Taking a Precision Cancer Medicine Approach to Develop Oncology Drugs That Target Mitosis

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Strategy for Oncology Drug Development

- Taking a precision cancer medicine approach to develop Onvansertib, a first-in-class, 3rd generation PLK1 inhibitor
- Leveraging a proven cancer target, PLK1
- Incorporating predictive clinical biomarkers
- Combining Onvansertib with already approved drugs
  - Phase 1b/2 trial of Onvansertib + cytarabine or decitabine in Acute Myeloid Leukemia (AML)
  - Phase 2 trial of Onvansertib + abiraterone acetate (Zytiga®)/prednisone in metastatic Castration-Resistant Prostate Cancer (mCRPC)
  - Phase 1b/2 trial of Onvansertib + FOLFIRI and bevacizumab in metastatic Colorectal Cancer (mCRC)

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Onvansertib – Pipeline Within a Molecule
Opportunities in Leukemias/Lymphomas and Solid Tumors

	Preclinical	Phase 1	Phase 2
Leukemias & Lymphomas	Acute Myeloid Leukemia – Orphan Drug Designation in the U.S. and Europe *Phase 1b/2 trial in combination with low-dose cytarabine (LDAC) or decitabine*		
	Metastatic Castration-Resistant Prostate *Phase 2 trial in combination with Zytiga® (abiraterone acetate)/prednisone*		
Solid Tumor Cancers	Colorectal (CRC)		
	Lung		
	Ovarian		
	Others (adrenocortical, sarcomas, head and neck, skin, liver, pancreatic, ampullary)		
	Triple Negative Breast		

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Licensed Drug Candidate from NMS
Onvansertib – Polo-like Kinase 1 (PLK1) Inhibitor

NERVIANO MEDICAL SCIENCES

Oncology Drug Discovery

- Largest oncology research and development company in Italy
- Developed anthracycline class of drugs (doxorubicin)
- Leader in protein kinase drug development (Polo-like Kinase Inhibitors)
- Identification and validation of molecular targets focused on driver oncogenes
- Excellent track record licensing innovative drugs to pharma/biotech companies including: Genentech (Roche), Ignyta (Roche), Novartis

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Developing Oncology Drugs That Target Mitosis

- Licensed global development and commercialization rights for Onvansertib
- Nerviano will continue manufacturing GMP API and finished drug
- Two active INDs in place with the FDA
- Financing in place to advance clinical programs into mid-2019

IND = Investigational New Drug

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Nerviano Oncology Portfolio Success

- Excellent track record licensing innovative drugs to pharma/biotech companies that have subsequently received FDA breakthrough status and priority review designation

Licensed	Preclinical	Phase 1	Phase 2	Phase 3	Registered
ARRAY BIOPHARMA	Encorafenib (B-RAF IP) Melanoma Braf mutation in combination with binimetinib				
Roche ignyta	Entrectinib (TRK, ROS, ALK) Non-Small Cell Lung				
tiziana LIFE SCIENCES	Milciclib (CDK, other kinases) Thymic Cancer				
trovagene	Onvansertib (PLK1 inhibitor) AML and mCRPC				
SERVIER Oncology	MPS1 Inhibitor Solid Tumors				
Genentech A Member of the Roche Group	ADC (PNU-652)				
OXFORD BioTherapeutics	ADC (NMS-P945)				

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Leveraging a Proven Cancer Target

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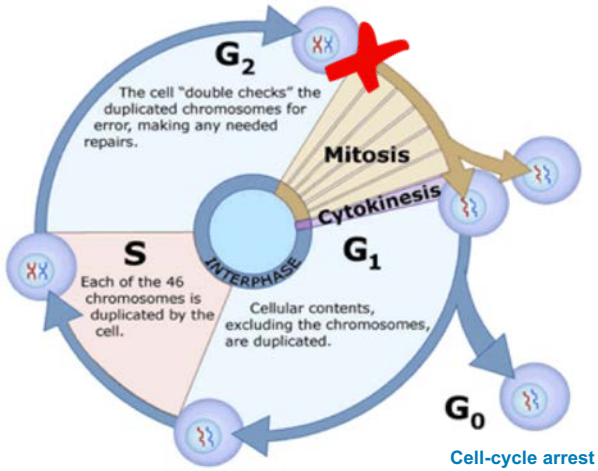
PLK1 – Established Target for Cancer Therapy

PLK1 Plays a Critical Role in Initiation, Maintenance and Completion of Mitosis



- Polo-like Kinase 1 (PLK1)
  - Belongs to a family of kinases (PLK1,2,3,4,5)
  - Dysfunction leads to cancer formation and progression
  - Over-expressed in dividing cancer cells
  - Inhibition leads to cancer cell death

[1]Liu et al- PLK1, A Potential Target for Cancer Therapy; Translational Oncology – Vol. 10 – pp. 22-32; February 2017

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PLK1 – Over-Expressed in Multiple Cancers

Publications

Over-Expression of PLK1 Observed in Numerous Cancers[1]	
Tumor Type	**PLK1 Fold Change Over-Expression**
AML	13.0
B-cell Lymphoma	56.3
Prostate	3.3
Adrenocortical	4.5
Lung Adeno	9.7
Lung Squamous	20.8
Breast	11.3
Esophageal	10.2
Stomach	4.8
Colon	2.5
Head & Neck	4.2
Pancreatic	2.2
Ovarian	31.7
Glioblastoma	12.4
Kidney	4.7
Liver	11.7
Uterine	21.3
Bladder	9.1

[1]Liu et al- PLK1, A Potential Target for Cancer Therapy; Translational Oncology – Vol. 10 – pp. 22-32; February 2017

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Developing Onvansertib First-in-Class 3rd Generation PLK1

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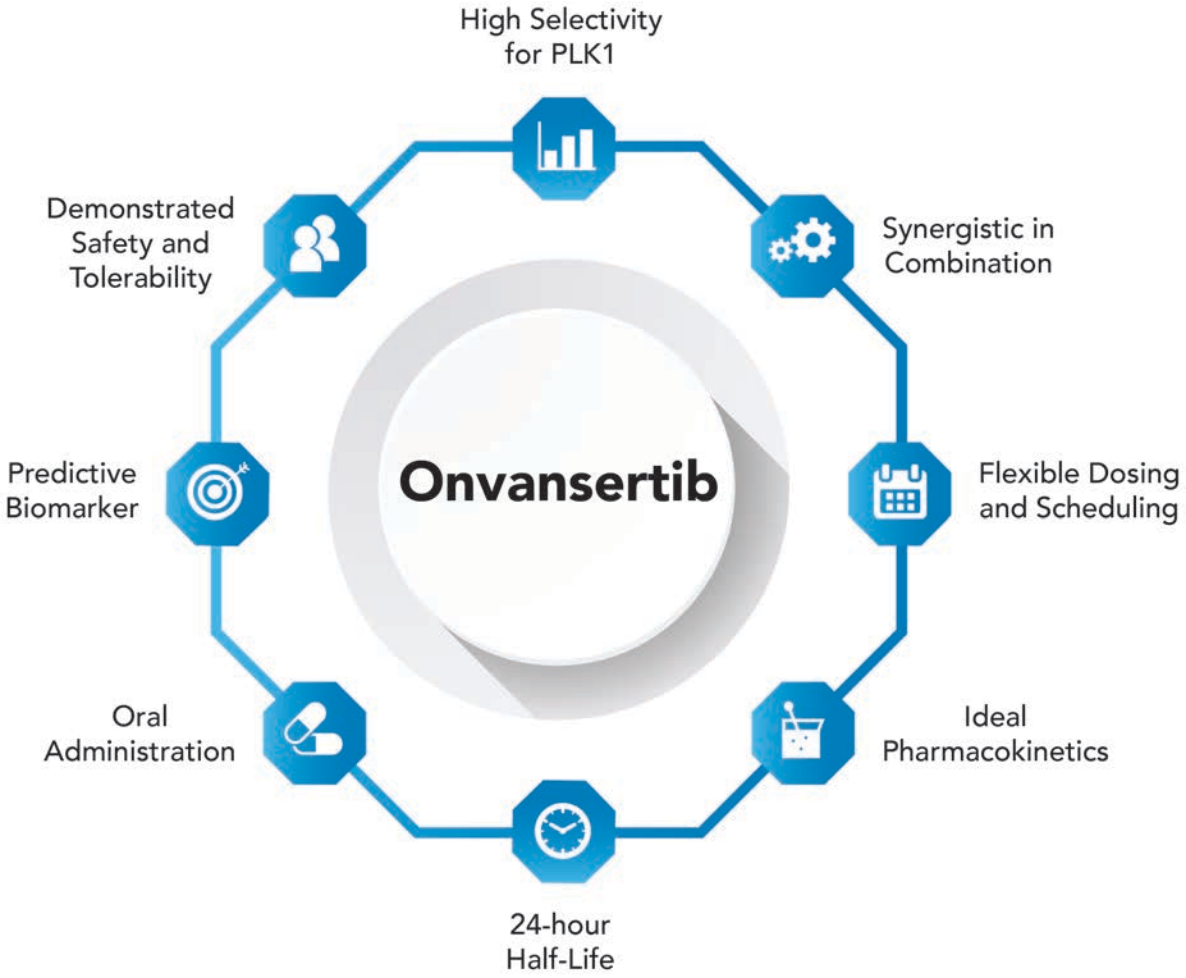
Onvansertib First-in-Class 3rd Generation PLK1
Best-in-Class Attributes



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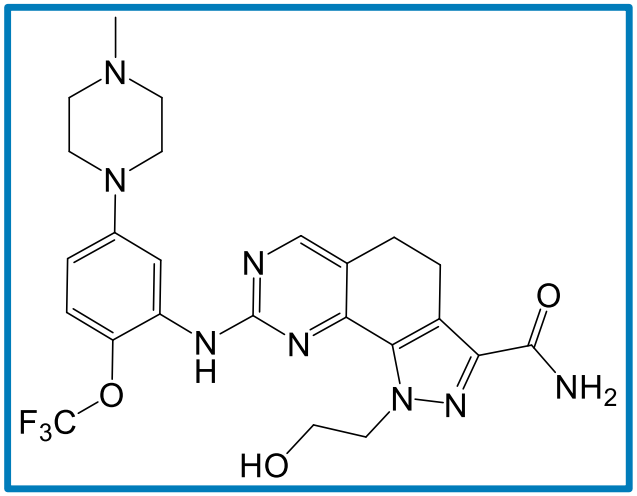
Onvansertib Intellectual Property

