# A Retrospective Clinical Audit of General Practices in Australia to Determine the Motivation for Switch to DTG/ABC/3TC and Clinical Outcomes

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## Background

We conducted a retrospective clinical audit at high HIV–caseload GP clinics in Australia to determine why virologically suppressed patients switched to dolutegravir/abacavir/lamivudine (DTG/ABC/3TC) fixed-dose combination and the clinical outcomes following switch.

## Methods

Patients identified across 6 clinics, who had received DTG/ABC/3TC alone for ≥1 day following a switch from suppressive antiretroviral therapy (<50 copies/mL), were included. Patient files were reviewed by each clinic and individual cases submitted via a systematic electronic survey. Time on treatment was calculated from the date of first DTG/ABC/3TC prescription and censored on 1 April 2016. Survival methods were used to determine time to DTG/ABC/3TC discontinuation.

## Results

We included 443 patients: 97% male, 91% white, 45% ≥50 years of age, 48% ≥3 prior ARV regimens, 45% >10 years of ART experience, 6.5% with evidence of any ART resistance. A summary of the most recent regimen prior to switch is shown in Table 1.

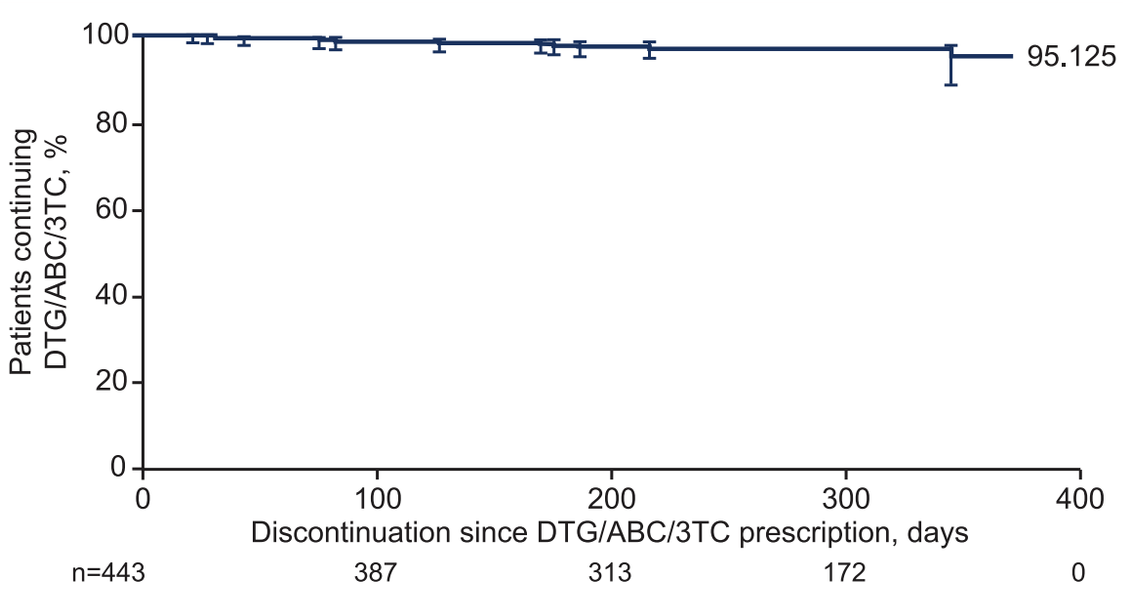
**Table 1. Summary of Most Recent Regimens Prior to Switch (N=443)**

| Demographics | | n (%) |
|---|---|---|
| Time on prior therapy, y | <2 | 242 (54.6) |
| | 2-5 | 81 (18.3) |
| | >5 | 120 (27.1) |
| Single-pill regimen | – | 50 (11.2) |
| Prior combination NRTI[a,b] | ABC/3TC | 300 (67.7) |
| | TDF/FTC | 119 (26.9) |
| | AZT/3TC | 5 (1.1) |
| | NRTI sparing | 5 (1.1) |
| Prior core agent[a,c] | INI | 258 (58.2) |
| | NNRTI | 118 (26.6) |
| | PI | 91 (20.5) |
| | EI | 2 (0.5) |
| | MI | 1 (0.2) |
| Prior DTG-based regimen[a] | DTG + ABC/3TC (alone) | 165 (37.2) |
| | Non-DTG–based regimen | 242 (54.6) |

ABC/3TC, abacavir/lamivudine; ART, antiretroviral therapy; ARV, antiretroviral; AZT/3TC; zidovudine/lamivudine; DTG, dolutegravir; EI, entry inhibitor; INI, integrase inhibitor; MI, maturation inhibitor; NNRTI, non-nucleoside reverse transcriptase inhibitor; NRTI; nucleoside reverse transcriptase inhibitor; PI, protease inhibitor; TDF/FTC, tenofovir/emtricitabine. [a]Most recent regimen before DTG/ABC/3TC. [b]Includes patients on single-pill regimens containing the combination NRTI; 14 patients had alternative combination NRTIs or a single NRTI in their regimen. [c]Some patients were on multiple core agents.

At time of censorship, the median time on DTG/ABC/3TC was 266 days (IQR 176-325). The probability of patients remaining on DTG/ABC/3TC therapy at 12 months was high (95.1%) by Kaplan-Meier estimate (Figure).

**Figure. Percentage of Patients Remaining on DTG/ABC/3TC Therapy After Switching by Kaplan-Meier Estimate**




Based on censored population (n=443).

