Efficacy and Safety Is Maintained in Adult Patients With Paroxysmal Nocturnal Hemoglobinuria Receiving Pegcetacoplan for Up to 3 Years

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CONCLUSIONS

- ✓ **Pegcetacoplan is the first proximal inhibitor demonstrating long-term efficacy and safety for a broad PNH population**
- ✓ **Hematologic improvements were maintained through 3 years in C5i-experienced patients (PEGASUS) and through 2.5 years in C5i-naive patients (PRINCE)**
- ✓ **Transfusion burden was markedly reduced after pegcetacoplan initiation, with 52% of patients avoiding transfusion through 3 years in PEGASUS and 67% through 2.5 years in PRINCE**
- ✓ **No new safety findings were identified**

INTRODUCTION

- Pegcetacoplan increased Hb concentrations in C5i-experienced and -naive adults with PNH in 2 phase 3 clinical trials (PEGASUS [NCT03500549] and PRINCE [NCT04085601], respectively)[1–3]
- Long-term safety and efficacy of pegcetacoplan are being assessed in the ongoing 307 OLE (NCT03531255)

OBJECTIVE

To report the longest continuous clinical trial data set for pegcetacoplan by conducting an integrated analysis of 2 phase 3 trials and the subsequent OLE

METHODS

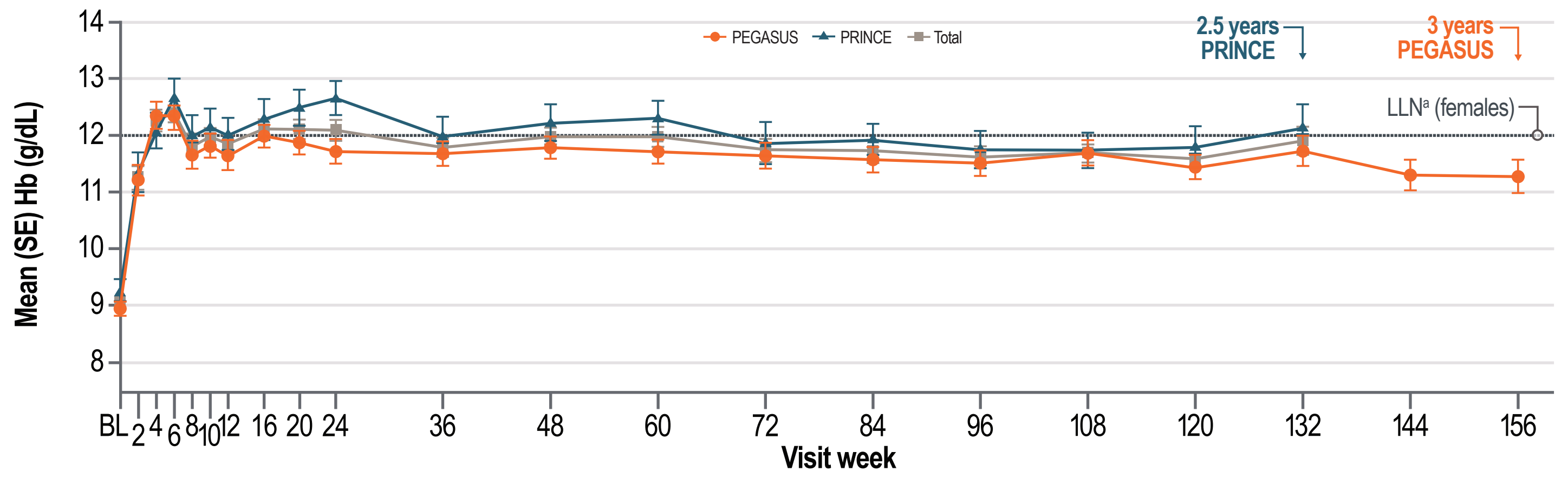
- Patients in the 307 OLE initially received pegcetacoplan 1080 mg subcutaneously twice weekly (dose escalations allowed)
- Efficacy was assessed from pegcetacoplan initiation up to 3 years (PEGASUS) and 2.5 years (PRINCE) by Hb, LDH, ARC, and indirect bilirubin values; FACIT-Fatigue scores; and transfusion avoidance rates
  - The Hb analysis accounted for transfusions; measures within 28 days before pegcetacoplan initiation and within 60 days of transfusion during pegcetacoplan treatment were excluded
- Safety during pegcetacoplan monotherapy was assessed

