

Categorized Hematologic Response to Pegcetacoplan in Patients with Paroxysmal Nocturnal Hemoglobinuria: Post Hoc Analysis of Data from Phase 1b (PADDOCK) and Phase 2a (PALOMINO) Trials

Antonio M. Risitano, MD, PhD^{1,2}, Raymond S. Wong, MBChB, MD³, Mohammed Al-Adhami, PhD⁴, Crystal Chen, MD⁴, and Régis Peffault de Latour, MD, PhD⁵

¹Hematology and BMT Unit, AORN, San Giuseppe Moscati, Avellino, Italy; ²Department of Clinical Medicine and Surgery, Federico II University of Naples, Naples, Italy; ³Sir YK Pao Centre for Cancer & Department of Medicine and Therapeutics, Prince of Wales Hospital, The Chinese University of Hong Kong, Shatin, NT, Hong Kong; ⁴Apellis Pharmaceuticals, Inc., Waltham, MA, United States; ⁵French Reference Center for Aplastic Anemia and Paroxysmal Nocturnal Hemoglobinuria, Assistance Publique – Hôpitaux de Paris, Université de Paris, Paris, France

CONCLUSIONS

- ✓ Post hoc analysis of data from the PADDOCK and PALOMINO trials demonstrated that a substantial proportion of patients with paroxysmal nocturnal hemoglobinuria (PNH) achieved Good, Major, or Complete hematological responses to pegcetacoplan at 16 Weeks, a trend which was sustained to 48 Weeks
- ✓ These results suggest that pegcetacoplan treatment in complement inhibitor-naïve PNH patients can lead to persistent clinical improvements in clinical and hematologic parameters

INTRODUCTION

- Paroxysmal nocturnal hemoglobinuria (PNH) is a rare, acquired, potentially life-threatening hematologic disease characterized by complement-mediated hemolysis, anemia, and thrombosis¹
- Despite treatment with C5-inhibitors to control intravascular hemolysis, anemia persists in approximately 70% of patients, primarily due to C3-mediated extravascular hemolysis²⁻⁴
- Pegcetacoplan, a C3-inhibitor recently approved by the Food and Drug Administration (FDA) for treatment of PNH, controls intravascular hemolysis and prevents extravascular hemolysis⁵
- The PADDOCK (Phase 1b; NCT02588833) and PALOMINO (Phase 2a; NCT03593200) trials assessed the safety and efficacy of pegcetacoplan in adult complement inhibitor-naïve patients
- Analysis of PADDOCK and PALOMINO trial data demonstrated pegcetacoplan’s improvement of key hematologic and clinical parameters, including hemoglobin level and freedom from transfusion⁶

AIMS

This post hoc analysis categorized patients’ hematologic response to pegcetacoplan treatment in the combined PADDOCK/PALOMINO trials.

METHODS

Trial Design

- PADDOCK was an open-label, multiple ascending dose pilot study of 2 cohorts (n=20). Cohort 1 received a suboptimal pegcetacoplan dose (180 mg/day subcutaneously) for 28 days. Cohort 2 received a pegcetacoplan dose of 270-360 mg/day subcutaneously for up to one year. Patients could be enrolled in both cohorts
- PALOMINO was an open-label study of a single cohort (n=4). Patients received a pegcetacoplan dose of 270-360 mg/day subcutaneously for up to one year

Post Hoc Analysis

- Categorization of hematologic response to pegcetacoplan at 16 Weeks and 48 Weeks for patients in the combined PADDOCK/PALOMINO trials (N=24) was performed manually by two independent, blinded observers, per criteria presented in Risitano AM, et al. *Front Immunol.* 2019;10:1157 (**Table 1**).⁷ Any discrepancies were resolved with a third observer, which was needed for 2 patients at 16 weeks and 3 patients at 48 weeks
- Patients missing data at one or both assessment timepoints were ignored

METHODS, continued

Table 1. Hematologic Response Criteria ⁶				
Response Category	PRBC Transfusions	Hb Level	LDH Level*†	ARC*
Complete	None	≥12 g/dL	≤1.5x ULN	and ≤150,000/μL‡
Major	None	≥12 g/dL	>1.5x ULN	or >150,000/μL‡
Good	None	≥10 and <12 g/dL	A. ≤1.5x ULN B. >1.5x ULN	Rule out bone marrow failure [°]
Partial	None or occasional (≤2 every 6 months)	≥8 and <10 g/dL	A. ≤1.5x ULN B. >1.5x ULN	Rule out bone marrow failure [°]
Minor#	None or occasional (≤2 every 6 months)	<8 g/dl		
	Regular (3–6 every 6 months)	<10 g/dL	A. ≤1.5x ULN B. >1.5x ULN	Rule out bone marrow failure [°]
	Reduction by ≥50%^	<10 g/dL		
No response#	Regular (>6 every 6 months)	<10 g/dL	A. ≤1.5x ULN B. >1.5x ULN	Rule out bone marrow failure [°]

Abbreviations: ARC, absolute reticulocyte count; Hb, hemoglobin; LDH, lactate dehydrogenase; PRBC, packed red blood cell; ULN, upper limit of normal
*Response categories are mostly based on red blood cell transfusion and Hb level, but LDH and ARC serve as ancillary indicators to discriminate between complete and major response, as well as within suboptimal response categories.
†A. and B. indicate subcategories without or with residual significant intravascular hemolysis, respectively.
‡To rule out increased erythropoietic response to compensate ongoing hemolysis; the value of 150,000/μL is a tentative index based on 1.5 x ULN (which in most laboratories is set at 100,000/μL).
°To assess the relative contribution of the degree of bone marrow failure to any response less than complete: a value of ARC below 60,000/μl could be a tentative index to establish such a contribution; bone marrow investigation may be appropriate.
^For patients with previous transfusion history (with a pre-treatment follow up of at least 6 months).
#For patients who do not accept red blood cell transfusions, minor response can be defined based on Hb level ≥6 and <8 g/dL, and no response based on Hb <6 g/dL. All Hb, LDH and ARC values should be assessed based on the median value over a period of 6 months.

