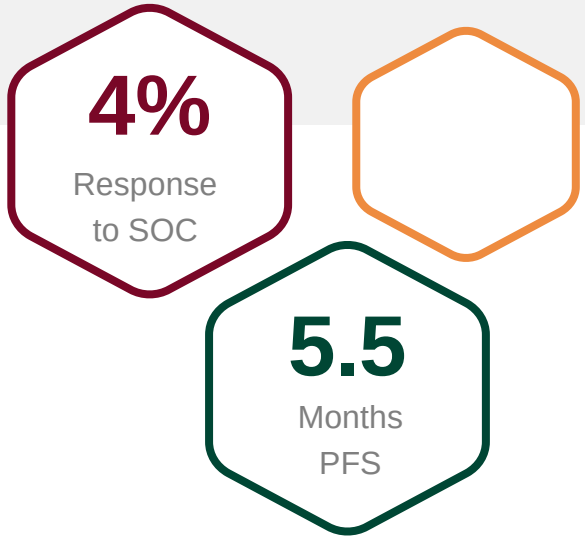
Principal Investigator: Dr. Heinz-Josef Lenz

New Second-Line Therapies are Needed to Improve Response and Increase Progression-Free Survival

50% of patients with mCRC have a KRAS mutation

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**



Significant limitations to standard-of-care (SOC)

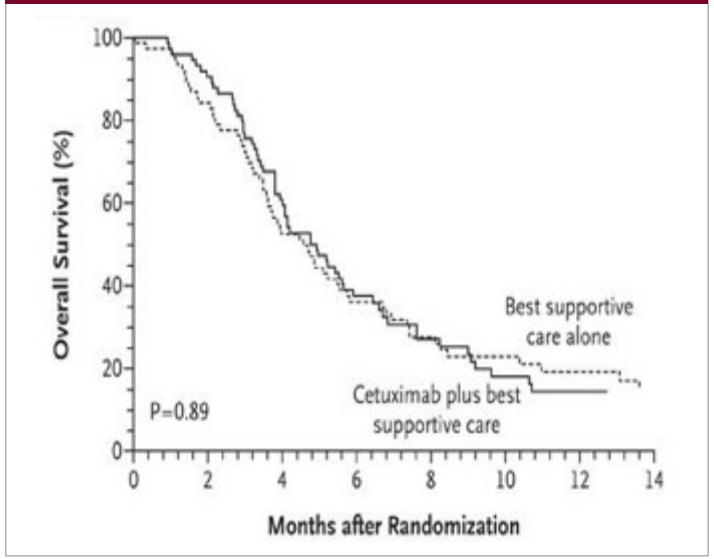
Historically, second-line standard-of-care treatment in KRAS-mutated mCRC has had an overall response rate of 4% and progression-free survival (PFS) of 5.5 months[1]

[1]Kubicka et al, Annals of Oncology 2013; 2342–2349; mCRC: Metastatic colorectal cancer

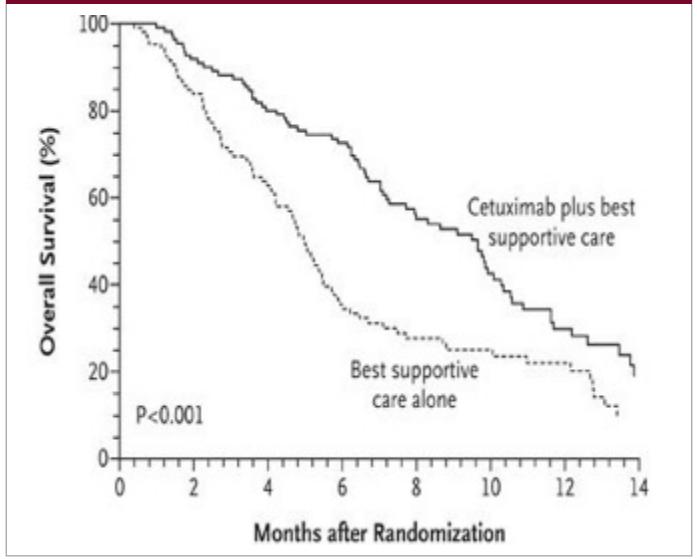
KRAS is a Pivotal Diagnostic Biomarker in the CRC Treatment Paradigm

- 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)

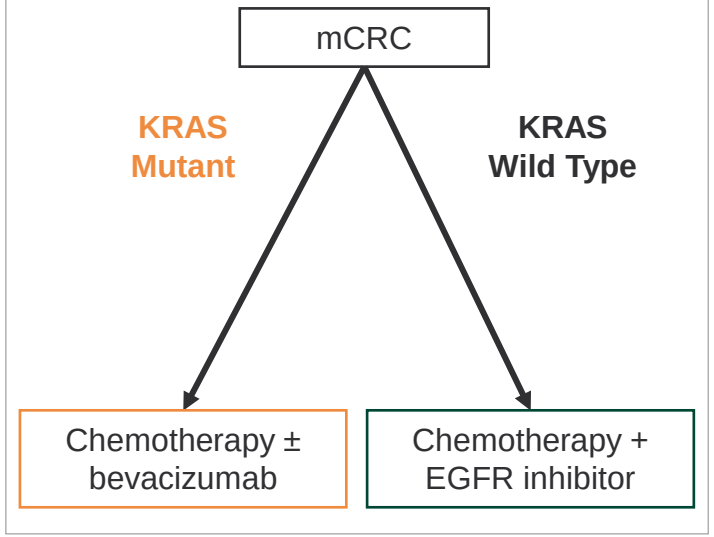
KRAS Mutant



KRAS Wild-type



Treatment Paradigm



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

Second-line Treatment: Real World Utilization in the US

Flatiron Health Data

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

FDA Approved Standard-of-Care, FOLFIRI + Bev, has an ORR Rate of 5% and PFS of 5.7 months in Pivotal Trial Used for Registration

Outcomes for patients in the 2nd line setting is poor

- Addition of bevacizumab to FOLFIRI improves outcomes[1]
- While KRAS WT patients benefit from the addition of bevacizumab, there was no statistically significant improvement in OS for KRAS-mutant patients[2]
- KRAS-mutant patients have lower ORR, PFS and OS[2]

KRAS	Treatment	ORR	PFS (months)	HR and significance of PFS	OS (months)	HR and significance of OS
All Patients[2]	FOLFIRI	3%	4.1	HR=0.68 (95 % CI 0.59-0.78) P <0.0001	9.8	HR=0.81 (95 % CI 0.69-0.94) P <0.0062
	FOLFIRI + Bev	5%	5.7		11.2	
KRAS WT[2]	FOLFIRI	5%	4.5	HR=0.61 (95 % CI 0.49-0.77) P <0.0001	11.1	HR=0.61 (95 % CI 0.53-0.90) P=0.0052
	FOLFIRI + Bev	7%	6.4		15.4	
KRAS MUTANT[2]	**FOLFIRI**	**3%**	**4.1**	HR=0.70 (95 % CI 0.56-0.89) P = 0.0027	10	HR=0.92 (95 % CI 0.71-1.18) P=0.4969
	FOLFIRI + Bev	**4%**	**5.5**		10.4	

- The anti-angiogenic agents aflibercept and ramucirumab, although used to a lesser extent, have an ORR of 11.8 – 13.4%[3-4]

