A RESEARCH REVIEW™
PRODUCT REVIEW

Dolutegravir (Tivicay®) in the Treatment of HIV Infection: An Update

Making Education Easy 2017

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ABOUT RESEARCH REVIEW

Research Review is an independent medical publishing organisation producing electronic publications in a wide variety of specialist areas. Product Reviews feature independent short summaries of major research affecting an individual medicine. They include a background to the particular condition, a summary of the medicine and selected studies by a key New Zealand specialist with a comment on the relevance to New Zealand practice. Research Review publications are intended for New Zealand medical professionals.

This narrative review summarizes some important aspects of the clinical use of dolutegravir (Tivicay), which is an orally-administered integrase strand transfer inhibitor (INSTI) that is approved for the treatment of human immunodeficiency virus type 1 (HIV-1) infection in combination with other antiretroviral agents in adults and adolescents. This review updates a previous Product Review, Dolutegravir (Tivicay®) in the Treatment of HIV Infection, and is sponsored by GlaxoSmithKline (NZ) Ltd.

LATEST RECOMMENDATIONS FOR ART

According to the 2016 recommendations of the International Antiviral Society-USA (IAS-USA),[1] clinical evidence supports the recommendation that all HIV-infected individuals with detectable plasma virus should be commenced on antiretroviral therapy (ART) as soon as possible following diagnosis. Also, as there are now many effective antiretroviral agents available, initial ART regimens can be based on considerations other than virological potency. Some of these considerations are:

- Ease of administration.
- Adverse effects.
- Drug interactions.
- Risk of resistance if virologic failure occurs.

Clinical evidence indicates that initial ART with two nucleoside reverse transcriptase inhibitors (NRTIs) plus a third agent from a different drug class achieves and maintains similar virologic suppression rates in nearly all patients.[1] The IAS-USA considers integrase strand transfer inhibitors (INSTIs), which currently include dolutegravir, elvitegravir, and raltegravir, as being optimal for initial ART. The recommended initial ART regimens for most patients with acute HIV infection are:

- Dolutegravir plus tenofovir/emtricitabine.
- Dolutegravir/abacavir/lamivudine.
- Elvitegravir/cobicistat/tenofovir/emtricitabine.
- Raltegravir plus tenofovir/emtricitabine.

DOLUTEGRAVIR

Dolutegravir (Tivicay) has been developed as a convenient INSTI therapy for use in combination with other antiretroviral agents for the treatment of treatment-naïve and treatment-experienced patients with HIV-1 infection. Dolutegravir is suitable for once-daily dosing without need for pharmacological boosting and can be taken with or without food.[2]

Dolutegravir is indicated for the treatment of HIV infection in combination with other antiretroviral agents in adults and adolescents aged >12 years and weighing ≥40kg.[2] The recommended dosage is 50mg once daily. (refer to the Data Sheet to find out when it should be dosed twice daily).[2] Dolutegravir is funded by PHARMAC, requiring Special Authority for subsidy.

Drug interactions

Due to being primarily metabolised by UGT1A1 in the liver, dolutegravir has limited propensity to affect drug-metabolising enzymes.[2,4,5] However, dolutegravir is a substrate of UGT1A3, UGT1A9, breast cancer resistance protein (BCRP), and P-glycoprotein and dolutegravir dosage modification may be required in patients using medications that induce or inhibit these enzymes.[2]

Anti-infective drugs

There are no interactions or dose adjustments required when dolutegravir is combined with the NRTIs.[2,5] Similarly, protease inhibitors (PIs), irrespective of ritonavir co-administration, can be safely used with dolutegravir.

