Imsidolimab, an Anti-IL-36 Receptor Monoclonal Antibody for the Treatment of Generalised Pustular Psoriasis: Results from the Phase 2 GALLOP Trial

Running heading: Imsidolimab for the treatment of GPP

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What is already known about this topic?

- Generalised pustular psoriasis (GPP) is a systemic inflammatory disease. Uncontrolled activation of IL-36 pro-inflammatory activity may underlie the pathogenesis of GPP. Currently, treatment options for GPP are limited.

What does this study add?

- Imsidolimab is being developed as a targeted therapy for GPP. Results from this Phase 2 study demonstrated a rapid resolution of symptoms and pustular eruptions in subjects with GPP flare after treatment with imsidolimab.

Abstract

Background Generalised pustular psoriasis (GPP) is a systemic inflammatory disease that can be severe, debilitating, and life-threatening. Uncontrolled activation of interleukin-36 (IL-36) pro-inflammatory activity may underlie the pathogenesis of GPP. Currently, GPP-specific treatment options are limited.

Objectives To evaluate the efficacy and safety of the anti-IL-36 receptor antibody imsidolimab in subjects with GPP.

Methods In an open-label, single-arm, multiple-dose study, subjects with GPP were treated with imsidolimab to assess clinical efficacy, tolerability, and safety. Subjects received an intravenous (IV) imsidolimab 750 mg dose on Day 1, followed by 3 doses of subcutaneous (SC) imsidolimab 100 mg administered on Days 29, 57, and 85. The primary efficacy endpoint was the proportion of subjects that achieved a clinical response at Week 4 and Week 16 following treatment with imsidolimab as measured by the Clinical Global Impression (CGI) scale.

Results A total of 8 patients were enrolled and 6 subjects completed the study. Responses were observed as early as Day 3, most rapidly for pustulation relative to other manifestations of GPP, with continued and consistent improvement across multiple efficacy assessments at Day 8, Day 29, and through Day 113. Most treatment-emergent adverse events (TEAEs) were mild to moderate in severity. No subject discontinued the study due to a non-serious TEAE. Two subjects experienced serious adverse events (SAEs) and no deaths were reported.

Conclusions Imsidolimab demonstrated a rapid and sustained resolution of symptoms and pustular eruptions in subjects with GPP. It was generally well-tolerated, associated with acceptable safety, and is advancing to Phase 3 trials. These data support targeting of IL-36 signalling with a specific antibody, imsidolimab, as a therapeutic option for this severely debilitating condition. The study was registered under EudraCT Number 2017-004021-33 and NCT 03619902.

Introduction

Generalised pustular psoriasis (GPP) is a rare, but severe and debilitating disease characterised by widespread sterile pustules on erythematous skin[1-4] that is often accompanied by systemic signs and symptoms such as fever, nausea, pain, anorexia, and general malaise.[1,4-6] Life-threatening complications of GPP can include sepsis, acute renal failure, high-output congestive cardiac failure, and acute respiratory distress syndrome.[6-7]

Factors that may trigger GPP onset include viral or bacterial infections, corticosteroid use, hypocalcaemia, psychological stress, and pregnancy.[7-9] Recurrent flares are common, even years after initial diagnosis.[10-11] While it is possible for GPP to manifest in the presence of psoriasis vulgaris (PV), studies suggest that the underlying pathophysiologic mechanisms of GPP and PV may differ and that the innate immune system plays a greater role in the pathogenesis of GPP.[11-14] Dysregulated interleukin-36 (IL-36) signalling was implicated in the pathogenesis of GPP following the identification of loss-of-function mutations in *IL36RN*, the gene encoding IL-36 receptor antagonist (IL-36RA)[15-18] in a subset of patients with GPP. IL-36 cytokines (IL-36α, IL-36β, and IL-36γ) engage with the IL-36 receptor (IL-36R) to initiate signalling events leading to pro-inflammatory responses.[19-21] IL-36RA normally opposes IL-36 mediated signalling.[22-24] Approximately 46-82% of GPP cases without PV have mutations in *IL36RN*[25-26], while the proportion of *IL36RN* mutant carriage is much lower (10-17%) in cases of GPP associated with PV.[27] It was subsequently determined that IL-36 is a dominant cytokine in GPP[28], suggesting that excessive IL-36 mediated pro-inflammatory activity may broadly underlie the pathogenesis of GPP. Therefore, targeting IL-36R represents a rational therapeutic strategy to control the pathological inflammatory cascade in GPP.[14, 29]

This Phase 2 study was designed to evaluate the efficacy and safety of imsidolimab in subjects with GPP flare. Imsidolimab is a high-affinity humanised immunoglobulin G4 (IgG4) monoclonal antibody (mAb) that specifically binds IL-36R, antagonising IL-36 signalling. Targeting IL-36R represents an elegant therapeutic strategy to control pathogenic pro-inflammatory IL-36 pathway activation in GPP. Results of a placebo-controlled clinical trial of spesolimab, another mAb against the IL-36R, showed significant efficacy in subjects with GPP flare.[35] Currently, GPP can be difficult to manage chronically[31], and there is no standard guidance for GPP therapy in most countries.[5, 30] While acitretin is indicated for extensive and severe refractory forms of psoriasis in the EU, and the biologic agents secukinumab, ixekizumab, brodalumab, and guselkumab have been approved in Japan to treat GPP[30-31], rigorous and well-controlled efficacy data in GPP are lacking. Therefore, there is a need for additional safe and more effective treatments to manage GPP.

Materials & Methods

Study Design and Participants

GALLOP was an open-label, single-arm, multiple-dose study to assess the clinical efficacy, tolerability, and safety of multiple doses of imsidolimab in subjects with active GPP.

Eligibility criteria included the following: subjects 18 to 75 years of age, with a clinically confirmed diagnosis of active GPP, Japanese Dermatology Association severity index (JDA-SI) total score of >6 with active pustules and erythema accounting for at least 10% of body-surface area (BSA) or had a Generalised Pustular Psoriasis Physician's Global Assessment (GPPPGA) score of at least moderate severity and must have been a candidate for systemic therapy or phototherapy. Patients were excluded if

they had any other forms of psoriasis except concomitant PV. Any concurrent therapies likely to have efficacy in GPP or psoriasis were washed out and their use was prohibited during participation.