- Four worldwide patent families
  - Genus, Compound, Combinations, Salt
- Mature portfolio
  - Granted in most major jurisdictions
- Patent term 2030 plus up to 5 years extension



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Onvansertib – Highly-Selective Only for PLK1

Selective PLK1 Inhibitor

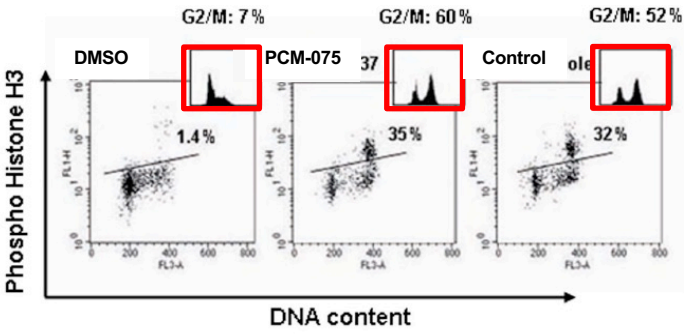
- Tested against >260 kinases
- PLK1 was the only active target (IC_{50} of 2nM)

PLK Member	Onvansertib IC50* (μM)
PLK1	0.002
PLK2	> 10
PLK3	> 10

Causes cancer cell death by G_2M arrest

- Onvansertib blocks cell division (mitosis)

AML-NS8 Patient-Derived Cells Treated with 200 nM Onvansertib for 24 Hrs[1]



[1]Data on File, Trovagene, Inc.

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Onvansertib Phase 1 Safety Trial[1]
Favorable First-in-Human Data

Phase 1 Dose Escalation Trial in Patients with Advanced or Metastatic Solid Tumors

Trial Design

Open-label dose escalation to assess safety and identify Phase 2 dose

19 patients administered Onvansertib orally, once daily for 5 consecutive days, every 21-days

Solid Tumors: colorectal, pancreatic, lung, sarcomas, hepatocellular, ampullary, prostate, ovarian, skin

Trial Results

1. Established safety and identified Phase 2 dose of 24 mg/m^2/day
2. 16 patients evaluable with 30% stable disease
3. Only mild to moderate side effects
4. No GI disorders, mucositis, or hair loss

[1]Weiss G et al., Phase I dose escalation study of NMS-1286937, an orally available Polo-like Kinase 1 inhibitor, in patients with advanced or metastatic solid tumors – Invest. New Drugs DOI 10.1007/s10637-017-0491-7

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Benefiting From Drug Class Experience

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Drawbacks Associated with 1st and 2nd Generation PLK Inhibitors

- Prior PLK inhibitors in development demonstrated significant clinical activity in combination with standard-of-care chemotherapy in AML
- Major drawbacks, unrelated to efficacy of the drug class, resulted in discontinuation of development

Non-Selective	panPLK inhibitors targeting both normal and tumor cells
Significant Toxicities	Serious adverse effects that are non-mechanism based
Sub-Optimal PK	Intravenous formulation; relatively long half-life
No Dosing/Schedule Flexibility	Fixed dose; no option to increase time between treatment
Lethal Infections	No mandated anti-infective prophylaxis
No Biomarker Strategy	Inability to identify patients most likely to respond

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Onvansertib – First-in-Class, 3rd Generation PLK1
Addresses Drawbacks of 1st and 2nd Generation

- Onvansertib product profile and clinical development program effectively addresses drawbacks associated with 1st and 2nd generation PLK inhibitors

Highly-Selective	Selective only for PLK1 which is overexpressed in tumor cells
Safe and Well Tolerated	Only mild to moderate side effects reported
Ideal PK Properties	Orally administered and relatively short half-life of ~24 hours
Dosing and Treatment Schedule Flexibility	Dose individualized to patients based on weight and body surface area; flexibility to increase time between treatment
Proactive Infection Management	Protocol mandated prophylactic anti-infectives for all patients
Biomarker Strategy	Ability to identify patients most likely to respond to therapy

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Combination Therapy Approach

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Onvansertib Combination Therapy Strategy

- Cornerstone of precision cancer medicine
- Onvansertib has demonstrated synergy with chemotherapies and targeted therapeutics
- Enhances efficacy (targets key pathways by synergy or additive effect)
- Reduces drug resistance, while providing therapeutic benefits

[1]Mokhtari, R et al - Combination Therapy in Combatting Cancer – Oncotarget, 2017, Vol. 8 (No. 23), pp: 38022-38043

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Onvansertib – Synergistic in Combination

- High PLK1 expression is associated with the most aggressive cancers
- Synergistic activity may enhance efficacy of standard-of-care therapies

Potentially Synergistic Drugs[1,2]
Abiraterone acetate
Bevacizumab
Bortezomib
Cisplatin
Cytarabine
Doxorubicin
FLT3 Inhibitors (Quizartinib)
Gemcitabine
HDAC Inhibitors (Belinostat)
Paclitaxel

Associated Cancers[2]
Leukemias/Lymphomas:
• Acute Myeloid Leukemia • Acute Lymphocytic Leukemia • Non-Hodgkin Leukemia • Multiple Myeloma
Solid Tumor Cancers:
• Castration-Resistant Prostate • Adrenocortical Carcinoma • Triple Negative Breast • Sarcomas • Small Cell Lung • Colon

[1]Alphabetical order. [2]Preclinical data on file with PCM-075 and these combined therapeutics

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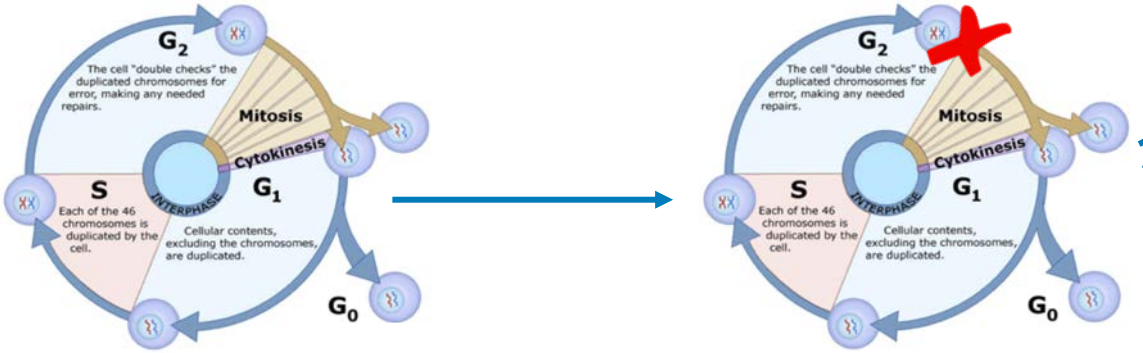
Onvansertib Rationale for Combination with DNA Damaging Agents[1,2]

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

G2/M Arrest



Mitosis

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

Active PLK1

PLK1 Inhibited

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

DNA Damaging Agents

- Cytarabine
- Doxorubicin
- Cisplatin

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

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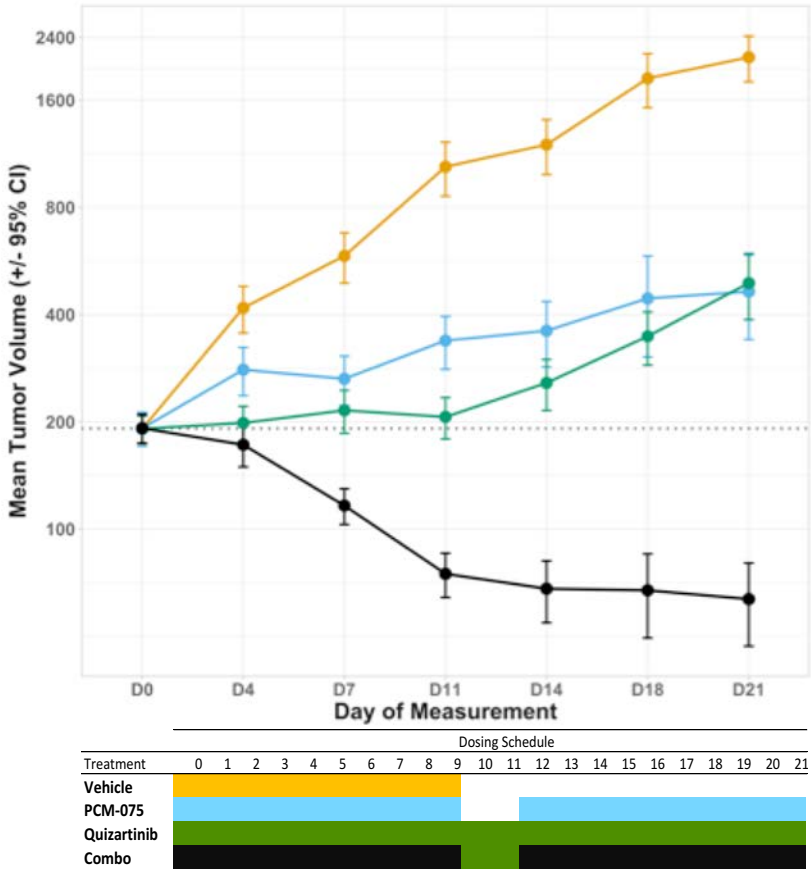
Onvansertib (PCM-075) + FLT3 Inhibitor
Acute Myeloid Leukemia (AML)

- 30% of AML patients have a FLT3 mutation[1]
- Quizartinib in Phase 3 clinical development[2]
- Combination of PCM-075 + quizartinib demonstrated:
  - 97% tumor growth inhibition
  - Regression in FLT3 AML xenograft model[3]

Evaluation of Efficacy of PCM-075 for MV-4-11 Human Acute Myeloid Leukemia (AML) Xenograft Model in NOD.SCID Mice



[1]Kindler et al, Blood 2010; 116:5089-10. [2]Stone et al, N Engl J Med 2017; 377:454-64. [3]Data on File at Trovagene, Inc.