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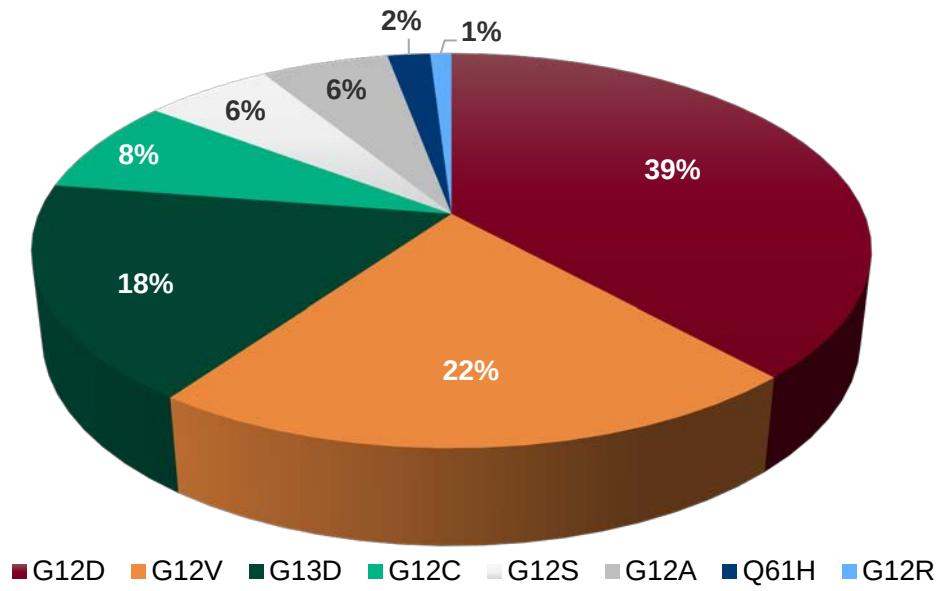
[1]Bennouna et al., Lancet Oncol. 2013; 14(1):29-37; [2]Kubicka, S, Annals of Oncology 2013, 24:2342-2349; CI: confidence interval, HR: hazard ration, ORR: objective response rate, PFS: progression-free survival, OS: overall survival, WT: wild-type, MUT: mutant; [3]Van Cutsem et al., Target Oncology 2016, 11:383-400 [4]Tabernero et al., Lancet Oncology 2015;16:499-508

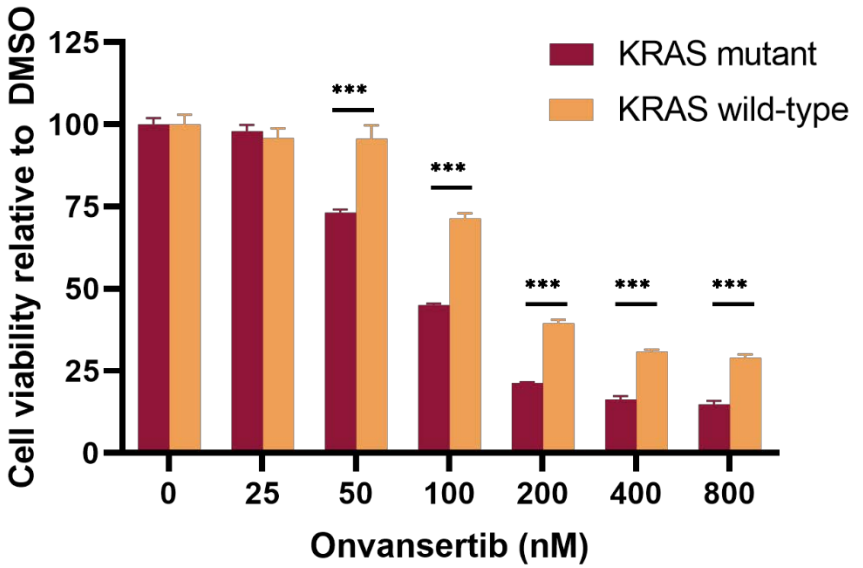
Synthetic Lethality: Cells with KRAS Mutations are Hypersensitive to Inhibition of PLK1

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



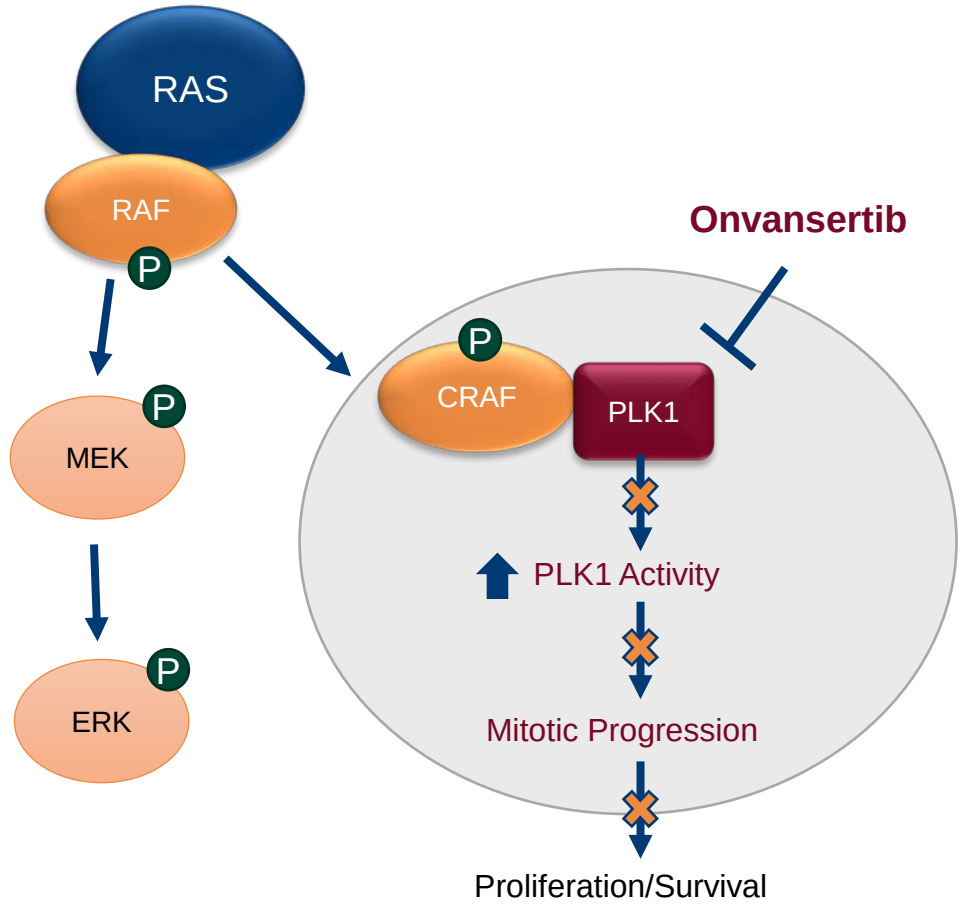
PLK1: Polo-like Kinase 1; mCRC: Metastatic colorectal cancer