Among the non-nucleoside reverse transcriptase inhibitors (NNRTIs), etravirine markedly reduces plasma concentrations of dolutegravir, probably mainly via induction of UGT1A1.[2,4-6] To attenuate the enzyme-inducing properties of etravirine, the dose of dolutegravir should be increased to 50mg twice daily when given with etravirine or dolutegravir should be co-administered with a ritonavir-boosted PI. Efavirenz also reduces dolutegravir plasma concentrations and the dose of dolutegravir should be 50mg twice daily when co-administered with efavirenz. Nevirapine has the potential to reduce plasma concentrations of dolutegravir

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but studies are lacking. In line with the dolutegravir Data Sheet, the recommended dose of dolutegravir is 50mg twice daily when co-administered with nevirapine. Alternative combinations that do not include nevirapine should be used where possible in INI-resistant patients.

Tuberculosis (Tb) co-infection is common in HIV-infection patients. Rifampicin results in lower dolutegravir plasma concentrations such that the dosage of dolutegravir should be increased to 50mg twice daily when given with rifampicin.[2,5]

Non-anti-infective drugs

Cationic antacids (e.g. Mg^{2+}, Al^{3+}, Ca^{2+}) can reduce the absorption of dolutegravir; therefore, dolutegravir should be taken 2 hours before or 6 hours after taking cationic antacids.[2,5] Such a schedule should also be followed if dolutegravir is co-administered with cation supplements such as iron and calcium. Alternatively, dolutegravir can be given with iron or calcium supplements if they are taken with food.

Some forms of ART are associated with an increased risk of developing type 2 diabetes mellitus, especially in HIV-infected individuals who have signs of metabolic syndrome prior to starting ART.[8,9] As the co-administration of dolutegravir and metformin results in elevated metformin plasma concentrations, monitoring and potential dose adjustment of metformin is recommended to maintain glycaemic control.[2,4] In an open-label study of the effect of dolutegravir on the pharmacokinetics of metformin in healthy adults, metformin was generally well tolerated when used in combination with dolutegravir despite a significant increase in plasma exposure.[10] Given the magnitude of the change in metformin plasma concentrations, the study investigators concluded that assessment of glycaemic control and consideration of metformin dose adjustment is warranted when co-administering dolutegravir and metformin.

Clinical efficacy

The virological efficacy of dolutegravir has been demonstrated in ART treatment-naïve patients with HIV-1 infection showing non-inferiority to raltegravir (SPRING-2) and superiority to efavirenz (SINGLE) and ritonavir-boosted darunavir (FLAMINGO) regimens in phase III randomised controlled trials (RCTs).[11-13] Notably, no treatment-emergent resistance was observed in patients with virological failure on dolutegravir compared with 21% NRTI resistance mutations in the raltegravir group of the patients with virologic failure on raltegravir in SPRING-2.[12]

The anti-viral efficacy of dolutegravir has also been demonstrated in treatment-experienced patients (i.e. when used as salvage therapy) showing superiority over raltegravir in a phase III RCT (SAILING) and efficacy in INSTI-resistant infection in a phase III open-label trial (VIKING-3).[7,14] Dolutegravir also demonstrated a statistically-significant lower rate of virological failure relative to raltegravir in treatment-experienced patients in the SAILING study.[7]

Drug resistance

Regarding drug resistance, dolutegravir has the highest genetic barrier to resistance of the currently-available INSTIs and it is comparable with ritonavir-boosted darunavir (FLAMINGO).[11] This is primarily attributable to its slower dissociation from the HIV-1 integrase-DNA complex (dissociation rate half-life 71 hours) compared with raltegravir (8.8 hours) and elvitegravir (2.7 hours) but also to its lower interindividual pharmacokinetic variability.[15,16] Additionally, dolutegravir appears to possess a different resistance profile to raltegravir and elvitegravir, which share several signature resistance mutations and have demonstrated cross-resistance.[4] As of August 2017, clinical resistance mutations to dolutegravir in treatment-naïve patients had not been reported.[4]

Switching therapy

Given that ART greatly extends the life-expectancy of most HIV-infected individuals, clinicians should be proactive in reviewing their patients' treatment needs, including consideration of switching to a different regimen.[17] In the setting of virologic suppression, the potential benefits of switching include improved tolerability, regimen simplification, increased adherence, and more favourable long-term health benefits.

