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THE IMPACT OF CHRONIC KIDNEY DISEASE AND CLINICAL EVENTS ON PATIENT HEALTH RELATED QUALITY OF LIFE IN DAPA-CKD

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Introduction: Chronic kidney disease (CKD) is a progressive condition characterised by declining renal function that is associated with increased risk of cardiovascular complications and death. Progressive loss of kidney function can also lead to anaemia, hyperkalaemia, increased risk of fractures and in severe cases requires renal-replacement therapy with dialysis or kidney transplantation, as such, CKD has a significant impact on quality of life (QoL). The DAPA-CKD clinical trial (NCT03036150) assessed the efficacy of dapagliflozin for the treatment of CKD in patients with stage 2-4 disease and albuminuria in comparison with placebo. Patient QoL, assessed through EQ-5D-5L questionnaires, was measured at baseline and subsequently every four months. The objective of this study was to estimate the impact of CKD progression and event incidence on patient QoL in the DAPA-CKD clinical trial.

Methods: A linear hierarchical multivariable regression model was developed based on pooled individual patient data from DAPA-CKD to estimate patient utility estimated from response to the EQ-5D-5L questionnaire, incorporating a subject specific random intercept. The regression model was adjusted for important patient characteristics including age, sex, comorbid type 2 diabetes (T2DM) status, CKD stage, dialysis, urinary albumin-creatinine ratio (UACR), heart failure and adverse events of interest from the DAPA-CKD clinical trial. In accordance with guidance issued by the National Institute for Health and Care Excellence, utility estimates were derived based on the application of UK-specific utility tariffs after mapping EQ-5D-5L responses to EQ-5D-3L values. Utility values were converted to utility decrements, with a larger value corresponding to poorer QoL.

Results: In total, 4,170 patients contributed 20,267 EQ-5D-5L questionnaires that were included in the regression analysis, with mean patient utility at baseline of 0.757 (95% confidence interval: 0.752-0.763). More advanced CKD was associated with poorer patient QoL, particularly in those patients progressing to dialysis during follow-up, with non-dialysis dependent CKD stage 5 patients having 0.028 (0.009-0.048) lower utility on average, increasing to 0.078 (0.050-0.105) in patients receiving dialysis when compared with stage 2 CKD patients. Similarly, patients with UACR >1,000 mg/g had 0.011 (0.002-0.020) lower utility than patients with UACR ≤1,000 mg/g. Hospitalisation for heart failure (HHF) was also associated with reduced QoL, with patients having 0.088 (0.016-0.159) lower utility within one month of the initial HHF event, and 0.071 (0.042-0.101) thereafter. Age, sex and comorbid T2DM were also associated with patient utility, with older patients (utility decrement of 0.012 [0.008-0.016] per 10 years), women (utility decrement of 0.049 [0.040-0.059]) and patients with T2DM (utility decrement of 0.042 [0.032-0.052]) having poorer quality of life.

Conclusions: CKD imposes a significant burden on patient QoL, which increases as the disease progresses, measured through either decline in renal function or the presence of albuminuria. Comorbidities and complications frequently associated with CKD are also associated with a loss in health related QoL. Interventions that can delay the progression of CKD may have the potential to improve QoL and reduce the burden of CKD.

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CANADIAN REAL-WORLD ASSESSMENT OF TOLVAPTAN IN ADPKD: C-MAJOR STUDY AND SAFETY MONITORING AND DISTRIBUTION PROGRAM

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Introduction: Tolvaptan is the only approved treatment in Canada for slowing renal function decline and kidney enlargement in ADPKD patients. As per Health Canada requirements, a patient registry evaluating long-term clinical outcomes (the C-MAJOR study) and a hepatic safety monitoring and distribution program (the HSMDP) to mitigate the risk of liver injury were implemented and have been ongoing nationally for 5 years. The aim of this interim analysis is to describe baseline characteristics of patients at initiation of tolvaptan treatment through the C-MAJOR study and to report on rates of treatment persistence and liver test abnormalities through the HSMDP.

Methods: C-MAJOR is a non-interventional, multi-centre study of Canadian ADPKD patients treated with tolvaptan. The HSMDP ensures tolvaptan is dispensed under controlled liver enzyme and function monitoring.

Results: As of April 2020, 398 patients, 51% female, were enrolled in C-MAJOR. At baseline, mean (SD) age was 45.1 (11.5) years, BP was 129.4 (13.4)/83.1 (10.0) mmHg and eGFR was 63.6 (27.8) mL/min/1.73 m². Total kidney volume was 1949 (1562) mL, 80.7% of patients had family history of ADPKD and 39.4% had family history of early end-stage renal disease. As per Mayo classification, 90.2% were at high risk for disease progression (1C-D-E). Most common ADPKD clinical manifestations were hypertension (83.2%), hepatic cysts (69.6%) and kidney pain (24.1%). Over a mean (SD) follow-up of 2.0 (1.0) years, adverse events were reported in 82.7% of patients, most common being polyuria (19.6%), fatigue (18.6%), and nocturia (15.1%).

Over a mean follow-up of 23.0 (SD = 17.6) months in the HSMDP, 2.4% (n=39) of the 1,600 patients who received at least one shipment of tolvaptan reported an elevation of transaminases >3x ULN. There were 0.3% (n=5) of patients meeting the guidelines for permanent discontinuation. No cases of drug-induced liver injury were reported. Treatment discontinuation rates at 12, 24 and 36 months were 14%, 21% and 26%, respectively.

Conclusions: This analysis provides Canadian real-world evidence of high-risk for disease progression at tolvaptan initiation, 3-y persistence data similar to phase III studies and HSMDP data showing that tolvaptan was permanently discontinued in 0.3% of patients because of hepatic effects. This abstract was also submitted for the ASN 2020 congress.

Conflict of Interest: Advisor, investigator and speaking bureau for Otsuka Pharmaceutical

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GASTRO-INTESTINAL ANGIODYSPLASIA IN PATIENTS WITH CHRONIC KIDNEY DISEASE

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Introduction: Angiodysplasia is an abnormal, dilated small blood vessel in the mucosal and submucosal layers of the gastrointestinal (GI) tract. It’s responsible for approximately 6% of lower GI bleeding cases and up to 8% of upper GI bleeds. Besides, it has been reported to be associated more with some pathologies, among others, end-stage chronic kidney disease (CKD). Yet under diagnosed because of current anemia and GI bleeding in patients with CKD, which present the main symptoms of angiodysplasia.