CLINICAL RESEARCH IN INFECTIOUS DISEASES

STATISTICAL ANALYSIS PLAN
for
DMID Protocol: 20-0013
Study Title:
A Multicenter Platform Trial of Putative Therapeutics for the Treatment of COVID-19 in Hospitalized Adults: ACTIV-5
APPENDIX 7 BET-C:
Danicopan/Standard of Care vs. Placebo/Standard of Care

NCT04988035

Version 1.0

DATE: 24-JAN-2022

STUDY TITLE

Protocol Number Code:	**DMID Protocol: 20-0013**
Development Phase:	Phase 2
Products:	Danicopan + Standard of Care Placebo + Standard of Care
Form/Route:	Danicopan/Placebo: oral Remdesivir: IV Other standard of care: form and route will vary depending on type of standard of care administered
Indication Studied:	COVID-19
Sponsor:	Division of Microbiology and Infectious Diseases National Institute of Allergy and Infectious Diseases National Institutes of Health
Clinical Trial Initiation Date:	July 21, 2021
Clinical Trial Estimated Completion Date:	TBD
Date of the Analysis Plan:	January 24, 2022
Version Number:	1.0

This study was performed in compliance with Good Clinical Practice.

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LIST OF ABBREVIATIONS

ACTIV	Accelerating COVID-19 Therapeutic Interventions and Vaccines
ACTT	Adaptive COVID-19 Treatment Trial
AE	Adverse Event
ALT	Alanine Aminotransferase
AST	Aspartate Aminotransferase
ATC	Anatomical Therapeutic Chemical
BET	Big Effect Trial
BLOQ	Below the Limit of Quantitation
CI	Confidence Interval
Cm	Centimeters
CoV	Coronavirus
COVID-19	Coronavirus Disease 2019
CP	Conditional Power
CRF	Case Report Form
CRP	C-Reactive Protein
CSR	Clinical Study Report
HLT	High-Level Term
DAIDS	Division of AIDS
DMID	Division of Microbiology and Infectious Diseases
DSMB	Data and Safety Monitoring Board
ECMO	Extracorporeal Membrane Oxygenation
eCRF	Electronic Case Report Form
eGRF	Estimated Glomerular Filtration Rate
Hgb	Hemoglobin
INR	International Normalized Ratio
ITT	Intent-to-Treat
JAK	Janus kinase
Kg	Kilograms
KM	Kaplan Meier
LLOD	Lower Limit of Detection
LLOQ	Lower Limit of Quantification
MedDRA	Medical Dictionary for Regulatory Activities
mL	Milliliter
N	Number (typically refers to subjects)
NAAT	Nucleic Acid Amplification Test
NEWS	National Early Warning Score
NIAID	National Institute of Allergy and Infectious Diseases

List of Abbreviations *(continued)*

NIH	National Institutes of Health
OP	Oropharyngeal
OR	Odds Ratio
PAP	Pulmonary Alveolar Proteinosis
PBMC	Peripheral Blood Mononuclear Cells
PCR	Polymerase Chain Reaction
PK	Pharmacokinetic
PLT	Platelet
PT	Preferred Term
Q1	First Quartile
Q3	Third Quartile
RR	Respiratory Rate
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SARS	Severe Acute Respiratory Syndrome
SARS-CoV-2	Severe Acute Respiratory Syndrome Coronavirus 2
SD	Standard Deviation
SOC	System Organ Class
SpO2	Blood Oxygen Saturation
TEAE	Treatment-Emergent Adverse Events
TFL	Tables, Figures, and Listings
TNF	Tumor Necrosis Factor
ULOQ	Upper Limit of Quantification
US	United States
WBC	White Blood Cell
WHO	World Health Organization

1. PREFACE

Refer to the master SAP.

2. INTRODUCTION

2.1. Purpose of the Analyses

This Statistical Analysis Plan (SAP) encompasses all analyses for endpoints that are specific to the BET-C study only. Details for the BET-C futility analysis are also included. Details of the rest of the secondary and some exploratory endpoints are covered in the master SAP. Details regarding PK and virology exploratory endpoints will be covered in separate SAPs.

