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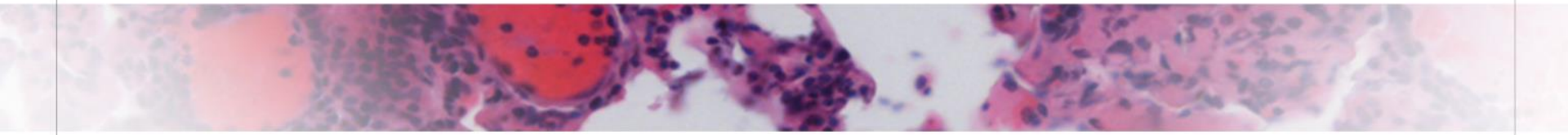
Abstract 2044



Phase 2 Study Evaluating the Efficacy and Safety of Parsaclisib in Patients With Relapsed or Refractory Mantle Cell Lymphoma Previously Treated With Ibrutinib (CITADEL-205)

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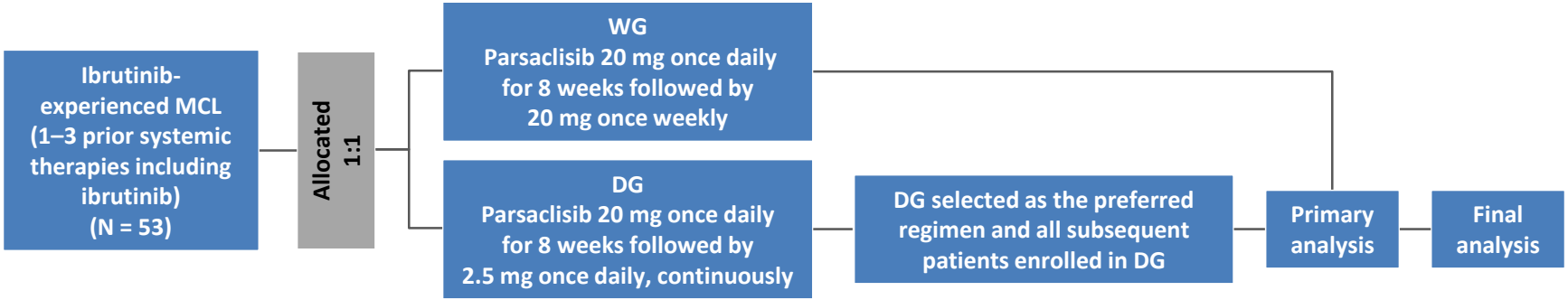
CITADEL-205 Cohort 1*: Study Design



- During the study, DG was selected as the preferred dosing regimen
- Patients in WG were allowed to switch to DG; therefore, WG (12 patients) contains a mixture of the 2 dosing regimens
- Data are presented for all patients overall and DG

*NCT03235544.
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 (must include ibrutinib)
- No prior PI3K 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 = 53)	Daily Group (N = 41)
Age, median (range), years	71.0 (48–89)	71.0 (48–89)
≥65 years, n (%)	37 (70)	29 (71)
Men, n (%)	41 (77)	30 (73)
Time since MCL diagnosis, median (range), years	4.7 (0.4–19.4)	4.3 (0.4–13.6)
Ann Arbor Staging, n (%)		
Stage I–II	10 (19)	10 (24)
Stage III–IV	43 (81)	31 (76)
ECOG performance status ≤1, n (%)	47 (89)	37 (90)
High-risk MIPI score, n (%)	29 (55)	22 (54)
Prior therapies		
Median (range) prior systemic therapy regimens	3 (1–3)	2 (1–3)
Refractory to most recent therapy, n (%)	23 (43)	18 (44)
Prior HSCT, n (%)	19 (36)	14 (34)

