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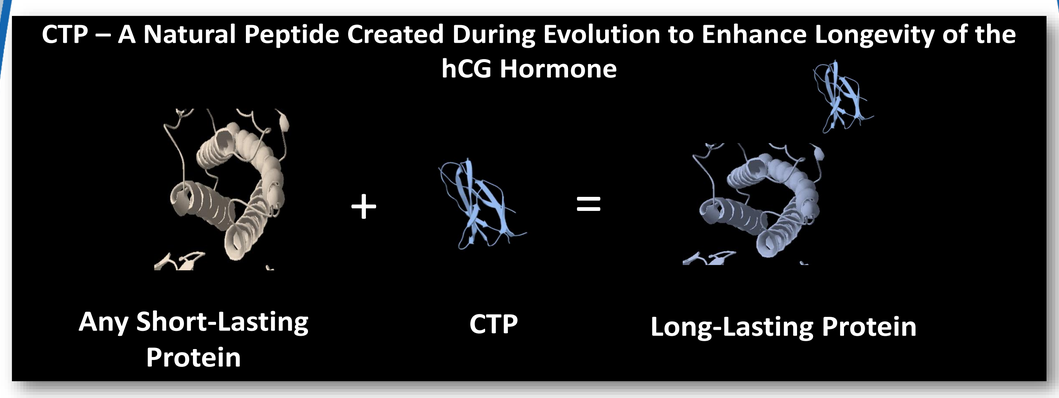
Safety and Tolerability of Once-Weekly Administration of CTP-Modified Human Growth Hormone (MOD-4023): 24-month Complete Dataset Results of a Phase 2 Study in Children with Growth Hormone Deficiency

Nataliya Zelinska, MD, PhD[1], Julia Skorodok, MD[2], Oleg Malievsky, MD, PhD[3], Ron G. Rosenfeld, MD[4], Zvi Zadik, MD[5], Ronit Koren, PhD[6], Shelly Vander, MSc[6], Gili Hart, PhD[6] and Klaudziya Radziuk, MD, PhD[7]

[1]Ukrainian Children Specialized Clinical Hospital, Kyev, Ukraine; [2]St. Petersburg State Pediatric Medical Academy, St. Petersburg, Russia; [3]Bashkir State Medical University, Ufa, Russia; [4]Oregon Health & Science University, Oregon, USA; [5] Kaplan Medical Center, Rehovot, Israel; [6]OPKO Biologics, Nes Ziona, Israel; [7] 2nd Children City Clinic, Minsk, Belarus. **Disclosure statement:** RGR: consultant for OPKO Biologics. KR, OM: Investigator, Ascendis Pharma. Nothing to disclose: NZ, JS, ZZ, RK, SV, GH.

Introduction

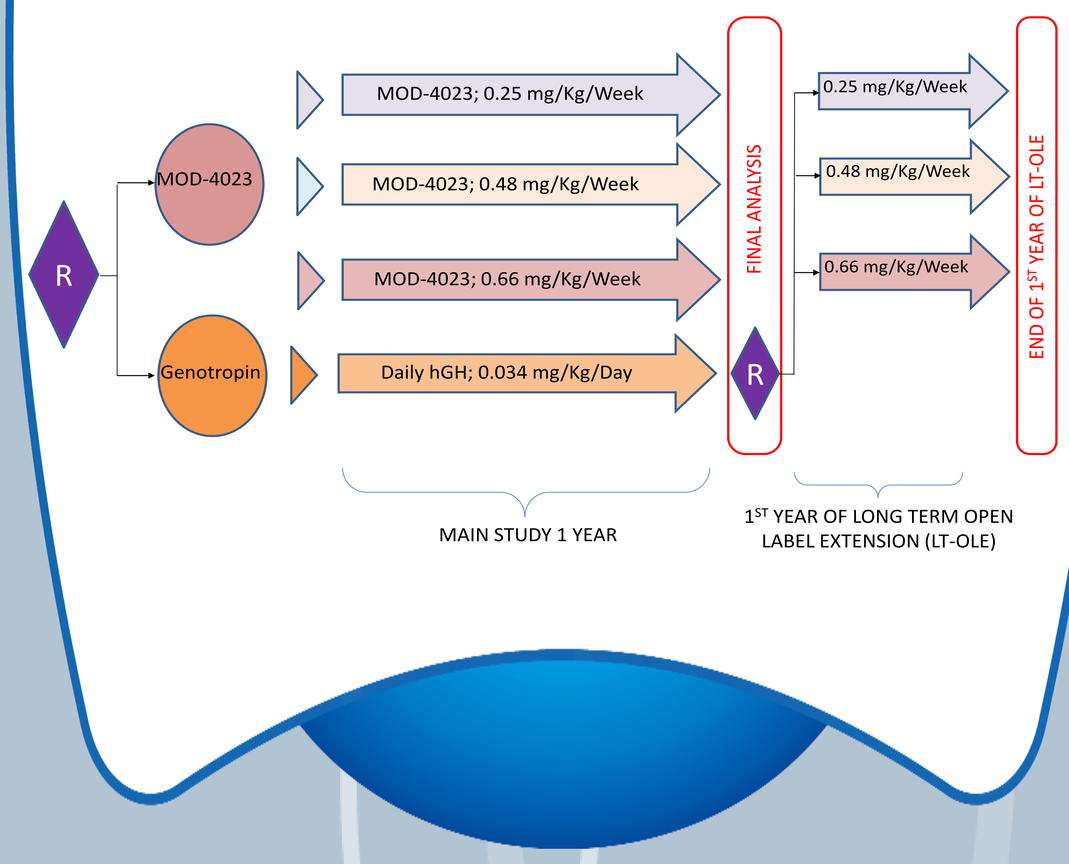
OPKO Biologics is developing bio-better long-acting versions of existing therapeutic proteins utilizing a technology called CTP.



