Effects of Age and Gender on the Pharmacokinetics of Fasiglifam (TAK-875)
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Purpose
Fasiglifam is a potent and highly selective agonist of GPR40 being developed as an adjunct to diet and exercise to improve glycemic control in patients with type 2 diabetes mellitus.

This study evaluates the effect of age and gender on the single-dose pharmacokinetics of fasiglifam in healthy subjects.

Methods
Twenty-four (six young males, six elderly males, six young females and six elderly females) were enrolled. Subjects received a single oral dose of fasiglifam 50 mg. Serial blood samples were collected up to 168 hours for quantitation of fasiglifam and its minor inactive metabolite fasiglifam M-I. The effect of age and gender on the pharmacokinetics of fasiglifam and fasiglifam M-I were evaluated via an analysis of variance with fixed effects for age, gender and age-by-gender interaction on $T_{\text{max}}$, $T_{1/2}$, and the natural logarithms of $C_{\text{max}}$ and $\text{AUC}_{0-\text{inf}}$.

Results
Elderly subjects (mean age: 70 years) had 20% and 25% greater fasiglifam and fasiglifam M-I $C_{\text{max}}$, respectively, than those of young subjects (mean age: 33 years). Elderly subjects had 20% and 27% greater fasiglifam and fasiglifam M-I $\text{AUC}_{0-\text{inf}}$, respectively, than those of young subjects. Fasiglifam $T_{\text{max}}$ and $T_{1/2}$ were comparable between elderly and young subjects while fasiglifam M-I $T_{\text{max}}$ was 2.5 hours longer than that in elderly subjects.

Female subjects had 14% and 60% greater fasiglifam and fasiglifam M-I $C_{\text{max}}$, respectively, than those in male subjects. Fasiglifam $\text{AUC}_{0-\text{inf}}$ were comparable between the genders while female subjects had 34% higher fasiglifam M-I $\text{AUC}_{0-\text{inf}}$ than male subjects. Fasiglifam $T_{\text{max}}$ and $T_{1/2}$ were comparable between genders while fasiglifam M-I $T_{\text{max}}$ was 2.83 hours shorter in female than male subjects.

Fasiglifam was well tolerated by all subjects with no hypoglycemia in any group.

Conclusion
Elderly subjects had higher exposure to fasiglifam than young subjects (20% higher peak and total exposure). Female subjects had slight differences in exposure to fasiglifam compared with male subjects (14% higher peak and no major difference in total exposure). These differences are small and unlikely to be clinically relevant.