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Background

Nowadays **Integrase Strand Transfer Inhibitors (INI)** are 1st line antiretroviral therapy (ART) regimens.

Specifically, increasing interest on **Dolutegravir (DTG)** has been reported, thanks to its high potency and efficacy, good tolerance, high barrier-to-resistance development, low risk of virologic failure and low risk of drug-to-drug interactions.

Nevertheless, several authors have arisen concerns around **DTG tolerance and safety profile in real-life settings**, due to the onset of *neuropsychiatric adverse effects* (NAE), *i.e.* sleep disturbances, headache, nervousness, poor concentration and unexplained pain or paraesthesia.

Aim of this study was to analyse the most frequent **adverse effects (AE)** leading to **DTG discontinuation** in our HIV outpatient.

Material and methods

We performed a **retrospective analysis** of a cohort of 632 HIV-infected patients who have started DTG between January 2015 and March 2018.

Data were obtained from the electronic outpatients chart of Modena Infectious Diseases Clinic.

We focused on the main AEs responsible for DTG withdrawal.

Table 1	n°	%	
Patients	632		
Males	427	67.5%	
Average age (years)	48.6	-	
Anamnesis with AIDS	156	24.7%	
HAART	Naïve	71	11.2%
	ABC backbone	37/71	52.0%
	TDF/TAF backbone	34/71	48.0%
	Experienced	561	88.8%
	Dual (3TC)	252	
	Triple with ABC	193	
	with TDF/TAF	274	
	Other *	80	
	DTG discontinuations	49	7.7%
	naïve	12	24.0%
experienced	37	76.0%	

Table 2	n	%		
Discontinuations due to AE	44 *	7.0%		
Males	26	59.0%		
Average age , years ± SD	49.1 ± 11.2			
Median time in DTG, days (IQR)	94 (20-181)			
Anamnesis with AIDS	15	34.0%		
Mean CD4 count , cell/mm ³ ± SD	668.7 ± 333.6			
TD	10	22.7%		
HAART	Naïve	9/71	12.7%	
	.ABC backbone	2/231	0.8%	
	.TDF/TAF backbone	7/114	6.0%	
	Experienced	35/561	6.2%	
	.Dual (3TC)	15 (12)		
	.Triple	20		
	.ABC backbone	12/231	5.2%	
	.TDF/TAF backbone	8/114	7.0%	
	AE	.Neuropsychiatric	32	5.0%
		.Gastrointestinal (including hypertransaminasemia)	11	1.7%
.Myalgia and arthralgia		6		
.Rash and itch		1		
.Unspecified		8		
Association of two or more class of symptoms		12	27%	

Results

DTG discontinuation due to AEs

44 out of 632 patients (7%) discontinued DTG because of AEs.

Among them 26 were males (59%), the average age was 49.1 years.

9 patients (12.7%) were **naïve** to ART and 7 of them started a TDF/TAF backbone.

Experienced patients discontinued *dual* therapy (mostly with 3TC) in 15 cases and *triple* ART in 20 cases (12 with an ABC- and 8 with a TAF/TDF-backbone).

The majority of patients who discontinued DTG complained **NAEs** (32 subjects, 5% of the total DTG cohort) or **gastrointestinal discomforts** (11 patients). Other reported AEs are enlisted in table 2.

DTG discontinuation due to NAEs

Among people suffering of NAEs, 5 patients were **naïve** to ART (2 ABC backbone) while 27 were **experienced**.

Among experienced, 13 subjects interrupted *dual* therapy and 14 a *triple* ART (7 ABC and 7 TDF/TAF).

Reported neuropsychiatric symptoms are enlisted in figure 1.

Moreover, 30 out of patients who experienced NAEs (93,7%) did not report neuropsychiatric symptoms after ART switch.

