

Home Self-Administration of Biologics – A German Survey among Omalizumab-Treated Patients with Severe Asthma and their Treating Physicians

Selbstapplikation von Biologika – eine Umfrage bei Omalizumab-behandelten Patienten mit schwerem Asthma und deren Ärzten

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 Appendix 1s

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ABSTRACT

In the EU, five biologics have been approved as add-on therapy for patients with severe asthma. Until recently, none of the biologics was approved for home use and had to be administered under medical supervision, a time-consuming schedule for both patients and physicians, accompanied by greater expenditure. However, over the last year, four out of the five biologics have been granted approval for patient self-administration at home. The objective of this multiple-choice survey was to understand how patients with severe asthma treated with omalizumab and their treating physicians view the potential home use of biologics exemplified by omalizumab. The questionnaires were answered by 120 physicians and 432 patients (response rate: 51.7% and 20.6%, respectively). Overall, 44.7% of patients were in favour of self-administration at home while 30.6% opposed this method of administration and 23.8% of patients were neu-

tral. Especially teenagers and young adults had a positive attitude towards self-administration. 76.7% of the questioned physicians were in favour of home use for certain patients. Time saving was the main advantage for self-administration mentioned by patients (53.2%) as well as by physicians (72.5%). The main concern for patients was ‘making a mistake while injecting’ (43.8%) while ‘forgetting to inject omalizumab’ (73.3%) was the main concern for physicians. 44.4% of patients expressed a wish for individual training and 70.8% of physicians agreed with this statement. The latter group also considered a starter kit including several information materials (54.2%) as well as an electronic reminder system (50.8%) as useful. In conclusion, self-administration of biologics has the potential to be time-saving for both patients and physicians.

ZUSAMMENFASSUNG

In der EU sind derzeit 5 Biologika als Add-on-Behandlung bei schwerem Asthma zugelassen. Bisher musste die Administration unter medizinischer Aufsicht erfolgen, was sowohl für Patienten als auch Arztpraxen mit einem erhöhten Zeit- und Kostenaufwand einhergeht. Im Laufe des letzten Jahres wurde allerdings die Selbstapplikation für 4 der 5 Biologika zugelassen. Ziel dieser Umfrage war es, mittels Multiple-Choice-Fragebögen das Potenzial einer Selbstapplikation von Biologika aus der Sicht von Patienten und Ärzten am Beispiel von Omalizumab einzuschätzen. In die Auswertung flossen 432 Patienten- und 120 Ärzte-Fragebögen ein (Rücklaufquote: 51,7% bzw. 20,6%). Insgesamt bewerteten 44,7% der Patienten eine Selbstapplikation positiv, 30,6% ablehnend und 23,8% neutral. V. a. in den Altersgruppen der Jugendlichen und jungen Erwachsenen wurde eine Selbstapplikation überwiegend positiv bewertet. 76,7% der befragten Ärzte würden eine Selbstapplikation für bestimmte Patienten befürworten. Als wichtigster Vorteil wurde bei Patienten bzw. Ärzten v. a. die Zeitersparnis (53,2% bzw. 72,5%) genannt. Bedenken äußerten die Patienten v. a. zu Fehlern beim Spritzen (43,8%), während bei Ärzten am häufigsten „vergessen Omalizumab zu spritzen“ (73,3%) genannt wurde. Von 44,4% der Patienten wurde der Wunsch nach einer persönlichen Schulung zur Selbst-

applikation als Unterstützung geäußert, während bei den Ärzten neben dieser Unterstützung (70,8%) v. a. auch ein Starterkit mit verschiedensten Infomaterialien (54,2%) sowie ein elektronisches Erinnerungs-System (App) als sinn-

voll erachtet wurden (50,8%). Zusammenfassend ergab die Umfrage, dass die praxisexterne Selbstapplikation von Biologika sowohl bei Patienten als auch Ärzten überwiegend befürwortet wurde und zu einer Zeitersparnis beitragen kann.

Background

Severe asthma is present in about 5–10% of asthma patients. These patients remain uncontrolled despite treatment with high dose inhaled corticosteroids plus a second controller [1]. The implementation of biologics has been a major advancement in the treatment of patients with severe asthma. Currently, 5 biologics have been approved in the EU as add-on therapy for patients with severe asthma. Until recently, however, no biologic was approved for at-home use and had to be administered under medical supervision, a time-consuming schedule for both, patients and physicians, accompanied by greater expenditure. However, over the last year, approval for patient self-administration at home has been granted for omalizumab, mepolizumab, benralizumab and dupilumab. This approval will allow patients to self-administer those biologics or to be injected by a trained caregiver if a physician considers it to be appropriate.

