

# Use of Supplementary Patient Education Material Increases Treatment Adherence and Satisfaction Among Acne Patients Receiving Adapalene 0.1%/Benzoyl Peroxide 2.5% Gel in Primary Care Clinics: A Multicenter, Randomized, Controlled Clinical Study

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## ABSTRACT

**Introduction:** Poor adherence to acne treatment may lead to unnecessary treatments, increased healthcare costs, and reduced quality of life (QoL). This multicenter study evaluated the effect of supplementary patient education material (SEM) (a short video, information card, and additional information available online) on treatment adherence and satisfaction among acne patients treated with the fixed-dose

combination adapalene 0.1%/benzoyl peroxide 2.5% gel (A/BPO) in primary care clinics versus (1) standard-of-care patient education (SOCPE) (package insert and oral instruction) and (2) SOCPE plus more frequent clinic visits.

**Methods:** Subjects with acne were randomized to receive once-daily A/BPO for 12 weeks plus (1) SEM in addition to SOCPE; (2) SOCPE only with two additional visits; or (3) SOCPE only. Other assessments included a subject appreciation questionnaire, a physician questionnaire, and safety.

**Results:** Ninety-seven subjects were enrolled. At baseline, most (87.6%) had mild to moderate acne. Better adherence was observed in the A/BPO + SEM group compared with A/BPO + more visits or A/BPO alone [mean 63.1%, 48.2% ( $p = 0.0206$ ), and 56.5%, respectively]. The A/BPO + SEM group had more subjects with greater than 75% adherence (45%, 30.4%, and 25%, respectively). According to the subject appreciation questionnaire, the SEM was more helpful to adhere to treatment (56.7%) versus more visits (32.3%) and A/BPO alone (15.2%), better use the product (70%, 61.3%, and 54.5%, respectively), and better manage skin irritation (53.3%, 48.4%, and 36.4%, respectively). All physicians were satisfied with the SEM and 90% would consider using it in their practice. Safety assessment showed fewer treatment-related adverse events in the A/BPO + SEM group.

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**Conclusion:** Use of the SEM may increase adherence of acne patients treated with once-daily A/BPO gel in primary care, consequently improving treatment and QoL in the long term.

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## INTRODUCTION

Acne vulgaris is a chronic and complex skin disease, affecting approximately 80% of adolescents and young adults [1, 2]. If left untreated, acne can have a profound negative impact on patient quality of life (QoL) and psychosocial development.

Combination therapies for acne, utilizing agents with different modes of action, facilitate the simultaneous targeting of multiple factors. A fixed-dose topical combination gel containing adapalene 0.1% and benzoyl peroxide (BPO) 2.5% (A/BPO) was developed for once-daily treatment of acne. The different mechanisms of action and favorable efficacy/safety profiles of adapalene and BPO make them logical choices for combination agents [3–5]. The efficacy and safety of A/BPO have been demonstrated in several studies [6–8].

While A/BPO was effective in numerous clinical studies, it may be less effective in clinical practice because of suboptimal adherence of acne patients to treatment [9]. In a small pilot study, the use of medication event monitoring system (MEMS) caps to objectively assess adherence to topical BPO gel has shown that adherence decreased after dispensation, with 82% of subjects applying medication on day 1 and only 45% at week 6 ( $p < 0.001$ ) [10]. According to a large-scale worldwide observational study using a short and validated questionnaire (ECOB) to assess the risk of poor adherence of acne patients, it was estimated that poor adherence occurred in 40% of patients treated with topical acne therapies [11, 12]. Similarly, low adherence to acne therapies was

found using subjective methods of data collection in various geographic zones of the world [13–15]. Effective strategies for the improvement of adherence include more frequent visits [16, 17], patient education through internet-based surveys, and demonstrations on the proper usage of the medication before dispensation [18, 19].

Poor adherence is independently correlated with lack of knowledge about acne treatment, consultation with a primary care physician, and the occurrence of side effects, among other factors [11]. Therefore, adherence to once-daily A/BPO treatment may be improved by a supplementary patient education intervention, providing information about the mode of action of the medication, the method of application, improvement expectations, and management of irritation if this occurs during treatment.