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

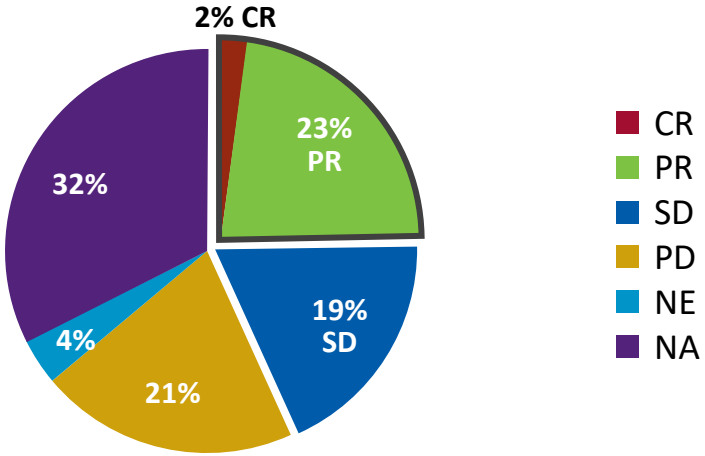
Patient Disposition

	All Treated Patients (N = 53)	Daily Group (N = 41)
Median (range) duration on parsaclisib, months	2.8 (0.1–19.6)	3.6 (0.1–19.6)
Median (range) duration of follow-up, months	14.0 (2.3–31.7)	11.0 (2.3–31.7)
Patients continuing on parsaclisib, n (%)	5 (9)	5 (12)
Primary reasons for discontinuing parsaclisib		
Progressive disease	40 (75)	30 (73)
Adverse event	4 (8)	3 (7)
Withdrawal/Physician decision	2 (4)	2 (5)
Death	2 (4)	1 (2)

Preliminary Response Rate by IRC

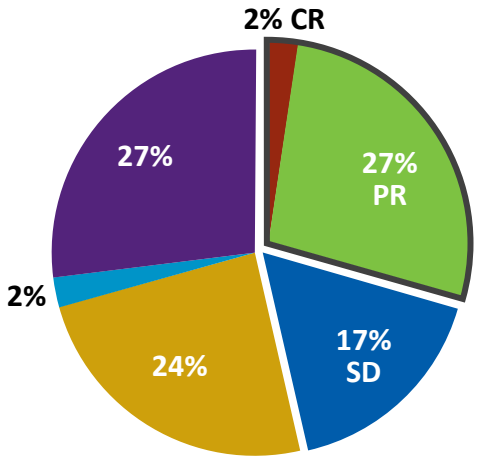
Overall ORR: 25% (95% CI: 14–38)

All Treated Patients (N = 53)



DG ORR: 29% (95% CI: 16–46)

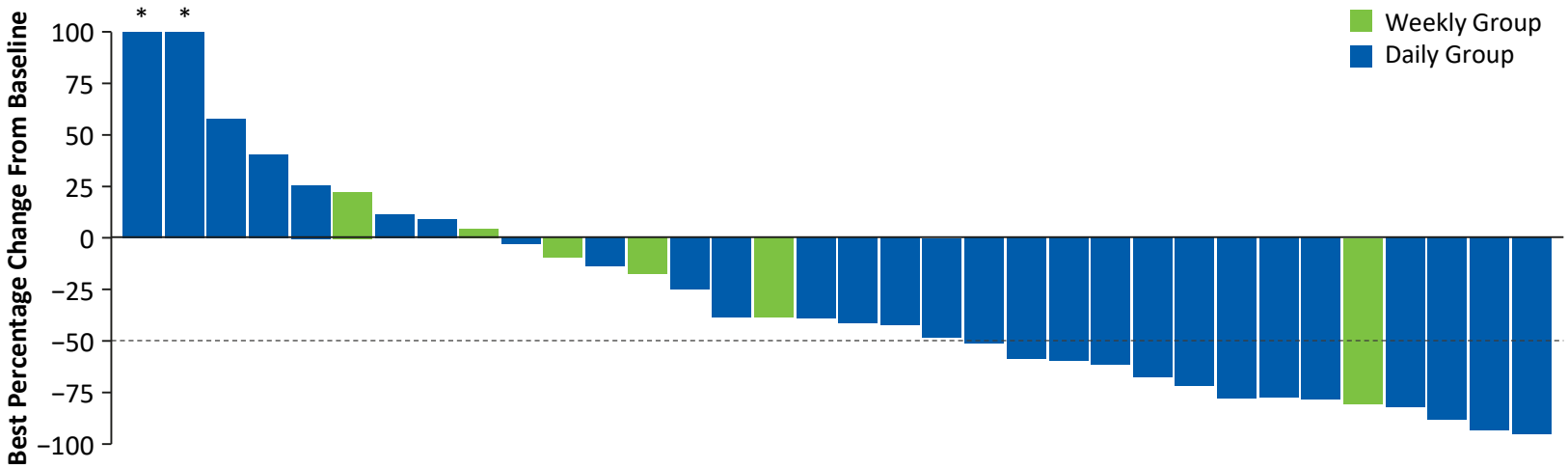
Daily Group (N = 41)



- ORR by investigator assessment: All Treated Patients 36% (95% CI: 23–50); Daily Group 44% (95% CI: 29–60)
- CR rate by investigator assessment: All Treated Patients 8% (4/53); Daily Group 10% (4/41)