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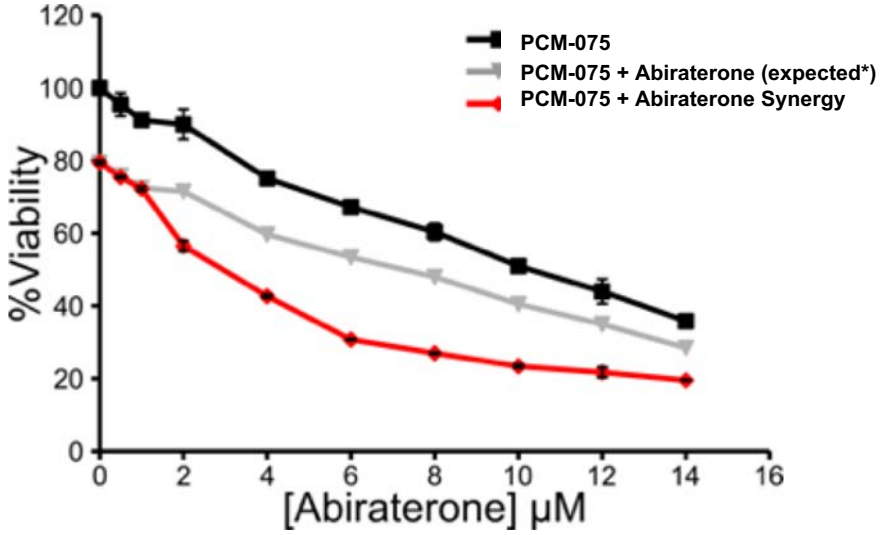
Onvansertib (PCM-075) + Abiraterone
Metastatic Castration-Resistant Prostate Cancer

- PCM-075 + abiraterone demonstrated synergy[1]
- Combination enhances PCM-075 mechanism of action[1]
- Medical need to increase duration of response to anti-androgen drugs

C4-2 Castration-Resistant Prostate Cancer Cells Increased Sensitivity to Abiraterone in the Presence of PCM-075



*Expected = the calculated value of the effect of the addition of each drug as calculated by Michael Yaffe, MD - MIT

[1]Yaffe, Michael, MD and Trovagene, 2017

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Onvansertib (PCM-075) Clinical Development

Phase 1b/2 Acute Myeloid Leukemia (AML)

Phase 2 metastatic Castration-Resistant Prostate Cancer (mCRPC)

Phase 2 metastatic Colorectal Cancer (mCRC)

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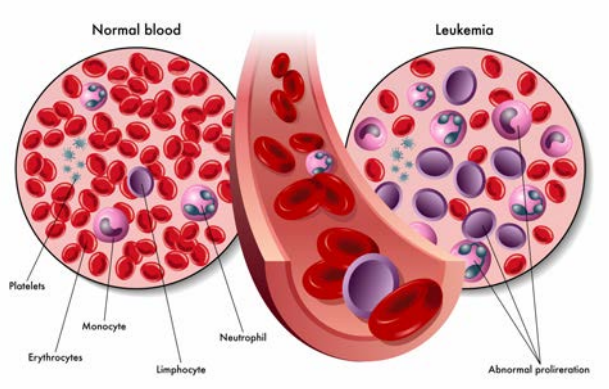
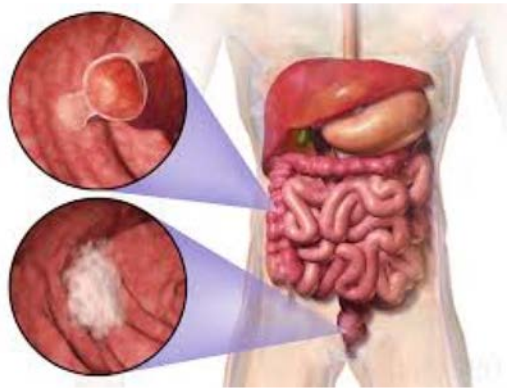
Clinical Development Roadmap

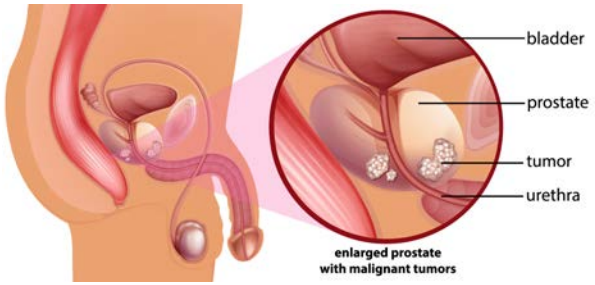
Acute Myeloid Leukemia



Colorectal Cancer



Prostate Cancer



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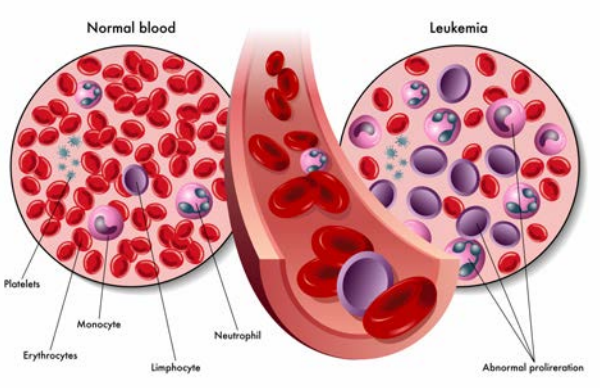
Acute Myeloid Leukemia[1]
Significant Need for New Treatment Options

- Aggressive hematologic malignancy of immature blood cells
- 20,000 new cases, 10,400 deaths annually, and 5 year survival rate of 25%
- Treatment options vary based on patient condition / age, but can include:
  - Chemotherapy / Radiation / Stem Cell Transplant
- Preclinical *in-vitro* and *in-vivo* data demonstrate efficacy of Onvansertib* as single agent and in combination with drugs used to treat AML

Acute Myeloid Leukemia



*Orphan Drug Designation granted for Onvansertib by the FDA September, 2017 and by the EMA in July, 2018 ;[1]National Cancer Institute SEER 2016; [2]Valsasina et al., Mol Cancer Ther; 11(4) April 2012

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AML Clinical Development Landscape[1]
Medical Need for New Therapeutic Options

- The majority of therapeutic advances for AML have not come from the introduction of novel therapeutics but instead from optimizing use of older drugs[2]
- With increased understanding of the molecular pathogenesis of AML in recent years there is a significant opportunity to introduce new targeted therapeutics[2]

Significant Opportunity for New Therapeutic Options

Company	Market Cap	Drug	Combination	Development
trovagene	$15M	Onvansertib (PLK1 inhibitor)	Cytarabine / Decitabine	Phase 1b/2
cti BIOPHARMA	$104M	Tosedosat (aminopeptidase activity inhibitor)	Cytrabine / 5-Azacytadine	Phase 1/2
AVEO ONCOLOGY	$288M	Ficlatuzumab (antibody targeting HGF)	Cytarabine	Phase 1
agios	$4.5B	Tibsovo (IDH1Inhibitor) AG-221 (IDH2 Inhibitor)	Single Agent Single Agent	FDA Approved Phase 1/2

[1]www.clinicaltrials.gov; [2]www.hematology.org/Thehematologist/Years-Best/8155.aspx

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Onvansertib (PCM-075) Scientific Rationale
Clinical Development in AML

- ***in-vitro* studies**[1]
  - High sensitivity of hematological tumor cell lines to PCM-075
- ***in-vitro and in-vivo* mode of action (MoA) studies**[2]
  - Xenograft model demonstrates dose dependent inhibition of PLK1 activity and G2/M arrest
- ***in-vivo* efficacy in AML xenograft models**[2]
  - Dose dependent efficacy of PCM-075 in
    - HL60 promyelocytic leukemia xenograft
    - Disseminated AML patient derived xenografts (AML-PS)
  - Combination of PCM-075 + cytarabine has greater survival than either agent alone (AML-PS)

[1]Source: Report No. N-0018670 Antiproliferative activity of NMS-1286937 in a panel of cell lines;[2]Valsasina et al., Mol Cancer Ther; 11(4) April 2012; [3]ClinicalTrials.gov, NCT03303339: PCM-075 in Combination With Either Low-dose Cytarabine or Decitabine in Adult Patients With Acute Myeloid Leukemia (AML) - Data-on-file, Trovagene 2018

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Orphan Drug Designation (ODD) in AML

- In the U.S. and Europe
- Regulatory and Financial Incentives
- Extended Market Exclusivity

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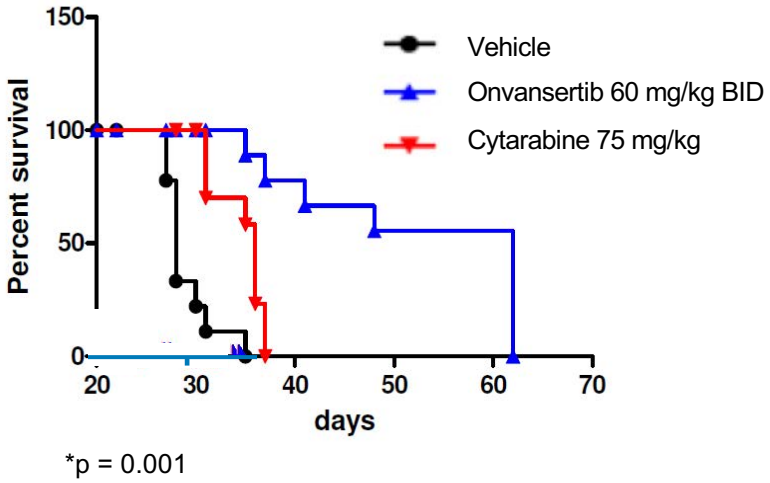
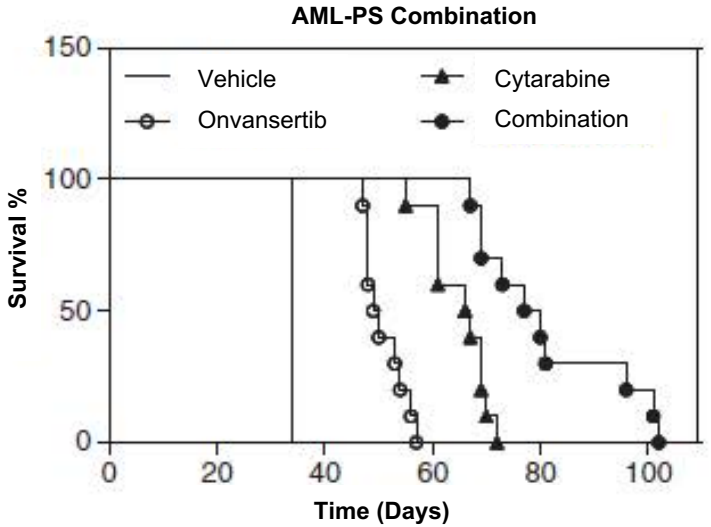
Onvansertib Comparative and Combination with Cytarabine in AML Models[1,2]

