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ESPEN
Virtual
CONGRESS



LIVE **VIRTUAL** on Clinical
CONGRESS Nutrition &
Metabolism

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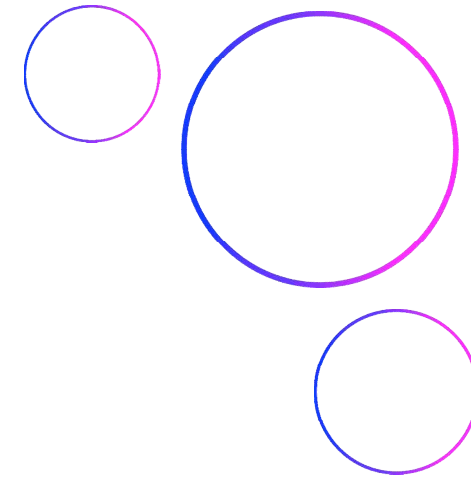
BENEFICIAL EFFECTS OF A LONG-ACTING GLP-2 ANALOG, HM15912, AFTER SWITCHING FROM DAILY OR WEEKLY GLP- 2 ANALOG DRUGS IN ANIMAL MODEL

Jin Bong Lee, Jae Hyuk Choi, Hyunjoo Kwon, Sung Min Bae, Dae Jin Kim, Young Hoon Kim, In Young Choi

Hanmi



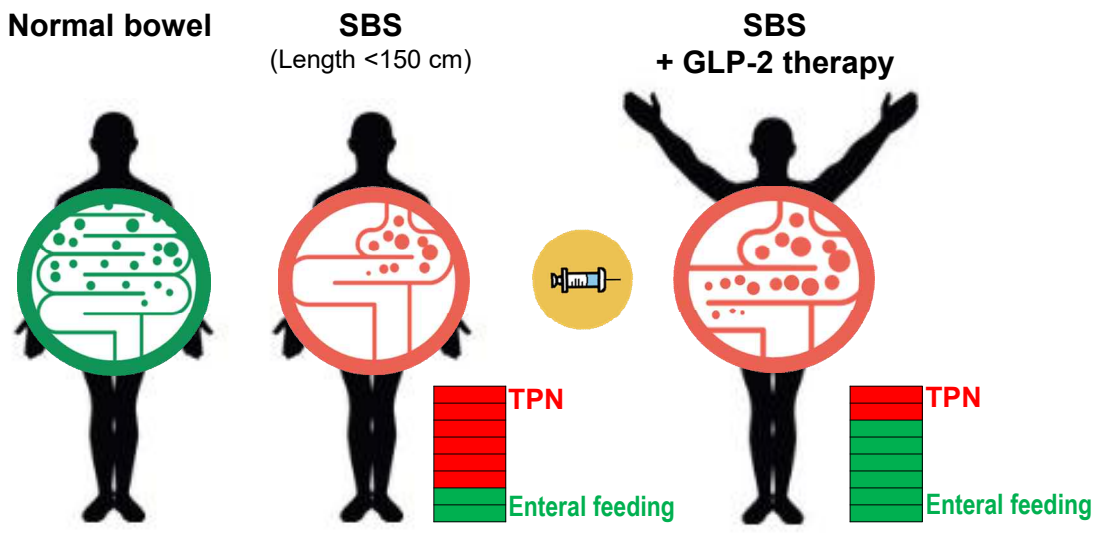
DISCLOSURES



Employee of Hanmi Pharm. Co., Ltd.



TREATMENT GOAL OF SHORT BOWEL SYNDROME AND BENEFITS OF GLP-2 THERAPY



Patients on IV nutrition

Suffer from malnutrition, liver failure, sepsis
Especially, 50% of pediatric patients died \leq age 3

