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STATISTICAL ANALYSIS PLAN

A Double-blind Randomized Parallel Group Study of the Efficacy and Safety of Tesevatinib in Subjects with Autosomal Dominant Polycystic Kidney Disease

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LIST OF ABBREVIATIONS

Abbreviation	Full Term
ADPKD	autosomal dominant polycystic kidney disease
AE	adverse event
ALP	alkaline phosphatase
ALT	alanine transaminase
ANCOVA	analysis of covariance
ARPKD	autosomal recessive polycystic kidney disease
ATC	American therapeutic chemical (classification)
CI	confidence interval
CM	concomitant medication
CRF	case report form
CTCAE	common terminology criteria for adverse events
ECG	electrocardiogram
EGFR	epithelial growth factor receptor
eGRF	estimated glomerular filtration rate
htTKV	height-adjusted total kidney volume
ICF	informed consent form
ICH	International Conference on Harmonisation
ITT	intent-to-treat
MDRD	modification of diet in renal disease
MedDRA	medical dictionary for regulatory activities
mITT	modified intent-to-treat
mL	milliliters
MMRM	mixed model repeated measures
MRI	magnetic resonance imaging
ms	millisecond
PKD	polycystic kidney disease
PT	preferred term
QD	once daily
QTcF	corrected QT interval using Fridericia's formula
SAE	serious adverse event
SAP	Statistical Analysis Plan
SOC	system organ class
TEAE	treatment-emergent adverse event

Abbreviation	Full Term
TLFs	tables, listings, and figures

1 INTRODUCTION

Polycystic kidney disease (PKD) is the most common inherited kidney disease in the United States, occurring in approximately 1 in every 1,000 live births. It affects more than 600,000 people in the United States and 12 million worldwide. It is the third most common single cause of kidney failure. Polycystic kidney disease is characterized by the growth of numerous renal cysts, which cause abnormalities in both structure and function of the kidneys. Cysts also develop in other organs, particularly in the liver. Other manifestations of PKD include high blood pressure, urinary tract infections, kidney stones, hematuria, and aneurysms. Pain in the back, abdomen, and pelvis affects many PKD patients. There are 2 types of PKD, autosomal dominant (ADPKD) and autosomal recessive (ARPKD). In ADPKD, the mutation in either the PKD1 or PKD2 gene results in the abnormal, uncontrolled growth of renal tubular epithelial cells. Epithelial growth factor receptor (EGFR) is overexpressed and mislocated from the basolateral to the luminal surface of renal tubular cells. Epithelial growth factor receptor ligands are secreted by tubular cells and are found in human PKD cyst fluids. The combination of EGFR mislocation and ligand secretion establishes an autocrine loop resulting in persistent renal tubular cell proliferation. Chronic proliferation results in renal cyst formation. The cysts then cause a structural distortion of the renal architecture, impeding normal nephron function. Cyst enlargement results in a massive increase in kidney volume and a progressive impairment of renal function. Associated clinical symptoms include hypertension, recurrent flank pain, hematuria, and recurrent pyelonephritis. Currently, there are no disease-modifying therapies for ADPKD; all existing treatment strategies are palliative and aimed at controlling symptoms.

This Statistical Analysis Plan (SAP) describes detailed statistical procedures to be used for study KD019-211 as specified in the protocol (Version 2.0, 31-August-2018): A Double-blind Randomized Parallel Group Study of the Efficacy and Safety of Tesevatinib in Subjects with Autosomal Dominant Polycystic Kidney Disease.

The SAP was written in accordance with the recommendations outlined in the International Conference on Harmonisation (ICH) E9 Guideline entitled “Guidance for Industry: Statistical Principles for Clinical Trials” and the most recent ICH-E3 Guideline, entitled “Guidance for Industry: Structure and Content of Clinical Study Reports.”

2 STUDY SUMMARY

2.1 Study Objectives

2.1.1 Primary Objectives

The primary objective of this study is to evaluate the change from baseline in height-adjusted total kidney volume (htTKV) as measured by magnetic resonance imaging (MRI) at Months 12, 18, 24, and 30 days post-dose in patients with ADPKD treated with tesevatinib or placebo.

