CLINICAL STUDY REPORT

FANCONI-TAF (FANTA) STUDY

Safety of tenofovir alafenamide (TAF) in patients with a history of tubulopathy on tenofovir disoproxil fumarate (TDF)

Sponsor Protocol Code:	FANTA
EudraCT Number:	2016-003345-29
IRAS Number:	211705
REC ref number	16/LO/1812
Investigational Drugs (IMPs):	Tenofovir alafenamide (co-formulated with Emtricitabine)
Indication:	HIV
Development Phase:	IV
Study Begin (FPFV):	21/02/2017
Study End (LPLV):	21/07/2023
Report Version & Issue Date:	1.7 – 26.11.2025
Sponsor Name and Address:	King's College NHS Foundation Trust, Denmark Hill, London, SE5 9RS
Sponsor contact details:	Ann-Marie Murtagh, R&I Director, annmariemurtagh@nhs.net
Chief Investigator:	Prof Frank Post

SIGNATURE PAGE

By signing below I approve the contents of this Clinical Study Report, and confirm that to the best of my knowledge it accurately describes the conduct and results of the study. The clinical trial reported herein was conducted in accordance with the principles contained in the Declaration of Helsinki, Good Clinical Practice (GCP) and all applicable laws and regulations.

This was a non-commercial academic trial, the results of this study are not intended to be used or a licensing application.

Chief Investigator: Prof Frank Post

Frank Post		26.11.2025
Printed name	**Signature**	**Date**

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APPENDICES

1. Ethics

Independent Ethics Committee or Institutional Review Board
The study protocol and amendments were reviewed and approved by a National Research Ethics Service (London – Dulwich Research Ethics Committee), REC reference 16/LO/1812.

Ethical conduct of the study
The trial was conducted according to the protocol and in compliance with the principles of the Declaration of Helsinki (1996) as amended, the principles of Good Clinical Practice (GCP) and in accordance with Medicines for Human Use (Clinical Trials) Regulations 2004, as amended, the Research Governance Framework for Health and Social Care, the Data Protection Act 1998 and other regulatory requirements as appropriate. The trial protocol and substantial amendments were reviewed by the United Kingdom (UK) Medicines and Healthcare products Regulatory Agency (MHRA)

Subject information and consent
All participants were provided with the current Patient Information Sheet, additional information and an opportunity to ask questions was provided prior to screening. All participants provided written informed consent.

2. Data Monitoring

A data monitoring committee (DMC) was established for the duration of the interventional phase of the study (week 0-96). The DMC consisted of Dr Ranjababu Kulasegaram, Dr John Booth and Dr Sophie Jose (statistician).

3. Sponsors, Investigators and Trial Sites

Sponsor	***King's College Hospital NHS Foundation Trust***
Chief Investigator	***Prof Frank Post***

4. Co-Investigator(s), Statistician, Laboratories, Database Management

Co-Investigator	***Prof. Margaret Johnson*** ***Dr. Deborah Williams*** ***Dr Angela Bailey/Prof. Alan Winston*** ***Dr. Lisa Hamzah***
Statistician	***Lucy Campbell*** ***Fowzia Ibrahim***
Laboratories	***Synnovis (KCH)*** ***Cambridge University Hospital NHS Foundation Trust***
Database Management	***Birgit Barbini***

5. Study Synopsis

Title of clinical trial	Safety of tenofovir alafenamide (TAF) in patients with a history of tubulopathy on tenofovir disoproxil fumarate (TDF)
Protocol Short Title/Acronym	FANCONI-TAF (FANTA) study
Study Phase	Phase IV
Sponsor name	King's College Hospital NHS Foundation Trust
Chief Investigator	Prof Frank Post
Eudract number	2016-003345-29
REC number	16/LO/1812
IRAS project ID:	211705
Medical condition or disease under investigation	HIV infection
Purpose of clinical trial	To assess long-term renal and bone safety of tenofovir alafenamide in patients with a history of tubulopathy / Fanconi syndrome while receiving tenofovir disoproxil fumarate
Primary objective	To determine the incidence of recurrent tubulopathy
Secondary objective (s)	To evaluate changes from baseline in renal function and bone biomarkers and bone mineral density
Trial Design	A trial consisting of 3 phases: a randomized, controlled phase (weeks 0-12), followed by a single arm interventional extension (week 12-96), followed by an observational extension (years 3-5)
Endpoints	(1) Treatment-limiting proximal renal tubulopathy (2) Changes in kidney function and bone biomarkers (3) Changes in bone mineral density
Planned number of subjects	40
Summary of eligibility criteria	Any person with well controlled HIV and a history of proximal tubulopathy (PRT, Fanconi syndrome) while receiving tenofovir disoproxil fumarate
IMP, dosage and route of administration	Tenofovir alafenamide (10 or 25 mg, co-formulated with emtricitabine 200 mg), taken orally daily
Active comparator product(s)	N/A
Maximum duration of treatment of a subject	5 years