Previously, biologics such as omalizumab were usually given in a physician's office due to the perceived risk of anaphylaxis. However, prevalence of anaphylaxis in omalizumab-treated patients is low (0.09%) and most of these cases appear during the first three injections [2]. On the other hand, the requirement to receive injections of biologics under medical supervision can be inconvenient for working patients, those in school, or those having to travel a long distance to their physician's office, and thus might affect therapy compliance. For some patients, the added travel expenses may also be a hindrance. Decreasing the number of regular visits allows patients the flexibility to fit their treatment around their lives, and subsequently might increase their quality of life. As for physicians, an increasing number of patients requiring repeated courses of biologics might limit their capacity for other patients needing more help. Giving patients the option to administer their therapy at home could therefore be a time- and cost-effective way for both patients and their treating physicians.

Self-administration of subcutaneous medications has been shown to be feasible for patients across a variety of therapeutic areas such as rheumatoid arthritis, multiple sclerosis and diabetes and is historically very common for patients with these diseases. However, for patients with respiratory diseases such as asthma, self-administration of injectables is new. To date, few studies have published experiences with self-administration of biologics at home in patients with severe asthma [3–6]. All studies showed that patients can safely and effectively self-administer biologics at home with appropriate training. No cases of anaphylaxis, suspected allergic reactions, or other serious adverse effects related to study medication were reported in any of the studies. However, less is known about patients' and physicians' perspectives regarding self-adminis-

tration of biologics and whether patient characteristics influence mode of administration. Here, we report the results of a multiple-choice survey conducted among patients with severe asthma treated with omalizumab and their treating physicians regarding the potential home use of biologics exemplified by omalizumab before EU approval was granted.

Material and methods

Design

This is a multicentre, observational, cross-sectional, questionnaire-based survey to collect representative views of people diagnosed with severe allergic asthma as well as their physicians regarding the home use of omalizumab. It was carried out in Germany between the 3rd of April and 17th of May 2018 (before approval of omalizumab self-administration was granted in the EU).

210 potential participating physicians received sealed packages containing one physician questionnaire and ten patient questionnaires. Only physicians with experience in omalizumab administration were selected and contacted by the study sponsor.

The physicians were requested to hand out the patient questionnaires to patients with current experience of omalizumab therapy. Completed patient questionnaires were returned to the physician in closed envelopes. Documents were sent to the contract research organisation (CROLLL GmbH, Nuremberg, Germany) for anonymous data analysis. The results of the survey are based on descriptive analyses, shown as percentages. Statistical tests were not performed.

Questionnaires

The patient questionnaire comprised 14 multiple-choice questions, covering demographics, current aspects of their omalizumab therapy, and several questions regarding acceptance/advantages as well as concerns about omalizumab self-administration. Furthermore, patients were asked what kind of support they would prefer regarding self-administration of omalizumab.

The physician questionnaire comprised six multiple-choice questions, regarding acceptance/advantages as well as concerns about omalizumab self-administration for their patients. Furthermore, physicians were asked what percentage of patients they would switch to home use of omalizumab and how much time this would save the practice in a month.

Questionnaires were not validated and were developed by the study sponsor's medical team with regards to evaluating patient's and physician's needs for antibody therapy and self-administration.

See **appendix 1s** for full questionnaires.

Results

Patient demographics

The questionnaires were answered by 120 physicians and 432 patients, corresponding to 51.7% and 20.6% of the surveys distributed to physicians and patients, respectively. ► **Table 1** gives an overview of the demographic characteristics of the patients. Among the patients, 54.4% were female. Most participants were ≥35 years old (66.9% of the total population between 35 and 64 years and 13.9% ≥65 years of age). About half of the patients received omalizumab for one to four years at the time of this survey, while 20.4% received omalizumab therapy for less than one year or for five to nine years, respectively. A minority of 5.8% had received omalizumab for more than ten years. At the time of the survey, 57.6% of patients received their omalizumab injections every four weeks, while 39.1% received them biweekly.

Views about current omalizumab therapy

In the patient questionnaire, opinions about the current omalizumab therapy scheme were asked. An overview of the different questions and answers is given in ► **Table 2**.

Views about the potential use of omalizumab at home

At the time of the survey, 44.7% of patients were in favour of omalizumab self-administration at home, while 30.6% were opposed to this method of administration (► **Fig. 1 a**). Especially teenagers (12–17 years of age) and young adults (18–34 years of age) had a positive attitude towards omalizumab self-administration with 61.9% and 59.2% being in favour of omalizumab self-administration, respectively (► **Fig. 1 b**). When looking at the data according to profession, students (58.3%) and working patients (51.8%) rated self-administration of omalizumab most favourable (► **Fig. 1 c**).