The study had a Screening Period of up to 42 days (6 weeks), treatment period of 12 weeks, and follow-up period of 12 weeks for a total duration of 30 weeks (Figure 1). Written informed consent was obtained from each subject prior to initiating any study-related procedures. Ethics Committee approvals were obtained at all participating centres; the study complied with the International Council for Harmonisation's Good Clinical Practice and local regulations, and the study was conducted according to the Helsinki declaration.

Study Treatments and Assessments

Subjects were to receive an intravenous (IV) imsidolimab 750 mg dose on Day 1, followed by 3 doses of subcutaneous (SC) imsidolimab 100 mg administered on Days 29, 57, and 85. The doses selected for this study have demonstrated favourable safety profile and prolonged pharmacodynamic (PD) activity in a Phase 1 study (ANB019-001). A loading dose of 750 mg IV was administered on Day 1 to enable steady state concentration to be reached faster at initiation of the imsidolimab 100 mg SC dose.

At study visits, changes in disease activity (response to study treatment), safety, and tolerability were monitored. Disease activity was evaluated using the Clinical Global Impression (CGI) scale according to the modified JDA-SI (mJDA-SI[32]). The mJDA-SI is a composite GPP instrument comprised of assessments of skin lesions (area of erythema with pustules, area of erythema [total], and area of oedema) and systemic manifestations and laboratory findings (fever, white blood cell count, C-reactive protein, and serum albumin). The CGI is an instrument that categorises overall GPP status as either "Very much improved", "Much improved", "Minimally improved", "No change", or "Worsened" based on the change in mJDA-SI total score from Baseline and/or descriptors of clinical severity. In addition, change in total BSA affected by GPP as measured by mJDA-SI, systemic manifestations, and laboratory findings as per mJDA-SI, GPPPGA scale[29], and quality of life (QoL), using the Dermatology Life Quality Index (DLQI)[34], was assessed. The GPPPGA scale is scored from 0 (clear) to 4 (severe), with morphological descriptors of each level of disease severity that encompass major signs of the disease (erythema, pustulation, scaling/crusting). For inflammatory skin conditions, a change in DLQI of at least 4 points is generally considered a minimally clinically important difference (MCID).

Safety assessments including adverse event (AE)/serious adverse event (SAE) monitoring, vital signs measurements, physical examination, electrocardiograms (ECGs), laboratory measurements, and urine assessments were performed during the study.

Endpoints

The primary efficacy endpoint was the proportion of subjects in the Full Analysis Set (N=8) that achieved a clinical response at Week 4 and at Week 16 following treatment with imsidolimab as measured by the CGI scale. Clinical response was defined as achieving "Very Much Improved," "Much Improved," or "Minimally Improved" on the CGI scale according to the mJDA-SI total score.

The secondary efficacy endpoints were the change in affected BSA of erythema with pustules, erythema, and oedema as measured by mJDA-SI by study visit, the change from Baseline in GPPPGA scores by study visit, and the change in DLQI by study visit.

Efficacy was also evaluated using the GPPPGA scale; however, the GPPPGA scale was added to the study after the first 3 subjects had already enrolled in response to a request from the FDA. Therefore, data on GPPPGA at Baseline was only available for 5 of 8 subjects. Additionally, one of the 5 subjects with a

Baseline GPPPGA score discontinued from the study at Day 29; thus only 4 of 5 subjects had GPPPGA scores from Week 4 onward.

Statistical Analysis

Statistical analysis was performed using statistical analysis system (SAS®) Version 9.4. The default summary statistics for continuous variables includes number of contributing observations (n), mean, standard deviation (SD), median, minimum, and maximum. Unless otherwise specified, "Baseline" was defined as the last non-missing measurement taken prior to the reference start date and time (this included unscheduled visits). For numerical variables, change from Baseline was calculated as the difference between the value of interest and the corresponding Baseline value. Point estimates were accompanied with 2-sided 95% confidence intervals (CI), where applicable.

Results

Demographic and Other Baseline Characteristics

Study participants (N=8) were enrolled at 5 sites in the UK and Poland and were 50% female, with a mean (SD) age of 51.3 (14.91) years, mean (SD) body mass index (BMI) of 28.86 (3.417) kg/m^2, and mean (SD) time since GPP diagnosis of 3.99 (6.48) years (Table 1). All but 1 subject was white. The mean (SD) Baseline total mJDA-SI Score was 9.1 (2.75), consistent with at least moderate disease severity (mild, n=1; moderate, n=5; severe, n=2). The mean (SD) area of erythema with pustules was 23.51% (18.15), and of the 5 subjects who were administered the GPPPGA scale, the Baseline score was 3.8 (moderate, n=1; severe, n=4). Genotypic testing, using Sanger sequencing, indicated homozygous wild-type *IL36RN*, *CARD14*, and *AP1S3* alleles for all 8 subjects treated in this study.

The Full Analysis Set included all subjects, regardless of whether treatment was received or not. A total of 8/8 subjects received the initial imsidolimab IV infusion and 6/8 (75%) subjects received all 3 follow-up SC doses. The 2 subjects who did not receive the follow-up SC imsidolimab doses had discontinued from the study early. One subject was discontinued due to use of a prohibited medication (infliximab). The second subject was discontinued due to lack of improvement.

Primary Efficacy Endpoint: Proportion of Subjects Achieving Clinical Response at Week 4 and Separately at Week 16 Following Treatment with Imsidolimab as Measured by the CGI Scale

At Weeks 4 and 16, 75% of subjects were CGI responders (Figure 2). Among responders, 50% were "Very much improved."