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

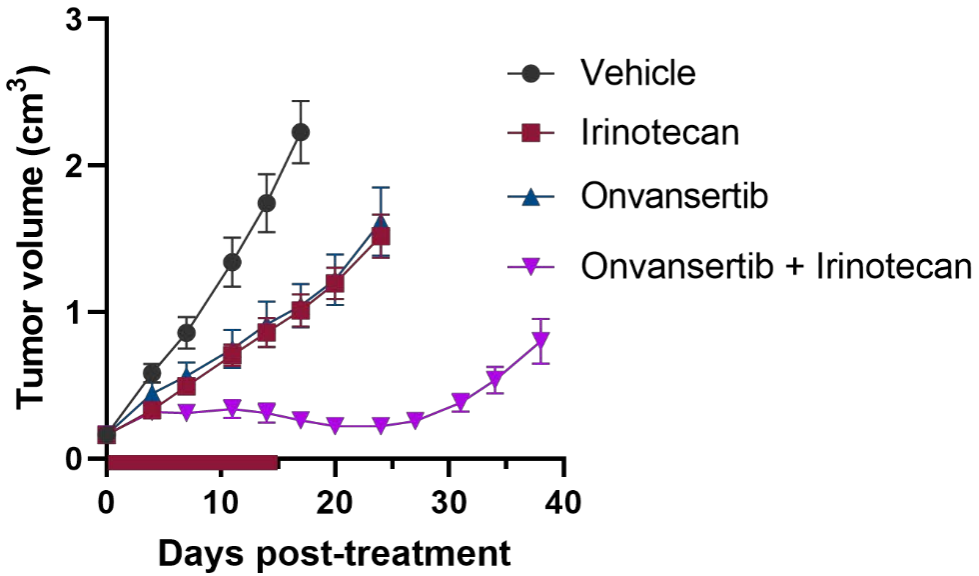


[1]Mielgo et al., Nat. Med. 2011; 17(12):1641-5

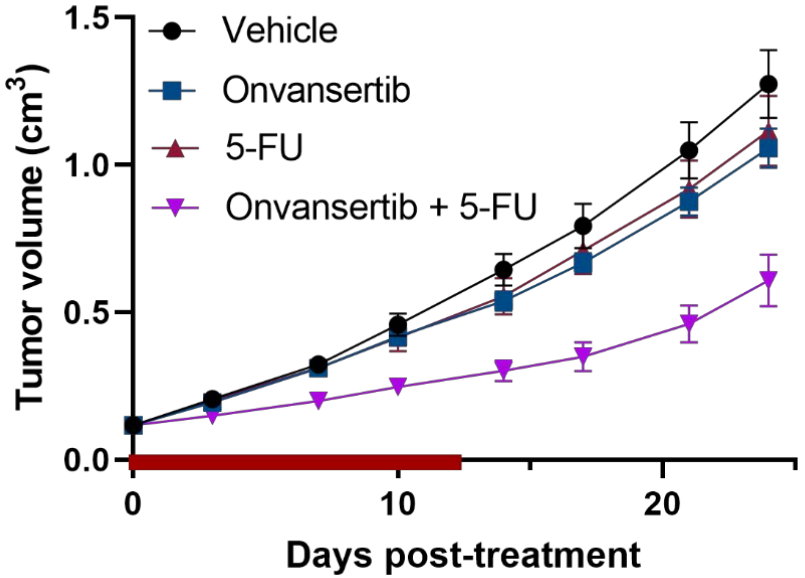
Synergy: Onvansertib in Combination with SOC Irinotecan and 5-FU

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

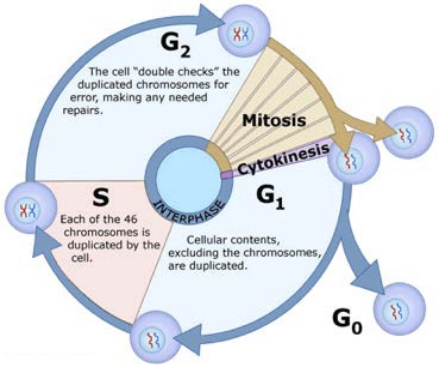


Synergy in Combination with 5-FU



PLK1 Regulates DNA Damage Response[1,2]

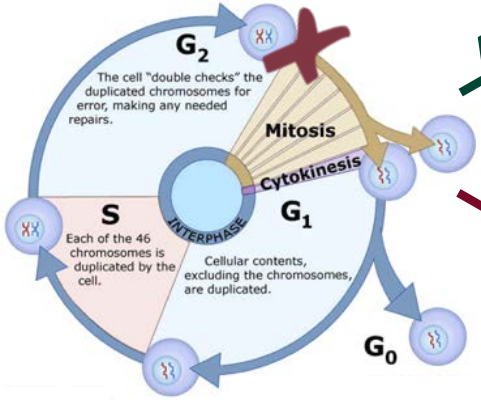
DNA Damaging Agents



- 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

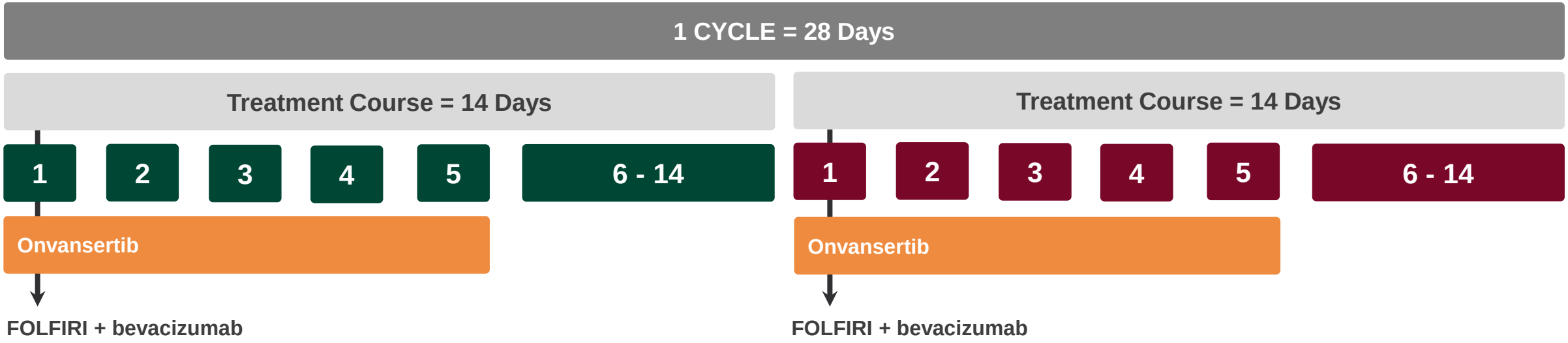
Cell Death

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

What is Clinical Trial Success

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

Phase 1b Enrollment and Patient Baseline Characteristics

Dose Escalation Patient Cohorts (as of 06-Jan-2021)

Number of Patients (N)	Dose Level 0 Onvansertib 12 mg/m^2	Dose Level +1 Onvansertib 15 mg/m^2	Dose level +2 Onvansertib 18 mg/m^2
Completed Cycle 1	5	6	5
Currently on Treatment	0	3	2

- Phase 1b: 3+3 dose escalation design to assess the safety of the combination and identify the maximum tolerated dose (MTD) and recommended Phase 2 dose (RP2D) of onvansertib

