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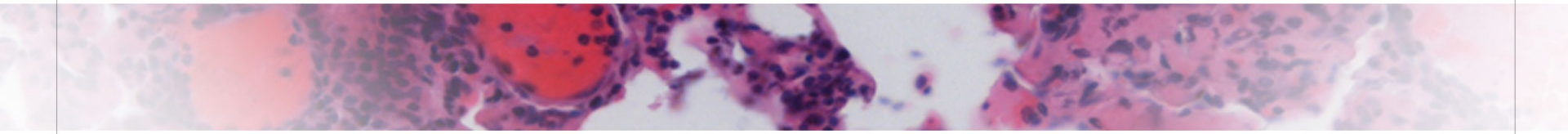

A Phase I Dose Escalation Study of PT-112 in Patients with Relapsed or Refractory Multiple Myeloma

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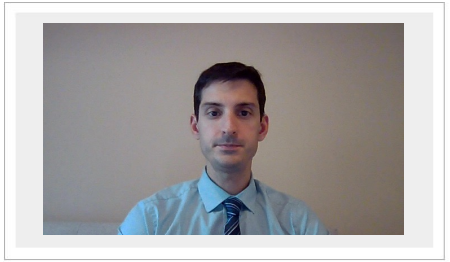
Disclosure Information



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There are no relevant conflicts of interest to disclose

Ames, Yim, Price

The above authors are employed by and hold interests in Phosplatin Therapeutics LLC.

Mr. Price is a member of the board of directors.

Jimeno

Dr. Jimeno is an advisory board member and holds interests in Phosplatin Therapeutics LLC

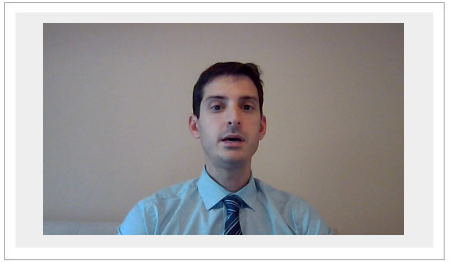
Background

PT-112 Non-Clinical Background

- The first pyrophosphate-platinum conjugate
- No susceptibility to DNA-repair resistance pathways
- Robust induction of Immunogenic Cell Death (ICD)
- Osteotropic biodistribution
- Activity in highly predictive Vk*MYC mouse model of multiple myeloma

PT-112 Clinical Background

- Two phase I studies in solid tumors reported:
  - First-in-human study of PT-112 monotherapy
  - Combination with anti-PD-L1 checkpoint inhibitor avelumab
- Durable partial responses observed as single agent and in combination across several cancer types



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PT-112 induces immunogenic cell death and synergizes with immune checkpoint blockers in mouse tumor models

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652. MYELOMA: PATHOPHYSIOLOGY AND PRE-CLINICAL STUDIES, EXCLUDING THERAPY: POSTER I | DECEMBER 7, 2017

Translational Research of PT-112, a Clinical Agent in Advanced Phase I Development: Evident Bone Tropism, Synergy *In Vitro* with Bortezomib and Lenalidomide , and Potent Efficacy in the Vk*MYC Mouse Model of Multiple Myeloma

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ABSTRACTS DEVELOPMENTAL THERAPEUTICS | VOLUME 29, SUPPLEMENT 8, VIII143, OCTOBER 01, 2018

PT-112: A well-tolerated novel immunogenic cell death (ICD) inducer with activity in advanced solid tumors

D.D. Karp • D.R. Camidge • J.R. Infante • T.D. Ames • J.M. Jimeno • A.H. Bryce

ABSTRACT ONLY | VOLUME 31, SUPPLEMENT 4, S708, SEPTEMBER 01, 2020

1026MO Phase Ib dose escalation study of novel immunogenic cell death (ICD) inducer PT-112 plus PD-L1 inhibitor avelumab in solid tumours

D.D. Karp • R.S. Dronca • R. Camidge • ... T.D. Ames • J.M. Jimeno • A.H. Bryce • Show all authors