The technology involves fusion of the C terminus peptide of hCG to one or both ends of the target protein. The MOD-4023 (hGH-CTP) is a long acting hGH, clinically validated and proven as a safe and efficient way for increasing the half-life of several therapeutic proteins while maintaining their biological activity.

Study Outline

A randomized, controlled Phase 2 study was conducted in pre-pubertal GHD children receiving SC injections of one of three MOD-4023 doses in a once weekly regimen (0.25, 0.48, and 0.66 mg/kg/week), or daily hGH- Genotropin (0.034 mg /kg/day) as control for 12 months. Safety assessments included monitoring of adverse events (AEs), injection site reactions, vital signs and physical condition. Laboratory assessments were also performed and included glucose and lipid metabolism, blood biochemistry, and immunogenicity.



General Safety

Summary of Lipid Metabolism Parameters and Changes from Baseline

Parameter	Statistic	Cohort 1 N=16			Cohort 2 N=17			Cohort 3 N=14			Total N=47		
		Baseline (Day 0)	18M	24M	Baseline (Day 0)	18M	24M	Baseline (Day 0)	18M	24M	Baseline (Day 0)	18M	24M
Total Cholesterol [mmol/L]	N	16	16	12	19	18	17	13	14	11	48	48	40
	Mean	4.45	4.34	4.29	4.39	4.1	4.05	4.51	4.46	4.42	4.44	4.29	4.22
LDL Cholesterol [mmol/L]	N	16	16	11	19	18	16	13	14	11	48	48	38
	Mean	2.78	2.57	2.39	2.79	2.51	2.31	2.81	2.66	2.62	2.79	2.57	2.42
Triglycerides [mmol/L]	N	15	16	11	19	18	16	13	14	11	47	48	38
	Mean	0.64	0.67	0.61	0.66	0.8	0.87	0.8	0.76	0.77	0.69	0.74	0.77
LP(a) Lipoprotein [mmol/L]	N	14		10	14		11	9		10	37		33
	Mean	20.42		47.33	25.5		25.27	8.88		16.5	19.54		30.63

No significant changes were observed for the lipid profile

Adverse Events

	Cohort 1 N=16	Cohort 2 N=18	Cohort 3 N=14	Total N=47
Patients reporting at least one AE	(68.75%) 11	(27.7%) 5	(50%) 7	(48.9%) 23
Patients with at least one mild or moderate AE	(68.75%) 11	(27.7%) 5	(50%) 7	(48.9%) 23
Patients reporting at least one severe AE	(0.0%) 0	(5.55%) 1	(0.0%) 0	(0.0%) 0
Patients reporting at least one unrelated or unlikely related AE	(68.75%) 11	(27.7%) 5	(50%) 7	(48.9%) 23
Patients reporting at least one possibly, probably or definitely related AE	(6.25%) 1	(0.0%) 0	(0.0%) 0	(0.0%) 0

No severe AEs were reported during MOD-4023 treatment.

Glucose Metabolism

Parameter	Statistic	Cohort 1			Cohort 2			Cohort 3			Total		
		Baseline (Day 0)	18M	24M	Baseline (Day 0)	18M	24M	Baseline (Day 0)	18M	24M	Baseline (Day 0)	18M	24M
Glucose [mmol/L] Normal =5.5-3.6	N	17	16	14	18	17	16	17	15	13	52	48	43
	Mean	4.37	4.43	4.35	4.45	4.74	4.93	3.98	4.49	4.57	4.27	4.56	4.64
Insulin [pmol/L] Normal= 0.0-210	N	3	8	5	7	13	12	4	8	10	14	29	27
	Mean	53.9	29.58	42.14	48.98	46.63	63.56	29.95	52.78	64.66	44.6	43.62	60
HbA1c [%HB] Normal= 4.5-5.7	N	16	15	15	18	16	17	15	15	13	49	46	45
	Mean	5.02	5.04	5.05	5.15	5.19	5.22	5	5.13	5.1	5.06	5.12	5.12

The mean glucose values across cohorts were within normal values. Fluctuations in mean glucose values between visits, and from baseline, were all ≤0.59 mmol/L with no apparent dose-dependent trends, and were not considered clinically significant. Fluctuations in mean insulin values between visits, and from baseline, were all ≤34.7 pmol/L with no apparent dose-dependent or time dependent trends, and were not considered clinically significant.

The mean HbA1c values were within normal values. Fluctuations in mean HbA1c values between visits, and from baseline, were ≤ 0.17% with no apparent dose-dependent or time dependent trends, and were not considered clinically significant.

Conclusions

The safety of MOD-4023 was demonstrated during the study:

- No severe AEs were reported during MOD-4023 treatment.
- A similar rate of adverse events was reported by patients treated with MOD-4023 and by patient in the daily treatment arm (Genotropin) .
- No unexpected AEs were considered as MOD-4023-related.
- No injection site-related reactions such as local discomfort, swelling, erythema or lipoatrophy were observed.
- Laboratory findings supported the tolerability of MOD-4023 treatment, and no significant overall changes were observed in glucose levels, insulin, HbA1c, or vital signs.

MOD-4023 demonstrated excellent safety and tolerability during treatment for up to 24 months in a dose range of 0.25-0.66 mg/kg/week. This supports the ongoing clinical development of MOD-4023 for once-weekly treatment of GHD children. Based on the above, a pivotal Phase 3 study will be initiated shortly at a dose of 0.66 mg/kg/week. In this phase II study , patients receiving the lower MOD-4023 doses will be switched to 0.66 mg/kg/week for long-term assessment.

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Gili Hart
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