2.1.2 Secondary Objectives

The secondary objectives of the study are to:

- Evaluate the safety and tolerability of tesevatinib50 mg QD in patients with ADPKD
- Evaluate the change in estimated glomerular filtration rate (eGFR) using the modification of diet in renal disease-4 (MDRD) formula at the Month 12, 18, 24, and 30 days post-dose time points

2.2 Study Design

This is a Phase 2b, multicenter, double-blind, randomized, parallel group study to evaluate the change from baseline in htTKV as measured by MRI in subjects with ADPKD treated with tesevatinib or placebo. Male and female subjects with ADPKD, 18 to 60 years of age and with an eGFR $\geqslant$ 30 mL/min/1.73 m2 and $\leqslant$ 80 mL/min/1.73 m2 will be enrolled. Up to 100 male and female subjects will be randomized 1:1 to receive 50 mg of tesevatinib once daily (QD) or placebo. The study will be conducted at approximately 25-30 sites in the United States.

Subjects will be screened up to 28 days before initiation of treatment with tesevatinib or placebo (certain screening assessments may be conducted up to 42 days prior to dosing). Screening assessments will include medical and PKD history, physical examination, vital signs, electrocardiograms (ECGs), clinical laboratory evaluation (including hematology, serum chemistry, coagulation, thyroid stimulating hormone, urinalysis, and pregnancy), ocular examination, echocardiogram, and MRI. Calculation of htTKV at screening for eligibility determination may be performed by a local radiologist.

Starting on Day 1, subjects will receive 50 mg QD of tesevatinib or placebo for up to 24 months. During the Early Treatment Period (Days 1 to 28), subjects will report to

the study site on Days 1, 14, and 28; subjects will be followed every 28 days from Months 2 to 12 and every other month from Months 12 to 24. Safety assessments will be performed at regular intervals throughout the study and will include physical examinations, vital signs, ECGs, clinical laboratory evaluations, ocular examination, and echocardiograms. Magnetic resonance imaging to determine the change from baseline in htTKV will be performed at Months 12, 18, and 24. Entry into the study will be based on local MRI readings, but central MRI readings and htTKV calculation will be performed at baseline and during the study.

All subjects will undergo an end-of-study evaluation approximately 30 days after the last dose of study drug.

2.3 Visit Schedule and Study Assessment

The flow chart of visit schedule and study assessments is given in Table 2 of the KD019-211 Protocol.

2.4 Efficacy Assessments

2.4.1 Height-Adjusted Total Kidney Volume

htTKV will be assessed by MRI at Months 12, 18, 24, and 30 days post-dose. htTKV, reported in milliliters (mL), is calculated using total kidney volume obtained from MRI divided by height in meter.

2.4.2 Estimated Glomerular Filtration Rate

eGFR will be assessed using the MDRD-4 formula as presented in Table 1. As indicated in Table 2 of the study protocol serum creatinine will be assessed at the Screening, Day 1, Day 14, Day 28, then monthly until Month 12, then every 2 months until Month 24; and 30 days from last dose.

Table 1: 4-Variable Modification of Diet in Renal Disease (MDRD-4) Formula

High Level Formula for Black or African-American Males: $eGFR = 175 \times (Scr^{-1.154}) \times (Age^{-0.203}) \times 1.212$
High Level Formula for Males NOT Black or African-American (any other option): $eGFR = 175 \times (Scr^{-1.154}) \times (Age^{-0.203})$
High Level Formula for Black or African-American Females: $eGFR = 175 \times (Scr^{-1.154}) \times (Age^{-0.203}) \times 1.212 \times 0.742$
High Level Formula for Females NOT Black or African-American (any other option): $eGFR = 175 \times (Scr^{-1.154}) \times (Age^{-0.203}) \times 0.742$

Note: Age is shown in years. Scr = serum creatinine

3 STATISTICAL METHODS

3.1 General Methods

3.1.1 Computing Environment

All statistical programming and data analyses will be performed using SAS® Version 9.4 on a Windows platform.