Secondary Efficacy Endpoint: Change in Affected BSA of Erythema with Pustules, Erythema, and Oedema as Measured by mJDA-SI by Study Visit

Concurrent and substantial improvement was observed in the 3 skin components of GPP: pustules, erythema, and oedema. Improvement was sustained through the duration of imsidolimab treatment. Following imsidolimab administration, BSA covered by erythema with pustules improved most rapidly based on the mJDA-SI skin component assessment. Mean BSA covered by erythema with pustules was 23.51% at Baseline (Figure 3A). The percent change from Baseline was -60% by Day 8 and -94% by Week 4 (Day 29) (Figure 3B). Mean BSA with erythema was 50.89% at Baseline (Figure 3C). The percent change from Baseline was -30% on Day 29 and -60% on Day 113 (Figure 3D). Mean BSA with oedema was 33.76% at Baseline (Figure 3E). The percent change from Baseline was -77% on Day 29 and

-78% on Day 113 (Figure 3F). Percent changes from Baseline were sustained throughout the duration of treatment.

Secondary Efficacy Endpoint: Change from Baseline in GPPPGA Scores by Study Visit

The severity of GPP was assessed using the GPPPGA scale, which captures the investigator's assessment of the overall disease severity at the time of evaluation. GPPPGA was added after the study started; therefore, a baseline assessment was only available for 5 of the study subjects and one discontinued prior to Day 29. Therefore, Weeks 4 and 16 GPPPGA assessments are only possible for 4 subjects.

Following imsidolimab treatment by Week 4, the mean (SD) change from Baseline GPPPGA score improved (decreased) by -2.5 (0.58) and the mean (SD) percent change from Baseline was -62.5% (14.4%) on the GPPPGA scale (Table 2). At Week 16, the mean (SD) change from Baseline was -3.0 (0.82) and the mean (SD) percent change from Baseline was -75.0% (20.4%).

Secondary Efficacy Endpoint: Change in Dermatology Life Quality Index (DLQI) Total Score by Study Visit

Consistent with the improvements observed in the other clinical measures of GPP severity, the subject-reported DLQI measure also improved over time following imsidolimab treatment (Figure 4). Subjects had a mean DLQI of 15.8 at Baseline, indicating a very large effect on the subjects' health-related QoL. Following administration of imsidolimab, DLQI continued to improve through Week 20 (Day 141). By Day 29, the DLQI total score improved (decreased) from Baseline to 11.7 and to 9.7 by Day 141.

Photographic Documentation of Disease Improvement

While photography was not captured for all subjects, observations on photographic images were consistent with improvements assessed in other clinical measures of GPP (Figure 5). The photographs documented a rapid and sustained improvement in disease severity following imsidolimab treatment for these subjects (n=2).

Safety Evaluation

No deaths occurred during the study and no subjects withdrew due to a TEAE. Overall, 6 out of 8 subjects (75.0%) experienced at least 1 TEAE during the treatment period (Table 3). The most commonly reported TEAEs by system organ classes (SOCs) (25.0% each) were Blood and Lymphatic System Disorders, Gastrointestinal Disorders, Infections and Infestations, Investigations, Respiratory, Thoracic and Mediastinal Disorders, and Skin and Subcutaneous Tissue Disorders. Two subjects reported TEAEs that were deemed moderate in severity and possibly related to study drug treatment: 1 subject experienced a moderate flare of plaque psoriasis, and the second subject experienced a moderate sore throat. No subjects reported TEAEs associated with infusion or injection site reactions.

Two SAEs were reported. One subject developed a SAE of SARS-CoV-2 infection that was deemed unrelated to study drug treatment. This subject fully recovered and resumed study treatment. Another subject developed sepsis while in the hospital that was assessed as possibly related to study drug treatment, following a non-serious AE of *S. aureus* bacteraemia. This subject fully recovered with appropriate antibiotic therapy and subsequently discontinued from the study upon use of a prohibited medication (infliximab) for treatment of GPP.

Discussion

Imsidolimab appeared generally well-tolerated and demonstrated a rapid and sustained improvement of symptoms and pustular eruptions in subjects with GPP flare, which was consistent across the clinical measures assessed. Taken together, these results indicate that imsidolimab may represent a useful approach to GPP treatment. In addition, an initial IV infusion of imsidolimab followed by monthly SC dosing, as utilised in this study, is an attractive approach for GPP treatment since rapid control of the flare and convenient maintenance of the underlying disease is desirable.

The onset of action of imsidolimab was rapid following the initial infusion, with responses observed as early as Day 3 (Figure 2). Continued and consistent improvement through Week 16 was observed with subsequent monthly SC maintenance dosing. A rapid onset of action and response is particularly desirable in GPP since patients often experience uncomfortable and potentially life-threatening systemic signs and symptoms during a pustular flare. The 2 subjects who discontinued the study before Week 4 both had a "Much Improved" score at their last observation on the CGI scale before study discontinuation. Reductions in pustules, oedema, and erythema were observed over the course of the study. The mJDA-SI skin component assessment of BSA covered with erythema with pustules was the most rapidly improved skin component of GPP following imsidolimab administration (Figure 3). Following imsidolimab treatment, by Week 4, the mean change from Baseline GPPPGA score also improved (decreased) (Table 2). Impact on subjects' QoL was assessed by quantifying responses to the patient-reported outcome measure DLQI. Consistent with the improvements observed in the objective clinical measures of GPP severity, the subject-reported DLQI measure also improved over time following imsidolimab treatment (Figure 4). Photographs documented rapid and sustained clinical improvement in disease severity following imsidolimab treatment for subjects (Figure 5). It is also notable that genotypic testing indicated homozygous wild-type *IL36RN*, *CARD14*, and *AP1S3* alleles for all 8 of the subjects treated in this study, which provides additional evidence that the pathogenic role of IL-36 activation in GPP extends beyond individuals with known *IL36RN* mutations.

The dosage utilised in this study, IV imsidolimab 750 mg dose on Day 1, followed by 3 doses of SC imsidolimab 100 mg administered on Days 29, 57, and 85, was generally well-tolerated. The majority of TEAEs were mild to moderate in severity and no deaths were reported. No subject discontinued the study due to a TEAE. Three subjects experienced TEAEs that were assessed as possibly related to study drug treatment.

