ISCHEMIA Schedule of Study Assessments and Procedures

	Screening visit	CCTA visit	Randomization visit (Baseline)	Catheterization & PCI or CABG	Follow up								
					1.5m[A] Visit 1	3m[A] Visit 2	6m[B] Visit 3	12m[A] Visit 4	18m[B] Visit 5	24m Visit 6	30m[B] Visit 7	36m[C] Visit 8	Frequency beyond 36 months
Eligibility screen	X												
Informed consent (including biorepository consent if applicable)	X												
Creatinine and pregnancy test[D]	X												
Medical History/Medical Status	X		X		X	X	X	X	X	X	X	X	Q6m
Cardiovascular medications	X		X		X	X	X	X	X	X	X	X	Q6m
Transmit Stress Test to Core Lab[E]	X												
NYHA* and CCS class**	X		X		X	X	X	X	X	X	X	X	Q6m
Release for medical records signed			X					X		X		X	Q12m
Coronary CT Angiography (CCTA)		X[F]											
Safety assessment[G]		X		X									
Vital signs, weight, height[H]			X		X	X	X	X	X	X	X	X	Q12m
Standard lab results[I]			X[J]			X	X	X	X	X	X	X	Q12m
Biorepository blood draw			X			X[K]							
Cardiac biomarkers[L]				X									
Electrocardiogram (ECG) [M]			X	X[N]				X		X			@ closeout
Lifestyle Assessment (PACE)***			X			X		X		X		X	Q12m
Lifestyle Counseling (PACE)***			X		X	X	X	X	X	X	X	X	Q6m
Morisky Green Levine Medication Adherence			X				X	X	X	X	X	X	Q6m
Full Quality of Life (QOL) assessment [O]			X[P]			X		X		X		X	@ closeout
Brief symptoms/QOL assessment[Q]			X		X	X	X	X	X	X	X	X	Q6m
Initiate Optimal Medical Therapy (OMT)			X										
Medical Therapy Evaluation and Optimization[R]					X	X	X	X	X	X	X	X	Q6m
Schedule catheterization for INV participants[S]			X										
Hospitalization assessment					X	X	X	X	X	X	X	X	Q6m
Endpoint assessment				X	X	X	X	X	X	X	X	X	Q6m

Follow-up visits will be scheduled based on time since the date of randomization (baseline).

Online Table S6. Schedule of Study Assessments and Procedures

*NYHA- New York Heart Association **CCS- Canadian Cardiovascular Society ***PACE- Patient-centered Assessment and Counseling for Exercise and nutrition (PACE) assessment and counseling

---

[A] 1.5, 3, and 12 month visits should be in clinic visits, depending on participant stability, risk factor control, and geography.

[B] 6, 18, and 30 month visits may be via telephone, email, or in clinic depending on participant stability, risk factor control, and geography.

[C] Following the 36 month visit, follow-up visits should be in clinic visits at least every 12 months. Clinic visits can be replaced by email or phone depending on participant stability, risk factor control, and geography.

[D] Creatinine if not done within 90 days and pregnancy test if premenopausal.

[E] Send ischemia test images (immediately following enrollment and before randomization), technical worksheets, and site interpretations/local reports from qualifying ischemia tests to core labs.

[F] CCTA not performed if estimated glomerular filtration rate < 60ml/min (unless requested by the treating physician) and not performed in other selected participants (see sections 4.1 and 5.5 and MOO); Blinded CCTA images and technical worksheets will be transferred to CCTA core lab for interpretation.

[G] Safety Assessment (refer to section 13.4).

[H] Height is only needed at randomization, assessments only required if visit is completed in clinic.

[I] Required labs include: lipids (preferably fasting) at 3 month visit then semiannually only, and HbA1c (at visit 4, 6, 8 and annually thereafter for diabetic participants. These lab results will be requested from the participant's physician. If these results are not available they should be obtained by either the participant's treating physician or study staff. Creatinine values obtained clinically for participants with eGFR <60 at the three month follow-up visit and annually will also be recorded.

[J] Additional lab required at randomization includes complete blood count Request from participant's physician, since it is expected that routine blood work will have been done within the last 6 months

[K] May be requested.

[L] For participants undergoing PCI: troponin and CK-MB pre-procedure and at 8-16 ± 2 hours post-PCI or at hospital discharge, whichever comes earlier. For participants undergoing CABG: troponin and CK-MB pre-procedure and at 18 ± 6 hours post-CABG. All biomarker measurements should be recorded on eCRF. A biomarker measurement should be obtained before and after all PCI and CABG procedures, whenever possible.

[M] Send to ECG core lab; ECG required for all cardiac admissions and revascularizations; year 1 ECG optional (filed on site) and closeout.

[N] ECG done following procedure (60±30 mins post-PCI, 3 days post-CABG).

[O] Seattle Angina Questionnaire/Duke Activity Status Index/Rand general health status item/Perceived Stress Scale/Patient Health Questionnaire/Life Orientation Test – Revised/EQ-5D/Demographic characteristics. Not required for the ISCHEMIA CKD ancillary trial.

[P] Sites may choose to obtain the baseline QOL at the time of the CCTA visit. The baseline QOL must be collected before reporting the assigned treatment strategy to participants.

[Q] Selected Seattle Angina Questionnaire/Rose dyspnea scale/EQ-5D

[R] At every follow-up visit the research team, in collaboration with the treating physician(s), will evaluate effectiveness of medical therapy and optimize as needed according to guideline recommendations and study algorithms.

[S] Planned cath and revascularization only in the INV group. See MOO for time windows for performing cath and revascularization after randomization. Catheterization and optimal revascularization treatment should be targeted within 30 days after randomization in the Invasive strategy group. In the Conservative group, catheterization and optimal revascularization is reserved for participants with refractory angina symptoms or acute ischemic events.