Comparing albuvirtide plus ritonavir-boosted lopinavir regimen to two nucleotide reverse transcriptase inhibitors plus ritonavir-boosted lopinavir in HIV-infected individuals who failed initial treatment: a retrospective comparative cohort study

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Background: Albuvirtide (ABT), a fusion inhibitor against human immunodeficiency virus (HIV) infection, has good efficacy and tolerability for HIV treatment. However, there is a paucity of data regarding ABT-based regimen as second-line therapy. This current study evaluated the efficacy and safety of switching to ABT + ritonavir-boosted lopinavir (LPV/r) treatment in a cohort of HIV-infected individuals who failed initial treatment.

Methods: This retrospective comparative cohort study included patients who failed initial treatment and switched to either ABT + LPV/r (the ABT group) or two nucleotide reverse transcriptase inhibitors (NRTIs) + LPV/r (the NRTI group) between November 2019 and December 2020 in the People's Hospital of Zhaojue County in Liangshan Yi Autonomous Prefecture, China. All individuals were followed up from baseline to 12 weeks after conversion, or until the patient developed unacceptable toxic effects or was lost of follow-up. The proportion of patients who achieved virological suppression (viral load <50 copies/mL) at week 12 was considered a primary efficacy endpoint. Safety outcomes included the incidence of adverse events and laboratory abnormalities. All participants underwent resistance testing before regimen conversion. The linear regression model was applied to evaluate the association of CD4⁺ T cell count with the patient's clinical characteristics.

Results: A total of 71 patients were included in this study, the two groups were comparable at baseline in terms of age, sex, CD4⁺ T cell count, and viral load. The suppression of HIV-1 RNA to levels <50 copies/mL was achieved in 82.4% (28/31) and 29.7% (11/34) of patients in the ABT group and the NRTI group, respectively (P<0.001). Older age (P=0.016) and higher alkaline phosphatase (ALP) levels (P=0.038), but not rescue regimen, were associated with attenuated CD4⁺ T cell recovery. Most adverse events mild in severity, with abdominal pain as the most reported event in two groups (26.8%, 19/71), and no severe adverse events were detected.

Conclusions: Conversion to ABT + LPV/r therapy appears to be an effective and safe strategy. This treatment regimen has great potential to be generalized in the HIV-infected population, although further testing in a larger patient population is required to verify these results.
**Introduction**

Human immunodeficiency virus (HIV) infections continue to be a major global public health issue. At the end of 2020, there was an estimated 37.7 million people living with HIV (PLWH), and 680,000 HIV-related deaths (https://www.who.int/news-room/fact-sheets/detail/hiv-aids). By October 2020, the number of PLWH in China had reached 1.05 million, with approximately 112,000 newly acquired HIV cases each year (http://www.nhc.gov.cn/wjw/). Initial antiretroviral therapy (ART) regimens comprise of an integrase strand transfer inhibitor (INSTI) together with one or two nucleotide reverse transcriptase inhibitors (NRTIs), as recommended by recent guidelines (1). In 2002, China implemented China’s National Free Antiretroviral Treatment Project (CNFATP), which is a policy of free universal access to ART for HIV-infected individuals and to date, 853,429 PLWH have benefited from this program (2). CNFATP provides a limited selection of medication, including four NRTIs [tenofovir disoproxil fumarate (TDF), azidothymidine (AZT), abacavir, and lamivudine (3TC)], two non-NRTIs (NNRTIs) [efavirenz (EFV) and nevirapine (NVP)], and one protease inhibitor (PI) [ritonavir-boosted lopinavir (LPV/r)]. However, the latest INSTI is not included (3). Therefore, CNFATP offers a first-line regimen of two NRTIs + one NNRTI. Patients failed to achieve a satisfactory virological response switch to two NRTIs + one PI as a second-line treatment regimen. LPV/r is the first PI prescribed and has good efficacy and lower side effects; therefore, it can be used in ART-experienced patients (4). Approximately 13% of patients fail to achieve complete virological response with first-line regimens over a 12-month period and require conversion to second-line regimens. Unfortunately, about 36% of these patients will still fail to achieve a complete virological response even after conversion to second-line regimens (2). This is partly due to the limited second-line drug options and the development of resistance mutations in patients with poor adherence (5). The DAWNING study found that treatment failure was related to the presence of integrase substitutions, including G118R or R263R/K, which can result in a prolonged binding of INSTIs and integrase-DNA complexes with G118R or R263K substitutions (6). A between-country comparison study suggested that interventions aimed at controlling the spread of first-line drug resistance is required by applying a dynamic transmission model (7). This situation raised the growing concern of regimen simplification to decrease the impact of comorbidities, minimize cumulative drug exposure, as well as improving adherence and tolerability (8).