A review of six clinical studies that evaluated switching patients who were virologically-suppressed on non-INSTI-based ART to regimens based on INSTIs concluded that INSTI-based regimens offer an important switch option for meeting and optimising the needs of many patients.[17] One of the six studies reviewed was the STRIIVING study, which demonstrated the non-inferiority of switching to once-daily ABC/DTG/3TC (see **Study Summary**).[18] Additional support for dolutegravir as a useful switch option is provided by a retrospective case chart analysis of HIV-1 infected patients in a large teaching hospital.[19] Of 68 patients with an undetectable viral load prior to being switched to dolutegravir from another ART regimen, 66 (97%) were still virologically suppressed 4 weeks after switching.

Dolutegravir/abacavir/lamivudine versus current ART in virally suppressed patients (STRIIVING): a 48-week, randomized, non-inferiority, open-label, Phase IIIb study[18]

Authors: Trottier B et al.

Aim and methods: The objective of STRIIVING was to investigate the efficacy and safety of switching from a PI-, INSTI-, or NNRTI-based therapy to ABC/DTG/3TC in virologically-suppressed HIV-infected adults (<50 copies/mL). Subjects were randomised to ABC//DTG/3TC on day one (early switch) or continued on current ART and switched at week 24 (late switch). Evaluation was carried out at 24 weeks (primary endpoint) and again at 48 weeks.

Results: Randomisation (1:1) of 553 patients enrolled resulted in 275 being assigned to the early-switch arm to ABC/DTG/3TC and 278 continuing current ART. At week 24, 85% of early-switch patients were virologically suppressed versus 88% of late-switch patients (**Figure 1**). Therefore, ABC/DTG/3TC was non-inferior to current ART (difference in proportion, -3.4%; 95% CI: -9.1 to 2.4). At week 48, the proportion of patients who were virologically suppressed was 83% in the early- and 92% in the late-switch groups. At week 24, adverse events were reported more frequently with ABC/DTG/3TC (66%) than with current ART (47%). In the late-switch group, 60% of patients reported adverse events post-switch. Discontinuations were infrequent and mostly due to low-grade adverse events. There were no further discontinuations due to adverse events in the early-switch arm post week 24 (4%) and a low discontinuation rate in the late-switch arm (2%). Switching to ABC/DTG/3TC was associated with improved scores on the HIV Treatment Satisfaction Questionnaire compared with current ART.

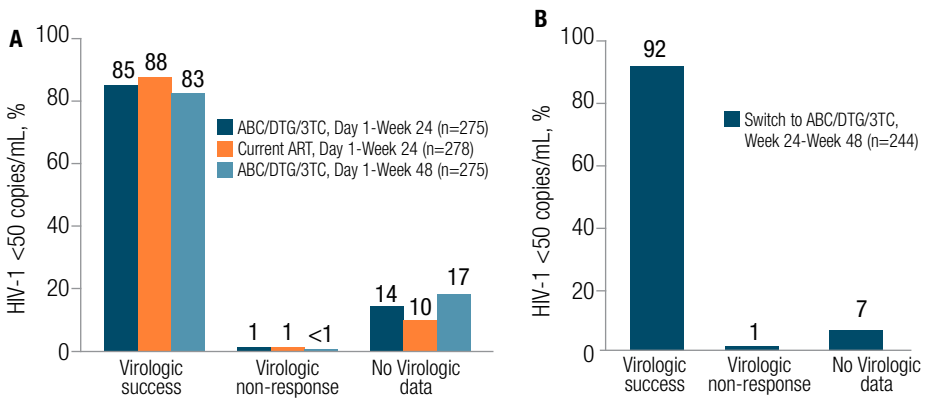

Figure 1. Virological outcomes in the STRIIVING Study. (A) Early-switch arm (on day one) (B) Late-switch arm (24 weeks)[18]

