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An accelerator mass spectrometry-enabled micro-tracer study to evaluate the human mass balance of KD101, an anti-obesity drug under development

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In clinical drug development, it is important to understand the absorption, distribution, metabolism and excretion (ADME) properties of a drug in humans. The micro-tracer study based on the accelerator mass spectrometry (AMS) is an ultrasensitive technique to obtain human ADME profiles with a negligible radiation dose. KD101 is a novel compound under development to treat obesity. The aim of this study was to investigate the absorption, metabolism and excretion properties of KD101 in obese subjects. A randomized, open-label, single-dose, one-treatment, one-period, one-sequence study was conducted in six males with a BMI ≥27, who received KD101 at 400 mg with 3.52 μg of [14C]-KD101 (180 nCi) in the fed state. Plasma, urine and feces samples were collected up to 288 hours post-dose for mass balance and metabolite profiling. Plasma concentrations of KD101 were determined using a validated GC method. Total radioactivity in the samples was determined using AMS. Safety and tolerability was evaluated based on vital signs, adverse events, clinical laboratory tests, and electrocardiography. All of the subjects completed the study with no clinically significant safety issue. Mean total recovery rate (range) was 85.21% (75.36-99.01%), consisting of 77.96% (68.31-92.33 %) for urine and 7.26% (5.91-8.51%) for feces, which differed greatly from the pre-clinical data. Oral absorption of [14C]-KD101 was rapid with the peak plasma concentration reaching at 5.83h post dose, which was consistent with the previous report. In the urine radiochromatogram, five large peaks were identified including a peak represented by the parent compound. KD101 is excreted predominantly through the urine in humans. Many of the excreted materials in the urine were considered metabolites. This study demonstrated effectiveness of the micro-tracer study enabled by AMS in humans to investigate the ADME property of KD101, which hugely differed from that seen in the preclinical animals.

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Biography

Howard Lee is the Founder and Director of the Center for Convergence Approaches in Drug Development (CCADD). He serves as a Professor at the Department of Transdisciplinary Studies, Graduate School of Convergence Science and Technology, Seoul National University. He is also appointed at Seoul National University College of Medicine and Hospital, affiliated with the Department of Clinical Pharmacology and Therapeutics. He previously served as the Head of Global Strategy and Planning, Clinical Trials Center, SNUH. As of August 2017, he was appointed as Chair of the Graduate Program in Clinical Pharmacology, Seoul National University. He has spearhead the introduction of Accelerator Mass Spectrometry (AMS)-enabled exploratory early clinical drug development studies to the Korean biopharmaceutical R&D sector, which has awarded him two government grants.

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