

Long-term Effectiveness of 9- δ -tetrahydrocannabinol:Cannabidiol Oromucosal Spray in Clinical Practice: results from a 18-months Multicenter Italian Study

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Objective:

We aimed to provide real life data on clinical outcomes of a large population of Italian patients with treatment-resistant multiple sclerosis (MS) spasticity receiving 9- δ -tetrahydrocannabinol and cannabidiol (THC:CBD) oromucosal spray (Sativex®).

Background: THC:CBD oromucosal spray is used as mono or add-on therapy for moderate to severe MS spasticity resistant to other medications.

Design/Methods: This 18-months observational, prospective, multicentre study evaluated patients with resistant MS spasticity treated with THC:CBD according to approved labelling. Data were collected from the mandatory Italian medicines agency (AIFA) e-registry from January 2015 to June 2018. Spasticity assessment with the 0-10 numerical rating scale (NRS) was performed at baseline, after 1 month of treatment (T1) and every 6 months until 18 months (T4) from the treatment initiation.

Results: A total of 1845 patients were recruited from 32 Italian MS centres. At T1, 1502 (81.4%) of patients reached an NRS improvement of $\geq 20\%$ and 814 (40.2%) a of $\geq 30\%$, with a mean NRS score reduction of 28.9% at T1 and of 36.8% at T4. Daily number of puffs was generally stable through the observation period (6.9 ± 2.4 at T1 vs 6.3 ± 3.1 at T4, $p=0.8$). At T4, 727 (39.4%) patients have discontinued treatment; 388 (53.4%) because of lack of effectiveness and 339 (46.6%) for adverse events: 127 (37.5%) reported vertigo, 118 (34.8%) sleepiness, 96 (28.3%) worsening of fatigue, and 54 (15.9%) cognitive symptoms. The multivariate analysis showed that higher NRS score at baseline (OR 2.21 95%CI 1.12-6.28, $p<0.01$) and higher difference of NRS between T1 and baseline (OR 2.03 95%CI 1.04-8.14, $p<0.05$) were associated to an increased probability to stay on therapy after 18 months.

Conclusions: Real-life data from a large Italian MS population confirmed the long-term effectiveness of THC:CBD for the treatment of resistant MS spasticity in everyday clinical practice. Treatment effects were sustained for 18-months with a relatively stable number of puffs/day.