Overall, most physicians were in favour of omalizumab home use. However, most of them would limit the self-administration method to certain patients (► **Fig. 2 a**). More than 70% of physicians could imagine omalizumab self-administration for at least 25% of their patients (► **Fig. 2 b**).

Time saving was the main advantage for omalizumab self-administration mentioned by patients as well as by physicians (► **Fig. 3 a and b**). Further advantages appreciated by patients and physicians included less doctor appointments, flexibility, and more time for other patients (physicians only).

Especially students and working patients cited multiple advantages when it came to self-administration of omalizumab, with time saving being the main factor (► **Fig. 4**).

Patients and physicians were also asked about any potential concerns related to self-administration of omalizumab at home (► **Fig. 5 a and b**). The two main concerns were 'making a mistake while injecting' (43.8%) and 'appearance of adverse events' (26.4%). However, about a third of patients (32.2%) had no concerns regarding omalizumab home use.

► **Table 1** Demographic characteristics of patients (N = 432).

Demographic characteristics	% of patients
Sex	
▪ Female	54.4
▪ Male	44.7
▪ Missing data	0.9
Age distribution of patients in years	
▪ < 12 years	2.1
▪ 12–17 years	4.9
▪ 18–34 years	11.3
▪ 35–64 years	66.9
▪ ≥65 years	13.9
▪ Missing data	0.9
Profession	
▪ Student	8.3
▪ Job seeking	4.9
▪ In Employment	50.5
▪ Housewife/Househusband	5.6
▪ Pensioner	30.1
▪ Missing data	1.6
Duration of omalizumab therapy	
▪ < 1 year	20.4
▪ 1–4 years	50.7
▪ 5–9 years	20.4
▪ > 10 years	5.8
▪ Missing data	3.0
Administration intervals	
▪ Biweekly	39.1
▪ Every four weeks	57.6
▪ Missing data	3.9
Injections per appointment	
▪ 1	13.0
▪ 2	45.1
▪ 3	25.9
▪ 4	18.8
▪ Missing data	1.4
Percentages may not add up to 100% due to rounding and (unrequested) multiple answers.	

► **Table 2** Views about current omalizumab therapy (N=432).

Question	% of patients
How flexible would you describe the omalizumab therapy?	
▪ Hardly flexible	29.2
▪ Flexible	51.9
▪ Very flexible	16.4
▪ Missing data	3.2
What are your personal expenses for each omalizumab therapy? ¹ (Euro)	
▪ <10	52.8
▪ 11–20	27.8
▪ 20–50	12.7
▪ >50	3.2
▪ Missing data	3.7
How many days per year do you invest due to omalizumab administration? ² (Days)	
▪ <1	39.6
▪ 1–10	21.5
▪ 11–20	22.9
▪ >20	8.3
▪ Missing data	7.9
Percentages may not add up to 100 % due to rounding and (unrequested) multiple answers.	
¹ e.g. travel expenses	
² e.g. having to take a day's leave from work	

Only 5.0% of physicians had no concerns regarding omalizumab home use by patients. The two main concerns were 'forget to administer omalizumab' (73.3%) and 'errors during injection' (60.8%).

Further, the surveys addressed the question of support related to omalizumab self-administration. 44.4% of patients expressed a wish for individual training and 70.8% of physicians agreed with this statement (► **Fig. 6 a** and **b**). More than half of the physicians also considered a starter kit including several information materials (54.2%) as well as an electronic reminder system (50.8%) as useful.