In Vivo Disseminated Leukemia Models



*p = 0.001

- Onvansertib 60 mg/kg BID (Days 1-2 with 5-day rest) + cytarabine 75 mg/kg IP Injection (Days 1-5 with 5-day rest)
- Onvansertib 120 mg/kg for 2 days repeated for 4 cycles with a 10-day rest



- Onvansertib 120 mg/kg for 2 days repeated for 4 cycles with a 10-day rest
- Cytarabine IP at 75mg/kg for 5 cycles of 5 consecutive days with 7-day rest
- The combination was given at the same schedule, doses, and routes of the single agents

- Onvansertib + cytarabine in combination showed increased survival compared to either agent alone

[1]Casolaro et al. (2013) PLOS One 8(3); [2]Valsasina et al. (2012), Mol Cancer Ther 11(4)

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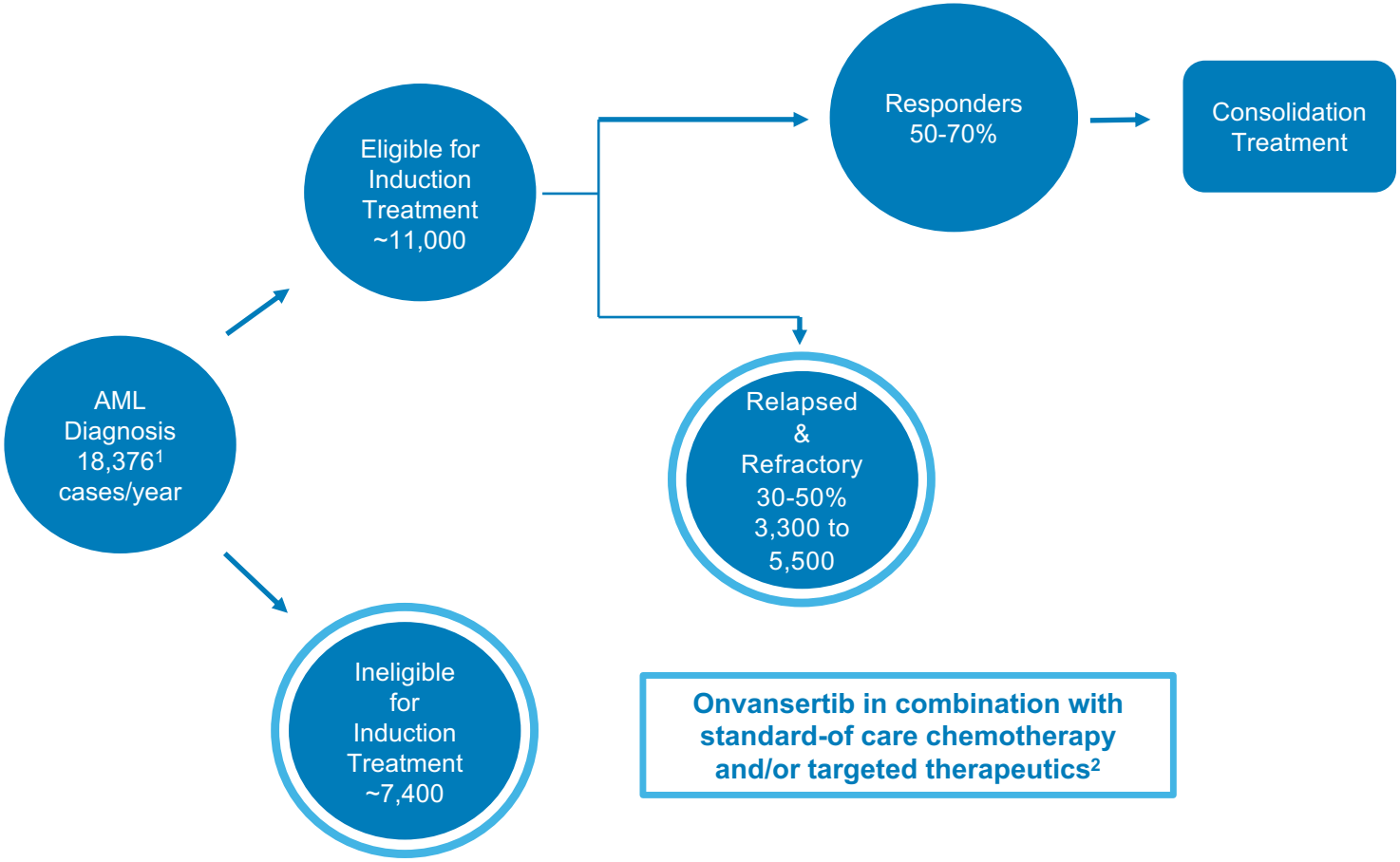
Onvansertib Positioning in AML
Patient Selection Algorithm



[1]Visser et al. (2012), Eur J Cancer (48). Estimated cases in EU27 per year; [2]e.g. Midostaurin for FLT3 mutation

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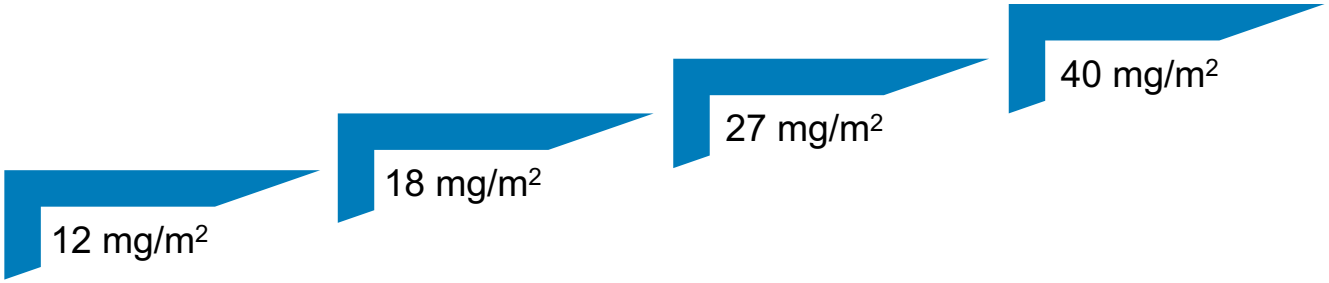
Ongoing Phase 1b/2 Clinical Trial in AML

Onvansertib in Combination with Either Low-Dose Cytarabine or Decitabine in Patients with Acute Myeloid Leukemia (AML)

Phase 1b: Dose escalation to assess safety and identify recommended Phase 2 dose



- Administered orally, once daily on days 1-5 of each cycle (21-28 days)

Phase 2: Assess safety and preliminary antitumor activity

- **Efficacy Endpoints:** Rate of complete response (CR + CRi) defined as morphologic leukemia-free state (MLF)
- **Exploratory Endpoints:** Evaluation of pharmacodynamic and correlative biomarkers

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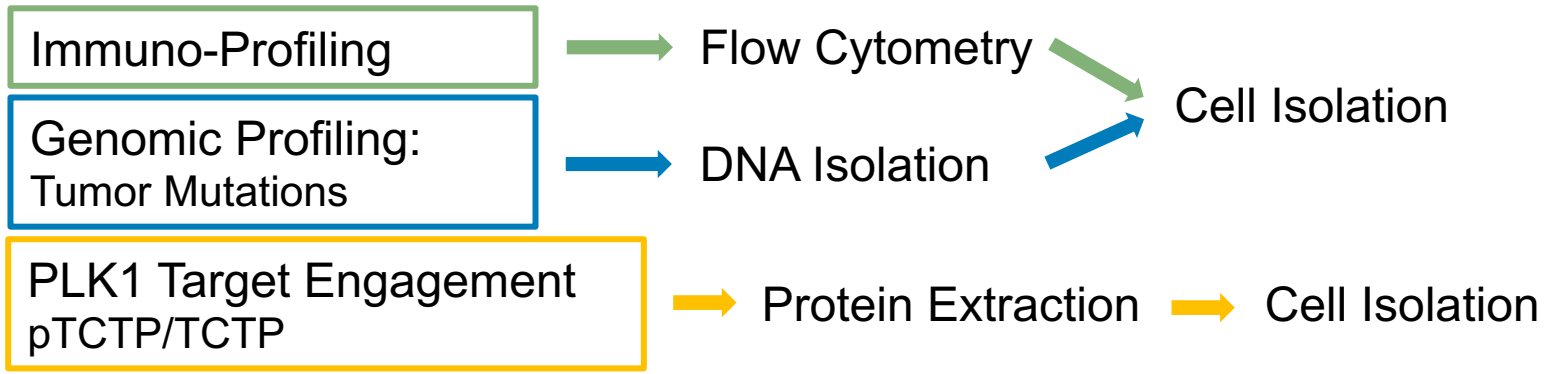
Biomarker Strategy in AML

- Biomarkers will be measured and correlated with pharmacokinetic drug levels to assess:
  - Treatment effects by measuring % blast cells in blood and bone marrow
  - Inhibition of PLK1 by Onvansertib (Target Engagement)
  - Correlating underlying tumor genetics with treatment response



