EViSCO

Epstein-Barr Virus Suppression in Chronic Obstructive Pulmonary Disease

(EViSCO)

Protocol Number:	14143JK-AS
EudraCT Number:	2017-004686-28

STATISTICAL ANALYSIS PLAN

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This document and all preceding versions will be stored in the Trial Master File for this trial

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ABBREVIATIONS

ABBREVIATION	DEFINITION
AE	Adverse Event
AR	Adverse Reaction
CAT	COPD Assessment Test
CI	Confidence Interval
COPD	Chronic Obstructive Pulmonary Disease
CRF	Case Report Form
CSR	Clinical Study Report
CTU	Clinical Trials Unit
EBV	Epstein-Barr Virus
EudraCT	European Clinical Trials Database
DMEC	Data Monitoring and Ethics Committee
DNA	Deoxyribonucleic Acid
EQ-5D-5L	EuroQol Quality of Life Questionnaire
FEV1	Forced Expiratory Volume in 1 Second
FVC	Forced Vital Capacity
GOLD	Global Initiative in Obstructive Lung Disease
ICAM-1	Intra Cellular Adhesion Marker 1
IL	Interleukin
ITT	Intention-To-Treat
NICTU	Northern Ireland Clinical Trials Unit
OR	Odds Ratio
PCR	Polymerase Chain Reaction
PP	Per-Protocol
RNA	Ribonucleic Acid
RSI	Reference Safety Information
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SAR	Serious Adverse Reaction

SD	Standard Deviation
SOP	Standard Operating Procedures
SSAR	Suspected Serious Adverse Reaction
SUSAR	Suspected Unexpected Serious Adverse Reaction
TMF	Trial Master File
TSC	Trial Steering Committee
QoL	Quality of Life
UAR	Unexpected Adverse Reaction

1. BACKGROUND AND DESIGN

The primary hypothesis is that treatment with valaciclovir is safe and will suppress Epstein-Barr virus in the sputum of patients with COPD.

This study seeks to establish if an antiviral therapy (valaciclovir) used to treat other herpes viruses is safe in patients with COPD. It also examines whether it is possible to supress Epstein-Barr virus (EBV) in the airways of patients with COPD and examine important outcome measures including lung function and markers of airway inflammation in the blood and sputum.

The EBV suppression in COPD (EViSCO) study will be a randomised double-blind placebo-controlled clinical trial. The EViSCO trial will recruit subjects with COPD (GOLD classification 2 and 3) and EBV detectable in their sputum samples. Trial participants will receive either valaciclovir one gram three times daily or a matching placebo for a total of 8 weeks. EViSCO trial participants will be recruited to the sub-study on a voluntary basis

1.1 Primary objective

- To evaluate the safety of valaciclovir (1 gram three times daily for 8 weeks) for the suppression of in patients with COPD.
- To suppress Epstein-Barr virus shedding in COPD..

1.2 Secondary objectives

- To determine the effect of EBV suppression on lung function (FEV1) in patients with COPD.
- To assess the tolerability of valaciclovir (1 gram three times daily for 8 weeks) by measuring participant compliance.

1.3 Exploratory objectives

- To measure the effect of EBV suppression on sputum and blood markers of inflammation in patients with COPD.

- To evaluate quality of life following EBV suppression in patients with COPD.

1.4 Inclusion and Exclusion Criteria

Patients will be eligible to participate in the study if they fulfil the following criteria:

Inclusion Criteria

1) Age over 18 years.
2) Clinical diagnosis of COPD as defined by the Global Initiative for Chronic Obstructive Lung Disease criteria (FEV1/FVC <70%) with GOLD 2 and GOLD 3 airflow obstruction (FEV1 30-80% predicted) with significant symptoms.
3) Presence of EBV on sputum PCR analysis.

Exclusion Criteria

1) Respiratory failure (defined as long-term oxygen therapy).
2) An acute exacerbation of COPD in the previous month (defined as an acute, sustained worsening of symptoms that is beyond normal day-to-day variations).
3) A diagnosis of asthma.
4) Patients with known hypersensitivity to valaciclovir or aciclovir.
5) Patients unable to swallow study drug capsules.
6) Established diffuse interstitial lung disease (e.g. Idiopathic Pulmonary Fibrosis).
7) Established diagnosis of symptomatic bronchiectasis*.
8) Patients known to be pregnant or breastfeeding.
9) Patients with an estimated creatinine clearance less than 50ml/minute**.
10) Known participation in investigational medicinal product trials within 30 days.
11) Patients who do not adequately understand verbal or written information.
12) Concomitant use of nephrotoxic medicinal products or medicines associated with altered renal tubular secretion. These inlcude aminoglycosides, organoplatinum compounds, methotrexate, pentamidine, foscarnet, ciclosporin, tacrolimus,tenofovir, cimetidine and probenecid. As iodinated

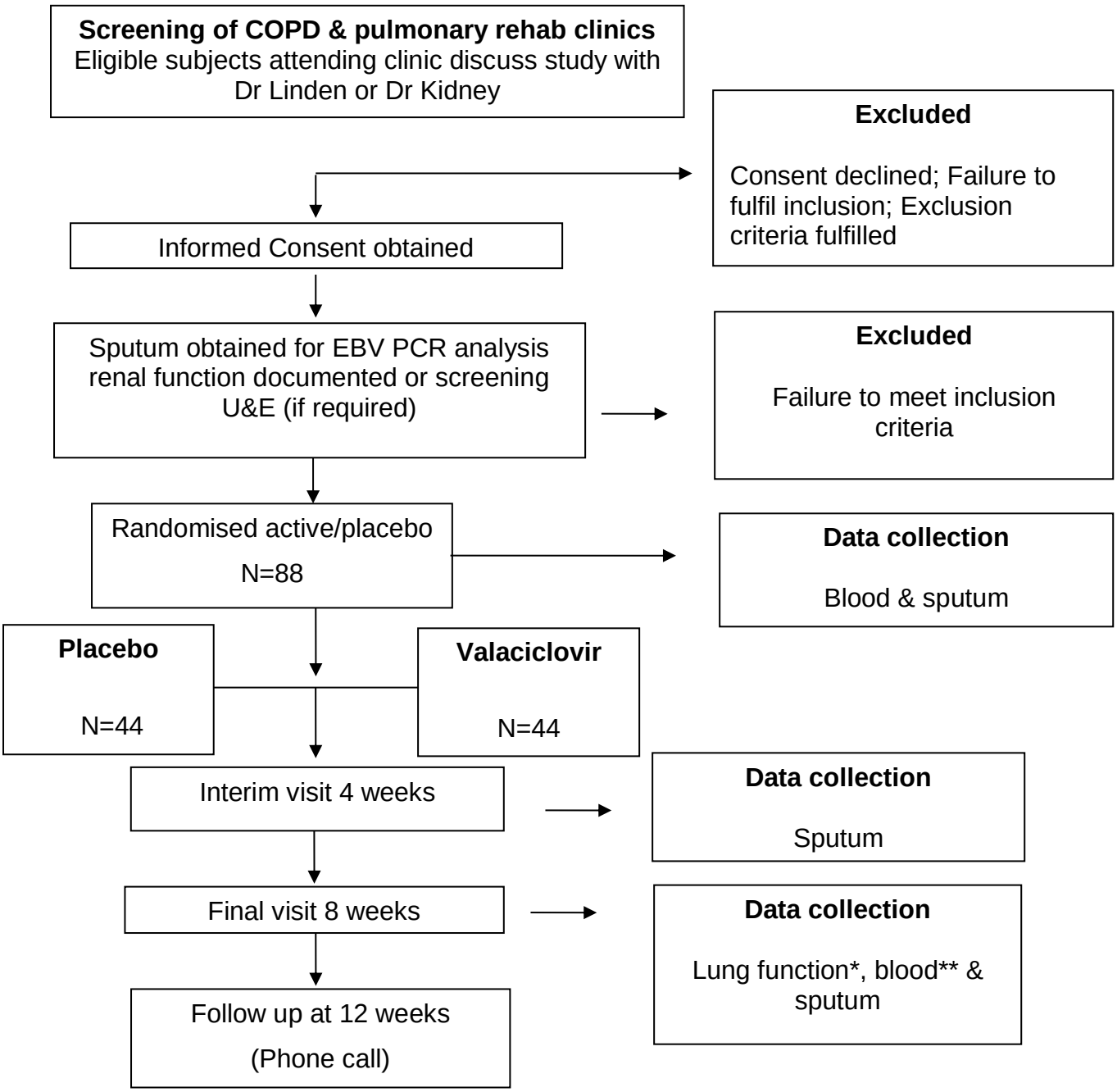
contrast used in radiological examinations can be nephrotoxicany patients with planned radiological contrast studies will be deferred for a reasonable time until after their contrast.