Version and date of protocol amendments	Protocol V2.0, 20/01/2017 (Substantial Amendment 1) Protocol V2.1, 28/06/2017 (Substantial Amendment 2) Protocol V3.0, 12/09/2018 (Substantial Amendment 3) Protocol V4.0, 02/09/2019 (Substantial Amendment 4)

6. Glossary of terms

N/A

7. Publications (reference)

Hamzah L, Willams D, Bailey AC, et al. Early safety of tenofovir alafenamide in patients with a history of tubulopathy on tenofovir disoproxil fumarate: a randomized controlled clinical trial.

HIV Med 2020; 21(3):198-203

Campbell L, Barbini B, Burling K, Cromarty B, Hamzah L, Johnson M, Jones R, Samarawickrama A, Williams D, Winston A, Post FA; FANTA Trial Team. Safety of tenofovir alafenamide in people with HIV who experienced proximal renal tubulopathy on tenofovir disoproxil fumarate.

JAIDS 2021; 88 (2): 214-219.

Campbell L, Barbini B, Cromarty B, Hamzah L, Williams D, Winston A, Post F, FANTA trial team. Safety of tenofovir alafenamide in people with HIV who experienced proximal renal tubulopathy on tenofovir disoproxil.

AIDS 2024; 38: 1442-1445.

8. Study period (years)

Overall study period: 2016 – 2024

Study Start Date (FPFV): 21/02/2017
Study End Date (LPLV): 21/07/2023

9. Phase of development

Phase IV

10. Objectives

To evaluate the effects of tenofovir alafenamide (TAF) on kidneys and bone in patients with a history of tubulopathy/Fanconi syndrome on tenofovir disoproxil fumarate (TDF).

11. Background and Context

TDF has been associated with renal tubular injury which may manifest as a reduction in estimated glomerular filtration rate (eGFR) and/or proximal renal tubulopathy (PRT, Fanconi syndrome and which may be accompanied by osteomalacia and fractures. Discontinuation of TDF typically results in resolution of PRT and improvement in eGFR – mostly to pre-TDF levels. Case reports have suggested TAF may be an option for this group of patients, but no formal studies have been conducted to confirm this. Hence, we studied the safety of TAF in this vulnerable population.

12. Methodology

Study Duration and Follow up visits

Phase 1 (weeks 0-12): open-label, randomised controlled study, with visits at baseline, week 4 and week 12

Phase 2 (weeks 12-96): single arm study with three monthly study visits

Phase 3 (years 3 -5): observational cohort study, with annual visits

Blood and urine samples to analyse kidney and bone biomarkers were obtained at each visit, and DEXA scans were performed at baseline, years 1, 2 and 5.

Table: Schedule of events

Immediate switch arm

Description	**Screening (week -8 to -2)**	**Baseline (Day 0)**	**Week 4**	**Week 8**	**Week 12**	**Week 24**	**Week 36**	**Week 48**	**Week 60**	**Week 72**	**Week 84**	**Week 96**
Informed consent	x											
Review eligibility	x	x										
Medical history	x											
Telephonic consultation				x								
Randomisation		x										
Adherence, adverse events and concomitant medications		x	x	x	x	x	x	x	x	x	x	x
Physical examination [1]	x	x	x		x	x	x	x	x	x	x	x
Urine dipstick analysis [2]	x	x	x		x	x	x	x	x	x	x	x
Pregnancy test [3]	x	x				x		x		x		x
Urine ACR/PCR		x										
Urine phosphate and plasma glucose		x	x		x	x		x				x
Kidney/bone profile [4]	x	x	x		x	x	x	x	x	x	x	x
Urate		x	x		x	x		x				x
Liver profile	x											
Lipid profile [5]		x						x				x
Thyroid function [6]		x										x