Total Patients N=18	Median [range] or n (%)
Age (years)	59 [37-83]
Sex	
Male	8 (44%)
Female	10 (56%)
ECOG	
0	8 (44%)
1	10 (56%)
Primary tumor site	
Colon	9 (50%)
Rectum	7 (39%)
Unknown	2 (11%)
Liver metastasis	
None	7 (39%)
Liver and other	8 (44%)
Liver only	2 (17%)
Number of metastatic organs	
1	7 (39%)
≥2	11 (61%)
Prior Bevacizumab treatment	
Yes	13 (72%)
No	5 (28%)

Phase 1b Safety Assessment

Most Common Treatment-Emergent AEs

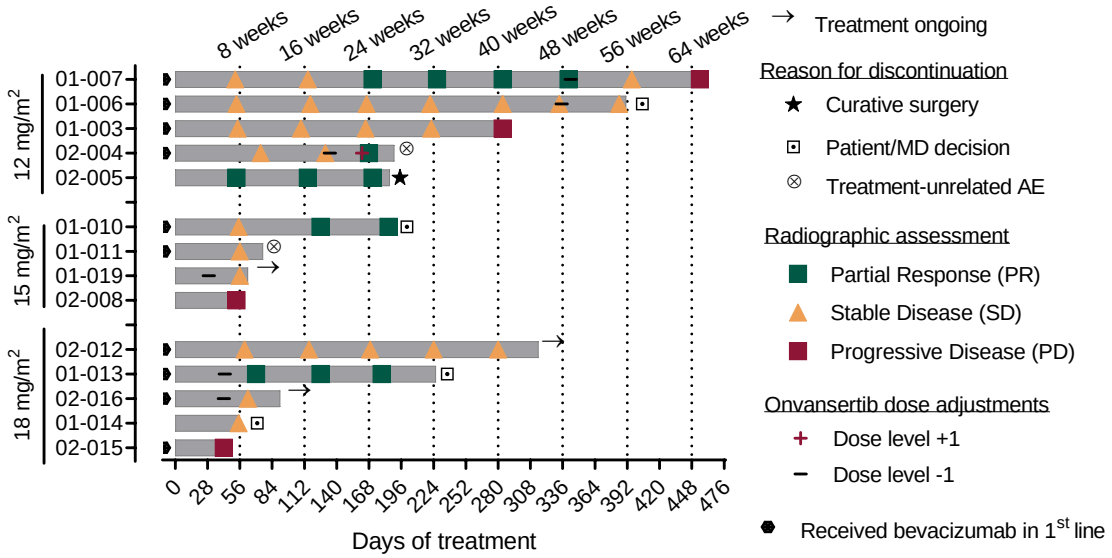
Adverse Events (AEs)	Grade 1	Grade 2	Grade 3	Grade 4	All Grades
Fatigue	4	7	1	0	12
Nausea	8	3	1	0	12
Neutropenia	1	2	4	4	11
Diarrhoea	7	2	0	0	9
Alopecia	6	1	0	0	7
Abdominal pain	1	4	1	0	6
Anaemia	4	1	0	0	5
WBC decrease	2	3	0	0	5
Vomiting	3	1	1	0	5
Stomatitis	4	1	0	0	5
Thrombocytopenia	2	2	0	0	4
Mucosal inflammation	1	2	0	0	3
Dyspepsia	3	0	0	0	3
ALT increased	2	1	0	0	3
Abdominal distension	3	0	0	0	3
Back pain	3	0	0	0	3
Epistaxis	3	0	0	0	3

n=number of patients (total N=18); WBC=white blood cells; ALT= alanine aminotransferase

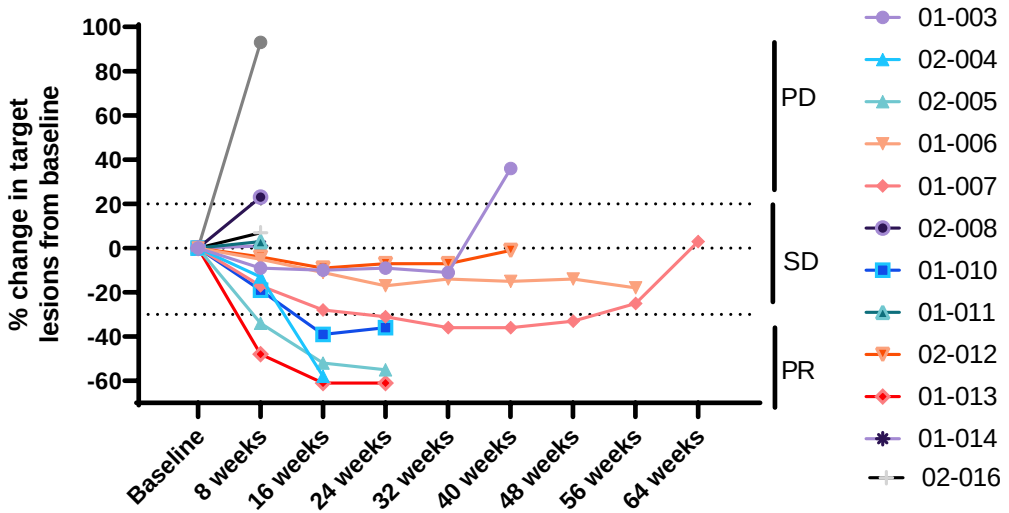
- 5 patients had G4 adverse events:
  - 1 patient had a G4 neutropenic fever at dose level 12 mg/m^2
  - 1 patient had a G4 neutropenia at dose level 15 mg/m^2
  - 3 patients had a G4 neutropenia dose level 18 mg/m^2
- The onvansertib RP2D was confirmed at 15 mg/m^2
- The combination regimen was well tolerated:
  - Of all AEs only 8% (17/202) 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; no patients went off trial due to neutropenia
- No major or unexpected toxicities were attributed to onvansertib

Phase 1b Preliminary Efficacy

Treatment Response and Duration (as of 06-Jan-2021)