3. STUDY OBJECTIVES AND ENDPOINTS

3.1. Study Objectives

3.1.1. Primary Objectives

Refer to Section 3.1. of master SAP for details regarding the primary objective.

3.1.2. Secondary Objectives

3.1.2.1. Key Secondary Objectives and Other Secondary and Exploratory Objective(s)

Refer to Section 3.1.2 and Section 3.1.3 of the master SAP for a list of secondary and exploratory objectives for this study.

3.1.2.2. Stage Specific Objective(s)

1. To evaluate Patient Reported Outcomes.
2. To evaluate danicopan pharmacokinetics (PK) and pharmacodynamics (PD) in selected subjects with COVID-19 at selected sites.

Details regarding this exploratory PK endpoint will be covered in a separate SAP addendum.

3.2. Endpoints

3.2.1. Primary Endpoint

Refer to Section 3.2.1 of the Master SAP for details regarding the primary endpoint.

3.2.2. Secondary and Exploratory Endpoints

Refer to Section 3.2.2 and Section 3.2.3 of the Master SAP for details regarding the secondary and exploratory endpoints.

3.2.3. Stage Specific Exploratory Endpoint (s)

1. SF-12 PCS and MCS scores at Day 29 and Day 60.
2. Incidence of progression to renal failure requiring dialysis at Day 29.

The SF-12 is a validated health-related quality of life (HR-QoL) instrument that is widely used across a broad spectrum of disease indications. Adapted from the 36-item SF survey that was designed to evaluate physical and mental health status, the SF-12 survey contains only 12 questions but covers the same 8 domains. There is a further stratification into 2 summary measures (Physical Component Summary (PCS) and Mental Component Summary (MCS)) as specified:

i. PCS:

1. General health (1 item)
2. Physical functioning (2 items)
3. Role physical (2 items)
4. Body pain (1 item)

ii. MCS

1. Vitality (1 item)
2. Social functioning (1 item)
3. Role emotional (2 items)
4. Mental health (2 items)

The PCS and MCS summary measures are scored using a norm-based method (i.e., mean = 5-, SD = 10)[1]. A PCS or MCS score of 50 indicates an average score with respect to a healthy population. Scores lower than 50 reflect less than average health and scores greater than 50 reflect better than average health [2]. This scoring will be performed using the Qualitymetric software. Scores will be produced for each of the 8 domains along with overall scores for the physical and mental health components. The SF-12 assumes a recall of 1 week before responding to questions. The survey is anticipated to be completed in several minutes and can be completed by the subject or via an interviewer (in-person or over the phone). This form will not be monitored. If it is not completed by the subject, it will not be considered a protocol deviation.

Details regarding the stage-specific PK endpoint will be covered in a separate SAP addendum.

3.3. Study Definitions and Derived Variables

Refer to the master SAP for the definition of study day, analysis visit windows, and laboratory sample collection study day windows.

4. INVESTIGATIONAL PLAN

4.1. Overall Study Design and Plan

See Section 4.1 of the master SAP.

4.2. Discussion of Study Design, Including the Choice of Control Groups

See Section 4.2 of the master SAP.

4.3. Selection of Study Population

Approximately 200 (100 Danicopan + standard of care and 100 shared placebo) male and non-pregnant female adults ≥18 years of age or older with COVID-19 and who meet all eligibility criteria will be enrolled at up to 70 domestic sites and 5 international sites. The target population should reflect the community at large. The estimated time from screening (Day -1 or Day 1) to end of study for an individual subject is approximately 60 days.