13) For the exploratory bronchoscopy sub-tudy patients will require adequate oxygen saturations, FEV1 >0.5 L and will not be performed while patients are taking aspirin or clopidogrel (BTS guidelines 2013).

** Patients with a primary respiratory diagnosis of established symptomatic bronchiectasis will be excluded. In order to fulfil this exclusion criteria patients must exhibit the clinical bronchiectasis phenotype and demonstrate computed tomography (CT) evidence of established multi-lobar bronchiectasis.*

*** Documented eGFR values from within the past 4 months will be used to confirm eligibility. If not available screening U&E will be completed.*

1.5 EViSCO Study Schematic Diagram



2. OUTCOME MEASURES

There are several study outcome measures:

2.1 Primary outcome measure(s)

- The primary safety outcome is the incidence of serious adverse reactions (SARs).
- The primary efficacy outcome is suppression of Epstein-Barr virus in the sputum of subjects with COPD and will be assessed using quantitative PCR at baseline and 8 weeks.

EBV is a DNA virus that may be suppressed beyond detection, however, it may be reverse transcribed and so it is possible that there will some detectable virus. For this this reason we will define EBV suppression as a 90% reduction in the viral load.

2.2 Secondary outcome measures

- Lung function measured by spirometry, the principal component will be the change in FEV1 from baseline to week 8*.
- Participant compliance measured by total number of tablets administered as a proportion of total number of tablets supplied.

* In light of the COVID19 lockdown lung function will not be measured in order to prevent unnecessary risk of exposure to study participants.

** Blood samples will no longer be taken in order to prevent unnecessary risk of exposure to study participants.

2.3 Exploratory Outcomes

Clinical Exploratory Outcomes

- Symptoms measured by CAT score and EQ-5D-5L from baseline to week 8.

Biological Exploratory Outcomes*

- Neutrophil activation biomarkers that may include but are not limited to measurement of neutrophil elastase and ICAM-1.
- Inflammatory response biomarkers that may include but are not limited to measurement of proteins, metabolites, cytokines (including but not limited to TNFα, IL-1β, IL-6, IL-8), proteases and anti-proteases.
- Nucleic acid analysis in sputum and blood including, viral/bacterial nucleic acid detection and gene expression. RNA sequencing, mRNA analysis and methylation analysis.

Exploratory Bronchoscopy Sub-study Outcome Measures*

- Measurement of epithelial ICAM-1 and airway neutrophilic inflammatory markers.
- Bronchial biopsy histology and immunohistopathology.
- Indices of nucleic acid expression in sputum and blood including viral and genomic DNA, viral RNA, microRNA and mRNA analysis & methylation analysis.

*These analyses are being undertaken outside of the NICTU and are not detailed in this statistical analysis plan

3. DATA

3.1 CRF Forms and variables

Full details of data collection and timing are described in the trial protocol (Version 4.0 / 22/04/2020). A copy of the CRF is presented in the Trial Master File (TMF).

3.2 Management of datasets

Below is the standard policy for management of data in the CTU as given in the CTU SOPs, at the time of analysis (including DMEC reports/Interim analysis (if required)):

The trial database will be stored in MACRO:

DMEC reports: - In collaboration with the Statistician, the Data Manager will create MACRO output files to support the analysis. This will act as the frozen dataset. It is the responsibility of the statistician to accurately record the date of freezing and ensure all data is retrieved. If there are no errors, the study database will be re-opened for further data entry.

If there are errors, the Study Statistician will report these to the Data Manager. The Data Manager in consultation with the Study Statistician, Data Project Manager and Senior Statistician will resolve the errors and determine which of the database closure activities are required to be undertaken. The Data Manager will re-create the MACRO output files to support the analysis. Database closure & lock: The same process for DMEC reporting will be followed for database closure and lock, the only difference being when the MACRO output files are created and there are no errors found for final analysis, the database should be locked as per SOP DM09.

3.3 Data completion schedule

The following table describes the schedule of assessments:

Table 1: Schedule of Assessments EViSCO Study

	Screening	Visit 1	Visit 2 week 4 (+/- 7days)	Visit 3 week 8 (+/- 7days)	Follow up week 12
Informed Consent	X				
Inclusion/Exclusion Criteria	X				
Demographic Data	X				
Medical History	X	X			
Medications	X	X	X	X	
Vital signs & BMI		X			
Documentation of exacerbations	X	X	X	X	X
Randomisation/ Registration		X			
CAT		X	X	X	
EQ-5D-5L		X	X	X	

Lung Function*	X			X	
Blood sample**	X	X		X	
Drug administration		X	X		
Sputum sample	X	X	X	X	
Bronchoscopy***		X		X	
Adverse events		X	X	X	X

*In some cases it may not be possible to facilitate lung function testing at the screening visit. In such cases patients who otherwise meet the trial eligibility criteria will be invited to return to have lung function measurement in order to complete the screening procedures. Confirmation of lung function indices must occur prior to trial enrolment.
**At the screening visit a U&E sample will only be sent if there are no previous U&E results from the previous 4 months. A screening U&E sample may be repeated at the discretion of the researcher if there is clinical concern that historic values are borderline.
***Bronchoscopy will only be performed in participants that consent to the sub-study. In addition bronchoscopy may not be undertaken on the same day as visit 1 and visit 3 but ideally will be facilitated within the bronchoscopy list.

3.4 **Data verification**

Data verification, consistency and range checks will have been performed at the data entry stage by the CTU, as well as checks for missing data (copies can be found in the TMF) according to SOP DM04. Additional range, consistency and missing data checks will be performed, as appropriate, when the analysis is performed (and when the datasets for analysis are constructed). All variables will be examined for unusual, outlying, unlabelled or inconsistent values.

