NOVARTIS

Clinical Trial Results Website

Sponsor

Novartis Pharmaceuticals

Generic Drug Name

PDR001

Trial Indication(s)

Advanced hepatocellular carcinoma (HCC)

Protocol Number

CPDR001G2101

Protocol Title

A phase Ib study of PDR001 in combination with sorafenib in patients with advanced hepatocellular carcinoma (HCC)

Clinical Trial Phase

Phase 1

Phase of Drug Development

Phase III

Study Start/End Dates

Study Start Date: April 2017 (Actual)
Primary Completion Date: February 2020 (Actual)
Study Completion Date: February 2020 (Actual)

Reason for Termination (If applicable)

Not applicable

Study Design/Methodology

This is a Phase Ib, open label, dose escalation study. The objective of this study is to establish a safe and tolerated dose of PDR001 in combination with sorafenib in patients with advanced HCC.

The study was comprised of 3 phases: screening, treatment and safety follow-up (30-day, 60-day, 90-day, 120-day and 150-day). Patients entered the survival follow-up once they completed the safety follow-up period or had disease progression as per Immune-related Response Evaluation Criteria in Solid Tumors (irRECIST).

During the study, PDR001 was administered intravenously every 4 weeks (Q4W) over a period of 30 minutes and sorafenib was administered orally once (QD) or twice (BID) a day as determined by the dose level assigned to a patient. Subjects could continue to receive the study treatment until one of the criteria for discontinuation were met.

An adaptive Bayesian Logistic Regression Model (BLRM) employing the escalation with overdose control (EWOC) principle was used to estimate the maximum tolerated dose (MTD) and/or recommended dose for expansion (RP2D). No more than one patient per day initiated the study treatment at each dose level explored. The first cohort of patients was treated with the starting dose of 400 mg of sorafenib taken orally once a day and 400 mg of PDR001 given intravenously Q4W. If no DLTs was observed at the first dose level, the study aimed to escalate the starting dose of sorafenib to evaluate the combination at the approved single-agent dose of sorafenib 400 mg twice a day and 400 mg of PDR001 infusion every 4 weeks.

Centers

7 centers in 6 countries: Canada(1), Germany(1), Japan(2), Taiwan(1), Italy(1), Hong Kong(1)

Objectives:

Primary objective:

- To characterize the safety and tolerability of PDR001 in combination with sorafenib and identify the MTD and/or RP2D in advanced HCC patients.

Secondary objectives:

- To characterize the pharmacokinetics of PDR001 and sorafenib in combination

- To assess preliminary anti-tumor activity of the combination based on overall response rate (ORR)

Test Product (s), Dose(s), and Mode(s) of Administration

The investigational drug in this study is PDR001 which was supplied in a vial as powder for solution for intravenous infusion.

The study treatment is defined as PDR001 in combination with sorafenib (available as oral tablets of 200mg).

Statistical Methods

The dose-escalation was guided by a Bayesian analysis of dose limiting toxicity (DLT) data for PDR001 and sorafenib in the first 56 days of treatment. The data reported from the study was summarized with respect to demographic and baseline characteristics, efficacy observations and measurements, safety observations and measurements, and all relevant pharmacokinetic (PK) measurements.

Study Population: Key Inclusion/Exclusion Criteria

Inclusion Criteria:
-Histologically or cytologically confirmed advanced (unresectable and/or metastatic) HCC
-Patients with advanced HCC not amenable for surgical or loco-regional treatment
- At least one measurable tumor lesion that has not been treated locally previously
-Patients with current cirrhotic status of Child-Pugh class A only (5-6 points with total bilirubin < 2 mg/dL for dose-escalation) with no encephalopathy and no clinical ascites (ascites controlled by diuretics is also excluded in this study).
-Patient has an Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1
-Patient must meet required laboratory values at the screening
-Normal electrocardiogram at screening

Exclusion Criteria:
-Known fibrolamellar HCC, sarcomatoid HCC, or mixed cholangiocarcinoma and HCC
-Invasion of the main portal vein and/or tumor involvement in more than 50% of the liver (applicable only for the dose-escalation part)
-Patients with Portal-caval shunts
-Prior or concomitant systemic anti-cancer treatment for advanced disease
-Systemic chronic steroid therapy (≥ 10mg/day prednisone or equivalent) or any immunosuppressive therapy 7 days prior to planned date for first dose of study treatment. Topical, inhaled, nasal and ophthalmic steroids are allowed.