RESULTS

- Of 133 patients in the phase 3 trials, 114 enrolled in the 307 OLE (PEGASUS, 64; PRINCE, 50)
- In the year before initial enrollment, ≥75% received a transfusion
- In PEGASUS and PRINCE, prior to pegcetacoplan initiation, mean (SD) Hb concentrations were 9.0 (1.1) g/dL and 9.3 (1.4) g/dL, respectively; median (IQR) LDH concentrations were 217 (185, 277) U/L and 1964 (1409, 2503) U/L; mean (SD) FACIT-Fatigue scores were 31.6 (11.7) and 36.6 (10.0); mean (SD) ARCs were 214 (79) ×10^9 cells/L and 181 (69) ×10^9 cells/L; mean (SD) indirect bilirubin concentrations were 33.2 (24.9) µmol/L and 32.3 (16.7) µmol/L

RESULTS (*continued*)

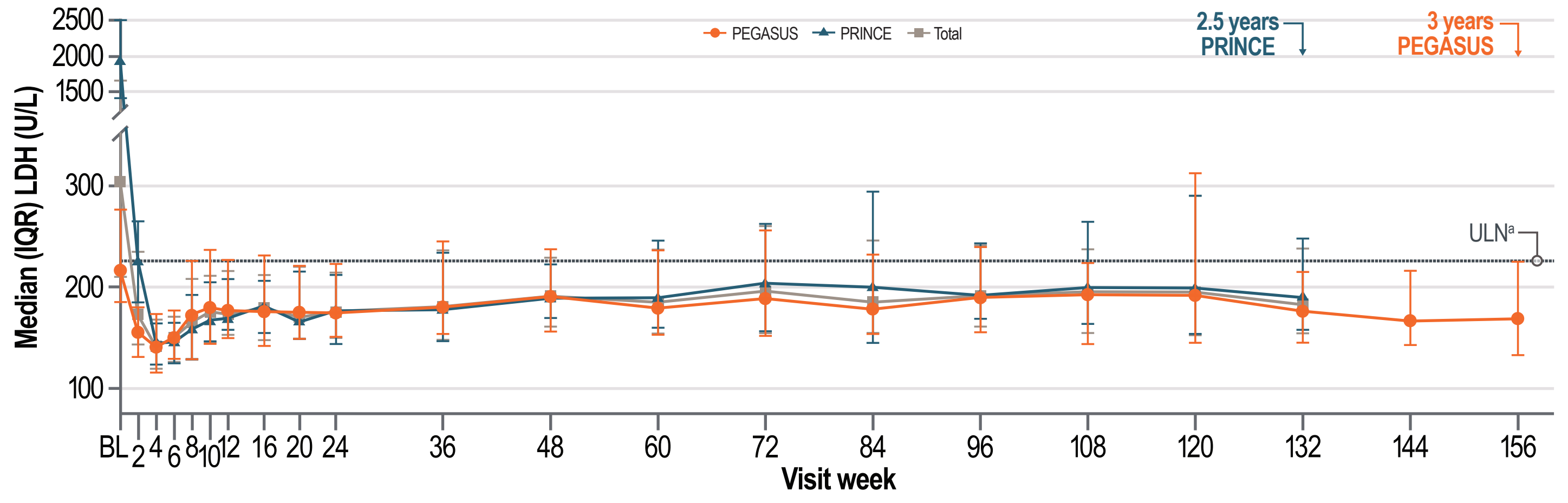
Figure 1. Hb concentrations through up to 3 years of pegcetacoplan treatment[a]



	BL	2	4	6	8	10	12	16	20	24	36	48	60	72	84	96	108	120	132	144	156
PEGASUS (n)	80	41	44	53	38	64	42	66	66	69	68	67	60	57	56	51	48	44	37	35	26
PRINCE (n)	52	18	22	22	36	41	47	42	39	44	49	47	46	45	45	41	43	37	32		
Total (n)	132	59	66	75	74	105	89	108	105	113	117	114	106	102	101	92	91	81	69		

[a]Patients who had a transfusion were not included in the Hb analysis for 60 days after the transfusion. [b]Normal ranges are per central laboratory; local laboratory values were normalized using central laboratory normal ranges.
BL, baseline (at pegcetacoplan initiation); Hb, hemoglobin; LLN, lower limit of normal (12 g/dL for female patients and 13.6 g/dL for male patients); SE, standard error.