Given the thorough nature of our follow-up procedure we expect the issue of missing data to be relatively minimal. We anticipate high compliance with initial data collection as this is close to the time of patient registration. If any clinical data is missing imputation will not be done. We expect there to be minimal data missing regarding study drug compliance, if a subject has compliance recorded for only one visit we will assume their overall compliance rate based on any compliance data captured.

Any problems with trial data will be queried with the Trial Managers, Data Managers, or statisticians, as appropriate. If possible, data queries will be resolved, although it is accepted that due to administrative reasons and data availability a small number of problems will continue to exist. This will be minimised.

3.5 **Data coding**

The variable codings will be as specified on the CRF.

4. DEFINITION OF TERMS

Term	Definition
Adverse Event (AE)	Any untoward medical occurrence in a participant to whom a medicinal product has been administered including occurrences which are not necessarily caused by or related to that product.
Adverse Reaction (AR)	Any untoward and unintended response in a participant to an investigational medicinal product, which is related to any dose administered to that participant.
Unexpected Adverse Reaction (UAR)	An adverse reaction the nature and severity of which is not consistent with the Reference Safety Information.
Serious Adverse Event (SAE) Serious Adverse Reaction (SAR)	An adverse event or adverse reaction that: results in death, is life-threatening, requires hospitalisation or prolongation of existing hospitalisation, results in persistent or significant disability or incapacity, consists of a congenital anomaly or birth defect, or any other important medical event(s) that carries a real, not hypothetical, risk of one of the outcomes above.
Suspected Serious Adverse Reaction (SSAR)	Any adverse reaction that is classed in nature as serious and is consistent with the Reference Safety Information (RSI)
Suspected Unexpected Serious Adverse Reaction (SUSAR)	Any adverse reaction that is classed in nature as serious and is not consistent with the Reference Safety Information
The EBV suppression	The EBV suppression is defined as 90% reduction in the viral load.
Per Protocol	The pre protocol population is defined as patients with overall study drug adherence of at least 70%
Overall Study Drug Adherence	Total number of tablets administered i.e. actual number of capsules taken / expected number of capsules taken
MMEF	Mid Expiratory Flow – MMEF 25-75% (L/s).

5. SAMPLE SIZE CALCULATIONS

A sample size of 31 subjects per group will have 90% power at a two-tailed significance level of 0.05 to detect a difference in the exploratory efficacy outcome EBV shedding of 70% in the treated group to 30% in the control group. With a dropout rate of approximately 30%, this study will require a total of 44 patients per group.

Sample Size in Bronchoscopy sub study

The exploratory bronchoscopy sub-study will be voluntary for participants recruited to the EViSCO trial and thus no formal sample size calculation has been performed.

6. RANDOMISATION AND BLINDING

6.1 Randomisation

Eligible participants will be randomised using a 1:1 allocation ratio into the two groups. All researchers will be blinded to the sequence. After informed consent has been obtained and eligibility has been confirmed, the researcher will contact the clinical trials pharmacist who will assign a unique patient identifier in accordance with the randomisation schedule and confirm the study drug pack numbers to be dispensed.

The researcher will then complete the patient registration form and submit this to the NICTU who will confirm the registration of the patient and that the unique patient identifier assigned is in accordance with the randomisation schedule. The pharmacist will also confirm the study pack numbers to be dispensed at visit 2.

6.2 Blinding and Allocation Concealment

As a placebo controlled, double-blind trial, patients, clinicians and the Chief Investigator will be blinded to treatment allocation. Patients will be given a Patient Study Card when they are enrolled in the trial. This will include 24-hour contact details of their treating clinician in the event that the patient needs to contact their clinician. Emergency unblinding may be requested on safety grounds, or if the treatment decision for a patient could be influenced by the knowledge of what the patient is

taking as part of the trial. If there is justification to unblind a patient, emergency unblinding will be performed by the Belfast Trust on call pharmacist. In the event unblinding occurs, the patient may discontinue study drug but will remain on the trial unless they decide to withdraw. Where unblinding has occurred this should be fully documented by the site and the Sponsor and NICTU informed.

7. ANALYSIS PRINCIPLES

The comparison of continuous outcomes will be carried out using t-tests followed by analysis of covariance adjusting for baseline FEV1 and other covariates if required. The mean and 95% confidence intervals will be reported. The categorical variables will be analysed using Fisher's Exact test or Chi-square test followed by logistic regression adjusting for baseline FEV1 and other covariates if required. The odds ratio and 95% confidence will be reported.

Statistical diagnostic methods will be used to check for violations of the assumptions, and transformations will be performed where required. Analyses will be on an intention-to-treat basis and all statistical tests will be at the 2-sided p-value of 0.05. A single final analysis is planned at the end of the trial.

Every effort will be made to minimise missing baseline and outcome data in this trial. The level and pattern of the missing data in the baseline variables and outcomes will be established by forming appropriate tables and the likely causes of any missingness will be investigated. This information will be used to determine whether the level and type of missing data has the potential to introduce bias into the analysis results for the proposed statistical methods, or substantially reduce the precision of estimates related to treatment effects. If necessary, these issues will be dealt with using multiple imputation or Bayesian methods for missing data as appropriate.

7.1 Analysis of primary outcome

Safety

The number of patients experiencing SAR in the two groups will be compared using Fisher's exact test, the relative risk and 95% confidence interval will be reported.

Efficacy

The number of patients experiencing suppression of Epstein-Barr virus in the two groups will be compared using Chi-Square test (or Fisher's exact if appropriate) followed by logistic regression adjusting for baseline FEV1 and other covariates if required. The odds ratio and 95% confidence interval will be reported.

The intention-to-treat basis analysis will use a significance level of ≤ 0.05 for the primary outcome. Per-protocol analysis will also be conducted which will involve a comparison of treatment groups that includes patients with overall study drug adeherence of at least 70%. Subgroup analyses will be performed on the primary outcome for compliance. In order to assess differences in treatment effects between the subgroups we will report odds ratio and 99% CI from the treatment*subgroup interaction model. Sensitivity analysis will be performed for the primary efficacy outcome excluding patients with a confirmed diagnosis of COVID-19

Additionally, change in viral load (Quantitative PCR) from baseline to week 8 in the two groups will be compared using independent t-test (or non-parametric alternative). The mean difference and 95% confidence interval will be reported.

7.2 Analysis of secondary, exploratory and other safety outcomes

The lung function outcomes will be reported using Mean (SD) or Median (p25 to p75) in patients with COPD. The change in lung function from baseline to week 8 in the two groups will be analysed using independent t-test or non-parametric alternative. The mean at baseline versus the mean at week 8 within each group will be analysed using a paired t-test or non-parametric alternative.

Exploratory subgroup analyses will be performed on the lung function outcomes for EBV suppression. Analysis of Covariance will be used to assess differences in

treatment effects between the subgroups and will be reported using mean difference and 99% CI.

Tolerability of valaciclovir will be assessed by measuring participant compliance at visit 2 and 3. The compliance (%) will be reported using mean (SD) or Median (p25 to p75) and will be analysed using independent t-test or non-parametric alternative

The change over time in CAT score and EQ-5D will be reported using Mean (SD) or Median (p25 to p75). The change from baseline to 8 weeks will analysed using independent t-test or non-parametric alternative.

