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Clinical Features and Outcomes of Patients Stopping DTG for Neuropsychiatric Symptoms

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INTRODUCTION

- In some cohorts dolutegravir (DTG) was associated with a higher rate of discontinuation for neuropsychological side effects (NPS)[1-7]
- Several associated factors have been described[8-13]
  - older age
  - female gender
  - abacavir co-administration
  - higher DTG exposure
  - *UGT1A1* (PK-mediated) and *SLC22A2* (PD-mediated) variants
- Pre-existing psychiatric disorders have not been associated with a higher risk of NPS symptoms in a large US cohort[14]
  - our group reported an association[15]
- A rise in moderate depression was described in 254 patients switching to DTG[16]

AIM OF THE STUDY

To describe the clinical features and outcomes of patients stopping DTG for NPS.

MATERIAL & METHODS:

- Prospective, observational study at two Italian outpatient clinics (Torino and Rome) - "DOLUOCT2"
  - Approved by the two Ethics Committees
  - All patients starting DTG (naïve and treated) and signing a written informed consent
  - Analysis of clinical, therapeutic, PK and PG variables with the risk of DTG discontinuation due to NPS;
- In this analysis we focused on patients stopping DTG for NPS in terms of:
  - pre-existing psychiatric comorbidities
  - outcomes after drug withdrawal
    - Symptoms were clinically assessed and resolution was recorded as no/partial/complete at the first available follow up after discontinuation
- Data expressed as number (percentage) or median (interquartile ranges) and tested using non-parametric tests

In the whole cohort (n=1455, median follow up of 30.7 months), 526 participants discontinued DTG (mostly because of treatment switches with no efficacy or tolerability issues, n=274). Discontinuation for NPS was recorded in 66 patients (4.5%).

RESULTS (n=66)

Participants discontinued DTG for NPS after a median of 5.1 months (1.3-14.7).

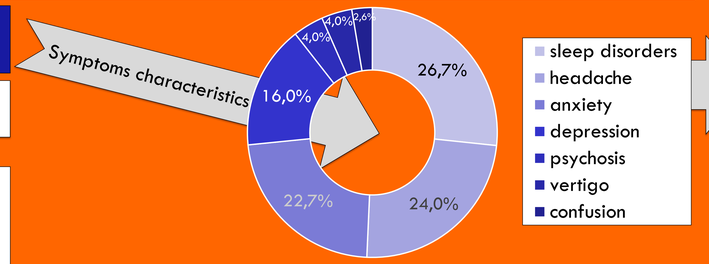
Patients' characteristics

- Age 54 years (48-63);
- BMI 24.5 Kg/m^2 (21.5-29.4)
- 44 born male (66.7%)
- 23 receiving abacavir (34.8%)

Pre-existing psychiatric conditions (n=21, 31.8%)

None	45 (68.2%)
Depression	12 (18.2%)
Anxiety	4 (6.1%)
Psychosis	1 (1.5%)
Alcohol abuse	1 (1.5%)
Previous IDU	1 (1.5%)
Insomnia	1 (1.5%)
Personality disorder	1 (1.5%)

Symptoms characteristics

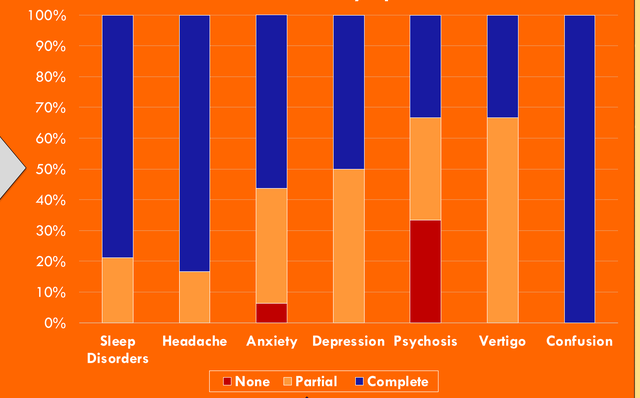


Symptoms according to pre-existing psychiatric comorbidities

Sleep	Headache	Anxiety	Depression	Psychosis	Vertigo	Confusion
35.6%	24.4%	28.9%	11.1%	2.2%	4.4%	4.4%
16.7%	33.3%	-	50%	8.3%	-	-
25%	50%	25%	-	-	25%	-
-	-	-	-	100%	-	-
-	-	100%	100%	-	-	-
-	100%	-	-	-	-	-
100%	-	100%	-	-	-	-
-	-	100%	-	-	-	-

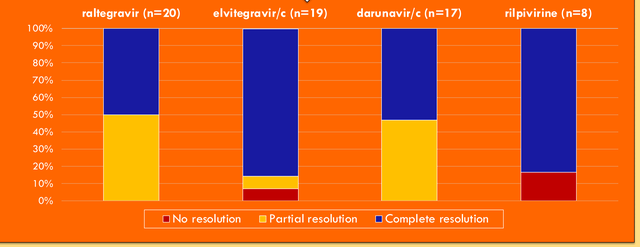
Pre-existing anxiety/depression was associated with a higher risk of discontinuing DTG (p=0.021, OR=4.4)

Resolution of symptoms



Headache (p=0.039) and sleep disorders (p=0.083) were associated with complete resolution of symptoms

DTG was replaced by



CONCLUSIONS

- In our prospective cohort of patients starting DTG, the drug was discontinued for NPS in 4.5% after a median of 5 months
- Despite the limitations of this observational small sample
  - NPS were heterogeneous with sleep disorders, headache and anxiety being the more incident
  - Pre-existing anxiety/depression was associated with a higher chance of discontinuing DTG for worsening depression
  - In the majority of cases (61.4%) a complete resolution of symptoms was observed (mostly headache and insomnia) however the incomplete resolution of certain NPS in almost one third of participants suggests alternative reasons (to DTG-associated toxicity)
  - No signal for a better switching strategy emerged

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