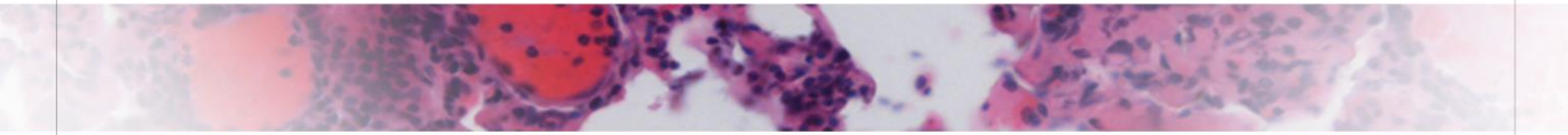
American Society of Hematology
Helping hematologists conquer blood diseases worldwide

Abstract 1121

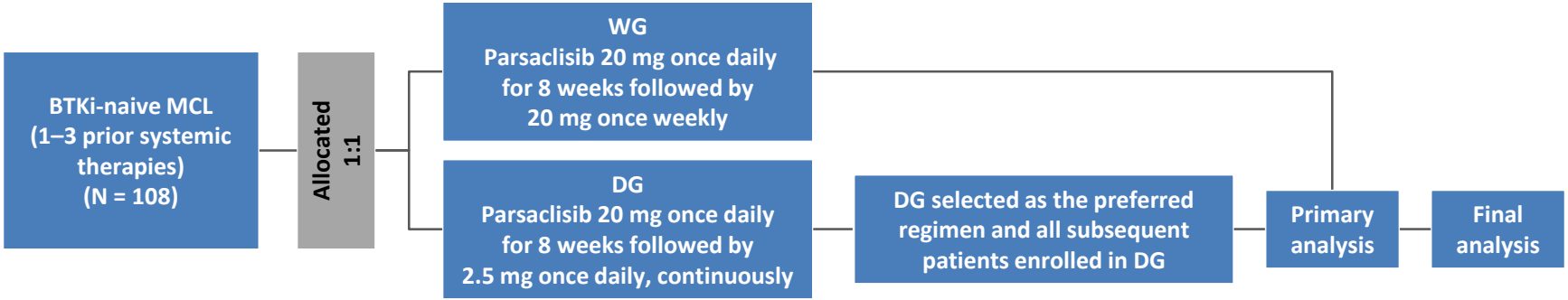


Phase 2 Study Evaluating the Efficacy and Safety of Parsaclisib in Patients With Relapsed or Refractory Mantle Cell Lymphoma Not Previously Treated With a BTK Inhibitor (CITADEL-205)

Amitkumar Mehta,[1] Marek Trněný,[2] Jan Walewski,[3] Vincent Ribrag,[4] Caroline Dartigeas,[5] Jacob Haaber Christensen,[6] Fabrizio Pane,[7] Guillermo Rodriguez,[8] Michal Taszner,[9] Parameswaran Venugopal,[10] Vittorio Ruggero Zilioli,[11] Fred Zheng,[12] Douglas J. DeMarini,[12] Wei Jiang,[12] Pier Luigi Zinzani[13]

[1]UAB School of Medicine, Birmingham, AL, USA; [2]Charles University, General Hospital, Prague, Czech Republic; [3]Maria Sklodowska-Curie National Research Institute of Oncology, Warsaw, Poland; [4]Institut Gustave Roussy, Villejuif, France; [5]CHRU Tours, Tours, France; [6]University of Southern Denmark, Denmark; [7]University of Naples Federico II, Naples, Italy; [8]Hospital Universitario Virgen del Rocío, Seville, Spain; [9]Medical University of Gdansk, Gdansk, Poland; [10]Rush University, Chicago, IL, USA; [11]ASST Grande, Ospedale Metropolitano Niguarda, Milan, Italy; [12]Incyte Corporation, Wilmington, DE, USA; [13]Institute of Hematology "Seràgnoli", University of Bologna, Bologna, Italy

CITADEL-205 Cohort 2*: Study Design



- During the study, DG was selected as the preferred dosing regimen
- Patients in WG were allowed to switch to DG; therefore, WG (31 patients) contains a mixture of the 2 dosing regimens
- Data are presented for all patients overall and DG

*NCT03235544.
BTKi, Bruton's tyrosine kinase inhibitor; DG, Daily Group; MCL, mantel cell lymphoma; WG, Weekly Group.