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

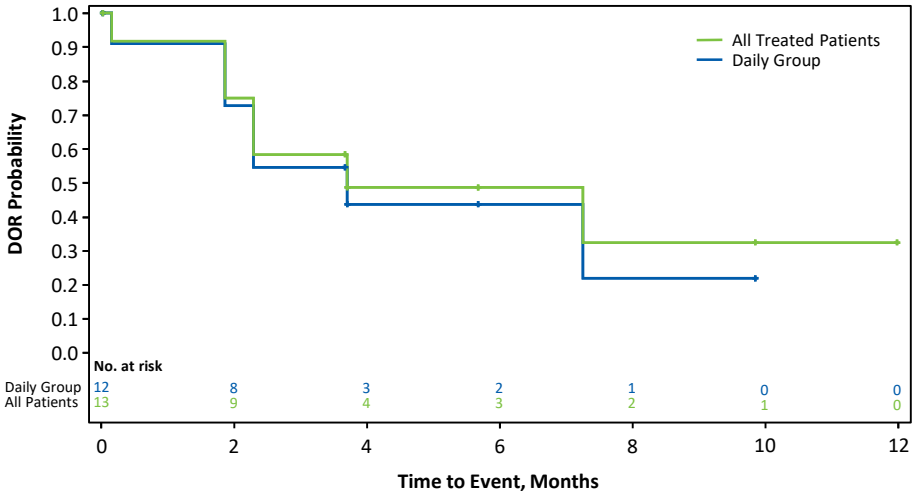


- 47% (25/53) of All Treated Patients and 51% (21/41) of patients in the Daily Group had tumor regression at target lesions

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

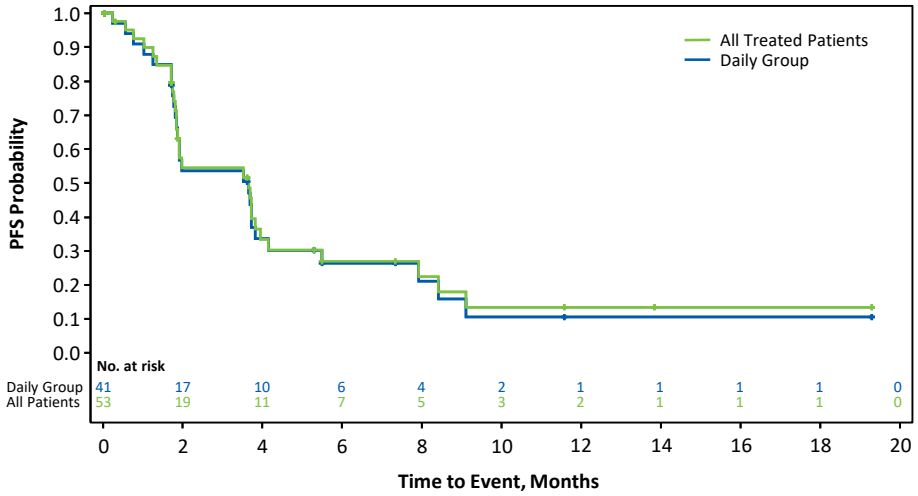
DOR and PFS by IRC

DOR



	All Treated Patients (13 Responders)	Daily Group (12 Responders)
Median DOR (95% CI), months	3.7 (1.9–NE)	3.7 (1.9–NE)

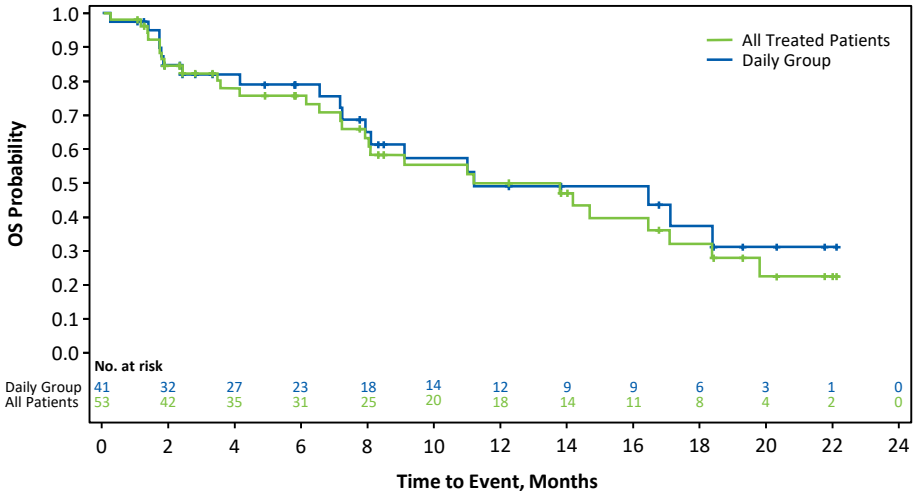
PFS



	All Treated Patients (N = 53)	Daily Group (N = 41)
Median PFS (95% CI), months	3.7 (1.8–3.9)	3.7 (1.8–4.1)