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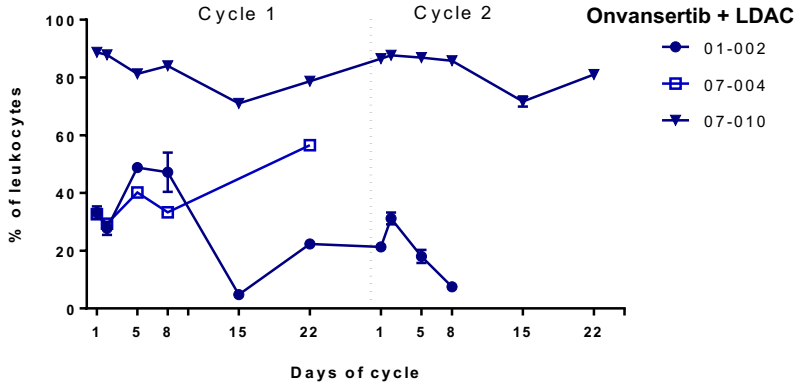
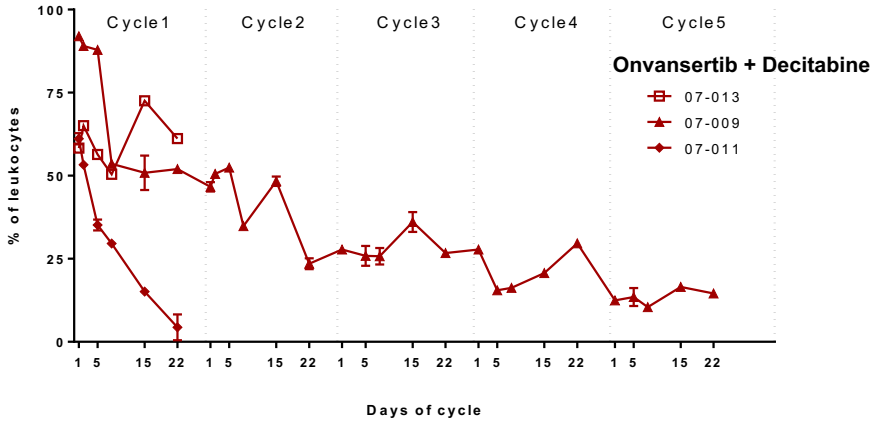
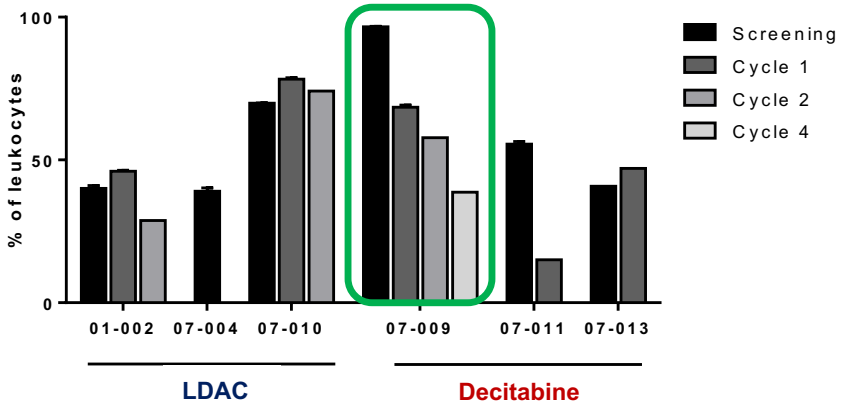
Immuno-Profiling: Monitoring Leukemic Blast Cells in Response to Treatment

% of Leukemic Cells in Blood

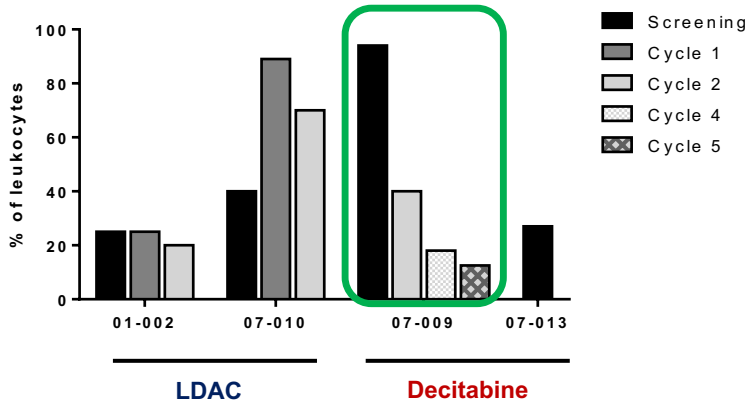




%Leukemic Cells in Bone Marrow (Trovagene analysis)



%Leukemic Cells in Bone Marrow (Clinical site analysis)



[1]NCT03303339, ClinicalTrials.gov; "Onvansertib in Combination With Either Low-dose Cytarabine or Decitabine in Adult Patients With Acute Myeloid Leukemia (AML)

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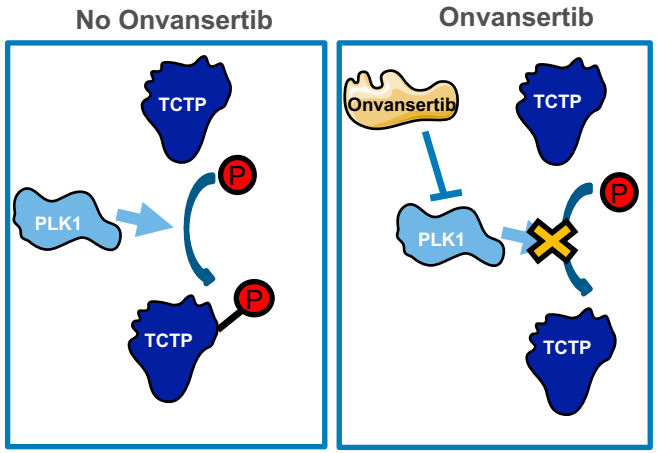
Target Engagement:
Monitoring PLK1 Inhibition Upon Treatment

The Translational Control Tumor Protein (TCTP) Identified as Specific Marker for PLK1 Activity In-Vivo[1]



- Onvansertib inhibits PLK1 kinase activity resulting in reduction in PLK1 substrates phosphorylation; Translational Control Tumor Protein (TCTP) is phosphorylated by PLK1

- PLK1 inhibition was assessed 3-hours following administration of Onvansertib at peak concentration (C_{max})

[1]Cusshi U. et al, Phosphorylation of TCTP as a Marker for Polo-like Kinase 1 Activity In Vivo – Anticancer Research December 2010 vol. 30 no. 12 pp. 4973-4985

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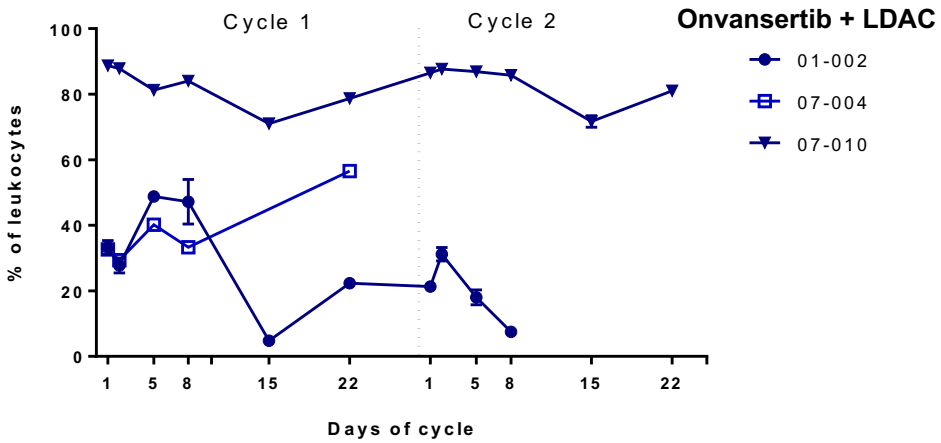
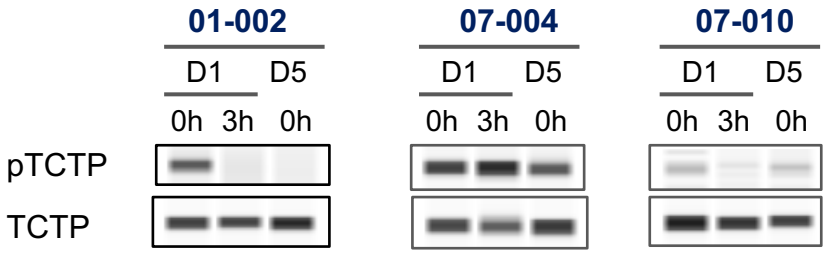
Correlation of Target Engagement and Treatment Response