Patients, Assessments, and Study Endpoints

Key inclusion criteria

- Age ≥18 years with pathologically confirmed R/R MCL
- Received 1–3 prior systemic regimens
- No prior PI3K or BTK inhibitors
- ECOG performance status ≤2
- Documented cyclin D1 overexpression or t(11;14) translocation

Assessments

- Response assessed by CT/MRI using the Lugano criteria[1]
- Adverse events assessed using CTCAE v4.03
- Data cutoff date: July 13, 2020

Primary endpoint

- Objective response rate (ORR)

Secondary endpoints

- Complete response rate
- Duration of response (DOR)
- Progression-free survival (PFS)
- Overall survival (OS)
- Best percentage change in target lesion size from baseline
- Safety and tolerability of parsaclisib
- Radiology-based endpoints determined by IRC

CT, computed tomography; CTCAE, Common Terminology Criteria for Adverse Events; ECOG, Eastern Cooperative Oncology Group; IRC, independent review committee; MRI, magnetic resonance imaging; R/R, relapsed/refractory; PI3K, phosphatidylinositol 3-kinase.

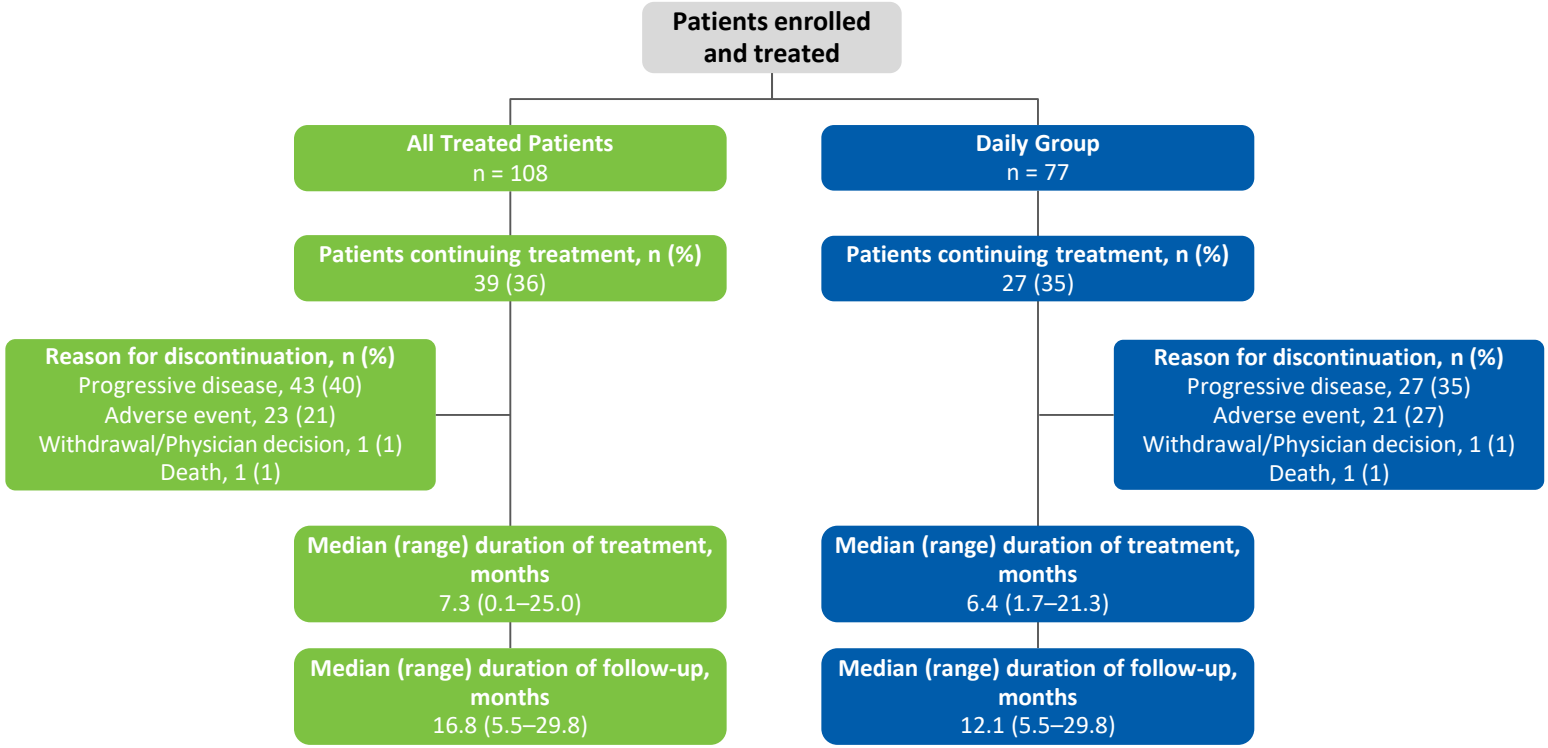
1. Cheson BD, et al. *J Clin Oncol.* 2014;32:3059–3068.

