Supplemental Material

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[a]*Celeste Lee passed away on February 9, 2017.*

SUPPLEMENTAL MATERIAL

TABLE 1:

Definitions

End point - End point is defined as a study outcome and how it is measured. Endpoints can be primary, secondary, exploratory; binary or continuous; single or composite. All study endpoints should be determined *a priori.*

A. Proportion calculation:

$$\frac{\text{(number of independent accesses with outcome)}}{\text{(number of total accesses that may have outcome during X timeframe)}}$$

The numerator is a subset of the denominator (always between 0 and 1 – or 0 and 100%)
Study example: Proportion of all fistulas created in the study that are patent at the end of study

B. Time to event calculation: The time from study start or index time (e.g. access creation) until occurrence of the outcome, study end or censoring event
Study example: Median time to loss of fistula patency was 8 months or the primary patency of fistulas was 62% at 6 months (reporting depends on survival methods used)

C. Descriptive statistics: For example, mean duration
Study example: The mean duration of fistula patency was 6 years in the study cohort.

D. Duration of Follow Up Calculations: Number of events in a specific number of patients over a fixed duration (patient days, patient months or patient years)
Study Example: The number of catheter related blood stream infections was 1.7 per 1000 patient days

It should be noted that in many of these situations, the access is the unit of evaluation, rather than the patient.

IDBD - The abbreviation IDBD refers to intervention, drug, biologic, device.

Arteriovenous Dialysis Access Circuit – The complete vascular circuit starting with the heart and including the complete feeding artery from its central origin, the arteriovenous dialysis access and the complete venous drainage up to the superior vena cava–right atrial junction, or inferior vena cava-right atrial junction in the case of a lower extremity dialysis access.

Components of the circuit

Inflow: Segment starting with central origin of the artery to 3-4 cms beyond the arteriovenous anastomosis.

Conduit: Needle access segment (NAS)

Peripheral Outflow: Segment beyond the needle access conduit to the origin of central veins.

Central outflow: ipsilateral central vein all the way up to the right heart.

Arteriovenous Dialysis Access Patency – The status (yes/no) of an arteriovenous dialysis access with detectable blood flow through and beyond the anastomosis demonstrated by either an imaging modality or physical examination (presence of a palpable thrill or audible bruit along some point of the arteriovenous dialysis access beyond the arteriovenous anastomosis).

Definitions of Arteriovenous Access Patency Durations – Definitions of AV access patency durations are timeframes that arteriovenous dialysis access are patent (defined above) and can be used for a variety of IDBD studies; thus, it may be necessary that patency be defined either from the time of initial arteriovenous dialysis access creation or from the time of an index intervention, or both, depending upon the nature of the study.

e.g. Duration of a Patent Arteriovenous Dialysis Access: = (Date of intervention/abandonment) – (Date of access creation) = patency duration

e.g. Proportion calculation: $\frac{\text{(\# Patent Accesses)}}{\text{\# Accesses evaluated in study during X timeframe)}}$ = percent patency

Note: Other qualifiers specific for the purposes of a vascular access IDBD study can be used, such as "functional patency" (below)

Physiologically mature AVF access: A physiologically mature access is a patent access that is not in use to provide dialysis but meets objective criteria for blood flow rate, conduit length, depth and diameter as defined *'a priori'* in the study protocol.

Functional Vascular Access - An AV access that can function adequately to provide the prescribed dialysis treatments as defined *a priori* in the study protocol.

Dialysis Vascular Access Abandonment - The act of discontinuing the clinical use of a dialysis vascular access because it is no longer functional and is considered to not be salvageable. An abandoned dialysis access is one that can no longer be used for one or two needle prescribed dialysis because it is unable to provide adequate blood flow and/or is deemed unsafe for the patient, and the associated problem cannot be corrected by any intervention either medical, endovascular or surgical. Possible scenarios are:

- The dialysis access that is not clinically functional (usable for dialysis) and a percutaneous intervention such as angioplasty, thrombolysis, stenting, embolization, or other intervention will not salvage the access in order for it to be clinically functional.
- A reasonable effort has been made to improve the condition of the access so that it can be used and has failed; for example, adequate elevation and time for rest of an infiltrated fistula.
- The access is viable, but there are complications that require the abandonment of the access, e.g., high cardiac output failure or severe dialysis access associated steal syndrome, serious access infection
- A surgical revision will not salvage the access in order for it to be useable for dialysis OR requires simultaneous replacement of 2 or more components (inflow, outflow, conduit) of the circuit.