OS Estimates by IRC

Kaplan-Meier Estimate of OS



	All Treated Patients (29 Deaths)	Daily Group (19 Deaths)
Median OS (95% CI), months	11.2 (7.9–17.1)	11.2 (7.9–NE)

Estimated Survival Rates

Survival Rate (95% CI)	All Treated Patients (N = 53)	Daily Group (N = 41)
Month 6	0.76 (0.61–0.85)	0.79 (0.62–0.89)
Month 12	0.50 (0.34–0.64)	0.49 (0.30–0.66)
Month 18	0.32 (0.17–0.48)	0.37 (0.18–0.57)

Common TEAEs and Laboratory Values of Interest

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

Event, n (%)	All Treated Patients (N = 53)		Daily Group (N = 41)	
	Any Grade	Grade ≥3	Any Grade	Grade ≥3
Any TEAE	44 (83)	28 (53)	34 (83)	22 (54)
Diarrhea	12 (23)	3 (6)	10 (24)	2 (5)
Anemia	10 (19)	6 (11)	7 (17)	4 (10)
Asthenia	8 (15)	0	8 (20)	0
Neutropenia	8 (15)	4 (8)	6 (15)	4 (10)
Cough	6 (11)	1 (2)	5 (12)	1 (2)
Decreased appetite	6 (11)	0	4 (10)	0
Pyrexia	6 (11)	0	5 (12)	0
Weight decreased	6 (11)	0	4 (10)	0

New or Worsening Laboratory Values

Event, n (%)	All Treated Patients (N = 53)			Daily Group (N = 41)		
	Any Grade	Grade 3	Grade 4	Any Grade	Grade 3	Grade 4
ALT elevation	8 (15)	0	0	8 (20)	0	0
AST elevation	8 (15)	0	0	5 (12)	0	0
Neutrophils decreased	17 (32)	5 (9)	2 (4)	14 (34)	5 (12)	1 (2)
Platelets decreased	11 (21)	5 (9)	0	6 (15)	2 (5)	0
Hemoglobin decreased	21 (40)	5 (9)	NA	14 (34)	3 (7)	NA

ALT, alanine transaminase; AST, aspartate aminotransferase; NA, not applicable; TEAE, treatment-emergent adverse event.

Serious TEAEs and Dose Modifications

Serious TEAEs in ≥2 Patients Overall*

Event, n (%)	All Treated Patients (N = 53)	Daily Group (N = 41)
Any serious TEAE	23 (43)	18 (44)
Diarrhea	4 (8)	3 (7)
Pneumonia	3 (6)	3 (7)
Colitis	2 (4)	2 (5)
Neutropenia	2 (4)	2 (5)
Peripheral swelling	2 (4)	2 (5)
Dehydration	2 (4)	2 (5)
Dyspnea	2 (4)	2 (5)

*Two deaths due to TEAEs not related to disease progression (1 patient with general health deterioration and respiratory tract infection, both attributed by the investigator not related to parsaclisib; 1 patient with dehydration and neutropenia, both attributed by the investigator not related to parsaclisib).

Dose Modifications Due to TEAEs (Any Grade)

	All Treated Patients (N = 53)	Daily Group (N = 41)
Interruption	17 (32)	13 (32)
Reduction	1 (2)	1 (2)
Discontinuation	5 (9)*	4 (10)

*Three of the 5 discontinuations overall (60%) were due to diarrhea/colitis events.

Time to Onset of High-Grade Diarrhea or Colitis Events

	All Treated Patients (N = 53)	Daily Group (N = 41)
Onset of grade ≥3 diarrhea/ colitis events, median (range), months	7.1 (3.8–19.8)	5.4 (3.8–19.8)

Summary

- Parsaclisib, a potent, highly selective, next-generation PI3Kδ inhibitor, demonstrated clinical activity in R/R MCL previously treated with ibrutinib
  - 29% ORR, 3.7 months median DOR, and 3.7 months median PFS in the Daily Group
- Parsaclisib showed an acceptable safety profile that was generally well tolerated

➢ Results of parsaclisib treatment in patients with R/R MCL who had not received prior BTKi therapy are presented at this meeting (Mehta et al, Abstract 1121)

BTKi, Bruton's tyrosine kinase inhibitor.

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

Zinzani: Consultant or advisor – *Bristol Myers Squibb, Celgene, Celltrion, EUSA Pharma, Gilead, Immune Design, Janssen-Cilag, Kyowa Kirin, MSD, Portola, Roche, Sandoz, Sanofi, Servier, and Verastem Oncology*; Speaker's bureau – *Bristol Myers Squibb, Celgene, Celltrion, EUSA Pharma, Gilead, Immune Design, Janssen-Cilag, Kyowa Kirin, MSD, Roche, Sandoz, Servier, Portola, and Verastem Oncology.*

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