8. ANALYSIS DETAILS

The results of the analyses will be reported following the principles of the ICH E3 guidelines on the Structure and Content of Clinical Study Reports.

8.1 Recruitment and follow-up patterns

- Screening, patient enrolment, treatment allocation, withdrawals, follow-up and inclusion in primary analysis will be reported using CONSORT diagram
- The numbers of exclusion will be summarized based on the exclusion and inclusion criteria

8.2 Baseline Characteristics

- Gender, n(%) by treatment arm
- Age(years), mean(SD) by treatment arm
- Height(m), mean(SD) by treatment arm
- Weight(kg), mean(SD) by treatment arm
- BMI(kg/m^2), mean(SD) by treatment arm
- Transfer Factor((TLCO) as a percentage of the predicted value(%)), mean(SD) by treatment arm
- Forced Expiratory Volume(FEV1 (L)), mean(SD) by treatment arm
- Forced Vital Capacity(FVC (L)), mean(SD) by treatment arm
- FEV1/FVC Ratio (%), mean(SD) by treatment arm
- Mid Expiratory Flow (MMEF 25-75% (L/s)), mean(SD) by treatment arm
- Peak Expiratory Flow(PEF (L/s)), mean(SD) by treatment arm
- Smoking Status, n(%) by treatment arm
- Pack Years, mean(SD) by treatment arm
- Presence of EBV, n(%) by treatment arm
- Quantitative PCR Titre(copies), mean(SD) by treatment arm
- Co-morbidities, n(%) by treatment arm
- Pre-existing Cardiovascular issues, n(%) by treatment arm
- Any exacerbations in past 12 months, n(%) by treatment arm

- Number of exacerbations in past 12 months, n(%) by treatment arm
- Number of exacerbations in past 12 months requiring steroids, n(%) by treatment arm
- Number of exacerbations in past 12 months requiring antibiotics, n(%) by treatment arm
- Number of exacerbations in past 12 months resulting in hospitalization, n(%) by treatment arm

8.3 Trial treatment

- Number of patients receiving at least one unit/dose of the drug, n(%) by treatment arm
- Duration of study drug (days), mean(SD) by treatment arm
- Overall compliance, mean(SD) by treatment arm
- Compliance, n(%) by treatment arm
- Time lapse between randomisation and study drug administration, mean(SD) by treatment arm
- Reason for study drug termination, n(%) by treatment arm
- Protocol Deviations/Violations, n(%) by treatment arm
- Premature withdrawals, n(%) by treatment arm

8.4 Trial Outcomes

- **Primary Safety Outcome**
    - Incidence of serious adverse reactions (SARs)Serious adverse reaction, n(%) by treatment group, Relative risk 95% CI
- **Primary Efficacy Outcome**
    - Suppression of Epstein-Barr virus in the sputum of subjects with COPD from baseline to week 8
        - Number of patients experiencing suppression of Epstein-Barr virus, n(%) by treatment arm, odds ratio and 95% CI (Note: Suppression as defined by a 90% reduction in Quantitative PCR at week 8 when compared to baseline) followed by logistic

regression adjusting for FEV1 and other covariates if required at baseline.

- Descriptive results for sputum sample including; presence of EBV (yes/no) at baseline, week 4 and week 8, n(%) by treatment arm

- Change in viral load (Quantitative PCR) from baseline to week 8, mean(SD) by treatment arm, difference in mean with 95% CI*
  - Descriptive results for quantitative PCR Tire(copies) at baseline, week 4 and week 8, mean(SD) by treatment arm

- Subgroup Analyses*
  - Compliance (≥80%, 60-79%, <60%), n(%) by treatment arm, odds ratio and 99% CI from the treatment*subgroup interaction model
- Sensitivity Analyses *
  - Sensitivity analysis will be performed for the primary outcome excluding patients with a confirmed diagnosis of COVID-19 reported as an adverse event.

- **Secondary Outcomes**
  - **Lung function**
    - Change in FEV1 from baseline to week 8, mean(SD) by treatment arm, difference in mean with 95% CI
      - Exploratory Subgroup Analysis*: EBV Suppression (as defined by 90% reduction in viral load) (Yes, No), mean(SD) by treatment arm, difference in mean and interaction term from ancova with 99% CI
    - Change in Forced Expiratory Volume in 1 second (FEV1 as a percentage of the predicted FEV1 value (%)) from baseline to week 8, mean(SD) by treatment arm, difference in mean with 95% CI
      - Exploratory Subgroup Analysis*: EBV Suppression (as defined by 90% reduction in viral load) (Yes, No),

mean(SD) by treatment arm, difference in mean and interaction term from ancova with 99% CI

- Change in FVC from baseline to week 8, mean(SD) by treatment arm, difference in mean with 95% CI
    - Exploratory Subgroup Analysis*: EBV Suppression (as defined by 90% reduction in viral load) (Yes, No), mean(SD) by treatment arm, difference in mean and interaction term from ancova with 99% CI
- Change in FEV1/FVC ratio from baseline to week 8, mean(SD) by treatment arm, difference in mean with 95% CI
    - Exploratory Subgroup Analysis*: EBV Suppression (as defined by 90% reduction in viral load) (Yes, No), mean(SD) by treatment arm, difference in mean and interaction term from ancova with 99% CI
- Change in MMEF from baseline to week 8, mean(SD) by treatment arm, difference in mean with 95% CI
    - Exploratory Subgroup Analysis*: EBV Suppression (as defined by 90% reduction in viral load) (Yes, No), mean(SD) by treatment arm, difference in mean and interaction term from ancova with 99% CI
- Change in PEF from baseline to week 8, mean (SD) by treatment arm, difference in mean with 95% CI
    - Exploratory Subgroup Analysis*: EBV Suppression (as defined by 90% reduction in viral load) (Yes, No), mean(SD) by treatment arm, difference in mean and interaction term from ancova with 99% CI
- Exploratory Subgroup Analysis*: EBV Suppression (as defined by 90% reduction in viral load) (Yes, No), mean(SD) by treatment arm, difference in mean and interaction term from ancova with 99% CIChange in TLCO from baseline to week 8, mean(SD) by treatment arm, difference in mean with 95% CI

- Exploratory Subgroup Analysis*: EBV Suppression (as defined by 90% reduction in viral load) (Yes, No), mean(SD) by treatment arm, difference in mean and interaction term from ancova with 99% CI

- Descriptive statistics for lung function including; FEV1, FEV1 as a percentage of the predicted FEV1 value, FVC, FEV1/FVC Ratio, MMEF, PEF and TLCO at baseline, week 4 and week 8, mean(SD) or median (IQR) by treatment arm.
- Difference between lung function measures at baseline and week 8 in the active and placebo groups separately for all lung function outcomes, mean (SD) within each treatment arm, mean difference and 95% CI

- Participant compliance measured by total number of tablets administered as a proportion of total number of tablets supplied, mean(SD) by treatment arm, mean difference and 95% CI

- **Exploratory Outcomes**

  - Clinical
    - Symptoms measured by CAT score and EQ-5D-5L from baseline to week 8, n(%) by treatment arm, mean difference and 95% CI
      - Descriptive statistics will also be presented at baseline, week 4 and week 8, mean(SD), median (IQR) or n(%) by treatment arm.
    - Suppression of Epstein-Barr virus in the sputum of subjects with COPD from baseline to week 4, n(%) by treatment arm, odds ratio and 95% CI*
    - Number of exacerbations reported between baseline and week 12, mean(SD) by treatment arm, mean difference and 95% CI *