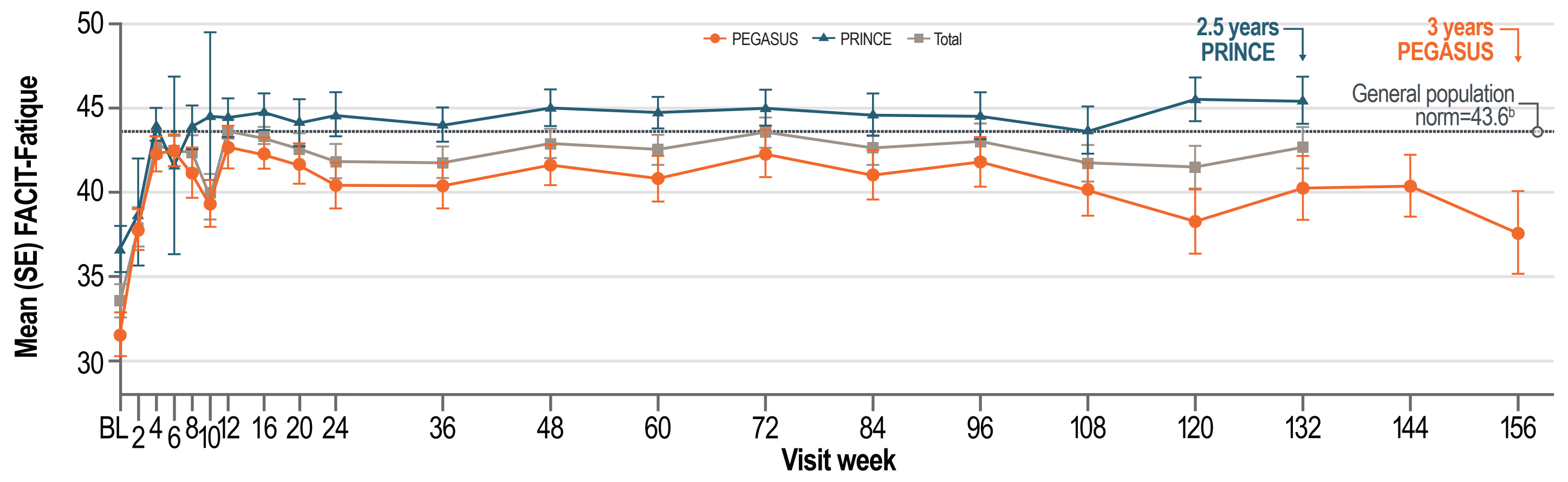
Figure 2. LDH concentrations through up to 3 years of pegcetacoplan treatment



	BL	2	4	6	8	10	12	16	20	24	36	48	60	72	84	96	108	120	132	144	156
PEGASUS (n)	80	80	74	77	47	68	46	75	74	72	73	67	63	56	58	52	53	47	41	34	27
PRINCE (n)	52	48	50	43	44	45	49	45	44	46	50	48	47	47	47	42	44	39	35		
Total (n)	132	128	124	120	91	113	95	120	118	118	123	115	110	103	105	94	97	86	76		

[a]Normal ranges are per central laboratory; local laboratory values were normalized using central laboratory normal ranges.
BL, baseline (at pegcetacoplan initiation); IQR, interquartile range; LDH, lactate dehydrogenase; ULN, upper limit of normal (226 U/L).

Figure 3. FACIT-Fatigue scores through up to 3 years of pegcetacoplan treatment[a]