Studies have shown the importance of IL-36 signalling in GPP, which represents a rational strategy to control the pathological inflammatory cascade in this condition, and the utility of this therapeutic approach was further validated by a recently reported placebo-controlled clinical trial of spesolimab.[15-16, 28, 35] While the GALLOP results provide useful and promising information about the emerging benefit-risk profile of imsidolimab in GPP, the small size and open-label design of this study are limitations. Double-blind, placebo-controlled, global multicentre Phase 3 trials of imsidolimab in GPP, designed to provide a more robust evaluation of this promising approach to GPP treatment, are currently ongoing (NCT05352893 and NCT05366855).

In conclusion, results from this Phase 2 study demonstrated that treatment with imsidolimab produced a rapid resolution of symptoms and pustular eruptions in subjects with GPP flare. These results suggest that specifically targeting IL-36 pathway activation, which is increasingly implicated as central to the pathophysiology of GPP, with a mAb to IL-36R could provide reliable, rapid, and sustained efficacy in patients experiencing GPP flare. This could potentially revolutionise GPP treatment in a manner similar to that produced by anti-cytokine therapies for PV.

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Figure legends

Figure 1 - Study Design

Figure 2 - Primary Efficacy Endpoint: Proportion and Number of Subjects Achieving Clinical Response on the CGI by Study Visit (Full Analysis Set)

Figure 3 - Secondary Efficacy Endpoint: Descriptive Statistics of Actual and Change from Baseline for Percentage Affected Area of Erythema with Pustules, Erythema and Oedema (Full Analysis Set). The affected BSA of erythema with pustules (A), percent change from Baseline of erythema with pustules (B), the affected BSA of erythema (C), percent change from Baseline of erythema (D), affected BSA of oedema (E), and percent change from Baseline of oedema (F).

Figure 4 - Secondary Efficacy Endpoint: Total Dermatology Life Quality Index (DLQI) Score by Study Visit (Full Analysis Set)

Figure 5 - Longitudinal Photographs of Two Subjects with GPP Treated with Imsidolimab

Demographics	Statistic	Safety Analysis Set (N=8)
Age (Years)	n	8
	Mean (SD)	51.3 (14.9)
	Median	53.0
	Min, Max	29, 69
Gender		
Male	n (%)	4 (50.0)
Female	n (%)	4 (50.0)
Ethnicity		
Hispanic or Latino	n (%)	0
Not Hispanic or Latino	n (%)	8 (100.0)
Race		
American Indian or Alaska Native	n (%)	0 (0.0)
Asian	n (%)	1 (12.5)
Black or African American	n (%)	0 (0.0)
Native Hawaiian or Other Pacific Islander	n (%)	0 (0.0)
White	n (%)	7 (87.5)
Other	n (%)	0 (0.0)
Missing	n (%)	0 (0.0)
Weight (kg) at Baseline	n	8
	Mean (SD)	78.8 (13.3)
	Median	75.0
	Min, Max	60.0, 98.0
Body Mass Index (BMI) (kg/m^2) at Baseline	n	8
	Mean (SD)	28.9 (3.4)
	Median	29.2
	Min, Max	24.5, 33.9
mJDA Severity Index Total Score at Baseline[a]	n	8
	Mean (SD)	9.1 (2.8)
	Median	8.5
	Min, Max	6, 14
mJDA Severity Index at Baseline	Mild [n (%)]	1 (12.5)
	Moderate [n (%)]	5 (62.5)
	Severe [n (%)]	2 (25.0)
Skin Lesions Score at Baseline (%)		
Area of erythema with pustules	n	8
	Mean (SD)	23.5 (18.2)
	Median	13.5
	Min, Max	8.0, 55.1
Area of erythema (total)	n	8
	Mean (SD)	50.9 (30.1)
	Median	45.6
	Min, Max	15.0, 91.0
Area of oedema	n	8
	Mean (SD)	33.8 (18.8)
	Median	27.5
	Min, Max	11.0, 60.0
GPPPGA Score at Baseline	Clear [n (%)]	0 (0.0)
	Almost Clear [n (%)]	0 (0.0)

Demographics	Statistic	Safety Analysis Set (N=8)
	Mild [n (%)]	0 (0.0)
	Moderate [n (%)]	1 (12.5)
	Severe [n (%)]	4 (50.0)
Number of years since GPP diagnosis	n	8
	Mean (SD)	4.0 (6.5)
	Median	1.1
	Min, Max	0.0, 19.0
PASI Score at Baseline[b]	n	5
	Mean (SD)	21.18 (16.768)

Age is relative to informed consent. If the date of birth is partial, age is calculated using the available parts of the date. If the Medical History start date of GPP is partial, number of years since GPP diagnosis is calculated using the available parts of the date. "Baseline" is defined as the last observed value of the parameter of interest prior to the first intake of study drug.
Abbreviations: GPP = generalised pustular psoriasis; GPPPGA = Generalised Pustular Psoriasis Physician's Global Assessment; mJDA = modified Japanese Dermatological Association; N = total number of subjects in the safety analysis set; n = number of subjects with available data; SD = standard deviation.
[a] The study population (N=8) includes 1 patient that did not meet the Inclusion Criterion JDA severity index total score >6 or present with active pustules and erythema accounting for at least 10% of BSA. This was considered a non-important protocol deviation.
[b] Change in PASI score from Baseline was used to assess response to imsidolimab treatment in subjects with concomitant plaque psoriasis.

Table 1 - Demography and Baseline Characteristics (Safety Analysis Set)

Visit Statistic	Total (N=5)		
	Result	Change from Baseline	% Change from Baseline
Baseline			
n	5	N/A	N/A
GPPPGA Mean (SD)	3.8 (0.45)	N/A	N/A
95% CI	(3.24, 4.36)	N/A	N/A
Median	4	N/A	N/A
Min, Max	3, 4	N/A	N/A
Week 4			
n	4	4	4
GPPPGA Mean (SD)	1.5 (0.58)	-2.5 (0.58)	-62.5 (14.4)
95% CI	(0.58, 2.42)	(-3.42, -1.58)	(-85.5, -39.5)
Median	1.5	-2.5	-62.5
Min, Max	1, 2	-3, -2	-75.0, -50.0
Week 16			
n	4	4	4
GPPPGA Mean (SD)	1.0 (0.82)	-3.0 (0.82)	-75.0 (20.4)
95% CI	(-0.30, 2.30)	(-4.30, -1.70)	(-107.5, -42.5)
Median	1	-3	-75
Min, Max	0, 2	-4, -2	-100.0, -50.0

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.
Baseline refers to the last non-missing measurement taken prior to the reference start date (including unscheduled assessments).
Abbreviations: CI = confidence interval; GPPPGA = Generalised Pustular Psoriasis Physician's Global Assessment; N = total number of subjects with GPPPGA at Baseline in the Full Analysis Set; n = number of subjects with available data; N/A = not applicable; PASI = Psoriasis Area Severity Index; SD = standard deviation.

