PS1883

Updated Results from Randomized Phase II Dose Optimization Study of Inobrodib (CCS1477), in Combination with Pomalidomide and Dexamethasone in Relapsed/Refractory Multiple Myeloma (RRMM)

Nisha Joseph,[1] Victoria Louise Campbell,[2] Sarah A. Holstein,[3] Dan Vogl,[4] Sarah Gooding,[5] Heather Oakervee,[6] Paula Rodríguez-Otero,[7] Matthew Jenner,[8] Jenny O'Nions,[9] Thomas Creasey,[10] Aristeidis Chaidos,[11] Dean Edward Smith,[12] Albert Oriol Rocafiguera,[13] Ceri Bygrave,[14] Charlotte Pawlyn,[15] Firas Al-Kaisi,[16] Sally Moore,[17] Gillian Brearton,[18] Pablo Bedano,[19] Victor Priego,[20] Tim Somervaille,[21] Tomasz Knurowski,[22] Karen Clegg,[22] Sofia Paul,[22] Kristopher Frese,[22] Emma Searle[21]

[1]Emory Winship Cancer Institute, Atlanta, GA, USA; [2]Western General Hospital, Edinburgh, UK; [3]University of Nebraska Medical Center, Omaha, NE, USA; [4]University of Pennsylvania, Philadelphia, PA, USA; [5]Oxford University Hospitals, Oxford, UK; [6]Barts Health NHS Trust, London, UK; [7]Universidad de Navarra, Pamplona, Spain; [8]University Hospital Southampton, Southampton, UK; [9]University College London Hospitals, London, UK; [10]Newcastle-Upon-Tyne Hospitals, Newcastle-Upon-Tyne, UK; [11]Imperial College Healthcare NHS Trust, London, UK; [12]Nottingham University Hospitals, Nottingham, UK; [13]Josep Carreras Leukaemia Research Institute, Badalona, Spain; [14]University Hospital Wales, Cardiff, UK; [15]The Royal Marsden NHS Foundation Trust, Sutton, UK; [16]Royal Derby Hospital, Derby, UK; [17]University Hospitals Bristol & Weston NHS Trust, Bristol, UK; [18]Clatterbridge Cancer Centre, Liverpool, UK; [19]Community Health Network, Indianapolis, IN, USA; [20]Center for Cancer and Blood Disorders, Bethesda, MD, USA; [21]The Christie NHS Foundation Trust, Manchester, UK; [22]CellCentric Ltd., Cambridge, UK

BACKGROUND

- Inobrodib (ino; CCS1477) is a first-in-class potent, selective, orally bioavailable inhibitor of the bromodomains of p300 and CBP, two closely-related histone acetyltransferases with oncogenic roles in hematological malignancies[1]
- *In vitro*, combining pomalidomide (pom), an immunomodulatory imide drug (IMiD), with a p300/CBP inhibitor significantly increased apoptosis and myeloma cell death compared with either agent alone[2]
  - Combining pom and ino represents a promising therapeutic strategy for patients with relapsed/refractory multiple myeloma (RRMM)
- Ino is currently being investigated as monotherapy and in combination across several hematological malignancies in an adaptive multi-arm/multi-stage trial (NCT04068597)
  - Preliminary clinical activity and a manageable safety profile were observed in patients with RRMM in the dose-escalation phase, which included two doses of pom (3 mg and 4 mg) and required patients to fast prior to dosing[3,4]
  - Here, we report the results of the randomized dose-expansion phase of ino plus pom and dexamethasone (dex; InoPd) in patients with RRMM, including those who relapsed on prior treatment with T-cell engagers (TCEs); these patients have particularly poor outcomes, with an estimated overall response rate (ORR) of 25–30%, and progression-free survival of 3–4 months[5,6]

