TITLE

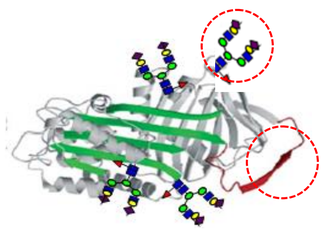
Human Phase 1 clinical data of ALT-P1 (hGH-NexP™) by Healthy Korean males

Sang Mee Lee[1], Jung-Soo Cho[1], Hye Shin Chung[2], Min Soo Park[3] and Soon Jae Park[1]

1 Alteogen, Inc., 62, Yuseong-daero 1628 Beon-gil, Yuseong-gu, Daejeon, Korea
2 Dept. of Biotechnology & Bioengineering, Han Nam University, Jeonmin-dong, Yuseong-gu, Daejeon, Korea
3 Dept. of Pediatrics, Yonsei University College of Medicine, Seoul, Korea

BACKGROUND

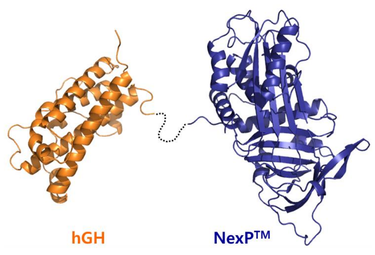
NexP™ Carrier



NexP™ is a long-acting fusion carrier developed by Alteogen, Inc.

- A further engineered human alpha-1 antitrypsin, which is abundant in human blood and its safety has been already proven.
- Increase of in vivo half life and reduced inherent proteinase inhibitor activity by genetic engineering

NexP™ Fusion Therapeutic Proteins



- Can be fused to **both C-terminus or N-terminus** of therapeutic proteins by recombinant technology
- **Prolonged in-vivo half life** of therapeutic proteins
- **Maintained in-vivo bioactivity** of therapeutic proteins
- Reduced **immunogenicity**
- High **productivity**

OBJECTIVES

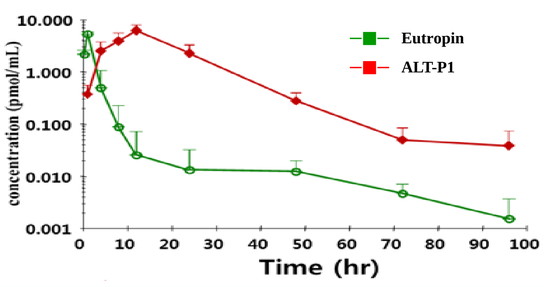
Currently available Growth Hormone (GH) is developed as daily injections, which cause inconvenience and poor compliance for patients. ALT-P1 was developed for once weekly administration in growth hormone deficient (GHD) adults and children. 1) Safety and tolerability, 2) pharmacokinetics and pharmacodynamics of once-weekly subcutaneous (SC) administration of ALT-P1 were evaluated in a Phase 1 study of Korean healthy male volunteers.

METHODS

This Phase 1, single-blinded, placebo-controlled, single-dosed, dose-escalated, randomized study was conducted by Yonsei University in Korea. A total of forty subjects were enrolled and randomized to one of the five dose cohorts: 0.03 mg/kg, 0.06 mg/kg, 0.12 mg/kg, 0.24 mg/kg, and 0.35 mg/kg. In each dose cohort, six subjects were randomized into the test cohort and two to the placebo group. The mean age was 25.7 ± 5.1 and the BMI was 22.0 ± 1.7 kg/m^2.

