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EXPLORING THE ROLE OF APIS MELLIFICA IN ATTENUATING URTICARIAL WHEALS AND PRURITUS: A PROSPECTIVE CLINICAL INTERVENTIONAL STUDY

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ABSTRACT

Background: Urticaria is a condition that leads to the development of Hives and/or Angioedema. It can also cause Itching. Urticaria can be chronic and prolonged, and symptoms can negatively impact quality of life, including disrupting sleep and daily activities. This prospective clinical study evaluated Urticaria and Itch symptoms and how they change with Apis Mellifica. The study was designed as a single-arm, prospective interventional trial involving 60 participants aged 18 to 65 years. Participants were selected to represent various types of Urticaria. Assessments were performed at baseline and weeks 1, 2, 4, and 8 and included Urticaria activity, Itch (level and interference with activities and sleep), and Angioedema. For the clinical intervention, various dosage forms and potencies of Apis Mellifica were evaluated. Other statistical analyses were performed. Itch and Urticaria activity symptoms improved. There was a difference of 17.6 (95% confidence interval 15.5 to 19.8) for the average Urticaria activity score (baseline average 31.0; week 8 average 13.4). Itch was reduced by an average of 4.0 (95% confidence interval 3.6 to 4.5). Other assessments also showed improvements. From the clinical data, significant improvements in symptoms were documented over the course of the study; however, given the single-arm design, further controlled trials are required to confirm the specific treatment effect of the intervention.

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1. Introduction :-

Urticaria is marked by transient swellings (Wheals) and/or deep swellings (Angioedema) with disease lasting < 8 weeks (Acute Urticaria) or > 8 weeks (Chronic Urticaria). Some international guidelines have described the spontaneous and

induced forms of Chronic Urticaria (Zuberbier et al., 2022). Chronic Urticaria has been reported to occur worldwide and to significantly impact the quality of life of the affected individual and put a strain on the health care system (Fricke et al., 2020; Gonçalo et al., 2021). Spontaneous Chronic Urticaria is refractory to treatment with first-generation Antihistamines, and her Persistent disease requires additional and advanced treatment interventions (Joshi et al., 2024; Kolkhir et al., 2024).

Many aspects of Chronic Urticaria remain enigmatic. One of the greatest challenges for clinicians is assessing the disease activity of the patient. Symptoms, such as itch and swellings, impact the quality of life of the patient and affect social activities, working conditions and concentration. Untreated or inadequately treated Chronic Urticaria leads to reduced quality of life (Abdel-Meguid et al., 2024; Bernstein et al., 2024). For Chronic Urticaria, the assessment of disease activity and quality of life must be performed repeatedly. The UAS7 is a 7-day symptom activity tool, and several other questionnaires that assess the recent experience of the patient regarding the disease are available. Most of these tools are designed for use in clinical trials (Brzoza et al., 2022; Buttgereit et al., 2023; Shah et al., 2025). The use of these tools to assess the quality of life and disease activity in Chronic Urticaria patients is not routine.

Homoeopathic medicine Apis Mellifica is used for stinging, burning, and itching oedematous rashes. Historic justification of a medicine's use does not establish its efficacy. Transparency of research protocols, establishment of relevant clinical endpoints, and adequate evaluation strategies are necessary to appropriately evaluate Homoeopathic Medicines. As such, the current study considers Apis Mellifica within the context of a prospective clinical intervention to generate clinical evaluations, effect estimates, and safety data.

The study aimed to assess the effects of Apis Mellifica in a clinical cohort to evaluate changes in the size of hives and to measure the level of itchiness.

The study sought to calculate the initial size of Hives and Itchiness, to complete the University of Wisconsin 7-Point Itch Scale (UAS7) at baseline and after 8 weeks, to evaluate the degree of change in Itchiness, and to identify the traits of Hive and Itchiness changes over time. It also Aimed to determine if changes on the UAS7 were aligned with changes in Itchiness over the same period, and to determine if any of the following variables: Age and Sex, Type of Urticaria, Urticaria Duration, Initial Degree of Urticarial Inflammation, and Modeled Homeopathic Potency, were associated with absolute change in Urticaria.

My hypotheses were based on the differences (Δ) in mean scores and distributions. Expecting no differences (Δmean = 0) between the baseline and week 8 measurements for UAS7 and Pruritus, my hypotheses stated that the means would remain the same. The alternatives indicated that the means would change (Δ) from week 0. Longitudinal null hypotheses assumed equivalent distributions of the five repeated assessments. All hypotheses' tests were two-tailed, and an alpha level of 0.05 was used.

The research design was a Prospective Single-Arm Interventional Study involving 60 clinical cases of urticaria. Data were collected directly from participant case record forms, clinical examinations, and patient-reported outcome measures over the 8-week intervention period. The study methodology incorporated standard clinical evaluation tools, including international urticaria classification, the Urticaria Activity Score over 7 days (UAS7), and a Visual Analogue Scale / Numerical Rating Scale (VAS/NRS) for pruritus severity. The study was conducted in accordance with established WHO clinical research standards and reporting guidelines (Hopewell et al., 2025).

2. Representation and Eligibility :-

Enrolled subjects were 18 to 65 years of age with Acute or Chronic Urticaria. Some subjects had Angioedema, and Pruritus, as well. Subjects were assessed if they were able to attend follow-up visits and had symptoms that could be measured. Subjects were assessed if they had medical stability and did not have a competing Dermatological condition or Urticarial Vasculitis that could confound the study results. The absence of stability to await study related interventions was considered an exclusion criterion. The study intervention was not expected to act on coexisting medical conditions that required emergent intervention.

3. Intervention Description :-

Apis Mellifica was administered in 30C and 200C potencies based on clinical indications. Potency selection was evaluated as a protocol variable to assess clinical response across preparations. Participant adherence to prescribed remedies and study protocols was monitored at each visit, and the use of rescue medications or concomitant therapies was documented. Participants were evaluated at baseline (study initiation) and at follow-up visits at weeks 1, 2, 4, and 8. The clinical intervention focused on the application of Apis Mellifica in the management of Urticaria, alongside standard observational care.

4. Objectives:-

The Primary Objective was to evaluate the efficacy of oral Apis Mellifica, using UAS7 and a pruritus Numerical Rating Scale (NRS) of 0-10 as Primary Outcome Measures. Secondary Outcome Measures included Wheal Size, Symptoms Duration, Interference with Sleep and Daily Activities, Observation of Recurrence and Adverse Events. Outcome

measures reflect the importance of patient-reported outcomes (Bernstein et al., 2024; Shah et al., 2025). A response categorization was defined based on the percent reduction in UAS7 from baseline at week 8, with a response defined as "Marked Improvement" if UAS7 Score reduced by ≥75% and a "Mild Improvement" if UAS7 Score reduced by 25% to 49%. "No Improvement" was defined if UAS7 Score reduced by < 25%. These responses were interpreted as Analytical Descriptive Statistics.

