Efficacy and Safety of Neihulizumab (AbGn-168H) in Patients with Active Psoriatic Arthritis: 24-week Results from a Phase II Open Label Study

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Background

- **Neihulizumab (AbGn-168H)** is a humanized monoclonal antibody which binds to human CD162 (PSGL-1) and preferentially induces apoptosis of late stage activated T cells. It has been tested in several T-cell mediated inflammatory diseases including psoriasis, ulcerative colitis and graft-versus-host disease.
- Psoriatic arthritis (PsA), a chronic inflammatory arthritis of unknown etiology which involves axial and peripheral joints, nails and entheses, is thought to be mediated by inflammatory elements including T cells, and the cytokine pathways they activate.
- We conducted a Phase IIa study of Neihulizumab in patients with psoriatic arthritis.

Study Objectives

Primary objective: to investigate efficacy of AbGn-168H in patients with moderately to severely active psoriatic arthritis following intravenous administration of multiple doses of AbGn-168H.

Secondary objective: to investigate safety, tolerability, and immunogenicity of AbGn-168H intravenous administration.

Study Design

Single arm, open label trial

Dose: 9 mg/kg; total 7 doses on Day 1 (Week 0), Day 8 (Week 1), Day 15 (Week 2), Day 29 (Week 4), Day 43 (Week 6), Day 57 (Week 8) and Day 71 (Week 10)

Mode of Administration: Intravenous infusion, infusion time approximately 1 hour

Duration of Treatment: AbGn-168H was administered as a total of 7 doses, Day 1 to 71 (Week 0 to 10), with follow-up at the end of Week 12 (Day 84), Week 16 (Day 112), Week 20 (Day 140), and Week 24 (Day 168).

Number of Centers: 7 (6 centers enrolled patients)

Diagnosis and Main Criteria for Inclusion

- The population for this study consisted of male or female patients, aged 18 to 75 years, inclusive, weighing <140 kg, and having psoriatic arthritis diagnosed according to the Classification Criteria for Psoriatic Arthritis (CASPAR) criteria, with moderate to severe activity (defined as ≥3 swollen joints and ≥3 tender or painful joints).
- Patients must have had active psoriatic skin lesions (diameter ≥2 cm) or documented psoriasis history, and a history of inadequate response or intolerance to non-steroidal anti-inflammatory drugs or disease modifying anti-rheumatic drugs.

Efficacy Endpoint

Primary endpoint: Proportion of patients reaching at least 20% improvement in American College of Rheumatology score (ACR20) in Week 12.

Secondary endpoints:

(1) Proportion of patients reaching ACR20, ACR50, and ACR70 at different time points;
(2) Disease Activity Score in 28 joints (DAS28) at different time points;
(3) Individual components of ACR assessment (Swollen Joint Count [SJC], Tender Joint Count [TJC], Patient Global Disease Activity Assessment [PtGDA], Patient Pain [PtPain], Physician's Global Disease Activity Assessment [PGDA], Health Assessment Questionnaire Disability Index [HAQ-DI], and C-reactive protein [CRP]) at different time points;
(4) and Target Lesion Psoriasis Severity Score (TLPSS) and static Physician's Global Assessment (sPGA) (for patients with active skin lesions) at different time points.

Safety Endpoint

Safety assessments included physical examinations, vital signs, 12-lead electrocardiograms (ECGs), safety laboratory tests, adverse events (AEs), and tolerability. The immunogenicity of AbGn-168H was evaluated by a qualitative bridging immunoassay for ADA.

Demographics

- The majority of the patients were female (12/20, 60.0%) and white (18/20, 90.0%). The mean age was 55.3 years. At Screening, the mean weight was 98.2 kg and mean height was 170.5 cm.
- Of the 36 individuals screened, 20 were enrolled; 15 completed treatment (7 doses of study drug) and 6 completed the study, including all follow-up visits.

Demographic and Baseline Characteristics

Female, n(%)	12 (60%)
Age (years), median (min, max)	55.5 (42, 72)
BMI (kg/m^2), median (min, max)	33.06 (24.50, 42.50)
Race, n (%)	
White	18 (90%)
African American	0
American Indian or Alaska native	0
Asian	0
Others	2 (10%)
Duration of psoriatic arthritis (years), median (min, max)	4.5 (0.7, 30)
Duration of psoriasis (years), median (min, max)	25 (1.9, 47)
Methotrexate current use, n (%)	11 (55%)
Prior exposure to biologics, n (%)	10 (50%)
Disease-related assessment-Baseline values, median (min, max)	
Swollen joint count (SJC)	16.5 (3, 57)
Tender joint count (TJC)	31.5 (5, 65)
Patient's assessment of Pain (VAS)	63.5 (18, 96)
Patient's global assessment of disease activity (VAS)	55.0 (10, 96)
Physican's global assessment of disease activity (VAS)	64.5 (38, 87)
HAQ-DI	1.4375 (0.25, 2.125)
C-reactive protein (mg/L)	0.608 (0.021, 4.346)
DAS28 (CRP), median (min, max)	5.588 (3.249, 7.585)
Static physician's global assessment (sPGA), n (%)	
Clear	0
Almost clear	2 (12.5%)
Mild	7 (43.8%)
Moderate	7 (43.8)
Severe	0
Target Lesion Psoriasis Severity Score (TLPSS), median (min, max)	5.5 (2.9)