-Cardiac or cardiac repolarization abnormality
-Patients with active Hepatitis B infection (HBsAg positive) that are not receiving antiviral treatment are excluded
-Patients with positive test for hepatitis C ribonucleic acid (HCV RNA)
-Loco-regional treatment within 4 weeks prior to initiation of study treatment.

Other inclusion/exclusion criteria might apply

Participant Flow Table

Overall Study

	PDR 400mg Q4W + SOR 400mg QD	PDR 400mg Q4W + SOR 400mg BID	Total
Arm/Group Description	PDR001 at 400 mg given intravenously every 4 weeks (Q4W) and sorafenib 400 mg taken orally once daily (QD)	PDR001 at 400 mg given intravenously every 4 weeks (Q4W) and sorafenib 400 mg taken twice daily (BID)	
Started	12	8	20
Completed	0	0	0
Not Completed	12	8	20
Adverse Event	2	5	7
Death	1	0	1
Progressive disease	6	3	9
Study terminated by sponsor	2	0	2
Subject/Guardian decision	1	0	1

Baseline Characteristics

	PDR 400mg Q4W + SOR 400mg QD	PDR 400mg Q4W + SOR 400mg BID	Total
Arm/Group Description	PDR001 at 400 mg given intravenously every 4 weeks (Q4W) and sorafenib 400 mg taken orally once daily (QD)	PDR001 at 400 mg given intravenously every 4 weeks (Q4W) and sorafenib 400 mg taken twice daily (BID)	
Number of Participants [units: participants]	12	8	20
Age Continuous (units: Years) Mean ± Standard Deviation			
	64.8±10.30	66.8±10.39	65.6±10.11
Sex: Female, Male (units: Participants) Count of Participants (Not Applicable)			
Female	2	5	7
Male	10	3	13
Race/Ethnicity, Customized (units: Participants) Count of Participants (Not Applicable)			
Caucasian	7	3	10
Asian	4	5	9

Black	1	0	1

Primary Outcome Result(s)

Number of participants with Adverse Events (AEs) and Serious Adverse Events (SAEs)

(Time Frame: From baseline until 30 days of last dose of study treatment, assessed for a median time of approximately 5 months)

	PDR 400mg Q4W + SOR 400mg QD	PDR 400mg Q4W + SOR 400mg BID
Arm/Group Description	PDR001 at 400 mg given intravenously every 4 weeks (Q4W) and sorafenib 400 mg taken orally once daily (QD)	PDR001 at 400 mg given intravenously every 4 weeks (Q4W) and sorafenib 400 mg taken twice daily (BID)
Number of Participants Analyzed [units: participants]	12	8
Number of participants with Adverse Events (AEs) and Serious Adverse Events (SAEs) (units: Participants) Count of Participants (Not Applicable)		
Adverse events (AEs)	12 (100%)	8 (100%)
Treatment-related AEs	11 (91.67%)	8 (100%)
Serious Adverse Events (SAEs)	3 (25%)	2 (25%)
Treatment-related SAEs	0 (%)	2 (25%)

Fatal SAEs	1 (8.33%)	0 (%)
AEs leading to discontinuation	5 (41.67%)	7 (87.5%)
Treatment-related AEs leading to discontinuation	4 (33.33%)	7 (87.5%)
AEs leading to dose adjustment/interruption	8 (66.67%)	8 (100%)
AEs requiring additional therapy	11 (91.67%)	8 (100%)

Number of participants with Dose Limiting Toxicities (DLTs)

(Time Frame: During the first 8 weeks of treatment)

	PDR 400mg Q4W + SOR 400mg QD	**PDR 400mg Q4W + SOR 400mg BID**
Arm/Group Description	PDR001 at 400 mg given intravenously every 4 weeks (Q4W) and sorafenib 400 mg taken orally once daily (QD)	PDR001 at 400 mg given intravenously every 4 weeks (Q4W) and sorafenib 400 mg taken twice daily (BID)
Number of Participants Analyzed [units: participants]	8	2
Number of participants with Dose Limiting Toxicities (DLTs) (units: Participants) Count of Participants (Not Applicable)		