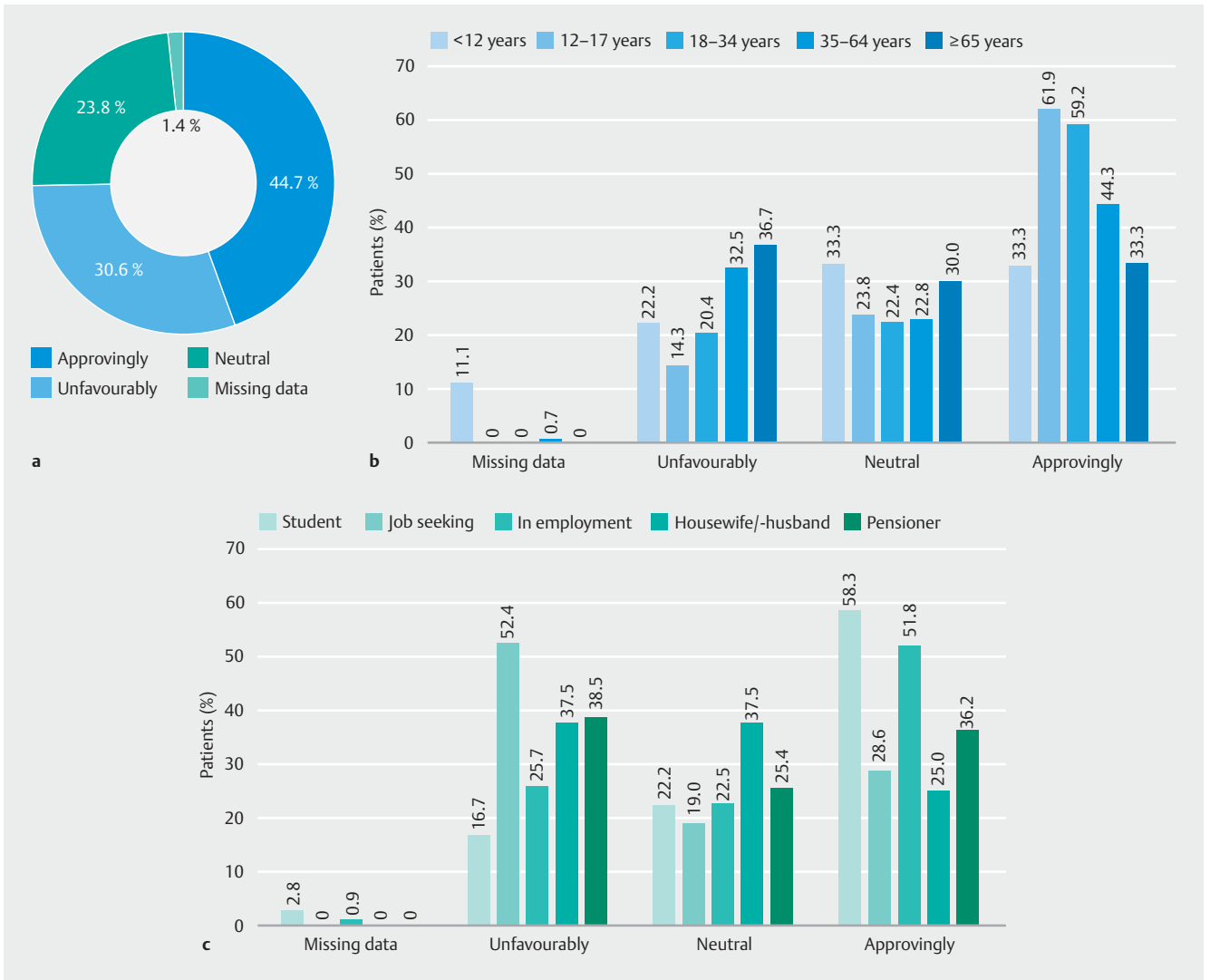
Discussion

Several clinical trials support the add-on therapy of biologics in patients with severe persistent allergic asthma [7–12]. However, administration of biologics is time-consuming as injections are given every two to eight weeks depending on medication used. This can impact patients' everyday life, as regular visits to the physician's office must be scheduled around day-to-day life, which may be challenging due to work or school. As a result of this, compliance to therapy may decrease over time. Self-administration of biologics at home could help overcome these chal-

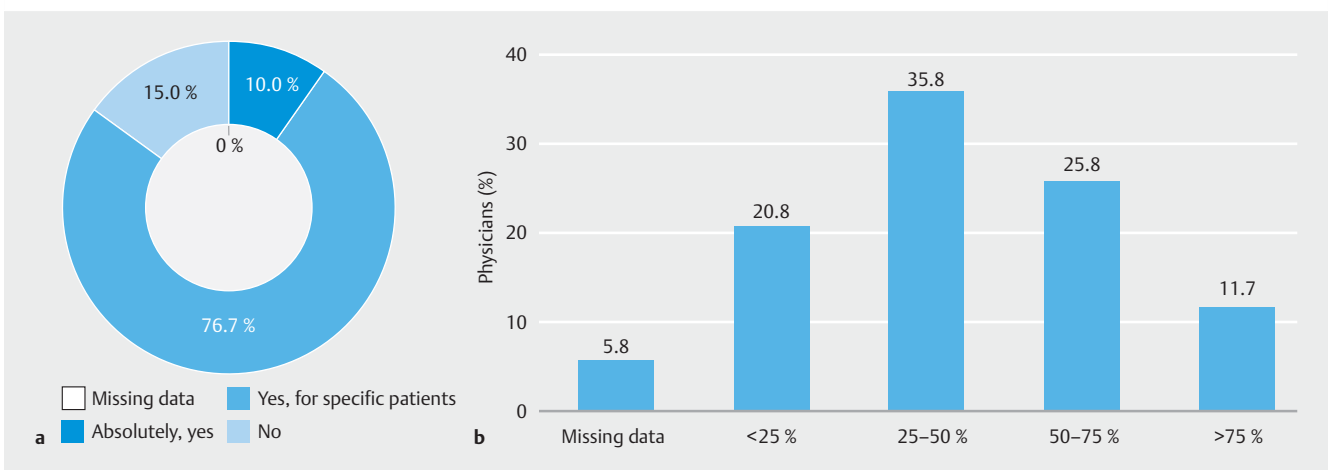
lenges. Effective self-administration at home has already been shown with other biological agents in rheumatoid arthritis [13] and psoriasis [14] as well as immunoglobulin-replacement therapy in primary immunodeficiency [14, 15].

