Qualification of Biomarker—Total Kidney Volume in Studies for Treatment of Autosomal Dominant Polycystic Kidney Disease

Guidance for Industry

This guidance represents the current thinking of the Food and Drug Administration's (FDA) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the Center for Drug Evaluation and Research (CDER) Biomarker Qualification Program (email: CDER-BiomarkerQualificationProgram@fda.hhs.gov).

Drug Development Tool (DDT) Type: Biomarker
Referenced Biomarker(s): Total Kidney Volume (TKV)

TKV is defined as the sum of the volume of the left and right kidneys.

I. SUMMARY OF GUIDANCE

A. Purpose of Guidance

This guidance provides a qualified context of use (COU) for the biomarker TKV in studies for the treatment of autosomal dominant polycystic kidney disease (ADPKD). This guidance also describes the experimental conditions and constraints for which this biomarker is qualified through the CDER Biomarker Qualification Program. This biomarker can be used by drug developers for the qualified COU in submissions of investigational new drug applications (INDs), new drug applications (NDAs), and biologics license applications (BLAs) without the relevant CDER review group reconsidering and reconfirming the suitability of the biomarker.

B. Application of Guidance

This guidance applies to the use of TKV in studies for the treatment of ADPKD. It does not change any regulatory status, decisions, or labeling of any medical imaging device used in the medical care of patients.

TKV use in drug development outside of the qualified COU will be considered by FDA on a case-by-case basis in regulatory submissions. In such cases, additional information relevant to the expanded use may be requested by the CDER product review team.

DDT Tracking Number: [DDTBMQ-000021]

II. CONTEXT OF USE

A. Use Statement

This guidance provides qualification recommendations for the use of TKV, measured at baseline, as a prognostic enrichment biomarker to select patients with ADPKD at high risk for a *progressive decline* in renal function (defined as a confirmed 30% decline in the patient's estimated glomerular filtration rate (eGFR)) for inclusion in interventional clinical trials. This biomarker may be used in combination with the patient's age and baseline eGFR as an enrichment factor in these trials.

B. Conditions for Qualified Use

1. *Quantitative Imaging Biomarker*

    TKV should be calculated from the left and right kidneys measured with a validated and standardized image acquisition and analysis protocol within the trial. (Please see supporting documentation for details at Biomarker Qualification Program: Qualified Biomarkers and Supporting Information.)

2. *TKV-Based Patient Selection in Clinical Trials*

    a. PATIENT POPULATION

    Patients with ADPKD should be at least 12 years of age

    b. PATIENT SELECTION

    Baseline TKV can be used in combination with the patient's age and baseline eGFR as an enrichment factor in ADPKD clinical trials to select ADPKD patients at high risk for a *progressive decline* in renal function. (Please see supporting documentation for details at Biomarker Qualification Program: Qualified Biomarkers and Supporting Information.)

    c. MEASUREMENT APPLICABILITY

Various imaging modalities and post-processing methods are available to determine TKV. These modalities have different levels of precision. For patients with ADPKD at high risk for a confirmed 30% decline in their eGFR, TKV was qualified based on a collection of data from multiple study sites, as well as on results from imaging modalities (i.e., magnetic resonance imaging (MRI), computed tomography (CT), or ultrasound (US)) and from analysis methodologies (i.e., stereology and ellipsoid calculations).