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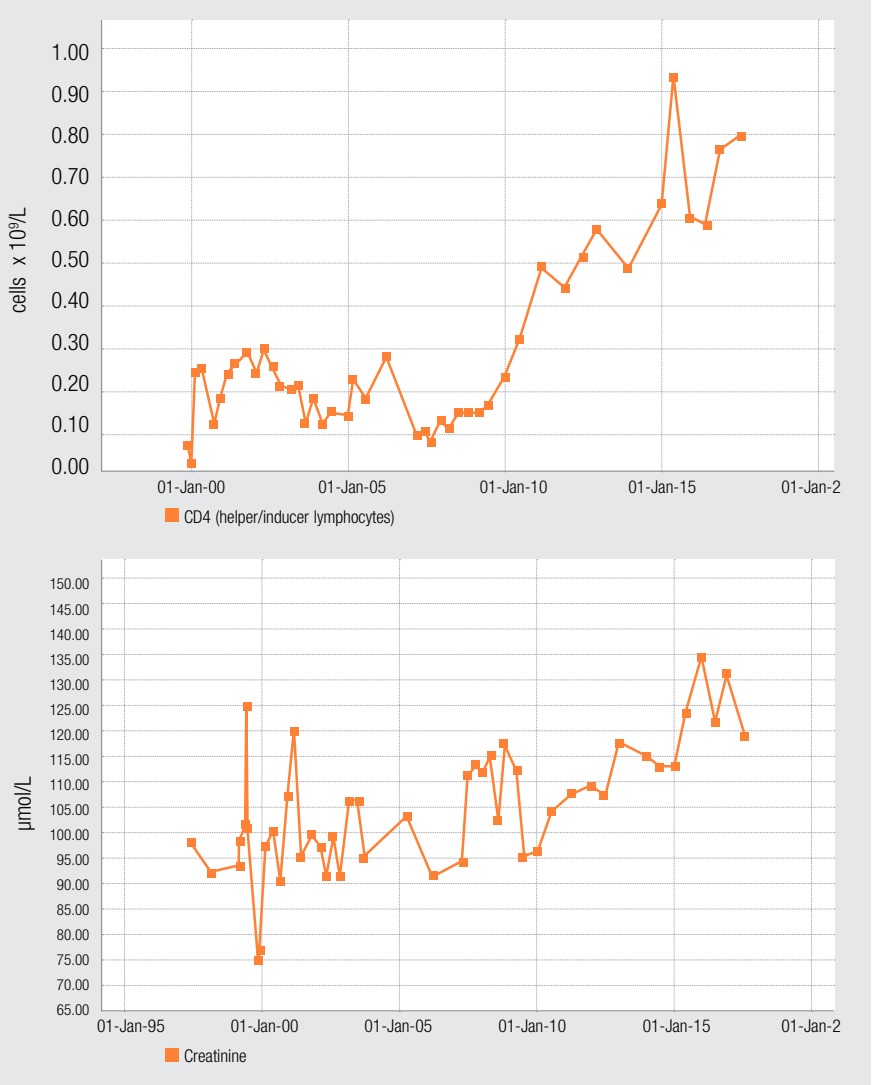
Comment (TB): As the authors comment, the study design was likely to be sensitive to any different side effects of a new regimen, as the participants were already long-established on their current regimen. This perhaps explains the paradox of greater satisfaction, but more side effects. It is a bit disappointing to be not told the effect of prior cART on the development of side effects. I would have thought those on raltegravir would potentially get more side effects on dolutegravir but I would not expect that to be true for the protease inhibitors or efavirenz. Personal experience tells me that most patients on long-term Atripla feel much better on dolutegravir, and those on atazanavir like the improvement in diarrhoea after changing to dolutegravir. These days, all the drugs seem to be highly effective in almost any combination. Short- and long-term side effects now dominate, and perhaps, as shown in this study, once-a-day convenience is important too.