3.1.2 Sample Size Justification and power calculations:

Based on the results presented in Caroli, et.al.[1] it is anticipated that the mean change from baseline in htTKV at 12 months will be 83.6 (± 90.0) mL in the placebo group. Assuming the mean change from baseline in htTKV at 12 months is 26.4 mL for the tesevatinib group, 40 subjects per group would yield approximately 80% power to detect a difference between treatment groups based on a 2-sided t-test with a Type I error rate of 0.05. Ten additional subjects per group will be added (i.e., for a total of 50 subjects per group) to adjust for dropouts and differences in analysis methodologies (e.g., the htTKV data will be log-transformed).

3.2 General Considerations

General considerations for descriptive statistics and presentation for continuous and categorical data are given below.

3.2.1.1 Continuous Variables

Continuous data will be described using descriptive statistics: number of observations (n), mean, standard deviation, median, minimum, and maximum.

Means, medians, standard deviations, and confidence intervals (CIs) will be reported to one decimal place more than the data reported on the case report form (CRF) or by the vendor. Minimum and maximum will be reported to the same number of decimal places displayed on the CRF or by the vendor. P-values will be reported to 4 decimal places.

3.2.1.2 Binary Endpoint and Other Categorical Variables

For endpoints with two possible outcomes (i.e., dichotomous endpoints) such as alive/otherwise or response/otherwise within specific periods, the 95% confidence interval will be calculated with Clopper-Pearson method. For other categorical variables, the counts and percent of each category within a parameter will be

calculated for observed data only. The denominator for all percentages, unless otherwise specified, will be the number of subjects in the treatment group or in the specified analysis population.

3.2.2 Study Day

The Study Day for all assessments prior to the first study drug administration is calculated as the difference between the date of the event or measurement (e.g., adverse event [AE] onset date, assessment date, sample collection date) and the start date of study treatment. The day before the start of study treatment is Study Day -1.

The Study Day for all post-assessments after the first study drug administration is calculated as the difference between the date of the event or measurement (e.g., AE onset date, assessment date, sample collection date) and the start date of study treatment plus one day. The first day of study treatment is Study Day 1.

3.2.3 Baseline

Baseline value is defined as the valid and last non-missing value obtained within 28 days prior to subject receiving the first study medication, unless otherwise stated under the related assessment section. Baseline can be the day before the first study medication or on the same day as the first study medication if a pre-dose assessment is available. Subjects without data on a parameter before the first study medication will have a missing baseline for this parameter.

3.2.4 Handling of Incomplete or Missing Data

Missing data will not be imputed in general and will be reported as missing in all listings. For categorical variables, patients with missing data are not included in calculations of percentages unless otherwise specified.

Missing start and end dates for AE and concomitant medication (CM)

The assumption will be the worst or most conservative judgment when imputing AE and CM start and end dates. The purpose of imputing a start date is to help define whether the AE/CM started while taking study drug.

For a partial or missing start date:

- If the day is missing, the first day of the month will be imputed. If the missing day is the same as the month of first dose of study drug, then the first dose date will be imputed.

- If the day and month are missing, the first day of January will be imputed. If the year is the same as the first dose date, then the first dose date will be imputed.
- If the date is completely missing, the first dose date will be imputed. If the end date suggests it could have started prior to this, the first day of January of the same year as the end date will be imputed.
- When imputing a start date, the start date will ensure that the new imputed date is sensible, i.e., is prior to the end date of the AE or CM.

For a partial or missing end date:

- If the day is missing, the last day of the month or the last assessment date, whichever is earlier, will be imputed.
- If the day and month are missing, the 31st of December or the last assessment date, whichever is earlier, will be imputed
- If the date is completely missing, there will be a need to look at whether the AE/CM is still ongoing before imputing a date. If the ongoing flag is missing, then it will be assumed that AE is still present, or CM is still being taken (i.e., do not impute a date). If the AE/CM has stopped, then the last assessment date will be imputed.

These data imputations are for categorization purpose only and will not be used in the listings.