4.4. Treatments

4.4.1. Treatments Administered

All subjects will receive remdesivir as a 200 mg intravenous (IV) loading dose on Day 1, followed by a 100-mg once-daily IV maintenance dose during hospitalization up to a maximum of 10 total doses (i.e., loading + maintenance doses received during study and pre-study if applicable). The duration of dosing may be adjusted by the site similar to what is described in the product label and based on a subject's clinical course and ultimate disease severity. Any dose of remdesivir that is delayed may be given later that calendar day. Any dose of remdesivir that is missed (not given that calendar day) is not made up. The treatment course continues as described above even if the subject becomes PCR negative.

In addition to receiving remdesivir, subjects in the BET-C trial will be randomized to receive danicopan or placebo as follows:

- ≥70 years of age: 300 mg oral (or via nasogastric [NG] or gastrostomy [G] tube) loading dose on Day 1, followed by 200 mg 4 times daily (QID) during hospitalization up to a maximum of 14 days.
    - At the end of the treatment course (discharge or 14 days, whichever comes first), treatment will be tapered as followed: 200 mg 3 times daily (TID) for 2 days, followed by 200 mg twice daily (BID) for 2 days, until complete cessation (total treatment duration up to 18 days or 4 days after discharge).
- <70 years of age: 400 mg oral (or via NG or G tube) loading dose on Day 1, followed by 250 mg QID during hospitalization up to a maximum of 14 days.
    - At the end of the treatment course (discharge or 14 days, whichever comes first), treatment will be tapered as followed: 250 mg TID for 2 days, followed by 250 mg BID for 2 days, until complete cessation (total treatment duration up to 18 days or 4 days after discharge).

4.4.2. Identity of Investigational Product(s)

Refer to Section 6.1.1 of the Appendix B - BET-C protocol.

4.4.3. Method of Assigning Subjects to Treatment Groups (Randomization)

See Section 4.4.3 of the master SAP.

4.4.4. Selection of Doses in the Study

The dose of remdesivir used in this stage will be the same dose shown to be efficacious in the ACTT-1 clinical trial and is the dose approved by the US FDA. The duration of dosing may be adjusted by the site according to clinical severity. The maximum number of doses to be given during hospitalization is ten doses. This includes the loading dose and all maintenance doses given during the study and pre-study if applicable.

For danicopan, the dosing strategy of 300 mg loading dose followed by 200 mg QID dose is proposed for age ≥ 70 years old, and the 400 mg loading dose followed by 250 mg QID dose is proposed for age < 70 years old was chosen for this study based on the simulation results. Plasma PK exposures for these proposed doses are predicted to achieve ≥90% FD inhibition in the majority of subjects during the entire dose interval. Considering the overall safety profile of danicopan and the transient nature of liver enzymes elevation observed in the clinical program thus far, coupled with the laboratory monitoring schedule in this study, these doses provide the optimal benefit to risk balance.

4.4.5. Selection and Timing of Dose for Each Subject

Remdesivir will be administered as a 200 mg intravenous (IV) loading dose on Day 1, followed by a 100-mg once-daily IV maintenance dose during hospitalization up to a maximum of 10 total doses.

For danicopan,

- ≥70 years of age: 300 mg oral loading dose on Day 1, followed by 200 mg 4 times daily during hospitalization up to a maximum of 14 days.
- <70 years of age: 400 mg oral loading dose on Day 1, followed by 250 mg 4 times daily during hospitalization up to a maximum of 14 days.

4.4.6. Blinding

See Section 4.4.6 of the master SAP.

4.4.7. Prior and Concomitant Therapy

Steroids and other concomitant therapies intended as specific treatment of COVID-19, as well as all biologics, will be assessed from 7 days prior to enrollment to Day 29. All other concomitant medications will be assessed from 7 days prior to enrollment to Day 15 or upon discharge, whichever comes first.

4.4.8. Treatment Compliance

Each dose of study product will be administered by a blinded member of the clinical research team who is qualified and licensed to administer the study product. Administration date and time, and whether any doses were slowed, halted or missed will be entered into the case report form (CRF).

4.5. Efficacy and Safety Variables

See Table 1 for schedule of study procedures. See Section 4.5 of the master SAP for additional details regarding efficacy and safety variables.