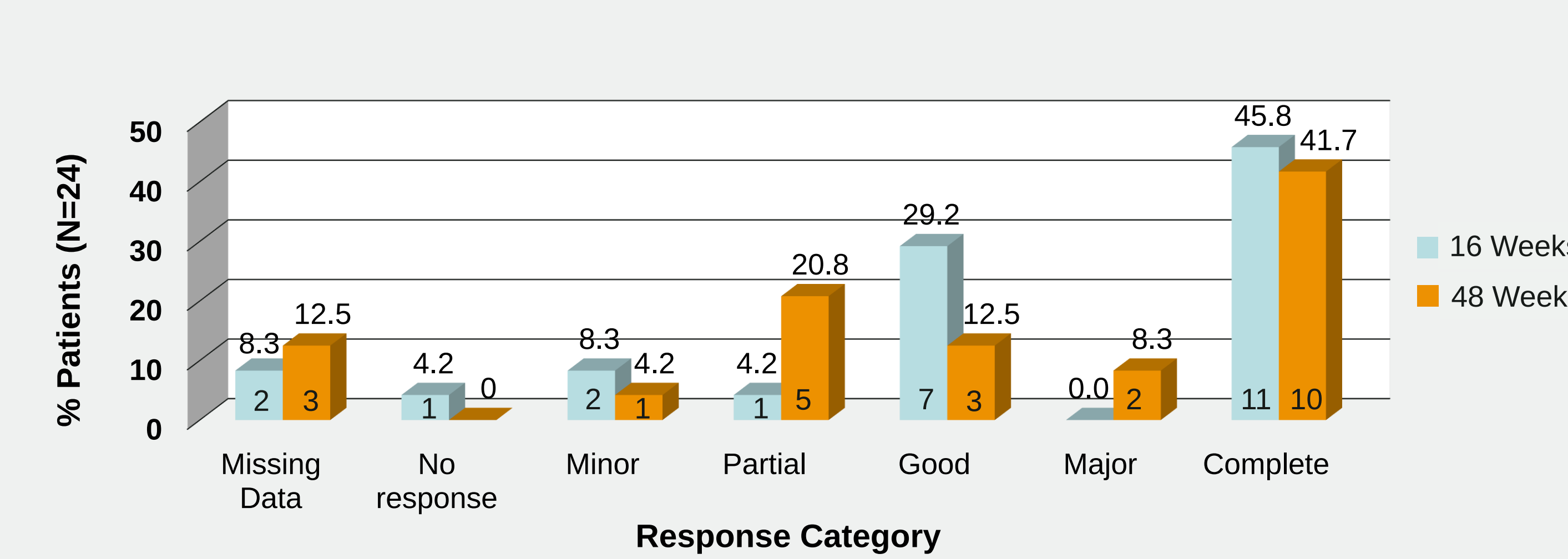
RESULTS

Most patients in the combined PADDOCK/PALOMINO trials achieved a Good, Major, or Complete hematologic response to pegcetacoplan at 16 Weeks (18/24; 75.0%) and 48 Weeks (15/24; 62.5%) (**Figure 1**). Data for the individual trials is presented in **Table 2**.

- In PADDOCK, 2 patients at 16 Weeks and 3 patients at 48 Weeks were unevaluable due to missing data
- Of those patients with evaluable data at 48 Weeks, 4/21 (19.0%) achieved at least 1 category of improvement in hematologic response at 48 Weeks when compared to 16 Weeks; 13/21 (62.0%) maintained the same response category, 4/21 (19.0%) experienced a decline in response category, which was comparable to a previous hematologic response analysis in patients treated with eculizumab over 12 months⁸

RESULTS, continued

Figure 1. Categorized Hematologic Response to Pegcetacoplan for Patients in the Combined PADDOCK/PALOMINO Trials at 16 Weeks and 48 Weeks



*Numbers within shaded bars represent *n* for associated percentages.

Table 2. Categorized Hematologic Response to Pegcetacoplan for Patients in the PADDOCK and PALOMINO Trials at 16 Weeks and 48 Weeks

Response Category	PADDOCK n=20 n (%)		Response Category	PALOMINO n=4 n (%)	
	16 Weeks	48 Weeks		16 Weeks	48 Weeks
Complete	9 (45.0)	7 (35.0)	Complete	2 (50.0)	3 (75.0)
Major	0 (0.0)	2 (10.0)	Major	0 (0.0)	0 (0.0)
Good	5 (25.0)	2 (10.0)	Good	2 (50.0)	1 (25.0)
Partial	1 (5.0)	5 (25.0)	Partial	0 (0.0)	0 (0.0)
Minor	2 (10.0)	1 (5.0)	Minor	0 (0.0)	0 (0.0)
No response	1 (5.0)	0 (0.0)	No response	0 (0.0)	0 (0.0)
Missing Data	2 (10.0)	3 (15.0)	Missing Data	0 (0.0)	0 (0.0)

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