Dolutegravir with enteral feeds in intensive care: nutrition vs viral suppression

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Introduction

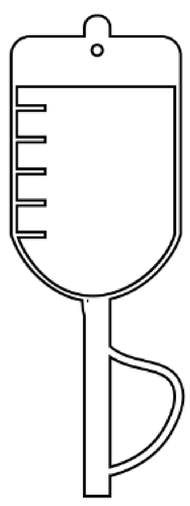
- People living with HIV requiring admission to intensive care often receive enteral nutrition via feeding tubes.
- Enteral feeds contain cations which may interfere with dolutegravir (DTG) absorption due to chelation [1].
- For this reason, temporal spacing (six hours before/two hours after DTG administration [2]) is recommended, possibly leading to suboptimal caloric intake [3].
- The clinical significance of the interaction between enteral feeds and DTG when co-administered is not fully understood and public data are sparse.

Method

- Review of prospectively collected data on therapeutic drug monitoring (TDM) and electronic patient records of patients on DTG and enteral feeds, whilst in intensive care unit (ITU) between 2022 and 2023.
- Maximum (C_{max}) and trough (C_{trough}) DTG concentrations were measured and compared to reference ranges (DTG 50 mg once daily: C_{max} 3340 ng/mL; C_{trough} 830 ng/mL) [4].

Results

- Six cases were identified with eight incidences of TDM sampling.
- In three of the eight samples, temporal spacing with enteral feeds occurred as per SPC guidance [2].
- DTG C_{max} and C_{trough} results are shown in the table.



Age, Gender, Ethnicity	Antiretroviral regimens	No of days in ITU	No of days into feeds	Dolutegravir TDM (ng/mL)		Separation of DTG from NG feed	Albumin (g/L)	Viral Loads (cp/ml)		
				C_{max}	C_{trough}			Pre-ITU	During feeds	Post-enteral feeds
48, M, Black	TAF/FTC + DTG OD	52	12	810	121	✓	19	75,800	2660	<50
33, F, Black	TAF/FTC + DTG OD	76	56	2201	389	×	26	56	116	<50
35, M, White	TDF/FTC + DTG OD	68	28	660	**44**	✓	19	372	144	70
	TDF/FTC + DTG **BD** (due to low plasma levels)		58	3171	1181	×	24			
44, M, White	TDF/FTC + DTG OD	37	30	929	146	✓	18	<50	71	<50
			31	1213	160	×	19			
29, M, Asian	TAF/FTC + DTG **BD** (rifampicin co-administration)	35	5	419	335	×	29	<50	<50	<50
33, F, White	TAF/FTC + DTG **BD** (rifampicin co-administration)	9	3	1144	**60**	×	23	356	<50	<50

TDF: tenofovir disoproxil fumarate; TAF: tenofovir alafenamide fumarate; FTC: emtricitabine; DTG: dolugravir; NG: nasogastric; OD: once daily; BD: twice daily.

Conclusions

- DTG C_{max} were lower than those observed in literature regardless of temporal spacing from enteral feeds.
- C_{trough} were also lower than expected in all cases.
- Six of eight C_{trough} were lower than the DTG minimum effective concentration (MEC) of 300 ng/mL [5], however, only one was below IC_{90} for wildtype virus (64 ng/mL [6]). Virological failure/onset of resistance were not observed in any of the patients.
- Multiple factors are likely to be contributing to low DTG concentrations, of which the most significant is likely impaired drug absorption, whilst nutritional feed co-administration seems to not be relevant.

References

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