Efficacy: Primary Endpoint

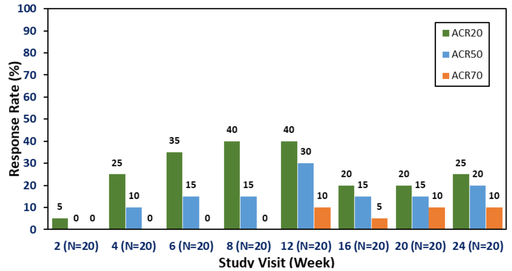
No formal confirmatory statistical testing is planned for this exploratory trial. All evaluations are reported for explorative purposes and are interpreted as such.

Using last observation carried forward (LOCF), s, 40.0% (8/20) of patients achieved ACR20 responder status at Week 12, and 12 (12/20, 60%) were classified as ACR20 non-responders.

For this trial, in which all patients who left the study before Week 12 were non-responders, analyses of the primary endpoint using LOCF and non-responder imputation (NRI, the usual primary method of analysis for ACR20 data) yield the same result.

Over the course of the study, the greatest response rates for ACR20, ACR50, and ACR70 were observed in Weeks 8 and 12. The ACR20 response rate peaked at 40%, the ACR50 response rate at 30%, and the ACR70 response rate at 10%.

ACR 20/50/70 Response Over Time (LOCF)



Efficacy Conclusion

- The overall efficacy analysis suggested that a substantial proportion of patients reached ACR20 at Week-12.
- Improvement was also observed in almost all the secondary endpoints at Week-12.
- Analysis by other endpoints such as DAS28 is very concordant. Among the eight (8) ACR responders, seven (7) showed ΔDAS28 > 1.2.
- It is important to note that the last treatment of AbGn-168H was at Week-10 and at least part of the therapeutic effects remained 14 weeks after AbGn-168H treatment.
- It is also important to note that 4 of the 8 responders had previously been exposed to biologics for psoriatic arthritis.

Summary of Efficacy Results at Week 12 and Week 14

Primary Endpoint	Week 12	Week 24*
ACR 20 (%)	40%	25%
Secondary Endpoints	Week 12	Week 24
ACR 50 (%)	30%	20%
ACR 70 (%)	10%	10%
ΔDAS28(CRP)	-1.0	-0.7
ΔPain-VAS#	-8.0	-4.0
ΔHAQ-DI#	-0.2	-0.2
ΔTLPSS#	-2.4	-2.5
sPGA (clear or almost clear, %)	53%	47%

*Last treatment at W10 # Mean change from baseline

Safety Conclusion

- Overall treatment was well tolerated in this population.
- A total of 20 patients were enrolled and received at least a partial dose of study drug, and 15 patients received all 7 doses.
- Sixty-five (65) percent of patients experienced a treatment-emergent AE (TEAE) during the treatment period.
- Thirty-five (35) percent of TEAE was treatment-related during the treatment period.
- There were no deaths and SAEs.
- One patient experienced a TEAE (foreign body reaction) that led to discontinuation of treatment and discontinuation from study.
- The most frequent TEAEs overall (including the treatment period and follow-up period) were urinary tract infection (15%), psoriatic arthropathy (15%), headache (10%), sinus congestion (10%), and hematoma (10%)
- There were no TEAEs that related to local tolerability at the injection site. Only one patient sample (an EOS time point for a patient who received all 7 doses of the study drug) tested positive for anti-AbGn-168H antibodies.

Overview of Adverse Events

Characteristics of Adverse Event (AE)	Treatment Emergent (N = 20)	Post-Treatment (N = 20)	Overall (N = 20)
With at least 1 AE	13 (65%)	5 (25%)	13 (65%)
With ≥ Grade 3 AEs	0	0	0
With at least 1 treatment-related AEs	7 (35%)	0	7 (35%)
With SAE	0	0	0
With AE leading to discontinuation of treatment*	1 (5%)	0	1 (5%)
With AE leading to discontinuation of study*#	1 (5%)	0	1 (5%)

*Foreign body reaction and #gout.

Study Conclusion

- In this open-label phase II study, improvement could be observed in each of the evaluated efficacy parameters (ACR20 at Week 12; ACR20/50/70, DAS28 scores, EULAR-response criteria , SJC, TJC, PtGDA, PtPain, PGDA, HAQ-DI, CRP, TLPSS, and sPGA assessments).
- The overall efficacy analysis suggests that 40% of all patients treated with AbGn-168H demonstrated meaningful responses by Week 12.
- The treatment was well tolerated in this population.
- Importantly, the results of an ad hoc analysis of patients who received all 7 doses of AbGn-168H and completed the study (Completed Set) identified 8 ACR20 responders (53.3%), 6 ACR50 responders (40%), and 2 ACR70 responders (13.3%) at Week 12, suggesting there may be clinical utility with this agent for the treatment of psoriatic arthritis.

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