Clinical trial results:
A Single Arm Multiple Dose Study to Assess the Efficacy and Safety of ANB019 in Subjects with Generalized Pustular Psoriasis

Summary

EudraCT number	2017-004021-33
Trial protocol	GB
Global end of trial date	20 January 2021

Results information

Result version number	v1 (current)
This version publication date	05 February 2022
First version publication date	05 February 2022

Trial information

Trial identification

Sponsor protocol code	ANB019-002

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03619902
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AnaptysBio, Inc.
Sponsor organisation address	10770 Wateridge Circle, Suite 210, San Diego, United States, 92121
Public contact	AnaptysBio Clinical Trials Info, AnaptysBio Inc, 001 858 3626387, clinicaltrialinfo@anaptysbio.com
Scientific contact	AnaptysBio Clinical Trials Info, AnaptysBio Inc, 001 858 3626387, clinicaltrialinfo@anaptysbio.com

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	20 January 2021
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	20 January 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

- To evaluate the efficacy of imsidolimab (ANB019) in subjects with active generalized pustular psoriasis (GPP) as measured by the Clinical Global Impression (CGI) scale according to the modified Japanese Dermatology Association (JDA) severity index total score.

- To assess the safety and tolerability of imsidolimab in subjects with GPP.

Protection of trial subjects:

This study was conducted in compliance with the protocol, the International Council for Harmonisation (ICH) Guidance for Industry E6(R2) Good Clinical Practice (GCP): Consolidated Guidance, the Declaration of Helsinki, Institutional Review Board (IRB)/Independent Ethics Committee (IEC) requirements, and all applicable national and local regulatory requirements.
The original protocol, protocol amendments, informed consent form (ICF), Investigator Brochure (IB), and other relevant documents (eg, advertisements) were submitted to an IRB/IEC by the investigators and reviewed and approved by the IRB/IEC before the study was initiated.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	30 January 2019
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Poland: 5
Country: Number of subjects enrolled	United Kingdom: 3
Worldwide total number of subjects	8
EEA total number of subjects	5

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)	7
From 65 to 84 years	1
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study was conducted at 5 centers that enrolled subjects in the UK and Poland.

Pre-assignment

Screening details:

The study included a screening period of up to 42 days, a 12-week treatment period, and a 12-week safety follow-up period. A total of 12 subjects were screened, with 8 subjects being enrolled in the study.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Imsidolimab

Arm description:

Participants received imsidolimab 750 mg intravenously (IV) on Day 1 followed by administration of 3 doses of subcutaneous (SC) imsidolimab 100 mg on Days 29, 57, and 85.

Arm type	Experimental
Investigational medicinal product name	Imsidolimab
Investigational medicinal product code	ANB019
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Subcutaneous use, Intravenous use

Dosage and administration details:

Imsidolimab was administered as a single dose of IV imsidolimab 750 mg followed by 3 doses of SC imsidolimab 100 mg administered on Days 29, 57, and 85.

Number of subjects in period 1	Imsidolimab
Started	8
Completed	6
Not completed	2
Termination of study by investigator	1
Use of excluded/prohibited medication	1

Baseline characteristics

Reporting groups	
Reporting group title	Imsidolimab
Reporting group description:	
Participants received imsidolimab 750 mg intravenously (IV) on Day 1 followed by administration of 3 doses of subcutaneous (SC) imsidolimab 100 mg on Days 29, 57, and 85.	

Reporting group values	Imsidolimab	Total	
Number of subjects	8	8	
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	51.3		
standard deviation	± 14.91	-	
Gender categorical Units: Subjects			
Female	4	4	
Male	4	4	
Race Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	1	1	
Black or African American	0	0	
Native Hawaiian or Other Pacific Islander	0	0	
White	7	7	
Ethnicity Units: Subjects			
Hispanic or Latino	0	0	
Not Hispanic or Latino	8	8	
Modified Japanese Dermatological Association Severity Index (JDA-SI) Total Score			
The JDA-SI includes assessment of skin lesions (area of erythema with pustules, area of erythema total, and area of edema) and fever, white blood cell count, C-reactive protein and serum albumin levels. The total score ranges from 0 to 17 (severe).			
Units: score on a scale			
arithmetic mean	9.1		
standard deviation	± 2.75	-	

End points

End points reporting groups

Reporting group title	Imsidolimab

Reporting group description:

Participants received imsidolimab 750 mg intravenously (IV) on Day 1 followed by administration of 3 doses of subcutaneous (SC) imsidolimab 100 mg on Days 29, 57, and 85.