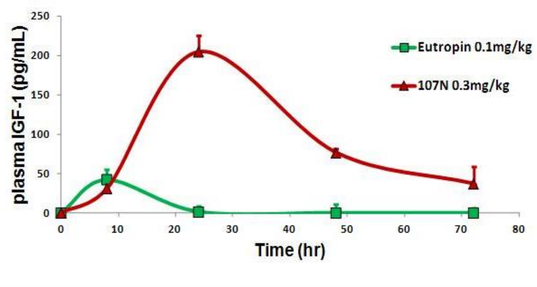
PRE-CLINICAL STUDIES

Rat hGH PK comparison



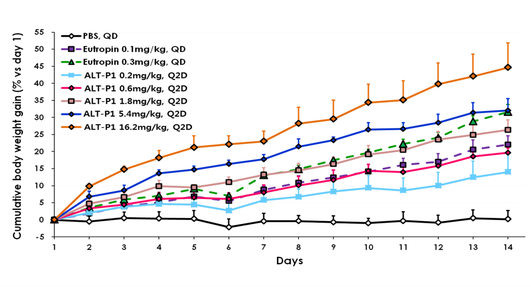
ALT-P1 in-vivo half life is much longer than 1st generation hGH

IGF-1 PD comparison



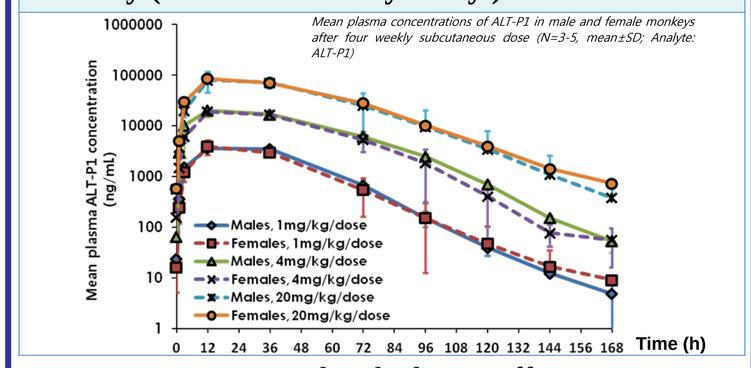
Higher IGF-1 concentration due to ALT-P1 injection than 1st generation hGH

Treatment-related growth



In case of every other day dose of ALT-P1, it showed linear growth and treatment-related growth

Monkey (4 week sc toxicity study)



- No treatment related adverse effect
- The safety and NOAEL at 20 mg/kg.
- Suitable as once-weekly injection

RESULTS

Injection dose and patient numbers

- A total of 40 subjects/ 5 dose cohorts
- 6 subjects to test and 2 subjects to placebo for each cohort
- Randomized/single-blinded/placebo-controlled/single-dosed/dose-escalated

Demographic data

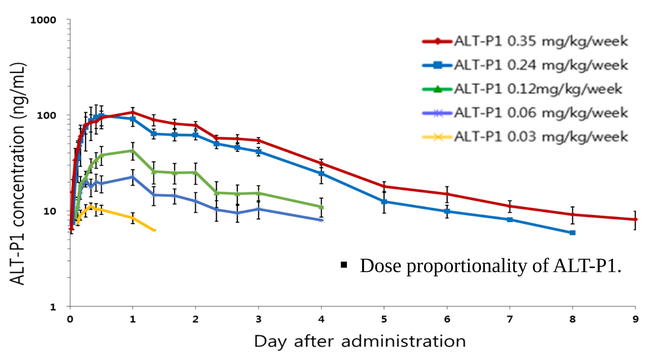
Demographic variables	Treatment(Mean±SD)						Total
	Placebo (N=10)	0.03mg/kg (N=6)	0.06mg/kg (N=6)	0.12mg/kg (N=6)	0.24mg/kg (N=6)	0.35mg/kg (N=6)	N=40
Age (years)	27.6±6.1	25.7±2.9	29.2±6.6	22.8±2.3	23.0±2.0	23.8±5.1	25.7±5.1
Weight(kg)	66.8±6.0	65.1±7.1	67.0±5.6	67.0±6.2	63.6±5.7	66.6±4.1	66.1±5.6
Height(cm)	173.0 ±3.5	171.2±4.8	173.7±3.4	175.2±6.7	172.7±8.2	170.6±5.2	172.9±5.2
BMI(kg/m^2)	22.1±1.8	22.1±2.0	22.1±1.9	21.7±0.7	21.3±1.9	22.9±2.0	22.0±1.7