5. SAMPLE SIZE CONSIDERATIONS

Refer to Section 5 of the master SAP.

6. GENERAL STATISTICAL CONSIDERATIONS

6.1. General Principles

Refer to Section 6.1 of the master SAP

6.2. Timing of Analyses

See Section 6.2.1 of the master SAP.

6.3. Analysis Populations

See Section 6.3 of the master SAP.

6.4. Covariates and Subgroups

See Section 6.4 of the master SAP.

6.5. Missing Data

See Section 6.5 of the master SAP.

6.6. Interim Analyses and Data Monitoring

Refer to Section 6.2.1 for details of the interim analyses for efficacy and futility.

6.7. Multicenter Studies

Refer to Section 6.7 of the master SAP.

6.8. Multiple Comparisons/Multiplicity

Refer to Section 6.8 of the master SAP.

7. STUDY SUBJECTS

7.1. Disposition of Subjects

Refer to Section 7.1 of the master SAP.

7.2. Protocol Deviations

Refer to Section 7.2 of the master SAP.

8. EFFICACY EVALUATION

8.1. Primary Efficacy Analysis

Refer to Section 8.1 of the master SAP for details regarding the primary analysis. Because of the background use of prophylactic antibiotics specific to this protocol, a supportive analysis will be performed by repeating the primary analysis to those subjects randomized to BET-C excluding any shared controls.

8.2. Secondary Efficacy Analyses

Refer to Section 8.1 of the master SAP.

8.3. Exploratory Efficacy Analyses

Refer to Section 8.3 of the master SAP for details regarding exploratory endpoints.

8.4. Stage Specific Exploratory Efficacy Analyses

8.4.1. SF-12 PCS and MCS Scores at Day 29 and Day 60

Functional scores of health and well-being include the MCS and PCS scores from the SF-12 health survey as described in Section 3.2.3. Results from the SF-12v2 health survey will be scored using Qualitymetric software to obtain MCS and PCS scores. No imputation will be performed for missing data, analyses will be based on observed non-missing data.

Summary statistics (mean, median, and quartiles) will be presented by treatment group (Table 2). P-value from Wilcoxon rank sum test will also be provided .

9. SAFETY EVALUATION

9.1. Demographic and Other Baseline Characteristics

Refer to Section 9.1 of the master SAP.

9.2. Measurements of Treatment Compliance

Refer to Section 9.2 of the master SAP.

9.3. Adverse Events

Refer to Section 9.3 of the master SAP regarding analysis of adverse events.

9.4. Deaths, Serious Adverse Events and other Significant Adverse Events

Refer to Section 9.4 of the master SAP.A summary of subjects who progressed to renal failure requiring dialysis at Day 29 is provided in Table 3. Renal failure events will be defined based on all Grade 4 renal failure adverse events. The number and proportion of subjects who progressed with 95% CI estimated using Blaker method are reported. A risk difference and 95% CI estimated using the Miettinen-Nurminen method is also provided.

9.5. Pregnancies

Refer to Section 9.5 of the master SAP.

9.6. Clinical Laboratory Evaluations

Refer to Section 9.6 of the master SAP.

9.7. Vital Signs and Physical Evaluations

Refer to Section 9.7 of the master SAP.

9.8. Concomitant Medications

Refer to Section 9.8 of the master SAP.

9.9. Other Safety Measures

No additional safety analyses are planned.

10. PHARMACOKINETICS

Details for PK analysis will be provided in a separate SAP.

11. IMMUNOGENICITY

Not Applicable.

12. OTHER ANALYSES

Not Applicable.

13. REPORTING CONVENTIONS

P-values ≥0.001 and ≤0.999 will be reported to 3 decimal places; p-values less than 0.0005 will be reported as "<0.001" and p-values greater than 0.9995 will be reported as ">0.999".