METHODS

- Patients with confirmed RRMM and ECOG performance status of 0/1, who had either exhausted standard-of-care options or, if pom-naïve, had received ≥2 prior therapies (including lenalidomide and a proteasome inhibitor), were randomized to one of three dose levels of oral ino (20 mg, 30 mg, or 40 mg) on an intermittent 4 days-on/3 days-off schedule in combination with a standard dosing regimen of pom 4 mg/day (Days 1–21) and dex 20 or 40 mg once weekly (based on age) on a 28-day cycle
  - Randomization was stratified according to pom exposure status
  - For convenience, patients were allowed to take ino with or without food
- The primary objective was to determine the optimal dose for pivotal studies of InoPd in accordance with FDA guidance (Project Optimus),[7] accounting for key aspects of both safety and efficacy
  - Adverse events (AEs) were investigator-assessed per Common Terminology Criteria for Adverse Events v5.0, and responses by International Myeloma Working Group criteria (2016)[8]
- Multiple secondary and exploratory objectives were also assessed, including pharmacodynamic profiling of paired bone marrow and serial peripheral blood mononuclear cell samples (data reported separately)

RESULTS

Patients

- Enrollment was completed at the time of data cut-off (February 16, 2026), with 63 response-evaluable patients randomized and treated with ino 20 mg (n=21), 30 mg (n=20), or 40 mg (n=22)
- Baseline patient and disease characteristics are presented in **Table 1**
  - Patients were heavily pretreated with a median 5 lines of prior therapy (range, 2–17)
    - 71% of patients had triple-class refractory disease, 54% were pom-refractory, and 65% had been previously treated with anti-B-cell maturation antigen (BCMA) therapy and/or a TCE
- Cohorts were balanced regarding prior pom (stratification factor), and while some differences in adverse risk characteristics were noted, all cohorts had multiple characteristics consistent with poor prognosis

Table 1. Baseline characteristics

Characteristic	InoPd 20 mg (n=21)	InoPd 30 mg (n=20)	InoPd 40 mg (n=22)	Total (N=63)
Median age (range), years	68 (50–80)	68 (44–83)	72 (49–81)	70 (44–83)
Male / White	16 (76) / 17 (81)	14 (70) / 19 (95)	12 (55) / 14 (64)	42 (67) / 50 (79)
United States	4 (19)	7 (35)	10 (46)	21 (33)
ECOG PS 0 / 1	5 (24) / 16 (76)	7 (35) / 13 (65)	2 (9) / 20 (91)	14 (22) / 49 (78)
BM involvement ≥50%	6 (29)	6 (30)	5 (23)	17 (27)
Plasmacytoma	11 (52)	6 (30)	6 (27)	23 (37)
ISS stage I / II / III[a]	4 (19) / 6 (29) / 3 (14)	7 (35) / 5 (25) / 3 (15)	7 (32) / 7 (32) / 3 (14)	18 (29) / 18 (29) / 9 (14)
IMWG CGS[9] standard risk / high risk[a]	1 (5) / 5 (24)	0 (0) / 8 (40)	5 (23) / 7 (32)	6 (10) / 20 (32)
Prior SCT 1 / 2[a]	9 (43) / 4 (19)	10 (50) / 3 (15)	12 (55) / 3 (14)	31 (49) / 10 (16)
Median no. of prior lines of therapy (range)	5 (2–9)	5 (2–15)	5 (2–17)	5 (2–17)
Triple-class[b] exposed	19 (91)	18 (90)	21 (96)	58 (92)
BCMA/TCE exposed	15 (71)	12 (60)	14 (64)	41 (65)
TCE exposed	15 (71)	10 (50)	13 (59)	38 (60)
Refractory				
Pom	10 (48)	12 (60)	12 (55)	34 (54)
Triple-class[b]	14 (67)	14 (70)	17 (77)	45 (71)
Penta-drug[c]	4 (19)	5 (25)	6 (27)	15 (24)

Data are n (%) unless otherwise specified.
[a]Total ≠ 100% because of missing data. [b]Exposed/refractory to an IMiD, PI, and an anti-CD38. [c]Refractory to ≥2 IMiDs, 2 different PIs, and an anti-CD38.
BCMA, B-cell maturation antigen; BM, bone marrow; ECOG PS, Eastern Cooperative Oncology Group performance status; IMiD, immunomodulatory imide drug; ISS, International Staging System; IMWG CGS, International Myeloma Working Group Consensus Genomic Staging; InoPd, inobrodib, pomalidomide, dexamethasone; PI, proteosome inhibitor; pom, pomalidomide; SCT, stem cell transplantation; TCE, T-cell engager.

