[RFC8.3] Efpegerglucagon in Congenital Hyperinsulinism: Preliminary Patient Baseline and Demographic Characteristics from the ACHIEVE Phase 2 Study

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INTRODUCTION

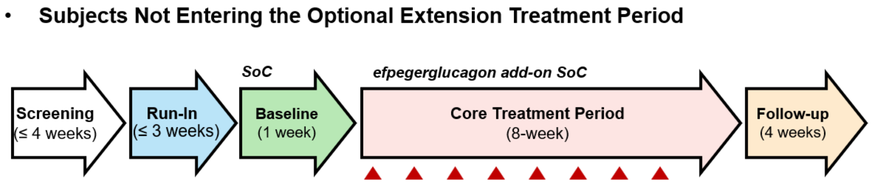
Congenital hyperinsulinism (CHI) is a serious disorder of dysregulated insulin secretion that causes recurrent hypoglycemia and may result in irreversible neurological damage, often leading to developmental delay. With only one approved pharmacologic therapy for hyperinsulinism, diazoxide, current nutritional, medical, and surgical approaches may provide incomplete control and contribute to treatment burden, supporting the need for new therapies. Efpegerglucagon is a long-acting glucagon analogue under investigation for CHI.

METHOD

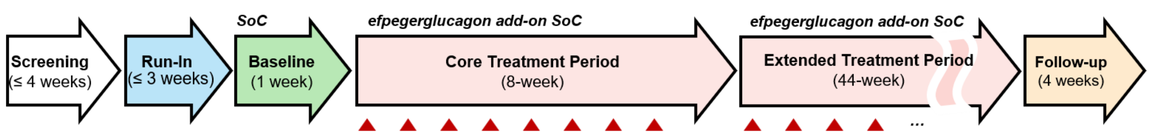
ACHIEVE is an ongoing Phase 2, multicenter, multiple ascending dose, open-label, proof-of-concept study (NCT04732416; EU CT 2024-515290-98-00). Subjects aged ≥ 2 years with persistent hypoglycemia (≥ 3 hypoglycemia events/week) despite stable standard of care (SoC) therapy receive once-weekly subcutaneous efpegerglucagon for an 8-week core treatment period, with a 44-week optional extension treatment (OET) period (Figure 1). Two sequential dose cohorts (0.04 mg/kg and 0.06 mg/kg) are evaluated, and enrollment for both Cohort 1 (N=8) and Cohort 2 (N=9) has been completed (Figure 2).

Figure 1. Study Periods

- **Subjects Not Entering the Optional Extension Treatment Period**

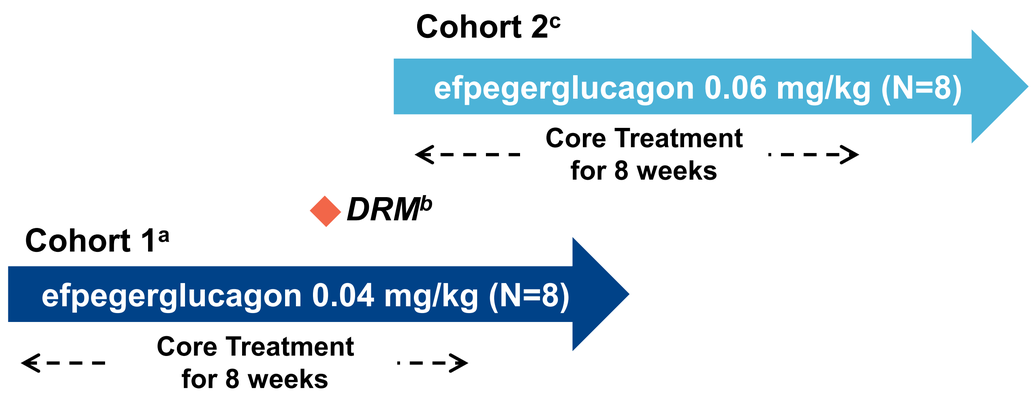


- **Subjects Entering the Optional Extension Treatment Period**



Note: Eligible subjects who are willing to continue in the optional extension treatment period will receive an additional 44 weeks of treatment.
▲ denotes efpegerglucagon treatment; SoC, standard of care therapy

Figure 2. Study Cohorts



a: The enrollment of subjects in Cohort 1 preceded the enrollment in Cohort 2, with no overlapping enrollment between the two cohorts.
b: After the sixth subject completed the 8-week treatment period in Cohort 1, a data review meeting (DRM) was held to determine dose escalation to Cohort 2.
c: Cohorts were planned to enroll approximately 8 subjects each; ultimately, 9 subjects were enrolled in Cohort 2.