The purpose of this study was to evaluate the effect of patient education on treatment adherence in primary care clinics. The study design was in line with routine practice in the UK and recommendations from the National Institute for Clinical Excellence for the treatment of acne in primary care [20]. The objective was to evaluate the effect of a supplementary patient education intervention on treatment adherence and satisfaction among acne patients treated with once-daily A/BPO gel in primary care clinics versus (1) standard-of-care patient education (SOCPE) and (2) more frequent clinic visits.

## METHODS

### Study Design

This was a multicenter, randomized, and controlled clinical study conducted in primary care clinics in the UK. The study included subjects aged at least 12 years with acne, randomized into three groups to receive once-daily A/BPO gel for 12 weeks:

- A/BPO + supplementary educational material (SEM): supplementary patient educational material in addition to SOCPE (package insert and oral instruction) with

visits at baseline and weeks 6 and 12. The SEM included a 3-min video about the mode of action of A/BPO, the method of application, treatment expectations, and management of irritation. Subjects also received an information card containing the key messages of the video, as well as additional information about acne and A/BPO available online. Briefly, the key messages contained in the video are as follows:

- Use A/BPO once a day in the evening.
- Cleanse all areas affected by acne with a gentle cleanser and dry with a clean towel.
- Use one small pea-sized amount of A/BPO spread over all affected areas, not just on the spots.
- Moisturize afterwards to help improve the condition of the skin.
- You should notice an improvement in 1–4 weeks.
- Manage irritation if it occurs by applying the treatment every other day at first.
- A/BPO + more visits: subjects received only SOCPE. However, these subjects attended two additional visits (baseline and weeks 3, 6, 9, and 12).
- A/BPO alone: subjects received only SOCPE with visits at baseline and weeks 6 and 12.

All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1964, as revised in 2013. Informed consent was obtained from all patients for being included in the study. ClinicalTrials.gov identifier: NCT02307266.

### Assessments

Treatment adherence was assessed using the MEMS to objectively evaluate subjects' adherence to the study treatment. The A/BPO gel pump was placed in a container fitted with a MEMS cap. The MEMS cap recorded the time and date every time it was opened and/or closed, and stored the data in an electronic chip. The MEMS cap was returned by the

subjects at the end of the study for data analysis. This assessment was performed without subjects' knowledge, to limit bias. Subjects were informed about this method of data collection at the end of the study.

Other assessments included a subject appreciation questionnaire at week 12, a physician questionnaire, and safety.

The 12-item subject appreciation questionnaire was completed at week 12 to evaluate subject satisfaction regarding the treatment used and the information they received.

The 14-item physician questionnaire was completed by the investigator at the end of the study regarding the SEM used.

Safety was assessed via monitoring of adverse events (AEs) throughout the study.

### Statistical Analysis

This was an exploratory study and no statistical rationale for sample size calculation was used. The plan to include 30 subjects per group was based on previous pilot studies using MEMS to study strategies for the improvement of treatment adherence [10].

Prior to study initiation, a randomization list was generated by a statistician. The RANUNI routine of the Statistical Analysis System (SAS Institute Inc., Cary, USA) was used for the generation of kit numbers. Randomization was conducted on a 1:1:1 ratio. This study did not have a blind design.

Comparison of the adherence variables between groups was performed using the Cochran–Mantel–Haenszel (CMH) test stratified by center after ridit transformation with the row mean difference statistics, testing the hypothesis of equality.

Two subject populations were analyzed: intent-to-treat (ITT)/worst-case population for adherence throughout the study period and ITT/observed population for adherence per week. The ITT/worst-case population consisted of all subjects who kept the product in the secondary container at all times. For subjects reporting an early termination, the missing values between the last visit and the theoretical

date of week 12 visit (84th day) was imputed as zero (no opening).

## RESULTS

### Disposition and Baseline Disease Characteristics

The study was conducted from November 2014 to June 2015 in nine primary care clinics in the UK. A total of 97 subjects (mean age 22.5 years) were enrolled. Of those, 82 subjects (84.5%) completed the study (Fig. 1). The majority of subjects (69.1%) were female and the most frequent skin phototypes were II and III. At baseline, 85 subjects (87.6%) had mild to moderate acne, with a third of those classified as moderate. Overall, mean acne duration was approximately 5 years in each group (Table 1).

