

## **Rosiglitazone-Associated Fractures in Type 2 Diabetes: An analysis from A Diabetes Outcome Progression Trial (ADOPT)**

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**OBJECTIVE**—The purpose of this study was to examine possible factors associated with the increased risk of fractures observed with rosiglitazone in A Diabetes Outcome Progression Trial (ADOPT).

**RESEARCH DESIGN AND METHODS**—Data from the 1,840 women and 2,511 men randomly assigned in ADOPT to rosiglitazone, metformin, or glyburide for a median of 4.0 years were examined with respect to time to first fracture, rates of occurrence, and sites of fractures.

**RESULTS**—In men, fracture rates did not differ between treatment groups. In women, at least one fracture was reported with rosiglitazone in 60 patients (9.3% of patients, 2.74 per 100 patient-years), metformin in 30 patients (5.1%, 1.54 per 100 patient-years), and glyburide in 21 patients (3.5%, 1.29 per 100 patient-years). The cumulative incidence (95% CI) of fractures in women at 5 years was 15.1% (11.2–19.1) with rosiglitazone, 7.3% (4.4–10.1) with metformin, and 7.7% (3.7–11.7) with glyburide, representing hazard ratios (95% CI) of 1.81 (1.17–2.80) and 2.13 (1.30–3.51) for rosiglitazone compared with metformin and glyburide, respectively. The increase in fractures with rosiglitazone occurred in pre- and postmenopausal women, and fractures were seen predominantly in the lower and upper limbs. No particular risk factor underlying the increased fractures in female patients who received rosiglitazone therapy was identified.

**CONCLUSIONS**—Further investigation into the risk factors and underlying pathophysiology for the increased fracture rate in women taking rosiglitazone is required to relate them to preclinical data and better understand the clinical implications of and possible interventions for these findings.

**Abbreviations:** ADOPT, A Diabetes Outcome Progression Trial