Safety

- The median duration of treatment was 153 days (20 mg, 169 days; 30 mg, 172 days; 40 mg, 142 days)
- Median treatment exposure was 88 and 109 days, respectively, for ino and pom
- Overall, 98% of patients had a treatment-emergent AE (TEAE) and 86% had an ino-related AE (**Table 2**)

Table 2. Safety summary

Patients with TEAE, n (%)	InoPd 20 mg (n=21)	InoPd 30 mg (n=20)	InoPd 40 mg (n=22)	Total (N=63)
Any-grade TEAE	21 (100)	20 (100)	21 (96)	62 (98)
Ino-related	18 (86)	17 (85)	19 (86)	54 (86)
Serious TEAE	12 (57)	14 (70)	16 (73)	42 (67)
Ino-related	8 (38)	6 (30)	10 (46)	24 (38)
Grade ≥3 TEAE	15 (71)	19 (95)	18 (82)	52 (83)
Ino-related	13 (62)	11 (55)	15 (68)	39 (62)
Grade 5 TEAE	2 (10)	1 (5)	0	3 (5)
Ino-related	0	0	0	0

ino, inobrodib; InoPd, inobrodib, pomalidomide, dexamethasone; TEAE, treatment-emergent adverse event.

- In the InoPd 20 mg cohort, of whom almost half were pom-refractory, 57% of patients had dose interruptions, and 5% and 57% of patients had dose reductions of ino and pom, respectively (**Table 3**)
- Overall, two patients had a TEAE that led to discontinuation of ino

Table 3. Treatment compliance

Patients, n (%)	InoPd 20 mg (n=21)	InoPd 30 mg (n=20)	InoPd 40 mg (n=22)	Total (N=63)
Dose modification				
Reduction of ino / pom	1 (5) / 12 (57)	5 (25) / 11 (55)	11 (50) / 9 (41)	17 (27) / 32 (51)
Interruption of ino / pom	12 (57) / 12 (57)	13 (65) / 14 (70)	14 (64) / 15 (68)	39 (62) / 41 (65)
TEAE leading to discontinuation of ino	1 (5)	0	1 (5)	2 (3)
Ino-related	0	0	0	0

ino, inobrodib; InoPd, inobrodib, pomalidomide, dexamethasone; pom, pomalidomide; TEAE, treatment-emergent adverse event.

- The most common grade 1/2 TEAEs were fatigue, diarrhea, and cytopenias (**Table 4**), and the most common grade 3/4 TEAEs were thrombocytopenia (38%), neutropenia (35%), and anemia (27%)
  - The incidence of thrombocytopenia increased with increasing dose of ino; however, in the 20 mg cohort, the rate and severity were similar to those observed with pom/dex in a less heavily pretreated population in the phase 3 DREAMM-3 study[10]
  - Bleeding events (MedDRA System Organ Class broad search) were reported in 24% of patients and most (19%) were mild or moderate; three patients had a grade 3 event (one in each dose level)
  - Grade 3/4 febrile neutropenia was reported in eight patients (20 mg, n=2; 30 mg, n=1; 40 mg, n=5)
  - Non-hematologic TEAEs were mostly grade 1/2