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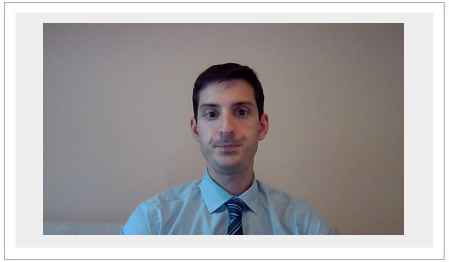
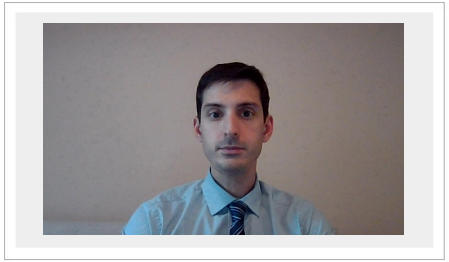
Trial Design and Patient Demographics



- 3+3 dose escalation design to determine the recommended phase 2 dose (RP2D)
- PT-112 mono-therapy given on a 28-day cycle (IV d1, 8, 15)
- Main enrollment criteria:
  - Relapsed/refractory multiple myeloma
  - Exhausted available therapies
  - Absolute neutrophil count ≥ 1.0 x 10^9/L
  - Platelet count ≥ 50 x 10^9/L
  - Hemoglobin ≥ 8.0 g/dL
  - Calculated creatinine clearance ≥ 30 mL/min
  - ECOG Performance Status 0-2

	Total Patients (n=24)
PT-112 Dose Levels	125 – 420 mg/m^2
Median Age (Range), Years	72 (50-85)
ECOG PS	
0	7 (29%)
1	16 (67%)
2	1 (4%)
Prior Systemic Therapy	
Median Prior Therapies (range)	7.5 (2-22)
Triple-Class Relapsed/Refractory	22 (92%)
Penta Relapsed/Refractory	19 (79%)
Prior BCMA-Targeted Therapy	5 (21%)
Prior Stem Cell Transplant	17 (71%)

Treatment Related Adverse Events (TRAEs)

