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Association of quality of life measures with afamelanotide treatment in patients with erythropoietic protoporphyria and x-linked protoporphyria: A retrospective cohort study

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Research letter

Association of quality of life measures with afamelanotide treatment in patients with erythropoietic protoporphyria and x-linked protoporphyria: A retrospective cohort study

To the Editor: Erythropoietic protoporphyria (EPP) and X-linked protoporphyria (XLP; EPP/XLP) are uncommon inherited heme-synthesis disorders characterized by painful cutaneous photosensitivity reactions from light-induced activation of accumulated protoporphyrin IX. Afamelanotide is the only medication with clinical effectiveness, favorable safety profile, and significantly improved EPP-specific quality of life (QoL; EPP-QoL).[1,2] However, full year-round symptom control is challenging in certain subgroups because of restrictions imposed by insurance companies on dose and frequency. We investigated how therapeutic responses to afamelanotide affect QoL in patients with EPP/XLP in a real-word, non-clinical trial setting.

This single-center retrospective study included all patients with EPP/XLP who were treated with afamelanotide between 2020 and 2021. QoL assessments were from the disease-specific EPP-QoL questionnaire completed at each visit before implantation (Supplementary Fig 1, available via Mendeley at https://doi.org/10.17632/7tcss39myf.2). Paired *t* tests were used to compare mean score changes from EPP-QoL questionnaires and EPP-QoL outcomes in documented treatment response subgroups. Two-sample *t* test was used to compare EPP-QoL outcomes to those of a phase III randomized placebo-controlled trial.[2] A larger positive change in EPP-QoL score from baseline indicates improvement in disease-specific QoL.

Of the 20 patients with EPP and 2 with XLP who received at least 1 afamelanotide dose, 21 (95.5%) returned for a second dose and 17 (77.3%) returned for a third dose within 1 year. A total of 77 EPP-QoL questionnaires were analyzed. Dropouts were due to missing or incomplete data, insurance reimbursement restrictions, or transfer to a different treatment center. No patients discontinued drug due to side effects or lack of efficacy. Waning efficacy between doses (around 6 weeks) was reported in 11 (50%) patients and persistently low tolerance to sunlight (≤1 hour) was described in 9 (40.9%) patients. EPP-QoL significantly increased from baseline at all timepoints ($P < .001$) and results were not significantly different from the phase III randomized placebo-controlled trial (Table I; $P > .1$).[2] Each consecutive implant showed incremental improvement in EPP-QoL from baseline, with the first implant showing the greatest change (+37.2, +48.7, +53.6; $P < .001$). Subgroup analysis revealed a smaller magnitude of improvement in those who experienced waning efficacy and persistently low tolerance to sunlight (Table II). A significantly smaller degree of EPP-QoL improvement was found in those who were unable to tolerate over 1 hour of sunlight with the first afamelanotide treatment (+14.6 vs +55.3, $P < .001$).

The EPP-QoL is the only QoL tool designed for EPP and, despite partial validation, captured treatment response was better than the Dermatology Life Quality Index in previous studies.[2] Although non-validated tools cannot be relied upon, consideration of the results is reasonable, since instrument validation is difficult for rare conditions such as EPP/XLP.[3] However, validated outcome measures are being developed.[4]

Table I. Changes in erythropoietic protoporphyria quality of life scores following each afamelanotide implant in patients with erythropoietic protoporphyria and x-linked protoporphyria compared to baseline and a multi-center phase III randomized placebo-controlled trial[2]

	Single-center		Multi-center phase III RCT[2]		Paired *t* test[†]	2-sample *t* test[‡]
Timepoint	ΔEPP QoL score (Mean ± SD)	No. of completed questionnaires (*n*)	ΔEPP QoL score (Mean ± SD)	No. of patients (*n*)	*P* value	*P* value
Baseline (Visit 1)	19.9 ± 11.8	20	26.6 ± 19.9	47	—	.166
Implant 1 (Visit 2 minus 1)	+37.2 ± 27.5	18	+17.4 ± 5.9	47	<.001*	.354
Implants 1 + 2 (Visit 3 minus 1)	+48.7 ± 26.9	13	+23.2 ± 6.5	46	<.001*	.895
Implants 1 + 2 + 3 (Visit 4 minus 1)	+53.6 ± 18.0	10	+24.5 ± 9.2	46	<.001*	.796