Table 2 - Secondary Efficacy Endpoint: Descriptive Statistics of Actual and Change from Baseline for GPPPGA Scores of Subjects with GPPPGA at Baseline (Full Analysis Set for Subjects with GPPPGA at Baseline)

Characteristic	Total (N=8) n (%)
Subjects with at least 1:	
TEAE	6 (75.0)
Related or Possibly Related TEAE	3 (37.5)
Severe TEAE	1 (12.5)
Serious TEAE	2 (25.0)
TEAE leading to discontinuation of study drug	1 (12.5)
TEAE leading to study discontinuation	0 (0.0)
Infusion-related TEAE or injection site reaction	0 (0.0)
MedDRA System Organ Class Preferred Term	
Blood and lymphatic system disorders	**2 (25.0)**
Anaemia	1 (12.5)
Lymphadenopathy	1 (12.5)
Gastrointestinal disorders	**2 (25.0)**
Nausea	1 (12.5)
Toothache	1 (12.5)
Vomiting	1 (12.5)
Infections and infestations	**2 (25.0)**
COVID-19	1 (12.5)
Nosocomial infection	1 (12.5)
Investigations	**2 (25.0)**
Blood folate decreased	1 (12.5)
Blood glucose increased	1 (12.5)
C-reactive protein increased	1 (12.5)
White blood cell count increased	1 (12.5)
Respiratory, thoracic and mediastinal disorders	**2 (25.0)**
Oropharyngeal pain	2 (25.0)
Skin and subcutaneous tissue disorders	**2 (25.0)**
Psoriasis	1 (12.5)
Skin haemorrhage	1 (12.5)

Abbreviations: COVID-19 = coronavirus disease of 2019; MedDRA = Medical Dictionary for Regulatory Activities; n = number of subjects with available data; N = total number of subjects in the safety analysis set; TEAE = treatment-emergent adverse event.

Table 3. Overview of Treatment-Emergent Adverse Events (Safety Analysis Set)

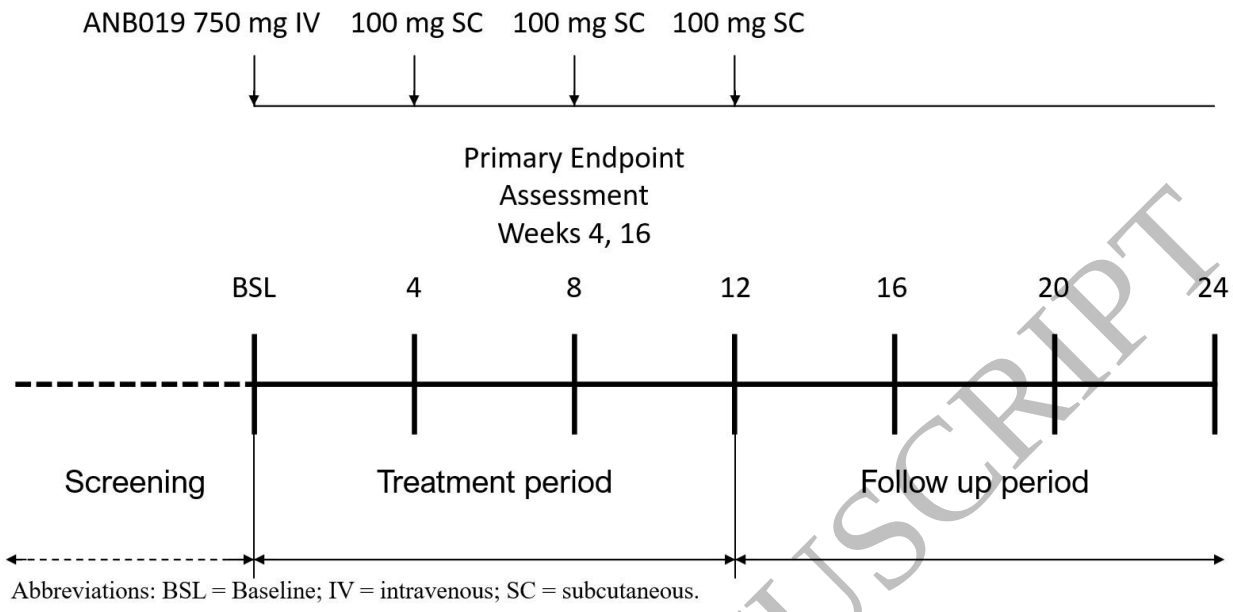

Figure 1
278x136 mm (x DPI)

