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Abstract (poster session)

Clinical safety of moxifloxacin: an analysis of "Valid for Safety" data from controlled phase II to phase IV studies performed between 1996 and 2010

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Objectives: Clinical Safety of Moxifloxacin (MXF) is approved for treatment of respiratory tract, skin, pelvic and intra-abdominal infections. Its safety profile is considered favourable in most reviews but has been challenged with respect to rare but potentially fatal adverse reactions. Our objective was to compare the MXF safety profile to that of comparators using the clinical trial database. Methods: Source of data: Double-blind and open-label, actively controlled, Phase 2-4 trials (valid for safety patients: n = 14,981 [MXF] vs 15,023 [comparators; standards of care and/or agreed upon with authorities]) (a) completed between 1996 and 2010 for both approved and other indications, (b) using the recommended MXF dosage (400 mg), administration route (oral, IV-only, or IV/oral), and precautions of use, and (c) including patients at risk (>= 65 y, diabetes, renal and hepatic impairment, cardiac disorders, BMI < 18 kg/m2). Patients with known contraindications were excluded from enrolment by design but any patient having entered a study, even if inappropriately, was included in the analysis. Analysis: Crude incidences and relative risk estimates (Mantel-Haenszel analysis) of patients with any adverse events (AEs), drug-related adverse events (ADRs), serious adverse events (SAEs), drug-related serious adverse events (SADRs), treatment discontinuation due to AEs and ADRs, fatal outcomes related to AEs and ADRs. Analyses were exploratory in nature and included systematic comparisons between groups and treatments. Results: Overall incidence rates of adverse events were similar in MXF and comparator groups, except for AEs and SAEs in IV-only double-blind studies, AEs, ADRs, SADRs in PO, SADRs in IV/PO, and premature discontinuation due to AEs in IV-only open-label studies, which were slightly more frequent in MXF-treated patients (mainly gastrointestinal disorders and "changes observed during investigations" such as asymptomatic QT prolongation). No medically-relevant differences in rates of AEs were seen between MXF and comparators in patients at risk. Incidence rates of hepatic disorders, tendon disorders, surrogates of QT prolongation, serious cutaneous reactions and Clostridium difficile-associated diarrhea were similar with MXF and comparators. Conclusions: No higher safety risk for MXF compared to standard therapies was seen in patients receiving the registered MXF dosage and for whom contra-indications and precautions of use (as in the product label) were taken into account.