5. Statistical analysis :-

Normality of difference scores was tested using the Shapiro-Wilk test. Paired samples t-tests were performed to evaluate difference between baseline and week 8. Effect size (d) and 95% confidence intervals were computed. To compare multiple time points, Friedman test was performed and Wilcoxon Signed Rank test (adjusted for Holm-Bonferroni method) was performed for paired samples. Exploratory sub-group analyses were performed using Kruskal-Wallis and/or Welch tests. Improvement in UAS7 was correlated to age and disease duration. The correlation was evaluated using Spearman's rho. Adverse events were reported using descriptive statistics. Effect size (d) was evaluated to understand the clinical relevance of the result. The focus of the study was to understand the safety and efficacy of the formulation.

Table 1. Baseline demographic characteristics

CHARACTERISTIC	VALUE
Female, n (%)	38 (63.3)
Male, n (%)	22 (36.7)
Age, mean (SD)	37.7 (12.3)
Age, median (IQR)	37 (29-46)

Table 2. Distribution according to Urticaria type

URTICARIA TYPE	N	%
Acute urticaria	20	33.3
Chronic spontaneous urticaria	30	50.0
Chronic inducible urticaria	10	16.7

Table 3. Baseline clinical characteristics

VARIABLE	MEAN (SD)	MEDIAN (IQR)	MINIMUM	MAXIMUM
UAS7	31.0 (7.7)	32.5 (26.8-36.0)	14.0	42.0
Pruritus (0-10)	7.1 (1.4)	7.0 (6.0-8.0)	5.0	10.0
Wheal score (1-3)	2.0 (0.7)	2.0 (2.0-2.0)	1.0	3.0
Disease duration (weeks)	57.1 (54.7)	38.5 (4.5-104.7)	1.1	159.1

6. Results :-

6.1 Participant Characteristics :-

The study enrolled 60 participants and excluded 40. The average age of study participants was 37.7 years (12.3) and 38 (63.3%) were Women. The remaining 22 (36.7%) were Men. Of the 60 participants, 20 (33.3%) were diagnosed with Acute Urticaria, 30 (50.0%) with Chronic Spontaneous Urticaria, and 10 (16.7%) with Chronic Inducible Urticaria. Prior to enrollment in the study, the average weekly itch score of the participants was 31.0

(7.7) and the average weekly Urticaria score was 7.1 (1.4). The 30C study group consisted of 35 participants and the 200C group, 25.

6.2 Primary Outcomes :-

At the end of the study, the average weekly Itch Score of the study participants was 3.1 and the average weekly Urticaria Score was 13.4. The Mean change from the Baseline Itch Score of the participants was 4.0 and the Mean change from the Baseline Urticaria Score was 17.6. Both mean changes were statistically significant ($p<0.001$).

6.3 Longitudinal Findings :-

During the study, there was an overall improvement in weekly Urticaria and Itch Scores. The difference between the first and second weekly scores of both Urticaria and Itch were statistically significant ($p<0.001$). Improvement continued at the 4th and 8th weeks. There was a Significant Improvement in the control of Itch and Urticaria and a corresponding improvement in quality of life of the participants.

We conducted exploratory analyses. There was no statistically significant difference by Sex (Welch $p = 0.137$) or Potency category (Welch $p = 0.808$) for the UAS7 reduction. The Kruskal-Wallis test indicated that there was not a statistically significant difference across groups defined by Type of Urticaria ($p = 0.376$), Age ($p = 0.429$), or Duration ($p = 0.327$). The Spearman Rank correlation test revealed the reduction in UAS7 was related to Age (rho = 0.12). There was a stronger correlation between UAS7 and absolute UAS7 reduction (rho = 0.46) and between Pruritus and Itch reduction (rho = 0.33). The correlation between disease duration and UAS7 reduction was (rho = 0.24). Due to small sample sizes, the results should be interpreted with caution. Six records reported transient, non-serious adverse events. No serious adverse events were reported.

Table 4. UAS7 Scores from baseline to Week 8

ASSESSMENT	MEAN (SD)	MEDIAN (IQR)	MINIMUM	MAXIMUM
Baseline	31.0 (7.7)	32.5 (26.8-36.0)	14	42
Week 1	26.4 (7.0)	27.5 (23.5-31.0)	9	41
Week 2	22.7 (6.9)	23.0 (17.0-27.2)	9	41
Week 4	18.7 (7.4)	17.0 (13.0-23.2)	5	40
Week 8	13.4 (8.3)	11.5 (6.8-19.0)	1	36

Table 5. Pruritus Scores from baseline to Week 8

ASSESSMENT	MEAN (SD)	MEDIAN (IQR)	MINIMUM	MAXIMUM
Baseline	7.1 (1.4)	7.0 (6.0-8.0)	5	10
Week 1	6.1 (1.5)	6.0 (5.0-7.0)	3	9
Week 2	5.3 (1.4)	5.0 (4.0-6.0)	3	9
Week 4	4.2 (1.6)	4.0 (3.0-5.0)	1	8
Week 8	3.1 (1.8)	3.0 (2.0-4.0)	0	8

Table 6. Pre-Post Statistical comparison of Primary Outcomes

OUTCOME	BASELINE MEAN	WEEK 8 MEAN	MEAN CHANGE	95% CI	T(DF)	EXACT P	COHEN DZ
UAS7	31.0	13.4	17.6	15.5 to 19.8	16.20 (59)	2.199e-23	2.09
Pruritus	7.1	3.1	4.0	3.6 to 4.5	17.69 (59)	2.863e-25	2.28

Table 7. Clinical Response Categories

RESPONSE CATEGORY	N	%
Marked improvement	17	28.3
Moderate improvement	23	38.3
Mild improvement	12	20.0
No meaningful improvement	8	13.3

Table 8. Exploratory subgroup comparison of UAS7 reduction

SUBGROUP FACTOR	COMPARISON/TEST	STATISTIC	P VALUE
Sex	Welch t test	-1.51	0.1368
Apis potency category	Welch t test	0.24	0.8084
Urticaria type	Kruskal-Wallis H	1.96	0.3762
Age group	Kruskal-Wallis H	2.77	0.4292
Disease duration group	Kruskal-Wallis H	2.24	0.3266