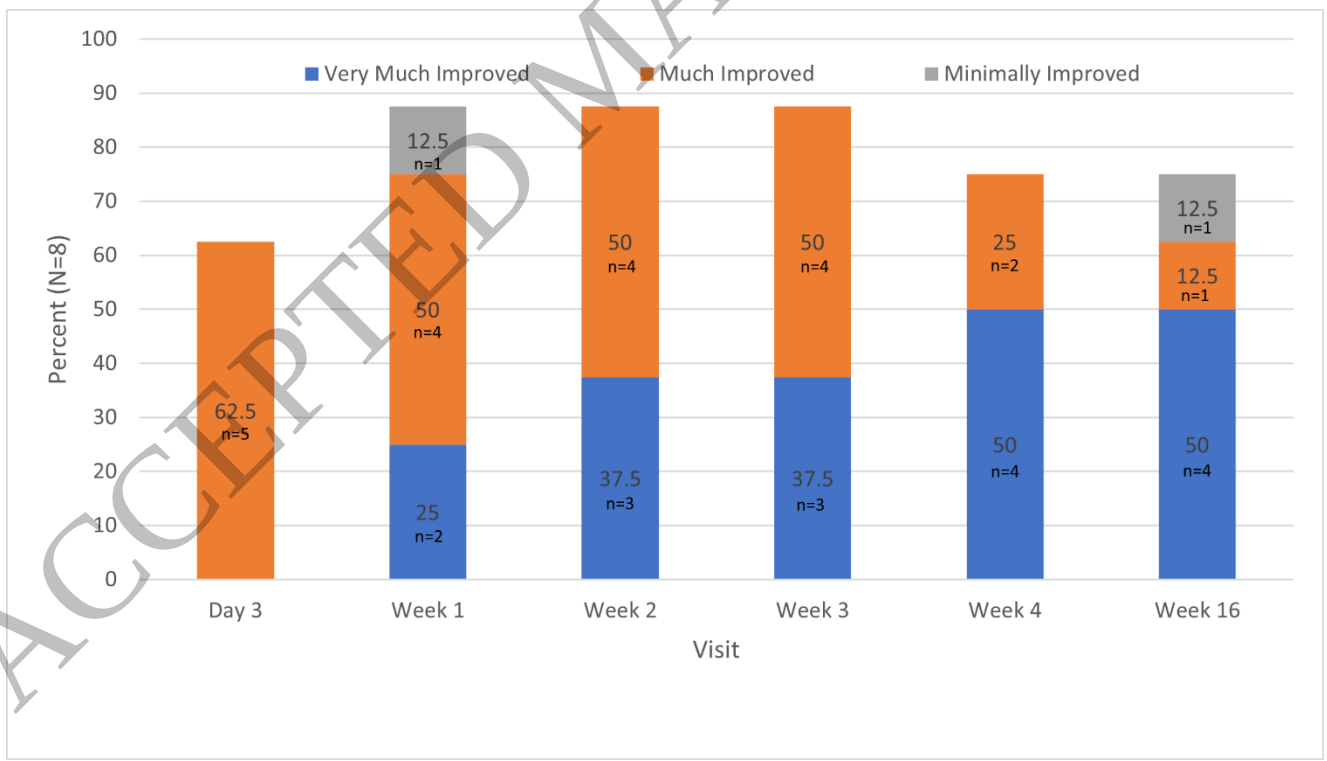

Figure 2
174x99 mm (x DPI)

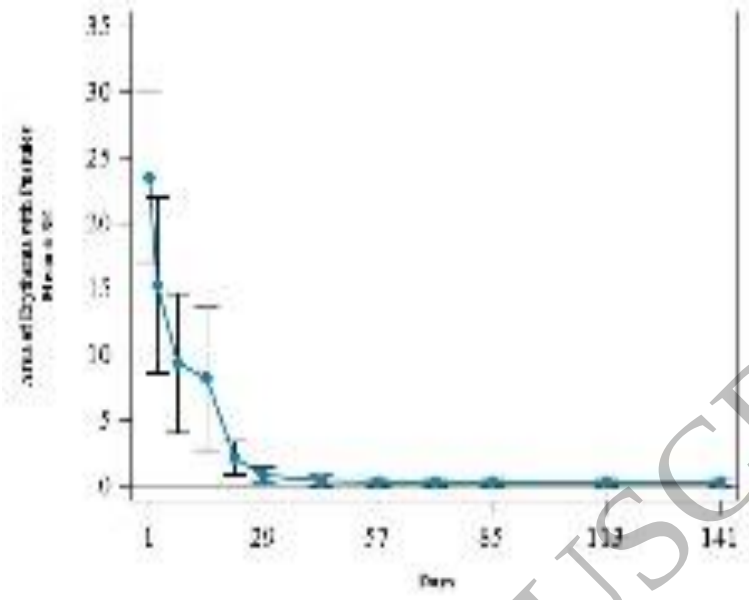

Figure 3
26x18 mm (x DPI)

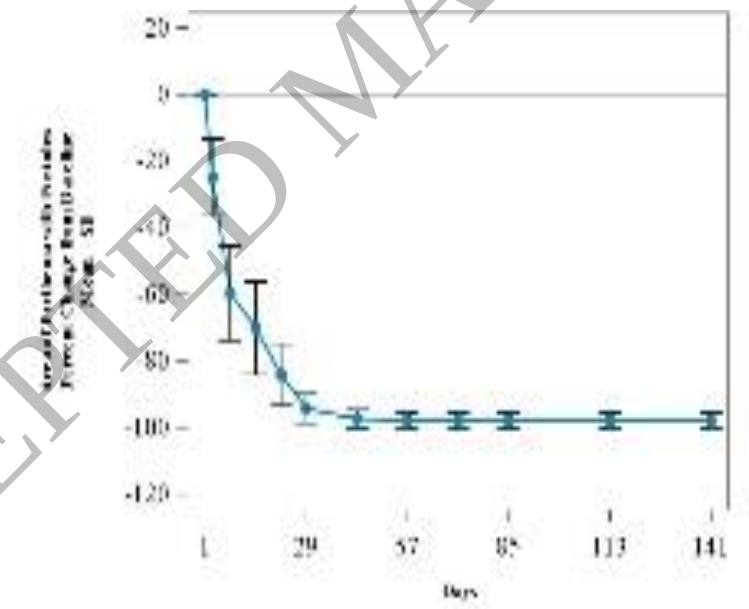

Figure 4
26x17 mm (x DPI)