### Assessment of Treatment Adherence (MEMS)

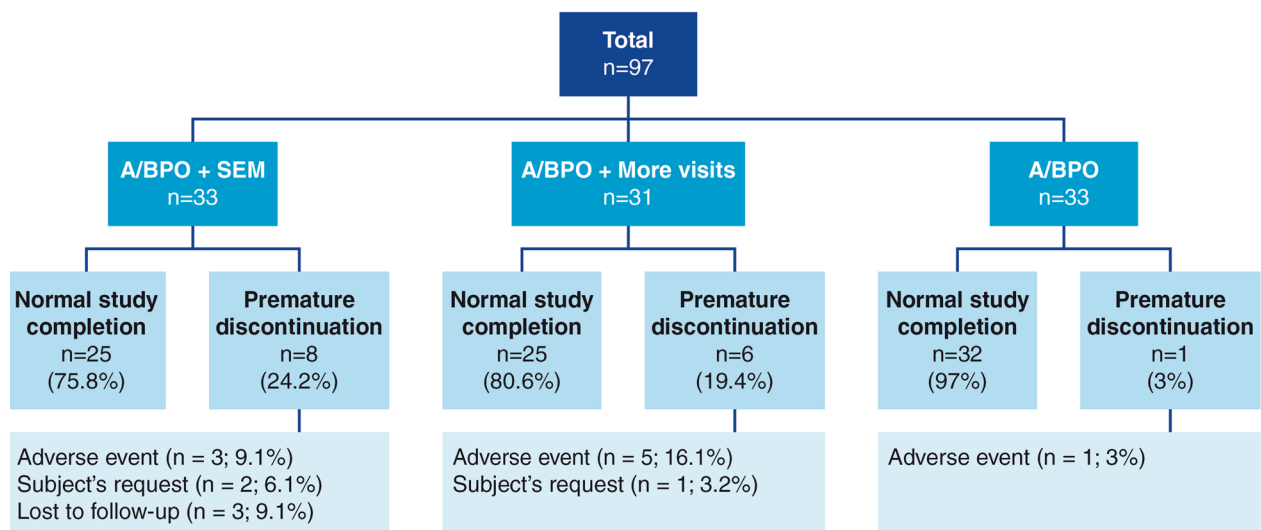
For the ITT/worst-case population, a better adherence was observed in the A/BPO + SEM group compared with the A/BPO + more visits or A/BPO alone groups (mean of 63.1%, 48.2%,

and 56.5%, respectively). The difference with the A/BPO + more visits group was significant ( $p = 0.0206$ ). In addition, the A/BPO + SEM group had more subjects with greater than 75% adherence (45%) compared with the A/BPO + more visits (30.4%) and A/BPO alone (25%) groups (Fig. 2).

For the ITT/observed population, the same trend was observed, with better adherence in the A/BPO + SEM group (66.9%) than in the A/BPO + more visits (55.2%) and A/BPO alone (56.5%) groups (Fig. 3). Additionally, more subjects in the A/BPO + SEM group had greater than 75% treatment adherence (50%) compared with the A/BPO + more visits (34.8%) and A/BPO alone (25%) groups.

### Subject Appreciation Questionnaire

According to the subject appreciation questionnaire, the SEM was more helpful to adhere to the treatment (56.7%) versus more visits (32.3%) and A/BPO alone (15.2%), better use the product (70%, 61.3%, and 54.5%, respectively), and better manage skin irritation (53.3%, 48.4%, and 36.4%, respectively) (Fig. 4). More subjects in the A/BPO + SEM group understood that an improvement was to be