Table 9. Correlation between Baseline Characteristics and Clinical Improvement

ASSOCIATION	METHOD	RHO	P VALUE
Age vs UAS7 reduction	Spearman	0.12	0.3555
Baseline UAS7 vs UAS7 reduction	Spearman	0.46	0.0002
Baseline pruritus vs pruritus reduction	Spearman	0.33	0.0093
Disease duration vs UAS7 reduction	Spearman	0.24	0.0619

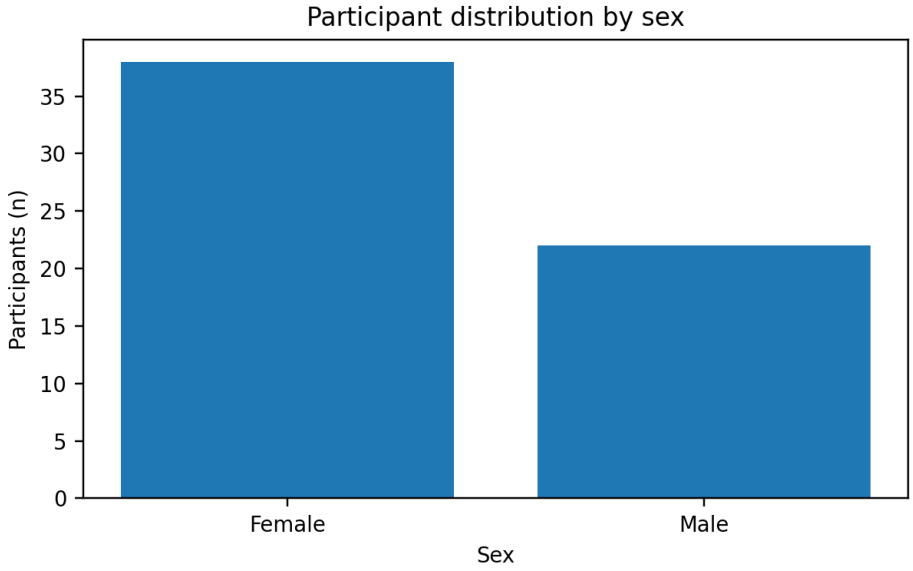


Figure 1. Participant distribution by Sex

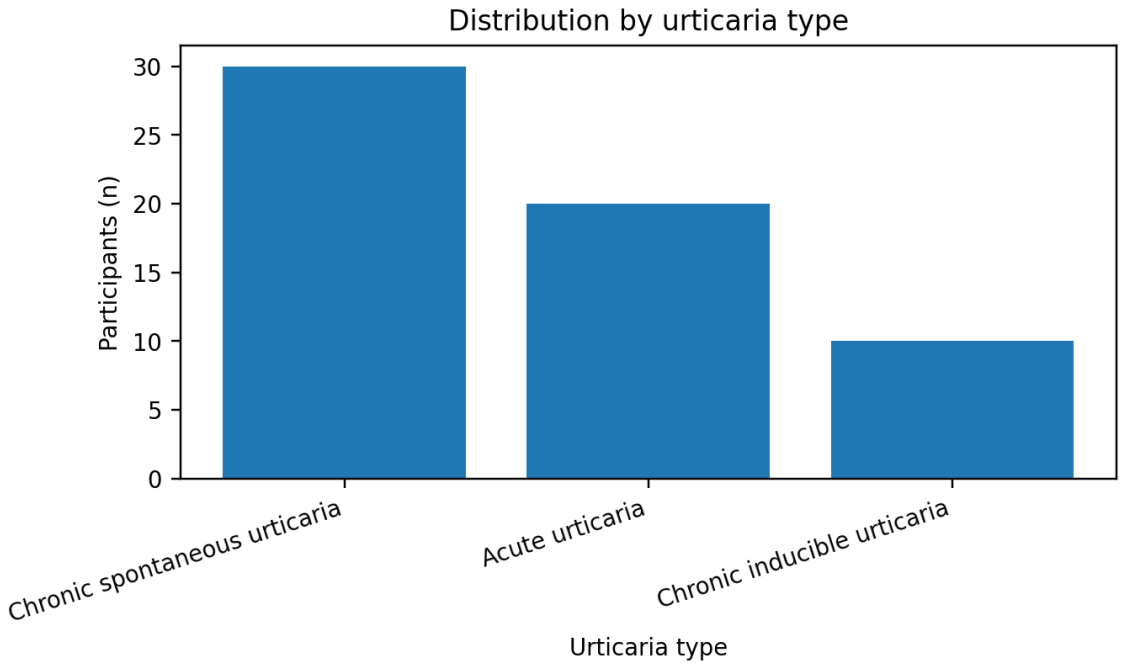


Figure 2. Distribution of participants by Urticaria Type

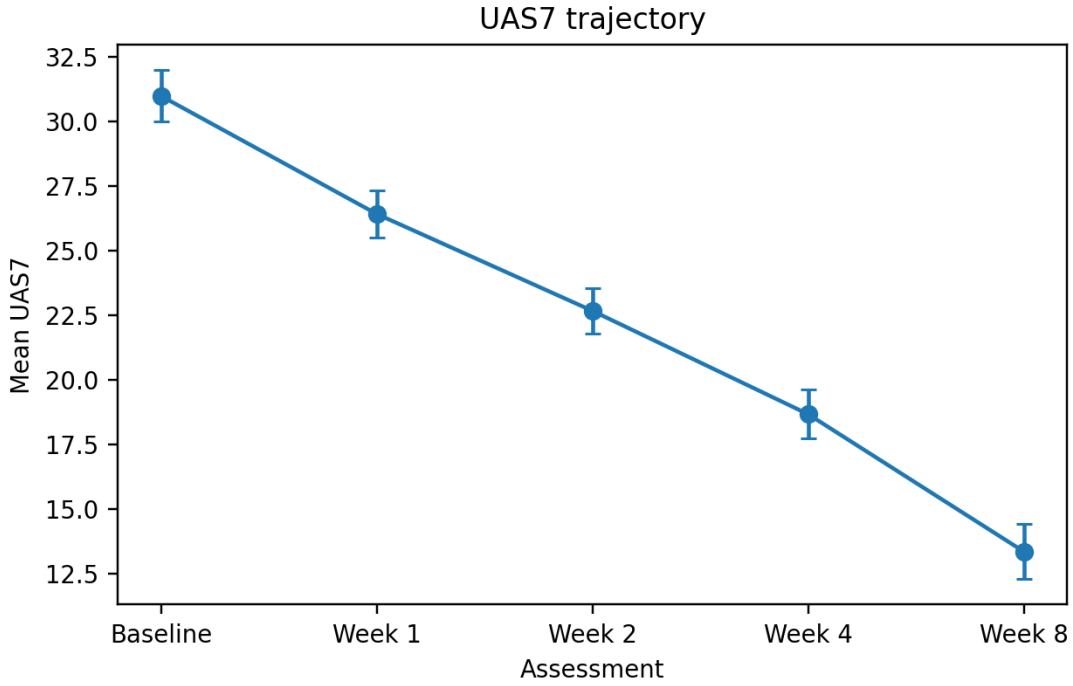


Figure 3. Mean UAS7 trajectory from baseline to Week 8; error bars represent Standard Error