Primary: Percentage of Participants Achieving Clinical Response on the Clinical Global Impression (CGI) Scale

End point title	Percentage of Participants Achieving Clinical Response on the Clinical Global Impression (CGI) Scale[1]

End point description:

Clinical response was defined as "Very much improved," "Much Improved," or "Minimally Improved" on the CGI scale according to the Modified Japanese Dermatological Association Severity Index (JDA-SI) total score.
The JDA-SI includes assessment of skin lesions (area of erythema with pustules, area of erythema total, and area of edema) and fever, white blood cell count, C-reactive protein and serum albumin levels. The total score ranges from 0 to 17 (severe).

CGI was assessed based on the JDA-SI according to the following:
- Very Much Improved: Reduction in JDA-SI total score by 3 or > points;
- Much improved: Reduction in JDA-SI total score by 1 or 2 points;
- Minimally improved: No change in JDA-SI total score and area of erythema with pustules reduced by <20% or clinically meaningful improvement in at least 1 other component of the modified JDA-SI.

The full analysis set (FAS) included all enrolled subjects. Participants with missing data were categorized as non-responders.

End point type	Primary

End point timeframe:

Week 4 and Week 16

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No formal hypothesis testing was performed in this single arm study.

End point values	Imsidolimab			
Subject group type	Reporting group			
Number of subjects analysed	8[2]			
Units: percentage of participants				
number (confidence interval 95%)				
Week 4	75.0 (34.91 to 96.81)			
Week 16	75.0 (34.91 to 96.81)			

Notes:

[2] - Full Analysis set

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change from Baseline in Body Surface Area of Erythema with

Pustules at Week 1 and Week 4

End point title	Percent Change from Baseline in Body Surface Area of Erythema with Pustules at Week 1 and Week 4

End point description:

End point type	Secondary

End point timeframe:

Baseline, Week 1, and Week 4

End point values	Imsidolimab			
Subject group type	Reporting group			
Number of subjects analysed	8[3]			
Units: percent change				
arithmetic mean (standard deviation)				
Week 1	-59.63 (± 39.895)			
Week 4	-94.17 (± 10.737)			

Notes:

[3] - FAS; N=6 at Week 4

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change from Baseline in Modified Japanese Dermatological Association - Severity Index (mJDA-SI) Total Skin Lesions Score at Week 1, Week 4 and Week 16

End point title	Percent Change from Baseline in Modified Japanese Dermatological Association - Severity Index (mJDA-SI) Total Skin Lesions Score at Week 1, Week 4 and Week 16

End point description:

The area of erythema with pustules, area of total erythema and area of edema were assessed by the Investigator and scored from 0 to 3 on the following scale:
0: 0% body surface area (BSA);
1: > 0%, < 10% BSA;
2: ≥ 10%, < 50% BSA;
3: ≥ 50% BSA.
The JDA-SI Total Skin Lesions Score is the sum of the area of erythema with pustules score, area of total erythema score and area of edema score and ranges between 0 and 9.

End point type	Secondary

End point timeframe:

Baseline, Week 1, Week 4, and Week 16

End point values	Imsidolimab			
Subject group type	Reporting group			
Number of subjects analysed	8[4]			
Units: percent change				
arithmetic mean (standard deviation)				
Week 1	-25.74 (± 26.369)			
Week 4	-55.65 (± 27.157)			
Week 16	-62.20 (± 29.757)			

Notes:

[4] - FAS; N=6 at Week 4 and Week 16

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Achieving a Generalized Pustular Psoriasis Physician's Global Assessment (GPPPGA) Score of 0 or 1 at Week 1 and Week 4

End point title	Percentage of Participants Achieving a Generalized Pustular Psoriasis Physician's Global Assessment (GPPPGA) Score of 0 or 1 at Week 1 and Week 4

End point description:

The GPPPGA scale was used to assess the impact and severity of GPP on the following scale:
0: Clear (normal skin or post-inflammatory hyperpigmentation, no visible pustules, no scaling or crusting).
1: Almost clear (faint, diffuse pink or slight red erythema, low density occasional small discrete pustules (noncoalescent), superficial focal scaling or crusting restricted to periphery of lesions).
2: Mild (light red erythema, moderate density grouped discrete small pustules (noncoalescent), predominantly fine scaling or crusting).
3: Moderate (bright red erythema, high density pustules with some coalescence, moderate scaling or crusting covering most or all lesions).
4: Severe (deep fiery red erythema, very high density pustules with pustular lakes, severe scaling or crusting covering most or all lesions).

