Dolutegravir and Treatment Noncompliance

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- Dolutegravir (DTG)-based HIV treatment regimens have reported high levels of effectiveness and acceptability[1] and it is now a recommended first- or second-line treatment for HIV, with the potential to reach 38 million patients worldwide.

- Concerns have been raised about potential poor adherence[2].

- Experiencing side Effects may result in poor adherence[3].

- Poor adherence to HIV treatment can be multifactorial with patient related and system of care components[4].

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Aim

Preliminary identification of cases of reported treatment noncompliance in combination with dolutegravir containing medications and a comparison to other anti-HIV medications.

- A search of VigiBase, the WHO global database of reported potential side effects of medicinal products, was performed on 19th June, 2023.

- Cases were identified when they reported both:
  - a reaction by the Preferred Term (PT) "**Treatment noncompliance**"; and
  - **dolutegravir** containing products in the WHODrug Standardised Drug Grouping (SDG) "Drugs for treatment of HIV infections".

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- Disproportionality measures, using the information component (IC), were calculated for the combination of the PT, Treatment Noncompliance and all DTG containing products combined.

- An IC_{025} of greater than 0 indicates positive disproportionate reporting with statistical significance[5].

Method (3)

- vigiPoint[6] was used to compare reporting for medications containing DTG to medications that do not contain dolutegravir in the WHODrug SDG "Drugs for treatment of HIV infections".

- A positive lower end of a 99% credibility interval of the calculated shrinkage log odds ratio (SLOR) highlights variables with an over-representation among the dolutegravir subset.

- A threshold of greater than 0.5 for the lower end of the SLOR 99% credibility interval (SLOR$_{005}$) highlights substantial deviation.

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Results (1)

- For all DTG containing active ingredients, a total of 311 reports were identified in VigiBase.

- The countries that contributed the largest number of reports were USA (n=102, 32.8%) and Italy (n=44, 14.1%) and reports were received from 19 countries in total.

- The IC_{025} value for this combination was 3.0 , thus there was statistically significant disproportionate reporting for this combination.

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- The PT "Treatment noncompliance" had two Low Level Terms (LLT): Treatment noncompliance (n=262, 84.2%) and Treatment nonadherence (n=49, 15.8%).

- There were 287 co-reported PTs, mostly side effects (n=335, 35.4%). The most common co-reported PTs were virologic failure (n=142, 15.01%) viral mutation identified (n=76, 8.03%) and pathogen resistance (n=68, 7.19%).

- The results of the vigiPoint analysis are shown in Table 1, with Preferred Terms related to treatment noncompliance.

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Table 1 (vigiPoint analysis Results)

Reported preferred terms (MedDRA)	No. Cases in DTG	No. Cases in Non-DTG	Proportion in DTG	Proportion in Non-DTG	SLOR
Product dose omission issue	1,139	2398	1.97	0.28	**2.85**
Treatment noncompliance	311	1184	0.54	0.14	**1.98**
Virologic failure	657	3750	1.14	0.44	**1.40**
Viral mutation identified	252	1081	0.44	0.13	**1.80**
Alcoholism	5	31	0.01	0.00	**1.26**
Pathogen resistance	239	855	0.41	0.10	**2.06**
Product dose omission in error	175	105	0.30	0.01	**4.64**
Drug resistance	158	2115	0.27	0.25	**0.16**
Treatment failure	146	1434	0.25	0.17	**0.60**
Substance abuse	3	22	0.01	0.00	**1.02**
Drug abuse	4	86	0.01	0.01	**-0.53**

Conclusion

- This potential signal warrants further investigation.

- Initial results indicates that treatment noncompliance may be associated with side effects and may result in treatment ineffectiveness.

- Treatment adherence programs should incorporate monitoring and management of side effects.

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References

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