Baseline Characteristics

Characteristics	All Treated Patients (N = 108)	Daily Group (N = 77)
Age, median (range), years	72 (43–90)	72 (51–90)
≥65 years, n (%)	85 (79)	60 (78)
Men, n (%)	86 (80)	60 (78)
Time since MCL diagnosis, median (range), years	3.5 (0.1–20.9)	3.5 (0.1–16.9)
Ann Arbor Staging, n (%)		
Stage I–II	26 (24)	21 (27)
Stage III–IV	79 (73)	55 (71)
Missing	3 (3)	1 (1)
ECOG performance status ≤1, n (%)	100 (93)	73 (95)
High-risk MIPI score, n (%)	59 (55)	41 (53)
Prior therapies		
Median (range) prior systemic therapy regimens	1 (1–3)	1 (1–3)
Refractory to most recent therapy, n (%)	47 (44)	34 (44)
Prior HSCT, n (%)	34 (31)	28 (36)

HSCT, hematopoietic stem cell transplant; MIPI, Mantle Cell Lymphoma International Prognostic Index.

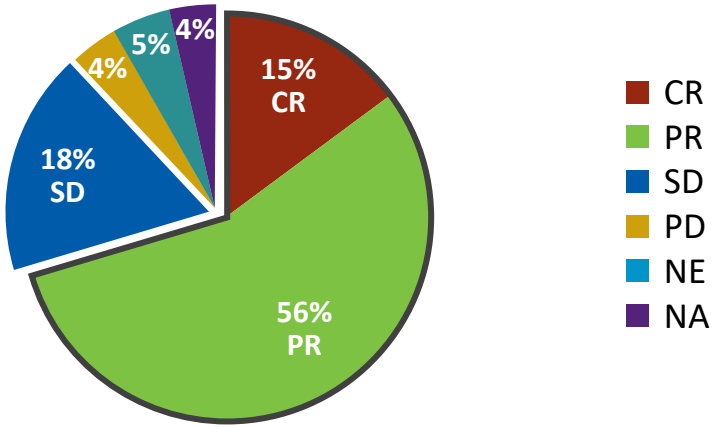
Patient Disposition



Preliminary Response Rate by IRC

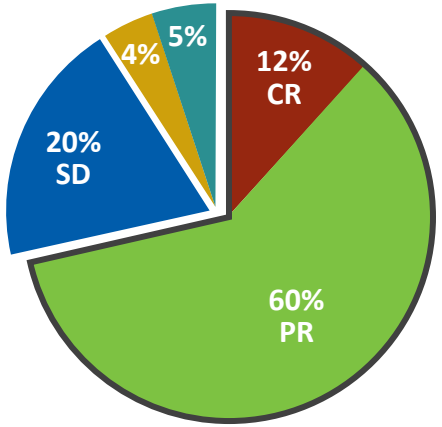
Overall ORR: 70% (95% CI: 61–79)

All Treated Patients (N = 108)



DG ORR: 71% (95% CI: 60–81)