	0 (%)	0 (%)

Number of participant with dose interruptions

(Time Frame: Until end of treatment, assessed for a median time of 4 months)

	PDR 400mg Q4W + SOR 400mg QD	PDR 400mg Q4W + SOR 400mg BID
Arm/Group Description	PDR001 at 400 mg given intravenously every 4 weeks (Q4W) and sorafenib 400 mg taken orally once daily (QD)	PDR001 at 400 mg given intravenously every 4 weeks (Q4W) and sorafenib 400 mg taken twice daily (BID)
Number of Participants Analyzed [units: participants]	12	8
Number of participant with dose interruptions (units: Participants) Count of Participants (Not Applicable)		
PDR001	5 (41.67%)	3 (37.5%)
Sorafenib	11 (91.67%)	8 (100%)

Dose intensity

(Time Frame: Until end of treatment, assessed for a median time of 4 months)

PDR 400mg Q4W + SOR 400mg QD	PDR 400mg Q4W + SOR 400mg BID

Arm/Group Description	PDR001 at 400 mg given intravenously every 4 weeks (Q4W) and sorafenib 400 mg taken orally once daily (QD)	PDR001 at 400 mg given intravenously every 4 weeks (Q4W) and sorafenib 400 mg taken twice daily (BID)
Number of Participants Analyzed [units: participants]	12	8
Dose intensity (units: milligram per day (mg/day)) Mean ± Standard Deviation		
PDR001	13.6 ± 1.47	13.1 ± 1.61
Sorafenib	304.2 ± 104.84	364.0 ± 209.40

Number of participants with dose reductions

(Time Frame: Until end of treatment, assessed for a median time of 4 months)

	PDR 400mg Q4W + SOR 400mg QD	PDR 400mg Q4W + SOR 400mg BID
Arm/Group Description	PDR001 at 400 mg given intravenously every 4 weeks (Q4W) and sorafenib 400 mg taken orally once daily (QD)	PDR001 at 400 mg given intravenously every 4 weeks (Q4W) and sorafenib 400 mg taken twice daily (BID)

Number of Participants Analyzed [units: participants]	12	8
Number of participants with dose reductions (units: Participants) Count of Participants (Not Applicable)		
Sorafenib	6 (50%)	8 (100%)

Secondary Outcome Result(s)

Overall Response Rate (ORR) per Response Evaluation Criteria in Solid Tumors (RECIST) v1.1 as per central radiology assessment

(Time Frame: Until end of treatment, assessed for a median time of 4 months)

	PDR 400mg Q4W + SOR 400mg QD	PDR 400mg Q4W + SOR 400mg BID
Arm/Group Description	PDR001 at 400 mg given intravenously every 4 weeks (Q4W) and sorafenib 400 mg taken orally once daily (QD)	PDR001 at 400 mg given intravenously every 4 weeks (Q4W) and sorafenib 400 mg taken twice daily (BID)
Number of Participants Analyzed [units: participants]	12	8
Overall Response Rate (ORR) per Response Evaluation Criteria in		

Solid Tumors (RECIST) v1.1 as per central radiology assessment (units: Percentage of participants) Number (95% Confidence Interval)		
	25.0 (5.5 to 57.2)	0 (0 to 36.9)

PDR001 trough concentration

(Time Frame: Pre-dose at Cycle 2, 3, 4, 6 , 8, 10, 12 on Day 1. Cycle=28 days)

	PDR 400mg Q4W + SOR 400mg QD	**PDR 400mg Q4W + SOR 400mg BID**
Arm/Group Description	PDR001 at 400 mg given intravenously every 4 weeks (Q4W) and sorafenib 400 mg taken orally once daily (QD)	PDR001 at 400 mg given intravenously every 4 weeks (Q4W) and sorafenib 400 mg taken twice daily (BID)
Number of Participants Analyzed [units: participants]	12	8
PDR001 trough concentration (units: nanogram/mililiter (ng/ml)) Mean ± Standard Deviation		
Cycle 2 Day 1, n= 9 / 7	19.6 ± 10.1	53.1 ± 69.4
Cycle 3 Day 1, n= 6 / 4	30.0 ± 18.9	23.9 ± 16.8
Cycle 4 Day 1, , n= 5 / 3	31.7 ± 19.7	30.1 ± 8.3
Cycle 6 Day 1, n= 5 / 0	45.1 ± 13.8	