Albuvirtide (ABT) is an injectable, long-acting fusion inhibitor that binds to the transmembrane glycoprotein gp41 of the HIV outer membrane and impedes its fusion with the host cell membrane, thereby blocking HIV replication (9,10). Dual therapy with intravenous ABT (320 mg) once weekly + LPV/r (400/100 mg) daily has been suggested as a potential treatment option, as it showed high efficacy and good tolerability (11,12), without reported drug interactions (13). A phase III randomized clinical trial (TALENT) also showed a non-inferiority endpoint of ABT + LPV/r regimen in patients who failed ART in a follow-up of 48 weeks (13).

ABT + LPV/r regimen has not been specifically mentioned in current guidelines mainly due to a lack of evidence from clinical trials under different clinical settings. This retrospective cohort study extended the duration time of patients’ initial treatment to 1 year, and limited the plasma HIV-1 RNA load to >1,000 copies/mL 1 month before the conversion. Second-line therapy usually depends on a patient’s previous treatment and characteristics, and is generally composed of two or three fully active agents, including one with a high resistance barrier (such as the HIV-1 integrase inhibitor dolutegravir) (1). However, regimens consisting of the integrase inhibitor are not covered by Chinese health insurance, with the exception of Genvoya (elvitegravir-containing). Integrase inhibitor-containing regimens are therefore non-affordable for many patients. ABT was included in the Chinese health insurance list in 2020, making it another second-line drug option,
especially for patients in resource-limited regions.

This current study examined the efficacy and safety of switching to ABT + LPV/r in individuals who failed initial treatment. Furthermore, the mutation sites related to first-line drugs were analyzed in patients who failed initial treatment. We present the following article in accordance with the STROBE reporting checklist (available at https://atm.amegroups.com/article/view/10.21037/atm-22-4369/rc).

Methods

Study design and selection criteria

A 12-week, retrospective comparative cohort study was conducted. The electronic health records of all individuals with HIV-1 infection who consulted at the People’s Hospital of Zhaojue County in Liangshan Yi Autonomous Prefecture between November 2019 and December 2020 were screened. HIV-1 infected adults, aged 18–65 years, were eligible for this study if they had received ART with two NRTIs + one NNRTI for at least 1 year as their first anti-HIV treatment and switched their regimen to ABT + LPV/r or two NRTIs + LPV/r. The plasma HIV-1 RNA of individuals should be >1,000 copies/mL 1 month before the conversion. Individuals with chronic hepatitis B co-infection or chronic hepatitis C co-infection were permitted to enroll. The collated data consisted of patient demographics, laboratory findings, therapeutic response of previous anti-HIV therapy, adverse events, HIV genotype, and drug resistance test results before regimen conversion.

The following exclusion criteria were applied: previous changes of ART to improve tolerability; the presence of active opportunistic infections, tumor, heart disease, cerebrovascular disease, and other life-threatening diseases before the regimen switch; pregnant or breastfeeding women; and abnormal essential laboratory data [white blood cell (WBC) <2×10^9/L or hemoglobin (HGB) <70 g/L, total bilirubin (TB) >50 μmol/L, alanine transferase (ALT) >200 IU/L, or estimated glomerular filtration rate (eGFR) <30 mL/min/1.73 m^2]. A flowchart detailing the patient evaluation process is shown in Figure 1.