RESULTS

Table 1. Baseline and Demographic Characteristics

Parameter	Cohort 1 (N=8)	Cohort 2 (N=9)	Total (N=17)
Age (years), mean (SD)	17.6 (13.8)	5.1 (2.8)	11.0 (11.3)
Sex, n (%)			
Male	4 (50)	5 (56)	9 (53)
Female	4 (50)	4 (44)	8 (47)
Baseline HbA1c (%) [a], mean (SD)	4.7 (0.6)	5.2 (0.3)	4.9 (0.5)
Cause of CHI (genetic mutations), n (%)			
ABCC8/KCNJ11	2 (25)	3 (33)	5 (29)
GCK	1 (13)	1 (11)	2 (12)
HK1	1 (13)	0 (0)	1 (6)
Other	2 (25)	0 (0)	2 (12)
None	2 (25)	5 (56)	7 (41)
Cause of CHI (syndromic status), n (%)			
Beckwith-Wiedemann Syndrome	0 (0)	1 (11)	1 (6)
Other	1 (13)	1 (11)	2 (12)
None	7 (88)	7 (78)	14 (82)
Pancreatic Histology Type, n (%)			
Diffuse	4 (50)	2 (22)	6 (35)
None	4 (50)	6 (67)	10 (59)
No Biopsy Performed	0 (0)	1 (11)	1 (6)
Pancreatectomy, n (%)			
None	6 (75)	9 (100)	15 (88)
Other[b]	1 (13)	0 (0)	1 (6)
Near-total	1 (13)	0 (0)	1 (6)
Current SoC Therapy, n (%)			
Diazoxide	6 (75)	5 (56)	11 (64.7)
Lanreotide	2 (25)	2 (22)	4 (23.5)
Octreotide	0 (0)	2 (22)	2 (11.8)

HbA1c, glycated hemoglobin; SD, standard deviation; SoC, standard of care
Note: Preliminary data as of 20 Aug 2026
a: Cohort 2 N=8, Total N=16
b: <10% of the pancreas was resected.

A total of 17 subjects were enrolled in the ACHIEVE Phase 2 study. Because enrollment of a younger pediatric population in Cohort 2 was allowed only after enrolling the adolescent population in Cohort 1 in some countries, subjects in Cohort 2 were generally younger than those in Cohort 1. Genetic etiologies were identified in 59% of subjects, with *ABCC8/KCNJ11* (KATP channel) mutation representing the most common cause. The 44-week OET period was implemented through a protocol amendment while Cohort 1 was ongoing, and most subjects in Cohort 2 entered the OET period.

CONCLUSIONS

The study population is representative of the heterogeneous CHI population with a persistent disease burden despite SoC therapy, underscoring the high unmet need for novel therapeutic options. The core treatment period of this phase 2 study has been completed, with safety and efficacy data forthcoming.

FOR MORE INFORMATION

To learn more about efpegerglucagon, please visit Hanmi Pharmaceutical's webpage by scanning the QR code.

ACKNOWLEDGEMENT / CONFLICTS OF INTEREST

- Grant received from the Korea Drug Development Fund by the Ministry of Science and ICT, the Ministry of Trade, Industry, and Energy, and the Ministry of Health and Welfare (RS-2021-DD118329, Republic of Korea)
- D. De León reports consulting for AmideBio, Zealand Pharma, Rhythm Pharmaceuticals, Fortress Biotech, Ultragenyx, Rezolute, NineSigma, Ligand Pharmaceuticals, Confo Therapeutics, Spruce Bioscience, and Twist Bioscience, and participation in industry-sponsored research funded by Zealand Pharma, Rezolute, Hanmi Pharm. Co., Ltd., Moderna, Rhythm, and Ultragenyx.
- I. Banerjee reports participation in industry-sponsored research funded by Zealand Pharma, Rezolute, and Hanmi Pharm. Co., Ltd.; receipt of research grants from the University of Manchester, Manchester BRC, and NIHR; and service as Chair of the ESPE Communications Committee and Associate Editor for Frontiers in Endocrinology.
- A. Dastamani, S. Empting, D. Zangen, C. Cheon reports participation in industry-sponsored research funded by Hanmi Pharm. Co., Ltd.
- M. Puri is an employee of Fortrea and serves as Medical Monitor for the study; E. Gwak, S. Kang, J. Byeon, and M. Lee are employees of Hanmi Pharm. Co., Ltd. The study is sponsored and funded by Hanmi Pharm. Co., Ltd.