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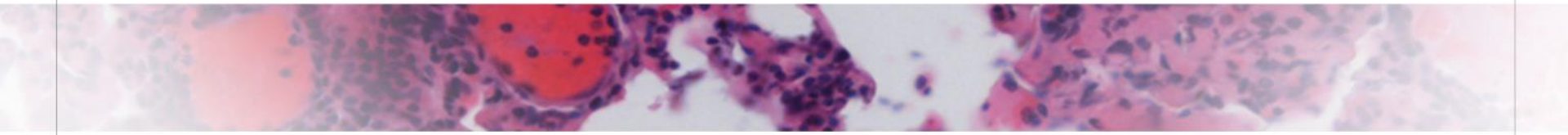
Abstract 2935



Phase 2 Study Evaluating the Efficacy and Safety of Parsaclisib in Patients With Relapsed or Refractory Follicular Lymphoma (CITADEL-203)

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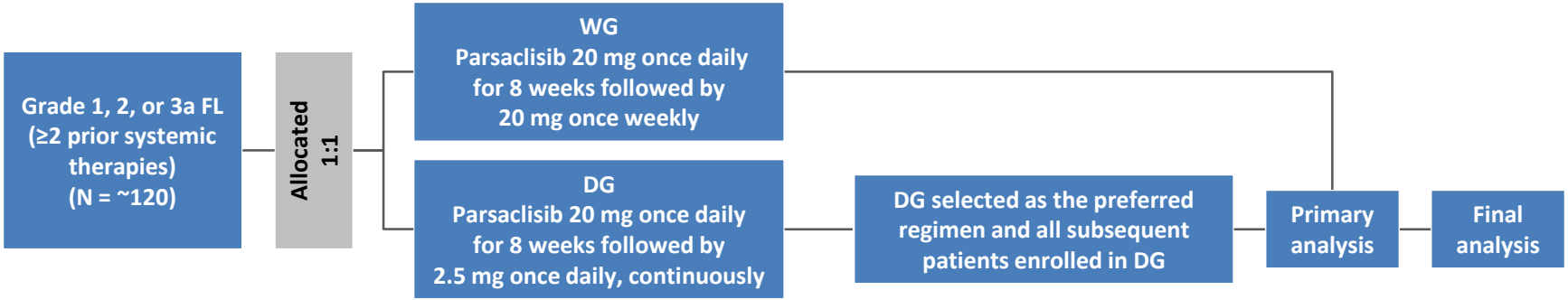
CITADEL-203*: Study Design

- Parsaclisib is a potent, highly selective, next-generation PI3Kδ inhibitor that has shown promising activity in NHL



- During the study, DG was selected as the preferred dosing regimen
- Patients in WG were allowed to switch to DG; therefore, WG (23 patients) contains a mixture of the 2 dosing regimens
- Data are presented for all patients overall and DG

*NCT03126019

DG, Daily Group; FL, follicular lymphoma; NHL, non-Hodgkin lymphoma; PI3K, phosphatidylinositol 3-kinase; WG, Weekly Group.

Patients, Assessments, and Study Endpoints

Key inclusion criteria

- Age ≥18 years with pathologically confirmed R/R FL
- Received ≥2 prior systemic regimens
- ECOG performance status ≤2
- No prior PI3K or BTK inhibitors
- Ineligible for stem cell transplantation

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
- Best percentage change in target lesion size from baseline
- Safety and tolerability of parsaclisib
- Radiology-based endpoints determined by IRC

BTK, Bruton's tyrosine kinase; 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.

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

Baseline Characteristics

Characteristics	All Treated Patients (N = 125)	Daily Group (N = 102)
Age, median (range), years	68.0 (40–88)	69.0 (40–88)
≥65 years, n (%)	76 (61)	64 (63)
Men, n (%)	69 (55)	57 (56)
Time since FL diagnosis, median (range), years	6 (0.2–32)	6 (0.2–32)
Current Ann Arbor Staging, n (%)		
Stage I–II	23 (18)	19 (19)
Stage III–IV	98 (78)	79 (77)
Missing	4 (3)	4 (4)
ECOG performance status ≤1, n (%)	117 (94)	96 (94)
Current FLIPI risk category ≥3, n (%)	57 (46)	50 (49)
Prior therapies		
Median (range) prior systemic therapy regimens	2 (1–8)	2 (1–8)
Anti-CD20, n (%)	122 (98)	99 (97)
Chemotherapy, n (%)	119 (95)	97 (95)
Refractory to most recent therapy, n (%)	62 (50)	50 (49)
Prior HSCT, n (%)	23 (18)	17 (17)

FLIPI, Follicular Lymphoma International Prognostic Index; HSCT, hematopoietic stem cell transplant.