This paper has some interesting snippets contained within it. Firstly, it gives a good account of the size of the effect on creatinine levels. The mean increase was 6-7 µmol/L, which is important when a switch in therapy is required because of declining renal function. This in practice often means changing people away from Atripla, which contains tenofovir, a well-known renal tubular toxin. A change to dolutegravir can make things look worse initially, so it is important to be able to warn patients about this predictable effect. This is shown in the following real patient example.

Patient example:

A man, who is currently aged 65 years, presented in 1999 with pneumocystis pneumonia and after initial treatment for that, was started on nelfinavir, zidovudine, and lamivudine. He had period of non-adherence related to a psychiatric decompensation, which has been controlled long term on depo-haloperidol. He was changed to indinavir/ritonavir, zidovudine, and lamivudine in 2004 and to atazanavir, tenofovir and emtricitabine in 2007. He developed angina, which has been well controlled for many years with metoprolol, aspirin and atorvastatin.

He was concerned about buttock and leg wasting but did not want to go off a once-daily regimen, and I was concerned about a rising creatinine as well. He was changed to dolutegravir, abacavir, and lamivudine in 2015, and was very happy with the convenience and actually found his appetite and sense of well-being improved dramatically. His key results are shown graphically opposite.



This case demonstrates a number of features.

Firstly, the miracle of long-term treatment of HIV in a man with mental health and social issues: the CD4 count is continuing to rise, and we joke that he is getting younger, not older! The viral load is not shown because it is always undetectable apart from the one major psychiatric episode.

The creatinine has stopped rising since the switch away from tenofovir in November 2015, and has stabilised and perhaps improved.

This patient serves as a counterpoint to the STRIIVING trial, demonstrating that a patient who wants to change is much more likely to be happy with the new regimen than a person randomised in a trial.

This patient also had no psychiatric issues with changing to dolutegravir, this may be because of the haloperidol, but in fact he is better overall now since the change because of a greater sense of well-being and improved appetite.

Other points are that I am happy to have patients with coronary artery disease on abacavir, when they are stable and well managed. This patient has given up smoking and so his cardiac risk has reduced dramatically.

Finally, this patient does not have a GP, so relies on mental health and infectious diseases services for all his prescriptions and treatment decisions . . . think how much better he would have done with a good GP!

Use in females

The majority of patients in the key clinical trials of dolutegravir performed to date have been male.[2] With there being limited clinical data of the use of dolutegravir in female patients with HIV-1 infection, the ARIA study was conducted to compare the safety and efficacy of dolutegravir-based ART compared with a boosted atazanavir-based regimen in treatment-naïve women.[20] ARIA showed superior virologic efficacy with ABC/DTG/3TC compared with atazanavir plus ritonavir plus tenofovir/emtricitabine (see **Study Summary**).

Women who were withdrawn from the ARIA study after becoming pregnant were offered entry to a ABC/DTG/3TC pregnancy pilot study (NCT02075593).[21] The primary aim of this ongoing open-label, single-arm, interventional study is to investigate the effects of pregnancy on the pharmacokinetics of dolutegravir. Results are not yet available. In the clinical practice setting, the use of dolutegravir is indicated during pregnancy only if the benefit outweighs the risk due to a lack of clinical trial data.[2]

Superior efficacy of dolutegravir/abacavir/lamivudine (DTG/ABC/3TC) fixed dose combination (FDC) compared with ritonavir (RTV) boosted atazanavir (ATV) plus tenofovir disoproxil fumarate/emtricitabine (TDF/FTC) in treatment-naïve women with HIV-1 infection (ARIA Study)[20,22]

Authors: Orrel C et al.

Aim and methods: The purpose of ARIA was to collect additional efficacy and safety data in women treated with ABC/DTG/3TC. ARIA was a randomised, open-label, non-inferiority multicentre phase IIIb study that compared the safety and efficacy of ABC/DTG/3TC with that of ATV+RTV+FTC/TDF in ART-naïve adult women with HIV-1 RNA ≥500 copies/mL.