CD4+ lymphocyte count/FBC	x									x				x
Plasma HIV RNA	x		x				x		x			x		x
Biobanking of blood/urine [7]	x		x		x		x		x			x		x
Urine pellet			x				x			x				
Early morning urine			x		x		x							
DXA scan (hip/spine)			x							x				x
Adherence questionnaire			x				x			x				x

Deferred switch arm

Description	**Screening** (wk -8 to -2)	**Baseline** (Day 0)	**Wk 4**	**Wk 12** (Day 0 - DESC)	**Wk 4**	**Wk 8**	**Wk 12**	**Wk 24**	**Wk 36**	**Wk 48**	**Wk 60**	**Wk 72**	**Wk 84**	**Wk 96**
Informed consent	x													
Review eligibility	x	x		x										
Medical history	x													
Telephonic consultation						x								
Randomisation		x												
Adherence, adverse events and concomitant medications		x	x	x	x	x	x	x	x	x	x	X	x	x
Physical examination [1]	x	x	x	x	x		x	x	x	x	x	X	x	x
Urine dipstick analysis [2]	x	x	x	x	x		x	x	x	x	x	X	x	x
Pregnancy test [3]	x	x		x				x		x		x		x
Urine ACR/PCR		x												
Urine phosphate and plasma glucose		x	x	x			x	x		x				x
Kidney/bone profile [4]	x	x	x	x	x		x	x	x	x	x	X	x	x
Urate		x	x	x	x		x	x		x				x
Liver profile	x													

Lipid profile [5]		x						x		x
Thyroid function [6]		x								x
CD4+ lymphocyte count/FBC	x							x		x
Plasma HIV RNA	x	x		x		x	x	x	X	x
Biobanking of blood/urine [7]	x	x	x	x	x	x	x	x	X	x
Urine pellet		x		x				X		
Early morning urine		x	x	x						
DXA scan (hip/spine)		x						x		x
Adherence questionnaire		x		x		x		x		x

1	Physical Examination (symptom directed except at screening: full physical examination)	5	Total Cholesterol, HDL, LDL, triglycerides (FASTING)
2	Measure plasma glucose if any glycosuria is present (local laboratory)	6	Thyroid stimulating hormone (TSH)
3	Women of child bearing potential (see 5.2)	7	10 ml EDTA plasma, 10 ml serum, 5 ml urine (see appendix A)
4	Should at least include the following: urea, creatinine, Na, K, Ca, P, albumin, uric acid, alkaline phosphate	NB	Day 0 and week 4, 12, 24, 48 and 96 are fasting visits

Observational extension

Description	**Week 96**	**Year 3**	**Year 4**	**Year 5**
Informed consent to participate in observational extension	x	x[1]		
Medical history, including renal and bone events		x	x	x
HIV and concomitant medications		x	x	x
Review and recording of laboratory results		x	x	x
Urine dipstick analysis		x	x	x
Urine ACR, PCR and phosphate		x	x	x
Kidney/bone profile [2] and glucose		x	x	x
Biobanking of blood/urine [3, 4]		x	x	x
DXA scan				x

1	If already past week 96 at the time of approval being granted
2	Should at least include the following: creatinine, phosphate, calcium, albumin, alkaline phosphate
3	10 ml EDTA plasma, 10 ml serum, 5 ml urine (see appendix A)
4	Biobanking will also be performed in case of (suspected) renal toxicity

Trial Medication
Tenofovir alafenamide (10 or 25 mg, co-formulated with emtricitabine 200 mg)

Dosing Regimen
Once a day

13. Number of patients (planned and analysed)

13.1 Planned 40

13.2 Analysed 31 (phase 1 and phase 2), 28 (phase 3)

Arm	Immediate	Deferred
# patients treated per study arm	17	14
# total patients completed study with extension	15	13
Reasons for non-completion	See below	See below