Over the last year, four out of the five biologics approved of treatment of severe asthma have been granted approval for patient self-administration at home. However, little is known about preferences of patients with severe asthma concerning self-administration of biologics and how physicians regard this type of administration that will be performed without medical supervision. To answer these questions, a multiple-choice survey was conducted among severe asthmatic patients and their treating physicians regarding the potential home use of biologics (in this case omalizumab) before EU approval was granted. Overall, nearly half of the patients welcomed the idea of self-administration at home, and time saving was the most favourable advantage. This is in accordance with a small study that described home self-administration of omalizumab in 68 patients with chronic spontaneous urticaria. Patients reported a preference to home treatment as it had a lower impact on their daily living [16]. In our survey, teenagers and young adults were particularly in favour of self-administration, while approval rating declined with age. This was also reflected looking at answers given according to profession. Students and employees had the most positive attitude. Time saving was the most mentioned advantage of home use, which could explain this age- and profession-dependent response. It is more difficult to make regular visits to the physician's office while having to go to work or school, as opposed to people with seemingly more flexibility in their day-to-day life (housewives, househusbands, pensioners and job seekers). Furthermore, young adults may value their independence more than other age groups, while pensioners may be more inclined to visit physicians on a routinely basis, anyway. Similar to our results, preference regarding self-administration was also age-dependent in patients with rheumatoid arthritis. Postal questionnaires and one-to-one interviews revealed that patients younger than 61 years old were more confident about self-administering treatment, while older patients preferred health care staff to administer treatment, as they find reassurance from contact with health care professionals and other patients with rheumatoid arthritis [17].

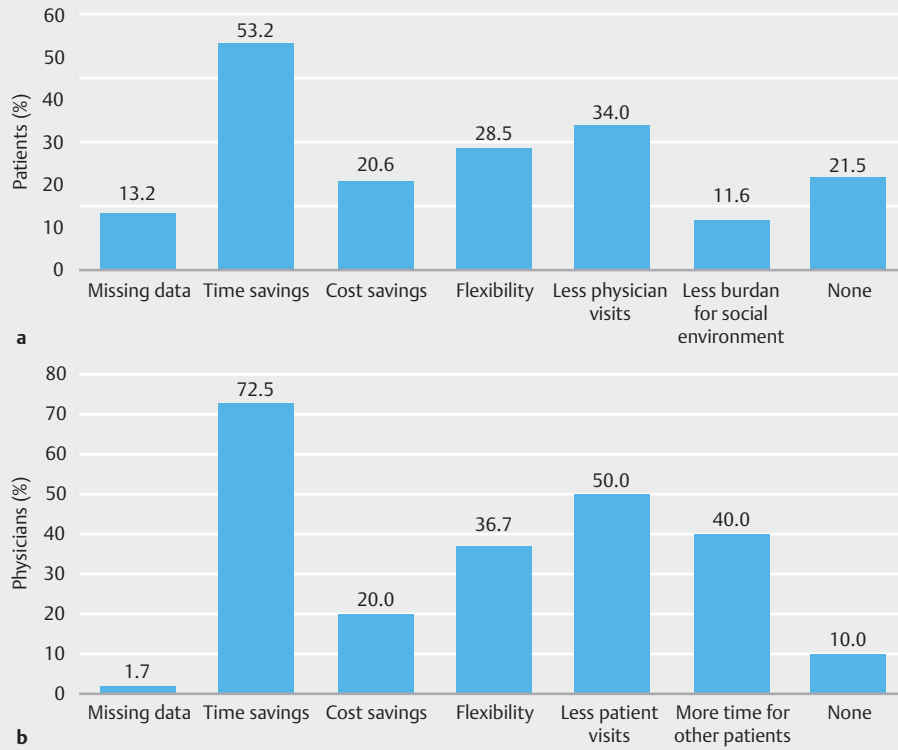
Understanding the individual preferences of patients regarding administration of biologics is a key for the treating physicians. As shown by the results of our survey, not all patients are in favour of self-administration. This is in accordance with the view of the questioned physicians, as most would limit self-administration to certain patients. It is therefore important for patients and physicians to discuss in detail the administration options, which may in turn improve adherence to therapy and well-being of the patient. Only a few patients had concerns about missing an injection at home, which may be due to the severity of their illness and recognizing the necessity of their therapy. On the other hand, more than two thirds of physicians quoted adherence problems (forgetting to inject omalizumab) as their main concern regarding self-administration at home. This concern may be unfounded. In a study by Denman et al., adherence