Results: A total of 495 women (median age 37 years) were randomized to receive ABC/DTG/3TC (n=248) or ATV+RTV+FTC/TDF (n=247) once daily. The two treatment groups were well matched for demographic and baseline characteristics. In the ITT analysis, 82% of patients who received ABC/DTG/3TC versus 71% who received ATV+RTV+FTC/TDF achieved the primary endpoint of a viral load of HIV-1 RNA <50 copies/mL at week 48 (adjusted difference 10.5%, 95% CI: 3.1–17.8%, p=0.005). The difference was attributable to a lower rate of discontinuations due to adverse events (4% vs 7%) and a lower rate of FDA Snapshot virologic failures (6% vs 14%) in the ABC/DTG/3TC versus ATV+RTV+FTC/TDF groups. Fewer drug-related adverse events (33% vs 49%) and fewer discontinuations due to adverse events (4% vs 7%) occurred in the ABC/DTG/3TC versus ATV+RTV+TDF/FTC groups. None of six ABC/DTG/3TC-treated women who met protocol-defined virologic withdrawal criteria had treatment-emergent primary INSTI or ABC/3TC resistance mutations. In comparison, one of four ATV+RTV+TDF/FTC-treated patients who met virologic withdrawal criteria had an emergent NRTI mutation (M184M/I/V). Five (2%) women in the ABC/DTG/3TC group and eight (3%) in the ATV+RTV+TDF/FTC group became pregnant and were withdrawn from the study.

Comment (RF): The ARIA study demonstrates a number of important issues in the treatment of HIV. It is a woman-only head-to-head comparison of a single-tablet regimen (STR) abacavir/lamivudine/dolutegravir (Triumeq) versus a ritonavir-boosted atazanavir/TDF/emtricitabine regimen. The STR combination performed better overall and with moderately fewer adverse effects than the boosted-PI combination.

It is not unexpected that the STR had a number of benefits over a regimen containing either three or four drugs. Better adherence with the STR may have to some extent influenced its superior efficacy over the multi-tablet regimen. Likewise, the moderately lower rate of adverse events is not surprising when comparing a INSTI/NRTI regimen with a boosted-PI regimen. The mean age of the women in both groups was relatively young so that any possible differences in cardiovascular outcome between atazanavir and abacavir would be unlikely to have shown up.

So, the ARIA study confirms ABC//DTG/3TC as an important first-line therapy for treatment-naïve HIV-positive women.

Patient example:

A 35-year-old woman, originally from Papua New Guinea (PNG), attended clinic with her husband. Both had recently been diagnosed HIV-positive (syphilis-, hepatitis-, and Tb-negative but with a reduced eGFR of 65 mmol/l and a normal renal ultrasound).

The couple had been together for a number of years, and there were no other partners involved. The length of time of her infection was unknown but her initial results of a HIV viral load of log 4.5 and CD4 of 230 suggested this wasn't a new infection for her. This couple travelled a lot as her husband was on a fly-in-fly-out contract to PNG, and her immediate family still lived in PNG.

What was needed was a simple regimen, one that had few side effects, would not make her renal function worse, and could be easily taken with her preferred oral contraceptive containing ethinyloestradiol and levonorgestrel.

As she was HLA-B*5701 negative, Tivicay and Kivexa fitted this role perfectly. After 3/12 she reported no side effect issues with medications, her adherence was excellent, her HIV viral load was undetectable (<20 copies/ml), and her renal function unchanged. Consequently, she was she was very happy with her regimen.

Tolerability and safety

Dolutegravir is generally well tolerated in patients with HIV infection.[4,23,24] Commonly reported adverse events include nausea, headache, and diarrhoea. Most treatment-emergent adverse events are of mild to moderate severity (the proportion of grade 3/4 adverse events is 1%[25]) and the rate of discontinuations due to adverse events is low. For example, in three large RCTs, the rate of discontinuations was 2–3% in treatment-naïve patients.[11-13,26]

Neuropsychiatric symptoms

Three retrospective cohort studies have been published suggesting that dolutegravir is associated with psychiatric events.[27-29]

