

Title: *Biomarkers of Kidney Injury and Recovery in Patients with Multiple Myeloma Receiving Daratumumab*

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BACKGROUND: Kidney impairment is a common complication of multiple myeloma (MM) and is associated with worse treatment response and outcomes. Daratumumab, an anti-CD38 monoclonal antibody, has demonstrated efficacy across MM disease states and has been associated with improved kidney function. Novel biomarkers reflecting distinct nephron injury and repair pathways have recently been validated, but their utility in monitoring kidney responses in MM remains unclear.

METHODS: We prospectively enrolled 20 adults with newly diagnosed MM at high risk for acute kidney injury initiating subcutaneous daratumumab between September 2024 and November 2025. Blood and urine samples were collected before treatment and approximately 30 days after initiation. Prespecified biomarkers included plasma dickkopf-3 (DKK-3; primary biomarker), soluble urokinase plasminogen activator receptor (suPAR), monocyte chemoattractant protein-1 (MCP-1), kidney injury molecule-1 (KIM-1), and urinary DKK-3, KIM-1, neutrophil gelatinase-associated lipocalin (NGAL), and clusterin (CLU).

RESULTS: Paired plasma (n=20) and urine (n=19) samples were analyzed. Following daratumumab initiation, plasma DKK-3, plasma suPAR, and urinary suPAR/creatinine increased significantly, with median rises of 19.8% (p=0.01), 22.1% (p=0.008), and 26.0% (p=0.01), respectively (Figure 1A). Increased plasma DKK-3 was associated with greater odds of early kidney recovery and showed a borderline association with improved 90-day eGFR slope (Figure 1B). Several secondary biomarkers demonstrated nominal associations with kidney outcomes, including baseline urine KIM-1/creatinine, plasma MCP-1, urine NGAL/creatinine, and change in urine CLU/creatinine; however, none remained significant after false-discovery-rate correction.

CONCLUSIONS: Although DKK-3 is traditionally viewed as a marker of tubular stress and progressive kidney injury, rising plasma DKK-3 after daratumumab initiation was associated with improved kidney recovery. These findings suggest that transient biomarker elevations may reflect adaptive tubular stress-response and remodeling during renal recovery rather than irreversible injury. Larger prospective studies are needed to validate these observations.