Real world data of using Triumeq (dolutegravir/abacavir/lamivudine; DTG/ABC/3TC): final outcomes of the 3-year German TRIUMPH cohort show good virologic effectiveness and safety in routine clinical practice

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Background

- TRIUMPH was a prospective, 3-year observational German cohort study in ART-naïve and pre-treated adult HIV-infected patients with negative HLA-B*5701 receiving Triumeq, an onepill-regimen consisting of dolutegravir/ abacavir/lamivudine (DTG/ABC/3TC).
- Primary and secondary outcomes include health care resource utilization, effectiveness and safety of DTG/ABC/3TC use in routine clinical care.

Objectives

- Frequency and type of monitoring measures while on DTG/ABC/3TC
- Virological effectiveness using an on-treatment (OT) analysis and a modified ITT (mITT) snapshot approach (HIV-RNA<50 cp/mL [visit window ≥month 33], discontinuation=failure, missing/loss-to-follow-up=excluded)
- 3-year persistence in the study and reasons for discontinuation
- Incidence of adverse drug reactions (ADRs) (coded with MedDRA preferred terms (PTs) and classified by system organ classes [SOCs])
- Time to study discontinuation due to ADRs (Kaplan-Meier analysis; discontinuations for other reasons than ADRs are censored)

Results

Study population

- The analysis population consisted of N=387 patients (40.1% ART-naïve).
- Of 232 pre-treated patients, 19.4% had ≥3 prior regimens and 47.8% were switched from a protease inhibitor (PI)-based regimen.

Table 1. Baseline characteristics	Overall (N=387)	ART-naïve (N=155, 40.1%)	Pre-treated (N=232, 59.9%)
Sex, male, n (%)	348 (89.9)	147 (94.8)	201 (86.6)
Age, years, median (IQR*)	42 (33 – 50)	38 (29 – 48)	45 (35 – 52)
CDC stage C, n (%)	60 (15.5)	8 (5.2)	52 (22.4)
HIV-RNA level, median (IQR*)	1.7 (1.7 – 4.3)	4.4 (3.9 – 4.9)	1.7 (1.7 – 1.7)
<50 cp/mL, n (%)		---	197 (84.9)
≥100,000 cp/mL, n (%)		28 (18.1)	---
CD4 cell count, median (IQR*)	533 (368 – 760)	450 (282 – 613)	600 (434 – 834)
<200 cells/µL, n (%)		20 (12.9)	---
Presence of comorbidities, N (%)	171 (44.2)	45 (29.0)	126 (54.3)
Comorbidities in >10% of patients			
Depression**, n (%)	76 (19.6)	18 (11.6)	58 (25.0)
Hypertension**, n (%)	43 (11.1)	14 (9.0)	29 (12.5)

*IQR, interquartile range; **8.5% of the cohort received antidepressants, 11.6% antihypertensives;*

Monitoring measures

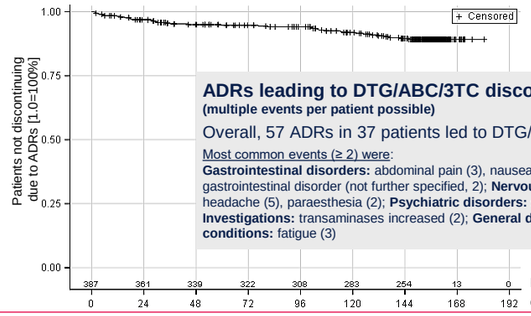
- The median number of documented visits to HIV specialists was 4.6 (IQR, 4.1 – 5.4) per patient year (PPY). The median number of referrals to specialists (excluding infectiologists) was 1.0 (IQR, 0.5 – 1.7).
- The median rates of monitoring measures such as HIV-RNA/CD4 cell controls or blood count/serum chemistry controls were 4.0 PPY (IQR, 3.5 – 4.3) and 4.1 PPY (IQR, 3.6 – 4.5), respectively. Urine tests or microbiological tests (including one or multiple tests) were performed 1.8 (IQR, 0.0 – 3.8) and 1.0 (IQR, 0.0 – 2.3) times PPY, respectively.