Table 4. All-cause TEAEs by grade 3/4 events reported in ≥5% of patients

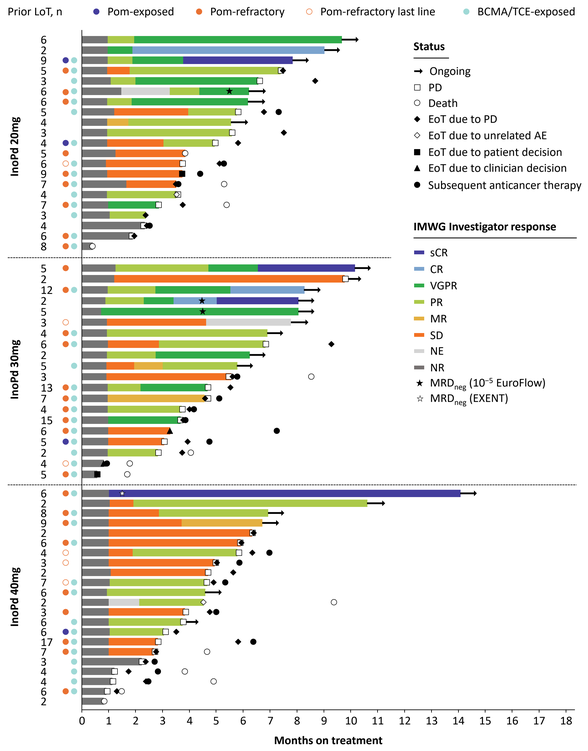
Patients with TEAE, n (%)[a]	InoPd 20 mg (n=21)		InoPd 30 mg (n=20)		InoPd 40 mg (n=22)		Total (N=63)	
	Grade 1/2	Grade 3/4	Grade 1/2	Grade 3/4	Grade 1/2	Grade 3/4	Grade 1/2	Grade 3/4
Hematologic								
Thrombocytopenia	2 (10)	6 (29)	4 (20)	6 (30)	3 (14)	12 (55)	9 (14)	24 (38)
Neutropenia	3 (14)	5 (24)	1 (5)	7 (35)	4 (18)	10 (46)	8 (13)	22 (35)
Anemia	3 (14)	5 (24)	2 (10)	5 (25)	3 (14)	7 (32)	8 (13)	17 (27)
Leukopenia	0	1 (5)	2 (10)	3 (15)	6 (27)	5 (23)	8 (13)	9 (14)
Febrile neutropenia	0	2 (10)	0	1 (5)	0	5 (23)	0	8 (13)
Non-hematologic								
Fatigue	11 (52)	2 (10)	8 (40)	3 (15)	7 (32)	1 (5)	26 (41)	6 (10)
Diarrhea	2 (10)	1 (5)	4 (20)	1 (5)	5 (23)	1 (5)	11 (18)	3 (5)
Acute kidney injury	1 (5)	3 (14)	1 (5)	1 (5)	1 (5)	1 (5)	3 (5)	5 (8)
Pneumonia	2 (10)	3 (14)	0	3 (15)	0	3 (14)	2 (3)	9 (14)
Sepsis	0	2 (10)	0	2 (10)	0	1 (5)	0	5 (8)

[a]Listed in order of frequency of grade 1/2 TEAEs in total population.
InoPd, inobrodib, pomalidomide, dexamethasone; TEAE, treatment-emergent adverse event.

Efficacy

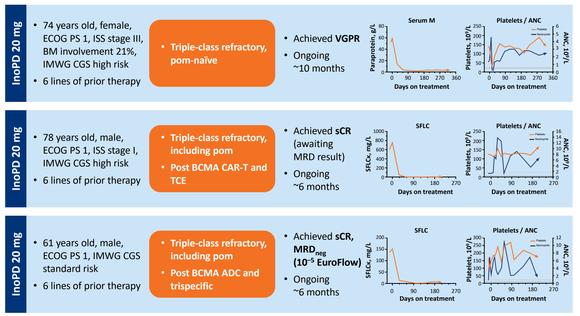
- As of February 16, 2026, median follow-up (range) among all patients was 217 (11–427) days
- Among patients treated with ino 20 mg, 30 mg, and 40 mg, the ORR was 67% (14/21), 60% (12/20), and 41% (9/22), respectively
- High response rates (67% in the 20 mg and 30 mg cohorts, and 43% in the 40 mg cohort) were noted in a population of unmet need (heavily pretreated and post-BCMA/TCE), with deep responses developing in pom-naïve patients (previously reported as MRD-negative complete responses[4]) and in heavily-pretreated patients, post-TCE (**Figures 1–3**)
- Several patients remained on treatment for >6 months (longest time on treatment >14 months)

Figure 1. Efficacy of InoPd in patients with RRMM



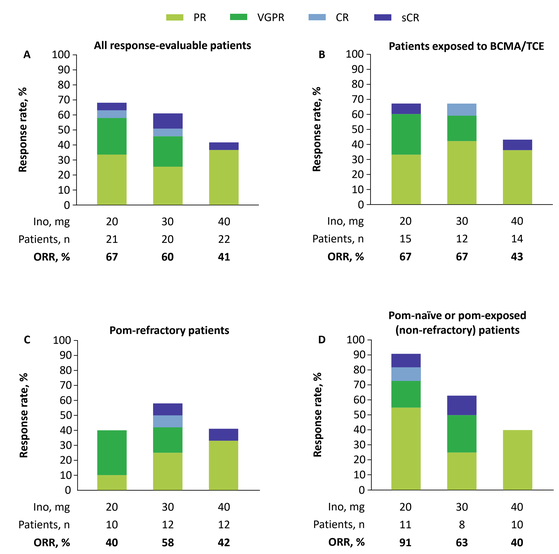
AE, adverse event; BCMA, B-cell maturation antigen; CR, complete response; EoT, end of treatment; InoPd, inobrodib, pomalidomide, dexamethasone; LoT, lines of therapy; MR, minimal response; MRD$_{neg}$, measurable residual disease negative; NE, not evaluable; NR, not reached; PD, progressive disease; pom, pomalidomide; PR, partial response; RRMM, relapsed/refractory multiple myeloma; sCR, stringent complete response; SD, stable disease; TCE, T-cell engager; VGPR, very good partial response.