If the assessment of the relationship of the AE to tesevatinib is missing, then it will be assumed that the AE is related to tesevatinib, and the AE considered as such in the frequency tables of possibly related AEs. No imputation should be done at the data level.

Missing event dates

Event date will be imputed only when day is missing, and the purpose of imputing an event date is to most conservatively calculate time to event.

If the day is missing, the first (mid, last) day of the month will be imputed for undesired (neutral, desired) event. If the missing day is the same as the month of first dose of study drug, then the first dose date will be imputed for undesired event.

These data imputations are for time to event calculation only and will not be used in the listings.

3.3 Analysis Populations

The following are the set of analysis populations.

Screened Population: All subjects who sign the Informed consent form (ICF) will be included in the Screened Population.

Safety Population: The Safety Population is defined as all subjects who receive at least 1 dose of study medication. Subjects will be analyzed according to the study drug they actually received.

Intent-to-treat (ITT) Population: The ITT population is defined as all randomized subjects. Subjects will be analyzed according to the study medication to which they were randomized.

Modified Intent-to-treat (mITT) Population: The mITT Population is defined as all subjects who receive at least 1 dose of study medication. The mITT Population will be used for tables of demography and baseline characteristics. Subjects will be analyzed according to the study medication to which they were randomized.

Efficacy Population: The Efficacy Population is defined as all subjects in the mITT population who complete at least 12 months of tesevatinib or placebo treatment and have a centrally read MRI at baseline and after 12 months of treatment. Subjects will be analyzed according to the study drug they actually received. This will be the primary population for efficacy analyses.

3.4 Subject Disposition and Evaluability

The analysis populations defined in Section 3.3 and the number of subjects discontinuing from the study and the primary reason for discontinuation will be summarized.

3.5 Protocol Deviations

All protocol deviations will be identified and classified as major or minor before clinical database lock and will be presented in a listing.

Major Deviation: Protocol deviation that may impact the accuracy, and/or reliability of the study data or that may impact subject rights, safety, or well-being.

Minor Deviation: Protocol deviation that does not impact the accuracy, and/or reliability of the study data or subject rights, safety, or well-being.

3.6 Demographics and Baseline Characteristics

3.6.1 Demographics

Descriptive summaries of demographic and baseline characteristics will be presented by treatment group and overall, for the mITT population. Demographics and baseline characteristics will be reviewed to assess the comparability of the treatment groups at baseline. Continuous variables such as subject age, weight and height will be summarized using number of observations, mean, standard deviation, median, minimum, and maximum values. Categorical variables such as subject sex and race will be summarized using number of observations and percentages for each category.

3.6.2 Medical History

Medical history will be summarized by primary System Organ Class (SOC) and Preferred Term (PT) for each treatment group. Medical history will be coded using Medical Dictionary for Regulatory Activities (MedDRA) Version 20.1 (or higher) terminology.

3.7 Prior and Concomitant Medications

Concomitant medications will be coded using the World Health Organization Drug Dictionary (MAR2017B2). Prior medications are defined as those medications that began and stopped before the start of study treatment. Concomitant medications are defined as medications taken after the start of study treatment and during the study period, including those began before but ongoing at the start of study treatment. If a medication start date is partially or fully missing and it is unclear as to whether the medication is prior or concomitant, it will be assumed that the medication is concomitant.

Number and percentage of incidence of prior and concomitant medications will be summarized according to Anatomical Therapeutic Class (ATC) and preferred drug name.

3.8 Treatment Exposure

Summary statistics for the duration of exposure to investigational product will be presented by treatment group. In addition, the number of dose interruptions will be provided in by-subject listings. The duration of exposure is defined as:

Duration of exposure (days) = (Date of last dose – Date of Study Day 1) + 1.

3.9 Efficacy Analyses

Listings for all efficacy data will be presented. Results will be presented by Treatment Group. The Efficacy Population will be the primary analysis population for efficacy analyses, with the mITT Population being used for sensitivity and supplemental analyses.