The mean, confidence intervals, median, IQR, and other statistics will be reported to 1 decimal place greater than the original data. The minimum and maximum will use the same number of decimal places as the original data.

Proportions will be presented as 2 decimal places; values greater than zero but <0.01 will be presented as "<0.01". Percentages will be reported to the nearest whole number; values greater than 0.5% but < 1% will be presented as "<1"; values greater than 99.5% but less than 100% will be reported as ">99".

For all other estimators, the NEJM statistical reporting guidelines will be followed: results will be presented with no more precision than is of scientific value and is meaningful. For example, measures of association, such as odds ratios, will be reported to two or three significant digits. Results derived from models will be limited to the appropriate number of significant digits.

14. TECHNICAL DETAILS

SAS version 9.4 or above, or R language and environment for statistical computing 3.6.1 or above, will be used to generate all tables, figures and listings.

15. SUMMARY OF CHANGES IN THE CONDUCT OF THE STUDY OR PLANNED ANALYSES

This is the first version of the BET-C SAP. There have been no changes in the planned analyses.

16. REFERENCES

1. Jenkinson C, Layte R, Jenkinson D, Lawrence K, Petersen S, Paice C, et al. A shorter form health survey: can the SF-12 replicate results from the SF-36 in longitudinal studies? *J Public Health Med*. 1997;19(2):179-86.
2. Ware J, Jr., Kosinski M, Keller SD. A 12-Item Short-Form Health Survey: construction of scales and preliminary tests of reliability and validity. Med Care. 1996;34(3):220-33.

17. LISTING OF TABLES, FIGURES, AND LISTINGS

Table, figure, and listing shells are presented in Appendices 1, 2, and 3.

APPENDICES

The tables and figures listed below are those that are specific to BET-C study. The rest of the tables will come from the master SAP. In all TFLs, Treatment A will be replaced by Danicopan + SOC and Treatment B will be replaced by Placebo + SOC.

APPENDIX 1. TABLE MOCK-UPS

LIST OF TABLES

9.5.1 Efficacy/Immunogenicity and Safety Measurements Assessed and Flow Chart

Table 1: Schedule of Study Procedures

	Screen	*Baseline*	*Study Intervention Period*	*Follow-up Visits*				
Day +/- Window	**−1 or 1**	**1**[1]	**Daily until hospital discharge (up to Day 29)**	**8**[3] **±2**	**15**[2] **± 2**	**22**[3] **± 3**	**29**[2] **± 3**	**60**[3] **± 3**
ELIGIBILITY								
Informed consent	X							
Demographics & Medical History	X							
Targeted physical exam	X							
Review SARS-CoV-2 results	X							
STUDY INTERVENTION								
Randomization		X						
Administration of investigational agent		Danicopan or placebo (see dosing above)						
Administration of prophylactic antibiotics		Prophylactic antibiotics (see Section 2.3.3 of the BET-C protocol)						
STUDY PROCEDURES								
Vital signs[4]		X[5]			X[2]		X[2]	
Clinical data collection[6]		X[5]	Daily until discharge	X	X	X	X	X[7]
Adverse event evaluation		X[5]	Daily until discharge	X	X	X	X	X
Concomitant medication review[8]		X[5]	Day -7 until discharge or Day 15	X	X	X	X	
SF-12							X	X
SAFETY LABORATORY								
Safety hematology, chemistry, and liver tests	X[9]	X[5,10,11]	Day 3, 5, 8, 11 (all ± 1 day) if hospitalized[10,11]		X[10]		X[10]	
Pregnancy test for females of childbearing potential	X[9]							
RESEARCH LABORATORY [12]								
Blood draw for serum and plasma		X	Day 3, 5, 8, 11 (all ± 1 day) if hospitalized		X		X	
Blood for RNA		X	Day 3, 8 (all ± 1 day) if hospitalized		X		X	
AT SELECTED SITES ONLY								
Danicopan pharmacokinetics and pharmacodynamics [13]		*X*	*Day 1: pre-dose prior to 1st and 2nd dose* *Day 3: pre-dose prior to 9th dose, 2hr, 4hr & 6hr post-9th dose (Day 3 samples may be collected before and after a subsequent dose while hospitalized)*		*X*		*X*	
Blood for PBMC[14]		*X*	*Day 3, 8 (all ± 1 day) if hospitalized*		*X*		*X*	

Notes:
[1] Day 1 is defined as the calendar day of randomization.