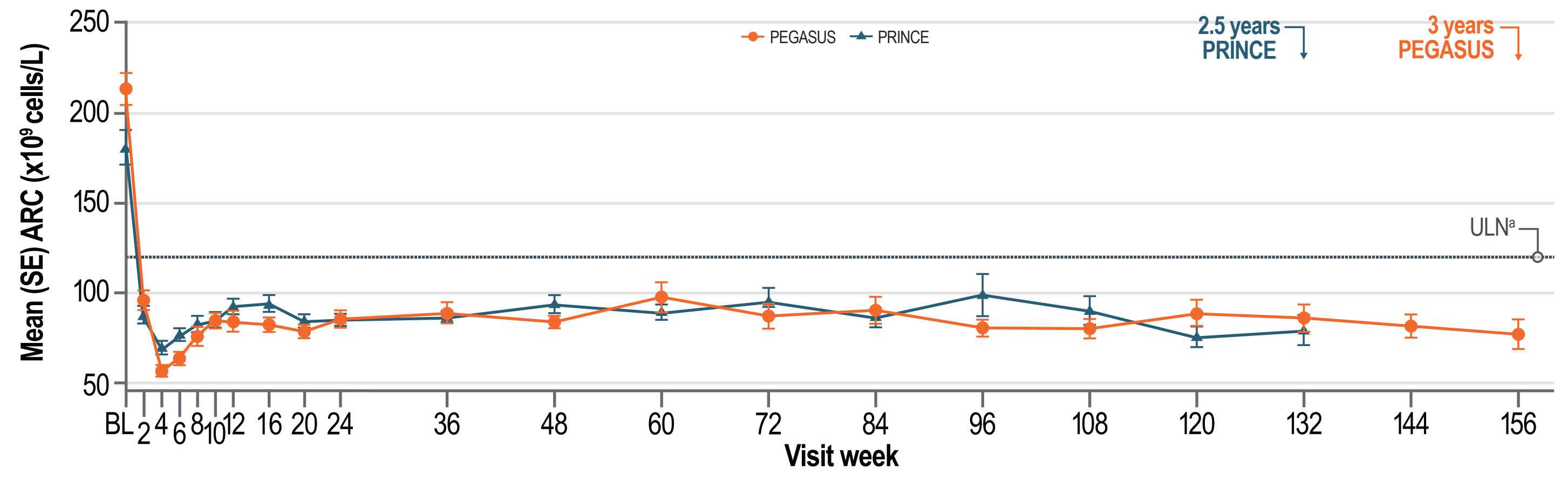


	BL	2	4	6	8	10	12	16	20	24	36	48	60	72	84	96	108	120	132	144	156
PEGASUS (n)	80	78	77	76	45	69	45	75	74	69	72	66	60	54	54	51	53	46	39	35	26
PRINCE (n)	52	11	42	5	34	6	40	39	41	35	44	40	47	46	44	41	42	37	33		
Total (n)	132	89	119	81	79	75	85	114	115	104	116	106	107	100	98	92	95	83	72		

[a]Greater FACIT-Fatigue scores indicate less fatigue. [b]Reported by Cella and colleagues.[4]
BL, baseline (at pegcetacoplan initiation); FACIT-Fatigue, Functional Assessment of Chronic Illness Therapy-Fatigue; SE, standard error.

- With pegcetacoplan, Hb (**Figure 1**) and LDH (**Figure 2**) concentrations markedly improved and remained stable through up to 3 years
- FACIT-Fatigue scores rapidly increased (indicating less fatigue) and were maintained near the general population norm of 43.6[4] (**Figure 3**)

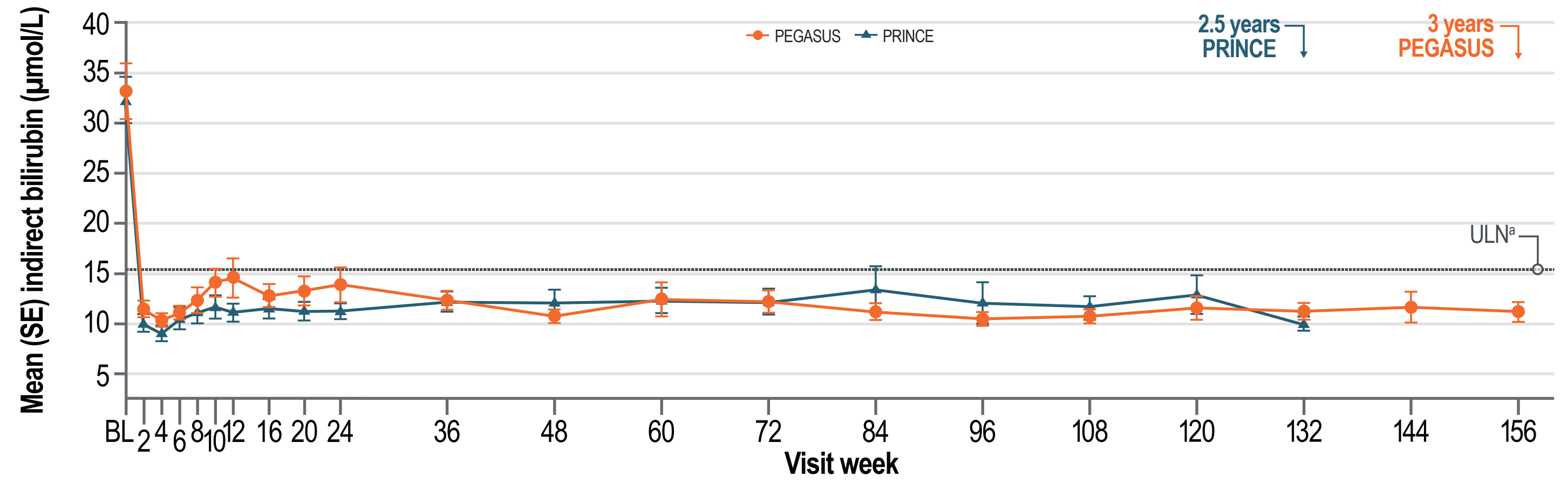
Figure 4. ARCs through up to 3 years of pegcetacoplan treatment