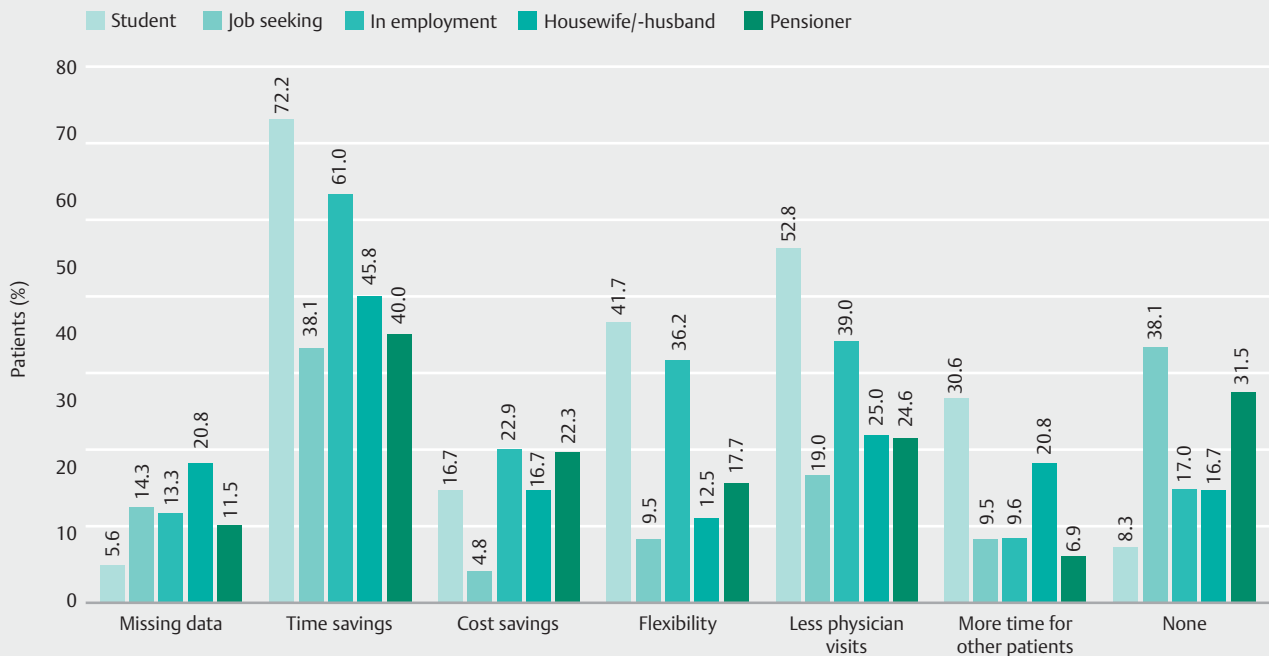
► **Fig. 1** Views about the potential use of omalizumab at home (unfavourably, neutral and approvingly) according to (a) all patients; b patients' age; c patients' profession. Note: Percentages may not add up to 100% due to rounding and (unrequested) multiple answers.



► **Fig. 2** a Physicians' view of omalizumab self-administration and (b) percentages of patients considered for omalizumab home use by their physicians.