Changes in Tumor Size From Baseline

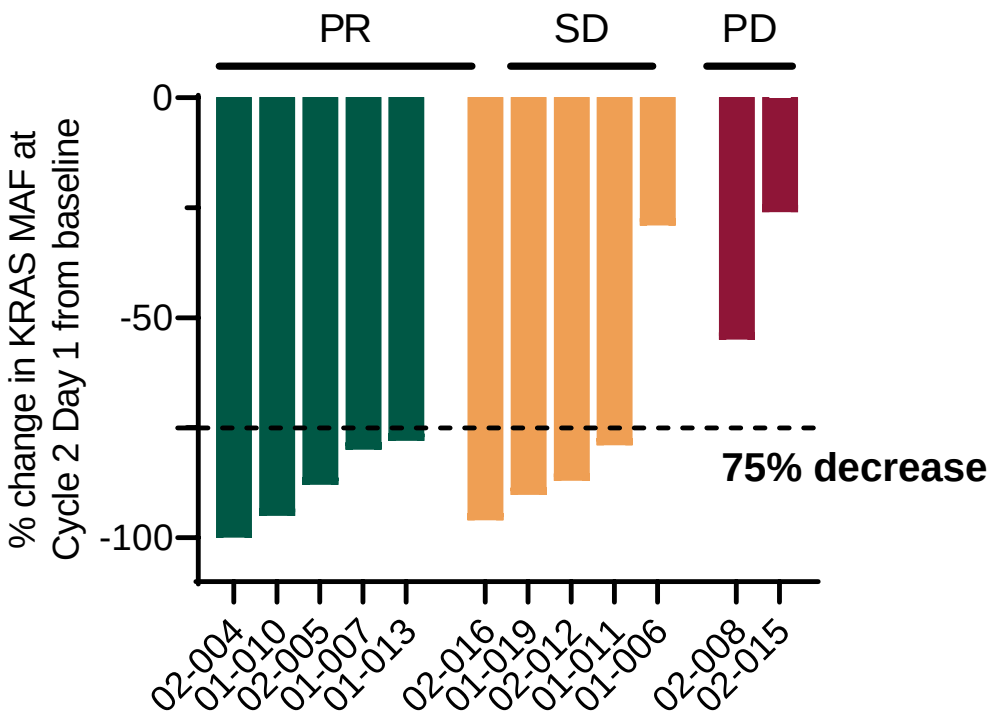


- 18 patients were treated in Phase 1b (6 patients at each dose level); 2 patients did not complete cycle 1 (1 at 12 mg/m^2 and 1 at 18 mg/m^2); 2 patients at 15 mg/m^2 completed cycle 1 of treatment, but have not reached their first 8-week scan
- 14 patients are currently evaluable for efficacy*:
  - 12 of 14 (86%) patients achieved a clinical benefit (SD + PR)
  - 5 (36%) patients have achieved a partial response (PR); 4 patients had a confirmed PR; 1 patient went on to have curative surgery; 1 patient with non-confirmed PR went off study following PR due to treatment-unrelated AE
  - Time to patients on trial achieving a PR ranges from 2 to 6 months

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

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)
- 12 of 14 patients had a KRAS mutation detected by ddPCR at baseline (all had a KRAS mutation detected by NGS)
- Clinical responses were observed across different KRAS mutations, including the 3 most common in CRC (G12D, G12V, G13D)
- The greatest decreases in KRAS MAF after 1 cycle of treatment were observed in patients achieving a PR
  - All 5 patients with a PR had >75% decrease
  - 4 of the 5 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; CXD1: Cycle X Day 1

Conclusions

- **Safety Assessment:**
  - The combination of onvansertib and FOLFIRI/Bev is well-tolerated
  - Onvansertib RP2D was established at 15 mg/m^2
- **Preliminary Efficacy:**
  - 12 of 14 (86%) patients evaluable for efficacy achieved a clinical benefit (SD + PR)
  - 5 (36%) patients achieved a partial response (PR), including 4 confirmed PRs; 1 patient proceeded to curative surgery
- **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 one cycle of therapy
- **Phase 2 Currently Enrolling at 7 trial sites:**
  - Further assess the safety and efficacy of onvansertib at the RP2D in combination with FOLFIRI + bevacizumab
  - Evaluate the value of KRAS liquid biopsy to predict treatment response

Catalysts and Milestones: KRAS-Mutated mCRC

Fast Track Designation enables more frequent interaction with the FDA and facilitates an accelerated clinical development pathway

May 2020: Fast Track Designation Granted by FDA

January 2021: ASCO-GI virtual poster presentation

Q2 2021: FDA End of Phase (EOP1b) meeting – potential path to approval discussion

ESMO 2021: ESMO mCRC Phase 2 Data

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

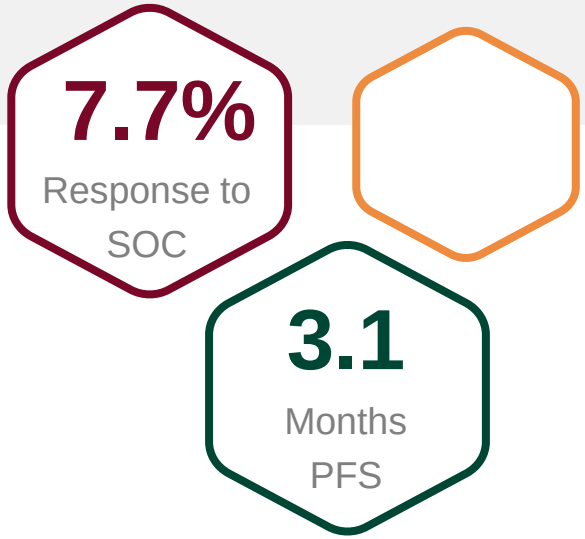
Principal Investigator: Dr. Daniel H. Ahn

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

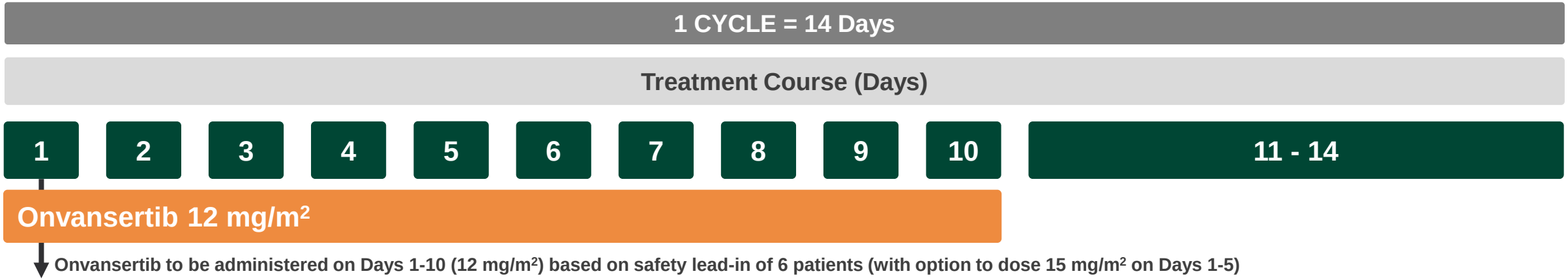
The promising response rates and impressive durability seen in KRAS-mutated mCRC with the combination of onvansertib + irinotecan + 5-FU, support onvansertib's potential in PDAC, where ~95% of patients have a KRAS mutation

Cardiff Oncology™

[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

Trial Design (~45 patients):



Eligibility Criteria

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

Primary Efficacy Endpoint

- Overall response rate (ORR)

What is Clinical Trial Success

- 8 of 39 (≥20%) patients achieve ORR

Projected Catalysts and Milestones: Metastatic PDAC

January 2021: Received FDA “Study May Proceed”

January 2022: ASCO-GI Phase 2 data presentation

April 2022: AACR biomarker data presentation

September 2022: ESMO Phase 2 data presentation

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

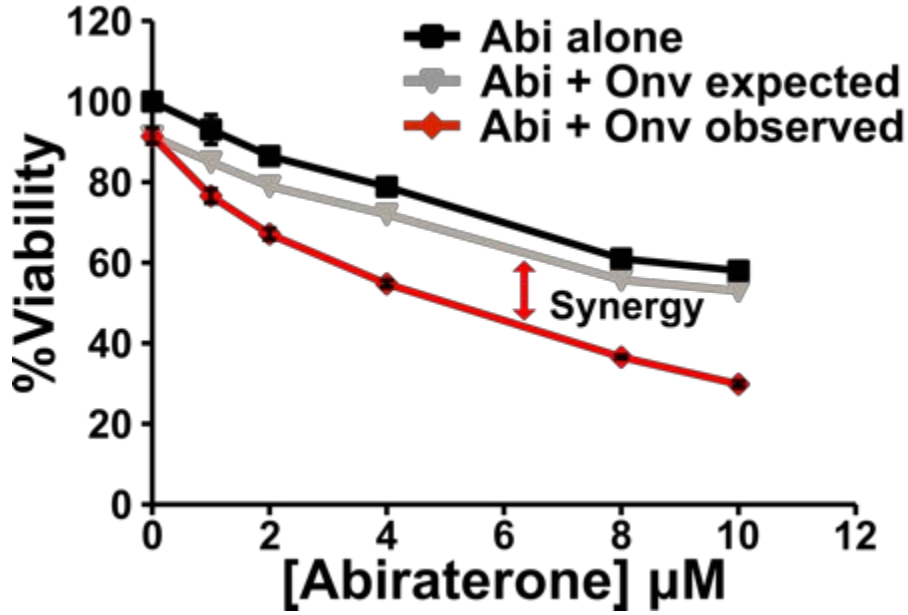
New treatment options are needed to extend the duration of response to ARSi's and increase overall survival