[2] In-person visits are preferred but recognizing quarantine and other factors may limit the subject's ability to return to the site for the visit. In this case, the visit may be performed by phone.

- *If still hospitalized at Days 15 and 29 or returns to the site for an in-person visit: assess adverse events, collect clinical data, vital signs, safety laboratory tests, and research laboratory samples (blood) as able.*
- *If phone call only on Days 15 and 29 and all Day 22 and Day 60 visits: assess adverse events, clinical status (ordinal scale), readmission to a hospital, and mortality only.*

[3] Day 8, 22 and Day 60 visits performed by phone if discharged from the site hospital.
[4] Vital signs include temperature, systolic blood pressure, heart rate, respiratory rate, O2 saturation and level of consciousness. In addition, height and weight are obtained only at baseline (height can be self-reported). Vital signs collected as part of standard care may be used.
[5] Baseline assessments should be performed prior to first drug administration. Laboratory tests performed as part of routine clinical care in the 24 hours prior to first dose will be accepted for the baseline safety laboratory tests. Baseline may be the same as the screening laboratory tests if obtained in the 24 hours prior to first dose.
[6] Refer to Section 8.1 of the protocol for details of clinical data to be collected including ordinal score, oxygen requirement, mechanical ventilator requirement, etc.
[7] Ordinal score only.
[8] Remdesivir, steroids and other therapies of COVID-19 will be assessed from 7 days prior to enrollment to enrollment. Then, all other concomitant medications (except those noted in 6.5.1) will be assessed from 7 days prior to enrollment to discharge or Day 15, whichever comes first. Antibiotics that will provide prophylaxis against meningococcal infections will be assessed until the end of the prescribed course.
[9] Screening laboratory tests include: ALT, AST, creatinine (and calculate an estimated glomerular filtration rate [eGFR] - the formula used is determined by the sites, but should be consistent throughout the study), and urine or serum pregnancy test for females of child-bearing potential. Laboratory tests performed as part of routine clinical care in the 48 hours prior to enrollment will be accepted for determination of eligibility.
[10] Safety laboratory tests include WBC count, differential, hemoglobin, platelet count, creatinine, total bilirubin, ALT, AST, INR, ferritin, fibrinogen, LDH, D-dimer, and C-reactive protein (CRP). Note: D-dimer and CRP values may predict severity and support assessment of outcomes and unlike other safety laboratory values, D-dimer and CRP should not be graded.
[11] Any laboratory tests performed as part of routine clinical care within the specified visit window can be used for safety laboratory testing.
[12] Blood draws for research labs may be omitted on any given study day if inappropriate for a subject's clinical status per site investigator judgment. In some instances, it may not be possible to collect blood for research laboratory investigations due to logistical reasons such as weekends or holidays or lack of necessary supplies. This will not constitute a deviation from the protocol.
[13] A convenience sample of approximately 20 subjects included in this study will be involved in a PK/PD analysis to confirm the dosing regimen. Only selected sites will participate in this collection.
[14] Only collected at selected sites capable of collecting PBMC.

