Abstract #0828

Similar Efficacy and Safety of Dolutegravir between Age Groups of Pediatric Patients

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BACKGROUND

Dolutegravir (DTG)-based cART are now approved for use in HIV⁺ children aged ≥ 6 years in many countries worlwide. However, published data about its efficacy and its safety profile in the pediatric population are scarce,[1,2] especially in youngest children. This retrospective monocentric study compared data about safety and efficacy of DTG in patients followed in a French pediatric unit, and divided into three groups of age at the time of DTG initiation: 5-12 (Group 1), 12-18 (Group 2) and ≥ 18 years old (Group 3).

METHODS

Clinical and biological data from 109 patients, who initiated DTG-based cART between January 2014 and December 2017 were retrospectively analysed: 33 in Group 1, 51 in Group 2 and 25 in Group 3. The primary endpoint was the proportion of patients who reached virological suppression (i.e. plasma viral load (PVL) <50 copies/mL obtained ≤ 3 months after DTG initiation) for viremic patients, and remained controlled until the last follow-up visit for all patients. The secondary endpoint was safety.

RESULTS

Baseline characteristics (Table 1)

Most of the individuals were antiretroviral–experienced (91,7%) and 12 (11%) were previously exposed to integrase strand transfer inhibitors (INSTI). INSTI-related resistance associated mutations were previously isolated in 4 patients: E157Q in 2 cases, N155H in 2 individuals (who were treated with twice-daily DTG).
At baseline, virological suppression was observed for ≥ 6 months in 58.7% of patients.

Efficacy (Table 2)

Sustained virological success was obtained in 79.8% of patients, with similar rates in the 3 groups of age (p=0,22).
With reinforced measures to improve adherence, undetectable VL was obtained at the last visit in 88.1% of patients, with similar proportions in the 3 groups (p=0,51).
In INSTI-experienced patients, sustained virological success and undetectable VL at the last visit were obtained in 91.7% and 100.0%, respectively.

ARV drug resistance

Genotypic resistance was assessed in samples from all 22 subjects presenting virological failure during follow-up. No selection of new RAMs in the RT, *protease* or *integrase* gene was observed in these patients during exposure to dolutegravir.

Tolerance (Table 2)

Only one patient (Group 2) stopped DTG for severe drug-related side effects (dizziness, sleep disturbance).
The three Grade 3 laboratory events was considered unrelated to DTG exposure (acute liver enzyme abnormalities, which spontaneously resolved without DTG interruption).