3.9.1 htTKV Logarithmic Transformation

To reduce heterogeneity, a logarithmic transformation (log_{10}) will be applied to the htTKV data prior to the analysis of covariance (ANCOVA) analyses (ie, defined in Sections 3.9.2) and mixed model repeated measures (MMRM) analyses (ie, defined in Section 3.10.1). The log10 transformation will apply to both the baseline and post-baseline htTKV assessments .

3.9.2 Primary Endpoint Analysis

The primary efficacy endpoint is the change from baseline in htTKV at Month 12. An ANCOVA model including treatment group as a factor and the baseline htTKV (log_{10} transformed) as a covariate will be used for efficacy analyses. The dependent variable is the log10 transformed change from baseline (ie, log_{10}(Month 12 htTKV) - log_{10}(Baseline htTKV)).

The 2-sided Type I error rate will be set at an alpha level of 0.05.

3.9.3 Secondary Endpoint Analyses: Change from Baseline in eGFR

A secondary endpoint is the change from baseline in eGFR at months 12, 18, 24, and 30 days post-dose using the MDRD-4 formula (see Table 1).

For the 30 days post-dose endpoint, the change in eGFR from baseline to post-treatment follow-up is annualized (divided) by each subjects' treatment duration (in years). This normalization is necessary, otherwise the treatment group having more dropouts or earlier dropouts may bias the results.

At each timepoint (ie, months 12, 18, 24, and 30 days post-dose) and analysis of covariance (ANCOVA) model will be used to evaluate treatment effect. The ANCOVA model has eGFR as the dependent variable, treatment group as the factor, and baseline eGFR, patient age, and baseline htTKV as covariates.

3.10 Supplementary and Sensitivity Analyses for Primary and Secondary Endpoints

The following are supplementary and sensitivity analyses for the primary and secondary endpoints:

- The primary and secondary efficacy endpoints will be performed on the mITT population.
- The htTKV at Months 18, 24, and 30 days post-dose will be analyzed in the manner as described in Section 3.9.2.
- A longitudinal analysis of htTKV (as described in Section 3.10.1)
- A longitudinal analysis of eGFR (as described in Section 3.10.23.10.1)

3.10.1 htTKV Longitudinal Analysis

An MMRM analysis will be performed on the htTKV data. The following is the MMRM model:

$$Y_{ij} = \beta_1 + \beta_2 \times Group_i + \beta_3 \times t_{ij} + \beta_4 \times t_{ij} \times Group_i + b_{1i} + b_{2i} \times t_{ij} + e_{ij}$$

Where:

Y_{ij}	is the $\log_{10}$(htTKV) values for subject i at visit j (ie, at baseline; months 12, 18, and 24; and 30-days post-dose)
$Group_i$	is the treatment group indicator for Subject i (=0 if placebo, =1 if KD019)
t_{ij}	is the time (in years) from baseline of the htTKV assessment
β_1	is the intercept for the placebo group
β_2	is the intercept increment for the KD019 group (ie, $\beta_1 + \beta_2$ is the intercept for the KD019 group)
β_3	is the slope for the placebo group
β_4	is the slope increment for the KD019 group (ie, $\beta_2 + \beta_4$ is the slope for the KD019 group)
b_{1i}	Is the random intercept term for subject i
b_{2i}	Is the random slope term for subject i
e_{ij}	Is the error term for subject i, visit j.

Note: the random effects, b_{1i} and b_{2i} are assumed to be normally distributed with mean 0 and unknown variance covariance structure (ie, an unstructured 2×2 covariance matrix will be modelled). The error terms in the model, e_{ij}, are assumed mutually independent and normally distributed; and they are also assumed to be independent of the random effects, b_{1i} and b_{2i}.

This model will test for a difference in slopes between placebo and KD019 (ie, testing the fixed effect parameter β_4).

The following is the corresponding sample SAS Proc Mixed code for this MMRM model:

Table 2: Sample SAS Code of Longitudinal MMRM Analyses

```
** Sample SAS Code for MMRM **;
Proc Mixed Data=XXX;
  Class Trt subject;
  Model  log_htTKV = treatment time treatment*time/s
  Random intercept time / type=un subj=subject;
Run;
```

3.10.2 eGFR Longitudinal Analysis

The slope of eGFR change will be analyzed by an MMRM analysis.