Intervention Rate - The number of IDBD interventions performed (type to be specified in protocol) upon a dialysis vascular access within a defined time period. For example, the term "intervention rate, post-intervention cumulative patency" would indicate the number of interventions performed during the post-intervention period from index procedure until access abandonment. Additionally, the types of intervention and any complications incurred should be clearly indicated, as per the study protocol.

Target Lesion – A predefined area toward which the IDBD used in the trial was directed. This should be defined *a priori* in the study protocol.

Target Zone - That area within the arteriovenous dialysis access circuit which encompasses the target lesion toward which the IDBD intervention is directed and the adjacent +/- "X" portion of the access. This should be defined *a priori* in the study protocol. *Example - target lesion ± 2 cm.*

Significant Dialysis Access Stenosis – A reduction in the vessel luminal diameter (graft or draining venous system) that is greater than or equal to a 50% reduction in normal vessel diameter (see note below) accompanied by hemodynamic, functional or clinical abnormalities, not explained by reasons other than the dialysis vascular access lesion. In general, the hemodynamic, functional or clinical abnormality should be present for 2 or more dialysis sessions. Example of abnormalities include:

- Significant change in physical examination characteristic of stenosis
- Elevated static venous pressures recorded during dialysis
- Detection of decreased intra-access blood flow at dialysis.
- Swollen extremity, chest, neck, face, breast
- Unexplained reduction in dialysis urea kinetic measurements
- Significant access recirculation

Determining percent stenosis - The method of percent stenosis determination should be clearly defined and specified *a priori* in the study protocol. The "normal" graft or vessel immediately upstream or downstream from the lesion, whichever is smallest, should serve as the reference vessel for this determination and should be clearly reported as such. The degree of stenosis reported should be the maximum observed diameter reduction. For example, with an extended stenotic lesion which has some variation in diameter throughout its length, the minimum diameter present within the lesion should be used for the determination. When possible, follow-up evaluations should use the same reference vessel as the pretreatment evaluation.

In the case of arterial anastomotic stenosis, significant stenosis should be determined by a comparison of the diameter of the anastomosis with the diameter of the adjacent feeding artery. If it is less than 50%, it should be considered to be stenotic when there is an accompanying decrease in the access flow.

Thrombosed Dialysis Vascular Access - An access that contains occlusive thrombus and has no blood flow.

Incomplete Dialysis Vascular Access Thrombosis - An access that contains thrombus that is not occlusive and the access can be demonstrated to have continuing blood flow.

B. Patency defined from the time of arteriovenous dialysis access creation – The following access patency definitions begin from the time of arteriovenous dialysis access creation.

When the creation of an arteriovenous dialysis access is defined *a priori* in the study protocol as a staged procedure with some variable time elapsing between the stages, the planned second procedure is not considered as an intervention for the purposes of determining duration of patency. Patency definitions for the staged access begin on the date that the first stage of the procedure is performed. If an intervention (angioplasty, thrombectomy, revision) is required, other than a planned staged procedure, then that intervention will affect the patency definition of the access.

