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Urinary Neuroendocrine Neoplasms (NENs) Treated in the "Modern Era": A Multicenter Retrospective Review

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BACKGROUND: Treatment of gastroenteropancreatic (GEP) and lung NENs has evolved substantially since 2010, with several new NCCN-recommended treatments available. Urinary NENs (UNENs) are very rare, thus treatment often extrapolated from NENs arising in other sites. We present an updated multicenter analysis of care patterns and overall survival (OS) in UNENs treated in the “modern era”.

METHODS: Multicenter retrospective review of patients diagnosed after 2005 and alive after 2010. Modern-era therapies (METs) were those FDA approved and recommended by NCCN after 2010 for any NEN primary, off-label immunotherapies, and therapy received in a clinical trial from 2010 onward. Duration of treatment efficacy measured using time to next treatment (TTNT). Log-rank and Cox proportional hazards used to test differences in OS.

RESULTS: 134 UNENs patients: 94 (70.1%) bladder, 32 (23.9%) kidney, 2 (1.5%) ureter, 2 (1.5%) urethra, 4 (3.0%) other urinary primary. 53 (39.6%) alive, 65 (48.5%) deceased, 16 (11.9%) lost follow up. Well differentiated NETs (WDNETs) in 20.2% of cases (78.1% kidney origin), 37.5% stage IV, median OS (mOS) (9.28 yrs); poorly differentiated NECs (PDNECs) in 70.9% (92.2% bladder origin), mOS (4.65 yrs), 26.6% stage IV. Patients received a median of two therapies (range 0-10); 47 (35%) received METs, mOS 7.89 yrs. DOTA-avidity, primary resection, and primary

site were significantly associated with OS. Bladder NENs demonstrated worse OS than other sites when adjusted for differentiation, smoking, DOTA-avidity, but not for those received METs.

CONCLUSION: This is the largest series of UNENs receiving METs. The results suggest that treatment patterns overlap with GEP and Lung NENs, with preliminary evidence suggesting comparable benefits in selected treatments for WD-UNENs. That said, WDNENs and PDNECs are two distinct entities, arising in different parts of the urinary tract with very different clinical pathologic features. Prospective studies need to validate application of GEP/lung treatment guidelines to U-NENs.

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