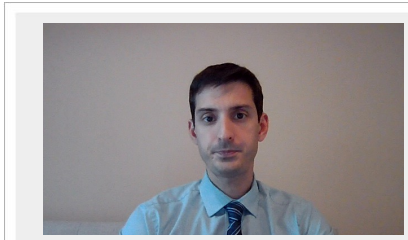


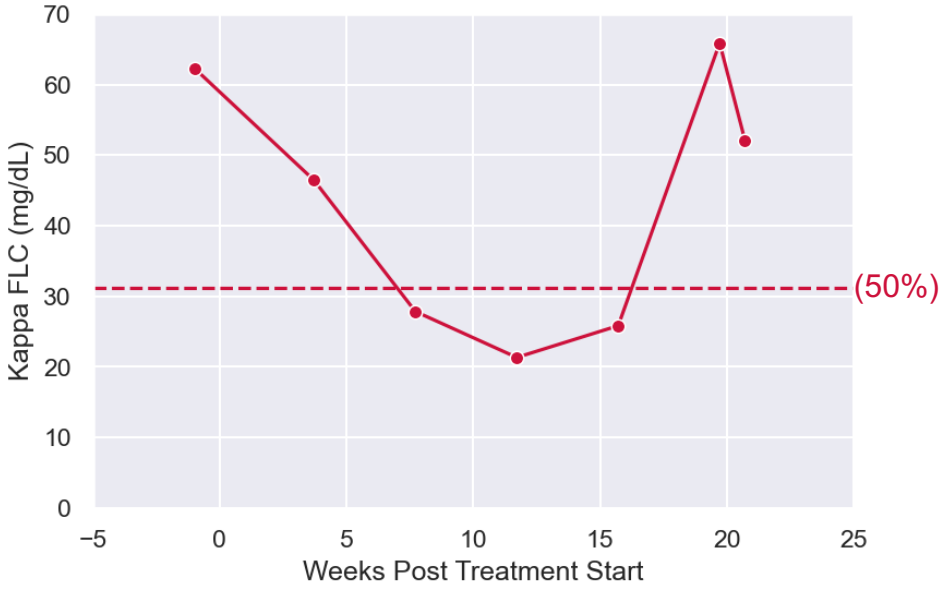
Dose Level in mg/m², number of patients	125-300, n=16			360, n=4			420, n=4			All Pts, n=24		
	G1-2	G3	G4	G1-2	G3	G4	G1-2	G3	G4	G1-2	G3	G4
All TRAEs – n (%)	7(44)	5(31)	2(12)	---	2(50)	1(25)	---	1(25)	3(75)	7(29)	8(33)	6(25)
Blood And Lymphatic System Disorders	5(31)	2(12)	2(12)	---	2(50)	1(25)	---	1(25)	3(75)	5(21)	5(21)	6(25)
Anemia	1(6)	1(6)	1(6)	---	1(25)	---	---	2(50)	---	1(4)	4(17)	1(4)
Leukopenia	1(6)	---	---	---	1(25)	---	---	---	1(25)	1(4)	1(4)	1(4)
Lymphopenia	1(6)	1(6)	---	---	1(25)	---	---	---	1(25)	1(4)	2(8)	1(4)
Neutropenia	4(25)	---	---	2(50)	---	---	---	1(25)	3(75)	6(25)	1(4)	3(12)
Thrombocytopenia	4(25)	1(6)	2(12)	---	2(50)	1(25)	---	1(25)	3(75)	4(17)	4(17)	6(25)
Gastrointestinal Disorders	6(38)	2(12)	---	2(50)	---	---	3(75)	1(25)	---	11(46)	3(12)	---
Abdominal pain	1(6)	---	---	1(25)	---	---	1(25)	---	---	3(12)	---	---
Diarrhea	2(12)	2(12)	---	2(50)	---	---	2(50)	1(25)	---	6(25)	3(12)	---
Nausea	8(50)	---	---	1(25)	---	---	---	---	---	9(38)	---	---
Vomiting	2(12)	---	---	1(25)	---	---	---	---	---	3(12)	---	---
General Disorders And Administration Site Conditions	4(25)	---	---	2(50)	---	---	3(75)	---	---	9(38)	---	---
Fatigue	4(25)	---	---	2(50)	---	---	2(50)	---	---	8(33)	---	---
Investigations	2(12)	---	---	1(25)	---	---	---	---	---	3(12)	---	---
Blood creatinine increased	2(12)	---	---	1(25)	---	---	---	---	---	3(12)	---	---
Metabolism And Nutrition Disorders	2(12)	3(19)	---	1(25)	1(25)	---	---	2(50)	---	3(12)	6(25)	---
Hypophosphatemia	1(6)	2(12)	---	---	1(25)	---	---	1(25)	---	1(4)	4(17)	---
Nervous System Disorders	1(6)	---	---	1(25)	2(50)	---	---	---	---	2(8)	2(8)	---
Neuropathy peripheral	1(6)	---	---	2(50)	1(25)	---	---	---	---	3(12)	1(4)	---
Respiratory, Thoracic And Mediastinal Disorders	1(6)	---	---	1(25)	---	---	1(25)	---	---	3(12)	---	---
Dyspnea	1(6)	---	---	1(25)	---	---	1(25)	---	---	3(12)	---	---

Treatment related adverse events (TRAEs) in ≥10% of patients. No G5 TRAEs were observed.

- PT-112 was generally well-tolerated
- No G4 non-hematologic toxicities were observed
- The frequency of G3 non-hematologic toxicities was 38%
- One DLT (G4 neutropenia) and frequent dose reductions and modifications at 420mg/m^2
- RP2D was declared at 360mg/m^2

Efficacy Outcomes: Partial Response (PR) at RP2D (1 of 4 patients)