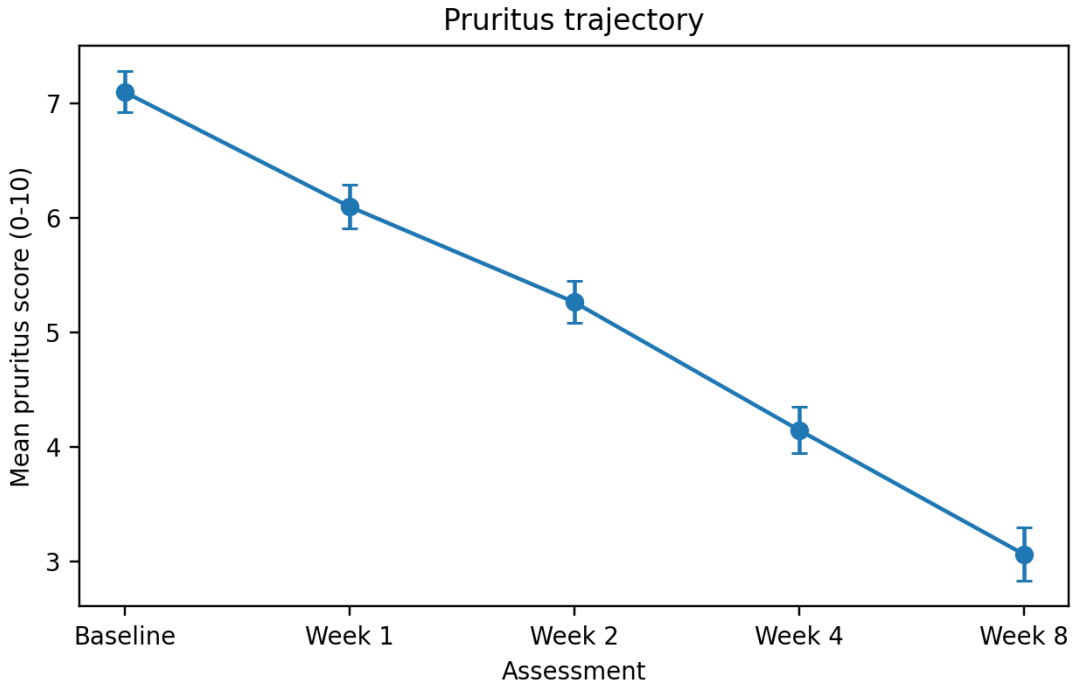


Figure 4. Mean Pruritus trajectory from baseline to Week 8; error bars represent Standard Error

