



Unexpectedly High Rate of Intolerance for Dolutegravir in Real Life Setting



Guido van den Berk, Josephine Oryszczyn, Willem Blok, Narda van der Meche, Rosa Regez, Daoud Ait Moha, **Kees Brinkman**
dept internal medicin OLVG, Amsterdam, The Netherlands – k.brinkman@olvg.nl

background

- Integrase inhibitors (INSTI) are now preferred antiretrovirals in first line cART.
- Dolutegravir (DGV) is possibly considered as one of the most efficacious, convenient and tolerated INSTI, with hardly any chance for drug-drug interactions.
- Since we encountered many patients who stopped DGV because of intolerance, we analyzed the experience with DGV in our whole patient population since licensing in the Netherlands (aug 2014)

methods

- OLVG cohort: ±3000 patients, (97,4% on cART)
- retrospective analysis of all patients who started DGV, either as initial therapy or after switching from other antiretrovirals for any reason.
- Baseline characteristics at the moment of DGV start were recorded.
- We calculated the proportion of patients who stopped DGV, analyzed the reason for interruption and evaluated potential risk factors.
- Chi-squared test and Z-score to check for significant differences between groups and proportions.

results

	total (N=387)		naives(N=65)		non-naives (N=322)		
median age (IQR)	48		46	(22)	48	(13)	ns
female	44	11,4%	8	12,3%	36	11,2%	ns
dutch origin	136	35,1%	28	43,1%	108	33,5%	ns
median CD4/mm ³ (IQR)	650		530	(395)	655	(345)	ns
median DGV days (IQR)	220		196	(147)	221	(148)	ns
DGV separate..	156		15		141		
DGV in STR..	231		50		181		
DGV stopped	62	16,0%	13	20,0%	49	15,2%	ns
median DGV days (IQR)	78		81	(71)	75	(99)	ns
female	5	11,4%	3	37,5%	2	5,6%	p=0.01
DGV separate	24	15,4%	1	6,7%	23	16,3%	ns
DGV in STR	38	16,6%	12	24,0%	26	14,4%	ns
reason for interruption							
other than toxicity*	6	9,7%	1	7,7%	5	10,2%	
toxicity	56	90,3%	12	92,3%	44	89,8%	ns
sleeping..	19	31,3%	5	38,5%	14	28,6%	ns
gastro-intestinal..	18	29,5%	4	30,8%	14	28,6%	ns
neuro-psychiatric..	12	19,7%	3	23,1%	9	18,4%	ns
paresthesia..	6	9,7%	0	0,0%	6	12,2%	ns
headache..	8	12,9%	0	0,0%	8	16,3%	ns
fatigue..	9	14,6%	1	7,7%	8	16,3%	ns
allergy..	1	1,7%	1	7,7%	0	0,0%	ns
other..	5	8,2%	1	7,7%	4	8,2%	ns

*LTFU, HBV protection, insurance, induction, patient request, interaction

results

DGV treatment was stopped in 62/387 (16,0%) patients. There were no virological failures. Main reason for DGV interruption was intolerance in 56/62 (90,3%) patients: 19/56 (31,3%) sleeping problems, 18/56 (29,5%) gastrointestinal problems, 12/56 (19,7%) psychiatric problems, 8/56 (12,9%) headache, 9/56 (14,6%) fatigue and 6/55 (10,9%). Some patients reported more than one toxicity.

Psychiatric reason to stop (n=12) varied from anxiety, depression and agitation to psychosis (n=2)

conclusion

In a real life setting a substantial proportion of patients unexpectedly interrupted DGV treatment for reasons of intolerance, in particular sleeping, gastrointestinal and psychiatric problems. This was much higher than reported in clinical trials.