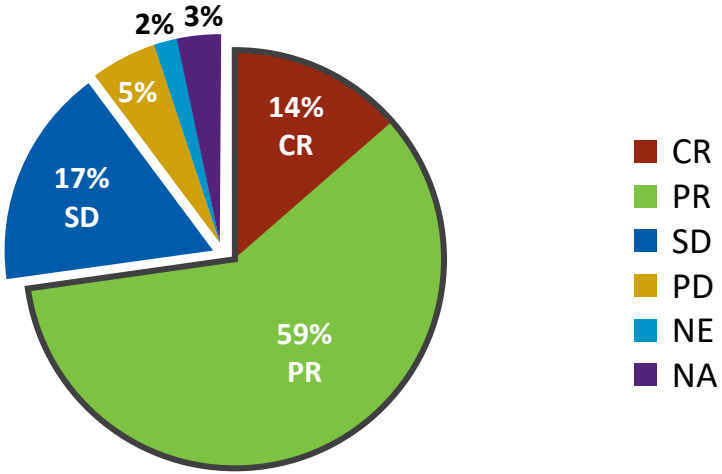
Patient Disposition

	All Treated Patients (N = 125)	Daily Group (N = 102)
Median (range) duration on parsaclisib, months	7.1 (0.2–21.0)	7.0 (0.2–21.0)
Median (range) duration of follow-up, months	14.5 (0.2–28.0)	11.7 (0.2–26.9)
Patients continuing on parsaclisib, n (%)	54 (43)	49 (48)
Primary reasons for discontinuing parsaclisib		
Progressive disease	36 (29)	24 (24)
Adverse event	24 (19)	20 (20)
Withdrawal/Physician decision	9 (7)	7 (7)
Other	2 (2)	2 (2)

Preliminary ORR by IRC

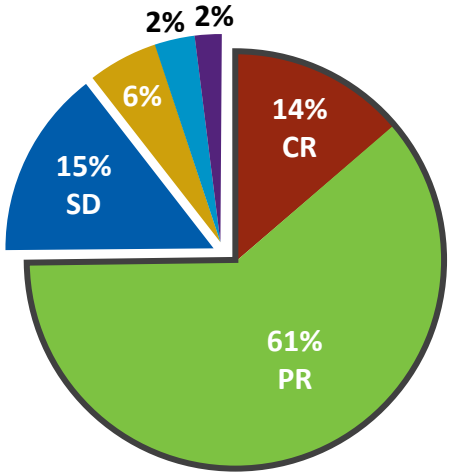
Overall ORR: 73% (95% CI: 64–81)

Efficacy Evaluable All Treated Patients (N = 118)*



DG ORR: 75% (95% CI: 65–83)