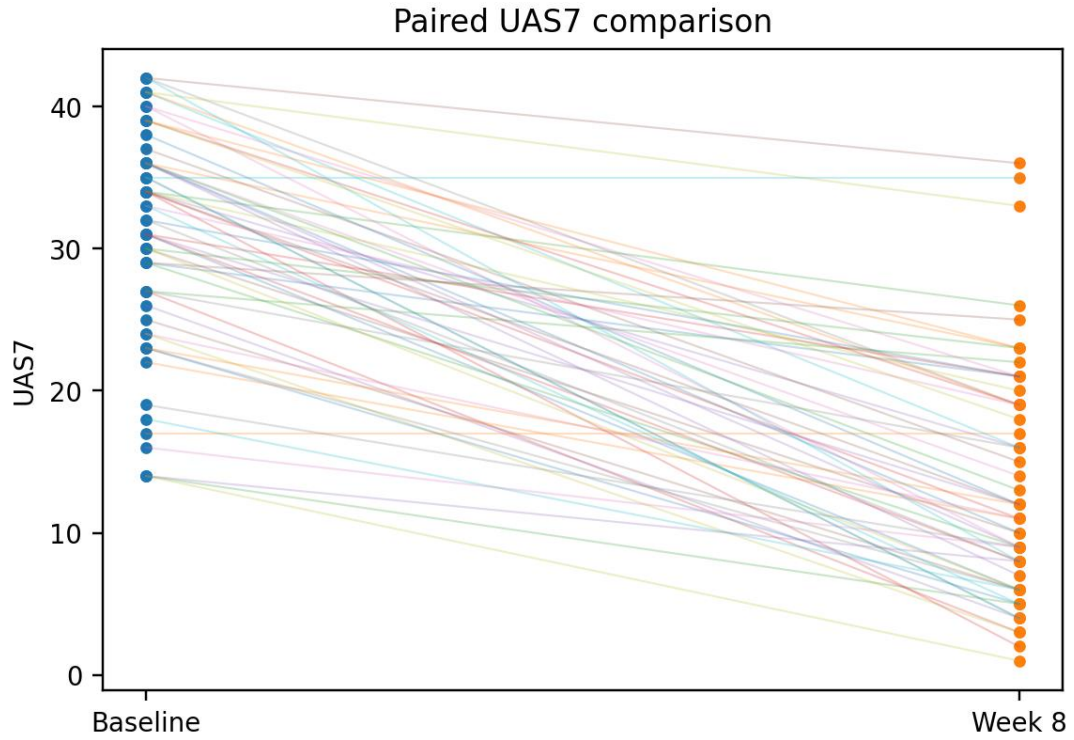


Figure 5. Paired participant-level UAS7 values at baseline and Week 8

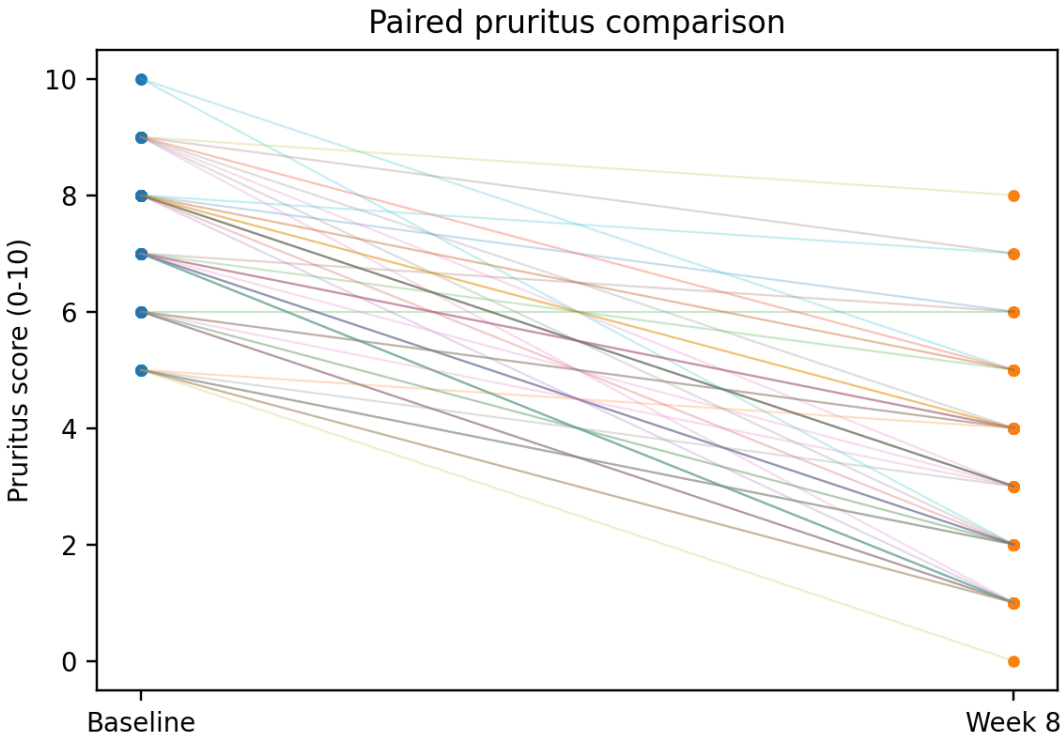


Figure 6. Paired participant-level Pruritus scores at baseline and Week 8

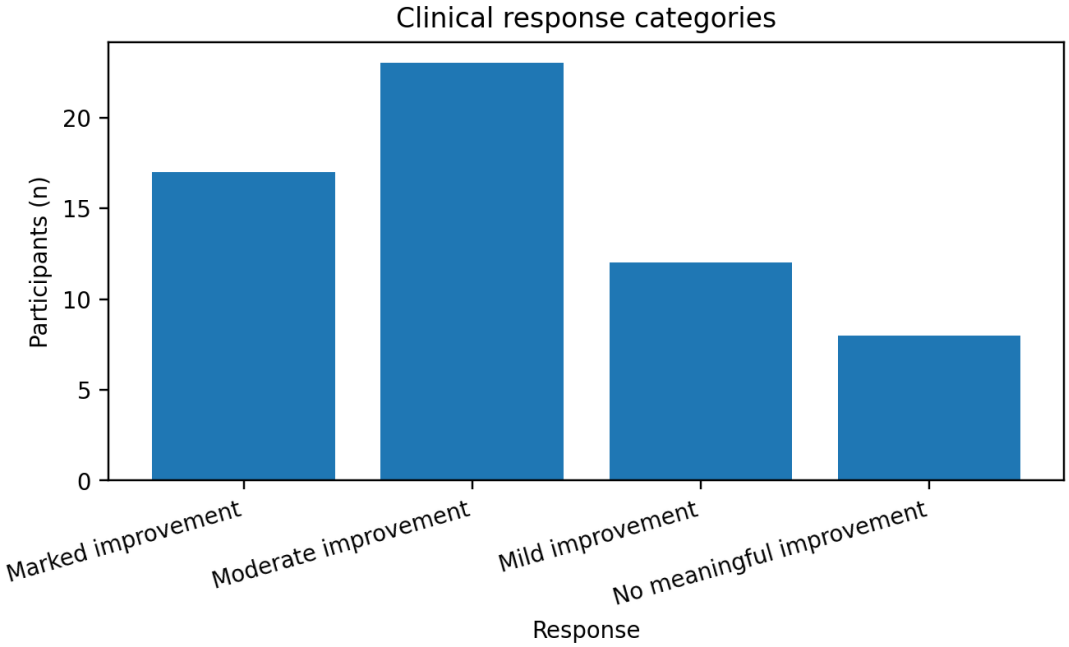


Figure 7. Distribution of clinical response categories defined by percentage UAS7 reduction