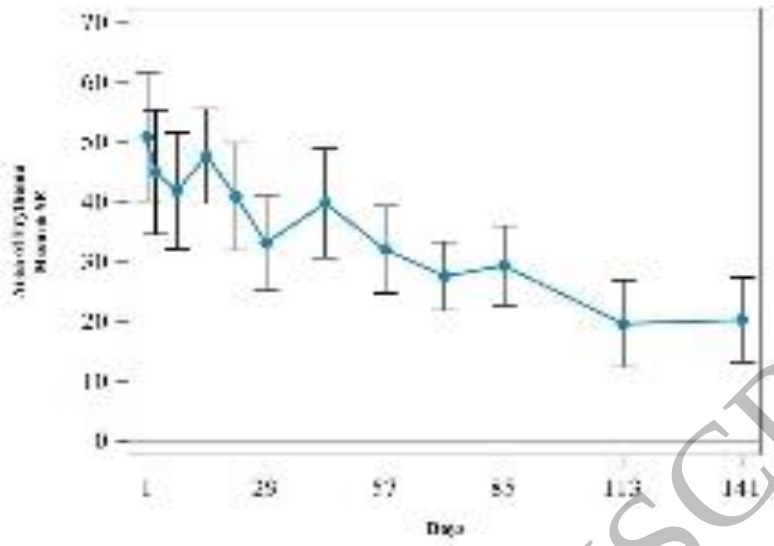

Figure 5
25x20 mm (x DPI)

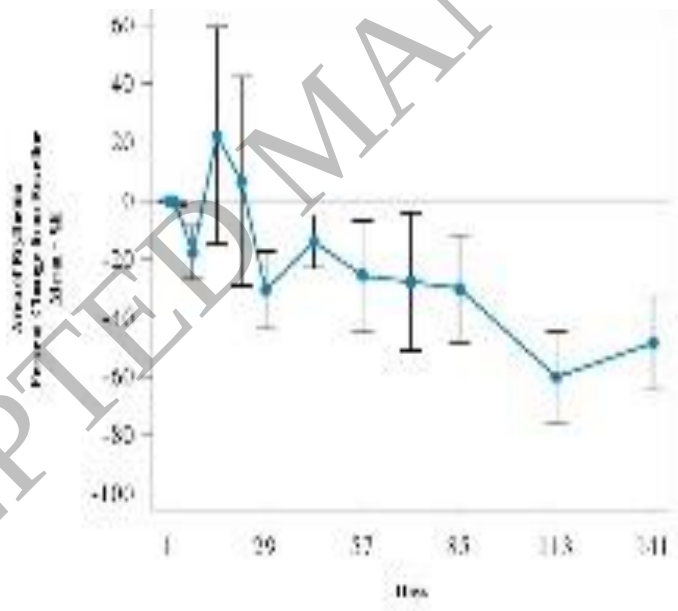

Figure 6
26x18 mm (x DPI)

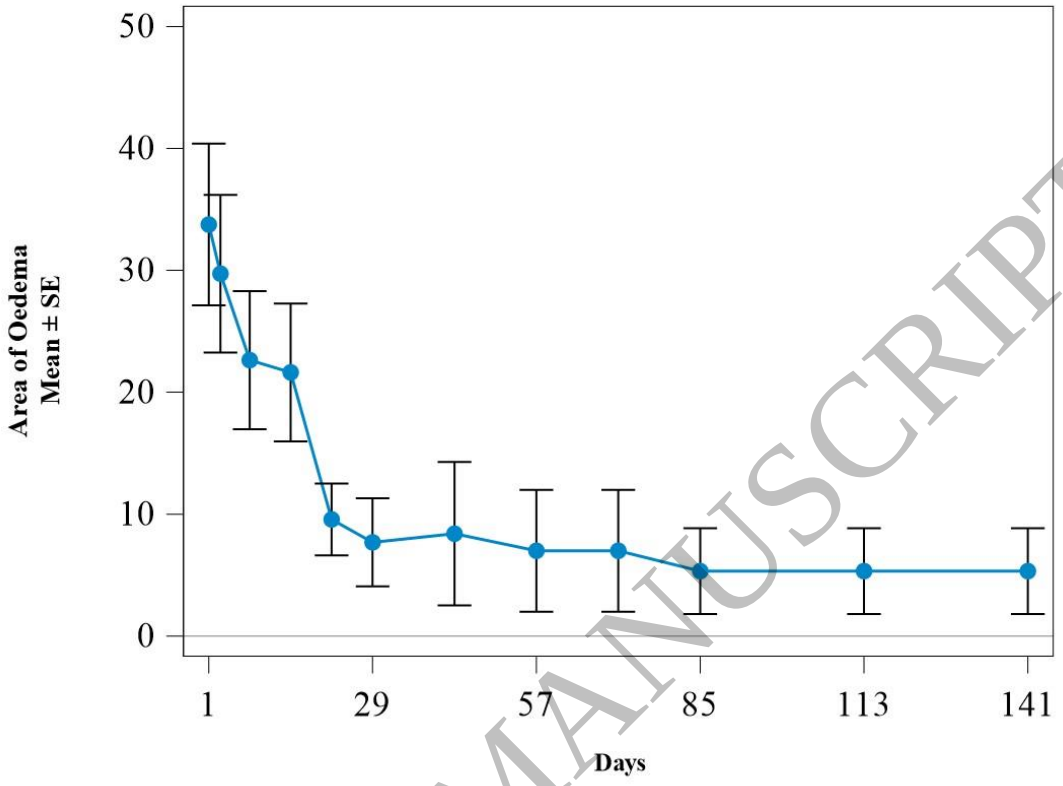

Figure 7
217x148 mm (x DPI)