GLP-2 receptor agonist is ideal therapy

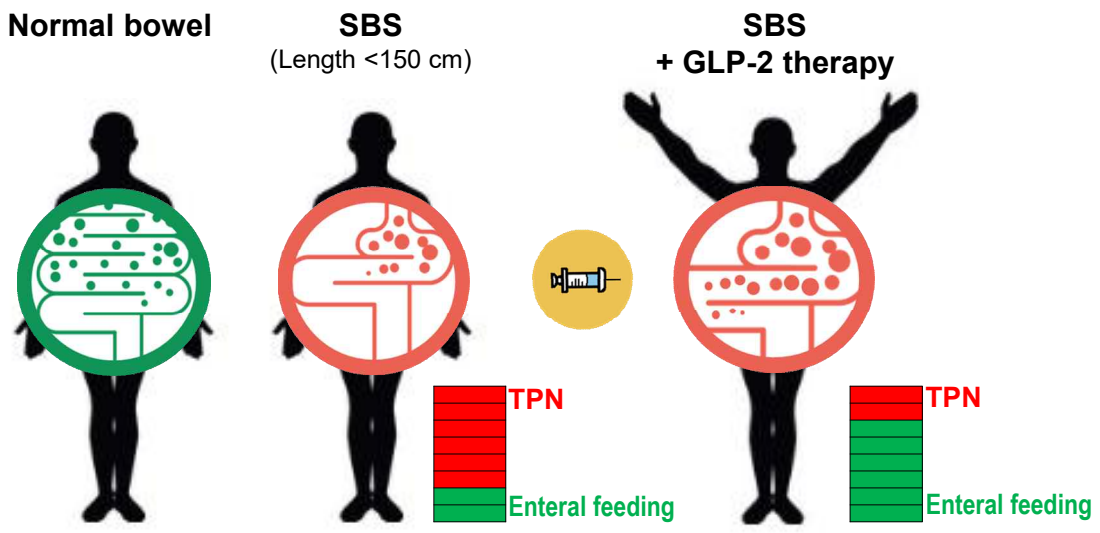
↓ PN dependency, ↑ patient's quality of life, But ...

Treatment burden in the patients who need long-term administration

More effective drug desired for further PN reduction



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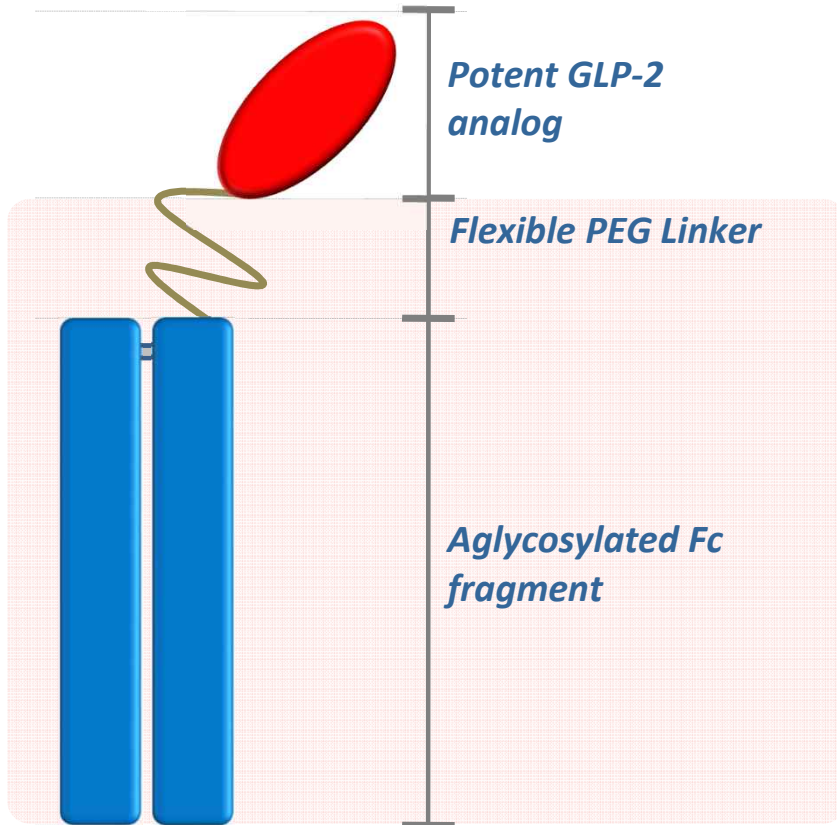
What is a medical requirement for the next generation for hormonal therapies?