% of Leukemic Cells in Blood

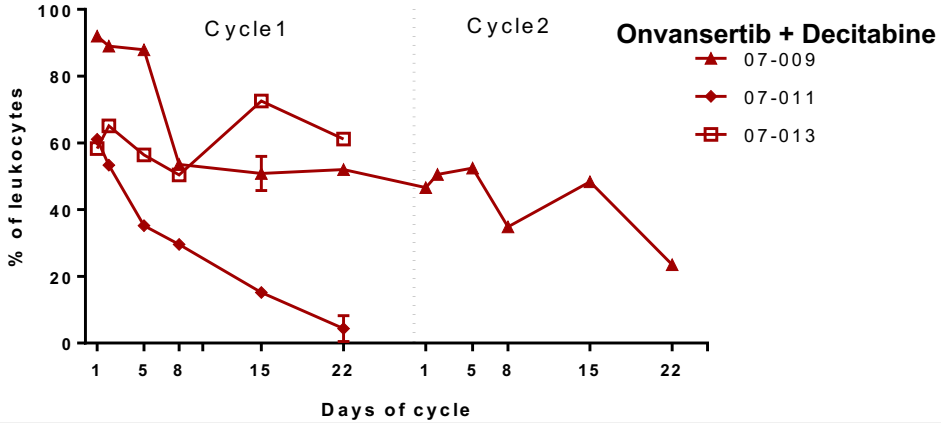


pTCTP status as a surrogate for PLK1 inhibition

Onvansertib 12mg/m^2 + LDAC

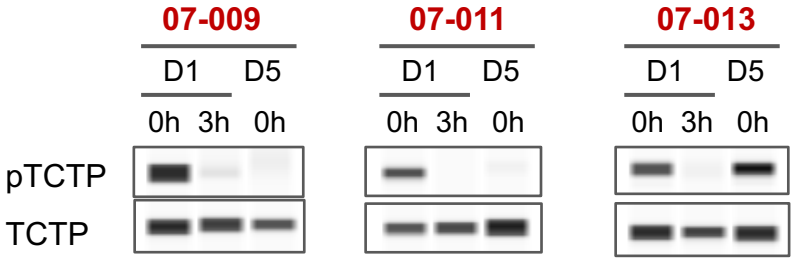


% of Leukemic Cells in Blood



pTCTP status as a surrogate for PLK1 inhibition

Onvansertib 12mg/m^2 + Decitabine



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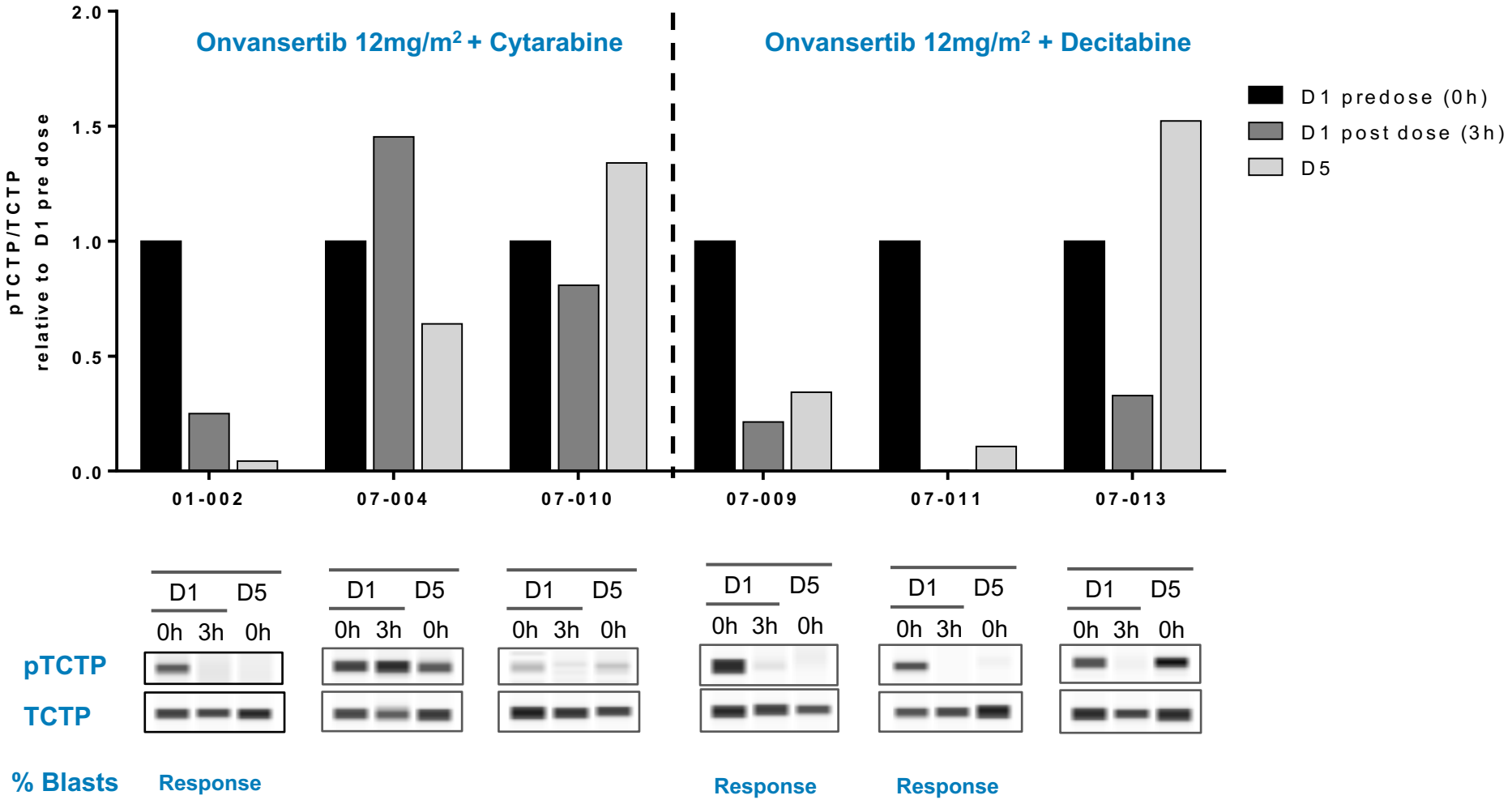
Summary of Target Engagement and Correlation to Treatment Response



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Predictive Response Strategy

Evaluating Patient Responsiveness to Onvansertib[1]

AML Patient

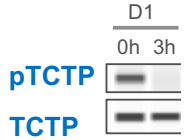
Pre-dose

Patient receives single dose Onvansertib

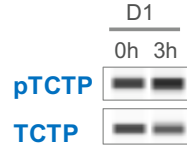
Assess target engagement of PLK1 by Onvansertib

3hr post-dose

Target Engagement Eligible Patient



NO Target Engagement Non-Eligible Patient



[1]Trovagene Patent Pending – PLK1 Target Phosphorylation Status and Treatment of Cancer with PLK1 Inhibitors

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Molecular Profiling and Patient Response in AML[1]

AML Genomic Subgroup	Frequency of Patients	Most Frequently Mutated Genes (%)	DNA Panel	RNA Panel
NPM1 mutation	27%	NPM1(100), DNMT3A(54), FLT3(39), NRAS(19), TET2(16), PTPN11(15)	X	
Mutated chromatin, RNA-splicing genes, or both	18%	RUNX1(39), MLLPTD(25), SRSF2(22), DNMT3A(20), ASXL1(17), STAG2(16), NRAS(16),TET2(15),FLT3ITD(15)	X	
TP53mutations, chromosomal aneuploidy, or both	13%	Complex karyotope(68), -5/5q(47), -7/7q(44), TP53(44), -17/17p(31), +8/8q(16)	X	X
inv(16)(p13.1q22) or t(16;16)(p13.1;q22);CBFB-MYH11	5%	inv(16) (100), NRAS(53), +8/8q(16), KIT(15), FLT3TKD(15)	X	X
biallelic CEBPA mutations	4%	CEBPAbiallelic(100), NRAS(30), WT1(21), GATA2(20)	X	
t(15;17)(q22;q12); PML-RARA	4%	t(15;17) (100), FLT3 ITD(35), WT1(17)	X	X
t(8;21)(q22;q22); RUNX1-RUNX1T1	4%	t(8;21) (100), KIT(38), -Y(33), -9q(18)	X	X
MLL fusion genes; t(x;11)(x;q23)	3%	t(x;11q23) (100), NRAS(23)	X	X
inv(3)(q21q26.2) or t(3;3)(q21;q26.2); GATA2,MECOM(EVI1)	1%	inv(3) (100), -7(85), KRAS(30), NRAS(30), PTPN11(30), ETV6(15), PHF6(15), SF3B1(15)	X	X
IDH2R172 mutations and no other class-defining lesions	1%	IDH2R172(100), DNMT3A(67), +8/8q(17)	X	
t(6;9)(p23;q34); DEK-NUP214	1%	t(6;9) (100), FLT3ITD(80), KRAS(20)	X	X

[1]Papaemmanuil et al. Genomic classification and prognosis in acute myeloid leukemia; NEJM 2016;374:2209-2221

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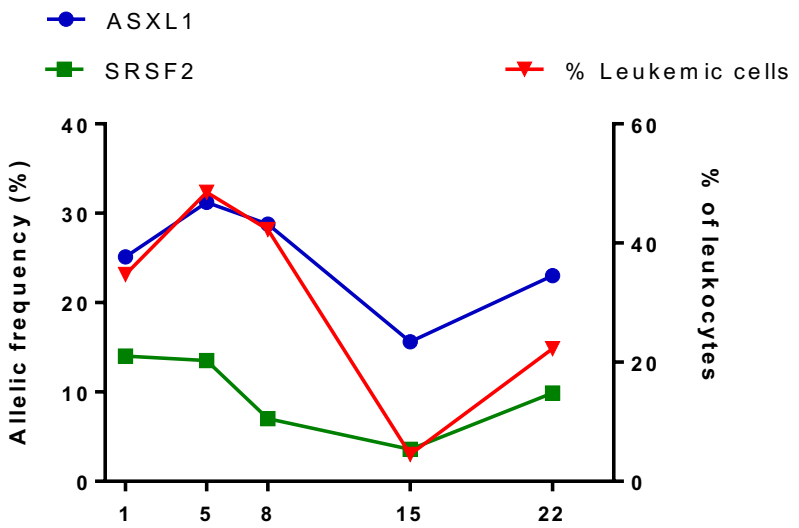
Genomic Profiling: Correlation of Mutation Detected in Blood and % Leukemic Cells

Patient	Mutations detected
01-002	ASXL1 c.1926_1927insG p.G646fs*12 SRSF2 c.284C>G p.P95R
07-004	TP53 c.955 A>T p.Lys319Ter
07-010	SRSF2 c.284C>G p.Pro95Arg RUNX1 c.511G>A p.Asp171Asn RUNX1 c.250A>C p.Thr84Pro TET2 c.3633T>A p.Cys1211Ter
07-009	SF3B1 c.1998G>T p.Lys666Asn FLT3 c.250G>T p.Asp835Tyr RUNX1 c.984_985delAG p.Ala329fs GATA2 c.829A>G p.Ser277Gly
07-011	TP53 c.773A>C p.Glu258Ala
07-013	PHF6 c.955C>T p.Arg319Ter GATA2 c.962T>C p.Leu321Pro

Mutations allelic frequencies and leukemic cells level in blood samples of patient 01-002



- Genomic analysis was performed on bone marrow and blood samples
- Mutations detected in bone marrow and blood were identical for all patients examined
- The mutation allelic frequencies detected in blood correlates with % of circulating leukemic cells