The MMRM model will be the same as the model described in Section 3.10.1 with the dependent variable being the subjects eGFR values. The model will include the baseline and all post-baseline eGFR assessments.

3.11 Subgroup Analyses

- Summary statistics and the ANCOVA analysis for htTKV described in Section 3.9.2 will be performed for each of the Mayo Classification groups (ie, Class 1A, 1B, 1C, 1D, and 1E). This will be done for the Month 12, 18, 24, and 30 days post-dose treatment visits.
  The formulas for the Mayo classification groups are derived from the methods in Irazabel (2015)[2] and are presented in Section 3.15.
- Summary statistics and the ANCOVA analysis for eGFR described in Section 3.9.3 will be performed for each of the Mayo Classification groups (ie, Class 1A, 1B, 1C, 1D, and 1E). This will be done for the Month 12, 18, 24, and 30 days post-dose treatment visits.

3.12 Multiplicity

The primary efficacy endpoint will be tested at the 2-sided 0.05 level. The secondary efficacy endpoints (ie, eGFR at months 12, 18, 24, and 30 days post-dose) will not be controlled for multiplicity for this Phase 2 study.

3.13 Safety Analysis

Safety assessments will include AEs, serious adverse events (SAEs), vital sign measurements, clinical laboratory evaluations (hematology and chemistry), and

electrocardiograms (ECGs). Unscheduled visits for safety assessments will not be presented in summary tables but will be in listings. All safety analyses will be performed using the Safety Population.

3.13.1 Adverse Events

AEs will be coded using the MedDRA dictionary (Version 20.0). Treatment-emergent AEs (TEAEs) are any AE occurring or worsening in severity after the first administration of study medication. All AEs (including SAEs) will be graded using the 5-point Common Terminology Criteria for Adverse Events (CTCAE) V5.0 scale (mild, moderate, severe, life-threatening, or death). Causality with tesevatinib will be classified as: definitely related; probably related; possibly related; unlikely related; or not related. Definitely related, probably related and possibly related will be combined to related, unlikely related and not related will be combined to unrelated in some safety analyses.

The number and percentage of patients who experienced at least one TEAE as well as the number and percentage of patients who experienced AEs of each specific system organ class (SOC) and preferred term (PT) will be presented. For the presentation of AE incidences, the SOCs and the PTs within each SOC will be presented by decreasing total frequency. Tabulation by maximum severity and relationship to tesevatinib will also be included by treatment group.

The TEAEs, Grade ≥ 3 TEAEs, SAEs, and TEAEs leading to dose modification/discontinuation will be summarized by treatment arm, SOC, and PT. These analyses will be repeated for events considered related (definitely related/probably related/possibly related) to tesevatinib.

Subject listings will be provided for SAEs, AEs resulting in study drug discontinuation, and deaths.

Adverse events will also be presented in listings. Time to onset and duration of AEs will be included in listings, along with action taken and outcome.

3.13.2 Clinical Laboratory Evaluation

The summary statistics (including number, mean, standard deviation, median, minimum, and maximum) of all laboratory variables and changes from baseline will be calculated for each visit or study assessment by treatment group. For parameters of white blood cell counts, neutrophils (absolute count), lymphocytes (absolute count),

monocytes (absolute count), hemoglobin, platelets, ALP, ALT, aspartate aminotransaminase, gamma glutamyl transferase, total bilirubin, glomerular filtration rate, plots of mean/mean changes from baseline with the corresponding standard error will be displayed.

For shift tables, laboratory results will be classified using the common terminology criteria for adverse events (CTCAE) Version 5.0. All graded laboratory parameters will be summarized separately for hematology and biochemistry. Corresponding shift tables comparing baseline to the worst post-baseline grade within the treatment period will be provided.