- "Less injection stress"** (30 inj. → Single inj. per month)
- "Convenient SC administration"** (Read-to-inject)
- "Accelerated adaptation"** (Rapid small bowel action)
- "Increase in PN wean-off rate"** (Potent intestintrophic effect)



WHAT A LONG-ACTING GLP-2 ANALOG IS?

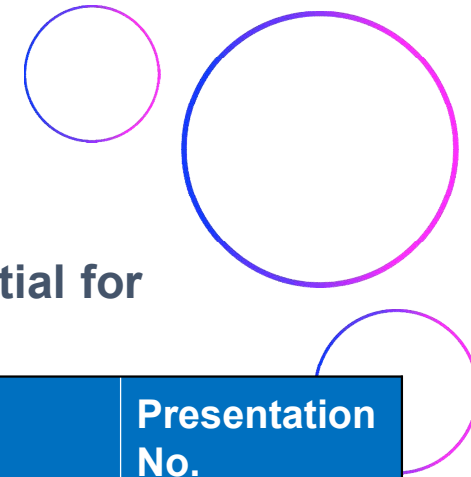


Hanmi's GLP-2 analog (HM15912) is conjugated with a human IgG4 Fc fragment *via* flexible linker





[General profile]

- Rationally designed GLP-2 analog to have a more potent intestinotrophic action vs human GLP-2
- Extended half-life allows once-monthly dosing
- Ready-to-inject with soluble formation
- Significant intestinotrophic efficacy in animal models

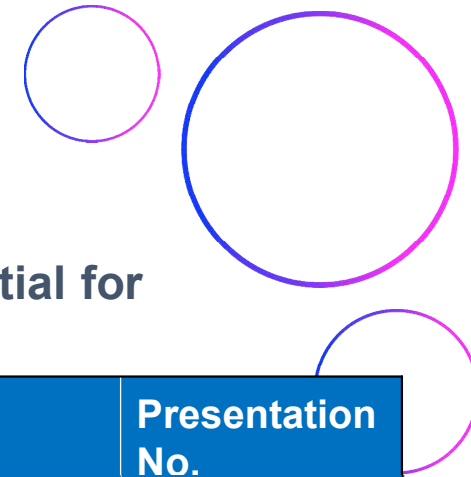
HYPOTHESIS & STUDY METHODS







HM15912, long-acting GLP-2 analog, is desired to have therapeutic potential for short bowel syndrome with significant efficacy

Purpose		Species / Strain	Induction method	Presentation No.
1. Best-in-class efficacy	Switching from Daily GLP-2 drug	 C57BL/6 mice	Normal	#O14
	Switching from Weekly GLP-2 drugs	 Sprague dawley rat	Normal	
2. Therapeutic potential	Efficacy in pathophysiological condition of SBS	 Sprague dawley rat	80% jejunioileal resection	#P249 (Poster)
3. Monthly potential	Various dosing interval	 C57BL/6 mice	Normal	