Treatment strategies

The following two treatment strategies both eligible to HIV/AIDS treatment were compared: (I) conversion to ABT + LPV/r until HIV-1 RNA ≤1,000 copies/mL (the ABT group), followed by sequential conversion to two NRTIs + LPV/r; and (II) immediate conversion to two NRTIs + LPV/r, followed by maintenance (the NRTIs group). ABT (320 mg) was administered by intravenous infusion once a day for the first 3 days of the first week, and once weekly on the first day of the week thereafter. LPV/r (400/100 mg) was administered as two tablets, twice daily. The dose was chosen after publication of a phase III clinical trial conducted by Su et al. for treating HIV (13). The plasma viral loads were collected every 4 weeks and the regimen was switched to two NRTIs + LPV/r if HIV-1 RNA ≤1,000 copies/mL at week 4 or 8, or ABT + LPV/r was continued. The decision to treat patients with ABT + LPV/r was based on the clinician’s opinion of its
effectiveness. Additionally, physicians decided upon the NRTIs according to the patient’s HIV genotype and drug resistance results before the conversion. TDF was replaced by AZT for those who had TDF resistance, and conversely, AZT was replaced by TDF for those who had AZT resistance. No changes to the regimen were made if 3TC resistant was found.

Start and end of follow-up

The follow-up for each individual started at the time of regimen conversion. All individuals were followed up from baseline to 12 weeks after conversion, or until the patient developed unacceptable toxic effects or was loss of follow-up, whichever occurred first.

Outcomes

The primary efficacy outcome was defined as the proportion of participants whose plasma HIV-1 RNA level was <50 copies/mL by week 12. The secondary efficacy outcome was the proportion of participants with plasma HIV-1 RNA level <50 copies/mL by week 4. The plasma HIV-1 RNA levels of the ABT group at week 8 were used as a descriptive indicator. The CD4 absolute cell count at week 12 and the CD4 cell count change from baseline to week 12 were considered as other prespecified tertiary efficacy endpoints. The incidence of adverse events and laboratory abnormalities were defined as safety outcomes.

Statistical analysis

Eligible patients were divided into ABT group and NRTIs group. The baseline demographics, virological and immunological parameters, and initial treatment strategies were compared between the two groups using the Pearson chi-square test for categorical characteristics and Student’s t-test for continuous characteristics. Use propensity score matching (PSM) for adjustment analysis if the two groups were not comparable. Quantitative data, including normally distributed data and non-normally distributed data, are described as mean ± standard deviation (SD), or median and interquartile range, and were compared using U tests. The chi-square test was used for qualitative data which are represented as frequencies (proportion). The linear regression model was applied to evaluate the association of CD4+ T cell count with the patient’s clinical characteristics.

Data were managed and analyzed using the SPSS v24.0 software (IBM, Armonk, NY, USA). A P value <0.05 was considered statistically significant in a two-sided test.

Ethical statement

The study was performed in accordance with the Declaration of Helsinki (as revised in 2013), and its relevant guidelines and regulations. This study was approved by the Ethics Committee of Biomedical Research, West China Hospital of Sichuan University (No. 2020-450). Given the study used routinely collected clinical data in an anonymized format, the requirement for written consent was waived.

Results

Clinical characteristics of the participants

Among the 74 patients enrolled for analysis between November 1, 2019, and December 31, 2020, 37 patients received ABT + LPV/r and 37 patients received two NRTIs + LPV/r. However, a total of 3 participants who received ABT + LPV/r were not eligible for the study, including 1 participant who developed hemoptysis due to bronchial dilation bleeding caused by tuberculosis, and 2 participants who discontinued the study due to traffic inconveniences caused by the COVID-19 pandemic. All other participants involved in the study completed the 12-week follow-up. To assess the effectiveness of ABT + LPV/r, the 34 participants who received ABT + LPV/r (the ABT group) were compared with the 37 patients who received two NRTIs + LPV/r (the NRTI group). The two groups were comparable at baseline in terms of age, sex, CD4+ T cell count, and viral load (Table 1).