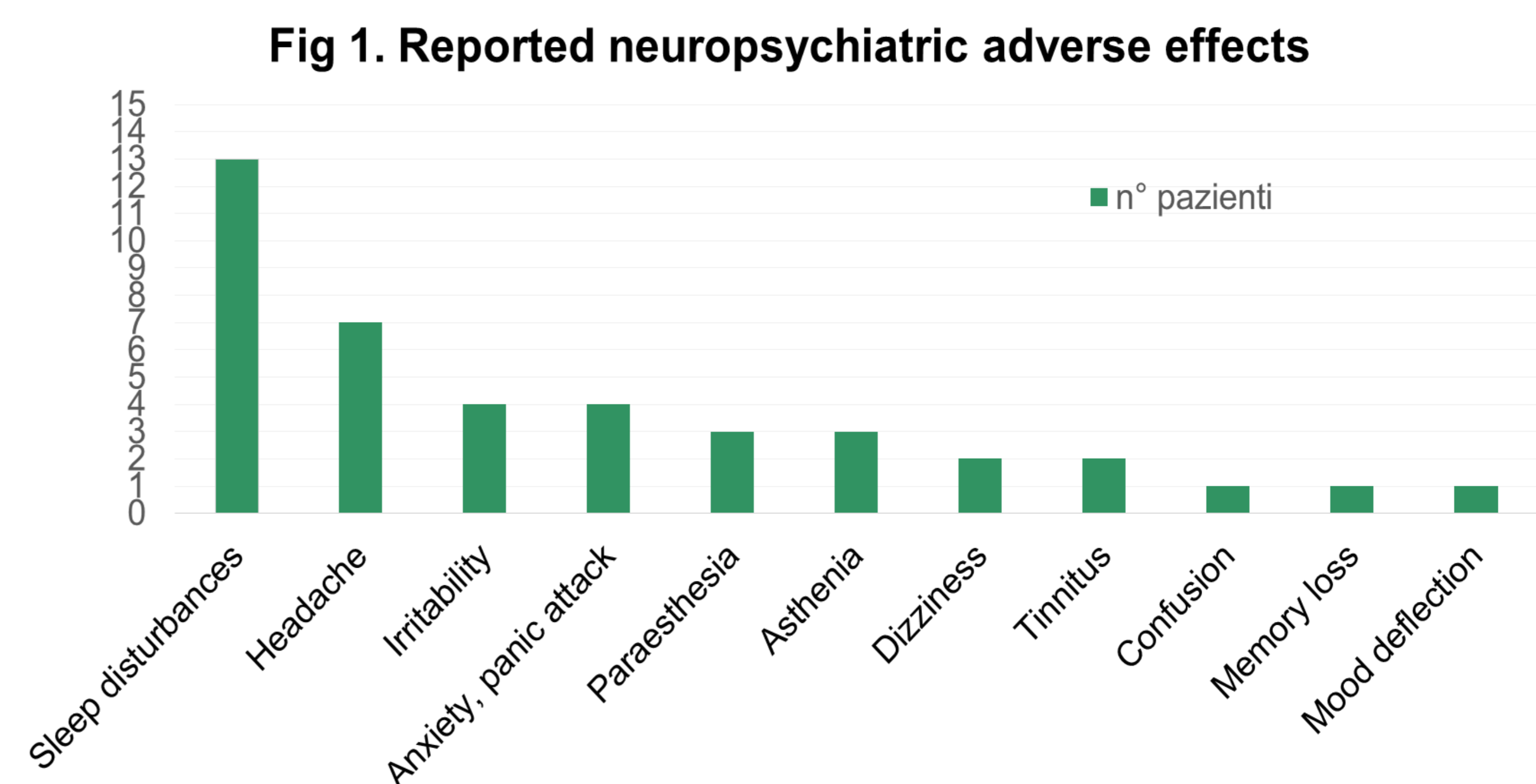


Table 3	n°	%
Discontinuations due to neuropsychiatric AEs	32	5.0%
Naïve	5	7.0%
.ABC backbone/n° tot ABC	2	0.9%
.TDF/TAF backbone/n° tot tenofovir	3	2.6%
Experienced	27	4.8%
.Dual	13	
.Triple:	14	
.ABC backbone/n° tot ABC	7	3.0%
.TDF/TAF backbone/n° tot tenofovir	7	6.1%
Association of two or more symptoms	16	50.0%
Previous neuropsychiatric disorders or psychiatric drugs	8	25.0%
Resolution after ART modification	30	93.7%

Conclusion

This study shows a **lower percentage of DTG interruption due to AEs** compared to the literature reported rates (7 vs 10.5%). However, we obtained similar results in appearance of NAEs (5 vs 5.4%).

In our cohort, **naïve** rate of DTG suspension due to AEs is **12.7%**, compared to a literature rate of 17.6%.

Among subjects who experienced **NAEs**, only 8 out of 32 patients either had previous records of neuropsychiatric disorders or were taking psychiatric drugs.

DTG discontinuation rate due to AEs results to be **higher** in **naïve** vs experienced patients (12.7% vs 6.2%, p<0.05) and **higher** in patients with **TDF/TAF** vs ABC-backbone (13% vs 6%, p<0.05)