Clinical trial results:
Clinical trial to determine the effect of Famciclovir on Epstein-Barr virus activity as measured by EBV shedding in saliva of patients with Multiple Sclerosis.

Summary

EudraCT number	2019-000169-19
Trial protocol	GB
Global end of trial date	10 April 2023

Results information

Result version number	v1 (current)
This version publication date	07 November 2024
First version publication date	07 November 2024
Summary attachment (see zip file)	Accepted paper (FamV paper_v3_revised_clean.docx) Protocol (CTIMP Protocol FCV_v5_tracked.docx)

Trial information

Trial identification

Sponsor protocol code	249627 v5

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05283551
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Queen Mary University of London
Sponsor organisation address	Mile End Road, London, United Kingdom, E1 4NS
Public contact	Dr Mays Jawad, Queen Mary University London, 0044 02078827260, research.governance@qmul.ac.uk
Scientific contact	Dr Mays Jawad, Queen Mary University London, 0044 02078827260, research.governance@qmul.ac.uk

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	07 June 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	10 April 2023
Global end of trial reached?	Yes
Global end of trial date	10 April 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary aim of this study is to explore the effect of famciclovir (500mg twice daily) on Epstein Barr virus shedding in the saliva of people with MS.

Protection of trial subjects:

Standard

Background therapy: -

Evidence for comparator:

N/A

Actual start date of recruitment	01 June 2019
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 30
Worldwide total number of subjects	30
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	29
From 65 to 84 years	1
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Recruited as per protocol

Pre-assignment

Screening details:

Screening as per protocol

Period 1

Period 1 title	Pre drug
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

Single arm internal case control design - pre drug

Arms

Arm title	Study population

Arm description:

Entire study population

Arm type	pre drug
Investigational medicinal product name	NONE
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Not assigned
Routes of administration	Not mentioned

Dosage and administration details:

NO DRUG GIVEN

Number of subjects in period 1	Study population
Started	30
Completed	29
Not completed	1
Consent withdrawn by subject	1

Period 2

Period 2 title	On drug
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details: Single arm internal control design

Arms

Arm title	Trial population
Arm description: Entire study population	
Arm type	Experimental
Investigational medicinal product name	famciclovir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: 500mg twice daily oral	

Number of subjects in period 2	Trial population
Started	29
Completed	24
Not completed	5
Consent withdrawn by subject	3
Adverse event, non-fatal	2

Period 3

Period 3 title	Post drug
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded
Blinding implementation details: Single arm internal control design	

Arms

Arm title	Study population
Arm description: Entire study population	
Arm type	No intervention
No investigational medicinal product assigned in this arm	

Number of subjects in period 3	Study population
Started	24
Completed	24

Baseline characteristics

End points

End points reporting groups

Reporting group title	Study population
Reporting group description: Entire study population	
Reporting group title	Trial population
Reporting group description: Entire study population	
Reporting group title	Study population
Reporting group description: Entire study population	

Primary: Salivary EBV DNA shedding

End point title	Salivary EBV DNA shedding
End point description: Viral shedding was defined as a salivary EBV concentration greater than 5.8 copies/ul, with viral presence defined as any detectable EBV DNA in saliva. The number of samples in each epoch with (a) viral shedding, and (b) viral presence, were recorded as a proportion of total samples	
End point type	Primary
End point timeframe: During study	

End point values	Study population	Trial population	Study population	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	21[1]	21[2]	21[3]	
Units: presence or absence				
Viral shedding	48	33	23	
Viral presence	48	40	54	
No viral DNA	52	60	46	

Notes:

[1] - those with at least one sample meeting QC requirements available across all epochs

[2] - those with at least one sample meeting QC requirements available across all epochs

[3] - those with at least one sample meeting QC requirements available across all epochs

Statistical analyses

Statistical analysis title	Primary outcome measure
Statistical analysis description: The primary outcome measure, the rate of EBV shedding in saliva, was assessed as a proportion in the pre-treatment and the on-treatment epochs. As the on-treatment groups were expected to be skewed, paired proportions were compared using the Wilcoxon Signed-Rank Test.	
Comparison groups	Study population v Trial population v Study population

Number of subjects included in analysis	63
Analysis specification	Pre-specified
Analysis type	superiority[4]
P-value	< 0.05
Method	Wilcoxon (Mann-Whitney)

Notes:

[4] - As above

Adverse events

Adverse events information	
Timeframe for reporting adverse events: From trial initiation until EoT	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	29
Reporting groups	
Reporting group title	Entire study population
Reporting group description: Entire study population	

Serious adverse events	Entire study population		
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 30 (10.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Uterine polypectomy	Additional description: Admitted for removal of uterine polyp		
subjects affected / exposed[1]	1 / 19 (5.26%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Pulmonary resection	Additional description: VATS wedge procedure for removal of nodule (subsequently found to be benign)		
subjects affected / exposed	1 / 30 (3.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Ankle fracture	Additional description: Required surgical management		
subjects affected / exposed	1 / 30 (3.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: Only females could be exposed to this AE given gender-specific AE (Uterine polypectomy). Of 30 participants, 19 were female (please see page 2 of "Accepted paper/FamV paper_v3_revised_clean.docx" in "Summary attachments" section.
1 subject was affected out of 19 female subjects that could be exposed to an Uterine polypectomy.

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Entire study population		
Total subjects affected by non-serious adverse events subjects affected / exposed	18 / 30 (60.00%)		
Cardiac disorders Tachycardia subjects affected / exposed occurrences (all)	1 / 30 (3.33%) 1		
Nervous system disorders Syncope subjects affected / exposed occurrences (all)	1 / 30 (3.33%) 1		
Fatigue subjects affected / exposed occurrences (all)	1 / 30 (3.33%) 1		
Sensory disturbance subjects affected / exposed occurrences (all)	1 / 30 (3.33%) 1		
Headache subjects affected / exposed occurrences (all)	1 / 30 (3.33%) 1		
Blood and lymphatic system disorders Haematoma subjects affected / exposed occurrences (all)	1 / 30 (3.33%) 1		
Ear and labyrinth disorders Ear infection subjects affected / exposed occurrences (all)	1 / 30 (3.33%) 1		
Eye disorders Conjunctivitis allergic subjects affected / exposed occurrences (all)	1 / 30 (3.33%) 1		
Gastrointestinal disorders			

Gastritis			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Diarrhoea			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Lower respiratory tract infection			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Pneumothorax	Additional description: Following VATS procedure (see SAE)		
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Herpes simplex reactivation			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Synovitis			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
COVID-19			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Tooth abscess			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Urinary tract infection			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
23 March 2020	COVID - related with gradual restart	-

Notes:

Limitations and caveats

None reported