Self-administration of Mepolizumab Liquid Using a Single-use Prefilled Autoinjector

Poster No. P696 (A1305)

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Background

- Mepolizumab is approved as an add-on maintenance treatment for patients with severe eosinophilic asthma (SEA) and has been shown to be well tolerated, reduce blood eosinophil counts and asthma exacerbations, and improve lung function and health-related quality of life.[1–6]
- Currently, mepolizumab is supplied as a lyophilized formulation to be reconstituted prior to subcutaneous (SC) injection and is administered once every 4 weeks by a healthcare professional (HCP) in the clinic.[1]
- A new formulation of mepolizumab as a liquid drug product in a single-use, ready-to-use prefilled syringe or prefilled autoinjector (AI) has been developed. Administration via either device has been shown to have a statistically comparable pharmacokinetic profile to that of the reconstituted lyophilized formulation (see related posters: Shabbir et al. P702 [A1311] and Bradford et al. P697 [A1306]).

Objective

- To evaluate the use of a single-use prefilled AI for the self-administration of mepolizumab (100 mg SC) by patients with SEA, or their caregivers, both in clinic and at home.

Methods

- This open-label, single-arm, repeat-dose, multicenter, Phase IIIa study (GSK ID: 204959; NCT03099096) included patients aged ≥12 years of age, diagnosed with asthma[7] for ≥2 years, who were either receiving mepolizumab (100 mg SC) prior to screening or not.
- Mepolizumab (100 mg SC; 1.0 mL) was self-administered via an AI once every 4 weeks over 12 weeks. If the caregiver performed the injections, all doses were injected by the same caregiver.
- Two different device labels were used based on guidance provided by regulatory agencies regarding device labeling preferences: the 'standard device label + pictogram AI (AI with pictogram)' and the 'standard device label AI (AI without pictogram)'.
- The first and third dose (Weeks 0 and 8, respectively) was self-administered under observation in clinic, whilst the second dose (Week 4) was self-administered unobserved at home.
- Injection success was determined by the investigators/site staff based on Observer and At-home Checklists, and visual inspection of the returned AI.
- The primary and secondary endpoints were the proportion of patients who successfully self-administered their third and second doses of mepolizumab, respectively.
- Other endpoints included the proportion of patients able to successfully self-administer all three doses, device usability and functionality, and safety assessments.
- The analysis population included all patients who attempted ≥1 self-administration of mepolizumab using an AI.

Results

- In total, 159 patients (or their caregivers) self-administered ≥1 mepolizumab dose. Of these, 104 (65%) used the AI with pictogram and 55 (35%) used the AI without pictogram and 157 (99%) completed the study. Patient demographics and baseline disease characteristics are shown in **Table 1**.
- Overall, seven patients using the AI with pictogram had their caregiver perform the first injection, while all patients using the AI without pictogram performed the first injection themselves.
- At Week 8, 99% of patients attempting an injection using the AI with pictogram and 98% of patients attempting an injection using the AI without pictogram successfully self-administered their third dose of mepolizumab in the clinic (**Table 2**).
- Almost all patients/caregivers attempting an injection successfully self-administered mepolizumab at every visit using either the AI with pictogram or the AI without pictogram (**Table 2**).

Table 1. Demographics and baseline disease characteristics

	Mepolizumab AI (N=159*)
Females, n (%)	98 (62)
Age (years)† Mean (SD) Range	 49.3 (16.2) 12–77
BMI (kg/m^2), mean (SD)‡	31.4 (7.6)
Disease duration (years) Mean (SD) Range	 23.3 (16.5) 2–68
Patients not currently receiving mepolizumab, n (%) Screening blood eosinophil count, cells/µL, median (range), n=74	75 (47) 320 (0–1760)

*157 patients completed the study. Two patients were withdrawn after self-administering their first dose of mepolizumab; one owing to serious adverse events relating to a traffic accident and one owing to physician decision (failure to comply with study procedures and unreliability); †birth day and month was imputed with 30 June; ‡BMI was collected for 158 patients.
BMI, body mass index; SD, standard deviation

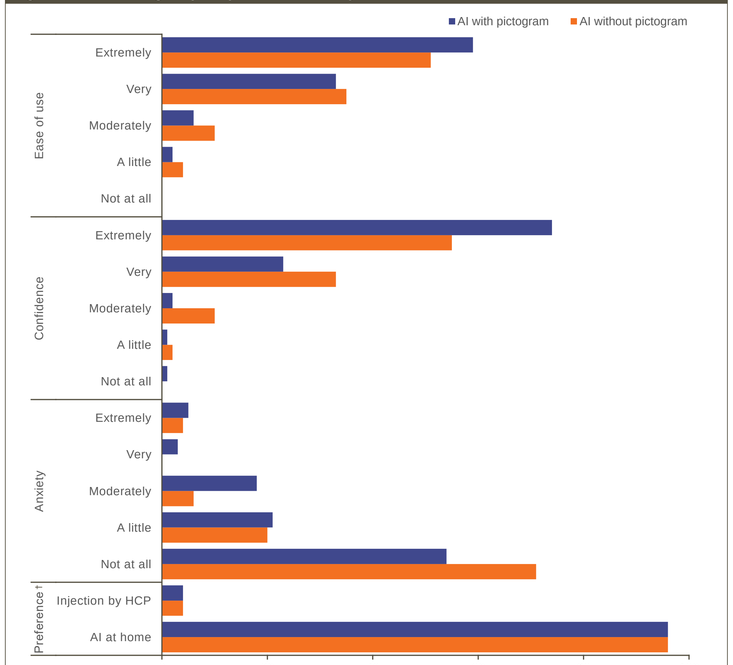
Table 2. Proportion of patients (or their caregivers) successfully able to self-administer mepolizumab (100 mg SC) using an AI by visit