EPP, Erythropoietic protoporphyria; *QoL*, quality of life; *RCT*, randomized controlled trial.
*Statistically significant, $P < .05$.
[†]*P* values for the single-center comparison of mean score change at each timepoint to baseline score were determined by the paired *t* test.
[‡]In the comparison of single-center to multi-center phase III randomized placebo-controlled trial, *P* values were determined by the 2-sample *t* test.[2]

Table II. Changes in erythropoietic protoporphyria quality of life scores following each afamelanotide implant in treatment response subgroups of patients with erythropoietic protoporphyria and x-linked protoporphyria

	Duration of full therapeutic response				
	<2 Months		≥2 Months		Paired *t* test
Timepoint	ΔEPP QoL score (Mean ± SD)	No. of completed questionnaires (*n*)	ΔEPP QoL score (Mean ± SD)	No. of completed questionnaires (*n*)	*P* value
Implant 1 (Visit 2 minus 1)	+29.4 ± 29.3	10	+46.9 ± 23.4	8	.190
Implants 1 + 2 (Visit 3 minus 1)	+38.2 ± 28.5	8	+65.6 ± 13.2	5	.071
Implants 1 + 2 + 3 (Visit 4 minus 1)	+46.8 ± 18.0	6	+63.9 ± 14.2	4	.149

	Length of tolerance to sunlight				
	≤1 Hour		>1 Hour		Paired *t* test
Timepoint	ΔEPP QoL score (Mean ± SD)	No. of completed questionnaires (n)	ΔEPP QoL score (Mean ± SD)	No. of completed questionnaires (*n*)	*P* value
Implant 1 (Visit 2 minus 1)	+14.6 ± 23.3	8	+55.3 ± 13.9	10	<.001*
Implants 1 + 2 (Visit 3 minus 1)	+28.9 ± 32.7	5	+61.1 ± 13.0	8	.092
Implants 1 + 2 + 3 (Visit 4 minus 1)	+38.9 ± 0	1	+55.2 ± 18.3	9	.421

EPP, Erythropoietic protoporphyria; *QoL*, quality of life.
*Statistically significant, $P < .05$. For all timepoints, *P* values for the comparison of mean score change within each therapeutic response subgroup were determined by the paired *t* test.

In summary, afamelanotide had a positive effect on QoL and showed a possible additive effect with subsequent administration in a real-word setting. Subgroups who reported treatment response variability had less robust QoL improvements. Higher or more frequent afamelanotide doses are under investigation for treatment of other diseases, such as vitiligo.[5] As such, further prospective studies investigating individualized afamelanotide dosing strategies are needed for patients with EPP/XLP to maximize treatment response.

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Conflicts of interest

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REFERENCES

1. Wensink D, Wagenmakers M, Barman-Aksözen J, et al. Association of afamelanotide with improved outcomes in patients with erythropoietic protoporphyria in clinical practice. *JAMA Dermatol*. 2020;156:570-575.
2. Langendonk JG, Balwani M, Anderson KE, et al. Afamelanotide for erythropoietic protoporphyria. *N Engl J Med*. 2015;373:48-59.
3. Rutter KJ, Ashraf I, Cordingley L, Rhodes LE. Quality of life and psychological impact in the photodermatoses: a systematic review. *Br J Dermatol*. 2020;182:1092-1102.
4. Biolcati G, Hanneken S, Minder EI, et al. Validation of a novel patient reported tool to assess the impact of treatment in erythropoietic protoporphyria: the EPP-QoL. *J Patient Rep Outcomes*. 2021;5:65.
5. Wu J, Cotliar R. Afamelanotide: an orphan drug with potential for broad dermatologic applications. *J Drugs Dermatol*. 2021;20:290-294.

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