HYPOTHESIS & STUDY METHODS



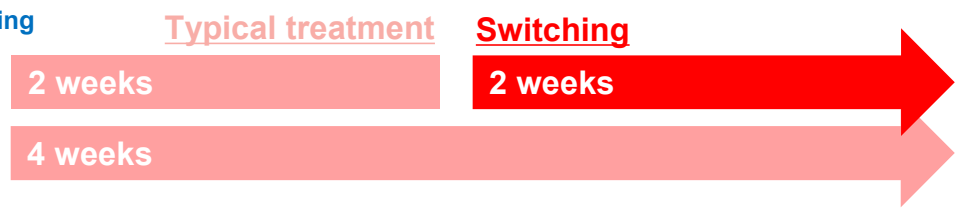
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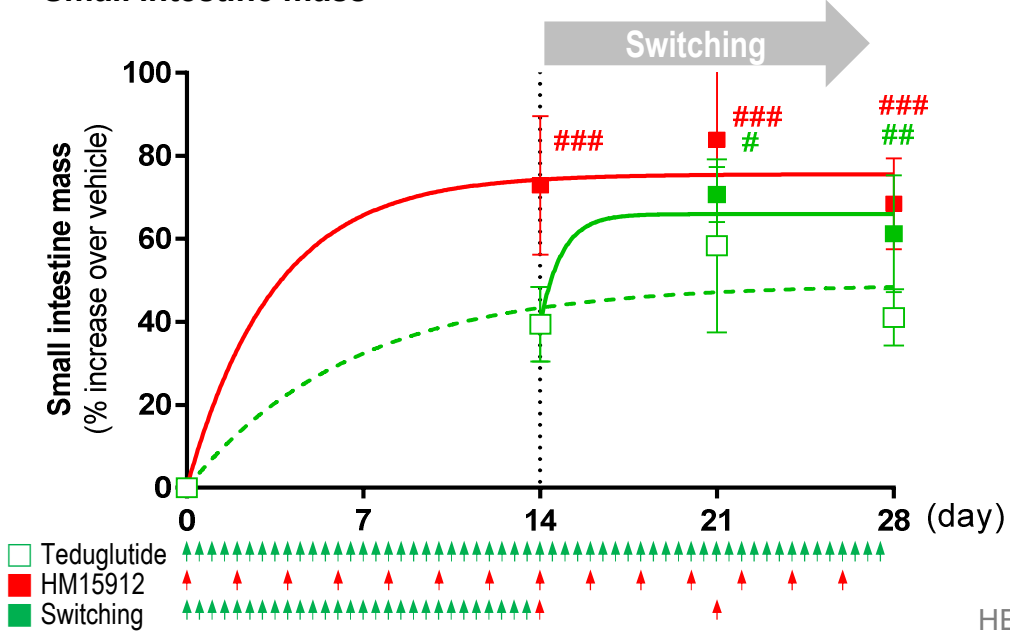
INTESTINOTROPIC EFFICACY AFTER SWITCHING FROM DAILY GLP-2 ANALOG

Experimental scheme

Study #1 : Daily GLP-2 (Teduglutide) → HM15912 switching



Small intestine mass



- Vehicle
- Teduglutide 15.0 nmol/kg/BID [E_{max}, EPAR]
- Teduglutide 15.0 nmol/kg/BID → HM15912 → 58.1 nmol/kg/QW [1.0 mg/kg/month HED]
- HM15912 16.6 nmol/kg/Q2D [0.25 mg/kg/week HED]

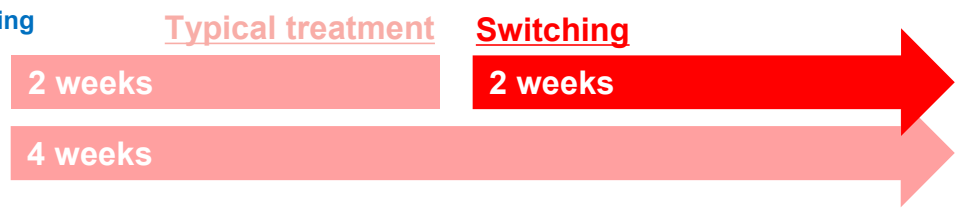
*p<0.05 vs. vehicle by One-way ANOVA
#p<0.05 vs. Teduglutide by One-way ANOVA

HED= Human equivalent dose; BID= twice a day; Q2D= every other day; QW= once a week

