ARTICLE

Effectiveness and patient satisfaction with the new sildenafil oral suspension formulation compared to sildenafil oro-dispersible film: a real-life study

Luca Boeri[1]✉, Giorgio Graps[1], Ester Zino[1], Agnese Zago[1], Andrea Li Puma[1], Fabio Ciamarra[1], Antonio Cimmino[1], Valentina Parolin[1], Michela Piccoli[1], Franco Gadda[1], Emanuele Montanari[1,2] and Giancarlo Albo[1,2]

Sildenafil is one of the most used phosphodiesterase type 5 inhibitor (PDE5i) for the treatment of erectile dysfunction (ED) in clinical practice. A new oral suspension formulation (OSF) of sildenafil has been introduced to overcome the drawbacks of previous formulations. We assess the efficacy and patients' experience with sildenafil 50 mg OSF in men with ED who were taking the sildenafil oro-dispersible film (ODF). Demographics and clinical data from 70 consecutive men with mild-moderate ED were analysed. Patients were treated with sildenafil 50 mg ODF for 12 weeks (follow-up 1), then, after 2-week washout, were administered sildenafil 50 mg OSF for 12 weeks (follow-up 2). At each follow-up, patients completed the International Index of Erectile Function (IIEF), the Patient Global Impression of Improvement (PGI-I), and the Psychological and Interpersonal Relationship Scales-Short Form (PAIRS-SF) questionnaires. Descriptive statistics described the whole cohort. The Wilcoxon Signed Rank Test assessed potential differences in psychometric scores at different follow-up assessments. Logistic regression analyses tested the associations between study variables and satisfaction after sildenafil OSF treatment. Overall, median age was 56 (51–62) years, and median IIEF-EF score was 14 (12–17). Compared to baseline, IIEF-EF scores significantly improved after sildenafil ODF and OSF treatment (all $p < 0.01$) with no differences between the two formulations. IIEF-overall satisfaction (OS) was higher after sildenafil OSF than ODF ($p < 0.001$). Similarly, median PGI-I score were better after sildenafil OSF than ODF ($p < 0.001$). The PAIRS-SF spontaneity scores were significantly higher after OSF than ODF ($p < 0.01$). At multivariable logistic regression analysis, younger age ($p = 0.02$) and lower baseline IIEF-EF scores ($p = 0.01$) were independent predictors of improved satisfaction with OSF compared to ODF. The sildenafil OSF and ODF had similar efficacy, however the new OSF provides higher satisfaction and spontaneity scores compared to the oro-dispersible film.

IJIR: Your Sexual Medicine Journal; https://doi.org/10.1038/s41443-025-01019-4

INTRODUCTION

Erectile dysfunction (ED) affects approximately 50% of men over the age of 40, often leading to significant distress, but it is also quite common in young individuals (26% of newly diagnosed in men <40 years) [1–3]. ED can severely impact men's quality of life by affecting their self-esteem, sexual well-being, and interpersonal relationships [4]. Given that sexual satisfaction is a key predictor of overall life satisfaction, addressing ED has the potential to enhance the quality of life of both affected individuals and their partners [5]. Moreover, since ED has been considered as a sentinel marker of co-existing, undiagnosed and future cardiovascular disease, its detection and comprehensive management are important in terms of preservation of the overall men's health [6–8].

Phosphodiesterase type 5 inhibitors (PDE5i), in clinical practice, are used as the first line treatment option in men with ED [7]. Several PDE5i are available in the market, each one with an individual pharmacokinetic and side effects profile [7]. Sildenafil, the first approved PDE5i in 1998, is the treatment of choice for men prioritizing a high efficacy [9]. Moreover, during its 25 years of existence, sildenafil has undergone several advancements to better address patients' needs and enhance their sexual life. Besides the classic film-coated tablets (25, 50 and 100 mg) an oro-dispersible film formulation (ODF) (25, 50, 75 and 100 mg) was developed to overcome the issue of swallowing disorders and the need of water for ingestion [10]. The sildenafil ODF showed similar efficacy, higher satisfaction but worse taste than the film-coated one [11]. However, other studies found no difference in patients' preference among the two formulations [12]. Real-life studies have shown that, irrespective of PDE5i efficacy, most users discontinue therapy during the first year of treatment due to medical (eg, fear of side effects, poor compliance) and psychosocial factors (eg, treatment cost, couple issues, perception of poor intercourse spontaneity) [13]. Therefore, the introduction of new PDE5i formulations that may meet patients' needs and expectations is of fundamental importance to improve treatment adherence.

[1]Department of Urology, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy. [2]Department of Clinical Sciences and Community Health, University of Milan, Milan, Italy. ✉email: dr.lucaboeri@gmail.com

Received: 6 December 2024 Revised: 31 December 2024 Accepted: 20 January 2025
Published online: 29 January 2025

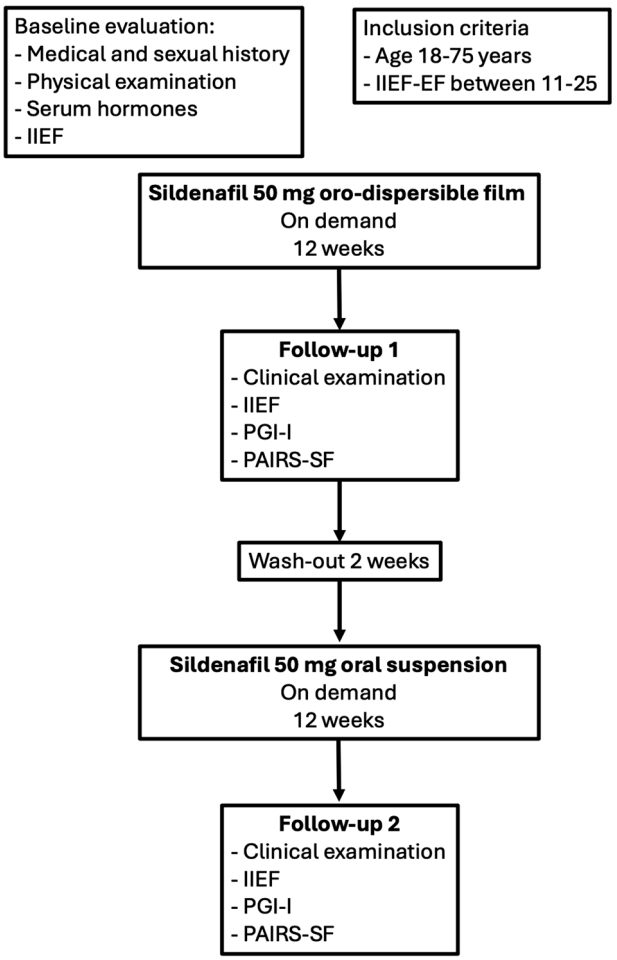

Fig. 1 Study protocol. IIEF international index of erectile function, EF erectile function, PGI-I patient global impression of improvement, PAIRS-SF psychological and interpersonal relationship scales – Short Form.

Recently, a new sildenafil oral suspension formulation (OSF) has been introduced and evaluated in Spain [14]. Physicians reported a higher patient satisfaction for sildenafil OSF, particularly for its ease of use and discretion, along with the possibility of adjusting the dose according to patient's response and circumstances [14]. The OSF of sildenafil has been recently introduced also in Italy, but there is a lack of data concerning its efficacy and impact on patients' sexual life.

In this study we evaluated the efficacy and patients' perception of the sildenafil OSF in men with ED who were taking the sildenafil ODF.

MATERIALS AND METHODS

The analyses of this cross-sectional study were based on a sample of 81 sexually active men consecutively assessed at a single tertiary-referral academic centre with the primary compliant of new onset sexual dysfunction between April 2023 and June 2024. ED was defined as the persistent inability to attain and maintain an erection sufficient to permit satisfactory sexual performance [7].

Patients were assessed with a detailed medical and sexual history including sociodemographic data. Comorbidities were scored with the Charlson Comorbidity Index (CCI) [15], which was categorised as 0 or ≥ 1. Body mass index (BMI) was calculated for each patient. Smoking habits were assessed, and patients were grouped into no smokers (never smoked/ex-smokers) and active smokers, respectively. Similarly, alcohol consumption was categorized as abstainers (no alcohol consumption) and drinkers (any amount per week) [16]. Relationship status was categorized as: sporadic/random vs. stable sexual relationship. Venous blood samples were drawn from each patient between 7 AM and 11 AM after an overnight fast. Serum concentrations of luteinising hormone (LH), follicle-stimulating hormone (FSH), total testosterone (tT) and prolactin were measured in each man.

At first evaluation, all patients were requested to complete the International Index of Erectile Function (IIEF) [17, 18]; to provide a frame of reference for objectively interpreting ED severity, we used the IIEF-erectile function domain (IIEF-EF) classification as proposed by Cappelleri et al. [19]. Moreover, we also considered IIEF sub-domains: orgasmic function (IIEF-OF), sexual desire (IIEF-SD), intercourse satisfaction (IIEF-IS), and overall satisfaction (IIEF-OS). Literacy problems as well as other reading and writing problems were excluded in all patients.

For the specific purpose of this study, we considered only participants (18–75 years old) with mild-to-moderate ED (IIEF-EF between 11 and 25 at baseline), eligible for PDE5i therapy according to current Guidelines [7], who were treated with sildenafil ODF 50 mg on-demand for 12 weeks (follow-up 1). Moreover, after two-week washout period from sildenafil ODF 50 mg, all enrolled patients were asked to take sildenafil OSF 50 mg on-demand for 12 weeks (follow-up 2) (Fig. 1). The OSF is a system releasing 0.5 mL of suspension containing 12.5 mg of sildenafil with each pulse, therefore patients had to perform 4 puffs to obtain 50 mg of treatment medication. Similar to the ODF, the oral suspension formulation of sildenafil was recommended 45 to 60 min before approaching the partner [11, 14]. Patients were encouraged to attempt sexual intercourse using the prescribed drug on at least 8 occasions during the period between visits.

We excluded: participants with tT < 3.5 ng/mL ($n = 2$) [20], with known hypersensitivity to sildenafil or its components ($n = 1$); with previous surgical treatment of the penis or pelvic area ($n = 3$); patients with a known history of depression or depressive symptoms, or those taking any antidepressant therapy ($n = 4$); participants who provided incomplete data at follow-up evaluations ($n = 5$). Therefore, a convenience sample of 70 patients was eventually included in the analysis.

To assess the impact of sildenafil ODF and OSF on sexual function, at follow-up 1 and 2, patients were evaluated by the treating physician and were asked to complete the IIEF, the Patient Global Impression of Improvement (PGI-I) [21], and the Psychological and Interpersonal Relationship Scales-Short Form (PAIRS-SF) questionnaire (Supplementary Material 1) [22]. The PGI-I is used to evaluate patient satisfaction after drug administration compared to the previous evaluation, and its scores range from 1 (very much better) to 7 (very much worse) [21]. The PAIRS-SF measures three conceptual domains: sexual self-confidence, spontaneity, and time concerns leading up to and during sexual encounters [22]. It was introduced to explore different outcomes than the ability to obtain a valid erection, already addressed by the IIEF, which are important to men and their partners, such as spontaneity and pleasure of the time before sexual intercourse. Treatment-related adverse events, patients' assessment of drug taste and ease of use were also investigated.

Data collection followed the principles outlined in the Declaration of Helsinki. All patients signed an informed consent agreeing to share their own anonymous information for other future studies. The study was approved by the Hospital Ethical Committee (Prot. 060182 – SilOros).

Statistical analyses

The sample size was calculated by using the paired t-test analysis. A previous study conducted in men with ED, treated with sildenafil film-coated and ODF, reported a mean IIEF-OS score difference of 1.0 point between the two formulations [11]. Therefore, we considered a true difference in means of 1 point and a variability (sigma) of 2.5. Considering Alpha = 0.05 and Beta = 0.20 (power = 1 - beta = 0.8) at least 55 participants are needed to achieve a power of 80% (Russ-Lenth applet for Windows). We included 70 participants in this study.

Distribution of data was tested with the Shapiro–Wilk test. Data are presented as medians (interquartile range; IQR) or frequencies (proportions). First, descriptive statistics were used to report baseline clinical and psychometric scores in the whole cohort. Second, the Wilcoxon Signed Rank Test assessed potential differences in IIEF scores at 12 weeks follow-up assessment (after sildenafil ODF treatment), compared to baseline. Similarly, the IIEF, PGI-I and PAIRS-SF scores were compared between the 12 weeks assessment (after sildenafil ODF treatment) and the 26 weeks follow up evaluation (after sildenafil OSF treatment).

Finally, univariate and multivariate logistic regression analyses tested the associations between study variables and PGI-I and IIEF-OS improvement (at least one point of improvement) after sildenafil OSF treatment compared to follow-up 1.

Statistical analyses were performed using SPSS v.26 (IBM Corp., Armonk, NY, USA). All tests were two sided and statistical significance level was determined at $p < 0.05$.

RESULTS

Table 1 details clinical characteristics of the whole cohort. Of all, median (interquartile range – IQR) age and BMI were 56 (51–62) years and 25.8 (23.2–27.9) kg/m^2, respectively. A stable sexual relationship was reported by 43 (61.4%) participants and median ED duration was 18 (10–21) months. Median total testosterone was 4.9 (3.8–7.2) ng/ml and 52 (74.2%) patients were PDE5i naïve. At first evaluation a moderate, mild-to-moderate and mild ED was reported by 12 (17.2%), 36 (51.4%) and 22 (31.4%) participants, respectively, with an overall median IIEF-EF score of 14 (12–17).

Figure 2 shows median IIEF sub-score values during the study protocol. Compared to baseline, IIEF-EF scores significantly improved after sildenafil ODF treatment [23 (22–26), $p < 0.01$] and was similar at follow-up 2, after sildenafil OSF therapy [24 (22–26), $p < 0.01$ vs baseline]. No differences were noted between the two drug formulations. Figure 3 depicts rates of ED severity at each follow-up assessment. Similar findings were observed for IIEF-SD scores. Of note, IIEF-OS and IIEF-IS improved at follow-up 1 compared to baseline (all $p < 0.01$) and further significantly improved at follow-up 2, after sildenafil OSF, compared to the end of the sildenafil ODF treatment (all $p < 0.01$). Supplementary Table 1 reports the numerical values of IIEF scores at different follow-up evaluations.

For the ODF formulation, median PGI-I score was 3 (3–4), but significantly improved after OSF compared to the previous treatment modality [3 (2–3), $p < 0.01$ vs ODF] (Table 2).

The PAIRS-SF self-confidence scores were similar after sildenafil ODF and OSF. However, spontaneity scores were significantly better after OSF than ODF [15 (14–16) vs. 13 (12–13), $p < 0.01$] (Table 2). PAIRS-SF time concerns values were similar at follow-up 1 and 2 evaluations.

After sildenafil ODF treatment, 64 (91.4%) participants complained about the bad taste and 15 (21.4%) reported a mild headache. After OSF use, 20.0% of men had mild headache while 85.7 and 72.7% of participants were enthusiastic about the taste and the ease of use.

Table 3 depicts univariate and multivariate logistic regression models testing the associations between clinical predictors and PGI-I/IIEF-OS improvement after OSF use. Younger age (OR 0.9, $p < 0.001$) and lower baseline IIEF-EF scores (OR 0.8, $p < 0.001$) were associated with PGI-I improvement. At multivariable analysis, only younger age (OR 0.9, $p < 0.01$) emerged as predictor of PGI-I improvement, after accounting for baseline IIEF-EF scores. Similarly, younger age (OR 0.7, $p < 0.001$) and lower baseline IIEF-EF scores (OR 0.7, $p < 0.01$) were associated with IIEF-OS improvement. At multivariable analysis, younger age (OR 0.8, $p = 0.02$) and lower baseline IIEF-EF (OR 0.7, $p = 0.01$) were found to be independent predictors of IIEF-OS improvement.

DISCUSSION

This study was specifically designed to investigate treatment efficacy and patients' perception of a new formulation of sildenafil (oral suspension), recently introduced in our country, compared to the established ODF in a cohort of men with ED. Current findings revealed that the two formulations had similar efficacy in improving EF; importantly, overall and intercourse satisfaction scores were better after sildenafil OSF compared to ODF.

Table 1. Demographic characteristics of the whole cohort of patients (No. = 70).

Age (years)	
Median (IQR)	56 (51–62)
Range	30–75
BMI (kg/m^2)	
Median (IQR)	25.8 (23.2–27.9)
Range	17.4–37.3
CCI (value)	
Median (IQR)	0.0 (0.0)
Range	0–3
CCI ≥1 [No. (%)]	10 (14.2)
Stable sexual relationship [No. (%)]	43 (61.4)
Smoking status [No. (%)]	
Never/former smokers	46 (65.8)
Current smokers	24 (34.2)
Alcoholic status [No. (%)]	
Abstainers	11 (15.7)
Current drinkers	59 (84.3)
LH (mUI/mL)	
Median (IQR)	3.8 (2.5)
Range	0.1–61.0
FSH (mUI/mL)	
Median (IQR)	5.1 (2.5–8.2)
Range	2.1–11.0
tT (ng/mL)	
Median (IQR)	4.9 (3.8–7.2)
Range	3.5–10.3
PRL (ng/mL)	
Median (IQR)	6.8 (4.1–12.7)
Range	1.5–18.7
Duration of ED (months)	
Median (IQR)	18 (10–21)
Range	9–24
PDE5i naïve [No. (%)]	52 (74.2)

BMI body mass index, *CCI* charlson comorbidity index, *tT* total testosterone, *ED* erectile dysfunction.

Furthermore, participants reported that their condition was improved (as scored with the PGI-I) after sildenafil OSF than after the ODF one. Of note, the OSF was associated with better spontaneity scores than the ODF. Younger men and those with more severe ED at baseline experienced greater satisfaction and improvements from the treatment.

It is known that, despite the existence of different PDE5i molecules (sildenafil, tadalafil, vardenafil, avanafil), with various formulations (film-coated, ODF) and dosages, ED patients are not completely satisfied since most of them discontinue the prescribed treatment within one year [13].

Therefore, the introduction of new PDE5i formulations is important in clinical practice to improve patient's adherence to treatment and their sexual life. Our interest was motivated by the recent introduction of the new formulation of sildenafil oral suspension in the market that could address the unmet needs of ED patients. Previous studies have reported that major expectations of patients from PDE5i are treatment efficacy and speed of action [23]. However, ED is a complex disease that involves

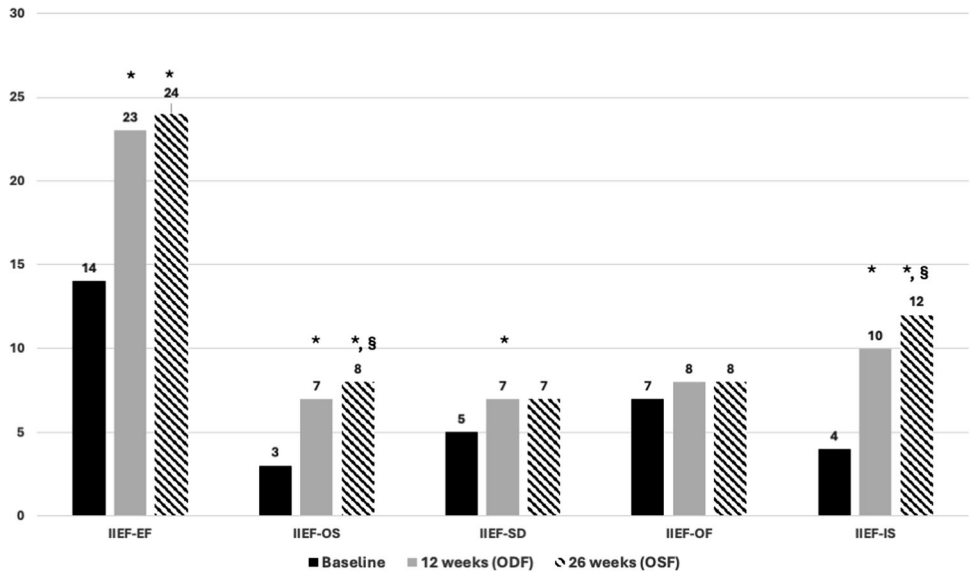

Fig. 2 Median IIEF scores of the study cohort at different follow-up evaluation. IIEF international index of erectile function, EF erectile function, OF orgasmic function, SD sexual desire, IS intercourse satisfaction, OS overall satisfaction. ODF oro-dispersible film, OSF Oral suspension formulation. *P* value according to the Wilcoxon signed-rank test; $^{*}p < 0.01$ vs. baseline; $^{§}p < 0.01$ vs. ODF group.

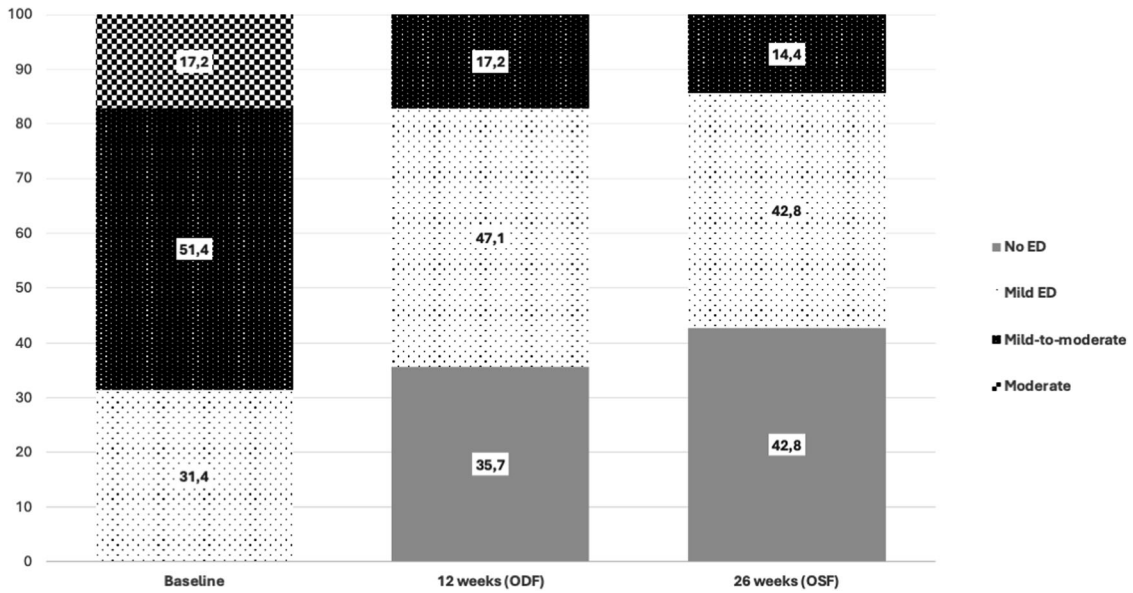

Fig. 3 Rate of erectile dysfunction severity at different follow-up.

organic but also psychological aspects related to the couple's intimacy and the use of medications to treat the disorder can also pose a barrier to the couple's mutual pleasure [24, 25]. For this reason, other PDE5i characteristics were found to be important for patient acceptability and compliance such as being discreet, comfortable and easy to use, with a good taste and not requiring water for ingestion [11, 14].

In terms of efficacy, previous meta-analyses have shown that sildenafil (at 50 mg and 100 mg) is the treatment of choice for men prioritizing high efficacy with a good safety profile [9, 26]. In this study we confirmed that sildenafil (both ODF and OSF) was highly effective in improving EF in men with ED. A minimal clinically important difference in EF scores (+2 points for mild ED and +5 points for moderate ED) [27] was obtained by 92.8 and 94.2% of participants after sildenafil ODF and OSF, respectively. The median IIEF-EF score was significantly improved after sildenafil treatment compared to baseline, irrespective of the formulation. Of clinical importance, after sildenafil OSF, patients reported higher satisfaction scores compared to the ODF treatment. The psychological aspect of patients taking sildenafil in this new formulation should be considered. Specifically, the OSF formulation could improve the quality of sexual life and psychological well-being of ED patients because its ease of administration and its good taste and discretion. Moreover, similar to the ODF one, it does not require water, glasses, or other objects necessary to take a tablet. Sildenafil ODF is available since 2017 and is already known by patients and partners as an established oral treatment for ED [10, 11]. Sociological studies have highlighted that the psychological impact of ED medication on men, coupled with poor communication and the partner's reluctance to

accept PDE5i use, are key factors influencing sexual intimacy and the use of PDE5i [28]. Therefore, the new oral suspension formulation, not yet "labeled" by the couple as a treatment for ED, could lead the patient to feel less ill about his condition and experience higher satisfaction after treatment compared to an old formulation. A previous study conducted in Spain corroborates our findings, since sildenafil OSF was associated with high satisfaction among ED patients [14].

The PAIRS-SF domain of self-confidence was similar between the ODF and OSF, reflecting that improved confidence is mainly related with erection quality, that was similar between the two formulations [29]. On the contrary, the OSF was associated with improved spontaneity scores compared to the ODF one. We speculate that this could be related to the new formulation since it is easy to use (as are other oral suspension medications), it is discreet (it does not require to open a package, carefully place a film on the tongue and leave a bad taste) and, from a psychological point of view, it might be perceived less as a medication for ED because of its novelty. These factors may have an impact on improved spontaneity and subsequently, on clinical outcomes.

Younger men and those with more severe ED experienced higher satisfaction after sildenafil OSF treatment. Despite most patients achieved a minimal clinically important improvement in EF scores it is likely that those with baseline higher severity of ED experienced greater satisfaction after treatment, confirming that sildenafil is effective irrespective of the degree of sexual function impairment [7]. Furthermore, younger men are likely to be more enthusiastic about a novel treatment modality than older men, thus reflecting the higher magnitude of satisfaction.

A potential strength of this study is that we investigated, for the first time, the efficacy and patient's perception of a new formulation of sildenafil, the oral suspension, compared to the ODF. We showed that both formulations are effective, but the OSF has some intrinsic characteristics that could further improve the couple's sexual experience. Our study is certainly not devoid of limitations. First, the study reports the results of a retrospective analysis of data prospectively collected in a homogenous cohort of white-European men with ED, thus deserving external validation with an independent, larger and more diverse sample. Second, a limitation is related to the methodology used, because this was not a randomized trial. However, the pre-post design helps limit potential differences between treatment groups. Lastly, since at the best of our knowledge, there is no published version of the Italian translation of the PGI-I and the PAIRS-SF questionnaires; therefore, we relied on the translation performed by a native English speaker and further validated by an uro-andrologist with international experience.

Table 2. Psychometric scores of the study cohort according to treatment received.

	12-weeks (ODF 50 mg)	26-weeks (OSF 50 mg)
PGI-I questionnaire		
Median (IQR)	3 (3–4)	3 (2–3)[§]
Range	1–5	1–4
PAIRS-SF questionnaire		
PAIRS-SF–Self confidence		
Median (IQR)	9 (9–10)	10 (9–10)
Range	9–10	6–11
PAIRS-SF–Spontaneity		
Median (IQR)	13 (12–13)	15 (14–16)[§]
Range	10–13	12–16
PAIRS-SF–Time concerns		
Median (IQR)	18 (18–19)	17 (16–18)
Range	16–20	16–20

ODF oro-dispersible film, *OSF* oral suspension formulation, *PGI-I* patient global impression of improvement, *PAIRS-SF* psychological and interpersonal relationship scales – Short Form.
P value according to the Wilcoxon signed-rank test. $p < 0.01$ vs. baseline.
[§]$p < 0.01$ vs. ODF group.

CONCLUSIONS

The 50 mg sildenafil oral-suspension formulation is equally safe and effective compared to the 50 mg ODF one. The new OSF provides higher satisfaction and spontaneity scores compared to the oro-dispersible film. This new formulation represents a further option to meet patients' expectations and adherence to PDE5i, thus enhancing the couple's sexual life.

Table 3. Logistic regression models predicting PGI-I and IIEF-OS improvements after OSF treatment compared to ODF (OR; *p* value [95%CI]) in the whole cohort.

	PGI-I improvement		IIEF-OS improvement	
	UVA model	**MVA model**	**UVA model**	**MVA model**
Age	0.9; <0.001 [0.71–0.94]	0.9; 0.01 [0.70–0.95]	0.7; <0.001 [0.72–0.96]	0.8; 0.02 [0.73–0.95]
BMI	1.1; 0.3 [0.96–1.21]		1.2; 0.5 [0.99–1.31]	
CCI	0.8; 0.3 [0.89–1.11]		0.7; 0.2 [0.91–1.11]	
Total Testosterone	1.1; 0.2 [0.81–1.16]		1.2; 0.1 [0.93–1.56]	
Stable sexual Relationship	0.9; 0.1 [0.82–1.05]		0.8; 0.3 [0.89–1.23]	
Baseline IIEF-EF	0.8; 0.01 [0.72–0.94]	0.8; 0.1 [0.75–0.95]	0.7; <0.01 [0.68–0.95]	0.7; 0.01 [0.63–0.91]

BMI body mass index, *CCI* charlson comorbidity index, *EF* erectile function, *IIEF* international index of erectile function, *MVA* multivariate model, *ODF* oro-dispersible film, *OSF* oral suspension formulation, *OS* overall satisfaction, *PGI-I* patient global impression of improvement, *UVA* univariate model.

DATA AVAILABILITY

Data are available from the corresponding author on reasonable request.

REFERENCES

1. Nehra A, Kulaksizoglu H. Global perspectives and controversies in the epidemiology of male erectile dysfunction. Curr Opin Urol. 2002;12:493–6. https://doi.org/10.1097/00042307-200211000-00009
2. Capogrosso P, Colicchia M, Ventimiglia E, Castagna G, Clementi MC, Suardi N, et al. One patient out of four with newly diagnosed erectile dysfunction is a young man-worrisome picture from the everyday clinical practice. J Sex Med. 2013;10:1833–41. https://doi.org/10.1111/jsm.12179
3. Pozzi E, Capogrosso P, Chierigo F, Pederzoli F, Ventimiglia E, Boeri L, et al. Clinical profile of young patients with erectile dysfunction: preliminary findings of a real-life cross-sectional study. Eur Urol Focus. 2020;6:184–9. https://doi.org/10.1016/j.euf.2018.10.003
4. Latini DM, Penson DF, Colwell HH, Lubeck DP, Mehta SS, Henning JM, et al. Psychological impact of erectile dysfunction: validation of a new health related quality of life measure for patients with erectile dysfunction. J Urol. 2002;168:2086–91. https://doi.org/10.1016/S0022-5347(05)64302-9
5. Althof SE. Quality of life and erectile dysfunction. Urology. 2002;59:803–10. https://doi.org/10.1016/s0090-4295(02)01606-0
6. Capogrosso P, Ventimiglia E, Boeri L, Capitanio U, Gandaglia G, Dehò F, et al. Sexual functioning mirrors overall men's health status, even irrespective of cardiovascular risk factors. Andrology. 2017;5:63–9. https://doi.org/10.1111/andr.12299
7. Salonia A, Bettocchi C, Boeri L, Capogrosso P, Carvalho J, Cilesiz NC, et al. European Association of Urology Guidelines on Sexual and Reproductive Health-2021 update: male sexual dysfunction. Eur Urol. 2021;80:333–57. https://doi.org/10.1016/j.eururo.2021.06.007
8. Pozzi E, Capogrosso P, Boeri L, Belladelli F, Baudo A, Schifano N, et al. Longitudinal risk of developing cardiovascular diseases in patients with erectile dysfunction-which patients deserve more attention? J Sex Med. 2020;17:1489–94. https://doi.org/10.1016/j.jsxm.2020.03.012
9. Chen L, Staubli SEL, Schneider MP, Kessels AG, Ivic S, Bachmann LM, et al. Phosphodiesterase 5 inhibitors for the treatment of erectile dysfunction: a trade-off network meta-analysis. Eur Urol. 2015;68:674–80. https://doi.org/10.1016/j.eururo.2015.03.031
10. Radicioni M, Castiglioni C, Giori A, Cupone I, Frangione V, Rovati S. Bioequivalence study of a new sildenafil 100 mg orodispersible film compared to the conventional film-coated 100 mg tablet administered to healthy male volunteers. Drug Des Devel Ther. 2017;11:1183–92. https://doi.org/10.2147/DDDT.S124034
11. Cocci A, Capece M, Cito G, Russo GI, Falcone M, Timpano M, et al. Effectiveness and safety of oro-dispersible sildenafil in a new film formulation for the treatment of erectile dysfunction: comparison between sildenafil 100-mg film-coated tablet and 75-mg oro-dispersible film. J Sex Med. 2017;14:1606–11. https://doi.org/10.1016/j.jsxm.2017.10.066
12. Manfredi C, Franco A, Ditonno F, Mathur R, Franco G, Lombardo R, et al. Treatment preferences of patients with erectile dysfunction: a systematic review of randomized controlled trials. Minerva Urol Nephrol. 2024;76:42–51. https://doi.org/10.23736/S2724-6051.23.05552-0
13. Corona G, Rastrelli G, Burri A, Serra E, Gianfrilli D, Mannucci E, et al. First-generation phosphodiesterase type 5 inhibitors dropout: a comprehensive review and meta-analysis. Andrology. 2016;4:1002–9. https://doi.org/10.1111/andr.12255
14. Peinado Ibarra F, García Gómez B, Luján Marco S, Segura Paños AM. Study UNICO: Perception of urologists and andrologists, in spain, about the use of sildenafil oral suspension in patients with erectile dysfunction. Arch Esp Urol. 2023;76:139–44. https://doi.org/10.56434/j.arch.esp.urol.20237602.15
15. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis. 1987;40:373–83.
16. National Institute of Alcohol Abuse and Alcoholism. The physicians' guide to helping patients with alcohol problems. U.S. Department of Health and Human Services, National Institutes of Health, Washington, DC. 1995. http://mpcmh.org/wp-content/uploads/2017/12/NIAAA_Clinicians_Guide_AandD_Screening.pdf. Accessed July 03, 2024.
17. Rosen RC, Riley A, Wagner G, Osterloh IH, Kirkpatrick J, Mishra A. The international index of erectile function (IIEF): a multidimensional scale for assessment of erectile dysfunction. Urology. 1997;49:822–30. https://doi.org/10.1016/s0090-4295(97)00238-0
18. D'Elia C, Cerruto MA, Cavicchioli FM, Cardarelli S, Molinari A, Artibani W. Critical points in understanding the Italian version of the IIEF 5 questionnaire. Arch Ital Urol Androl Organo Uff Soc Ital Ecogr Urol E Nefrol. 2012;84:197–201.
19. Cappelleri JC, Rosen RC, Smith MD, Mishra A, Osterloh IH. Diagnostic evaluation of the erectile function domain of the international index of erectile function. Urology. 1999;54:346–51. https://doi.org/10.1016/s0090-4295(99)00099-0
20. Boeri L, Capogrosso P, Ventimiglia E, Cazzaniga W, Pederzoli F, Moretti D, et al. Does calculated free testosterone overcome total testosterone in protecting from sexual symptom impairment? findings of a cross-sectional study. J Sex Med. 2017;14:1549–57. https://doi.org/10.1016/j.jsxm.2017.10.070
21. Gill TM, Feinstein AR. A critical appraisal of the quality of quality-of-life measurements. JAMA. 1994;272:619–26.
22. Swindle R, Cameron A, Rosen R. A 15-item short form of the psychological and interpersonal relationship scales. Int J Impot Res. 2006;18:82–8. https://doi.org/10.1038/sj.ijir.3901381
23. Jiann B-P, Nakajima K, Dighe S, Harshman-Smith CD, Hassan TA. Degree of planning of sexual intercourse among men from China, Japan, and Taiwan taking medication for erectile dysfunction: findings of an observational, cross-sectional survey. Sex Med. 2019;7:54–60. https://doi.org/10.1016/j.esxm.2018.10.006
24. Cai Z, Song X, Zhang J, Yang B, Li H. Practical approaches to treat ED in PDE5i nonresponders. Aging Dis. 2020;11:1202–18. https://doi.org/10.14336/AD.2019.1028
25. Pozzi E, Fallara G, Capogrosso P, Boeri L, Belladelli F, Corsini C, et al. Primary organic versus primary psychogenic erectile dysfunction: findings from a real-life cross-sectional study. Andrology. 2022;10:1302–9. https://doi.org/10.1111/andr.13212
26. Madeira CR, Tonin FS, Fachi MM, Borba HH, Ferreira VL, Leonart LP, et al. Efficacy and safety of oral phosphodiesterase 5 inhibitors for erectile dysfunction: a network meta-analysis and multicriteria decision analysis. World J Urol. 2021;39:953–62. https://doi.org/10.1007/s00345-020-03233-9
27. Rosen RC, Allen KR, Ni X, Araujo AB. Minimal clinically important differences in the erectile function domain of the International Index of Erectile Function scale. Eur Urol. 2011;60:1010–6. https://doi.org/10.1016/j.eururo.2011.07.053
28. Carvalheira A, Forjaz V, Pereira NM. Adherence to phosphodiesterase type 5 inhibitors in the treatment of erectile dysfunction in long-term users: how do men use the inhibitors? Sex Med. 2014;2:96–102. https://doi.org/10.1002/sm2.31
29. Tsujimura A, Kiuchi H, Soda T, Takezawa K, Okuda H, Fukuhara S, et al. Sexual life of Japanese patients with erectile dysfunction taking phosphodiesterase type 5 inhibitors: an Internet survey using the psychological and interpersonal relationship scales-short form questionnaire. Int J Urol Off J Jpn Urol Assoc. 2014;21:821–5. https://doi.org/10.1111/iju.12429

AUTHOR CONTRIBUTIONS

LB wrote the paper, GG, EZ, AZ, ALP, FC, AC, VP, MP, collected data; FG, EM and GA supervised the paper, approved the final version of the manuscript.

COMPETING INTERESTS

The authors declare no competing interests.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

All methods were performed in accordance with the relevant guidelines and regulations; all patients signed an informed consent agreeing to share their own anonymous information for other future studies. The study was approved by the Hospital Ethical Committee (Prot. 060182 – SilOros).

ADDITIONAL INFORMATION

Supplementary information The online version contains supplementary material available at https://doi.org/10.1038/s41443-025-01019-4.

Correspondence and requests for materials should be addressed to Luca Boeri.

Reprints and permission information is available at http://www.nature.com/reprints

Publisher's note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.