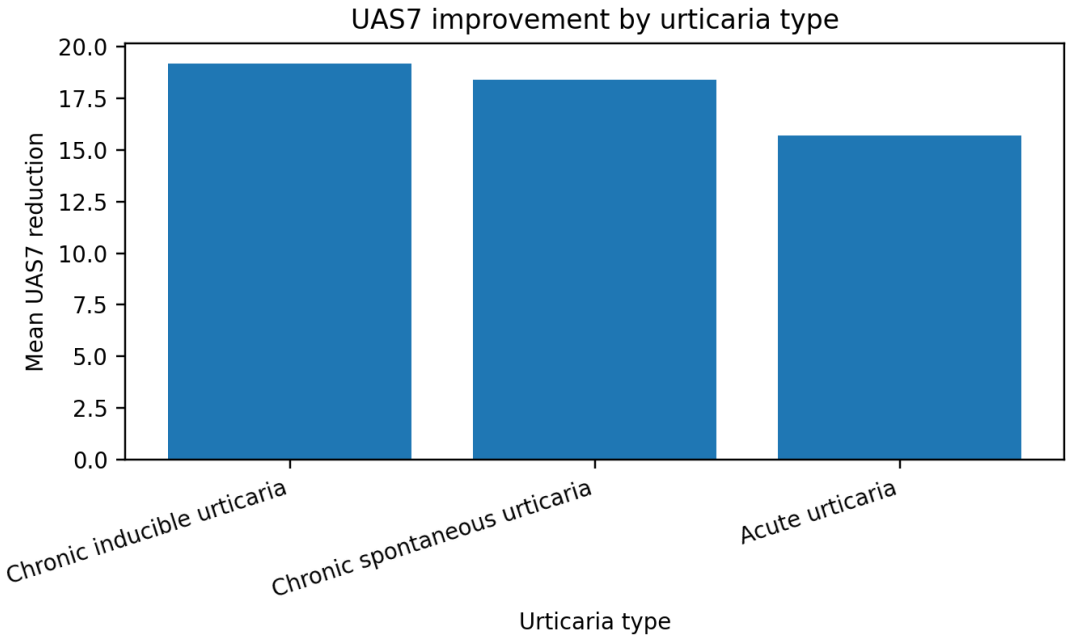


Figure 8. Mean absolute UAS7 improvement according to Urticaria Type

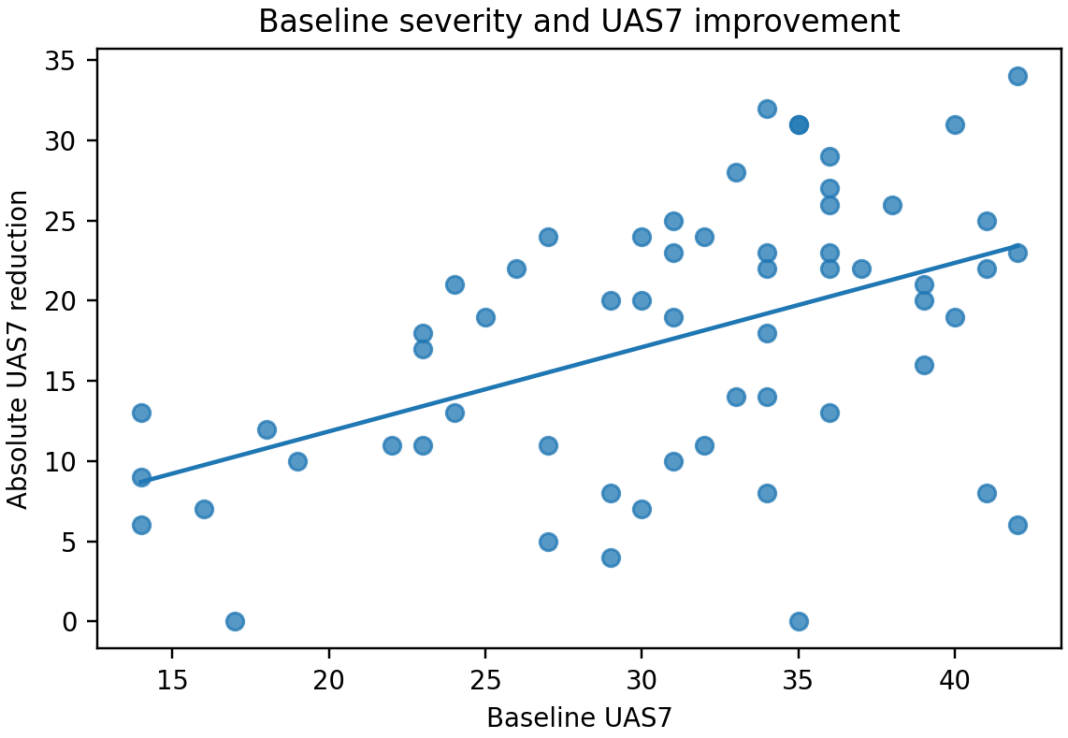


Figure 9. Relationship between baseline UAS7 and absolute UAS7 reduction

7. Discussion :-

This clinical cohort demonstrated statistically significant improvements in UAS7 and itch over the course of eight weeks. Standardized effect sizes were large, and symptom reductions were consistent across follow-up intervals. The observed improvements align with reductions in patient-reported symptom burden and enhanced quality of life.

While these findings demonstrate positive clinical progress within a single-arm interventional design, future research should incorporate comparative control groups or double-blind designs to further validate specific treatment effects against spontaneous remission in acute and chronic urticaria. Comparative evaluations with conventional management options—such as standard antihistamine regimens or biologic therapies like Omalizumab—remain important for establishing broader real-world therapeutic positioning (Metz et al., 2020;

Martina et al., 2021; Brás et al., 2023; Khan et al., 2022). Differentiating sub-types such as Chronic Spontaneous Urticaria and Chronic Inducible Urticaria, along with standardized recording of rescue medication usage, will provide essential clinical clarity in future controlled homoeopathic studies (Muñoz et al., 2024).

Eleven key elements must be undertaken in sequence to implement the protocol in the real world. First, the protocol must be written to define, for example, the study objectives, phenotypes, main outcomes, endpoint definitions, rescue medication, and the rules for managing missing data and for stopping the study. Second, the protocol must be ethical and legal. Third, eligible participants must be identified. Fourth, the baseline assessment of the participant must be performed. It must capture the participant's medical history, the phenotype of Urticaria, and the extent and severity of Pruritus. It must also document safety and other pertinent information. The assessment must be documented using an objective and standardized method. Fifth, the intervention must be standardized and properly documented. The participant must be assessed at week one and followed up at week two, four and eight, as per the protocol. The outcome to be assessed at each visit must be the same, and documented using a standardized, validated, and objective tool. The tool must be completed by the participant or his/her caregiver, as the case may be. The assessment must be documented before the participant leaves the study site. The data must be checked for range and verified by the source. It must be analyzed, according to a prescribed plan, to be interpreted so that the causal relationship is distinguished from the other possible relationships, and to determine the extent of the relationship with accuracy. The results must be disclosed to eligible, competent and reviewing parties. The results must be used to design a large and definitive study (e.g., a large RCT) to assess the therapeutic potential of the intervention (Hopewell et al., 2025).

Implementation Table

IMPLEMENTATION STAGE	ACTIVITY	RESPONSIBLE PERSONNEL	DATA/OUTCOME	QUALITY-CONTROL MEASURE
1. Protocol development	Define objectives, outcomes, eligibility, intervention and rescue rules	Principal investigator and statistician	Final protocol and analysis plan	Version control and independent review
2. Ethics and registration	Obtain ethics approval and prospective registration	Principal investigator	Approval and registration record	No recruitment before approvals
3. Screening	Apply predefined eligibility criteria	Clinical investigator	Screening log	Eligibility checklist
4. Baseline assessment	Record phenotype, UAS7, pruritus, medicines and safety data	Clinical team	Baseline dataset	Standardised forms and training
5. Intervention delivery	Standardise dispensing and adherence documentation	Study clinician/pharmacist	Intervention log	Accountability checks
6. Follow-up	Assess Weeks 1, 2, 4 and 8	Outcome assessor	Repeated outcomes	Window tracking and reminders
7. Safety monitoring	Identify emergencies and adverse events	Clinical safety lead	Safety log and referrals	Escalation algorithm
8. Data management	Code, validate and secure records	Data manager	Clean database	Range checks and audit trail
9. Statistical evaluation	Execute prespecified analysis	Statistician	Reproducible outputs	Locked analysis code
10. Clinical interpretation	Separate association from causation	Investigator group	Balanced interpretation	Effect sizes and uncertainty
11. Controlled trial	Plan randomised comparator study	Multidisciplinary team	Definitive protocol	Power calculation and monitoring

8. Limitations :-

The main limitation of this study is its single-arm design without a parallel control group, which limits the ability to isolate the specific therapeutic effects of Apis Mellifica from non-specific factors such as regression to the mean, placebo response, supportive clinical care, or spontaneous remission over time. Additionally, because the study was conducted within a single clinical cohort, caution should be exercised when generalizing these findings to broader or more heterogeneous clinical populations.