Mutations and drug resistance

All participants underwent genotypic resistance testing before regimen conversion. No virological resistance to LPV/r was found, while 14 (41.2%) individuals in the ABT group and 13 (35.1%) in the NRTI group were found to have mutations related to NRTIs or NNRTIs or both. Single-site mutation associated with NRTIs were found in 3 participants in the ABT group and 2 participants in the NRTI group. Multiple point mutations associated with NRTIs (≥2 sites) were detected in 1 participant in the ABT group and 2 participants in the NRTI group. A total of 8 participants in the ABT group developed a NNRTIs-
associated single mutation and 6 had a NNRTIs-associated multiple point mutation (≥2 sites), while 9 participants in NRTI group had a NNRTIs-associated single mutation and 4 had a NNRTIs-associated multiple point mutation (≥2 sites) (Table 2). According to the detected mutations, drug-resistance against five current national, freely available NRTIs (TDF, AZT, and 3TC) and NNRTIs (EFV and NVP) were stratified into five different levels (high-level resistance, intermediate resistance, low-level resistance, potential low-level resistance, and susceptible). The baseline distribution of drug resistance is shown in Figure 2. There was no significant difference between the two groups (AZT,
P=0.264; TDF, P=0.517; 3TC, P=0.703; EFV, P=0.871; and NVP, P=0.411).

### Virological and immunological assessment

The ABT group showed improved virological suppression than the NRTI group at week 12 (82.4% vs. 29.7%, P<0.001; Table 3). Secondary outcomes supported the primary efficacy outcome. At week 4, the proportion of participants whose plasma HIV-1 RNA level was <50 copies/mL varied significantly (38.2% vs. 5.4%, P<0.001). Nine individuals in the ABT group had plasma HIV-1 RNA levels above 1,000 with a median of 32,744 copies/mL [1,610–214,000] at week 8. The mean change from baseline to week 12 in absolute CD4+ T cell count increased from 226 to 321 cells/μL in the ABT group, and from 216 to 280 cells/μL in the NRTI group. There was no discernible difference in CD4+ T count from baseline to week 12 between groups after adjusting for baseline CD4+ T cell count (P=0.869).

The outcome of patients under ART including virological response and immunological response. However, in our study, not all the patients have good recovery. A linear regression model was applied to identify the independent risk factors related to insufficient cellular immune recovery (Table 4). The rescue regimen, age, gender, body mass index (BMI), transmission routine, previous regimen, treatment duration, World Health Organization (WHO) grading, baseline viral load, CD4+ T cell count, CD8+ T cell count, HGB, platelet (PLT), WBC count, TB, aspartate...
transaminase (AST), alanine transaminase (ALT), albumin (ALB), alkaline phosphatase (ALP), and eGFR were examined. In univariate analysis, age, previous treatment duration, baseline CD4+ T cell count, CD8+ T cell count, HGB were found significantly related to insufficient cellular immune recovery. However, in multivariate analysis, only older age \( \beta: -8.073; 95\% \text{ confidence interval (CI)}: -14.581 \text{ to } -1.566; P=0.016 \) and higher ALP levels \( \beta: -1.015; 95\% \text{ CI}: -1.969 \text{ to } -0.060; P=0.038 \) were associated with attenuated recovery. Interestingly, different rescue regimen with only 12 weeks' duration did not show any influence on CD4+ T cell recovery.

**Safety**

Both treatments were well tolerated. Most adverse events were mild and no severe adverse events occurred (Table 5). No drug discontinuation occurred due to adverse events. Of the 71 patients who received either treatment, there was a significant difference in the proportion of participants who reported pain at the puncture site, including 4 (11.8%) participants in the ABT group and none in the NRTIs group \( P=0.032 \). Fewer participants in the ABT group reported a decrease in WBC count \( P=0.014 \). Changes from baseline to week 12 in the levels of PLT, ALT, and creatine were also reported, but no significant differences were found between the groups.