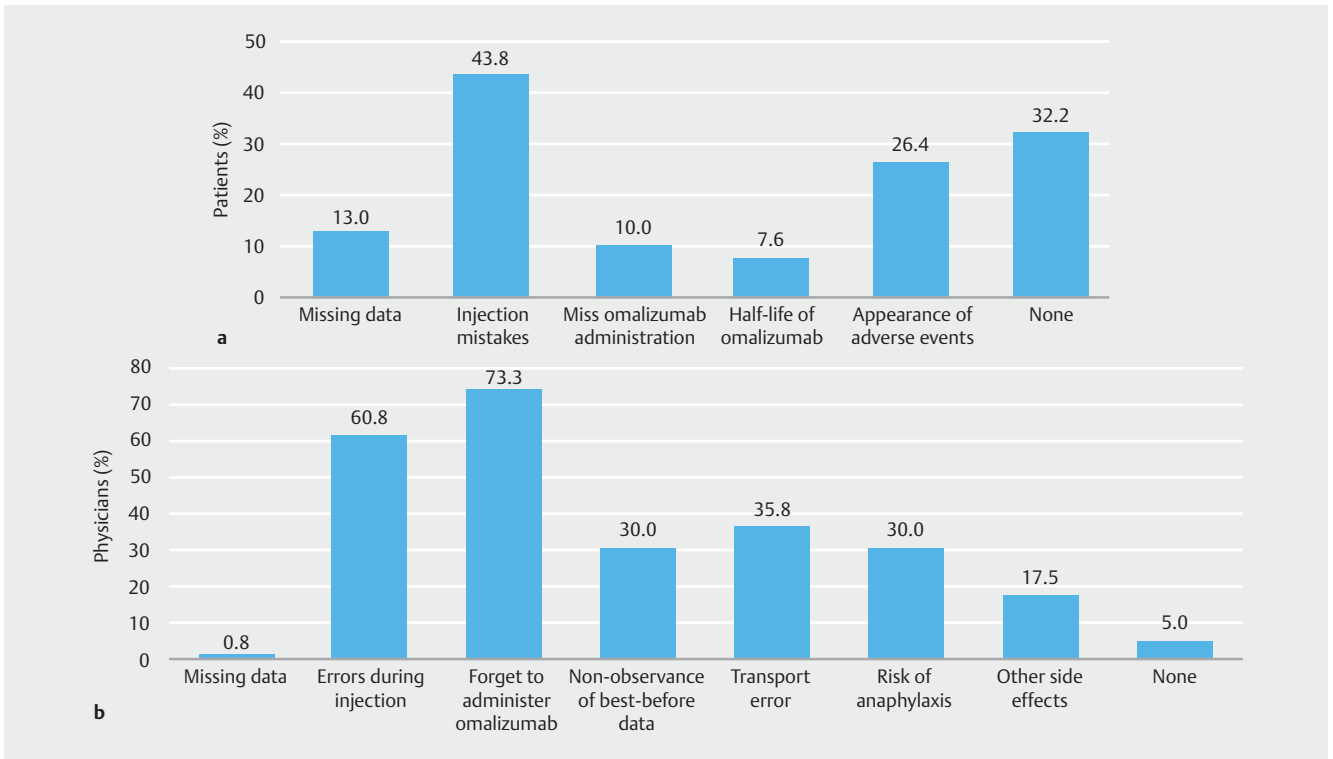


► **Fig. 3** Advantages of omalizumab self-administration for (a) patients and (b) physicians (multiple answers possible).