Table: The reasons for patient withdrawal from the study

Patient	Comments
1	Discontinued TAF treatment: treatment simplification
2	Discontinued TAF: pre-emptive switch during critical care unit admission for COVID-19
3	Transient HIV viraemia (200 – 1000 copies/mL)
4	Transient HIV viraemia (200 – 1000 copies/mL)
5	Renal/bone adverse events (renal colic, traumatic rib fracture)

14. Diagnosis and main criteria for inclusion

People aged 18 years and older with HIV-1 who, while receiving TDF, had experienced Fanconi syndrome or treatment-limiting PRT, defined by at least 2 of the following: proteinuria [≥1+ on urinary dipstick or protein to creatinine ratio (PCR) >30 mg/mmol]; normoglycemic glycosuria (≥1+ on urinary dipstick); hypophosphatemia (serum phosphate <0.64 mmol/L); rapid eGFR decline (>5 mL/min/1.73 m^2/yr with >25% reduction from baseline; or a renal biopsy showing acute tubular injury not explained by other causes, with clinical resolution of the PRT on TDF discontinuation. Participants were required to be virologically suppressed (plasma HIV-1 RNA <200 copies per mL) on a stable ART regimen not containing TDF and be naive to TAF. Individuals with diabetes mellitus,

glycosuria ≥1+ at screening or baseline, proteinuria ≥2+ or urine PCR ≥100 mg/mmol at screening, or creatinine clearance <30 mL/min (Cockcroft-Gault) were ineligible.

15. Test product, dose and mode of administration

Tenofovir alafenamide (10 or 25 mg, co-formulated with emtricitabine 200mg), one tablet daily, with investigator selected other antiretroviral agents

16. Duration of treatment

Five years

17. Reference therapy, dose and mode of administration

N/A

18. Criteria for evaluation: Endpoints

Primary endpoint: recurrent tubulopathy
Secondary endpoints: changes in kidney function (eGFR by creatinine, eGFR by cystatin C, urine protein/creatinine, albumin/creatinine, and retinol-binding-protein/creatinine ratios, and fractional excretion of phosphate); changes in bone biomarkers (25-OH vitamin D, parathyroid hormone, total procollagen type 1 N-terminal propeptide (P1NP, a marker of bone formation) and C-terminal telopeptide (CTX, a marker of bone resorption) [weeks 0-96 only]; bone mineral density by Dual X-ray Absorptiometry (DEXA).

18.1 Efficacy

Not assessed

18.2 Safety

Safety Parameters: Assessment of adverse events and concomitant medications

No cases of recurrent proximal tubulopathy were encountered. No adverse effects of the IMP on kidney function, bone biomarkers or bone mineral density were observed. No IMP-adverse events were observed.

19. Statistical Methods

Repeated measures/multi-level mixed effects linear regression models were used to analyse changes in biomarkers from baseline to week 96 (including data from all study visits), and from baseline to year 5 (including data for baseline and yearly visits post-baseline for soluble biomarkers and from baseline, years 1, 2 and 5 for bone mineral density).

20. Changes in the Trial Plan

At the end of the initial 96-week trial, a decision was made to close the trial and extend this a further 3 years as an observational phase.

20.1 Protocol Deviations

No serious breaches or major protocol deviations occurred throughout the study period.

21. Summary – Conclusions

21.1 Demographic data

In summary, 31 participants (97% male, 87% white ethnicity), with a median age of 55 (IQR 51-60) years, 97% male gender, were enrolled.

The following tables summarise the demographics of the study population:

Number of Subjects			
Age (years)	**Male**	**Female**	**Total**
Pre-term new-born infants (<37 weeks)	0	0	0
New-borns (0-27 days)	0	0	0
Infants and toddlers (28 days – 23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	28	1	29
Elderly (≥65 years)	2	0	2
Total	30	1	31

Number of Subjects				
	White British	**White Other**	**Black African**	**Asian Other**
Male	22	50	2	1
Female	0	0	1	0
Total	22	5	3	1

21.2 Primary outcome

No cases of recurrent tubulopathy were encountered.

