(S149) PHARMACOKINETICS OF BG-12 ALONE AND WITH INTERFERON BETA-1A OR GLATIRAMER ACETATE

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Background: BG-12 is an oral therapy that exhibits anti-inflammatory and potentially neuroprotective mechanisms of action. It is currently being tested in phase 3 clinical trials for relapsing-remitting multiple sclerosis (RRMS). Two drugs commonly used to treat RRMS are interferon beta-1a (IFNβ-1a) and glatiramer acetate (GA). It is possible that BG-12 could be given with IFNβ-1a or GA. Objectives: To assess the potential drug interaction for co-administration of BG-12 + intramuscular (IM) IFNβ-1a or subcutaneous (SC) GA. Methods: Two phase 1, open-label, single-center, randomized, crossover studies each enrolled 26 healthy volunteers. Dosing sequences comprised two dosing periods separated by 7 days. Treatment consisted of BG-12, 240 mg twice a day, for 2 or 3 days alone (GA and IFNβ-1a studies, respectively) or given with a single IM IFNβ-1a 30-g or SC GA 20-mg injection administered on day 2. Pharmacokinetic (PK) parameters, vital signs, electrocardiographic findings, and adverse events (AEs) were assessed. Results: Twenty-five subjects completed the BG-12 + GA study, and 24 subjects completed the BG-12 + IFNβ-1a study. BG-12 metabolite (monomethyl fumarate [MMF]) concentrations in all treatment groups were comparable, suggesting no clinically significant effect of IM IFNβ-1a or GA on BG-12 disposition. The most common AEs were flushing with BG-12 alone (both studies) and BG-12 + GA, and flu-like symptoms with BG-12 + IM IFNβ-1a. There were no serious AEs or deaths. One subject with a transient, moderate increase in liver enzymes and neutropenia following BG-12 + IM IFNβ-1a treatment withdrew from the study. In the BG-12 + GA study, 1 subject discontinued after receiving BG-12 alone because of a mild erythematous facial nodule; 1 subject discontinued because of mild nausea after receiving BG-12 + GA. A mild increase in temperature and pulse was observed only following IM IFNβ-1a administration; no subject withdrew for these reasons. Hematologic shifts were observed in subjects receiving BG-12 alone and BG-12 + GA (mild neutropenia and anemia); no subject withdrew for these reasons. No clinically significant abnormalities on physical examination or ECG were observed. Conclusions: The PK profile of BG-12 was not altered by co-administration with IM IFNβ-1a or GA, indicating no drug interaction. No safety profile change or new safety signals were identified.

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