Evaluation of Novel Urinary Biomarkers in Beagle Dogs With Amphotericin B-Induced Kidney Injury

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Abstract

Next-generation urinary protein biomarkers have been qualified to enable monitoring for drug-induced kidney injury in toxicology studies conducted in rats. However, there is limited literature on the utility of these biomarkers in dogs. To add to the existing body of knowledge on the utility of the next-generation drug-induced kidney injury (DIKI) biomarkers, we evaluated the value of these biomarkers for the early detection of DIKI in Beagle dogs using a differentiated nephrotoxicant, Amphotericin B (AmpB). In dogs with AmpB-induced kidney injury, we monitored the response of urinary albumin, total protein, clusterin, kidney injury molecule 1, neutrophil gelatinase-associated lipocalin and N-acetyl-beta-D-glucosaminidase. We also measured blood urea nitrogen, serum creatinine and cystatin C. The results showed that urinary clusterin (up to ? 112x) was much more sensitive to AmpB-induced kidney injury relative to other biomarkers. Moreover, other than urinary clusterin and to a much lesser extent urinary albumin and total protein, none of the other biomarkers analyzed in this study were more sensitive than blood urea nitrogen and serum creatinine. The AmpB related tubular alterations were characterized by minimal to mild, multifocal necrosis, degeneration, regeneration, dilatation and mineralization. The mild nature of these histopathologic findings further attested to the sensitivity of urinary clusterin to AmpB-induced kidney injury in dogs. These results will help drug developers make informed decisions when selecting urinary biomarkers for monitoring DIKI in dogs for toxicology studies.

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