*Not detailed in study protocol

8.5 Toxicity/ Symptoms

- AEs, no.events (%) by treatment arm, no. patients(%) by treatment arm, Risk ratio with 95% CI
- ARs, no.events (%) by treatment arm, no. patients(%) by treatment arm, Risk ratio with 95% CI
- SAEs, no. events (%) by treatment arm, no. patients (%) by treatment arm, Risk ratio with 95% CI
- SARs, no. events (%) by treatment arm, no. patients (%) by treatment arm, Risk ratio with 95% CI
- UARs, no. events (%) by treatment arm, no. patients (%) by treatment arm, Risk ratio with 95% CI
- SUSARs, no. events (%) by treatment arm, no. patients (%) by treatment arm, Risk ratio with 95% CI
- Fatal AEs/SAEs, no. events (%) by treatment arm, no. patients (%) by treatment arm, Risk ratio with 95% CI
- Safety bloods, mean(SD) by treatment arm at baseline and week 8

AEs, ARs, SAEs, SARs, UARs and SUSARs will also be presented by system organ class.

9. ADDITIONAL INFORMATION

9.1 Data Monitoring and Ethics Committee (DMEC)

A DMEC will be appointed with responsibility for safeguarding the interests of trial patients, they will monitor the main outcome measures including safety and efficacy so as to protect the validity and credibility of the trial. The committee members will be independent of the study team and will comprise of at least two respiratory specialists and one statistician. The DMEC Charter will outline the terms of reference of the DMEC including roles/responsibilities, membership, organisation of meetings, reporting, decision-making and the relationship with the other trial committees.

The DMEC will discuss trial progress as and when required, but at least every 9 months, meetings will be held and will be formally minuted. The Trial Statistician will produce reports for the DMEC including recruitment, baseline, adverse event, compliance and outcome data to enable them to monitor the trial and guide overall progress. An interim analysis of efficacy is not planned, although this can be requested by the DMEC as required.

The DMEC will function primarily as a check for safety reviewing adverse events (AEs). They will specifically review the incidence of ARs, SAEs and SUSARs and produce a recommendation following each meeting. They will report any issues pertaining to safety to both the study sponsor and the Chief Investigator. If concerns exist about participant safety it will be the responsibility of both to take appropriate action to halt the trial immediately.

10. SIGNATURES OF APPROVAL

Date: 28/10/2020

Version: 2.0 Final

This document has completed a final review and is understood and approved by the following:

Dr Joe Kidney		
Chief Investigator Name	*Chief Investigator Signature*	Date dd/mm/yyyy
Clíona McDowell		
Senior Statistician or designee Name	*Senior Statistician or designee Signature*	Date dd/mm/yyyy
Christina Campbell		
Study Statistician Name	*Study Statistician Signature*	Date dd/mm/yyyy

APPENDIX 1: EXAMPLE DRAFT SUMMARY TABLES, FIGURES AND LISTINGS

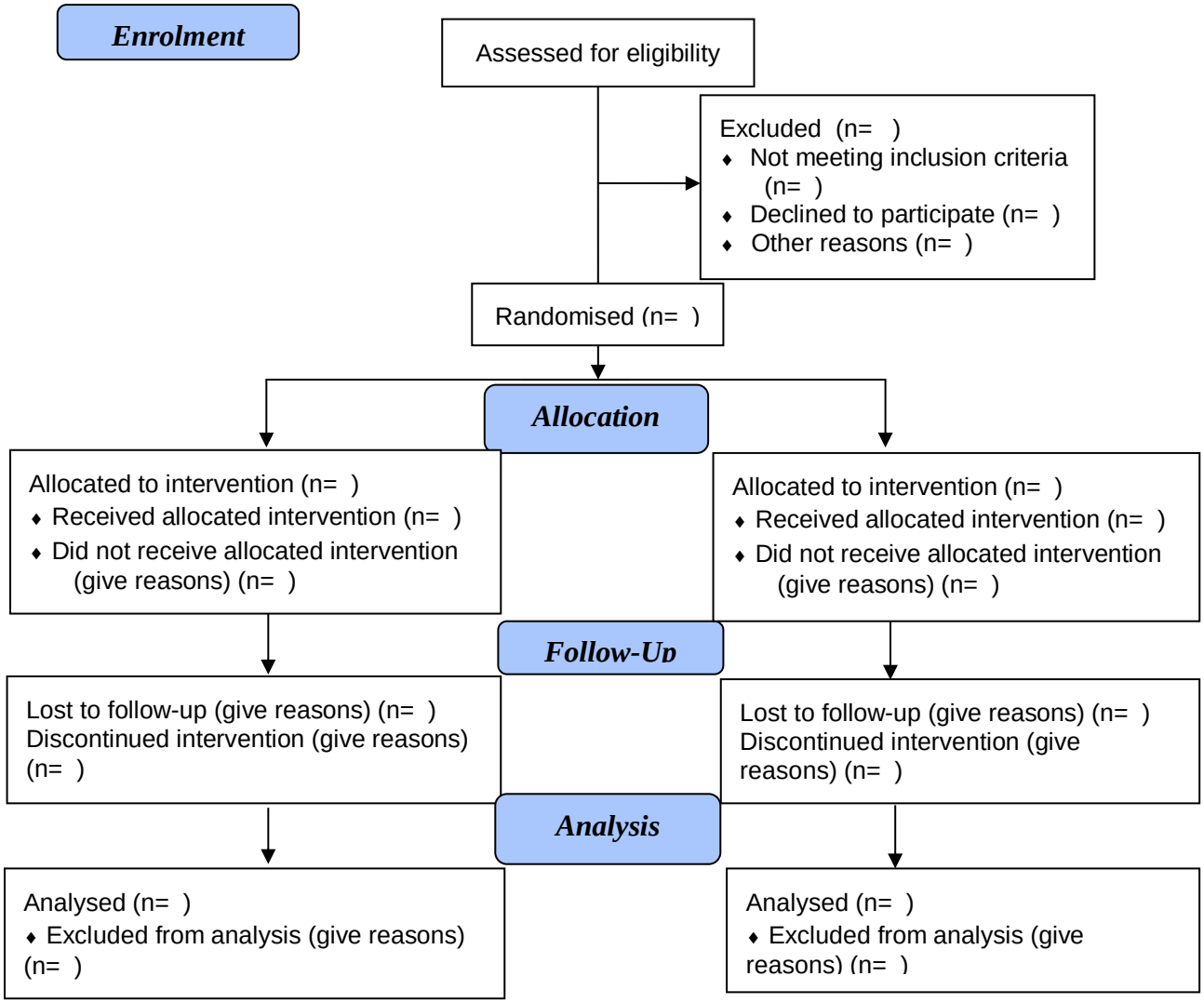


Figure A1. The CONSORT Diagram

Table x.x: Reason for Exclusion From the Study

Total number of patients screened		n
Total number of patients recruited		n
Total number of patients excluded		n
Reasons for Exclusion	The patient is not over 18 years of age?	n
	The patient does not have a clinical diagnosis of COPD	n
	The patient does not display the presence of Epstein-Barr virus on sputum PCR analysis?	n
	Respiratory failure (defined as long-term oxygen therapy).	n
	An acute exacerbation of COPD in the previous month	n
	A diagnosis of asthma.	n
	Patient has known hypersensitivity to valaciclovir or aciclovir.	n
	Patient unable to swallow study drug capsules.	n
	Established diffuse interstitial lung disease (e.g. Idiopathic Pulmonary Fibrosis).	n
	Established diagnosis of symptomatic bronchiectasis.	n
	Patient known to be pregnant or breastfeeding.	n
	Patient has an estimated creatinine clearance less than 50ml/minute.	n
	Patient is known to have participated in investigational medicinal product trials within 30 days.	n
	Patient does not adequately understand verbal or written information.	n
	Concomitant use of nephrotoxic medicinal products or medicines associated with altered renal tubular secretion.	n
	Other	n