Patients disposition after 3 years and reasons for study discontinuation (multiple responses permitted)

- In 36.2% of patients (n=140) premature study discontinuation was reported.
- Most common reasons were stopping DTG/ABC/3TC (18.3%; reasons see Table 2), loss to follow-up (13.4%) and patient decision/withdrawal of consent (5.7%).

Table 2. Study or DTG/ABC/3TC discontinuations and most common reasons (multiple responses permitted)		Overall (N=387)	ART-naïve (N=155)	Pre-treated (N=232)
Patients with study discontinuation, n (%)		140 (36.2)	53 (34.2)	87 (37.5)
Reasons for study disc. (>5%)	Loss to follow-up, n (%)	52 (13.4)	18 (11.6)	34 (14.7)
	Patient decision/withdr. consent, n (%)	22 (5.7)	6 (3.9)	16 (6.9)
	Patients stopping DTG/ABC/3TC, n (%)	71 (18.3)	24 (15.5)	47 (20.3)
Reasons for stopping DTG/ABC/3TC	ADRs, n (%)	37 (9.6)	15 (9.7)	22 (9.5)
	Patient wish, n (%)	33 (8.5)	8 (5.2)	25 (10.8)
	Virologic failure, n (%	3 (0.8)	2 (1.3)	1 (0.4)
	Comorbidity/comedication, n (%)	2 (0.5)	1 (0.6)	1 (0.4)
	Other, n (%)	9 (2.3)	1 (0.6)	8 (3.4)

Figure 1. Time to study discontinuation due to ADR



ADRs leading to DTG/ABC/3TC discontinuation
(multiple events per patient possible)

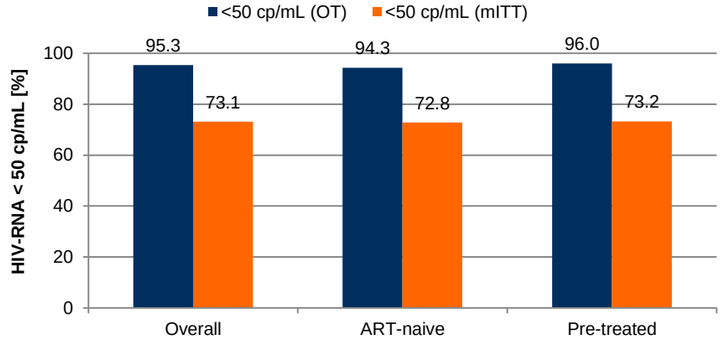
Overall, 57 ADRs in 37 patients led to DTG/ABC/3TC discontinuation.

Most common events (≥ 2) were:
Gastrointestinal disorders: abdominal pain (3), nausea (3), diarrhoea (2), flatulence (2), gastrointestinal disorder (not further specified, 2); **Nervous system disorders:** dizziness (3), headache (5), paraesthesia (2); **Psychiatric disorders:** sleep disorder (4), depression (4); **Investigations:** transaminases increased (2); **General disorders and administration site conditions:** fatigue (3)

Virological effectiveness after 3-year follow-up

- Virologic effectiveness was 73.1% (mITT; 244/334) [ART-naïve 72.8 (99/136), pre-treated 73.2% (145/198)].
- In OT analysis, HIV-RNA was <50 cp/mL in 95.3% (244/256) [ART-naïve 94.3% (99/105), pre-treated 96.0% (145/151), see Figure 2].

Figure 2. Virologic effectiveness of DTG/ABC/3TC use in routine care



Adverse drug reactions (ADRs)

- Overall, 92 ADRs (81 non-serious ADRs in 59 patients, 11 SADRs in 6 patients) were reported resulting in an event rate of 0.097 PPY.
  - SADRs (N=11): sleep disorder, depression, hyperlipidaemia, headache, psychiatric decompensation (6 events in 1 patient), acute myocardial infarction
- 77.2%, 12.0% and 10.9% of ADRs occurred in years 1, 2 and 3.

Conclusions

- During the course of the 3-year TRIUMPH cohort, the good safety profile and high virological effectiveness of the onepill-regimen DTG/ABC/3TC in clinical trials was confirmed in real-life with discontinuation rates for intolerance or virologic failure of 9.6% and 0.8%, respectively.
- Moreover, ADR rates decreased over time.
- Monitoring measures were mainly related to routine quarterly controls of HIV-disease, reflecting local HIV treatment guidelines.

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