**Discussion**

Currently, there is a paucity of data examining the performance of ABT + LPV/r regimen for HIV-infected individuals who failed initial treatment. Herein, a cohort study was conducted using real-world data from routine care to evaluate the efficacy and safety of ABT (320 mg/day) + LPV/r (400/100 mg/day) as a second-line ART in a population of 71 patients diagnosed with HIV infection. Conversion to ABT + LPV/r was superior to maintenance on NRTI regimen, with a larger proportion of individuals in the ABT group having plasma HIV-1 RNA levels <50 copies/mL at both week 4 (38.2% vs. 5.4%) and week 12 (82.4% vs. 29.7%). The different rescue regimen of 12 weeks' duration did not have any influence on CD4+ T cell recovery, and there were no significant differences in mean CD4+ T count changes from baseline to week 12. Both regimens were well tolerated, and no participant discontinued the study due to adverse events. Adverse event profiles were similar between groups, except for pain at the puncture site.

Virological failure is defined as ART that fails to suppress and sustain a person’s viral load to less than 200 copies/mL (1), or two consecutive HIV-1 RNA levels above 1,000 copies/mL, despite interval intensive adherence counseling in resource-limited settings (14). This is a complex and clinically significant complication of HIV infection. Factors that can contribute to virologic failure include drug resistance, drug toxicity, and poor adherence to ART (1,15,16). Virological failure without resistance mutations is rare in patients with a high level of ART compliance. Virological failure with drug resistance mutations may arise due to both pretreatment HIV drug resistance (PDR) and acquired drug resistance (17). In many regions, the prevalence of PDR is 10% or greater, mainly due to resistance from NNRTIs, while PDR in other segments of the population remains low (18). In cases of virological failure, it is recommended that genotypic resistance testing be performed, so as to facilitate the selection and optimization of treatment options with at least two different classes of two active drugs (17,18). In our study cohort, individuals who switched to second-line regimens are often from resource-limited areas and nearly

| Table 3 The therapeutic response in patients from the two groups |
|-----------------|----------------|----------------|
| Variables       | ABT group (n=34) | NRTI group (n=37) | P value |
| HIV-1 RNA (copies/mL) at week 4 | <0.001 |
| <50             | 13 (38.2)        | 2 (5.4)         |
| <1,000          | 25 (73.5)        | 14 (37.8)       |
| ≥1,000          | 9 (26.5)         | 23 (62.2)       |
| HIV-1 RNA (copies/mL) at week 12 | <0.001 |
| <50             | 28 (82.4)        | 11 (29.7)       |
| ≥50             | 6 (17.6)         | 26 (70.3)       |
| CD4 cell count at week 12 | 0.869 |
| 50–199          | 11 (32.4)        | 12 (32.4)       |
| 200–349         | 13 (38.2)        | 16 (43.2)       |
| 350–500         | 4 (11.8)         | 7 (18.9)        |
| >500            | 6 (17.6)         | 2 (5.4)         |

Missing data treated as participant exclusion

34/37 (91.9) 37/37 (100.0)

Unless otherwise indicated, data are presented as n (%) or n/N (%). HIV, human immunodeficiency virus; ABT, albuvirtide; NRTI, nucleotide reverse transcriptase inhibitor.
half were predicted to have mutations related to NRTIs or NNRTIs or both, indicating that both poor adherence and resistance to ART drugs may account for initial treatment failure. According to our observation, two participants in the ABT group replaced AZT with TDF in sequential treatment after ABT, and two participants replaced TDF with AZT to achieve better virological suppression. With regards to patient compliance to ART, our study shows that patients who previously took ART ≥3 tablets per day or twice daily had increased compliance after switching to ABT + LPV/r.