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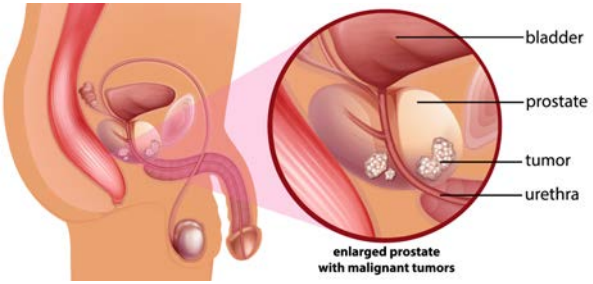
Metastatic Castration-Resistant Prostate Cancer
Opportunity to Increase Duration of Response to Therapy

- 25,000 men die from metastatic prostate cancer annually and the five-year survival rate is 37%[2]
- Treatments
  - Zytiga® (Johnson & Johnson)/prednisone
  - Xtandi® (Astellas/Pfizer)
- Ongoing need to increase duration of response to treatment
  - Patients develop resistance within 9-15 months[4] and do not respond well to subsequent therapies
- Preclinical studies demonstrate synergy between Onvansertib and Zytiga®
  - PLK1 inhibition improves abiraterone efficacy by repressing the androgen signaling pathway[3,4]

Prostate Cancer



[1]2017 Annual Report on Prostate Disease – Harvard Health Publications; [2]GlobalData. Prostate Cancer—Global Drug Forecast and Market Analysis to 2023. Apr, 2015; [3] National Cancer Institute Metastatic cancer. Mar, 2013. Available at: http://www.cancer.gov/about-cancer/what-is-cancer/metastatic-fact-sheet; [4]GAntonarakis, Emmannel – Current Understanding of Resistance to Abiraterone and Enzalutamide in Advanced Prostate Cancer; Clinical Advances in Hematology & Oncology – May 2016 – Volume 14, Issue 5

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PLK1 and Abiraterone Acetate (Zytiga®)
Metastatic Castration-Resistant Prostate Cancer (mCRPC)

- All metastatic prostate cancer patients become castration-resistant
- PLK1 dependent microtubule dynamics promotes androgen receptor (AR) signaling[1,2]
- PLK1 inhibition improves abiraterone efficacy[3]
- Inhibition of PLK1 represses androgen signaling pathway[4]
- PLK1 inhibitors may add important therapeutic benefit for the treatment of castration-resistant prostate cancer patients[5]

[1]Xianzeng, Hou, Zhiguo, Li – PLK1-Dependent Microtubule Dynamics Promotes Androgen Receptor Signaling in Prostate Cancer; Prostate. 2013 September; 73(12): 1352–1363. doi:10.1002/pros.22683; [2] Arpaporn, Deeraksa, Jing, Pan - Plk1 is upregulated in androgen-insensitive prostate cancer cells and its inhibition leads to necroptosis; Oncogene. 2013 June 13; 32(24): 2973–2983. doi:10.1038/onc.2012.309; [3]Clemens, Thoma – Prostate Cancer: PLK-1 Inhibition Improves Abiraterone Efficacy; Nature Reviews Urology volume11, page603 (2014); [4]Zhang Z1, Chen L – Inhibition of PLK1 Represses Androgen Signaling Pathway in Castration-Resistant Prostate Cancer; Cell Cycle. 2015;14(13):2142-8. doi: 10.1080/15384101.2015.1041689; [5]Klaus, Strebhardt - Drugging Plk1: An attractive approach to inhibit androgen receptor signaling; Cell Cycle. 2015 Jul 18; 14(14): 2193–2194

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Ongoing Phase 2 Clinical Trial in mCRPC

Onvansertib in Combination with Zytiga® and Prednisone in Patients with Metastatic Castration-Resistant Prostate Cancer (mCRPC)

Dosing Regimen	Duration	Evaluation
Onvansertib – 24 mg/m^2 Days 1-5 (21-Day Cycle) + Zytiga®/prednisone daily	4 Cycles = 12 Weeks	Disease Control based on PSA level

Efficacy Endpoints

Effect of Onvansertib in combination with Zytiga®/prednisone on disease control assessed by prostate-specific antigen (PSA) decline or stabilization pre- and post-treatment

Safety Endpoint

Safety of Onvansertib in combination with Zytiga®/prednisone

Exploratory Endpoint

Target inhibition of PLK1, evaluation of relevant biomarkers and correlation with patient response and genomic profile

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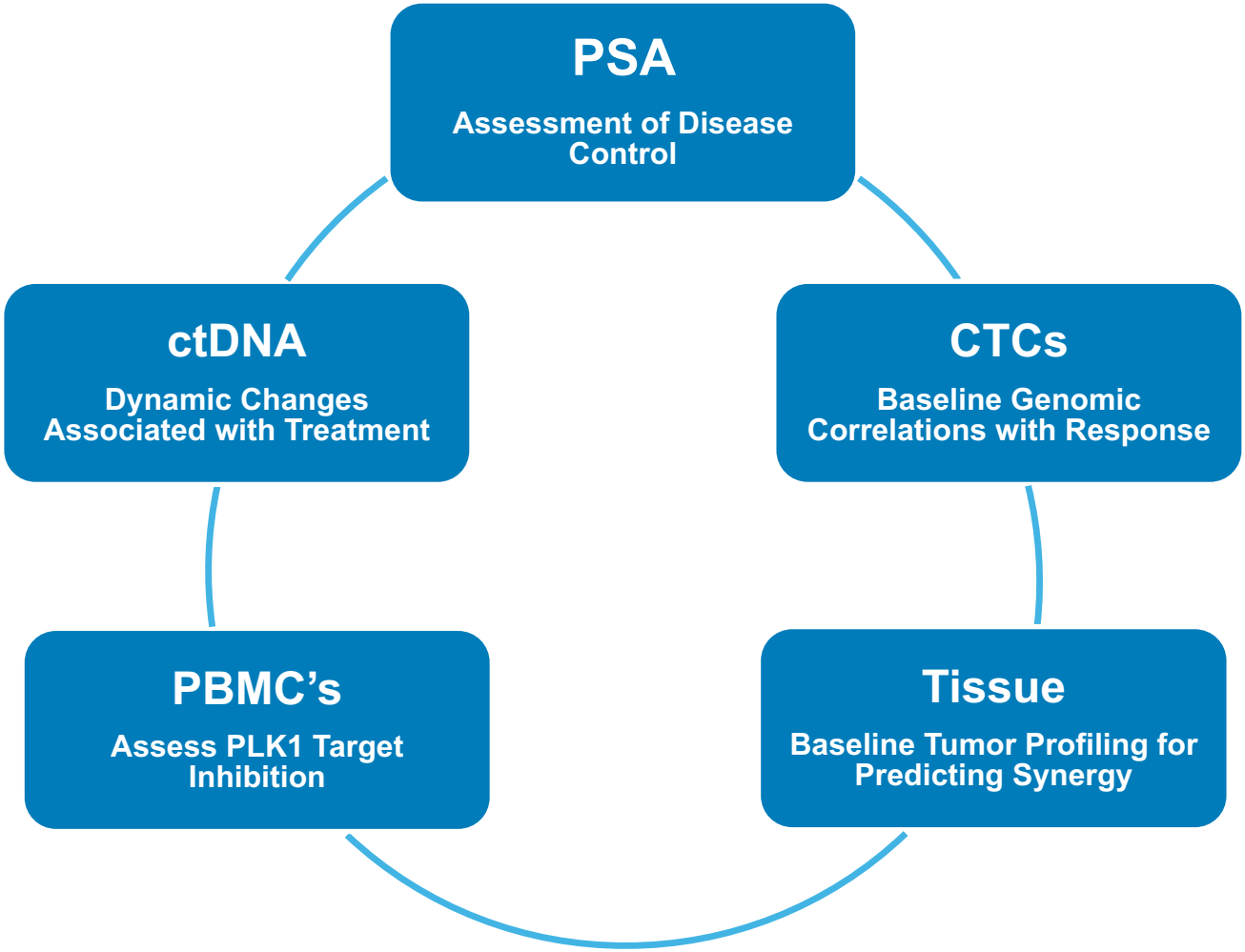
Biomarker Strategy in mCRPC



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PSA: NCCN Recommended Biomarker
Trial Eligibility and Efficacy for mCRPC[1]

- PSA is a validated biomarker assessing disease stability or progression
- Prostate Cancer Clinical Trials Working Group (PCWG)[1] has set criteria for the use of blood PSA levels:
  - Trial eligibility (defining progression)
  - Initial assessment of efficacy