[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

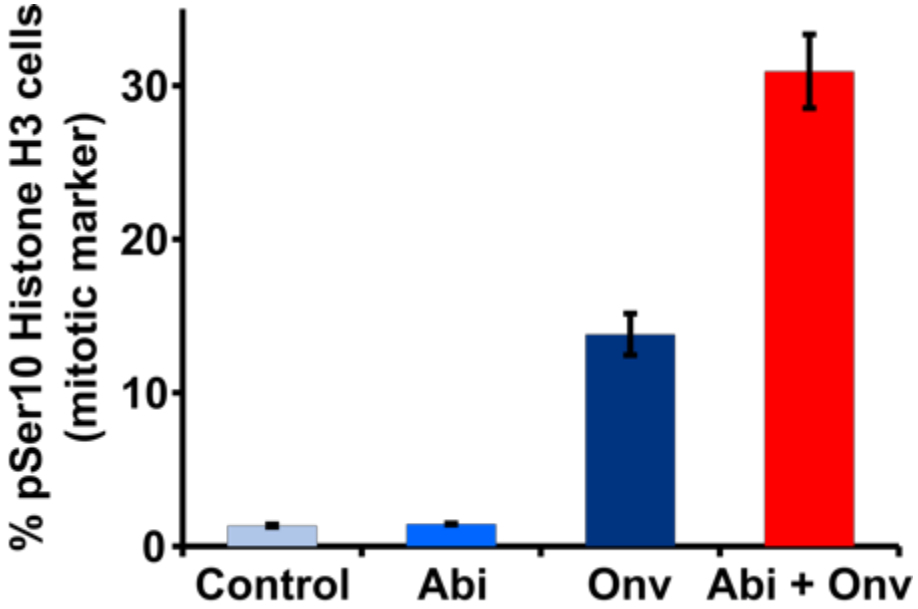
Onvansertib Extends the Response to Androgen Receptor Signaling Inhibitors

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]

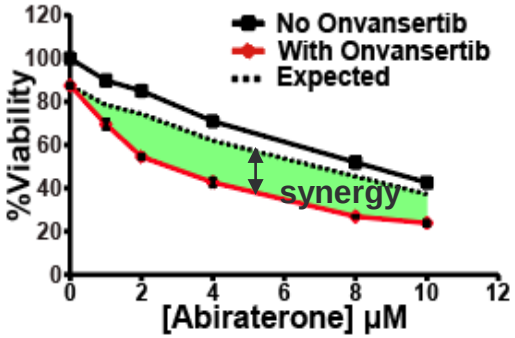


[1]Patterson & Yaffe, 2019, MIT; mCRPC: Metastatic castration resistant prostate cancer

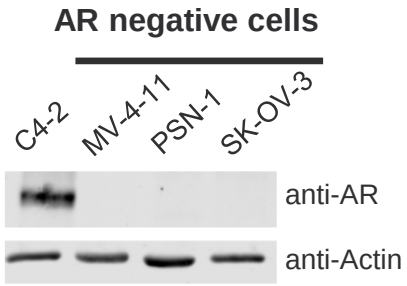
Clinical Trial Background and Rationale

- 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

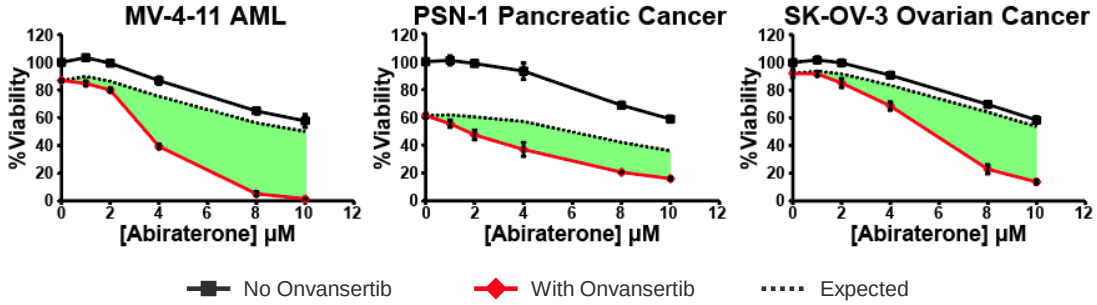
Synergy In Vitro in C4-2 Cells



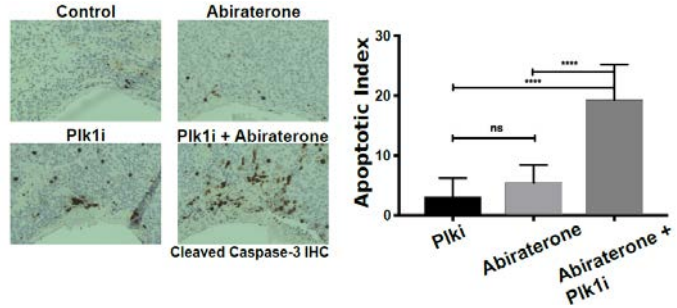
AR Expression



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)

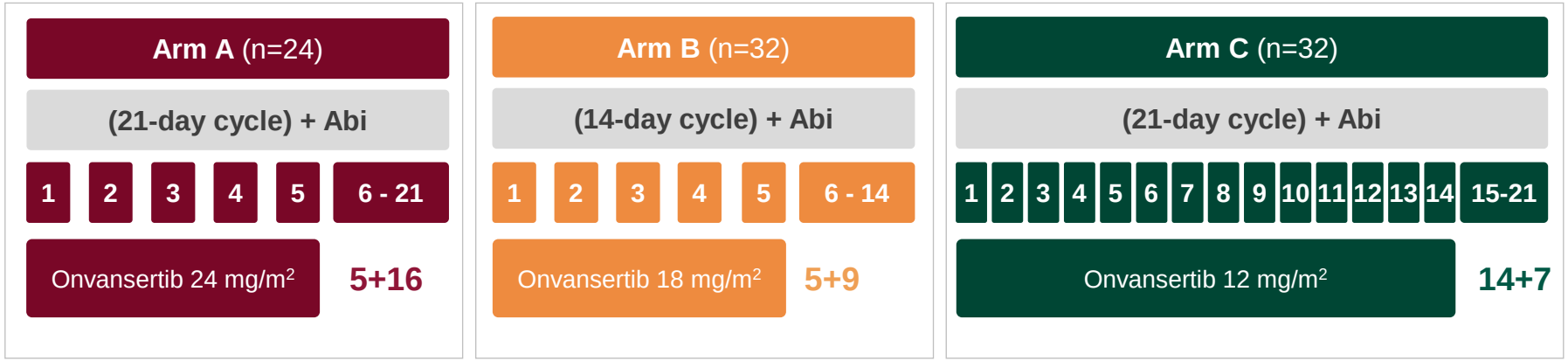
Key Eligibility Criteria:

