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Clinical pharmacokinetic pilot study of Gador dimethyl fumarate in healthy volunteers

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The hypothesis for the design of this project was that the extended release formulation containing Dimethyl fumarate 240 mg, developed by Gador will present similar bioavailability with respect to the reference formulation, measured in terms of speed and absorption. A clinical study of single-dose bioequivalence (in 2 stages) was designed to be carried out in healthy subjects. This study was opened of two periods, two sequences, crossed, randomized under fasting conditions. Eight out of ten subjects involved in this pilot study (stage-1) were randomized and completed the 2 periods of administration of the treatments. Data of all the subjects who completed the 2 periods of treatment administration were used for pharmacokinetic purposes. The design of the study was adequate to determine the bioequivalence of the test and reference products. The 7-day washout period was sufficient to allow the complete elimination of the formulations before the next dosing period. In relation to Monomethyl fumarate; the extended release formulation containing Dimethyl fumarate 240 mg, developed by Gador presents similar bioavailability, measured in terms of speed and extension of absorption in relation to the reference formulation. Intrasubject CVs were on the order of 30% to 40% for the 3 pharmacokinetic parameters; indicating that the molecule and/or the formulation shows high variability in absorption and must be considered for the calculation of sample size of stage-2. This improved process will serve for clinical assessment in patients. Individual plasma concentrations showed results lower than the lower limit of quantification of the validated analytical method. It is suggested to adjust the method by lowering said level for stage-2. It is possible to consider extending the range of bioequivalence for C_{max} to 70-143% in stage-2; since the intrasubject CV was >30% and the reference geometric mean is between 0.80-1.25 in stage-1.

Biography

Maligne Guillermo E is the Chief of Clinical Research and BA/BE Management at Gador S.A., Buenos Aires, Argentina. He has over 12 years of experience working in the pharmaceutical industry, 17 years medical development as Physician, 4 years in basic research project CONICET Fellowship (National Scientific Council), 8 years of experience advising oncologist clinical trials in early and late phases for clinical research.

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