Conversely, other data has shown that there are no new safety signals associated with dolutegravir use. In order to characterize psychiatric symptoms (insomnia, depression, anxiety, and suicidality) occurring in patients during HIV-1 treatment with dolutegravir compared with other key antiretroviral agents (atazanavir, darunavir, efavirenz, or raltegravir), Fettiplace et al. analysed dolutegravir post-marketing data from three sources:[30]

1. Five RCTs of dolutegravir in patients with ≥48 weeks of data (SPRING-2, FLAMINGO, SINGLE, ARIA, and SAILING).[7,11-13,20]
2. The Observational Pharmaco-Epidemiology Research and Analysis (OPERA) database cohort of patients who started dolutegravir-, efavirenz-, raltegravir-, or darunavir-based regimens.[30]
3. The ViiV Healthcare Global Safety Database that included spontaneously reported post-marketing cases of psychiatric symptoms in patients treated with dolutegravir or dolutegravir/abacavir/lamivudine.[30]

In the RCTs, psychiatric symptoms were reported at low and similar rates in 672 patients receiving dolutegravir and 1681 receiving comparator antiretroviral agents.[30] Insomnia was the most commonly reported symptom, with the highest rates being observed in the SINGLE study (dolutegravir 17% vs efavirenz 12%) and consistently lower rates in the four other RCTs (dolutegravir 3–8% vs comparators 3–7%).[7,11-13,20] More efavirenz-treated patients withdrew because of psychiatric symptoms than patients treated with the other key antiretroviral agents (4% vs <1%).[30] In the OPERA database (6,347 HIV-positive who initiated DTG-,

EFV-, RAL- or DRV-based regimens), despite a history of psychiatric symptoms at baseline being lowest in efavirenz-treated patients compared with patients treated with dolutegravir, raltegravir, or darunavir, the prevalence and incidence during treatment were similar across the four agents.[30] Treatment discontinuation rates due to psychiatric symptoms were lowest for dolutegravir (0.1–0.6%) and highest for raltegravir (0–2.5%).[30] In the ViiV Global Safety Database, rates of spontaneously-reported depression, anxiety, and suicidality were ≤0.55 per 1000 patient-years with either dolutegravir or ABC/DTG/3TC whereas cases of insomnia occurred at higher rates with either regimen (**Figure 2**).[30]

Based on the analysis of clinical trial and real world data sources, Fettiplace et al. concluded that rates of the four psychiatric symptoms were low among dolutegravir-treated individuals and rarely necessitated discontinuation.[30]

This conclusion is supported by the findings of a meta-analysis of six RCT trials that compared dolutegravir, elvitegravir, or raltegravir to efavirenz, PIs (atazanavir or darunavir) or another INSTI, which was conducted by the FDA in response to case reports of neuropsychiatric symptoms with INSTIs.[31] The meta-analysis showed that the risk of neuropsychiatric adverse events, analysed at the level of pooled Depression and Suicide/Self-Injury and the Psychosis and Psychotic Disorders Standardized MedDRA Query, was similar for INSTIs and efavirenz. There was a trend toward a lower risk for neuropsychiatric adverse events with INSTIs compared with EFV and the risk was similar between INSTIs and PIs.

Effects on renal function

Due its minor inhibition of the organic cation transporter 2 (OCT2) in the proximal renal tubules, dolutegravir reduces tubular secretion of creatinine and slightly increases serum creatinine levels but does not affect glomerular filtration.[2,4]

Small increases in serum creatinine generally occur during the first 4 weeks of treatment with dolutegravir but remain stable over time and are not considered clinically relevant.[2,4] Serum creatinine and creatinine clearance changes with dolutegravir observed in a real-world clinical setting were similar to those that have been seen in clinical trials, with no renal-related serious adverse events or discontinuations noted.[32] As renal excretion is a minor pathway of elimination for dolutegravir, no dose adjustment is required in patients with renal impairment (mild, moderate, or severe).[2] Caution is warranted for patients with certain INI-associated resistance or clinically-suspected INI resistance and severe renal impairment, as there may be a loss of therapeutic effect and development of resistance to dolutegravir or other co-administered antiretroviral agents.