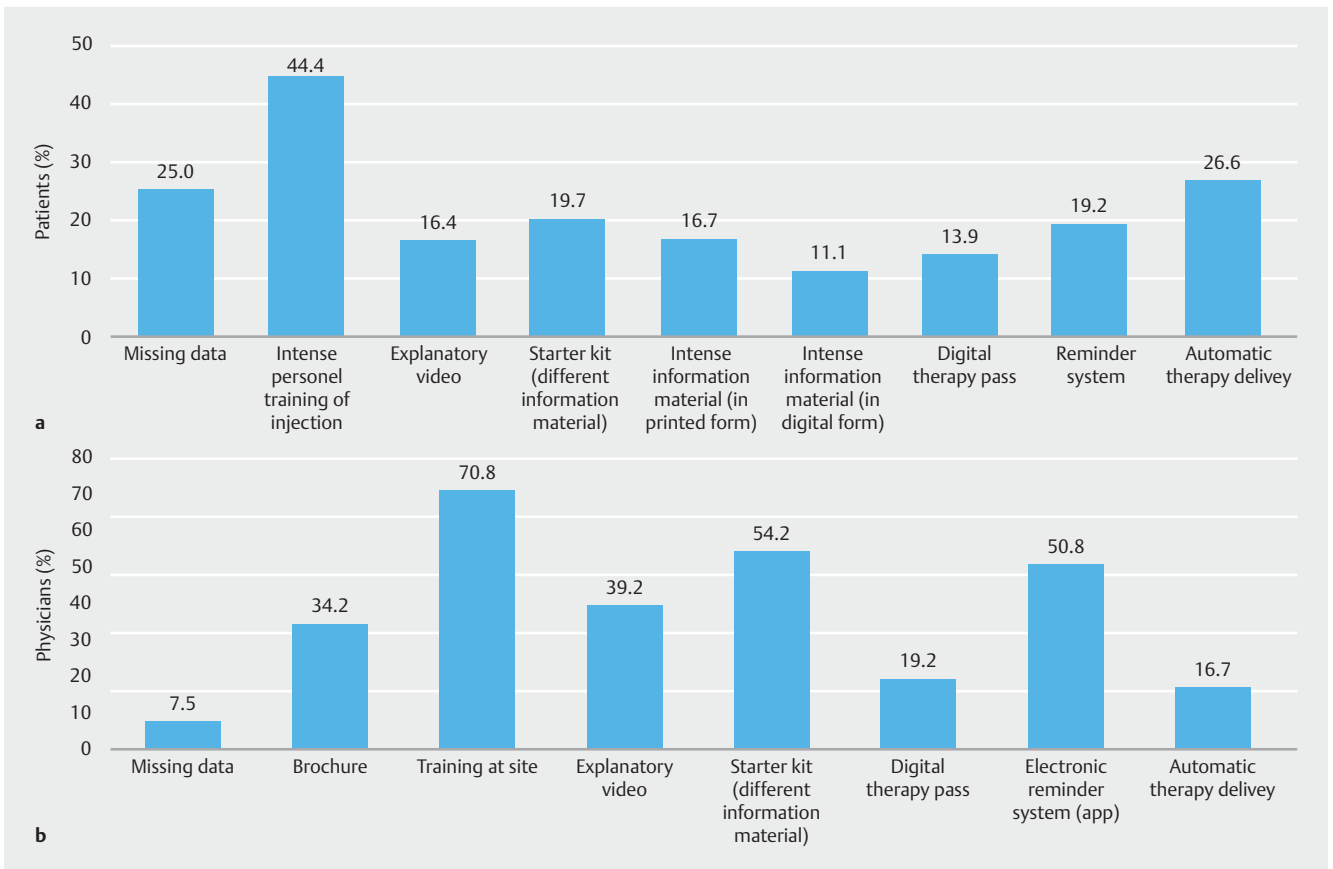


► **Fig. 4** Advantages of omalizumab self-administration according to profession of patients (multiple answers possible).

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► **Fig. 5** Concerns about omalizumab self-administration from (a) patients and (b) physicians (multiple answers possible).



► **Fig. 6** Support materials as wished for by (a) patients and (b) physicians (multiple answers possible).

to biologic self-administration in patients with chronic spontaneous urticaria appeared to be excellent (self-reported adherence) [16], and high treatment adherence with self-administration has also been observed in other diseases such as multiple sclerosis (objectively assessed using electronic injection logs) [18]. Nonetheless, reasons for non-adherence can be manifold and include injection anxiety or injection pain as well as forgetfulness and not knowing exactly how to administer the medicine, which was also reflected by the results of our survey. The main concern of the patients regarding self-administration was 'making a mistake while injecting'. Most of such barriers can be overcome with appropriate training, enabling patients to administer doses safely and effectively at home. In our survey, individual training was the most common request expressed by patients and also reflected in the physicians' answers. An educational video may be a good supplement to standard in-person teaching and can decrease training time [19]. To facilitate adherence, smartphone apps with reminder systems and tips for administration are a novel approach to improve medication-taking behaviour [20]. However, only a fifth of patients questioned in our survey expressed their wishes for an explanatory video or reminder systems, respectively, so it remains to be seen whether these are beneficial in real life.

Approximately one third of physicians was concerned about the potential anaphylaxis risk of patients administering omalizumab at home. However, in four studies no cases of treatment-associated anaphylaxis were reported during self-administration of biologics, including omalizumab [3–6]. Furthermore, long-term experience in real-life setting has shown that prevalence of anaphylaxis in omalizumab-treated patients with asthma is in general very low (zero cases over a period of nine years) [21]. If anaphylaxis occurred, it was most frequently within the first three doses [2, 22]. Even under expanded approval, the first three doses still have to be administered under medical supervision. This will allow physicians to determine whether self-administration at home is appropriate for individual patients. Only those with no known history of anaphylaxis are allowed to self-administer omalizumab or be injected by a trained caregiver from the fourth dose onwards.

Overall, self-administration of biologics, in this survey exemplified by omalizumab, is seen positively by patients and physicians as it is timesaving for both groups. Whether patients are eligible for self-administration is the decision of the treating physician. Individual patient selection and training of self-administration are key factors, and patient adherence must be guaranteed.

Conclusion

Overall, nearly half of the patients questioned were in favour of biologic (exemplified by omalizumab) self-administration at home, citing time saving as the main advantage. Especially teenagers and young adults had a positive attitude towards self-administration. Most physicians were also supportive of home use. In conclusion, self-administration of biologics has the potential to be timesaving for both patients and physicians.

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Conflict of interest

Claudia Mailänder is an employee of Novartis Pharma GmbH. Hartmut Timmermann has received consultancy fees from several pharmaceutical companies (Astra-Zeneca, Ammirall, Astellas, Bayer, Boehringer, Berlin Chemie AG, GSK, Leti, Meda, Mundipharma, Novartis, Nycomed, Pfizer, Sanofi, Takeda und Teva). Financial support: The study was sponsored by Novartis Pharma GmbH, Germany. Novartis Pharma GmbH, Germany, provided financial support for the preparation of the manuscript, including all article-processing charges.

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