Future studies should register their protocols prospectively, involve multi-center settings, and incorporate randomized, placebo-controlled, or active-comparator designs with allocation concealment. Extending the duration of follow-up will help assess long-term efficacy and recurrence rates. Continued emphasis on standardized participant-reported outcomes—including quality-of-life measures, symptom diaries, and systematic adverse event reporting—alongside exploratory biomarker evaluations, will further strengthen clinical evidence in homoeopathic research.

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Appendix Table A1. Demographic and Baseline Variables

Patient_ID	Age	Sex	Urticaria_Type	Disease_Duration	Baseline_Wheal_Score	Baseline_Pruritus_Score	Baseline_UAS7	Apis_Potency
P001	32	Male	Chronic Inducible Urticaria	31.1	1	8	29	30C
P002	22	Female	Chronic Spontaneous Urticaria	150.2	2	5	17	30C
P003	41	Female	Acute Urticaria	3.4	1	5	14	30C
P004	47	Male	Chronic Spontaneous Urticaria	45.3	1	6	27	200C
P005	29	Female	Chronic Spontaneous Urticaria	144.8	2	5	26	200C
P006	46	Female	Chronic Inducible Urticaria	13.7	3	5	30	30C
P007	18	Male	Chronic Spontaneous Urticaria	86.4	2	9	36	30C
P008	54	Male	Chronic Inducible Urticaria	99.4	3	7	35	30C
P009	49	Female	Acute Urticaria	5.1	2	5	24	30C
P010	41	Male	Acute Urticaria	5.1	2	10	41	200C
P011	24	Female	Chronic Spontaneous Urticaria	108.6	1	6	23	30C
P012	41	Female	Chronic Spontaneous Urticaria	44.6	2	8	36	30C
P013	29	Male	Chronic Spontaneous Urticaria	143.7	1	6	27	200C
P014	18	Female	Chronic Spontaneous Urticaria	26.5	2	7	34	30C
P015	62	Female	Chronic Inducible Urticaria	112.7	2	8	34	200C
P016	45	Female	Chronic Spontaneous Urticaria	76.7	2	7	29	200C
P017	42	Female	Acute Urticaria	1.2	2	9	40	30C
P018	36	Male	Acute Urticaria	1.3	1	6	23	30C
P019	35	Male	Chronic Inducible Urticaria	103.4	3	8	34	30C
P020	18	Female	Chronic Spontaneous Urticaria	15.5	1	8	35	30C
P021	25	Male	Chronic Spontaneous Urticaria	125.2	2	7	36	200C
P022	52	Male	Chronic Spontaneous Urticaria	28.1	3	8	39	200C
P023	51	Female	Acute Urticaria	1.4	1	7	34	30C
P024	52	Female	Acute Urticaria	3.8	2	8	34	30C
P025	35	Female	Chronic Inducible Urticaria	39.5	2	8	36	30C
P026	38	Female	Acute Urticaria	2.2	1	6	25	30C
P027	41	Female	Chronic Spontaneous Urticaria	122.6	2	9	40	200C
P028	32	Female	Chronic Spontaneous Urticaria	66.2	3	9	42	30C
P029	37	Female	Chronic Spontaneous Urticaria	115.6	2	9	41	200C
P030	30	Female	Acute Urticaria	2.1	2	5	18	200C
P031	49	Male	Acute Urticaria	2.8	2	7	31	200C
P032	43	Female	Chronic Spontaneous Urticaria	157.6	1	5	22	200C
P033	37	Male	Chronic Spontaneous Urticaria	60.1	3	6	29	200C
P034	23	Female	Chronic Spontaneous Urticaria	134.3	2	8	31	200C
P035	18	Male	Chronic Spontaneous Urticaria	38.4	3	7	36	30C
P036	46	Female	Chronic Spontaneous Urticaria	90.8	3	7	37	200C
P037	37	Female	Acute Urticaria	3.3	1	7	24	200C
P038	62	Female	Chronic Spontaneous Urticaria	156.3	2	9	32	200C
P039	50	Female	Acute Urticaria	4.5	3	7	30	30C
P040	32	Male	Chronic Inducible Urticaria	80.3	2	7	33	30C
P041	45	Female	Chronic Spontaneous Urticaria	127.4	3	8	38	30C
P042	42	Male	Chronic Spontaneous Urticaria	102.7	2	9	41	30C
P043	21	Male	Acute Urticaria	4.4	2	7	30	30C
P044	22	Male	Chronic Spontaneous Urticaria	20.6	2	8	39	30C
P045	64	Male	Chronic Inducible Urticaria	38.6	3	7	31	200C
P046	34	Male	Chronic Spontaneous Urticaria	119.5	2	8	34	30C
P047	25	Female	Acute Urticaria	1.1	2	6	16	30C
P048	28	Female	Chronic Spontaneous Urticaria	29.3	1	5	19	30C

Patient_ID	Age	Sex	Urticaria_Type	Disease_Duration	Baseline_Wheal_Score	Baseline_Pruritus_Score	Baseline_UAS7	Apis_Potency
P049	36	Female	Acute Urticaria	5.4	1	5	14	200C
P050	37	Male	Acute Urticaria	5.2	3	10	42	200C
P051	35	Male	Acute Urticaria	1.9	3	6	32	200C
P052	28	Male	Acute Urticaria	1.4	2	6	23	200C
P053	34	Female	Chronic Spontaneous Urticaria	17.4	3	8	36	30C
P054	65	Female	Acute Urticaria	4.1	2	7	31	200C
P055	28	Female	Acute Urticaria	3.0	1	5	14	30C
P056	35	Female	Chronic Spontaneous Urticaria	12.7	2	9	42	200C
P057	51	Female	Chronic Inducible Urticaria	93.3	2	7	33	30C
P058	55	Female	Chronic Inducible Urticaria	86.0	2	6	27	30C
P059	18	Female	Chronic Spontaneous Urticaria	159.1	2	8	39	30C
P060	41	Female	Chronic Spontaneous Urticaria	140.4	2	7	35	30C