However, the effect of dolutegravir on creatinine clearance should be considered when dolutegravir is co-administered with drugs for which dosage adjustments are guided by estimated creatinine clearance.[2]

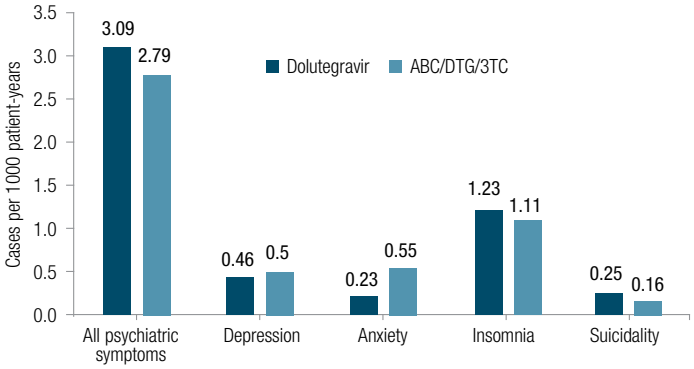


Figure 2. Summary of spontaneous reporting rates of psychiatric symptoms in patients treated with dolutegravir or ABC/DTG/3TC according to a global safety database.[30]

EXPERTS' CONCLUDING COMMENTS

Tim Blackmore

Dolutegravir is a very useful addition to the HIV medicine list in NZ. There appears little doubt from the clinic that the integrase inhibitors are popular with patients, and the advantage of being once a day really helps a lot of people, particularly if they get home at varying times in the evening.

There are two practical issues from my experience. Firstly, the neuropsychiatric side effects can be quite disabling, but seem to only a be problem in those who are quite elderly or with pre-existing morbidity making their brains "fragile". At least there is not the concern around vivid dreams, which can be a major reason to avoid efavirenz in those with bad experiences or PTSD. The other practical issue is the rise in creatinine. It is not a cause of concern itself, but it does make it important to explain to the patient that the switch away from efavirenz/emtricitabine/tenofovir disoproxil fumarate (Atripla) to dolutegravir/abacavir/lamivudine may not actually make the eGFR look any better!

Rick Franklin

My experience over the past 2 years of using dolutegravir in NZ is strongly positive. It is generally very well tolerated and has few side effects or interactions. Those interactions that are present are well known and can be easily managed.

Patients on a twice-daily INSTI regimen were delighted to be able to move to once-daily dosing and adherence improved in a number of patients with viral load blips that were most likely related to poor adherence with a twice-daily schedule. More recently, my experience in Australia with Tb-coinfected HIV clients has demonstrated the usefulness of medications that can be combined in dual therapies.

Overall, dolutegravir has rapidly become a mainstay of HIV therapy because of its ease of use and high genetic barrier to resistance and patient tolerability.

KEY MESSAGES

- Dolutegravir is recommended as a first-line option for treatment-naïve HIV-1 infected patients.
- Dolutegravir can be given as a once-daily ART without the need for boosting.
- Dolutegravir has a low propensity for drug-drug interactions; in particular, it does not require dosage adjustment when co-administered with NRTIs and PIs (except for tipranavir).
- Dolutegravir has demonstrated high virological efficacy in treatment-naïve patients and as salvage therapy.
- The STRIIVING study demonstrated that dolutegravir-based ART is a useful switch option for long-term use in virologically-suppressed patients.
- In the ARIA study, dolutegravir-based ART demonstrated superior efficacy compared with a boosted atazanavir-based regimen in treatment-naïve women.
- Dolutegravir is generally well tolerated and is associated with few discontinuations due to adverse events.
- Recent analyses of RCT and real-world data indicate that the risk of neuropsychiatric adverse events with dolutegravir is similar to that with other INSTIs, efavirenz, and PIs.

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