21.3 Safety results

Kidney function, as assessed by eGFR, proteinuria and fractional excretion of phosphate, remained stable through five years of follow up.

Bone turnover makers were unaffected up to week 96, and no changes in lumbar spine bone mineral density up to year 5 were observed. Participants experienced small reductions in total hip bone mineral density, which was not unexpected given the prolonged follow up of the study participants.

Table: Listing of Adverse Events for all patients

Adverse Events	**Immediate arm**	**Deferred arm**
Total Number of AEs per Study Arm	100	135
Subjects affected by non-serious adverse events:	As above	As above

Table: Listing of Serious Adverse Events for all patients

Serious Adverse Events	**Immediate arm**	**Deferred arm**
Total Number of SAEs per Study Arm	15	2
Total number of all cause deaths per Study Arm	0	0
Total number of deaths resulting from adverse events per Study Arm	0	0

Within the per protocol population (n= 31), a total of 235 AEs, including “17” SAE, were identified and included in the safety analysis. Summary tables for AEs and SAEs are presented in the appendix of this

synopsis.

Overall, 31 patients (100%) patients experienced at least one AE. The proportion that experienced at least one SAE was 19.35% (n=6).

There were no incidences of adverse drug reactions (ADRs).

There were zero Serious Adverse Reactions (SARs), zero unexpected SARs and zero SUSARs.

22. Conclusion

The FANTA Study has shown that TAF is a safe, well-tolerated and effective treatment for individuals with HIV who experienced PRT on TDF.

23. Date of Report

This is version 1.7 of the Clinical Study Report synopsis, dated 26/NOV/2025.

APPENDICES

i) Summary of treatment-emergent AEs in the per protocol population

System Organ Class *(Current list of MedDRA SOC)*	**Preferred Term**	**Number of Subjects Experiencing the AE in Immediate Arm** *(ideally list number and percentage e.g. 10 /12 subjects would be listed as 10 (83.33%)*	**Total Number of Occurrences of the AE in the Immediate Arm** *(10 subjects may have experienced the same AE multiple times throughout the trial e.g. there were 20 occurrences of the same event)*	**Number of Subjects Experiencing the AE in Deferred Arm** *(ideally list number and percentage e.g. 10 /12 subjects would be listed as 10 (83.33%)*	**Total Number of Occurrences of the AE in the Deferred Arm** *(10 subjects may have experienced the same AE multiple times throughout the trial e.g. there were 20 occurrences of the same event)*
Blood and lymphatic system disorders		0	0	0	0
Cardiac disorders	*Atypical chest pain *Fainting episode	0	0	2 / 14 (14.3%)	2
Congenital, familial and genetic disorders		0	0	0	0
Ear and labyrinth disorders	*Labyrinthitis	0	0	1 / 14 (7.1%)	1
Eye Disorders	*Floater left eye *Lens of eye opacification *Genetic peripheral retinal atrophy *MSSA Eyes	4 / 17 (23.5%)	4	0	0
Gastrointestinal disorders	*Heartburn *Gastroenteritis	8 / 17 (47.1%)	12	8 / 14 (57.1%)	19

	*Diarrhoea *Nausea *Norovirus *Vomiting *Cramping *Aphthous ulcer *Stomach discomfort *Hemorrhoids *Stool darkening *Mouth dryness *Looser stool *Gastritis *Constipation *Lower abdominal discomfort *Abdominal bloating				
General disorders and administration site conditions	*Chills *Tiredness *Fatigue *Fever *Temperature *Leg Swelling	4 / 17 (23.5%)	5	1 / 14 (7.1%)	1
Hepatobiliary disorders		0	0	0	0
Immune system disorders	*Hayfever	1 / 17 (5.9%)	1	0	0
Infections and infestations	*Gonorrhoea (throat) *Non-gonoccocal urethritis *Possible Syphilis *Tooth infection *Rectal chlamydia *Right lower gum infection *Viral URTI *Genital, Oral, Perianal HSV *Pharyngeal candida	2 / 17 (11.7%)	3	7 / 14 (50%)	13
Injury, poisoning and procedural complications	*Fall on stairs *Pain post fall *Aches from fall *Bike accident	0	0	3 / 14 (21.4%)	4