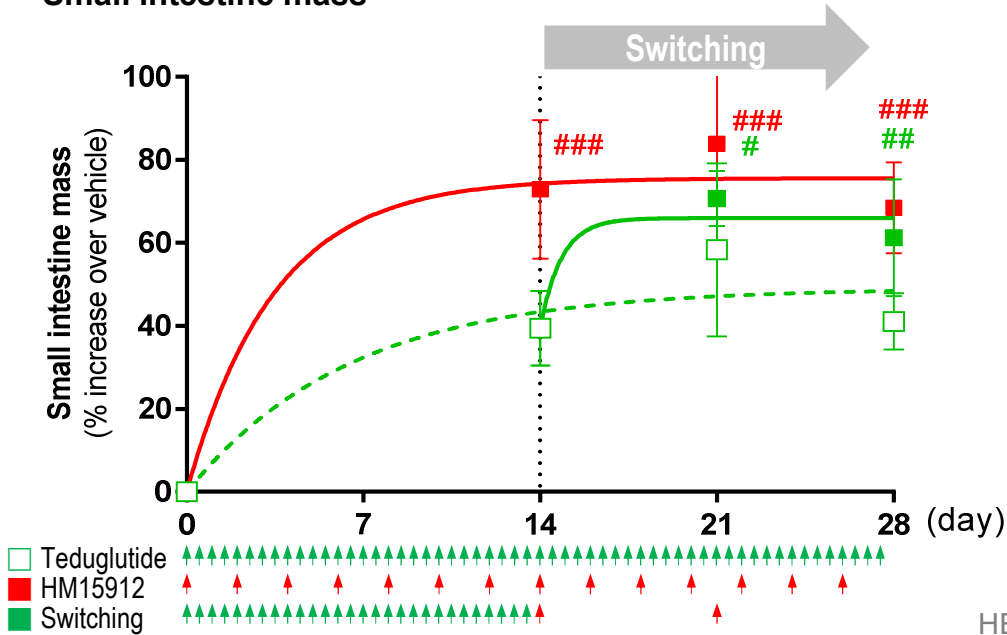
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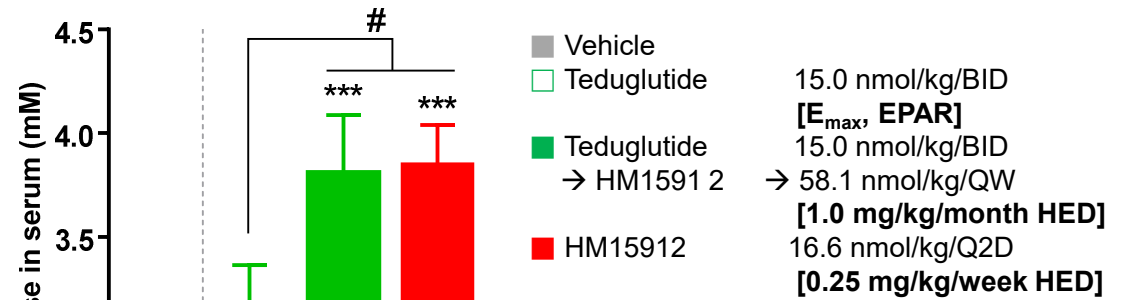
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Small intestine mass