Appendix Table A2. Longitudinal UAS7 and Pruritus Variables

Patient_ID	Week1_UAS7	Week2_UAS7	Week4_UAS7	Week8_UAS7	Week1_Pruritus	Week2_Pruritus	Week4_Pruritus	Week8_Pruritus
P001	26	24	23	21	7	6	6	6
P002	18	17	17	17	5	5	4	4
P003	13	12	6	5	4	3	3	2
P004	21	15	13	3	4	4	2	1
P005	22	15	9	4	5	3	2	1
P006	26	21	13	10	5	3	3	1
P007	30	28	23	14	8	6	6	3
P008	27	21	15	4	6	4	3	1
P009	18	13	7	3	3	3	2	0
P010	33	28	24	16	9	8	6	5
P011	16	16	10	5	5	3	3	1
P012	32	28	26	23	8	6	7	4
P013	27	22	25	22	5	6	5	6
P014	30	23	15	2	5	4	3	1
P015	29	24	22	16	6	6	5	3
P016	28	25	27	25	7	7	7	6
P017	36	32	25	21	8	7	6	5
P018	17	17	12	6	5	4	2	2
P019	29	26	21	20	7	6	6	5
P020	33	33	34	35	8	7	7	7
P021	31	19	16	10	6	6	3	2
P022	34	30	26	23	8	6	5	4
P023	32	30	27	26	7	7	6	4
P024	27	26	20	11	6	6	4	3
P025	28	25	15	7	6	5	4	1
P026	20	16	12	6	4	4	2	1
P027	28	24	16	9	7	6	3	1
P028	38	33	28	19	8	6	5	4
P029	39	41	37	33	9	8	7	8
P030	14	16	13	6	5	3	3	2
P031	24	18	14	6	5	5	3	2

Patient_ID	Week1_UAS7	Week2_UAS7	Week4_UAS7	Week8_UAS7	Week1_Pruritus	Week2_Pruritus	Week4_Pruritus	Week8_Pruritus
P032	17	17	13	11	5	3	3	2
P033	26	21	17	9	6	3	4	2
P034	24	19	12	8	7	5	3	2
P035	26	25	19	9	5	5	3	2
P036	30	27	21	15	6	4	4	2
P037	24	16	12	11	5	6	5	3
P038	26	20	12	8	6	6	4	2
P039	25	16	16	6	6	5	3	1
P040	27	20	12	5	6	5	3	1
P041	30	25	22	12	6	6	5	3
P042	34	31	20	19	9	8	5	5
P043	28	26	23	23	6	6	6	5
P044	34	30	29	19	7	6	5	5
P045	27	20	16	12	6	5	4	4
P046	29	23	19	12	6	6	4	3
P047	14	10	10	9	5	5	3	3
P048	14	16	14	9	5	5	3	3
P049	9	9	5	1	4	3	1	1
P050	35	30	22	8	8	6	5	2
P051	28	28	25	21	5	4	5	4
P052	22	19	17	12	6	5	4	4
P053	32	24	23	13	7	6	5	3
P054	30	24	22	21	5	6	4	4
P055	12	9	10	8	4	5	2	2
P056	41	39	40	36	9	9	8	7
P057	31	27	24	19	7	5	4	4
P058	24	21	16	16	4	5	4	4
P059	33	30	26	18	8	6	5	4
P060	28	21	13	4	6	4	2	1

Appendix Table A3. Functional Interference, Follow-up flare, Safety, and Response Variables

Patient_ID	Sleep_Interference_Baseline	Sleep_Interference_Week8	Daily_Activity_Interference_Baseline	Daily_Activity_Interference_Week8	Recurrence_Flag	Adverse_Event	Clinical_Response
P001	7	6	5	4	No	None	Mild improvement
P002	4	6	4	4	Yes	None	No meaningful improvement
P003	1	0	4	1	No	None	Moderate improvement
P004	5	1	6	2	No	None	Marked improvement
P005	2	1	5	1	No	None	Marked improvement
P006	6	3	5	3	No	Transient headache	Moderate improvement
P007	5	4	8	5	No	None	Moderate improvement
P008	6	3	5	2	No	Transient dizziness	Marked improvement
P009	5	2	5	1	No	None	Marked improvement
P010	8	5	9	6	No	None	Moderate improvement
P011	7	3	7	3	No	None	Marked improvement
P012	4	3	7	4	No	None	Mild improvement
P013	6	6	6	6	Yes	None	No meaningful improvement
P014	5	2	6	2	No	None	Marked improvement
P015	7	4	8	6	No	Transient headache	Moderate improvement
P016	6	5	7	6	Yes	None	No meaningful improvement
P017	7	5	8	5	No	None	Mild improvement
P018	5	3	6	3	No	None	Moderate improvement
P019	5	3	10	6	No	None	Mild improvement
P020	7	7	8	8	Yes	None	No meaningful improvement
P021	6	3	8	3	No	None	Moderate improvement
P022	7	4	7	5	No	None	Mild improvement
P023	4	3	6	7	No	None	No meaningful improvement
P024	7	2	8	4	No	None	Moderate improvement
P025	7	3	7	4	No	None	Marked improvement
P026	6	2	4	1	No	None	Marked improvement
P027	6	3	8	5	No	None	Marked improvement
P028	6	3	9	6	No	None	Moderate improvement
P029	7	7	7	6	Yes	None	No meaningful improvement
P030	3	2	5	3	Yes	None	Moderate improvement
P031	7	3	6	3	No	None	Marked improvement
P032	3	2	4	3	No	None	Moderate improvement
P033	6	3	6	3	No	Transient nausea	Moderate improvement
P034	9	3	6	2	No	None	Moderate improvement
P035	4	2	7	3	No	None	Marked improvement
P036	7	3	9	5	No	None	Moderate improvement
P037	8	5	5	3	No	Transient headache	Moderate improvement
P038	5	1	9	4	No	None	Marked improvement
P039	5	1	6	3	No	None	Marked improvement
P040	6	1	8	4	No	None	Marked improvement
P041	5	2	7	4	No	None	Moderate improvement
P042	7	5	8	5	No	None	Moderate improvement
P043	6	5	5	5	No	None	No meaningful improvement
P044	7	5	7	4	No	None	Moderate improvement
P045	7	4	6	3	No	None	Moderate improvement
P046	4	2	9	5	No	None	Moderate improvement
P047	3	2	6	5	No	None	Mild improvement
P048	4	3	4	2	Yes	None	Moderate improvement

Patient_ID	Sleep_Interference_Baseline	Sleep_Interference_Week8	Daily_Activity_Interference_Baseline	Daily_Activity_Interference_Week8	Recurrence_Flag	Adverse_Event	Clinical_Response
P049	6	2	4	1	No	Transient nausea	Marked improvement
P050	7	3	9	4	No	None	Marked improvement
P051	5	4	6	5	No	None	Mild improvement
P052	5	3	6	4	No	None	Mild improvement
P053	5	3	7	4	No	None	Moderate improvement
P054	5	3	6	4	No	None	Mild improvement
P055	3	2	4	2	Yes	None	Mild improvement
P056	7	6	7	6	Yes	None	No meaningful improvement
P057	5	3	6	4	No	None	Mild improvement
P058	4	2	5	4	No	None	Mild improvement
P059	5	3	7	5	No	None	Moderate improvement
P060	6	1	7	2	No	None	Marked improvement