The most common reasons patients switched to DTG/ABC/3TC were simplification, toxicity/intolerance, or patient preference (73%,13%, and 12%, respectively). Less than 2% of patients switched for reasons attributed to cost, suboptimal adherence, or drug:drug interactions. The most common toxicities/intolerances leading to switch to DTG/ABC/3TC were nervous system, renal and urinary, and gastrointestinal disorders. Pre-existing toxicity/intolerance events resolved in 43/58 (74%) of patients who switched for this reason to DTG/ABC/3TC (Table 2).

**Table 2. Toxicity/Intolerance Events Based on MedDRA System Organ Classes Leading to Switch to DTG/ABC/3TC and Resolved After Switching to DTG/ABC/3TC**

| Toxicity/Intolerance | Number of patients with pre-existing events | Number of patients with resolved events |
|---|---|---|
| Nervous system disorders | 13 | 9 |
| Renal and urinary disorders | 12 | 8 |
| Gastrointestinal disorders | 10 | 10 |
| Psychiatric disorders | 6 | 4 |
| General system disorders | 4 | 4 |
| Musculoskeletal and connective tissue disorders | 4 | 1 |
| Metabolism and nutrition disorders | 4 | 3 |
| Hepatobiliary disorders | 2 | 2 |
| Endocrine disorders | 1 | 1 |
| Blood and lymphatic system disorders | 1 | 1 |
| Skin and subcutaneous tissue disorders | 1 | 0 |
| Total | 58 | 43[a] |
| Events attributed to ARVs prior to DTG/ABC/3TC | 55 (95%) | 43 (100%) |

Note: Only one defining event per patient. [a]For patients with unresolved pre-existing toxicity/intolerance events (15), median time on DTG/ABC/3TC treatment was 191 days (IQR 100-239.5), lower than that of the overall population, which was 266 days (IQR 176-325).

Fourteen patients (3.2%) discontinued DTG/ABC/3TC; none of these were due to virologic failure. Discontinuations were mainly related to adverse events (2.5%); <1% of patients discontinued due to a psychiatric event. The discontinuation rates for all subgroups were similar (0%-5.6%) regardless of time on treatment, number of previous regimens, time on most recent regimen, core agent or NRTI combination in the most recent regimen, and rationale for switch, including switch from non-DTG–based regimens. Nine patients of those who discontinued DTG/ABC/3TC (n=14) were switched back to their prior regimen (Table 3), and all 14 patients maintained virologic control.

**Table 3. Patients Who Discontinued DTG/ABC/3TC**

| Prior regimen[a] | Reason for DTG/ABC/3TC discontinuation[d] | Event | Subsequent regimen[h] | AE ceased |
|---|---|---|---|---|
| DTG + ABC/3TC | Toxicity/Intolerance | Headache[e] | DTG + ABC/3TC | Yes |
| ATV/r + ABC/3TC | Blip | Single event of 63 copies/mL | ATV/r + ABC/3TC | |
| DTG + ABC/3TC | Toxicity/Intolerance | Creatinine | EVG/c/TDF/FTC | No |
| ATV/r + TDF/FTC | Toxicity/Intolerance | Abdominal discomfort | ATV/r + TDF/FTC | Yes |
| RAL + ABC/3TC | Toxicity/Intolerance | Insomnia | RAL + ABC/3TC | Yes |
| NVP + TDF/FTC[b] | Toxicity/Intolerance | Anxiety[f] | NVP + TDF/FTC | Yes |
| RAL + ABC/3TC[b] | Toxicity/Intolerance | Dry mouth | RAL + ABC/3TC | Yes |
| RAL + TDF/FTC | Toxicity/Intolerance | Rash | RAL + TDF/FTC | Yes |
| DTG + ABC/3TC | Drug-drug interactions | Cigarettes and risk of CVD | ATV/r + TDF/FTC | |
| DTG + ABC/3TC[c] | Toxicity/Intolerance | Malaise[g] | NVP + ABC/3TC | Yes |
| NVP + ABC/3TC | Patient preference | | NVP + ABC/3TC | |
| DTG + ABC/3TC | Toxicity/Intolerance | Anxiety | DRV/r + ABC/3TC | Yes |
| RAL + DRV/r + ABC/3TC | Toxicity/Intolerance | Rhabdomyolysis[h] | RPV/TDF/FTC | Yes |
| RAL + NVP + 3TC | Toxicity/Intolerance | Nausea | RAL + NVP + 3TC | Yes |

AE, adverse event. [a]Switched from prior regimens for simplification, with 3 exceptions. [b]Discontinued prior regimen due to a pre-existing toxicity/intolerance. [c]Discontinued prior regimen due to patient preference. [d]Median time on DTG/ABC/3TC treatment was 147.5 (IQR 75-195.75) days in these patients. [e]This subject was entered 2 days after study closure. [f]History of anxiety. [g]Aches, shortness of breath, tight chest, coughing, fatigue. [h]Serious AE: onset bilateral arms, required hospitalization.

## Conclusions

In this real-world, retrospective audit, switching to DTG/ABC/3TC from a range of other regimens shows a low rate of discontinuation. Few patients were reported to discontinue due to adverse events and no patients due to virologic failure, supporting this as a viable treatment strategy. These results are consistent with previous clinical trial data with DTG/ABC/3TC.[1]

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**Reference: 1.** Koteff J, Brennan C, Aboud M, et al. Measuring safety and satisfaction of ABC/DTG/3TC in a switch trial: secondary endpoints from the STRIIVING study. Presented at: 15th European AIDS Conference; October 21-24, 2015; Vancouver, Canada.

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