Cycle 8 Day 1, n= 5 / 0	40.9 ± 14.8
Cycle 10 Day 1, n= 2 / 0	50.9 ± 4.0
Cycle 12 Day 1, n= 2 / 0	51.4 ± 0.2
Cycle 18 Day 1, n= 1 / 0	56.9 ± NA[1]

[1] NA= The value was not estimable due to insufficient number of participants

Maximum concentration (Cmax) of sorafenib

(Time Frame: Cycle 3 Day 1 Pre-dose, 1h, 3h and 8 h post-dose. Cycle=28 days)

	PDR 400mg Q4W + SOR 400mg QD	**PDR 400mg Q4W + SOR 400mg BID**
Arm/Group Description	PDR001 at 400 mg given intravenously every 4 weeks (Q4W) and sorafenib 400 mg taken orally once daily (QD)	PDR001 at 400 mg given intravenously every 4 weeks (Q4W) and sorafenib 400 mg taken twice daily (BID)
Number of Participants Analyzed [units: participants]	6	5
Maximum concentration (Cmax) of sorafenib (units: Nanogram per milliliter) Geometric Mean (Geometric Coefficient of Variation)		
	3710 (94.7%)	5380 (35.7%)

Time to reach maximum concentration (Tmax) of sorafenib

(Time Frame: Cycle 3 Day 1 Pre-dose, 1h, 3h and 8 h post-dose. Cycle=28 days)

	PDR 400mg Q4W + SOR 400mg QD	PDR 400mg Q4W + SOR 400mg BID
Arm/Group Description	PDR001 at 400 mg given intravenously every 4 weeks (Q4W) and sorafenib 400 mg taken orally once daily (QD)	PDR001 at 400 mg given intravenously every 4 weeks (Q4W) and sorafenib 400 mg taken twice daily (BID)
Number of Participants Analyzed [units: participants]	6	5
Time to reach maximum concentration (Tmax) of sorafenib (units: hours) Median (Full Range)		
	2.80 (0 to 6.12)	2.83 (1.00 to 8.25)

Area under the plasma concentration-time curve of sorafenib from time zero to 8 hours after administration (AUC0-8)

(Time Frame: Cycle 3 Day 1 Pre-dose, 1h, 3h and 8 h post-dose. Cycle=28 days)

	PDR 400mg Q4W + SOR 400mg QD	PDR 400mg Q4W + SOR 400mg BID
Arm/Group Description	PDR001 at 400 mg given intravenously every 4 weeks (Q4W) and sorafenib 400	PDR001 at 400 mg given intravenously every 4 weeks (Q4W) and sorafenib 400

	mg taken orally once daily (QD)	mg taken twice daily (BID)
Number of Participants Analyzed [units: participants]	0	2
Area under the plasma concentration-time curve of sorafenib from time zero to 8 hours after administration (AUC0-8) (units: hours*nanogram/mililiter) Geometric Mean (Geometric Coefficient of Variation)		
		21100 (30.3%)

Safety Results

All-Cause Mortality

	PDR 400mg Q4W+ SOR 400mg QD N = 12	PDR 400mg Q4Wv+ SOR 400mg BID N = 8	All subjects N = 20
Arm/Group Description	PDR001 at 400 mg given intravenously every 4 weeks (Q4W) and sorafenib 400	PDR001 at 400 mg given intravenously every 4 weeks (Q4W) and sorafenib 400	All subjects

	mg taken orally once daily (QD)	mg taken twice daily (BID)	
Total participants affected	3 (25.00%)	1 (12.50%)	4 (20.00%)

Serious Adverse Events by System Organ Class

Time Frame	Adverse events were collected from first dose of study treatment until end of study treatment plus 30 days post treatment, up to maximum duration of 121 weeks
Additional Description	Any sign or symptom that occurs during the study treatment plus the 30 days post treatment
Source Vocabulary for Table Default	MedDRA (22.1)
Assessment Type for Table Default	Systematic Assessment