	BL	2	4	6	8	10	12	16	20	24	36	48	60	72	84	96	108	120	132	144	156
PEGASUS (n)	80	79	74	75	47	66	46	71	70	71	72	67	62	56	52	49	47	42	39	34	26
PRINCE (n)	52	45	45	35	31	29	36	37	36	42	49	46	47	44	44	41	41	38	34		

[a]Normal ranges are per central laboratory; local laboratory values were normalized using central laboratory normal ranges.
ARC, absolute reticulocyte count; BL, baseline (at pegcetacoplan initiation); SE, standard error; ULN, upper limit of normal (120x10^9 cells/L).

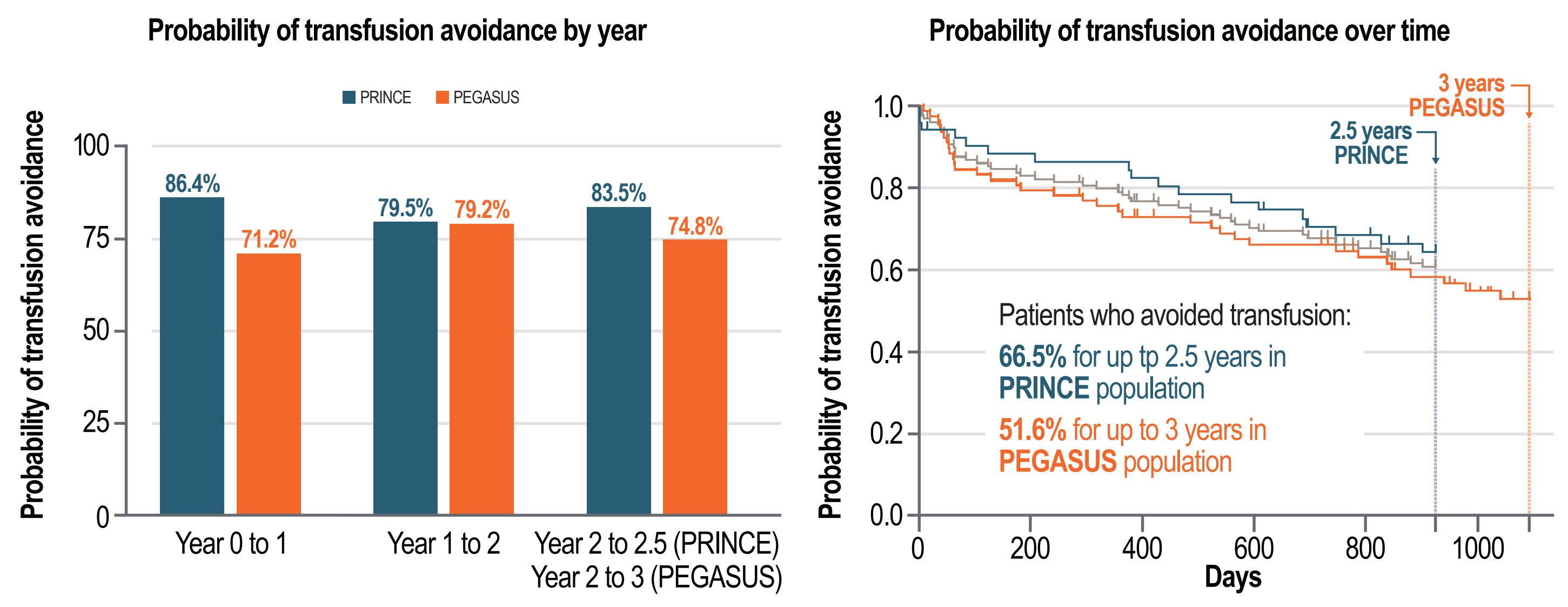
Figure 5. Indirect bilirubin levels through up to 3 years of pegcetacoplan treatment



	BL	2	4	6	8	10	12	16	20	24	36	48	60	72	84	96	108	120	132	144	156
PEGASUS (n)	80	80	74	77	47	68	46	74	74	69	72	67	59	53	52	48	51	42	39	34	27
PRINCE (n)	52	48	49	42	43	43	48	44	44	45	50	48	48	47	46	42	43	37	34		

[a]Normal ranges are per central laboratory; local laboratory values were normalized using central laboratory normal ranges.
BL, baseline (at pegcetacoplan initiation); SE, standard error; ULN, upper limit of normal (15.4 µmol/L).

