

Title: *Resolution of Bevacizumab-Associated Hypertension and Proteinuria After Drug Cessation In Patients with OBGYN Cancers: A Real-World Cohort Study*

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Background: Bevacizumab is associated with hypertension (HTN) and proteinuria in patients with gynecologic cancers. The natural history of resolution of these toxicities after drug cessation has not been well-characterized.

Methods: We used the TriNetX US Collaborative Network to identify adult female patients with gynecologic malignancies who received and subsequently discontinued bevacizumab. Drug cessation was defined at 21 days after the last noted administration. Primary endpoints were time to resolution of *de novo* Grade 3+ HTN (SBP ≥ 160 or DBP ≥ 100 mmHg) and *de novo* Grade 2+ proteinuria (UPCR ≥ 1.0 g/g, UACR ≥ 300 mg/g, or dipstick $\geq 2+$). A secondary composite renal outcome (dialysis initiation, new CKD Stage 5, or $\geq 40\%$ sustained eGFR decline confirmed ≥ 30 days apart) was assessed using Fine-Gray hazard models with death as a competing event, applying a 90-day survivor landmark post-cessation.

Results: Of 6,960 patients, 1,255 met inclusion criteria (median age 63 years [IQR 54–71]). During active treatment, 339/1,255 (27.0%) developed *de novo* Grade 3+ HTN (median 105 days) and 574/1,255 (45.7%) developed *de novo* Grade 2+ proteinuria (median 104 days). Among patients with Grade 3+ HTN, 138 (40.7%) achieved full resolution (median 124 days), 106 (31.3%) achieved BP normalization requiring antihypertensive class escalation (improved to Grade 1), and 95 (28.0%) had persistent uncontrolled BP at last follow-up. Among 574 patients with Grade 2+ proteinuria, only 100/574 (17.4%) achieved full resolution (median 172 days), while 474/574 (82.6%) had proteinuria at final follow-up. *De novo* Grade 3+ HTN was associated with the composite renal outcome (sHR 1.37, 95% CI 1.12–1.67, $p=0.002$), while *de novo* Grade 2+ proteinuria was not (sHR 1.10, 95% CI 0.91–1.33, $p=0.314$).

Conclusion: In this real-world cohort, *de novo* Grade 3+ HTN resolved in ~72% of patients within 12 months of cessation. In contrast, *de novo* Grade 2+ proteinuria was largely refractory.

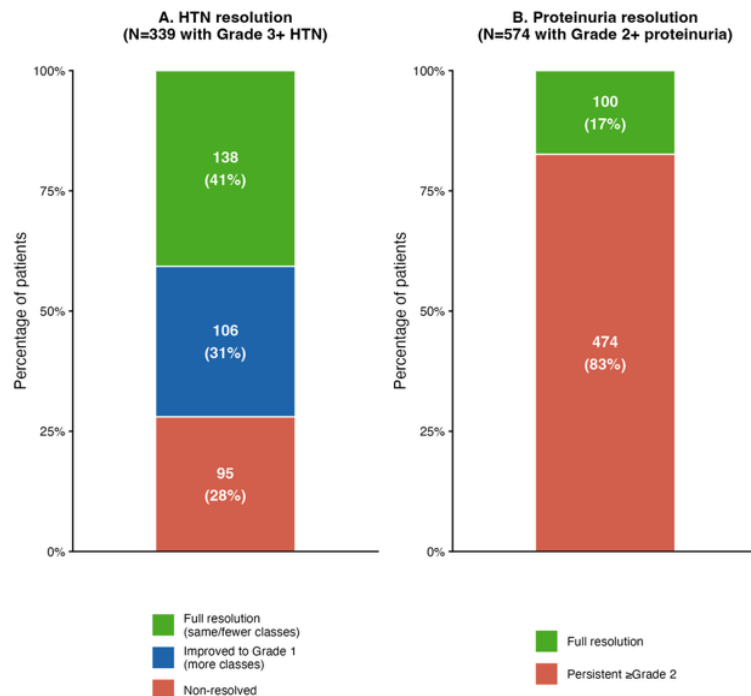


Figure 1: HTN and Proteinuria resolution. Toxicities were defined using CTCAE v5.0 criteria and required *de novo* onset (absence of qualifying readings in the 12 months preceding bevacizumab initiation).