	PDR 400mg Q4W+ SOR 400mg QD N = 12	**PDR 400mg Q4Wv+ SOR 400mg BID N = 8**	**All subjects N = 20**
Arm/Group Description	PDR001 at 400 mg given intravenously every 4 weeks (Q4W) and sorafenib 400 mg taken orally once daily (QD)	PDR001 at 400 mg given intravenously every 4 weeks (Q4W) and sorafenib 400 mg taken twice daily (BID)	All subjects
Total participants affected	3 (25.00%)	2 (25.00%)	5 (25.00%)

Gastrointestinal disorders			
Varices oesophageal	1 (8.33%)	0 (0.00%)	1 (5.00%)
Hepatobiliary disorders			
Hepatitis	0 (0.00%)	1 (12.50%)	1 (5.00%)
Infections and infestations			
Sepsis	1 (8.33%)	0 (0.00%)	1 (5.00%)
Metabolism and nutrition disorders			
Hyperglycaemia	0 (0.00%)	1 (12.50%)	1 (5.00%)
Nervous system disorders			
Transient ischaemic attack	1 (8.33%)	0 (0.00%)	1 (5.00%)
Skin and subcutaneous tissue disorders			
Erythema	0 (0.00%)	1 (12.50%)	1 (5.00%)
Rash maculo-papular	0 (0.00%)	1 (12.50%)	1 (5.00%)

Other Adverse Events by System Organ Class

Time Frame	Adverse events were collected from first dose of study treatment until end of study treatment plus 30 days post treatment, up to maximum duration of 121 weeks
Additional Description	Any sign or symptom that occurs during the study treatment plus the 30 days post treatment
Source Vocabulary for Table Default	MedDRA (22.1)
Assessment Type for Table Default	Systematic Assessment

Frequent Event Reporting Threshold 5%

	PDR 400mg Q4W+ SOR 400mg QD N = 12	PDR 400mg Q4Wv+ SOR 400mg BID N = 8	All subjects N = 20
Arm/Group Description	PDR001 at 400 mg given intravenously every 4 weeks (Q4W) and sorafenib 400 mg taken orally once daily (QD)	PDR001 at 400 mg given intravenously every 4 weeks (Q4W) and sorafenib 400 mg taken twice daily (BID)	All subjects
Total participants affected	12 (100.00%)	8 (100.00%)	20 (100.00%)
Blood and lymphatic system disorders			
Anaemia	0 (0.00%)	1 (12.50%)	1 (5.00%)
Neutropenia	1 (8.33%)	0 (0.00%)	1 (5.00%)
Cardiac disorders			
Cardiac disorder	0 (0.00%)	1 (12.50%)	1 (5.00%)
Ear and labyrinth disorders			
Ear discomfort	1 (8.33%)	0 (0.00%)	1 (5.00%)
Eye disorders			
Eyelid oedema	0 (0.00%)	1 (12.50%)	1 (5.00%)
Gastrointestinal disorders			

Abdominal distension	3 (25.00%)	0 (0.00%)	3 (15.00%)
Abdominal pain	3 (25.00%)	0 (0.00%)	3 (15.00%)
Abdominal pain lower	1 (8.33%)	0 (0.00%)	1 (5.00%)
Abdominal pain upper	2 (16.67%)	0 (0.00%)	2 (10.00%)
Constipation	3 (25.00%)	1 (12.50%)	4 (20.00%)
Diarrhoea	4 (33.33%)	1 (12.50%)	5 (25.00%)
Dry mouth	2 (16.67%)	0 (0.00%)	2 (10.00%)
Dysphagia	0 (0.00%)	1 (12.50%)	1 (5.00%)
Faeces soft	1 (8.33%)	0 (0.00%)	1 (5.00%)
Gingival bleeding	2 (16.67%)	0 (0.00%)	2 (10.00%)
Nausea	3 (25.00%)	1 (12.50%)	4 (20.00%)
Odynophagia	1 (8.33%)	0 (0.00%)	1 (5.00%)
Oral pain	1 (8.33%)	0 (0.00%)	1 (5.00%)
Proctalgia	1 (8.33%)	0 (0.00%)	1 (5.00%)
Stomatitis	1 (8.33%)	2 (25.00%)	3 (15.00%)
Vomiting	3 (25.00%)	1 (12.50%)	4 (20.00%)
General disorders and administration site conditions			
Asthenia	1 (8.33%)	1 (12.50%)	2 (10.00%)
Fatigue	4 (33.33%)	1 (12.50%)	5 (25.00%)
Malaise	1 (8.33%)	0 (0.00%)	1 (5.00%)
Peripheral swelling	2 (16.67%)	0 (0.00%)	2 (10.00%)
Pyrexia	3 (25.00%)	3 (37.50%)	6 (30.00%)
Hepatobiliary disorders			
Hepatitis	0 (0.00%)	1 (12.50%)	1 (5.00%)