**Fig. 1** Subject disposition

**Table 1** Demographics and baseline disease characteristics

	A/BPO + educational material ( <i>N</i> = 33)	A/BPO + more visits ( <i>N</i> = 31)	A/BPO ( <i>N</i> = 33)	Total ( <i>N</i> = 97)
Gender				
Male	11 (33.3%)	12 (38.7%)	7 (21.2%)	30 (30.9%)
Female	22 (66.7%)	19 (61.3%)	26 (78.8%)	67 (69.1%)
Age				
Mean	24.1	22.5	21.0	22.5
Min, max	12, 49	12, 51	12, 44	12, 51
Race				
White	29 (87.9%)	27 (87.1%)	26 (78.8%)	82 (84.5%)
Asian	3 (9.1%)	4 (12.9%)	6 (18.2%)	13 (13.4%)
Other	1 (3.0%)	0	1 (3.0%)	2 (2.1%)
Phototype				
I	2 (6.1%)	2 (6.5%)	3 (9.1%)	7 (7.2%)
II	11 (33.3%)	11 (35.5%)	9 (27.3%)	31 (32.0%)
III	14 (42.4%)	12 (38.7%)	13 (39.4%)	39 (40.2%)
IV	5 (15.2%)	4 (12.9%)	6 (18.2%)	15 (15.5%)
V	1 (3.0%)	2 (6.5%)	2 (6.1%)	5 (5.2%)
IIGA				
1: Almost clear	8 (24.2%)	3 (9.7%)	1 (3.0%)	12 (12.4%)
2: Mild	17 (51.5%)	20 (64.5%)	22 (66.7%)	59 (60.8%)
3: Moderate	8 (24.2%)	8 (25.8%)	10 (30.3%)	26 (26.8%)
Mean ± SD	2.0 ± 0.7	2.2 ± 0.6	2.3 ± 0.5	2.1 ± 0.6
Acne history (duration in years)				
Mean ± SD	5.7 ± 9.3	4.7 ± 5.6	4.4 ± 4.6	4.9 ± 6.8

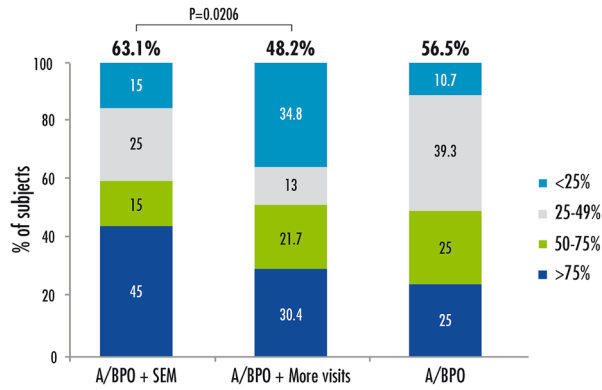
expected after 1–4 weeks of treatment (82.8%) compared with more visits (61.3%) and A/BPO alone (48.5%) (Fig. 4), and the treatment was to be applied over the entire face avoiding eyes and lips (63.0% versus 54.8% and 54.5%, respectively).

In addition, more subjects in the A/BPO + SEM group understood how to reduce side effects observed at the beginning of treatment without affecting efficacy by applying the

treatment every other day for the first 2 weeks (30.0% versus 6.5% and 15.2%, respectively), and were not at all bothered by the side effects of the treatment (51.7%, 38.7%, and 42.4%, respectively).

### Physician Questionnaire

The physicians were asked to provide their opinion on the SEM used in this study. All



**Fig. 2** Subject adherence to treatment according to the medication event monitoring system (ITT/worst-case population)

physicians were satisfied with the video, found that it was easy for the target population to understand, and that the information was relevant and complete for their patients.

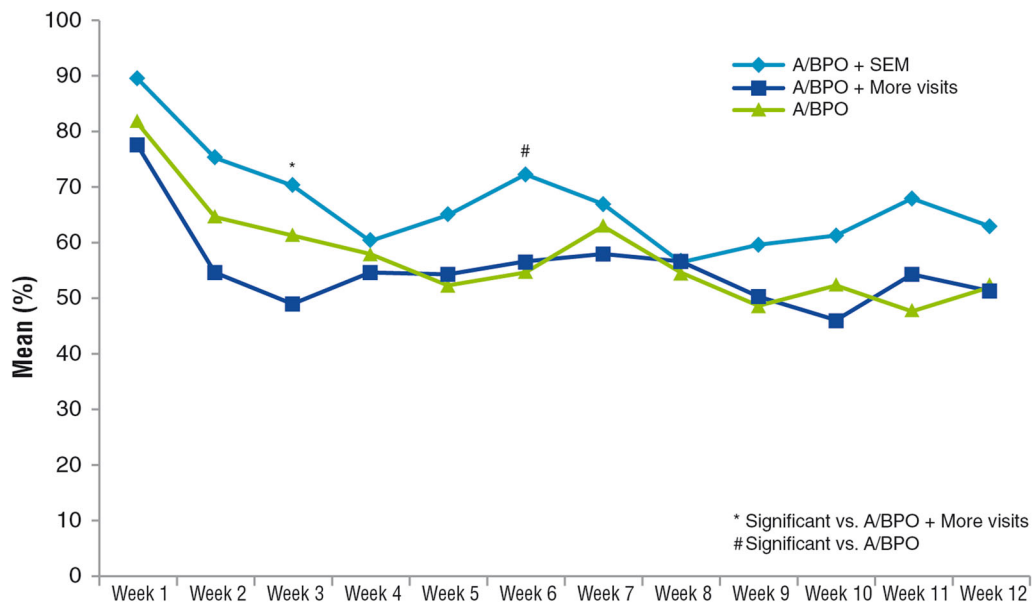
The majority of physicians considered that it better managed patients’ expectations (55.6%) and saved time explaining how to use A/BPO (66.7%). Nearly all physicians (88.9%) would consider using this video in their practice in the future. The trend was similar for the patient information card.