- 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%)

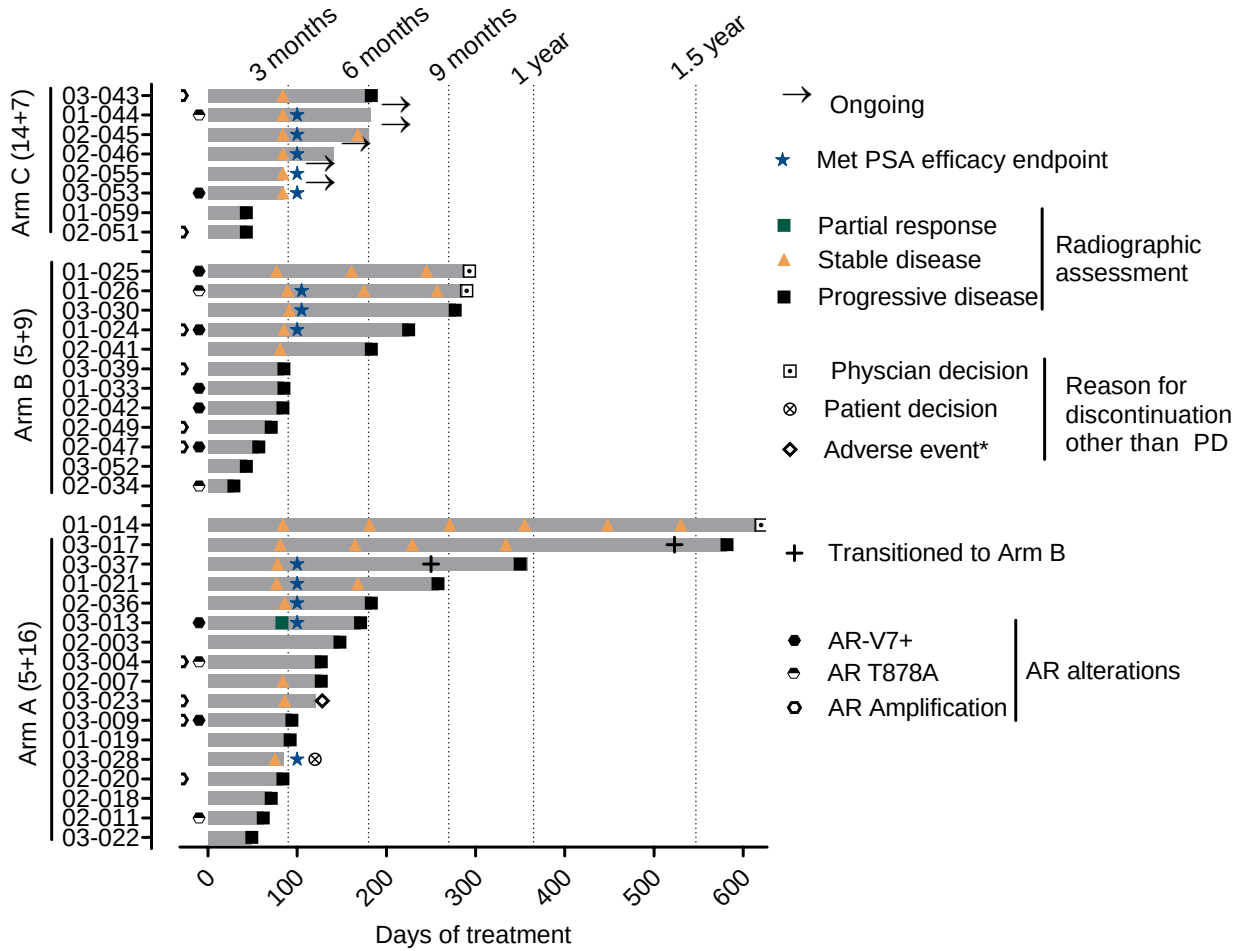
n= number of patients (total N=51)

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

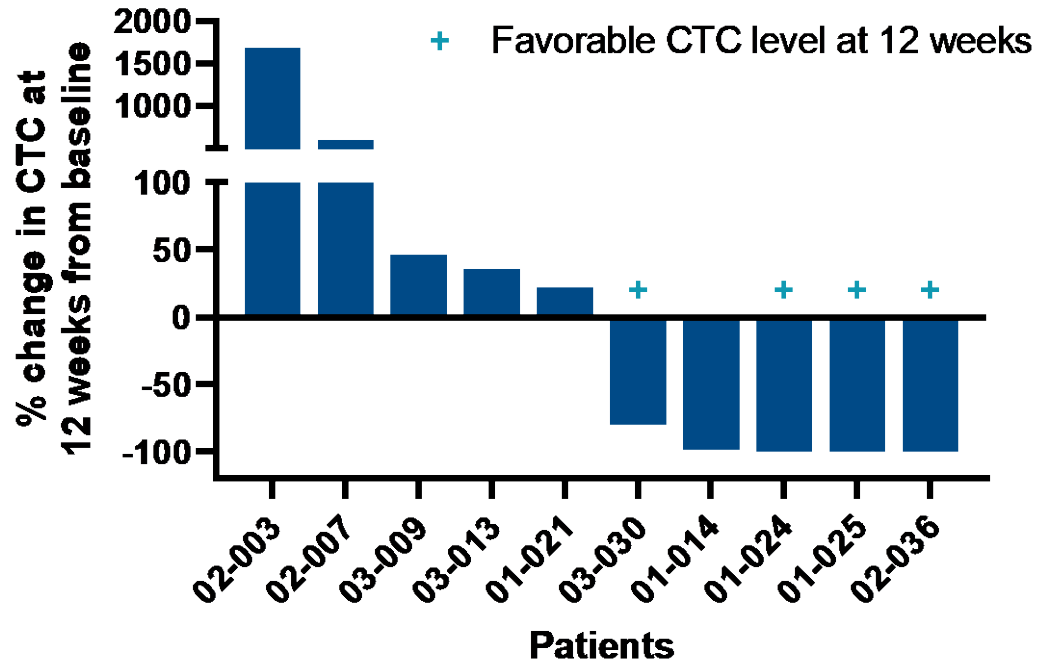
Onvansertib-Induced Circulating Tumor Cell Decrease is Associated with Progression-Free Survival

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

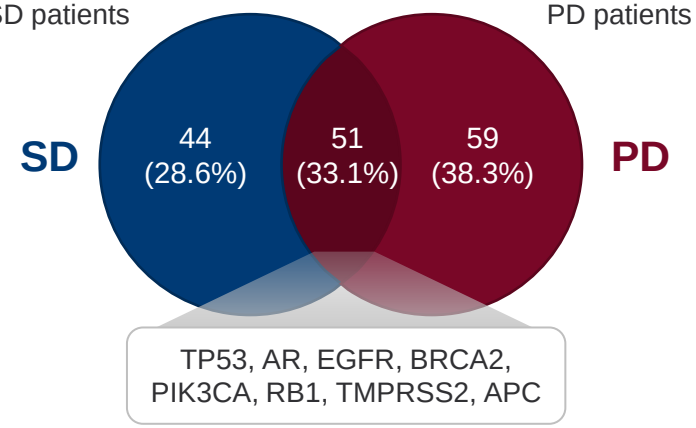
Analysis of Genes Differentially Mutated in SD and PD Patients