Investigations	*Deranged UPCR / UACR *Abnormal LFTs	2 / 17 (11.7%)	2	0	0
Metabolism and nutritional disorders	*Vitamin D deficiency *Folate deficiency *Hypercho-lesterolaemia *Mixed hyper-lipidemia *Glucose intolerance *Weight gain *Low plasma folate	1 / 17 (5.9%)	1	5 / 14 (35.7%)	8
Musculoskeletal and connective tissue disorders	*Left flank pain *Back pain *Knee pain *Shoulder pain *Hip pain *Finger pain *Joint pain *Gout *Osteopenia *Bilateral sacroiliitis *Sciatica *Strained tendon *Weakness *Torn knee cartilage *Arthralgia	9 / 17 (52.9%)	15	11 / 14 (78.6%)	22
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	*Squamous cell carcinoma *Polycythaemia	2 / 17 (11.7%)	2	0	0
Nervous system disorders	*Dizziness *Peripheral neuropathy *Headache *Leg numbness *Transient global amnesia *Worsening short term memory *Blackouts	6 / 17 (35.3%)	6	6 / 14 (42.9%)	11

	*Seizures *Daytime somnolence				
Pregnancy, puerperium and perinatal conditions		0	0	0	0
Product issues		0	0	0	0
Psychiatric disorders	*Low mood *Vivid dreams *Memory problems *Depression *Concentration difficulties *Insomnia	1 / 17 (5.9%)	1	5 / 14 (35.7%)	9
Renal and urinary disorders	*Haematuria *Urinary frequency *Urinary tract infection *Kidney pain *Acute urinary retention *Renal stones *Benign prostatic hypertrophy *Nocturia *Drop>25% in eGFR	4 / 17	5	7 / 14 (50%)	9
Reproductive system and breast disorders	*Nipple pain *Itching foreskin *Testicular pain *Swollen penis head	2 / 17 (11.7%)	2	2 / 14 (14.3%)	2
Respiratory, thoracic and mediastinal disorders	*Dental abscess *Root Canal *Flu *Cold *Cough *Oral thrush *Asthma *Chest infection *Coryzal symptoms *Tonsillitis *Nose bleeding *Upper respiratory tract infection	10 / 17 (58.8%)	27	11 / 14 (78.6%)	22

	*Breathlessness *Dental work *Sinus infection *Infective exacerbation of COPD *Lower respiratory tract infection *Epitaxis				
Skin and subcutaneous tissue disorders	*Skin infection *Cellulitis *Seborrheic warts *Ingrown hair *Dermatitis *Nail infection *Psoriasis *Rash *Cyst *Multiple small wounds *Sporotrichosis *Echtym / MSSA *Night sweats *Itchiness no rash *Back lump	6 / 17 (35.3%)	15	5 / 14 (35.7%)	5
Social circumstances		0	0	0	0
Surgical and medical procedures	*Tooth Extraction *CT guided nerve root block	0	0	2 / 14 (14.3%)	2
Vascular disorders	*Hypertension	2 / 17 (11.7%)	2	2 / 14 (14.3%)	2

ii) Summary of treatment-emergent ARs in the per protocol population

Not Applicable – no AR/SAR occurred in this trial.

iii) Summary of treatment-emergent SAEs in the study population

System Organ Class *(Current list of MedDRA SOC)*	**Preferred Term**	**Number of Subjects Experiencing the SAE in Immediate Arm** *(ideally list number and percentage e.g. 10 /12 subjects would be listed as 10 (83.33%)*	**Total Number of Occurrences of the SAE** *(10 subjects may have experienced the same AE multiple times throughout the trial e.g. there were 20 occurrences of the same event)*	**Number of Subjects Experiencing the SAE in Deferred Arm** *(ideally list number and percentage e.g. 10 /12 subjects would be listed as 10 (83.33%)*	**Total Number of Occurrences of the SAE** *(10 subjects may have experienced the same AE multiple times throughout the trial e.g. there were 20 occurrences of the same event)*
Blood and lymphatic system disorders		0	0	0	0
Cardiac disorders		0	0	0	0
Congenital, familial and genetic disorders		0	0	0	0
Ear and labyrinth disorders		0	0	0	0
Eye Disorders		0	0	0	0
Gastrointestinal disorders	*Acute pancreatitis	1 / 17 (5.9%)	2	0	0
General disorders and administration site conditions		0	0	0	0
Hepatobiliary disorders		0	0	0	0
Immune system disorders		0	0	0	0
Infections and infestations		0	0	0	0
Injury, poisoning and procedural complications	*Fractures	1 / 17 (5.9%)	1	0	0
Investigations		0	0	0	0
Metabolism and nutritional		0	0	0	0