Table 2: Summary Statistics for SF-12 PCS and MCS Results on Day 29 and Day 60 – mITT Population

Time Point	Baseline Ordinal Score	Danicopan + SOC (N=X)					Placebo + SOC					P-value[a]
		n	Mean	Q1	Median	Q3	n	Mean	Q1	Median	Q3	
Mental Component Summary												
Day 29	Baseline Ordinal Score 5	x	xx.x	xx	xx	xx	x	xx.x	xx	xx	xx	
	Baseline Ordinal Score 6	x	xx.x	xx	xx	xx	x	xx.x	xx	xx	xx	
	Baseline Ordinal Score 7	x	xx.x	xx	xx	xx	x	xx.x	xx	xx	xx	
	Any Baseline Ordinal Score	x	xx.x	xx	xx	xx	x	xx.x	xx	xx	xx	x.xxx
Day 60	Baseline Ordinal Score 5	x	xx.x	xx	xx	xx	x	xx.x	xx	xx	xx	
	Baseline Ordinal Score 6	x	xx.x	xx	xx	xx	x	xx.x	xx	xx	xx	
	Baseline Ordinal Score 7	x	xx.x	xx	xx	xx	x	xx.x	xx	xx	xx	
	Any Baseline Ordinal Score	x	xx.x	xx	xx	xx	x	xx.x	xx	xx	xx	x.xxx
Physical Component Summary												
Day 29	Baseline Ordinal Score 5	x	xx.x	xx	xx	xx	x	xx.x	xx	xx	xx	
	Baseline Ordinal Score 6	x	xx.x	xx	xx	xx	x	xx.x	xx	xx	xx	
	Baseline Ordinal Score 7	x	xx.x	xx	xx	xx	x	xx.x	xx	xx	xx	
	Any Baseline Ordinal Score	x	xx.x	xx	xx	xx	x	xx.x	xx	xx	xx	x.xxx
Day 60	Baseline Ordinal Score 5	x	xx.x	xx	xx	xx	x	xx.x	xx	xx	xx	
	Baseline Ordinal Score 6	x	xx.x	xx	xx	xx	x	xx.x	xx	xx	xx	
	Baseline Ordinal Score 7	x	xx.x	xx	xx	xx	x	xx.x	xx	xx	xx	
	Any Baseline Ordinal Score	x	xx.x	xx	xx	xx	x	xx.x	xx	xx	xx	x.xxx

N = Number of subjects in the mITT population.
n = Number of subjects with non-missing SF-12 score data.
[a] P-value calculated using Wilcoxon rank-sum test.

Table 3: Incidence of Progression to Renal Failure Requiring Dialysis at Day 29– Safety Population

Actual Baseline Ordinal Score	Treatment	Number of Subjects Progressed to Renal Failure[a]			Risk Difference	
		n	%	95% CI	Estimate	95% CI[b]
Baseline Ordinal Score 5	Danicopan + SOC (N=X)	x	x	x.x, x.x	x	x.x, x.x
	Placebo + SOC (N=X)	x	x	x.x, x.x		
Baseline Ordinal Score 6	Danicopan + SOC (N=X)	x	x	x.x, x.x	x	x.x, x.x
	Placebo + SOC (N=X)	x	x	x.x, x.x		
Baseline Ordinal Score 7	Danicopan + SOC (N=X)	x	x	x.x, x.x	x	x.x, x.x
	Placebo + SOC (N=X)	x	x	x.x, x.x		
Any Baseline Ordinal Score[c]	Danicopan + SOC (N=X)	x	x	x.x, x.x	x	
	Placebo + SOC (N=X)	x	x	x.x, x.x	x	

N=Number of subjects in safety population. n= Number of unique subjects that satisfies the row criteria.
[a] Number of subjects who progressed to renal failure requiring dialysis at Day 29. Confidence intervals estimated using Blaker method.
[b] 95% CI for risk differences calculated using the Miettinen-Nurminen method.
[c] [X] additional subjects with an actual baseline ordinal score of 4 are included in the 'Any Baseline Ordinal Score' group.

APPENDIX 2. GENERAL PROGRAMMING NOTES FOR SAP FIGURES

- Use the same color for a treatment on the different graphs (SAS standard colors):
  - Danicopan + SOC = Blue
  - Placebo + SOC = Red
- For severity graphs (SAS standard colors):
  - 5 = green
  - 6 = blue
  - 7 = red
  - Death = black