Pharmacokinetic (PK) Profile of EBP05/EB613 Oral hPTH(1-34) (teriparatide) Tablets in Women of Menopausal Age Versus Young Adult Men

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BACKGROUND

EB613 is an oral, daily tablet formulation of teriparatide [hPTH(1-34)] being developed by Entera Bio for the treatment of osteoporosis. EBP05 is the specific formulation that was selected during early clinical development and used in Phase 2 studies, including a 6-month, 161-patient, placebo-controlled Phase 2 study, (ENT-07-2019; NCT04003467; ASBMR 2021 poster FRI-237, oral presentation LB-1116), which showed rapid dose-proportional increases in biochemical markers of bone formation, decreases in markers of bone resorption, and increased lumbar spine, total hip, and femoral neck Bone Mineral Density (BMD) in postmenopausal women with low BMD or osteoporosis. The 2.5 mg daily dose of 0.5 mg [hPTH(1-34)] EBP05 tablets was selected for evaluation in a planned registrational Phase 3 study.

An earlier Phase 1 study in young male volunteers (ENT-02-2013; NCT02202603) and a Phase 2 study in female and male patients with hypoparathyroidism (ENT-04-2018; NCT03516773; ASBMR 2019: LB SUN-972) also evaluated the PK profile of EBP05 tablets, 0.75 mg hPTH(1-34) each, with a total dose of 2.25 mg. Both studies were performed at the Hadassah Clinical Research Center. The tablets were administered with 100 ml water in the morning, following an overnight fast. The production process of the EBP05 tablets was optimized following the Phase 1 study and manufactured at an international CDMO using a scalable process to accommodate future commercial supply.

The current retrospective analysis compares data from the 2 PK studies, using the same tablet strength of 0.75 mg, from two different production processes and same 2.25 mg total dose in two different populations - young adult men vs. women of menopausal age.

METHODS

PK profiles were obtained from nine young healthy men (mean age of 23, range 21-26) in a Phase 1 study (ENT-02-2013), and from six women from a Phase 2 study (ENT-04-2018) in hypoparathyroidism patients of menopausal age (mean age of 60, range 49-63). Subjects in study ENT-04-2018 received up to 3 administrations of 2.25 mg EBP05 dose on different treatment days. For the current comparative analysis, each administration is regarded as an independent event, resulting in a total of 11 evaluable PK profiles obtained from the women of menopausal age. Data were obtained from the respective clinical study reports.

RESULTS

Following the administration of a 2.25 mg dose of EBP05, the PK parameters obtained in young men and in women of menopausal age were found to be similar (Figure 1).

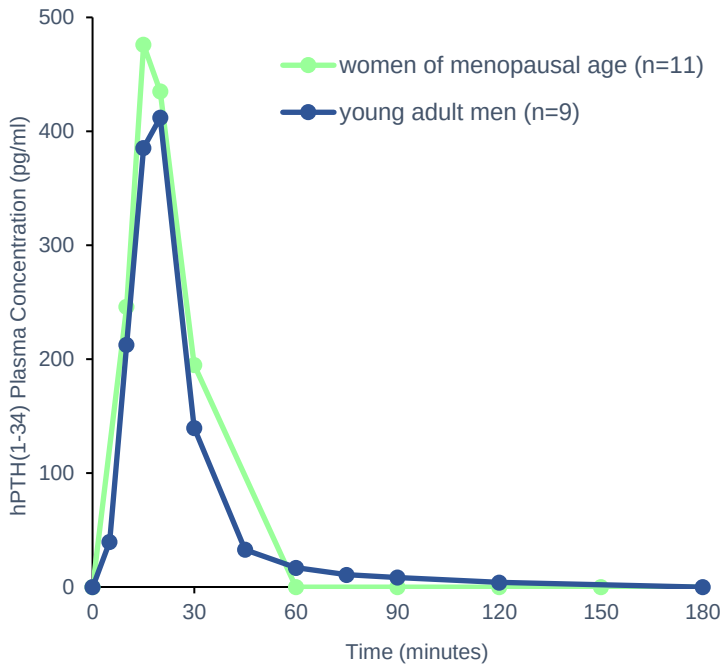

Figure 1. *Median hPTH(1-34) after oral EBP05 2.25 mg (3x0.75 mg tablets)*

No serious adverse events were reported. All adverse effects were mild or moderate and self-resolving.

The profile of drug related adverse events reported in one or more subjects in either study is characteristic of PTH receptor activating drugs and included headache, palpitations, nausea, dizziness, erythema, and fatigue.

RESULTS

Median Cmax was 425 (IQR 272 - 625) pg/ml vs 521 (IQR 279 - 1720) pg/ml and median AUC_{last} was 157 pg*hour/ml (IQR 64 - 218) vs 158 (IQR 75 - 589) pg*hour/ml in young men and women of menopausal age, respectively (Table 1).

Study ID	N	Age (years)	Cmax (pg/ml)	Tmax (min)	AUClast (pg*hour/ml)
ENT-02-2013	9	22 (21 - 26)	425 (272 - 625)	20 (10 - 20)	157 (64 - 218)
ENT-04-2018	11	62 (49 - 63)	521 (279 - 1720)	20 (15 - 30)	158 (75 - 589)

Table 1*. Median PK parameters (with IQR for Cmax and AUClast and range for Tmax and age) of hPTH(1-34) after oral administration of a 2.25 mg dose of EBP05 (3x0.75 mg tablets) to young healthy men (study ENT-02-2013) and to women of menopausal age (study ENT-04-2018).*

CONCLUSION

This retrospective analysis compares a 2.25 mg dose of EBP05 in healthy young males versus female patients of menopausal age with hypoparathyroidism. The data showed a consistent PK profile based on median Tmax, Cmax, and AUClast values.

Therefore, the PK profile of Entera's novel oral peptide delivery of hPTH(1-34) appears to be reproducible across populations which differ in gender and age.

The baseline age characteristics of these female patients in ENT-04-2018 is similar to that of the reported Phase 2 and planned Phase 3 of EBP05 oral hPTH(1-34) once daily tablets in post-menopausal osteoporosis.

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