Table x.x: Baseline Characteristics at Trial Entry

Baseline Characteristics		Treatment Group		Total
		Valaciclovir	Placebo	
		N	n	n
Gender	**Male**	n (%)	n (%)	n (%)
	Female	n (%)	n (%)	n (%)
Age (years)		xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)
Height(m)		xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)
Weight(kg)		xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)
BMI(kg/m2)		xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)
Transfer Factor((TLCO) as a percentage of the predicted value(%))		xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)
Forced Expiratory Volume(FEV1 (L))		xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)
Forced Vital Capacity(FVC (L))		xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)
FEV1/FVC Ratio (%),		xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)
Mid Expiratory Flow (MMEF 25-75% (L/s))		xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)
Peak Expiratory Flow(PEF (L/s)),		xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)
Smoking Status	**Current Smoker**	n (%)	n (%)	n (%)
	Ex-Smoker	n (%)	n (%)	n (%)
	Never Smoked	n (%)	n (%)	n (%)
Pack years		xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)
Presence of EBV	**Yes**	n (%)	n (%)	n (%)
	No	n (%)	n (%)	n (%)
Quantitative PCR Titre(copies)		xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)

Relevant co-morbidities		n (%)	n (%)	n (%)
Pre-existing Cardiovascular issues		n (%)	n (%)	n (%)
Any exacerbations in past 12 months	**Yes**	n (%)	n (%)	n (%)
	No	n (%)	n (%)	n (%)
If Yes, Number of exacerbations in past 12 months		x.x (x.x to x.x)	x.x (x.x to x.x)	x.x (x.x to x.x)
If Yes, Number of exacerbations in past 12 months requiring steroids		x.x (x.x to x.x)	x.x (x.x to x.x)	x.x (x.x to x.x)
If Yes, Number of exacerbations in past 12 months requiring antibiotics		x.x (x.x to x.x)	x.x (x.x to x.x)	x.x (x.x to x.x)
If Yes, Number of exacerbations in past 12 months resulting in hospitalization		x.x (x.x to x.x)	x.x (x.x to x.x)	x.x (x.x to x.x)

Mean (SD) (or median (IQR)) presented for continuous variables and no. (%) for all categorical variables.

Table x.x: Treatment after Trial Entry Treatment Termination, Protocol Deviation

		Valaciclovir N = <n>	Placebo N = <n>
Number of patients who received at least one dose of treatment		n (xx.x%)	n (xx.x%)
Duration of study drug (days)		xx.x (x.x)	xx.x (x.x)
Overall compliance		xx.x (x.x)	xx.x (x.x)
Compliance	**≥80%**	n (xx.x%)	n (xx.x%)
	60-79%	n (xx.x%)	n (xx.x%)
	<60%	n (xx.x%)	n (xx.x%)
Time from randomisation to start of study drug (hours)		xx.x (xx.x to xx.x)	xx.x (xx.x to xx.x)
Reasons for termination of study drug			
1) Study Drug related AE		n (xx.x%)	n (xx.x%)
2) Study Drug related SAE		n (xx.x%)	n (xx.x%)
3) Study Drug Expiry Date		n (xx.x%)	n (xx.x%)
4) Patient Request		n (xx.x%)	n (xx.x%)
5) Clinician's Request		n (xx.x%)	n (xx.x%)
6) Other		n (xx.x%)	n (xx.x%)
Protocol deviations/ violations			
Eligibility		n (xx.x%)	n (xx.x%)
Consent		n (xx.x%)	n (xx.x%)
Study Drug Administration			
Did not receive allocated treatment[a]		n (xx.x%)	n (xx.x%)
Received treatment of other group[b]		n (xx.x%)	n (xx.x%)
Study drug omitted in error[c]		n (xx.x%)	n (xx.x%)
Study drug received in error		n (xx.x%)	n (xx.x%)
SAE reporting timelines		n (xx.x%)	n (xx.x%)
Visit outside schedule		n (xx.x%)	n (xx.x%)
Other		n (xx.x%)	n (xx.x%)
Premature Withdrawals			
Adverse Event		n (xx.x%)	n (xx.x%)
Serious Adverse Event		n (xx.x%)	n (xx.x%)
Protocol deviation/ non-compliance		n (xx.x%)	n (xx.x%)
Lost to Follow Up		n (xx.x%)	n (xx.x%)
Withdrawal of patient consent		n (xx.x%)	n (xx.x%)
Death		n (xx.x%)	n (xx.x%)
At clinician's request		n (xx.x%)	n (xx.x%)
Other		n (xx.x%)	n (xx.x%)

[a]-Numbers based on study drug administration data, [b]- Numbers based on the randomisation listing held by trial Statistician,[c]- Numbers based on Protocol deviation data

Table x.x: Primary Efficacy Outcome Analyses

		Valaciclovir N = <n>	**Placebo N = <n>**	Difference (95% CI)	p-value
Number of patients experiencing suppression of Epstein-Barr virus in the sputum of subjects with COPD will be assessed using quantitative PCR at baseline and 8 weeks.*	Intention to Treat#	N(%)	N(%)	xx.x (xx.x – xx.x)	0.xx
	Per Protocol	N(%)	N(%)	xx.x (xx.x – xx.x)	0.xx
Change in viral load from baseline to week 8	Intention to Treat	xx.x(xx.x)	xx.x(xx.x)	xx.x (xx.x – xx.x)	0.xx
Change in viral load from baseline to week 8	Per Protocol	xx.x(xx.x)	xx.x(xx.x)	xx.x (xx.x – xx.x)	0.xx

**Odds Ratio and 95% Confidence Interval Presented*
#Primary Analysis

Table x.x: Primary Efficacy Outcome Subgroup

EBV Supression (Yes)		**Valaciclovir N = <n>**	**Placebo N = <n>**	**OR (99% CI)**
Overall Compliance	**≥80%**	N(%)	N(%)	x.xx (xx.x – xx.x)
	60-79%	N(%)	N(%)	x.xx (xx.x – xx.x)
	<60%	N(%)	N(%)	x.xx (xx.x – xx.x)

*Odds Ratio and 99% CI from the treatment*subgroup interaction models are presented*