End point type	Secondary

End point timeframe:

Week 1 and Week 4

End point values	Imsidolimab			
Subject group type	Reporting group			
Number of subjects analysed	5[5]			
Units: percentage of participants				
number (confidence interval 95%)				
Week 1	0.0 (0.00 to 52.18)			
Week 4	50.0 (6.76 to 93.24)			

Notes:

[5] - Subjects with any GPPPGA assessment; N=4 at Week 4

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Dermatology Life Quality Index (DLQI) Total Score at Week 1, Week 4, and Week 16

End point title	Change from Baseline in Dermatology Life Quality Index (DLQI) Total Score at Week 1, Week 4, and Week 16

End point description:

The DLQI is a 10-item questionnaire that asks participants to evaluate the degree that their skin problem has affected their quality of life in the last week in the following 6 aspects: symptoms and feelings, daily activities, leisure, work or school activities, personal relationships and treatment related feelings. Participants answer the 10 questions on a scale from 0 (not at all) to 3 (very much). The DLQI is calculated by summing the scores of the 10 questions, resulting in a maximum of 30 and a minimum of 0 with higher scores indicating more impaired quality of life. A negative change from Baseline indicates improvement.

End point type	Secondary

End point timeframe:

Baseline and Week 1, Week 4, and Week 16

End point values	Imsidolimab			
Subject group type	Reporting group			
Number of subjects analysed	8[6]			
Units: score on a scale				
arithmetic mean (standard deviation)				
Week 1	-0.9 (± 3.56)			
Week 4	-6.0 (± 9.08)			
Week 16	-10.7 (± 9.16)			

Notes:

[6] - FAS; N= 6 at Week 4 and Week 16

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From first dose of study treatment up to end of follow-up period; 24 weeks.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	23.1

Reporting groups	
Reporting group title	Imsidolimab
Reporting group description:	
Participants received imsidolimab 750 mg intravenously (IV) on Day 1 followed by administration of 3 doses of subcutaneous (SC) imsidolimab 100 mg on Days 29, 57, and 85.	

Serious adverse events	Imsidolimab		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 8 (25.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Infections and infestations			
COVID-19			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nosocomial infection			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Imsidolimab		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 8 (75.00%)		
Vascular disorders			
Hypertension			

subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1		
General disorders and administration site conditions Peripheral swelling subjects affected / exposed occurrences (all) Swelling face subjects affected / exposed occurrences (all)	 1 / 8 (12.50%) 1 1 / 8 (12.50%) 1		
Reproductive system and breast disorders Vaginal haemorrhage subjects affected / exposed occurrences (all)	 1 / 8 (12.50%) 1		
Respiratory, thoracic and mediastinal disorders Oropharyngeal pain subjects affected / exposed occurrences (all)	 2 / 8 (25.00%) 2		
Investigations Blood folate decreased subjects affected / exposed occurrences (all) Blood glucose increased subjects affected / exposed occurrences (all) C-reactive protein increased subjects affected / exposed occurrences (all) White blood cell count increased subjects affected / exposed occurrences (all)	 1 / 8 (12.50%) 1 1 / 8 (12.50%) 1 1 / 8 (12.50%) 1 1 / 8 (12.50%) 1		
Injury, poisoning and procedural complications Humerus fracture subjects affected / exposed occurrences (all)	 1 / 8 (12.50%) 1		
Cardiac disorders			

Mitral valve prolapse subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1		
Myxomatous mitral valve degeneration subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1		
Nervous system disorders Presyncope subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1		
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1		
Lymphadenopathy subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 3		
Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1		
Toothache subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1		
Vomiting subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1		
Skin and subcutaneous tissue disorders Psoriasis subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1		
Skin haemorrhage subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1		
Renal and urinary disorders			