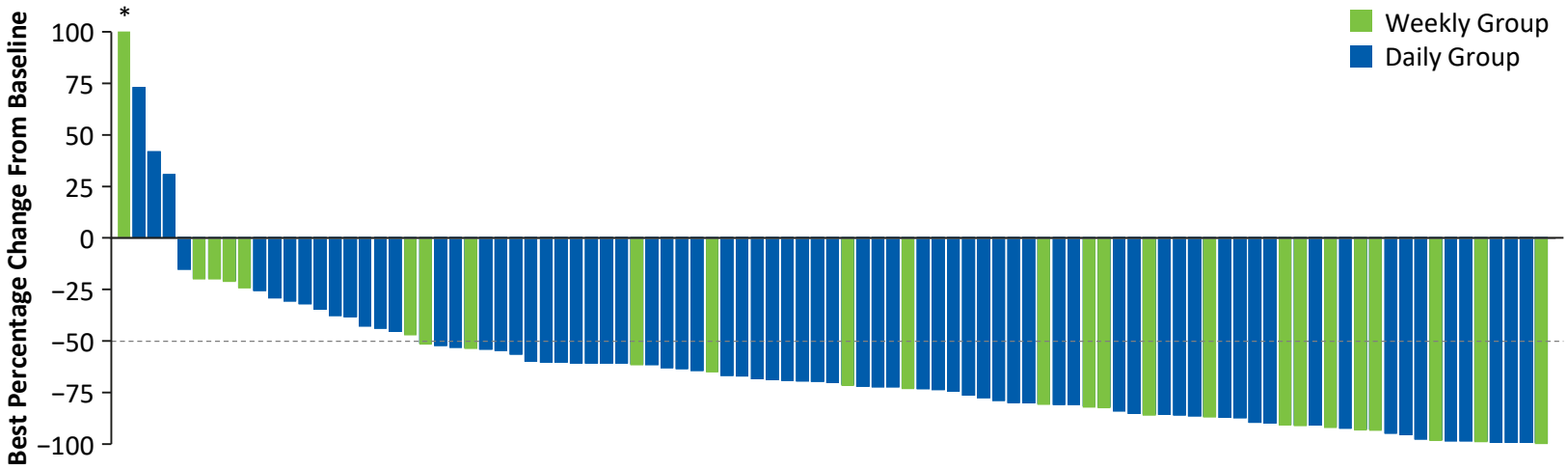
Daily Group (N = 77)



- 87% of responses occurred by the first IRC assessment
- ORR by investigator assessment: All Treated Patients 79% (95% CI: 70–86); Daily Group 81% (95% CI: 70–89)

CI, confidence interval; CR, complete response; NA, not assessed (no post-baseline response data available); NE, not evaluable; PD, progressive disease; PR, partial response; SD, stable disease.

Change From Baseline in Target Lesion Size by IRC

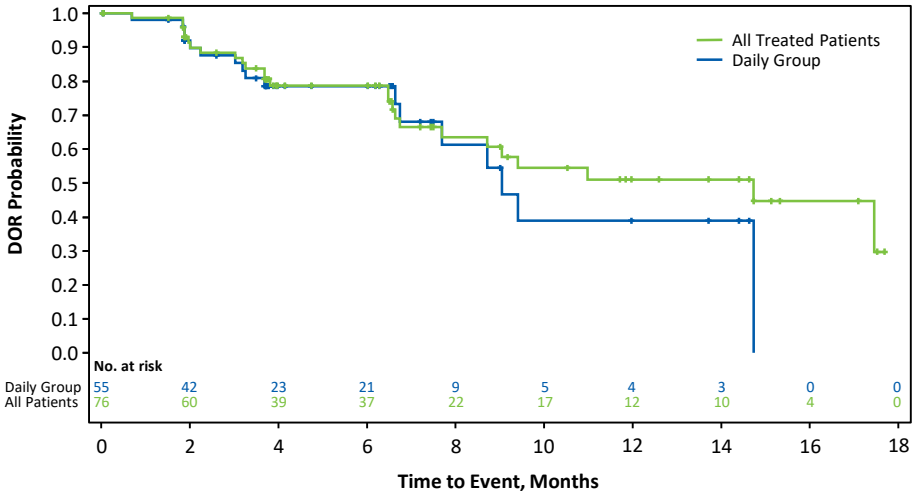


- 84% (91/108) of All Treated Patients and 87% (67/77) of patients in the Daily Group had tumor regression at target lesions

*Patient had best percentage change from baseline >100%.