Figure 6. Transfusion avoidance through up to 3 years of pegcetacoplan treatment



Patients who avoided transfusion:
66.5% for up tp 2.5 years in PRINCE population
51.6% for up to 3 years in PEGASUS population

- ARC improvements were maintained below the ULN (**Figure 4**), as were indirect bilirubin concentrations (**Figure 5**)
- Annual transfusion avoidance ranged from 71.2%–79.2% (PEGASUS) to 79.5%–86.4% (PRINCE) (**Figure 6**)
- In the PEGASUS population, 51.6% avoided transfusion for up to 3 years; in the PRINCE population, 66.5% avoided transfusion for up to 2.5 years (**Figure 6**)

Table. TEAEs during pegcetacoplan monotherapy for up to 3 years

Patients with events, n (%)	**PEGASUS N=80**	**PRINCE N=52**	**Total N=132**
TEAEs	79 (98.8)	50 (96.2)	129 (97.7)
Considered related to pegcetacoplan	43 (53.8)	17 (32.7)	60 (45.5)
Serious TEAEs	43 (53.8)	23 (44.2)	66 (50.0)
Considered related to pegcetacoplan	5 (6.3)	1 (1.9)	6 (4.5)
TEAEs leading to pegcetacoplan discontinuation	16 (20.0)	1 (1.9)	17 (12.9)
TEAEs leading to death	1 (1.3)	3 (5.8)	4 (3.0)
Considered related to pegcetacoplan	0	0	0
TEAEs of special interest	70 (87.5)	46 (88.5)	116 (87.9)
Hypersensitivity	27 (33.8)	16 (30.8)	43 (32.6)
Infections	63 (78.8)	35 (67.3)	98 (74.2)
Serious infections	17 (21.3)	10 (19.2)	27 (20.5)
Sepsis	4 (5.0)	2 (3.8)	6 (4.5)
Meningitis	0	0	0
Thrombosis	3 (3.8)	0	3 (2.3)
Breakthrough hemolysis[a]	23 (28.8)	16 (30.8)	39 (29.5)
Patients with 1/2 events	14 (17.5) / 4 (5.0)	10 (19.2) / 3 (5.8)	24 (18.2) / 7 (5.3)

[a]Clinically significant (as reported by investigators) and laboratory-confirmed events. AE, adverse event; TEAE, treatment-emergent adverse event (AEs with a start date on or after the first dose of pegcetacoplan monotherapy or with a start date before the date of the first dose of pegcetacoplan but increased in severity on or after the date of the first dose of drug. Did not include AEs occurring more than 8 weeks after the last dose of pegcetacoplan). Patients with multiple occurrences of an AE were counted only once.

- Most patients had a TEAE during up to 3 years of pegcetacoplan monotherapy (**Table**)
- Serious TEAEs occurred in 50.0% of patients overall, and 4.5% of all patients had a serious TEAE deemed pegcetacoplan related
- Overall, 17 patients discontinued pegcetacoplan due to a TEAE; of those, 9 discontinued due to a hemolytic disorder, with 7 of these discontinuing within 1 year of starting pegcetacoplan
- In all, 4 (3.0%) TEAE-related deaths occurred (none deemed pegcetacoplan related) and 3 (2.3%) patients had a thrombotic event
- Breakthrough hemolysis occurred in 28.8% (23 of 80) of patients in PEGASUS and 30.8% (16 of 52) of patients in PRINCE
- No meningitis cases were reported

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Abbreviations:

ARC, absolute reticulocyte count; BL, baseline; C5i, complement component 5 inhibitor; FACIT-Fatigue, Functional Assessment of Chronic Illness Therapy-Fatigue; Hb, hemoglobin; IQR, interquartile range; LDH, lactate dehydrogenase; LLN, lower limit of normal; OLE, open-label extension; PNH, paroxysmal nocturnal hemoglobinuria; SD, standard deviation; SE, standard error; TEAE, treatment-emergent adverse event; ULN, upper limit of normal.

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