D-xylose absorption at week 4



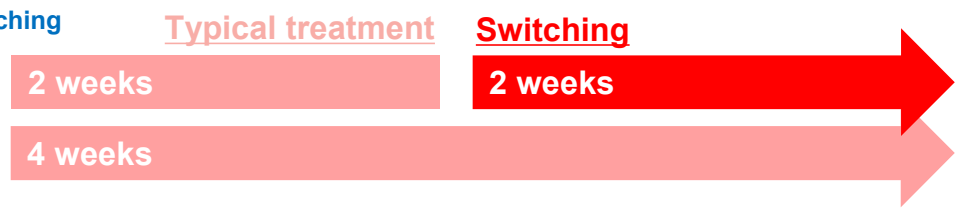
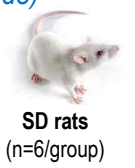
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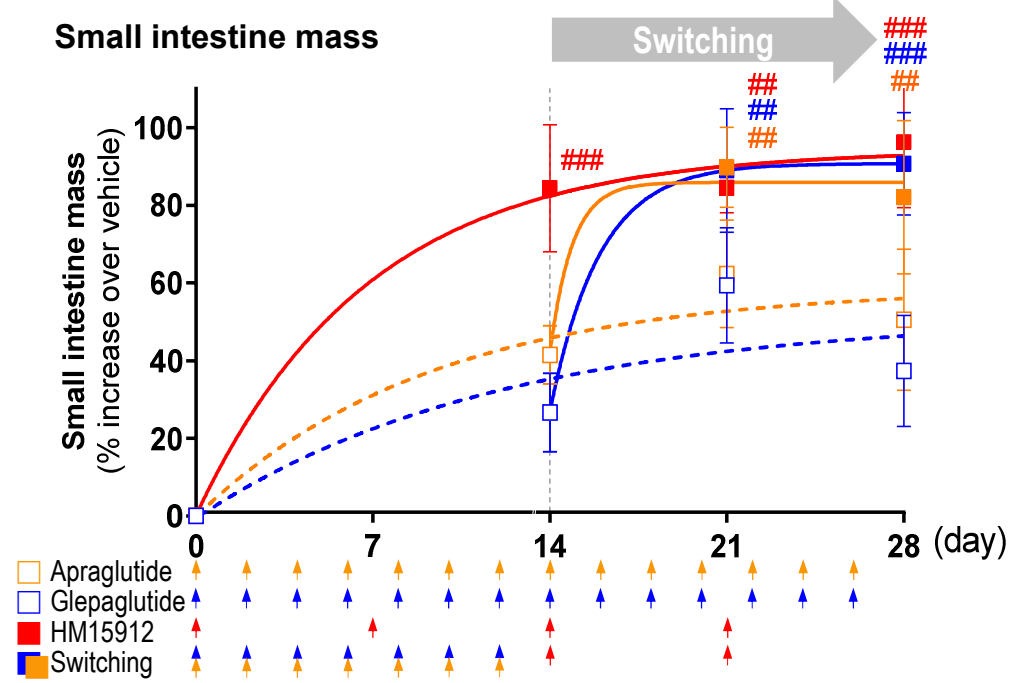
INTESTINOTROPIC EFFICACY AFTER SWITCHING FROM WEEKLY GLP-2 ANALOGS

Experimental scheme

Study #2 : Weekly GLP-2 → HM15912 switching
 (Apraglutide, Glepaglutide)
 * In-house synthesized



Small intestine mass



- Vehicle
- Apraglutide 63.7 nmol/kg/Q2D [10 mg/week HED]
- Glepaglutide 55.6 nmol/kg/Q2D [10 mg/week HED]
- HM15912 57.9 nmol/kg/QW [2 mg/kg/month HED]
- Switching, Apraglutide → HM15912
- Switching, Glepaglutide → HM15912

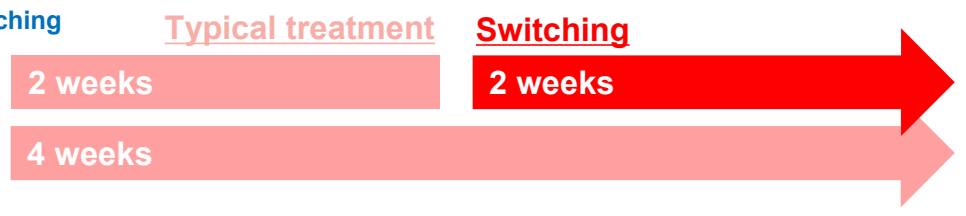
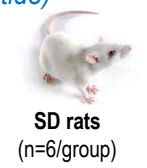
*p<0.05 vs. vehicle by One-way ANOVA
 #p<0.05 vs. weekly GLP-2RA (synthesized) by One-way ANOVA