**Safety**

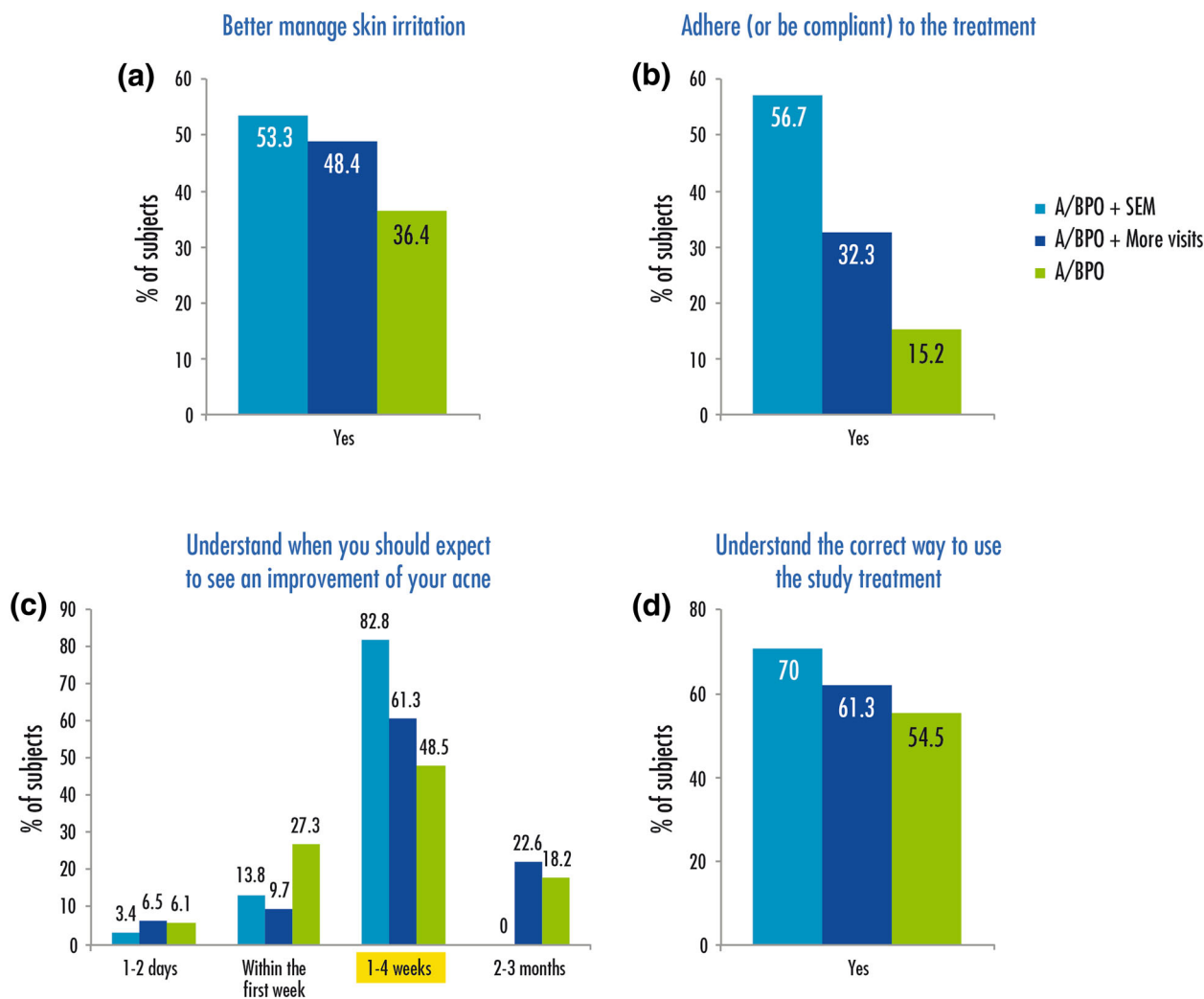
A total of 22 AEs in 17 subjects (17.5%) were considered as treatment-related, all of which were of dermatological nature. Fewer treatment-related AEs were reported in the A/BPO + SEM group compared with the A/BPO + more visits and A/BPO alone groups (4, 12, and 6, respectively). The most frequent AEs related to the study drug were dry skin (4.1%) and erythema, rash, and skin irritation (3.1% each).