Safety and tolerability data

	Placebo (N=10)	0.03 mg (N=6)	0.06 mg (N=6)	0.12 mg (N=6)	0.24 mg (N=6)	0.35 mg (N=6)
ADA	negative	negative	negative	negative	negative	negative
Tenderness	4 [5]	1[1]	2[2]	2[3]	3[4]	2[4]
Ache	-	-	-	1[1]	-	-
ALT increased	-	-	-	1[1]	-	-
Myalgia	-	-	-	1[1]	-	-

*Data are presented as patient number [Adverse effect cases]

ALT-P1 Pharmacokinetics

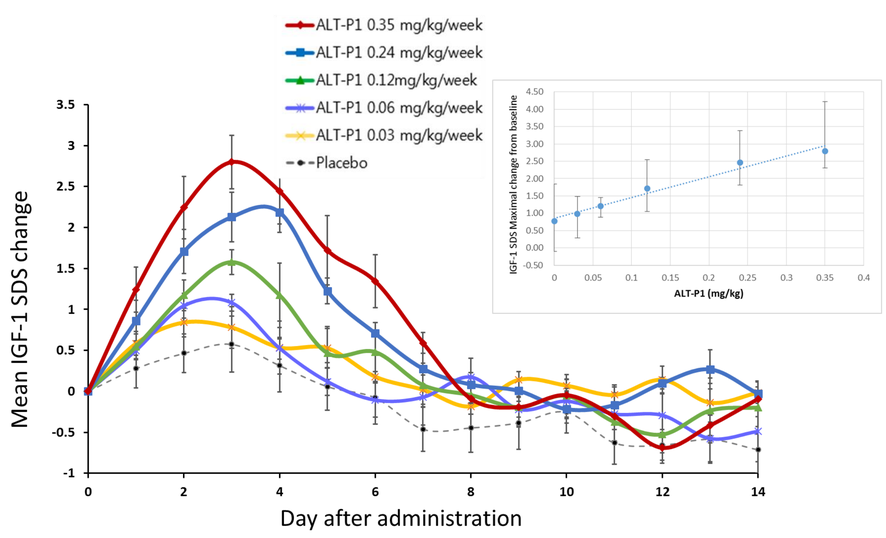


- Dose proportionality of ALT-P1.

Dose	0.12 mg/kg	0.24 mg/kg	0.35 mg/kg
AUCinf (h*ng/mL)	2230.32 ±1104.31	6275.97 ±2427.31	8588.28 ±2173.01
t1/2 (h)	19.09±6.66	26.81±3.31	39.50±20.34

- No severe adverse events
- Only 11.1% as drug related adverse effects that are typically reported adverse effects of hGH.
- Mild tenderness and pain in some subjects around injection sites
- Anti-drug antibody formation was not observed.

ALT-P1 Pharmacodynamics



Dose	0.12 mg/kg	0.24 mg/kg	0.35 mg/kg
Mean IGF-1 SDS	1.57-fold	2.12-fold	2.44-fold
Maximal change of IGF-1 SDS	1.72-fold	2.47-fold	2.80-fold

CONCLUSIONS

- **ALT-P1 is a long-acting recombinant hGH fused to NexP™ protein carrier.**
- **In animal studies, ALT-P1 showed its safety and pharmacological chracteristics that indicates the potential in clinical use.**
- **In Phase 1 clinical trials by use of healthy male volunteers, ALT-P1 showed the increase of in vivo half life from 19 hrs (0.12mg/kg) to 40 hrs (0.35mg/kg) along with increase of IGF-1 levels.**
- **No ADA (anti-drug antibody) was detected in human bloods by injection of ALT-P1.**
- **The results of the current study warrant further developments and clinical studies of ALT-P1 in adult and pediatric GHD patients.**
- **The human clinical study proved that ALT-P1 was safe and suitable for at least one injection per week in the tested dose range of 0.12mg/kg and 0.35mg/kg.**

- **Acknowledgement : This work was conducted jointly with CJ Healthcare Corp**

55ESPE 598--P1

Growth

Soon jae

DOI: 10.3252/pso.eu.55ESPE.2016

Poster presented at: ESPE 2016 PARIS 10-12 SEPTEMBER