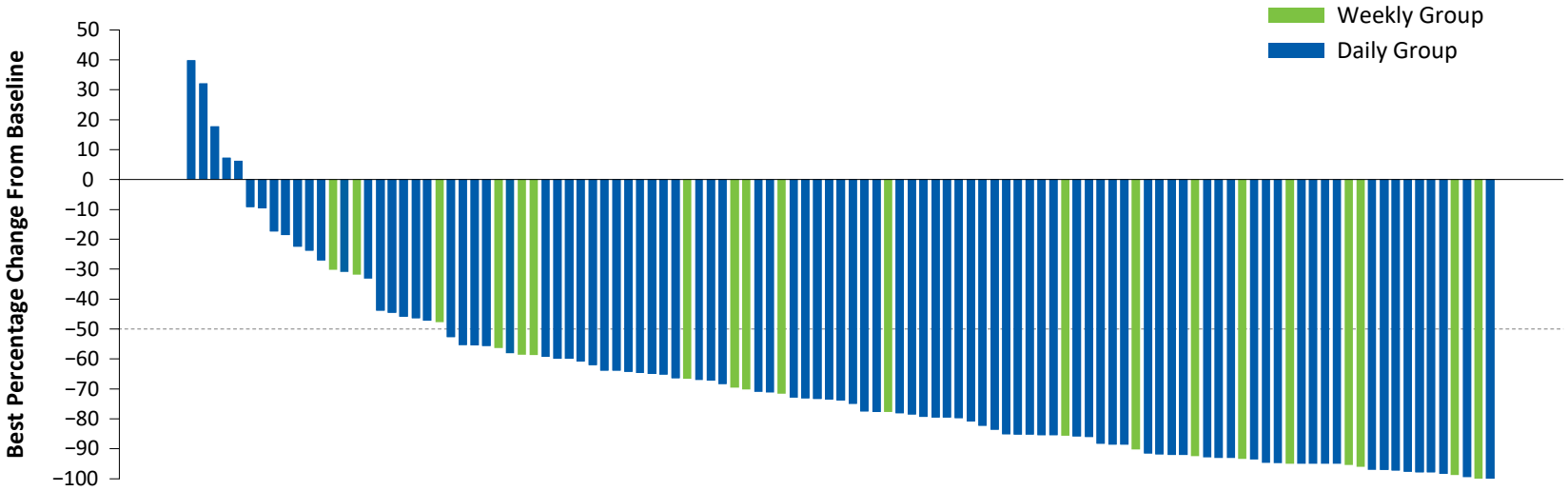
Efficacy Evaluable DG (N = 95)*



- 77% of responses occurred at first assessment
- ORR by investigator assessment: efficacy evaluable All Treated Patients 73% (95% CI: 64–81), Daily Group 74% (95% CI: 64–82)

*Efficacy evaluable population consists of treated patients who had at least 9 weeks of follow-up or had at least 1 post-baseline disease assessment or had discontinued the study prematurely.
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.

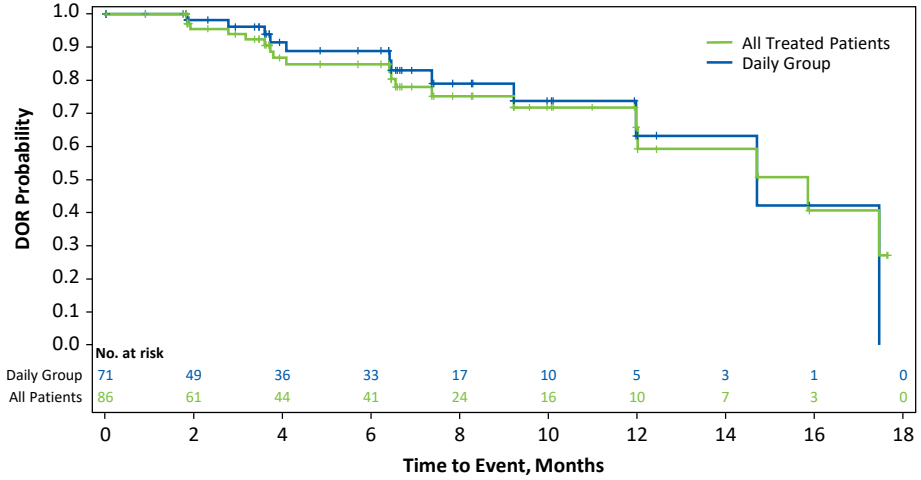
Change From Baseline in Target Lesion Size by IRC



- 90% (106/118) of efficacy evaluable All Treated Patients and 91% (86/95) of efficacy evaluable patients in the Daily Group had tumor regression at target lesions

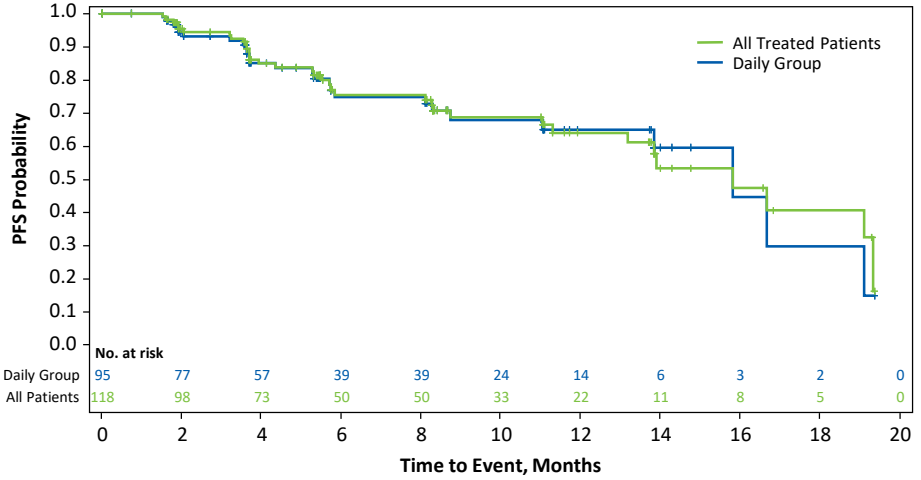
DOR and PFS by IRC

DOR



	Efficacy Evaluable All Patients (86 Responders)	Efficacy Evaluable Daily Group (71 Responders)
Median DOR (95% CI), months	15.9 (12.0–NE)	14.7 (12.0–17.5)