[1]PCWG2: Sher et al, JCO, 2008, PCWG3: Sher et al, JCO, 2016

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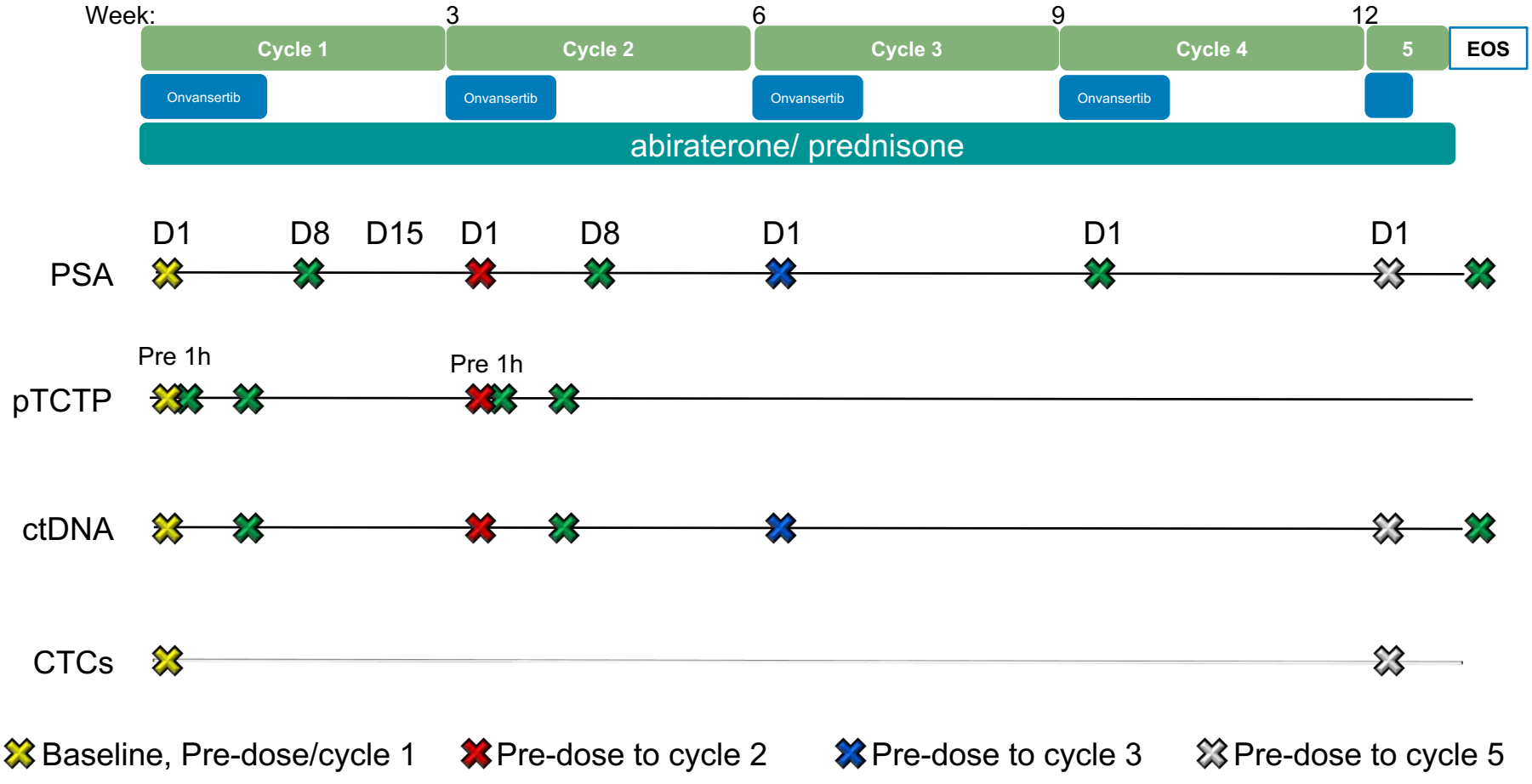
Biomarker Assessment Schedule



- Primary Endpoint: Proportion of patients achieving disease control after 12 weeks of study treatment, as defined by lack of PSA progression

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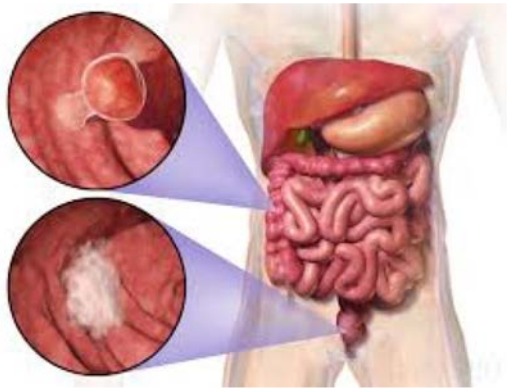
Colorectal Cancer: Unmet need in mCRC

- 140K new cases of CRC in 2018 with 64.5% 5 year survival[1]
  - ~51K deaths per year from mCRC[1]
- Tumor biomarkers drive therapy decisions for 1st line mCRC therapy[2]
  - ~50% mCRC is RAS mutant (KRAS): FOLFOX/FOLFIRI/FOLFOXIRI
- Large unmet need in RAS mutant CRC[2]
  - No targeted therapies are available for RAS mutant CRC
  - 2nd line therapies have ~5% response rate in metastatic CRC (mCRC)



[1]https://seer.cancer.gov/statfacts/html/colorect.html; [2]King et al, Frontline Strategies for Metastatic CRC, 2016, Amer J Hem/Onc; Loree&Kopetz, Recent Developments in treatment of mCRC, 2017, Ther Adv Med Onc;

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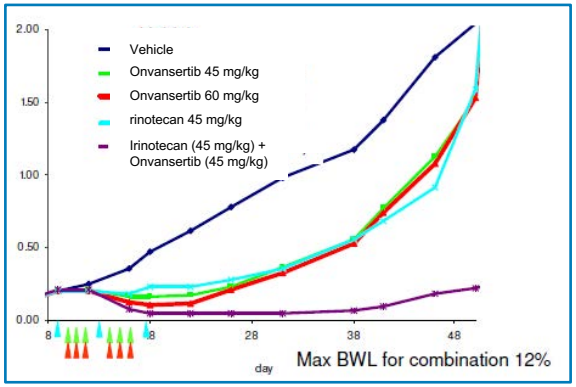
Onvansertib in Pre-Clinical CRC Synergy with Irinotecan[1]

- **In vitro:**
  - CRC cell lines are sensitive to Onvansertib:

    25/27 cell lines tested had an IC50<1uM and 10 had an IC50<0.1uM
  - Onvansertib is synergistic with paclitaxel, cisplatin, SN-38 and irinotecan
- **In-vivo:**
  - Onvansertib inhibits tumor growth of CRC xenograft models
    3 independent models were tested and Onvansertib induces maximal tumor regression of ~84% compared to vehicle
  - The combination of Onvansertib with Irinotecan significantly reduces tumor growth compared with vehicle or either single agent treatment



[1]Data on File at Trovagene, Inc.

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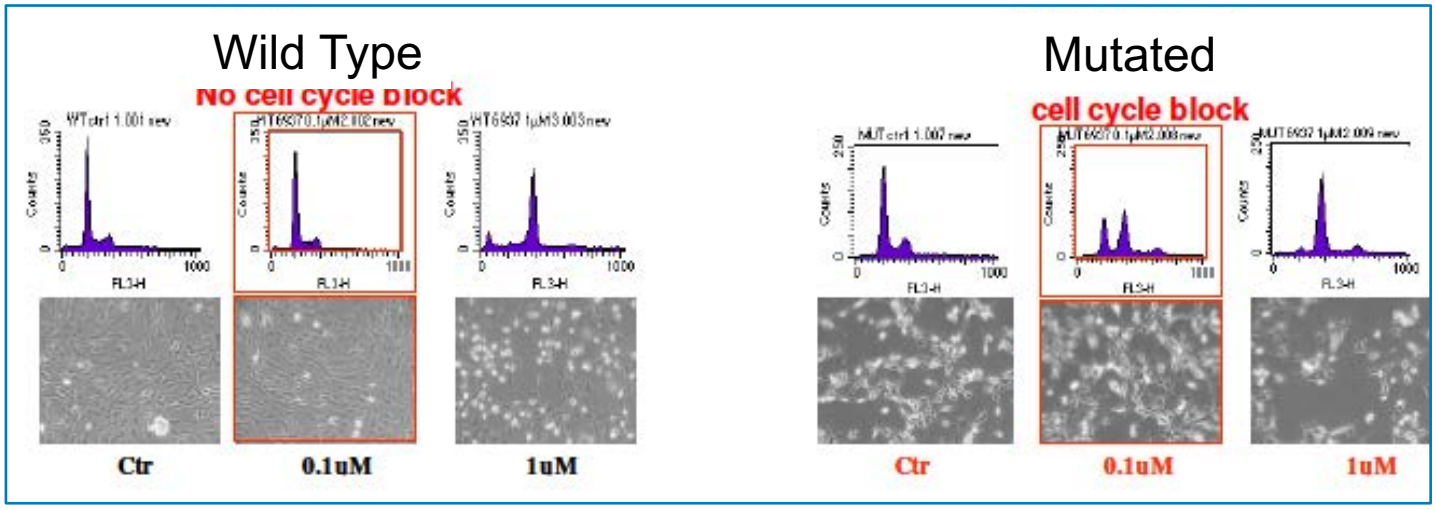
KRAS Mutation: Multiple *in-vitro* Studies Indicate Mutation is Biomarker for Onvansertib Sensitivity

- In a genome-wide RNAi screen there was found a synthetic lethal interactions (profound mitotic block/death) with KRAS oncogene and PLK1; Tested in 2 mutant & isogenic cell lines[1]
- KRAS-mutant cancer cell lines are more sensitive to PLK1 inhibition (BI2536)[2]
- KRAS mutated NIH3T3 cells showed higher sensitivity to onvansertib compare to KRAS wild-type (WT) cells[3]



[1]Luo J, Elledge SJ, Cell. 2009; [2]Wang J., Liu M., Nat.Comm,2016; [3]Investigator Brochure, Data-on-file, Trovagene

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Summary

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Value Creating Milestones

Q4'18
- ✓ AML – ASH Presentation
- ✓ Efficacy and Safety Data Readouts (AML, mCRPC)
- ✓ mCRC IND & Protocol Filed to FDA

Q1'19
- ✓ AML – Reach MTD and RP2D
- ✓ Begin Enrolling AML Phase 2 trial
- ✓ mCRPC – ASCO GU Presentation
- ✓ Efficacy and Safety Data Readouts (AML and mCRPC)
- ✓ Evaluate Expanding Clinical Program to Europe
- ✓ Formalize Japan Partnering

Q2'19
- ✓ Initiate mCRC Phase 1b/2 Trial
- ✓ Efficacy and Safety Data Readouts (AML, mCRPC)
- ✓ AACR Presentation (AML, mCRPC)
- ✓ Complete Enrollment of AML Phase 2
- ✓ Complete Enrollment of mCRPC Phase 2
- ✓ AML Companion Diagnostic

Q3'19
- ✓ Efficacy and Safety Data Readouts (AML and mCRPC)
- ✓ Assess Dose Escalation – Phase 1b mCRC Trial – Identify Phase 2 Dose
- ✓ Begin Enrolling mCRC Phase 2

Q4'19
- ✓ Data Readouts (AML, mCRPC, mCRC)
- ✓ Begin Enrolling Phase 2 mCRC
- ✓ AML – ASH Presentation

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Summary

- Precision Cancer Medicine, predictive biomarker approach
- Leveraging a proven cancer target, PLK1
- Onvansertib – first-in-class, 3rd generation, oral PLK1 inhibitor
- Synergy strategy – Onvansertib in combination with approved drugs

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