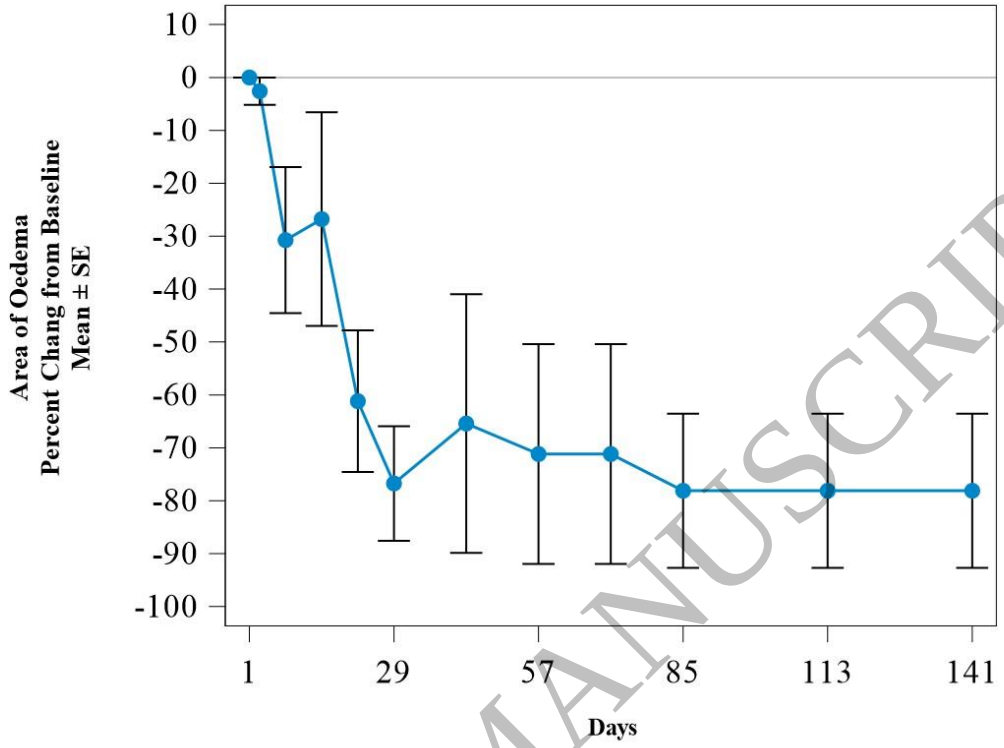

Figure 8
207x150 mm (x DPI)

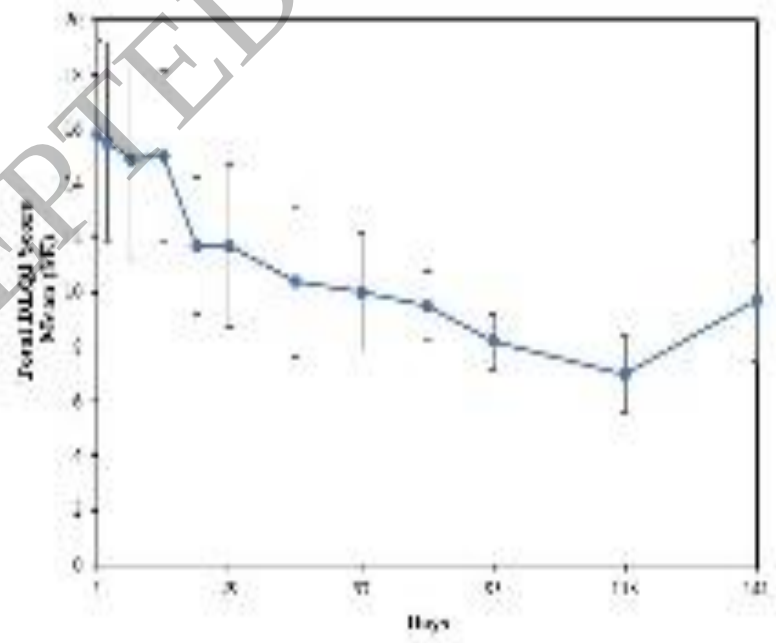

Figure 9
25x17 mm (x DPI)

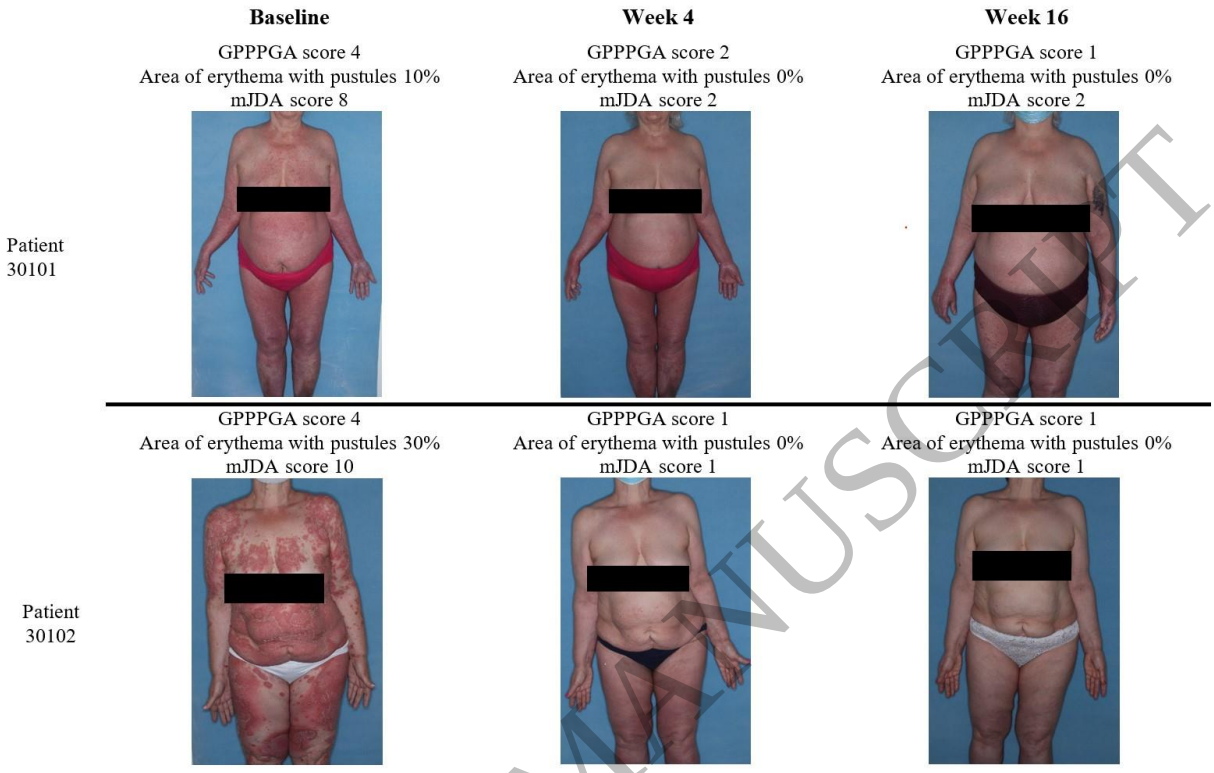

Figure 10
282x178 mm (x DPI)