**DISCUSSION**

Acne is a chronic disease requiring long-term management. It may be necessary to continue treatment for prolonged periods of time to ensure therapeutic success and prevent disease relapse. Despite the availability of efficacious and safe therapeutic options for topical treatment, poor adherence of patients to such therapies may lead to unnecessary treatments, increased healthcare costs, and reduced patient QoL. Dréno et al. previously identified factors associated with poor adherence including the



**Fig. 3** Subject adherence to treatment according to the medication event monitoring system per week (ITT/observed population)



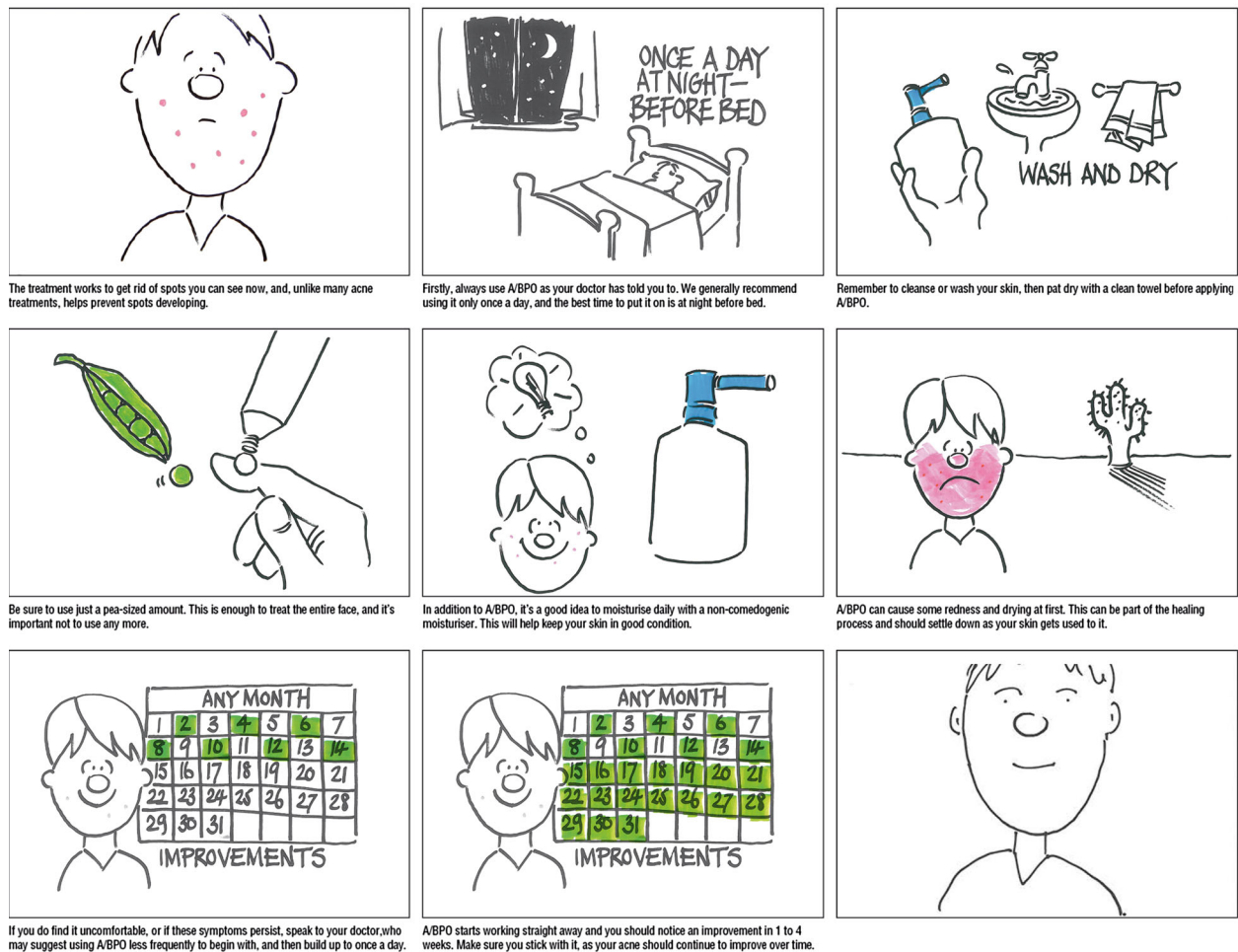
**Fig. 4** Subject appreciation questionnaire: the information you have received in the study about the treatment helps you to **a** better manage skin irritation? **b** adhere (or