Infections and infestations			
Cellulitis	1 (8.33%)	0 (0.00%)	1 (5.00%)
Conjunctivitis	0 (0.00%)	1 (12.50%)	1 (5.00%)
Gingival abscess	0 (0.00%)	1 (12.50%)	1 (5.00%)
Herpes zoster	1 (8.33%)	0 (0.00%)	1 (5.00%)
Infected cyst	1 (8.33%)	0 (0.00%)	1 (5.00%)
Nasopharyngitis	1 (8.33%)	1 (12.50%)	2 (10.00%)
Sinusitis	0 (0.00%)	1 (12.50%)	1 (5.00%)
Upper respiratory tract infection	1 (8.33%)	0 (0.00%)	1 (5.00%)
Viral upper respiratory tract infection	0 (0.00%)	1 (12.50%)	1 (5.00%)
Injury, poisoning and procedural complications			
Procedural pain	1 (8.33%)	0 (0.00%)	1 (5.00%)
Skin abrasion	1 (8.33%)	0 (0.00%)	1 (5.00%)
Investigations			
Alanine aminotransferase increased	7 (58.33%)	2 (25.00%)	9 (45.00%)
Amylase increased	1 (8.33%)	0 (0.00%)	1 (5.00%)
Aspartate aminotransferase increased	9 (75.00%)	4 (50.00%)	13 (65.00%)
Blood alkaline phosphatase increased	2 (16.67%)	0 (0.00%)	2 (10.00%)

Blood bicarbonate decreased	1 (8.33%)	0 (0.00%)	1 (5.00%)
Blood bilirubin increased	1 (8.33%)	3 (37.50%)	4 (20.00%)
Blood creatinine increased	1 (8.33%)	0 (0.00%)	1 (5.00%)
C-reactive protein increased	1 (8.33%)	0 (0.00%)	1 (5.00%)
Gamma-glutamyltransferase increased	4 (33.33%)	1 (12.50%)	5 (25.00%)
Lipase increased	5 (41.67%)	0 (0.00%)	5 (25.00%)
Lymphocyte count decreased	0 (0.00%)	1 (12.50%)	1 (5.00%)
Neutrophil count decreased	0 (0.00%)	1 (12.50%)	1 (5.00%)
Platelet count decreased	1 (8.33%)	1 (12.50%)	2 (10.00%)
Weight decreased	1 (8.33%)	1 (12.50%)	2 (10.00%)
White blood cell count decreased	1 (8.33%)	1 (12.50%)	2 (10.00%)
Metabolism and nutrition disorders			
Decreased appetite	3 (25.00%)	2 (25.00%)	5 (25.00%)
Hyperglycaemia	0 (0.00%)	1 (12.50%)	1 (5.00%)
Hyperkalaemia	1 (8.33%)	0 (0.00%)	1 (5.00%)
Hyperuricaemia	1 (8.33%)	0 (0.00%)	1 (5.00%)
Hypoalbuminaemia	0 (0.00%)	1 (12.50%)	1 (5.00%)
Hypokalaemia	1 (8.33%)	2 (25.00%)	3 (15.00%)
Hyponatraemia	0 (0.00%)	1 (12.50%)	1 (5.00%)