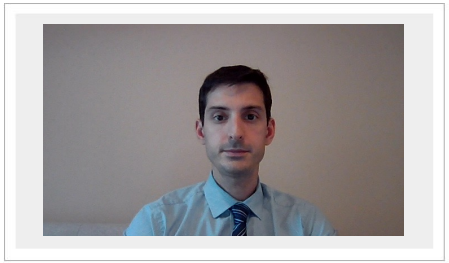


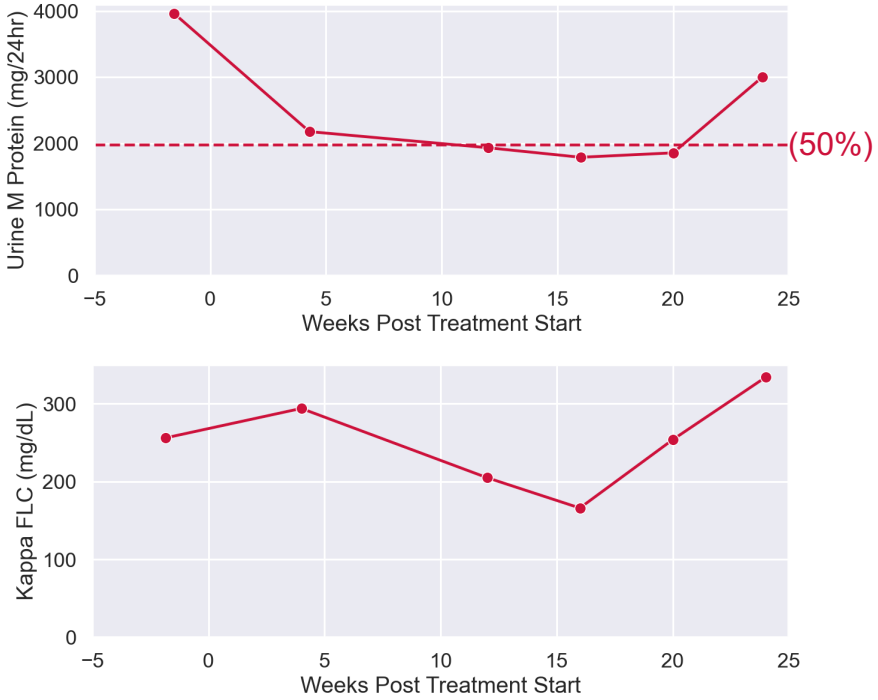


One of four (25%) patients treated at the RP2D of 360mg/m^2 experienced a PR

- 79-year-old male with 5 prior lines of therapy
- Serum M protein negative
- Enrolled at RP2D of 360 mg/m^2
- Achieved a confirmed partial response, with 66% reduction in serum free light chain (FLC)
- Experienced improvement in daily activities
- Gr 3 thrombocytopenia, peripheral neuropathy
- Progression free for 4.5 months

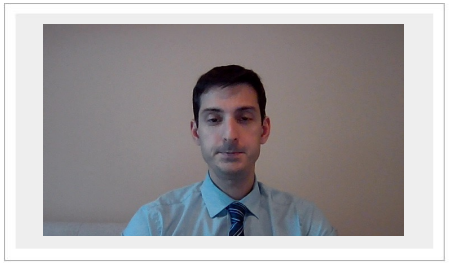
Efficacy Outcomes: Minimal Response (MR) at 420mg/m^2





- 72-year-old female with 22 prior lines of therapy, including prior BCMA CAR-T (non-responder)
- Serum M protein negative
- Enrolled at 420 mg/m^2 dose level, dose reduced to 250 mg/m^2
- Achieved a confirmed minimal response, with 55% reduction in urine M protein
- Concomitant reduction of 35% in FLC level
- Gr 3-4 pancytopenia, Gr 3 diarrhea
- Progression free for 5.5 months

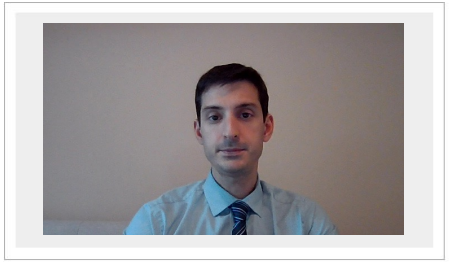
Efficacy Outcomes: Additional Evidence of PT-112 Activity



At 420 mg/m^2, two additional patients had reduction in disease markers. Both experienced short PFS and passed away due to underlying disease and co-morbidities without documented disease progression.

- 85-year-old female with 9 lines of prior therapy, M protein 1.3 g/dL at baseline. Prior to cycle 2:
  - M protein no longer detected
  - Concomitant 50% decline in serum FLC levels
  - Gr 3 acute kidney injury, assessed as unrelated to PT-112
- 82-year-old female, 5 lines of prior therapy, no measurable M protein. Prior to cycle 2:
  - FLC level declined by 70% from baseline
  - Had G2 metabolic encephalopathy with electrolyte abnormalities, assessed as unrelated to PT-112

Conclusions



- PT-112 monotherapy treatment was feasible and well tolerated in heavily pre-treated, relapsed or refractory multiple myeloma patients
- The RP2D is 360 mg/m^2 given on days 1, 8, and 15 of a 28-day cycle
- Cases of confirmed responses and other signals of biological activity were observed with monotherapy PT-112
  - The heavy degree of pretreatment in this patient population suggest a lack of cross-resistance with other standards of care for multiple myeloma
- Further clinical study of PT-112 in multiple myeloma in a phase 2 setting is warranted, including incorporation of dexamethasone