be compliant) to the treatment? **c** understand when you should expect to see an improvement of your acne? and **d** understand the correct way to use the study treatment?

occurrence of side effects, lack of knowledge about acne and acne treatment, consultation with a primary care physician, and lack of patient satisfaction with treatment, among others [11]. Snyder et al. stated that a physician’s ability to convey information about the medication is critical for treatment success and patient satisfaction [9]. For effective patient education and counselling on the treatment of chronic disease, various means of information such as reading materials, videos, and reminders may be utilized [21–23]. Recent studies have shown that written counselling significantly

improved adherence in acne patients [24]. Moreover, evidence from an observational study has shown that A/BPO gel leads to good treatment adherence for the majority of patients [25].

This multicenter, randomized, and controlled study assessed the effect of patient education on treatment adherence and satisfaction among acne patients receiving once-daily A/BPO gel treatment in primary care clinics in the UK versus SOCPE and more frequent clinic visits. Figure 5 is an excerpt from the SEM video shown to subjects.



**Fig. 5** Excerpt from the supplementary educational material video

Overall, better adherence was observed in the A/BPO + SEM group compared with the A/BPO + more visits or A/BPO alone groups, as measured by MEMS. The similar adherence between the group with extra visits and the A/BPO alone group may be due to the timing of the additional visits. These visits took place on weeks 3 and 9, whereas treatment-related irritation is more likely to occur earlier, which may explain why the extra visits had little effect on adherence. According to the subject appreciation questionnaire, the SEM helped them adhere to treatment, better use the product, and manage their expectations and side effects. Subjects were also more satisfied in terms of safety in the A/BPO + SEM group. All physicians were satisfied with the SEM provided and the

vast majority would consider using it in their practice.

A/BPO was well tolerated in this study, with related AEs as expected from previous studies and post-marketing experience. All related AEs were mild to moderate in intensity and resolved quickly and spontaneously. Although the A/BPO + SEM group reported more premature discontinuation compared with the other groups (8, 6, and 1, respectively), only one of those was related to the study treatment. A possible explanation for the higher premature discontinuation reported in the A/BPO + SEM group is that more subjects in this group were “almost clear” at baseline and if they achieved a “clear” status at an early stage of the treatment they may not have wanted to continue treatment.



A limitation of this study is that the MEMS used may not be a user-friendly system. The subjects had to open and close the cap on every application in order to record data on treatment adherence. This may potentially introduce more missing values during the data collection process.

## CONCLUSIONS

This educational material is easy to understand and use. Use of this material may increase adherence of patients treated with once-daily A/BPO gel for acne in primary care, consequently improving treatment and QoL in the long term. Physicians could consider using this material in their practice to enhance patient satisfaction and treatment outcome. Future studies are warranted to confirm that improved treatment adherence should translate into improved efficacy.

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Nestle Skin Health-Galderma R&D. T. McCormack served as an investigator for Nestle Skin Health-Galderma R&D. N. Kerrouche is an employee of Nestle Skin Health-Galderma R&D.

**Compliance with Ethics Guidelines.** All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1964, as revised in 2013. Informed consent was obtained from all patients for being included in the study.

**Data Availability.** The datasets generated during and/or analyzed during the current study are not publicly available as they are proprietary data, but all of the conclusions drawn in the manuscript are based on data included in the publication and supporting literature has been provided.

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