Acute kidney injury subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1		
Metabolism and nutrition disorders Hypokalemia subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 January 2018	Changes included the following: -Revised to indicate a minimum three-hour observation period after the first and second subcutaneous injections (from no such limit for study center observation after SC administration). - Revised Inclusion Criteria to specify that in addition to prohibition on sperm donation for the specified duration, ova donation for assisted reproduction is also prohibited. The duration for males was revised to 220 days (from 6 months).
26 July 2018	Changes included the following: - Overall Design revised to remove a minimum of 7 days screening period requirement and updated 'up to 28 days', and updated the number of Investigators and number of study centers from 3 to 5. - Updated Background to reflect Phase I Study results (ANB019-001). - Inclusion Criteria: Added SI and conventional units for hemoglobin, white blood cell count, platelets, and serum creatinine. - Exclusion Criteria: Text revised to clarify the requirement to stop all systemic conventional therapies (eg. cyclosporine, methotrexate, and retinoid) the day the study drug is administered and remove definition of regular alcohol consumption and excessive smoking. - Removed Meals and Dietary Restrictions. - included guidance for using rescue medication in the form of topical corticosteroids (eg. betamethasone valerate ointment and cream, mometasone furoate ointment and cream) and guidance for adding any systemic psoriasis medication that is likely to impact psoriasis signs and symptoms (eg. cyclosporine, methotrexate, retinoid). - Removed the section 8.1.4 describing assessment of body surface area affected by GPP. - Updated timing of bidirectional posterior-anterior and lateral view chest X-ray. - Added text regarding follow-up visits in case of early discontinuation. - Added text to indicate that a minimum 3 hour observation period is required after the first and second SC injections. - Storage duration of biomarker samples and immunogenicity samples was updated to 5 years from 1 year. - Added text to indicate that “only samples within the stability window of the assay will be analyzed”.

03 April 2019	Changes included the following: - Updated the number of Investigators and number of study centers from 5 to 8-10. - Added an additional secondary endpoint to assess the proportion of subjects achieving a score of 0 or 1 on the Generalized Pustular Psoriasis Physician's Global Assessment scale. Additional wording added to the secondary endpoints for PK analysis; moved immunogenicity objective (to assess ADA) from exploratory to secondary endpoint; retitled tertiary/exploratory endpoints section to exploratory endpoints. - Revised the screening period from "up to 28 days" to "up to 42 days (Week -0)." - Added Table to detail the sample collection and time points for PK and ADA testing. - Inclusion Criteria revised to to increase the upper age limit from 65 to 75, define the limit of ALT and AST to ≤ 2 × ULN, and revise disease criteria for study entry. - Exclusion criteria revised to remove 2 examples of other forms of psoriasis that were excluded from participation. - Added wording to clarify that study treatment may be interrupted only once before being permanently discontinued. - New section added to describe the GPPPGA scale. - Clarified that ECGs will be reviewed by the central laboratory "for quality and interpretation" and that ECG data would not be entered into EDC with the exception of clinical significance. Photography language was revised to describe a standardized approach for collection of photographs and the process for transfer and quality review. - Added a clarification that Investigator may review laboratory assessments to make a decision about safety or to determine subject eligibility for the study. - Genetics language revised to characterize additional DNA/RNA testing and optional pharmacogenomic testing. - Text added to better characterize the presentation of statistical data for ADA status and efficacy and safety endpoints - Added 3 references - Added new appendix to support added secondary endpoint of the GPPPGA assessment.
30 August 2019	Changes included the following: - Revised the secondary objectives to remove change from Baseline in GPPPGA score at all study visits and to assess change in Dermatology Life Quality Index (DLQI) total score instead of improvement in DLQI total score at all visits. Exploratory endpoint was revised for skin biopsies to assess IL-8 dendritic cells, not IL-6 dendritic cells. Removed references to logistic regression model using logit link. - Added one paragraph in Benefit/Risk Assessment about an SAE of sepsis that has been reported during the study for 1 subject. - Inclusion Criteria that specified the enrollment of subjects with or without a history of PP and PsA was removed. A statement was added that any laboratory values that are out-of-range at Screening will be left to the Investigator's discretion as to whether or not a subject is eligible. - Exclusion Criteria modified to include squamous cell carcinoma deemed fully treatable by the Investigator as permissible. - Clarified the language around dose administration and to state that infusions may be slowed for subjects experiencing infusion-related reactions. - Revised the statement on collection of AEs to include any occurring through End of Study. - Clarified PK sample collection and documentation. - Removed the ITT Analysis Set and replaced with Full Analysis Set (FAS). Removed any references to randomization. The PPS will now be based on the FAS instead of the ITT set. Additional text was added to clarify use of the PK analysis set. - Added a clarification on the analysis of clinical response and Clinical Global Impression (CGI) score. - Clarified that secondary endpoints will be analyzed at all study visits through Week 16 for modified JDA SI score, descriptive statistics, GPPPGA score, and PASI. - Included a statement that summary statistics will be provided for average DLQI scores instead of absolute scores, in addition to the percent change from Baseline through Week 16.

29 October 2019	Changes included the following: - The sentence permitting the Investigator to assess eligibility in consultation with the Medical Monitor and the Sponsor, for those subject who fail to meet laboratory screening criteria, has been removed.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported