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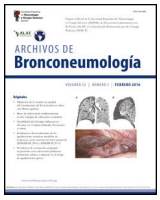

Scientific Letter

The DESTINA Study: An Observational Cross-sectional Study to Evaluate Patient Satisfaction and Tolerability of Cytisine for Smoking Cessation in Spain

To the Director,

Tobacco contributes to more than 8 million deaths each year worldwide. Quitting smoking reduces significantly the risk of death, particularly before the age of 40.[1] The combination of psychological counseling with pharmacological treatment is key for a successful smoking cessation process; for years, the first-line drugs in Western Europe were nicotine replacement therapy (NRT), varenicline and bupropion,[2] but currently, also cytisine should be considered as advisable pharmacological smoking cessation aid.

Here, we present the first study ever done in Spain to evaluate the role of cytisine (Todacitan®) for smoking cessation which, at the recommended doses of 1.5–9 mg per day for 25 days, has been shown to be more effective than placebo and NRT in several clinical trials,[3–6] and to be non-inferior and present less adverse events (AE) than varenicline.[7]

The present study was an observational, multicenter, multidisciplinary, cross-sectional study conducted in 7 Spanish centers, including primary care centers and hospitals. It was based on the review of real-life data from medical records and a patient's interview at the routine visit after the end of cytisine treatment (post-treatment visit). The information was collected using an electronic case report form, from March to July 2022.

The main objective was to evaluate, in routine clinical practice, the satisfaction of patients who had received cytisine for smoking cessation in the last 3 months before study initiation. The study also evaluated the tolerability and safety, the adherence and the effectiveness of cytisine for smoking cessation.

A total of 105 patients were included in the study. This sample size was lower than the initially estimated in the protocol (140), but enough to achieve the pre-defined aimed precision for the primary endpoint (±0.2 units with a SD of 1 unit).

The mean age of patients was 56.9 (SD: 10.2) years; 52.4% were women. Patients were, in average, 15.9 years (SD: 4.3) old when they started smoking and, at the initial visit, they were smoking 22 (SD: 8.4) cigarettes per day and 40.8 (SD: 21.7) pack-year. A 81.9% of patients had previously tried to quit smoking; the last attempt was with pharmacological treatment in 59.2% of patients. Among the treatments used, varenicline was the most common (68.9%). 70.5% of patients had a high or very high degree of dependence to tobacco (Table 1).

Patients were satisfied (38.1%) or very satisfied (39.0%) with the treatment. These results were independent of sex, previous treatment attempts, degree of dependence and reinforcement pattern. At the post-treatment visit, 76% of patients were abstinent. Using

Table 1
Study patient's characteristics.

Variable	Valid *N*	Mean (SD)	*n* (%)
Age (years)	105	56.9 (10.2)	
Sex	105		
Male			50 (47.6%)
Female			55 (52.4%)
Age at starting smoking (years)	105	15.9 (4.3)	
Number of cigarettes per day	105	22.0 (8.4)	
Number of pack-year	100	40.8 (21.7)	
Number of previous quit attempts without treatment	105		
0			19 (18.1%)
1			32 (30.5%)
2			21 (20.0%)
3			24 (22.9%)
>3			9 (8.6%)
Number of previous quit attempts with treatment	104		
0			40 (38.5%)
1			40 (38.5%)
2			19 (18.3%)
3			4 (3.8%)
>3			1 (1.0%)
Time since last attempt (months)	74	53.3 (77.3)	
Did you use treatment in the last quit attempt?	103		
No			42 (40.8%)
Yes			61 (59.2%)
Nicotine replacement therapy (gum)			3 (4.9%)
Nicotine replacement therapy (mouth spray)			0 (0.0%)
Nicotine replacement therapy (tablets)			1 (1.6%)
Nicotine replacement therapy (patches)			5 (8.2%)
Varenicline			42 (68.9%)
Bupropion			7 (11.5%)
Other			4 (6.6%)
Patients motivated to quit smoking before the start of treatment			
EVA scale	96	8.1 (1.5)	
Qualitative scale	58		
Yes			58 (100.0%)
No			0 (0%)
Levels of CO in inspired air (ppm)	66		23.4 (11.5)

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Table 1 (*Continued*)

Variable	Valid *N*	Mean (SD)	*n* (%)
Fagerström Questionnaire Score	105		
Very low (0–1)			0 (0.0%)
Low (2–3)			2 (1.9%)
Moderate (4–5)			29 (27.6%)
High (6–7)			50 (47.6%)
Very high (8–10)			24 (22.9%)
Reinforcement Questionnaire	97		
Negative reinforcement			56 (57.7%)
Positive reinforcement			41 (42.3%)
Glover-Nilsson test	96		
Mild dependency			11 (11.5%)
Moderate dependency			58 (60.4%)
High dependency			27 (28.1%)
Time from start of cytisine treatment to date of visit (months)	104	1.2 (0.9)	

Table 2
Results of the study for the total population.

Variable	Valid *N*	Mean (SD)	*n* (%)
Patient satisfaction with treatment	105		
Very satisfied			41 (39.0%)
Satisfied			40 (38.1%)
Neutral			13 (12.4%)
Unsatisfied			7 (6.7%)
Very unsatisfied			4 (3.8%)
Percentage of self-reported days of complete abstinence (cigarettes = 0) between the start of treatment and the study visit	104	64.9% (35.7)	
Number of patients that reported being abstinent all days (completely or partially) between the start of treatment and the study visit	104		45 (43.3%)
Abstinent patients at the study visit	104		79 (76.0%)
Self-reported treatment adherence	105		
Very good			64 (62.1%)
Good			21 (20.4%)
Average			8 (7.8%)
Low			4 (3.9%)
Very low			4 (3.9%)

a Likert scale, adherence to treatment was reported as very good (62.1%) or good (20.4%). On average, patients consumed a total of 90.3 (SD: 21.1) pills over 23.2 (SD: 5.8) days of treatment (Table 2).

The study shows that cytisine is a treatment with a manageable AE profile: 37.1% of patients experienced an AE of any degree. Sleeping disorders, usually related to smoking cessation itself, were the most common AE. Other AE included nauseas (12.4%) and vomits (3.8%). Most AE were mild (36.4%) or moderate (54.5%).

Cytisine has been shown to be more effective than placebo and NRT in several clinical trials, and to be non-inferior to varenicline and associated with fewer adverse effects.[3,4,6–9] At one month, different continuous abstinence rates have been reported, including 40%[6] and 59.3%[9] in two independent studies conducted in New Zealand, and 57.2% in a study conducted in Italy.[10] Similarly, the adverse events reported in the previous studies also include gastrointestinal events and sleeping disorders as the most prevalent ones.[3,8,9]

Some study limitations include the lack of concurrent control group, missing values for some variables and limited time between treatment initiation and post-treatment visit. Future studies are necessary to test the effectiveness of long-term treatment with cytisine.

In summary, the study shows that most patients (77.1%) are satisfied with the treatment with cytisine for smoking cessation and are abstinent (76%) at the post-treatment visit.

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Conflict of Interests

CAJR reports grants and personal fees from Aflofarm, Gebro, GSK, Johnson&Johnson, Pfizer and Menarini. JARM reports grants and personal fees from Aflofarm, GSK, Pfizer, Novartis AG, Menarini, Boehringer Ingelheim, Astra-Zeneca, Gebro, and Laboratorios Rovi. JSCM has received honoraria as medical advisor, for presentations and publications from Aflofarm, AstraZeneca, Boerhinger, Ferrer, GSK, Menarini, Novartis, Pfizer and Rovi. JST declares to have received honoraria from Aflofarm as a clinical advisor. AMP, RSM and JLDM declare no conflicts of interest.

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References

1. World Health Organization. Tobacco 2022. World Health Organization; 2022. https://www.who.int/news-room/fact-sheets/detail/tobacco [accessed 23.09.22].
2. NICE. Tobacco: preventing uptake, promoting quitting and treating dependence. NICE guideline; 2021.
3. West R, Zatonski W, Cedzynska M, Lewandowska D, Pazik J, Aveyard P, et al. Placebo-controlled trial of cytisine for smoking cessation. N Engl J Med. 2011;365.
4. Cahill K, Lindson-Hawley N, Thomas KH, Fanshawe TR, Lancaster T. Nicotine receptor partial agonists for smoking cessation. Cochrane Database Syst Rev. 2016:2016, http://dx.doi.org/10.1002/14651858.CD006103.PUB7.
5. Tutka P, Vinnikov D, Courtney RJ, Benowitz NL. Cytisine for nicotine addiction treatment: a review of pharmacology, therapeutics and an update of clinical trial evidence for smoking cessation. Addiction. 2019;114:1951–69, http://dx.doi.org/10.1111/ADD.14721.
6. Walker N, Howe C, Glover M, McRobbie H, Barnes J, Nosa V, et al. Cytisine versus nicotine for smoking cessation. N Engl J Med. 2014;371:2353–62, http://dx.doi.org/10.1056/NEJMOA1407764.
7. Courtney RJ, McRobbie H, Tutka P, Weaver NA, Petrie D, Mendelsohn CP, et al. Effect of cytisine vs varenicline on smoking cessation: a randomized clinical trial. JAMA. 2021;326:56–64, http://dx.doi.org/10.1001/JAMA.2021.7621.
8. Hajek P, McRobbie H, Myers K. Efficacy of cytisine in helping smokers quit: systematic review and meta-analysis. Thorax. 2013;68:1037–42, http://dx.doi.org/10.1136/thoraxjnl-2012-203035.
9. Walker N, Smith B, Barnes J, Verbiest M, Parag V, Pokhrel S, et al. Cytisine versus varenicline for smoking cessation in New Zealand indigenous Māori: a randomized controlled trial. Addiction. 2021, http://dx.doi.org/10.1111/ADD.15489.
10. Principe R, Tinghino B, Zagà V, Cardellicchio S, Siracusano L, Zelano G, et al. Use of cytisine for smoking cessation in Italian Centers for Tobacco Treatment. Eur Respir J. 2017;50:PA4476, http://dx.doi.org/10.1183/1393003.CONGRESS-2017.PA4476.

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