disorders					
Musculoskeletal and connective tissue disorders	*Right hip pain *Torn Achilles tendon	1 / 17 (5.9%)	1	1 / 14 (7.1%)	1
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		0	0	0	0
Nervous system disorders	*Alcohol withdrawal symptoms	1 / 17 (5.9%)	1	0	0
Pregnancy, puerperium and perinatal conditions		0	0	0	0
Product issues		0	0	0	0
Psychiatric disorders	*Suicidal ideation	1 / 17 (5.9%)	1	0	0
Renal and urinary disorders		0	0	0	0
Reproductive system and breast disorders		0	0	0	0
Respiratory, thoracic and mediastinal disorders	*Chest infection *Pneumonia *Respiratory failure *Exacerbation of COPD	2 / 17 (11.7%)	7	1 / 14 (7.1%)	1
Skin and subcutaneous tissue disorders	*Cellulitis *Abscess	2 / 17 (11.7%)	2	0	0
Social circumstances		0	0	0	0
Surgical and medical procedures		0	0	0	0
Vascular disorders		0	0	0	0

iv) Summary of treatment-emergent SARs in the study population

Not Applicable – no AR/SAR occurred in this trial.

Table 1: Listing of Adverse Events and Serious Adverse Events for all patients in FANTA Week 96 analyses:

	F/TAF (n=31)
Any adverse event (N=207)	29 (93.5%)
Mild (N=135)	28 (90.3%)
Moderate (N=66)	19 (61.3%)
Severe (N=6)	4 (12.9%)
Adverse events noted in >10% of the study population	
Musculoskeletal pain	19 (61.3%)
Respiratory tract infection	19 (61.3%)
Gastro-intestinal complaints	11 (35.5%)
Dental issues	6 (19.4%)
Headache	5 (16.1%)
Depression	4 (12.9%)
Serious adverse events (N=8; none related to study drug): Infection (N=6), accident (N=1), chest tightness (N=1)	3 (9.7%)
Study drug-related adverse events (probably/definitely): Headache (1), vivid dreams (1), diarrhoea (1) [all resolved with continuation study drug]	3 (9.7%)
Adverse events leading to temporary study drug discontinuation (10 and 30 days respectively, for gout and peripheral neuropathy; both considered unrelated to study drug)	2 (6.5%)
Death	0

Numbers in the left-hand column indicate the total number of reported adverse events, data in the right-hand column the number and proportion of participants with the relevant adverse events.

Table 2: Listing of all Serious Adverse Events for all patients in FANTA:

	SAE description	Included in FANTA Trial week 96 analysis (Y/N)
1	Cellulitis	Y
2	Pneumonia	Y
3	Chest tightness	Y
4	Chest Infection	Y
5	R antecubital fossa abscess	Y
6	Pain in right hip	Y
7	Fractures in foot	Y
8	Community acquired pneumonia	Y
	Infected right arm abscess	N - duplicate
	Suicidal Ideation	N - not SAE, IME
1	Chest Infection	N *
2	Acidotic type 2 respiratory failure, resolved with medical management and home NIV	N *
3	Exacerbation of COPD	N *
4	Acute Pancreatitis	N *
5	Damage to ligaments and Achilles tendon left foot (agreed SAE as inability to move around)	N *
6	Respiratory problems (existing COPD)- Infective COPD	N *
7	Pancreatitis	N *
8	Started as exacerbation of COPD, then diagnosed as pneumonia and gastroenteritis	N *

****** This single individual with multiple SAEs was included in the week 12 randomised phase of the study but was*

in poor health at Baseline and did not participate beyond week 12 and thus not included in the week 96 or year 5 analyses.

Consort diagram