3.13.3 Vital Signs

Descriptive statistics for vital signs (weight, temperature, blood pressure, pulse rate, and respiratory rate) values and the change from baseline will be presented for each scheduled assessment time point.

3.13.4 ECG

Descriptive statistics for ECG parameters (i.e., PR interval, QRS interval, and QTcF interval) at each time point with triplicate ECGs will be presented for the values and change from baseline scores. (QTcF is the QT interval using Fridericia's correction which is calculated by $QTcF = QT/(RR^{(1/3)})$.)

The number and percentage of subjects with observed QTcF values that satisfy the following conditions will be presented by treatment group and study visit and categorized as: ≤ 450 ms; > 450 to 480 ms; > 480 to 500 ms; and > 500 ms.

The number and percentage of subjects having change from baseline QTcF values that satisfy the following conditions will be presented by treatment group and study visit and categorized as: ≤ 0 ms; > 0 to ≤ 30 ms; > 30 to ≤ 60 ms; and > 60 ms.

3.13.5 Echocardiogram

The results of the echocardiogram (ie, normal, abnormal, and abnormal clinically significant) will be summarized by treatment group for each valve (ie, aortic, mitral, tricuspid, and pulmonic) at each scheduled assessment timepoint.

3.13.6 Physical Examination

Significant abnormal physical exam findings were reported as adverse events.

3.14 Interim Analysis

There is no interim analysis for this study.

3.15 Mayo Classification Formula

Table 3 lists the Mayo Classifications (ie, 1A, 1B, 1C, 1D, and 1E) htTKV criteria for a given age as presented in Irazabel (2015)[2]; supplemental Table S2.

For classes 1A, 1B, 1C, and 1D the upper limits of htTKV are presented, for class 1E, the minimal value is presented (ie, as such the values in Table 3 for the 1D and 1E columns are equivalent).

For example, a 40 year old with an htTKV of 650 would have a classification of 1C.

Figure 1 provides an illustration of the Mayo Classification categories, as copied from "Figure 3" of Irazabel (2015)[2].

Table 3: Mayo Classification HtTKV Limits for Age

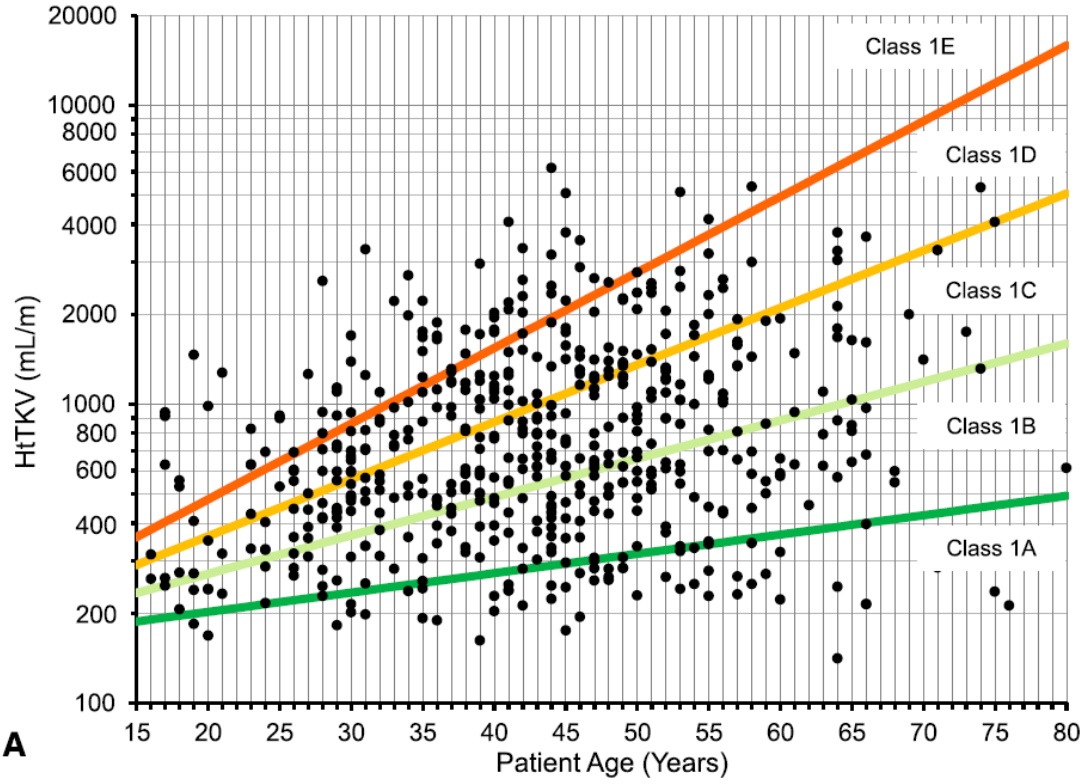
Age (years)	1A*	1B*	1C*	1D*	1E†
15	188	234	290	359	359
16	190	241	303	381	381
17	193	248	317	404	404
18	196	255	331	428	428
19	199	263	346	454	454
20	202	271	362	481	481
21	205	279	378	510	510
22	208	287	395	541	541
23	211	296	413	573	573
24	214	305	431	607	607
25	218	314	451	644	644
26	221	323	471	682	682
27	224	333	492	723	723
28	228	343	514	767	767
29	231	353	538	813	813
30	234	364	562	862	862
31	238	375	587	913	913
32	242	386	613	968	968
33	245	398	641	1026	1026
34	249	410	670	1088	1088
35	253	422	700	1153	1153
36	256	435	732	1222	1222
37	260	448	765	1295	1295