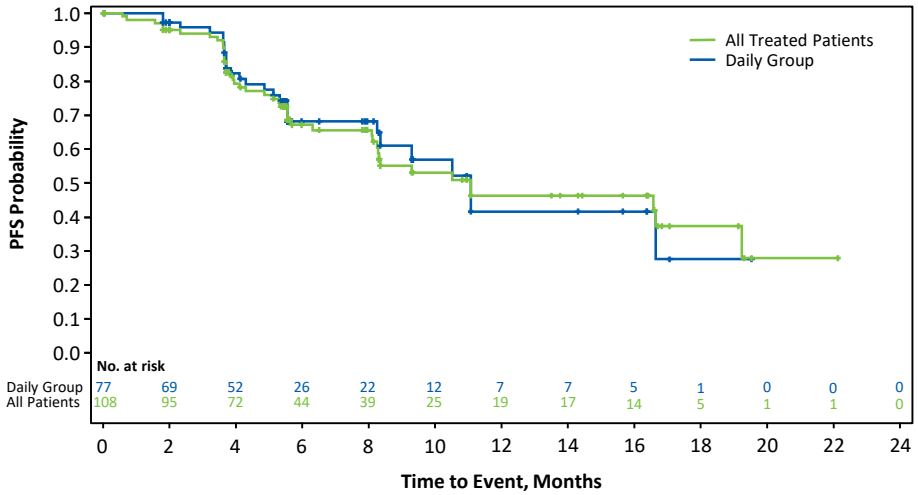
DOR and PFS by IRC

DOR



	All Treated Patients (76 Responders)	Daily Group (55 Responders)
Median DOR (95% CI), months	14.7 (7.7–NE)	9.0 (6.7–14.7)

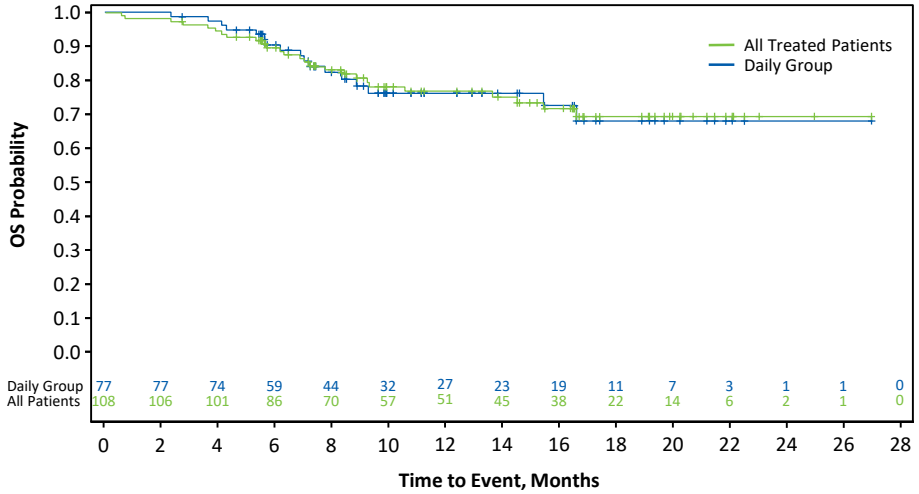
PFS



	All Treated Patients (N = 108)	Daily Group (N = 77)
Median PFS (95% CI), months	11.1 (8.3–19.2)	11.1 (8.3–NE)

OS Estimates by IRC

Kaplan-Meier Estimate of OS



	All Treated Patients (26 Deaths)	Daily Group (17 Deaths)
Median OS (95% CI), months	NR (NE–NE)	NR (NE–NE)

NR, not reached.

Estimated Survival Rates

Survival Rate (95% CI)	All Treated Patients (N = 108)	Daily Group (N = 77)
Month 6	0.90 (0.82–0.94)	0.90 (0.81–0.95)
Month 12	0.77 (0.66–0.84)	0.76 (0.63–0.85)
Month 18	0.69 (0.57–0.78)	0.68 (0.51–0.80)