Musculoskeletal and connective tissue disorders			
Arthralgia	3 (25.00%)	2 (25.00%)	5 (25.00%)
Axillary mass	1 (8.33%)	0 (0.00%)	1 (5.00%)
Bone pain	0 (0.00%)	1 (12.50%)	1 (5.00%)
Joint swelling	1 (8.33%)	0 (0.00%)	1 (5.00%)
Muscle spasms	1 (8.33%)	0 (0.00%)	1 (5.00%)
Myalgia	2 (16.67%)	0 (0.00%)	2 (10.00%)
Pain in extremity	2 (16.67%)	0 (0.00%)	2 (10.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Keratoacanthoma	1 (8.33%)	0 (0.00%)	1 (5.00%)
Skin papilloma	1 (8.33%)	0 (0.00%)	1 (5.00%)
Nervous system disorders			
Amnesia	1 (8.33%)	0 (0.00%)	1 (5.00%)
Dysarthria	1 (8.33%)	0 (0.00%)	1 (5.00%)
Dysgeusia	1 (8.33%)	0 (0.00%)	1 (5.00%)
Headache	3 (25.00%)	1 (12.50%)	4 (20.00%)
Hepatic encephalopathy	1 (8.33%)	0 (0.00%)	1 (5.00%)
Hypoaesthesia	1 (8.33%)	0 (0.00%)	1 (5.00%)
Hypogeusia	1 (8.33%)	0 (0.00%)	1 (5.00%)
Neuropathy peripheral	1 (8.33%)	0 (0.00%)	1 (5.00%)
Psychiatric disorders			

Depression	1 (8.33%)	0 (0.00%)	1 (5.00%)
Insomnia	0 (0.00%)	1 (12.50%)	1 (5.00%)
Renal and urinary disorders			
Albuminuria	0 (0.00%)	1 (12.50%)	1 (5.00%)
Dysuria	1 (8.33%)	0 (0.00%)	1 (5.00%)
Pollakiuria	1 (8.33%)	0 (0.00%)	1 (5.00%)
Proteinuria	0 (0.00%)	2 (25.00%)	2 (10.00%)
Reproductive system and breast disorders			
Nipple pain	1 (8.33%)	0 (0.00%)	1 (5.00%)
Respiratory, thoracic and mediastinal disorders			
Cough	2 (16.67%)	1 (12.50%)	3 (15.00%)
Dysphonia	4 (33.33%)	4 (50.00%)	8 (40.00%)
Dyspnoea exertional	1 (8.33%)	0 (0.00%)	1 (5.00%)
Hiccups	1 (8.33%)	0 (0.00%)	1 (5.00%)
Oropharyngeal pain	2 (16.67%)	1 (12.50%)	3 (15.00%)
Pneumonitis	0 (0.00%)	1 (12.50%)	1 (5.00%)
Skin and subcutaneous tissue disorders			
Alopecia	3 (25.00%)	3 (37.50%)	6 (30.00%)
Dry skin	2 (16.67%)	0 (0.00%)	2 (10.00%)
Erythema	3 (25.00%)	3 (37.50%)	6 (30.00%)
Palmar-plantar erythrodysaesthesia syndrome	5 (41.67%)	4 (50.00%)	9 (45.00%)

Pruritus	3 (25.00%)	1 (12.50%)	4 (20.00%)
Purpura	1 (8.33%)	0 (0.00%)	1 (5.00%)
Rash	6 (50.00%)	3 (37.50%)	9 (45.00%)
Rash erythematous	1 (8.33%)	0 (0.00%)	1 (5.00%)
Rash maculo-papular	1 (8.33%)	1 (12.50%)	2 (10.00%)
Skin exfoliation	1 (8.33%)	0 (0.00%)	1 (5.00%)
Vascular disorders			
Hot flush	1 (8.33%)	0 (0.00%)	1 (5.00%)
Hypertension	2 (16.67%)	4 (50.00%)	6 (30.00%)

Other Relevant Findings

None

Conclusion:

The combination of PDR001 and sorafenib, showed preliminary anti-tumor efficacy. The safety profile was consistent across the 2 dosing groups, and the AEs were largely managed by treatment discontinuation/ dose reductions, and the majority of the AEs were attributed to the underlying disease.

Date of Clinical Trial Report

16-Jul-2020