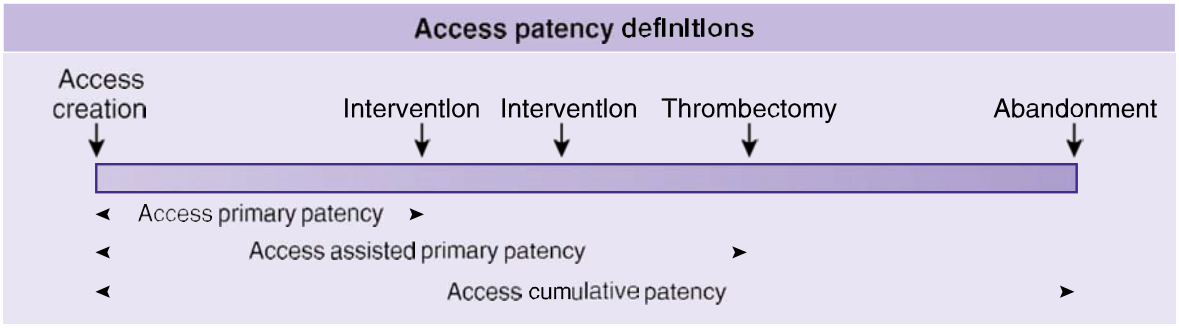

Figure 1. Access patencies from the time of creation

Access primary patency - the time from arteriovenous dialysis access creation until the first of one of the following events: access thrombosis, any intervention designed to facilitate, maintain or reestablish patency, the access reaches a censoring event as specified *a priori* in the study protocol, or study end.

Access assisted primary patency – Term used to describe an access that needed assistance to maintain continued patency (Fig. 1) during the study period. It is calculated as the time from arteriovenous dialysis access creation until the first of one of the following events: access thrombosis, the access reaches a censoring event as specified *a priori* in the study protocol, or study end. This period includes all intervening interventions (surgical or endovascular) designed to maintain the functionality of the dialysis vascular access as long as patency is not lost.

Access cumulative patency - the time from arteriovenous dialysis access creation until access abandonment, or the access reaches a censoring event as specified *a priori* in the study protocol, or study end, including intervening manipulations (surgical or endovascular interventions) designed to maintain the functionality of the access. The term secondary patency has also been used in this context; however, this term has been misused in the literature which makes it confusing. Hence it is not used in this document.

C. Patency defined from the time of an index intervention – this may relate to the dialysis access circuit, the target zone, or both as defined *a priori* in the study protocol (fig. 2)

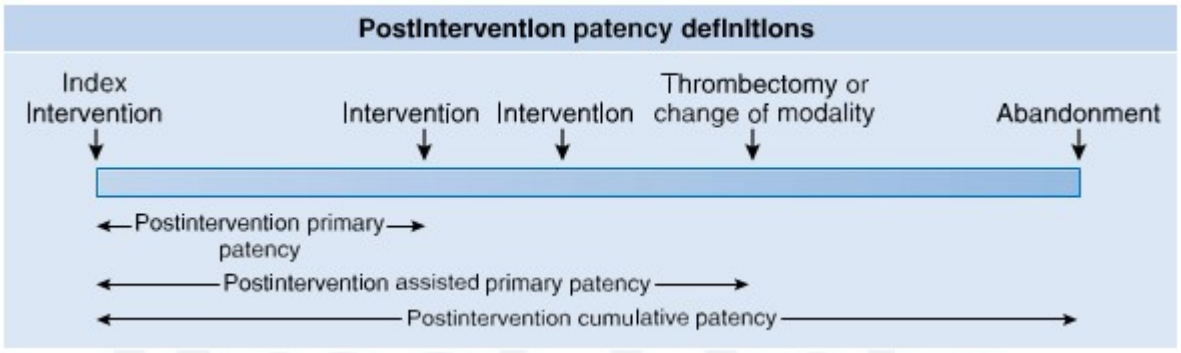

Figure 2. Post intervention access patencies

Post-intervention primary patency - the time from the index IDBD until the first of one of the following events: access thrombosis, any intervention designed to facilitate, maintain or reestablish patency, the access reaches a censoring event as specified *a priori* in the study protocol, or study end.

Post-intervention assisted primary patency - Term used to describe an access that needed assistance to maintain continued patency during the study period. It is calculated as the time from the index IDBD intervention until the first of one of the following events: access thrombosis or until a surgical intervention that excludes the treated lesion from the dialysis access circuit, or the patient reaches a censored event as

defined *a priori* in the study protocol. This period includes all intervening interventions (surgical or endovascular) designed to maintain the functionality of dialysis vascular access.

Post-intervention Cumulative Patency - the time from the index IDBD intervention until the access is abandoned including intervening manipulations (surgical or endovascular interventions) designed to maintain the functionality of a patent access, the patient reaches a censoring event as defined *a priori* in the study protocol, or study end. The term secondary patency has also been used in this context; however, this term has been misused in the literature which makes it confusing. It is recommended that it not be used.