Figure 2. Illustrative case studies[a]



[a]Data cut-off: April 2026.
ADC, antibody-drug conjugate; ANC, absolute neutrophil count; BCMA, B-cell maturation antigen; BM, bone marrow; CAR-T, chimeric antigen receptor T-cell therapy; ECOG PS, Eastern Cooperative Oncology Group performance status; IMWG CGS, International Myeloma Working Group Consensus Genomic Staging; MRD$_{neg}$, measurable residual disease negative; InoPd, inobrodib, pomalidomide, dexamethasone; ISS, International Staging System; sCR, stringent complete response; SFLC(κ), serum free light chain (kappa); TCE, T-cell engager; VGPR, very good partial response.

Figure 3. Overall response rates in (A) all response-evaluable patients, (B) patients exposed to BCMA/TCE, (C) pom-refractory patients, and (D) pom-naïve or pom-exposed (non-refractory) patients



BCMA, B-cell maturation antigen; CR, complete response; ino, inobrodib; ORR, overall response rate; pom, pomalidomide; PR, partial response; sCR, stringent complete response; TCE, T-cell engager; VGPR, very good partial response.

CONCLUSIONS

- The combination of InoPd has promising clinical activity, including in populations of high unmet need (e.g., patients previously treated with TCEs)
  - Observed response rates in this limited dataset at 67% in the 20 mg and 30 mg cohort appear at least two-fold higher than previously published real-world data for a similar population
- In the pom-naïve (or pom-exposed, but not refractory) setting, high ORR was noted at 91% and 63% in 20 mg and 30 mg cohorts, respectively
- Responses among pom-refractory patients, including those who were progressing with pom as the last line of therapy, further confirm previously generated clinical data as well as nonclinical data that show exquisite synergy with IMiDs
- Ino 20 mg twice daily on a 4 days-on/3 days-off schedule in combination with standard pom and dex had the best benefit/risk profile and was selected as the optimal dose for the pivotal DOMMINO-1 (NCT07096778) and DOMMINO-2 clinical trials
- This all-oral regimen with a novel mechanism of action has the potential to benefit diverse populations of patients with RRMM, many of whom are treated in the community setting

REFERENCES

1. Nicosia L, et al. *Cancer Cell*. 2023;41(12):2136–2153.e13.
2. Welsh SJ, et al. *Blood Cancer Discov*. 2024;5(1):34–55.
3. Searle E, et al. Poster presentation at EHA 2023 (P863).
4. Searle E, et al. Oral presentation at ASH 2024 (Abstract #1023).
5. Costa LJ, et al. *Leukemia*. 2025;39(3):543–554.
6. Weisel K, et al. Poster presentation at EHA 2024 (P913).
7. FDA. Optimizing the Dosage of Human Prescription Drugs and Biological Products for the Treatment of Oncologic Diseases. Guidance for Industry (August 2024).
8. Kumar S, et al. *Lancet Oncol*. 2016;17(8):e328–e346.
9. Avet-Loiseau H, et al. *J Clin Oncol*. 2025;43(24):2739–51.
10. Dimopoulos MA, et al. *Lancet Haematol*. 2023;10(10):e801–e812.

ACKNOWLEDGMENTS

We thank the patients, their families, the investigators, and the site staff.
Medical writing support was provided by Fiona Bolland, PhD, CMPP, and Farhana Burnett, PhD, CMPP, of Twist Medical, and funded by CellCentric Ltd.
The study is sponsored by CellCentric Ltd., Cambridge, UK.

Corresponding author: Nisha Joseph, MD (nisha.sara.joseph@emory.edu)

Presented at the EHA 2026 Congress; Stockholm, Sweden; June 11–14, 2026