	Age at the time of DTG initiation			Total (n=109)
	Group 1 5-12 years (n=33)	Group 2 12-18 years (n=51)	Group 3 ≥18 years (n=25)	
Male sex (n, %)	16 (48.5)	33 (64.8)	14 (56.0)	63 (57.8)
Place of birth of the child (n, %)				
Sub-Saharan African country	**16 (48.5)**	**32 (62.7)**	**11 (44.0)**	**59 (54.1)**
France	12 (36.4)	10 (19.6)	9 (36.0)	31 (28.4)
Another country	5 (15.2)	9 (17.6)	5 (20.0)	19 (17.4)
Place of birth of the mother				
Sub-Saharan African country	**27 (81.8)**	**37 (72.6)**	**18 (72.0)**	**82 (75.2)**
France	1 (3.0)	6 (11.8)	3 (12.0)	10 (9.2)
Another country	5 (15.2)	8 (15.7)	4 (16.0)	17 (15.6)
ART history				
Previous exposure to ARV (n, %)	**30 (90.9)**	**45 (88.2)**	**25 (100.0)**	**100 (91.7)**
Previous exposure to RAL and/or EVG/c (n, %)	1 (3.0)	2 (3.9)	9 (36.0)	12 (11.0)
Viral subtype (n, %)				
B	0 (0.0)	5 (9.8)	2 (12.0)	8 (7.3)
CRF02_AG	14 (42.4)	8 (15.7)	3 (12.0)	25 (22.9)
Other non-B subtypes	**15 (45.4)**	**38 (74.5)**	**19 (76.0)**	**72 (66.1)**
Unknown	4 (12.1)	0 (0.0)	0 (0.0)	4 (3.7)
INSTI-related RAMs prior to DTG initiation (n%)				
None	**18 (54.5)**	**43 (84.3)**	**16 (64.0)**	**77 (70.6)**
E92Q + N155H	0 (0.0)	1 (2.0)	0 (0.0)	1 (0.9)
N155H	0 (0.0)	0 (0.0)	1 (4.0)	1 (0.9)
E157Q	2 (6.0)	0 (0.0)	0 (0.0)	2 (1.8)
Unknown	13 (39.4)	7 (13.7)	8 (32.0)	28 (25.7)
Background regimen associated with DTG				
2 NRTI (n, %)	**22 (66.7)**	**48 (94.1)**	**18 (72.0)**	**88 (80.7)**
1 NRTI (n, %)	7 (21.2)	2 (3.9)	0 (0.0)	9 (8.3)
1 PI/r (n, %)	2 (6.0)	1 (2.0)	3 (12.0)	6 (5.5)
1 NNRTI (n, %)	2 (6.0)	0 (0.0)	2 (8.0)	4 (3.7)
Other regimen (n, %)	0 (0.0)	0 (0.0)	2 (8.0)	2 (1.8)
Immuno-virological status				
CD4 count (/mm³)) (median, IQR)	829 (20-2570)	695 (60-1496)	631 (40-1452)	728 (20-2570)
Patients with VL < 50 copies/mL (n, %)	**22 (66.7)**	**28 (54.9)**	**14 (56.0)**	**64 (58.7)**
VL of patients with detectable viremia (log_{10} copies/mL) (median, range)	4.3 (1.8-5.1)	3.6 (1.7-5.3)	4.1 (1.8-5.1)	4.1 (1.7-5.3)

Table 1. Characteristics of the 109 patients at the time of DTG initiation

	Total (n=109)	Age at the time of DTG initiation		
		Group 1 5-12 years (n=33)	Group 2 12-18 years (n=51)	Group 3 ≥18 years (n=25)
Duration of follow-up (months) (median, range)	24 (6-54)	12 (6-36)	24 (6-54)	24 (6-48)
Virological follow-up				
Sustained virological success (n, %)	87 (79.8)	29 (87.9)	37 (72.5)	21 (84.0)
VL <50 copies/mL at the last visit (without ARV change) (n, %)	**96 (88.1)**	**31 (93.9)**	**43 (84.3)**	**22 (88.0)**
Emergence of RAMs in patients with virological failure (n, %)	**0 (0.0)**	**0 (0.0)**	**0 (0.0)**	**0 (0.0)**
Safety				
Grade I/II clinical events	7 (6.4)	0 (0.0)	2 (3.9)	5 (20.0)
Grade I/II biological events	30 (27.5)	8 (24.2)	13 (25.5)	9 (36.0)
Grade III/IV biological events	3 (2.8)	0 (0.0)	2 (3.9)	1 (4.0)
Stop for intolerance	**1 (0.9)**	**0 (0.0)**	**1 (2.0)**	**0 (0.0)**

Table 2. Clinical and virological follow-up of the 109 patients during DTG treatment.

DISCUSSION

- In virologically-suppressed patients, DTG was generally introduced as a simplification strategy, to decrease the number of pills taken daily and/or the daily dosing frequency. All patients had suppressed viremia at the last visit
- The low rate of severe drug-related adverse events is similar to those reported in previous trials in adults [3,4,5] and adolescents[1,2]

CONCLUSION

Virological efficacy and safety of dolutegravir were similar between the 3 groups of age.

Because of its high genetic barrier to resistance and small pill burden, DTG could be especially useful in the pediatric population, in which the risk of poor treatment adherence is high.

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