HED= Human equivalent dose; Q2D= every other day; QW= once a week

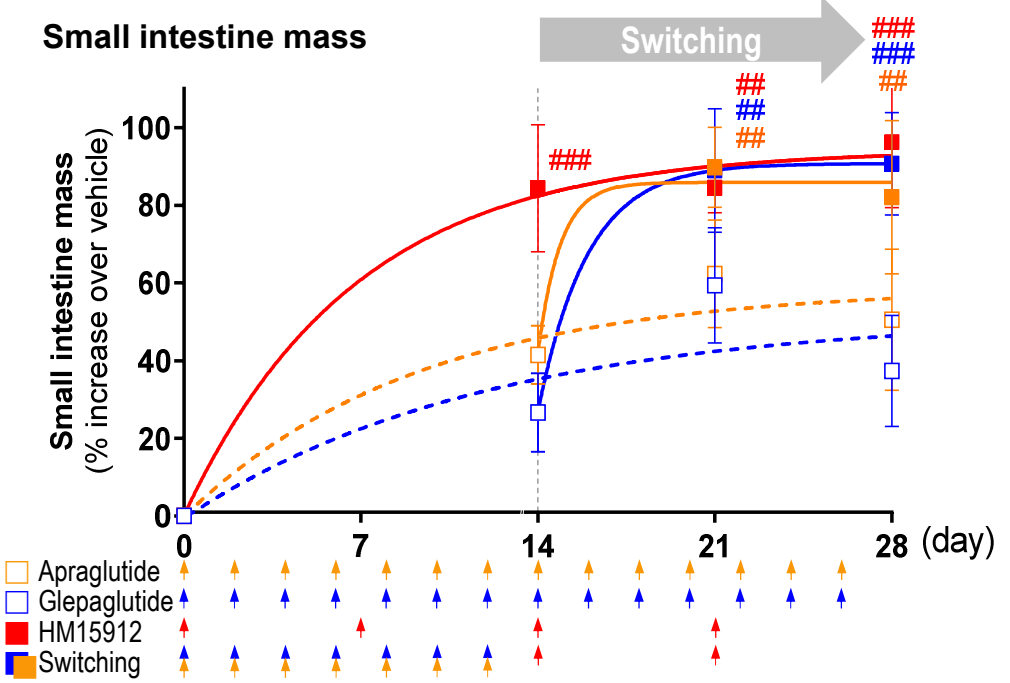
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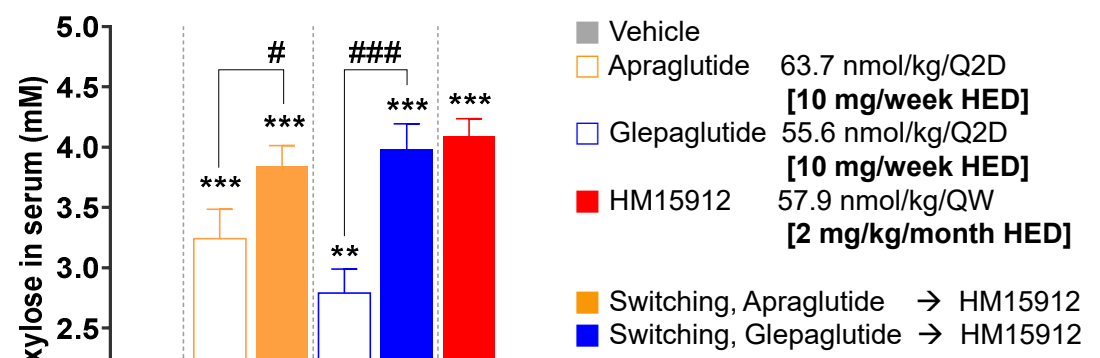
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Small intestine mass



D-xylose absorption at week 4



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 #p<0.05 vs. weekly GLP-2RA (synthesized) by One-way ANOVA

HED= Human equivalent dose; Q2D= every other day; QW= once a week

EXECUTIVE SUMMARY

- **HM15912 treatment significantly increased small intestine mass compared to teduglutide or weekly GLP-2 analogs after 2 weeks treatment.**
- **After 2 more weeks treatment, while showing the maintained or slightly increased small intestine weight in teduglutide or weekly GLP-2 analogs treated groups, respectively, it was further increased after switching to HM15912.**
- **In consensus with increase in small intestine weight, absorption capacity was also significantly improved after switching to once weekly administration of HM15912, which is mimicking once monthly administration in human.**

- **Significant effect on intestinal growth after switching from daily or weekly GLP-2 drugs to HM15912 with extended dosing interval mimicking once-a-month in human supports that HM15912 will provide a less PN dependency and more convenient treatment option (monthly) to SBS patients.**
- **ODD granted in US and EU, RPD in US**
- **P2 clinical study is on-going in SBS patients (US).**

Please note poster presentation reporting more information about HM15912:

#P249 Intestintrophic effect of a novel long-acting GLP-2 analog, HM15912, in animal model of short bowel syndrome and potential as monthly administration