Summary of Statistical Analysis Plan for MYTHIC Study

[Draft: April 26, 2020]

Part	Patient Group(s)	Outcome	Statistical Analysis[a]
1	Arm 1 (ITT)	SVR12	- estimated probability of SVR12 and 95% confidence interval (CI) - exact binomial calculations
2	Arm 1 (ITT)	Virologic failure (VF)	- estimated probability of SVR12 and 95% confidence interval (CI) - exact binomial calculations
3	Arm 1 (ITT)	Post-treatment virologic relapse	- estimated probability of SVR12 and 95% confidence interval (CI) - exact binomial calculations
4	All patients	HCV-viremic kidney transplant (KT); i.e., Arm 1 KT	- cumulative incidence and 95% CI - death and other KT types treated as competing risk - estimate non-parametrically, using Lin (1997) which proceeds through the cause-specific hazards, or Fan (2013) which uses Inverse Probability of Censoring Weighting (IPCW).
5	All patients	Non-HCV-viremic KT; i.e., Arm 2A-2B KT	- same as for component (4).
6	All, by Arm	Hospital admissions	- Arm treated as a time-dependent treatment - crude hospitalization rate per 100 patient-years (PY) and 95% CI - use robust variance estimator, to account for correlation among hospital admissions within-patient
7	All, by Arm	Hospital admissions	- Arm treated as a time-dependent treatment - proportional rates model (Lin et al., 2000) - robust SEs, to account for clustering within-patient
8(a)	All, and SRTR* controls	Kidney transplant	- exclude, from SRTR, all patients who indicated consent to receive an HCV-viremic KT (hereafter: SRTR*) - estimate prognostic score using SRTR* patients: KT as event - 1:5 matching (MYTHIC : SRTR*) based on prognostic score with caliper - Cox regression, with MYTHIC as lone covariate, stratified by matched set

8(b)	All, and SRTR* controls	Kidney transplant	Same as 9(a), but using exact matching on small set of predictors, with prognostic score used to break ties among potential matches
9	Arm 1 – ITT	Compliance	Treated as repeated binary (0/1) data, with 1 indicating compliance (i.e., having taken 80-120% of prescribed pills)
10	Arm 1 – ITT	Death	Time to event; Cox regression
11	Arm 1 – ITT	Graft failure	Time to event; Cox regression
12	Arm 1	Delayed graft function	DGF: binary (0/1) response. Compute OBS/EXP, where OBS=observed number of DGFs for Arm 1 and EXP= expected count based on logistic regression model fitted to HCV-negative UNOS patients from large academic centers
13	Arm 1	Acute allograft rejection	AAR: Binary (0/1) response. Compute OBS/EXP, where OBS=observed number of AARs for Arm 1 and EXP= expected cunt based on logistic regression model fitted to HCV-negative UNOS patients from large academic centers
14	Arm 1	ALT elevation	Binary (0/1), with '1' corresponding to peak ALT > 5 x ULN, where ULN=upper limit of 'normal'.
15	All, by arm	Serious Adverse Event	SAE: recurrent event Arm treated as a time-dependent factor Proportional rates model, robust SEs to account for within-patient clustering
16	Arm 1, 2AB	eGFR	Repeated continuous response Linear mixed model, to account for clustering by patient
17	Arm 1, 2AB	Proteinuria	Binary response; logistic regression
18	Arm 1, 2AB	BK virus	Binary response; logistic regression

Notes:

a) Each of the above-listed analyses will be accompanied by appropriate summary statistics (e.g., mean, median, IQR, etc).