38	264	461	799	1373	1373
39	268	475	835	1456	1456
40	272	489	872	1543	1543
41	276	504	912	1635	1635
42	280	519	953	1734	1734
43	285	535	996	1838	1838
44	289	551	1040	1948	1948
45	293	567	1087	2065	2065
46	298	584	1136	2189	2189
47	302	602	1187	2320	2320
48	307	620	1241	2459	2459
49	311	638	1297	2607	2607
50	316	658	1355	2763	2763
51	321	677	1416	2929	2929
52	325	698	1480	3105	3105
53	330	719	1546	3291	3291
54	335	740	1616	3488	3488
55	340	762	1688	3698	3698
56	345	785	1764	3919	3919
57	350	809	1844	4155	4155
58	356	833	1927	4404	4404
59	361	858	2014	4668	4668
60	366	884	2104	4948	4948
61	372	910	2199	5245	5245
62	378	938	2298	5560	5560
63	383	966	2401	5893	5893
64	389	995	2509	6247	6247
65	395	1024	2622	6622	6622
66	401	1055	2740	7019	7019
67	407	1087	2863	7440	7440
68	413	1119	2992	7887	7887
69	419	1153	3127	8360	8360
70	425	1188	3268	8861	8861
71	432	1223	3415	9393	9393
72	438	1260	3568	9957	9957
73	445	1298	3729	10554	10554
74	451	1337	3897	11187	11187
75	458	1377	4072	11859	11859
76	465	1418	4255	12570	12570
77	472	1461	4447	13324	13324
78	479	1505	4647	14124	14124
79	486	1550	4856	14971	14971

80	494	1596	5075	15869	15869

*Upper limits shown for classes A, B, C and D.
†Minimal values shown for Class 1E

Figure 1: Illustration of Mayo Classification



4 LIST OF TABLES, FIGURES, AND LISTINGS

The list of TLFs and corresponding shells will be presented in a separate document.

5 REFERENCES

1. Caroli A, Perico N, Perna A, et al. Effect of longacting somatostatin analogue on kidney and cyst growth in autosomal dominant polycystic kidney disease (ALADIN): a randomised, placebo-controlled, multicentre trial. *Lancet*. 2013;382(9903):1485-1495.
2. Irazabal MV, Rangel LJ, Bergstralh EJ, et al. Imaging classification of autosomal dominant polycystic kidney disease: a simple model for selecting patients for clinical trials. *J Am Soc Nephrol*. 2015;26(1):160-172. doi:10.1681/ASN.2013101138