	Mepolizumab AI with pictogram (N=104)		Mepolizumab AI without pictogram (N=55)	
Visit	**Attempted injections, n**	**Successful injections*, n (%) [95% CI]**	**Attempted injections, n**	**Successful injections*, n (%) [95% CI]**
Week 0, first dose (observed in clinic)	104	101 (97) [92, 99]	55	52 (95) [85, 99]
Week 4, second dose (unobserved at home)	103	101 (98) [93, 100]	54	52 (96) [87, 100]
Week 8, third dose (observed in clinic)	103	102 (99) [95,100]	54	53 (98) [90, 100]
Weeks 0, 4, and 8 (all doses)	103	98 (95) [89, 98]	54	48 (89) [77, 96]

*The denominator for the percentage of successful injections was the number of attempted injections.
CI, confidence interval

- Overall, 12 injection failures were reported by 11 patients, all due to user errors; reasons included using the incorrect injection site (arm [allowed only for caregiver] instead of thigh or abdomen) and the AI being pulled away before the end of the injection. There were no device failures.
- Patient/caregiver perception of AI usability is summarized in **Figure 1**. Of those patients receiving mepolizumab at screening, 96% (n=69/72) preferred receiving mepolizumab using the AI at home compared with an injection administered by a HCP in the clinic.

Figure 1. Patient/caregiver perception of AI usability*



*Patients (AI with pictogram, n=102; AI without pictogram, n=51) were asked the following questions: how easy was it to give yourself an injection using the pen at home?; at the end of the study, how confident were you about your ability to use the pen in the correct way on your own when you were not at the doctor's office?; how anxious did you feel about administering mepolizumab using the pen at home?; what is your preference for receiving mepolizumab using the pen at home or by injection administered by a doctor/nurse?; The AI was referenced as the 'pen' in the device usability/functionality questionnaire; †refers to patients receiving mepolizumab at baseline (AI with pictogram, n=47; AI without pictogram, n=25).

- Immediately after the first injection, 60% of patients reported pain, which was generally mild and considered acceptable (**Table 3**). A decrease in the proportion of patients experiencing pain was seen following each of the subsequent injections.
- Overall, 56 (35%) patients reported on-treatment adverse events (AEs), and five patients experienced drug-related AEs. Nine on-treatment serious AEs were reported by four patients (not considered related to study treatment). The incidence of anti-drug antibodies was low (1%) and none were neutralizing.

Table 3. Injection pain summary

Dose interval	Mepolizumab AI (N=159) number of patients, n (%)		
	Time following self-administration		
	Immediately	1 hour	24 hours
Week 0, first dose, n	141	140	136
Patients experiencing any pain (VAS score >0)	85 (60)	51 (36)	30 (22)
Pain acceptable*	85 (100)	51 (100)	30 (100)
Pain greater than expected	12 (14)	4 (8)	2 (7)
VAS score			
Mean (SD)	10.5 (17.1)	3.3 (8.4)	1.8 (5.8)
Week 4, second dose, n	129	109	134
Patients experiencing any pain (VAS score >0)	73 (57)	32 (29)	33 (25)
Pain acceptable*	72 (99)	32 (100)	31 (94)
Pain greater than expected	9 (12)	5 (16)	6 (18)
VAS score			
Mean (SD)	8.4 (16.6)	3.7 (12.3)	2.3 (8.1)
Week 8, third dose, n	150	130	116
Patients experiencing any pain (VAS score >0)	65 (43)	27 (21)	18 (16)
Pain acceptable*	65 (100)	27 (100)	18 (100)
Pain greater than expected	13 (20)	2 (7)	0
VAS score			
Mean (SD)	7.3 (16.2)	2.2 (8.2)	1.0 (4.5)

*All patients were asked if the pain was acceptable, despite the degree of pain experienced and the relative pain to expectation. VAS score: 0 (no pain) to 100 (worst possible pain).
VAS, visual analogue scale

Conclusions

- Mepolizumab (100 mg SC) was self-administered successfully by patients (or their caregivers) using an AI both in the clinic and at home.
- The safety profile was similar to that observed in previous trials with the reconstituted lyophilized formulation[2–5] and no new safety concerns were identified over the 12-week treatment period.
- These results demonstrate that the self-administration of mepolizumab administered via a ready-to-use AI by patients (or their caregivers) is a convenient and flexible alternative to the current reconstituted lyophilized formulation delivered in the clinic.

References

1. GSK. Nucala. US Prescribing information. December 2017. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/125526s004lbl.pdf [last accessed January 2019]; 2. Pavord ID, et al. *Lancet* 2012;380:651–9; 3. Bel EH, et al. *N Engl J Med* 2014;371:1189–97; 4. Ortega HG, et al. *N Engl J Med* 2014;371:1198–207; 5. Chupp GL, et al. *Lancet Respir Med* 2017;5:390–400; 6. Lugogo N, et al. *Clin Ther* 2016;38(9):2058–70 e1; 7. Global Initiative for Asthma. Global strategy for asthma management and prevention. 2018. Available from: www.ginasthma.org [last accessed January 2019].

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