Table x.x: Lung Function/ Sputum Sample Descriptive Statistics

		Valaciclovir			Placebo		
		Baseline	**Week 4**	**Week 8**	**Baseline**	**Week 4**	**Week 8**
		n=<n>	n=<n>	n=<n>	n=<n>	n=<n>	n=<n>
Lung Function							
Forced Expiratory Volume (FEV1 (L))		xx.x (x.x)	xx.x (x.x)	xx.x (x.x)	xx.x (x.x)	xx.x (x.x)	xx.x (x.x)
Forced Expiratory Volume in 1 second (FEV1 as a percentage of the predicted FEV1 value (%))		xx.x (x.x)	xx.x (x.x)	xx.x (x.x)	xx.x (x.x)	xx.x (x.x)	xx.x (x.x)
Forced Vital Capacity (FVC (L))		xx.x (x.x)	xx.x (x.x)	xx.x (x.x)	xx.x (x.x)	xx.x (x.x)	xx.x (x.x)
FEV1/FVC Ratio (%)		xx.x (x.x)	xx.x (x.x)	xx.x (x.x)	xx.x (x.x)	xx.x (x.x)	xx.x (x.x)
Mid Expiratory Flow (MMEF 25-75% (L/s))		xx.x (x.x)	xx.x (x.x)	xx.x (x.x)	xx.x (x.x)	xx.x (x.x)	xx.x (x.x)
Peak Expiratory Flow(PEF (L/s))		xx.x (x.x)	xx.x (x.x)	xx.x (x.x)	xx.x (x.x)	xx.x (x.x)	xx.x (x.x)
Transfer Factor (TLCO (as a percentage of the predicted value) (%))		xx.x (x.x)	xx.x (x.x)	xx.x (x.x)	xx.x (x.x)	xx.x (x.x)	xx.x (x.x)
Sputum Sample							
Quantitative PCR Titre(copies)		xx.x (x.x)	xx.x (x.x)	xx.x (x.x)	xx.x (x.x)	xx.x (x.x)	xx.x (x.x)
Presence of EBV	Yes	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
	No	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)

Table x.x Secondary Outcomes(Lung Function)

	Valaciclovir	Placebo	Difference (95% CI)	P-Value
Change in Forced Expiratory Volume (FEV1 (L)) from baseline to week 8	xx.x (x.x)	xx.x (x.x)	xx.x (xx.x – xx.x)	0.xx
Change in Forced Expiratory Volume in 1 second (FEV1 as a percentage of the predicted FEV1 value (%)) from baseline to week 8	xx.x (x.x)	xx.x (x.x)	xx.x (xx.x – xx.x)	0.xx
Change in Forced Vital Capacity (FVC (L)) from baseline to week 8	xx.x (x.x)	xx.x (x.x)	xx.x (xx.x – xx.x)	0.xx
Change in Mid Expiratory Flow (MMEF 25-75% (L/s)) from baseline to week 8	xx.x (x.x)	xx.x (x.x)	xx.x (xx.x – xx.x)	0.xx
Change in Peak Expiratory Flow(PEF (L/s)) from baseline to week 8	xx.x (x.x)	xx.x (x.x)	xx.x (xx.x – xx.x)	0.xx
Change in FEV1/FVC Ratio (%) from baseline to week 8	xx.x (x.x)	xx.x (x.x)	xx.x (xx.x – xx.x)	0.xx
Change in Transfer Factor (TLCO (as a percentage of the predicted value) (%)) from baseline to week 8	xx.x (x.x)	xx.x (x.x)	xx.x (xx.x – xx.x)	0.xx

Table x.x Lung Function Exploratory Subgroups

	EBV Suppression	Valaciclovir N = <n>	Placebo N = <n>	Difference (99% CI)	Interaction Term*
Change in Forced Expiratory Volume (FEV1 (L)) from baseline to week 8	Yes	xx.x (x.x)	xx.x (x.x)	xx.x (xx.x – xx.x)	0.xx
	No	xx.x (x.x)	xx.x (x.x)	xx.x (xx.x – xx.x)	
Change in Forced Expiratory Volume in 1 second (FEV1 as a percentage of the predicted FEV1 value (%)) from baseline to week 8	Yes	xx.x (x.x)	xx.x (x.x)	xx.x (xx.x – xx.x)	0.xx
	No	xx.x (x.x)	xx.x (x.x)	xx.x (xx.x – xx.x)	
Change in Forced Vital Capacity (FVC (L)) from basleine to week 8	Yes	xx.x (x.x)	xx.x (x.x)	xx.x (xx.x – xx.x)	0.xx
	No	xx.x (x.x)	xx.x (x.x)	xx.x (xx.x – xx.x)	
Change in Mid Expiratory Flow (MMEF 25-75% (L/s)) from baseline to week 8	Yes	xx.x (x.x)	xx.x (x.x)	xx.x (xx.x – xx.x)	0.xx
	No	xx.x (x.x)	xx.x (x.x)	xx.x (xx.x – xx.x)	
Change in Peak Expiratory Flow(PEF (L/s)) from baseline to week 8	Yes	xx.x (x.x)	xx.x (x.x)	xx.x (xx.x – xx.x)	0.xx
	No	xx.x (x.x)	xx.x (x.x)	xx.x (xx.x – xx.x)	
Change in FEV1/FVC Ratio (%) from baseline to week 8	Yes	xx.x (x.x)	xx.x (x.x)	xx.x (xx.x – xx.x)	0.xx
	No	xx.x (x.x)	xx.x (x.x)	xx.x (xx.x – xx.x)	
Change in Transfer Factor (TLCO (as a percentage of the predicted value) (%)) from baseline to week 8	Yes	xx.x (x.x)	xx.x (x.x)	xx.x (xx.x – xx.x)	0.xx
	No	xx.x (x.x)	xx.x (x.x)	xx.x (xx.x – xx.x)	

**Interaction term from ancova*

Table x.x Secondary Outcomes(Participant Compliance)

	Valaciclovir	Placebo	Difference (95% CI)	P-Value
Overall Compliance	xx.x (x.x)	xx.x (x.x)	xx.x (xx.x – xx.x)	0.xx

Table x.x: Paired analysis for lung function in active and placebo groups

		Valaciclovir N = <n>	Difference (95% CI)	P value	Placebo N = <n>	Difference (95% CI)	P value
Forced Expiratory Volume (FEV1 (L))	Baseline	xx.x (x.x)	xx.x (xx.x – xx.x)	0.xx	xx.x (x.x)	xx.x (xx.x – xx.x)	0.xx
	Week 8	xx.x (x.x)			xx.x (x.x)		
Forced Expiratory Volume in 1 second (FEV1 as a percentage of the predicted FEV1 value (%))	Baseline	xx.x (x.x)	xx.x (xx.x – xx.x)	0.xx	xx.x (x.x)	xx.x (xx.x – xx.x)	0.xx
	Week 8	xx.x (x.x)			xx.x (x.x)		
Forced Vital Capacity (FVC (L))	Baseline	xx.x (x.x)	xx.x (xx.x – xx.x)	0.xx	xx.x (x.x)	xx.x (xx.x – xx.x)	0.xx
	Week 8	xx.x (x.x)			xx.x (x.x)		
Mid Expiratory Flow (MMEF 25-75% (L/s))	Baseline	xx.x (x.x)	xx.x (xx.x – xx.x)	0.xx	xx.x (x.x)	xx.x (xx.x – xx.x)	0.xx
	Week 8	xx.x (x.x)			xx.x (x.x)		
Peak Expiratory Flow (PEF (L/s))	Baseline	xx.x (x.x)	xx.x (xx.x – xx.x)	0.xx	xx.x (x.x)	xx.x (xx.x – xx.x)	0.xx
	Week 8	xx.x (x.x)			xx.x (x.x)		
FEV1/FVC Ratio (%)	Baseline	xx.x (x.x)	xx.x (xx.x – xx.x)	0.xx 0.xx	xx.x (x.x)	xx.x (xx.x – xx.x)	0.xx

	Week 8	xx.x (x.x)			xx.x (x.x)		
Transfer Factor (TLCO (as a percentage of the predicted value) (%))	Baseline	xx.x (x.x)	xx.x (xx.x – xx.x)	0.xx	xx.x (x.x)	xx.x (xx.x – xx.x)	0.xx
	Week 8	xx.x (x.x)			xx.x (x.x)		

Continuous outcomes reported as Mean (SD). Paired sample t-test used to determine if any difference between lung function measures at baseline and week 8 in the active and placebo groups separately.