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

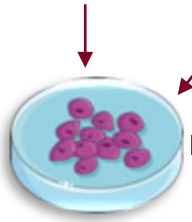
Pathways enriched in PD patients
UV Response
Wnt-beta Catenin Signaling
KRAS Signaling Up
Apoptosis
Myogenesis
PI3K/AKT/mTOR Signaling
Notch Signaling
TNF-alpha Signaling via NF-kB
Apical Junction
IL-6/JAK/STAT3 Signaling

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

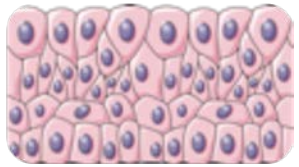
DECIPHER BIOSCIENCES

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

Catalysts and Milestones: mCRPC

October 2020: Prostate Cancer Foundation (PCF)

February 2021: ASCO-GU presentation

April 2021: AACR Preclinical data presentation

October 2021: Prostate Cancer Foundation (PCF)

New Clinical Programs Planned

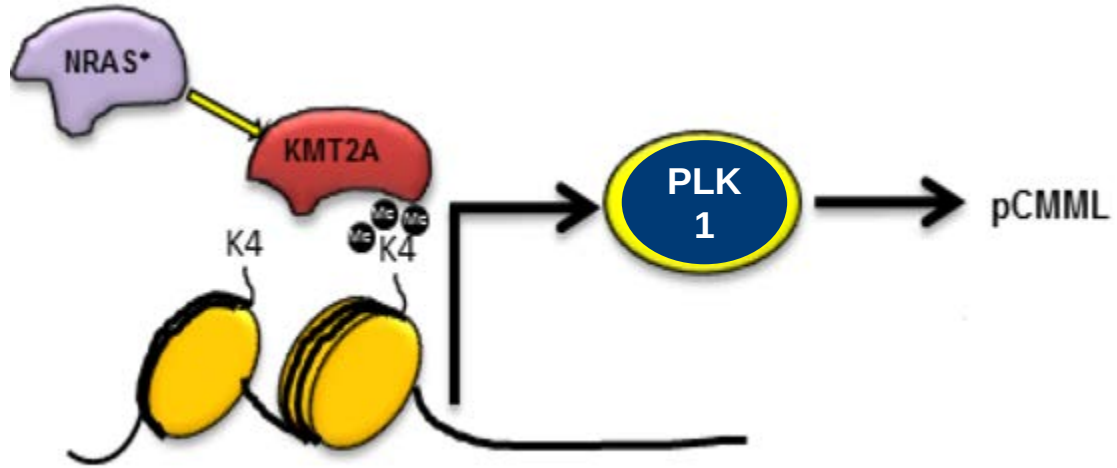
Chronic Myelomonocytic Leukemia (CMML)

Phase 2 Study to Evaluate the Safety and Efficacy of Onvansertib in RAS-Pathway Mutant CMML

Study Rationale

- Proliferative CMML is enriched for activating RAS pathway mutations such as NRAS, KRAS, CBL, PTPN11 and NF1, all of which have been associated with adverse outcomes
- RAS pathway mutations drive proliferative CMML via a novel RAS-KMT2A-PLK1 axis, which can be therapeutically targeted with PLK1 inhibitors
- In-vitro and in-vivo experiments with onvansertib as a single agent have shown a dose-dependent inhibition of CMML cell growth, with improved cell differentiation

Activating RAS Pathway Can Be Therapeutically Targeted with PLK1 Inhibitors



Phase 2 Two-Arm Randomized Trial of Onvansertib +/- Decitabine in RAS-Pathway Mutated CMML

Determine the safety and efficacy of onvansertib, a novel oral PLK1 inhibitor in RAS-pathway mutant chronic myelomonocytic leukemia

Trial Design:

	Dosing Schedule	Duration	Efficacy Endpoint
Two Arms: **Arm A (n=32) Treatment Naïve** **Arm B (n=32) Relapsed/Refractory**	Onvansertib 15 mg/m^2 Days 1-14 (21-day cycle)	3 cycles monotherapy (option to add decitabine at cycle 4 if lack of efficacy with single agent)	Interim analysis of first 18 patients after 3 cycles to evaluate objective response

Eligibility Criteria:

- Newly diagnosed or relapsed/refractory to prior therapy
- RAS pathway mutant: NRAS, KRAS, PTPN11, CBL and NF1 with frequency allele of ≥5%

Efficacy Endpoint:

- Rate of complete remission (CR)

What is Clinical Trial Success

- Achieve ≥25% CR rate in treatment naïve cohort
- Achieve ≥12.5% CR rate in the relapsed and refractory cohort

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 10/31/20)	$131.8M
Q1 – Q3, 2020 Average Quarterly Cash Burn	$3.8M
Headquarters	San Diego, CA

Investment Highlights

3rd Generation, 1st-in-class, Oral PLK1 Inhibitor

Onvansertib overcomes the shortcomings of prior PLK inhibitors:

- Highly selective for PLK1
- Orally administered
- 24-hour half-life
- Flexible dose and schedule

Specifically targets a known mechanism of cell division that is required for tumor cell viability

Preliminary clinical data demonstrate the safety, tolerability and efficacy of onvansertib in combination with SOC across multiple indications

Strong Lead Program in KRAS-mutated mCRC

Supported by compelling preliminary clinical data from a Phase 1b/2 trial showing a ten-fold improvement in ORR compared to SOC

Preclinical data support:

- MOA of synthetic lethality between KRAS mutant mCRC and PLK1 inhibition
- Synergy with irinotecan and 5-FU

First Indication: 2nd line treatment in patients who have failed 1st line treatment with FOLFOX with/without bevacizumab

FDA Fast Track Designation

Diversified Pipeline Across Numerous Cancers

Clinical data from ongoing trials support the use of onvansertib in combination regimens across numerous aggressive cancers:

- mCRC Phase 1b/2 trial
- mCRPC Phase 2 trial
- PDAC Phase 2 trial
- AML Phase 2 trial

Expansion opportunities:

- Chronic myelomonocytic leukemia
- Triple negative breast cancer
- Lung cancer
- Ovarian cancer

Integrated Biomarker Strategy

Circulating Tumor DNA: changes in KRAS mutational burden in blood are predictive of subsequent tumor shrinkage (mCRC)

Circulating Tumor Cells: changes are predictive of overcoming anti-androgen resistance (mCRPC)

Circulating Tumor DNA: changes are predictive of decreases in leukemic bone marrow cells (AML)

Cardiff Oncology™

PLK: Polo-like Kinase; SOC: Standard-of-care; ORR: Overall response rate; MOA: Mechanism of action; mCRC: metastatic colorectal cancer; mCRPC: metastatic castration resistant prostate cancer; PDAC: Pancreatic ductal adenocarcinoma; AML: Acute myeloid leukemia

Thank You

for more information contact:

ir@cardiffoncology.com