PFS



	Efficacy Evaluable All Patients (N = 118)	Efficacy Evaluable Daily Group (N = 95)
Median PFS (95% CI), months	15.8 (13.2–19.3)	15.8 (13.8–19.1)

Common TEAEs and Laboratory Values of Interest

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

Event, n (%)	All Treated Patients (N = 125)		Daily Group (N = 102)	
	Any Grade	Grade ≥3	Any Grade	Grade ≥3
Any TEAE	114 (91)	68 (54)	91 (89)	55 (54)
Diarrhea	41 (33)	12 (10)	38 (37)	11 (11)
Nausea	32 (26)	1 (1)	26 (25)	1 (1)
Cough	28 (22)	0	25 (25)	0
Fatigue	19 (15)	1 (1)	16 (16)	1 (1)
Pyrexia	19 (15)	3 (2)	17 (17)	3 (3)
Rash	17 (14)	3 (2)	11 (11)	2 (2)
Neutropenia	16 (13)	12 (10)	14 (14)	10 (10)
Asthenia	14 (11)	1 (1)	12 (12)	1 (1)
Hypokalemia	11 (9)	2 (2)	11 (11)	2 (2)

New or Worsening Laboratory Values

Event, n (%)	All Treated Patients (N = 125)			Daily Group (N = 102)		
	Any Grade	Grade 3	Grade 4	Any Grade	Grade 3	Grade 4
ALT elevation	32 (26)	2 (2)	0	26 (25)	2 (2)	0
AST elevation	29 (23)	0	0	26 (25)	0	0
Neutrophils decreased	54 (43)	12 (10)	5 (4)	44 (43)	10 (10)	4 (4)
Hemoglobin decreased	35 (28)	3 (2)	NA	30 (29)	2 (2)	NA
Platelets decreased	25 (20)	0	0	20 (20)	0	0

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 = 125)	Daily Group (N = 102)
Any serious TEAE	53 (42)	43 (42)
Diarrhea	9 (7)	8 (8)
Colitis	8 (6)	8 (8)
Pyrexia	4 (3)	4 (4)
Pneumonitis	3 (2)	2 (2)
Febrile neutropenia	2 (2)	2 (2)
Lower respiratory tract infection	2 (2)	2 (2)
Pleural effusion	2 (2)	2 (2)
Rash	2 (2)	2 (2)
Vomiting	2 (2)	2 (2)
Acute kidney injury	2 (2)	1 (1)
Dehydration	2 (2)	1 (1)
Respiratory tract infection	2 (2)	1 (1)

*One death due to TEAEs (Stevens-Johnson syndrome; attributed by the investigator not related to parsaclisib).

Dose Modifications Due to TEAEs (Any Grade)

	All Treated Patients (N = 125)	Daily Group (N = 102)
Interruption	59 (47)	49 (48)
Reduction	13 (10)	12 (12)
Discontinuation	26 (21)*	22 (22)

*Eleven of the 26 discontinuations overall (42%) were due to diarrhea/colitis events.

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

	All Treated Patients (N = 125)	Daily Group (N = 102)
Onset of grade ≥3 diarrhea/ colitis events, median (range), months	5.8 (0.2–12.9)	6.5 (0.2–12.9)
Improvement to grade ≤2 diarrhea, median (95% CI), days	23.5 (6.0–32.0)	24.0 (6.0–32.0)

Summary

- Parsaclisib, a potent, highly selective, next-generation PI3Kδ inhibitor, has demonstrated excellent efficacy in R/R FL to date
  - 75% ORR, 14.7 months median DOR, and 15.8 months median PFS in the Daily Group
- Parsaclisib has a favorable safety profile
  - Significant transaminase elevations were uncommon
  - Diarrhea and colitis were manageable and reversible
- The primary analysis is planned for Q1 2021

Acknowledgments

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Disclosures

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