Table x.x: CAT Questionnaire Descriptive Statistics

	Valaciclovir			Placebo		
	Baseline	**Week 4**	**Week 8**	**Baseline**	**Week 4**	**Week 8**
Cough	xx.x (x.x)	xx.x (x.x)	xx.x (x.x)	xx.x (x.x)	xx.x (x.x)	xx.x (x.x)
Phlegm/ mucus	xx.x (x.x)	xx.x (x.x)	xx.x (x.x)	xx.x (x.x)	xx.x (x.x)	xx.x (x.x)
Chest Tightness	xx.x (x.x)	xx.x (x.x)	xx.x (x.x)	xx.x (x.x)	xx.x (x.x)	xx.x (x.x)
Breathlessness	xx.x (x.x)	xx.x (x.x)	xx.x (x.x)	xx.x (x.x)	xx.x (x.x)	xx.x (x.x)
Limited Activities at Home	xx.x (x.x)	xx.x (x.x)	xx.x (x.x)	xx.x (x.x)	xx.x (x.x)	xx.x (x.x)
Confidence in Leaving Home	xx.x (x.x)	xx.x (x.x)	xx.x (x.x)	xx.x (x.x)	xx.x (x.x)	xx.x (x.x)
Sleeps Soundly	xx.x (x.x)	xx.x (x.x)	xx.x (x.x)	xx.x (x.x)	xx.x (x.x)	xx.x (x.x)
Energy	xx.x (x.x)	xx.x (x.x)	xx.x (x.x)	xx.x (x.x)	xx.x (x.x)	xx.x (x.x)
Total	xx.x (x.x)	xx.x (x.x)	xx.x (x.x)	xx.x (x.x)	xx.x (x.x)	xx.x (x.x)

Table x.x: EQ-5D Descriptive Statistics

EQ: 5D (sub scales)		Valaciclovir			Placebo		
		Baseline	Week 4	Week 8	Baseline	Week 4	Week 8
Numbers reporting some problem – score 2 or above	Mobility	n/N (%)	n/N (%)	n/N (%)	n/N (%)	n/N (%)	n/N (%)
	Self-care	n/N (%)	n/N (%)	n/N (%)	n/N (%)	n/N (%)	n/N (%)
	Usual activities	n/N (%)	n/N (%)	n/N (%)	n/N (%)	n/N (%)	n/N (%)
	Pain/discomfort	n/N (%)	n/N (%)	n/N (%)	n/N (%)	n/N (%)	n/N (%)
	Anxiety/Depression	n/N (%)	n/N (%)	n/N (%)	n/N (%)	n/N (%)	n/N (%)
EQ: 5D (VAS)		x.x (x.x to x.x)	x.x (x.x to x.x)	x.x (x.x to x.x)	x.x (x.x to x.x)	x.x (x.x to x.x)	x.x (x.x to x.x)
Index Score		x.x (x.x to x.x)	x.x (x.x to x.x)	x.x (x.x to x.x)	x.x (x.x to x.x)	x.x (x.x to x.x)	x.x (x.x to x.x)

Table x.x Exploratory Outcomes

	All patients	Valaciclovir	Placebo	Difference (95% CI)	p-value
CAT Score	xx.x (x.x)	xx.x (x.x)	xx.x (x.x)	xx.x (x.x to x.x)	0.xxx
EQ-5D-5L	xx.x (x.x)	xx.x (x.x)	xx.x (x.x)	xx.x (x.x to x.x)	0.xxx
Suppression of Epstein-Barr virus in the sputum of subjects with COPD from baseline to week 4*	N(%)	N(%)	N(%)	xx.x (xx.x – xx.x)	0.xx
Number of exacerbations reported between baseline and week 12	xx.x (x.x)	xx.x (x.x)	xx.x (x.x)	xx.x (x.x to x.x)	0.xxx

Continuous outcomes reported as Mean (SD) (or median(IQR) if appropriate). Categorical outcomes reported as n(%).

**odds ratio and 95% CI presented*

Table x.x: Safety Outcomes

	Number of Events			Number of Patients				
	Total (n=)	**Valaciclovir (n=)**	**Placebo (n=)**	**Total (n=)**	**Valaciclovir (n=)**	**Placebo (n=)**	**RR (95%I)**	**p-value**
Adverse Events	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	x.x (x.x to x.x)	x.xx
Adverse Reactions	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	x.x (x.x to x.x)	x.xx
Unexpected Adverse Reactions	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	x.x (x.x to x.x)	x.xx
Serious Adverse Events	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	x.x (x.x to x.x)	x.xx
Serious Adverse Reactions *	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	x.x (x.x to x.x)	x.xx
Suspected Unexpected Serious Adverse Reactions	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	x.x (x.x to x.x)	x.xx
Fatal Serious Adverse Events	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	x.x (x.x to x.x)	x.xx

**Primary safety outcome (incidence of serious adverse reactions)*

AEs, ARs, SAEs, SARs, UARs and SUSARs will also be presented by system organ class.

Table x.x: Safety Bloods

	Valaciclovir		Placebo	
	Baseline	**Week 8**	**Baseline**	**Week 8**
Haematology Blood				
Haemoglobin (g/L)	xx.x (x.x)	xx.x (x.x)	xx.x (x.x)	xx.x (x.x)
Platelet Count (x10⁹/L)	xx.x (x.x)	xx.x (x.x)	xx.x (x.x)	xx.x (x.x)
Total White Cell Count (x10⁹/L)	xx.x (x.x)	xx.x (x.x)	xx.x (x.x)	xx.x (x.x)
Eosinophils (x10⁹/L)	xx.x (x.x)	xx.x (x.x)	xx.x (x.x)	xx.x (x.x)
Eosinophils (%)	xx.x (x.x)	xx.x (x.x)	xx.x (x.x)	xx.x (x.x)
Lymphocytes (x10⁹/L)	xx.x (x.x)	xx.x (x.x)	xx.x (x.x)	xx.x (x.x)
Neutrophil (x10⁹/L)	xx.x (x.x)	xx.x (x.x)	xx.x (x.x)	xx.x (x.x)
Neutrophil/Lymphocyte Ratio	xx.x (x.x)	xx.x (x.x)	xx.x (x.x)	xx.x (x.x)