Common TEAEs and Laboratory Values of Interest

TEAEs Occurring in ≥10% of All Treated Patients or Daily Group

Event, n (%)	All Treated Patients (N = 108)		Daily Group (N = 77)	
	Any Grade	Grade ≥3	Any Grade	Grade ≥3
Any TEAE	94 (87)	61 (57)	66 (86)	44 (57)
Diarrhea	34 (31)	14 (13)	28 (36)	13 (17)
Pyrexia	19 (18)	2 (2)	13 (17)	1 (1)
Constipation	15 (14)	1 (1)	12 (16)	0
Asthenia	12 (11)	2 (2)	10 (13)	1 (1)
Neutropenia	12 (11)	9 (8)	9 (12)	7 (9)
Rash	11 (10)	1 (1)	10 (13)	1 (1)
Cough	10 (9)	0	8 (10)	0
Fatigue	10 (9)	1 (1)	8 (10)	1 (1)
Hypokalemia	9 (8)	4 (4)	8 (10)	3 (4)

Select New or Worsening Laboratory Values

Event, n (%)	All Treated Patients (N = 108)			Daily Group (N = 77)		
	Any Grade	Grade 3	Grade 4	Any Grade	Grade 3	Grade 4
ALT elevation	32 (30)	4 (4)	0	24 (31)	2 (3)	0
AST elevation	26 (24)	3 (3)	0	18 (23)	2 (3)	0
Neutrophils decreased	55 (51)	5 (5)	5 (5)	44 (57)	5 (7)	4 (5)

ALT, alanine transaminase; AST, aspartate aminotransferase; TEAE, treatment-emergent adverse event.

Serious TEAEs and Dose Modifications

Serious TEAEs in ≥2 Patients Overall*

Event, n (%)	All Treated Patients (N = 108)	Daily Group (N = 77)
Any serious TEAE	42 (39)	33 (43)
Diarrhea	10 (9)	10 (13)
Colitis	4 (4)	4 (5)
Hypokalemia	4 (4)	3 (4)
Pyrexia	3 (3)	2 (3)
Cytomegalovirus infection	2 (2)	2 (3)
Pulmonary embolism	2 (2)	1 (1)

*Two deaths due to TEAEs not related to disease progression (1 patient with leukocytosis, acute kidney injury, and AML, all attributed by the investigator to be related to parsaclisib; 1 patient with endocarditis staphylococcal and septic shock, both attributed by the investigator not related to parsaclisib).

AML, acute myeloid leukemia.

Dose Modifications Due to TEAEs (Any Grade)

	All Treated Patients (N = 108)	Daily Group (N = 77)
Interruption	44 (41)	35 (45)
Reduction	5 (5)	2 (3)
Discontinuation	24 (22)*	21 (27)

*Fourteen of the 24 discontinuations overall (58%) were due to diarrhea/colitis events.

Time to High-Grade Onset and Improvement (Diarrhea or Colitis Events)

	All Treated Patients (N = 108)	Daily Group (N = 77)
Onset of grade ≥3 diarrhea/ colitis events, median (range), months	3.9 (1.0–11.0)	4.0 (1.5–11.0)
Improvement to grade ≤2 diarrhea, median (95% CI), days	11.0 (5.0–25.0)	11.0 (5.0–25.0)

Summary

- Parsaclisib, a potent, highly selective, next-generation PI3Kδ inhibitor, has demonstrated excellent activity in R/R MCL to date
  - 71% ORR, 9 months median DOR, and 11.1 months median PFS in the Daily Group
- Parsaclisib showed an acceptable safety profile that was generally well tolerated
- Parsaclisib represents a potentially new treatment option for BTKi-naive R/R MCL and a first-in-class PI3Kδ inhibitor for MCL

➢ Results of parsaclisib treatment in patients with R/R MCL who had received prior ibrutinib therapy are presented at this meeting (Zinzani et al, Abstract 2044)

Acknowledgments

The authors wish to thank the patients and their families, the investigators, and the site personnel who participated in this study.

Medical writing assistance was provided by Kakuri Omari, PhD, CMPP, of Envision Pharma Group (Philadelphia, PA), and funded by Incyte Corporation.

Scan code to download a copy of the slides and audio narration

Disclosures

Mehta: Consultant – *Bristol Myers Squibb, Celgene, Kite Pharma, and Spectrum Pharmaceuticals*; Speaker's bureau – *AstraZeneca, Gilead, and Kite Pharma*; Research funding – *Bristol Myers Squibb, Epizyme, Incyte Corporation, Merck, Roche, and Seattle Genetics*.

This study was sponsored by Incyte Corporation (Wilmington, DE).