ABT is an injectable long-acting HIV-1 fusion inhibitor. It acts by forming a stable α-helical conformation with the target sequence of gp41, blocking the formation of fusion-active six-helix bundle (6-HB) in a dominant-negative manner, thereby preventing viral fusion and entry, as well as HIV replication (19). ABT has been shown to be effective in 28 different HIV-1 clinical isolates collected in China, with half maximal inhibitory concentration (IC_{50}) values ranging from 1.3–18.1 nmol/L, including variants resistant to T20. It is the first United States Food and Drug Administration (US FDA)-approved HIV entry inhibitor (19). ABT also reacts to serum ALB, extending its half-life in humans to 11–12 days compared to the first FDA-approved HIV-1 fusion inhibitor enfuvirtide [with half-life of 3.46–4.35 hours in humans (20)], thereby allowing for once-weekly administrations of the drug (11). The efficacy of ABT + LPV/r therapy has been investigated in 2 other clinical trials. The dose of ABT (320 mg) and LPV/r (400/100 mg) was shown to exhibit a superior anti-HIV activity and was safe for treatment-naïve HIV-1 infected patients in a 47-day observation period, with a decline of

| Variables                                      | Coefficient | 95% CI           | P   | Coefficient | 95% CI           | P   |
|------------------------------------------------|-------------|------------------|-----|-------------|------------------|-----|
| ABT + LPV/r                                    | −32.465     | −110.509 to 45.578 | 0.409 | −8.073     | −14.581 to −1.566 | 0.016 |
| Age (years)                                    | −5.117      | −10.198 to −0.035  | 0.048 |             |                  |     |
| Male                                           | 70.430      | −24.051 to 164.911 | 0.142 |             |                  |     |
| BMI (kg/m^2)                                   | 6.103       | −10.794 to 23.000  | 0.474 |             |                  |     |
| Transmission routine                            | −20.008     | −128.184 to 88.169  | 0.713 |             |                  |     |
| Previous treatment duration (years)            | 16.434      | 1.247 to 31.625    | 0.034 |             |                  |     |
| Previous regimen                                | −5.860      | −53.916 to 42.197  | 0.809 |             |                  |     |
| WHO grading                                     | 60.420      | −8.920 to 129.760   | 0.087 |             |                  |     |
| Baseline viral load (log10 copies/mL)          | −33.144     | −82.229 to 15.941   | 0.182 |             |                  |     |
| Baseline CD4 (cells/μL)                        | −0.424      | −0.756 to −0.092    | 0.013 |             |                  |     |
| Baseline CD8 (cells/μL)                        | −0.128      | −0.222 to −0.035    | 0.008 |             |                  |     |
| Baseline HGB (g/L)                             | 1.671       | 0.015 to 3.327      | 0.048 |             |                  |     |
| Baseline PLT (10^9/L)                           | −0.103      | −0.656 to 0.451     | 0.712 |             |                  |     |
| Baseline WBC (10^9/L)                           | −7.667      | −31.879 to 16.546   | 0.530 |             |                  |     |
| Baseline TB (IU/L)                             | −0.836      | −6.878 to 5.206     | 0.783 |             |                  |     |
| Baseline ALT (IU/L)                            | −0.221      | −1.204 to 0.761     | 0.654 |             |                  |     |
| Baseline ALB (g/L)                             | −1.448      | −7.699 to 4.803     | 0.645 |             |                  |     |
| Baseline ALP (IU/L)                            | −0.330      | −1.106 to 0.446     | 0.399 | −1.015     | −1.969 to −0.060  | 0.038 |
| Baseline eGFR                                  | 0.102       | −1.553 to 1.757     | 0.903 |             |                  |     |

ABT, albuvirtide; LPV/r, ritonavir-boosted lopinavir; BMI, body mass index; WHO, World Health Organization; HGB, hemoglobin; PLT, platelet; WBC, white blood cell; TB, total bilirubin; ALT, alanine transaminase; ALB, albumin; ALP, alkaline phosphatase; eGFR, estimated glomerular filtration rate; CI, confidence interval.
Table 5 A summary of the adverse events

| Adverse events          | Total (n=71) | ABT group (n=34) | NRTI group (n=37) | P value |
|-------------------------|-------------|------------------|-------------------|---------|
| Pain at the puncture site | 4 (5.6)     | 4 (11.8)         | 0                 | 0.032   |
| Abdominal pain          | 19 (26.8)   | 10 (29.4)        | 9 (24.3)          | 0.629   |
| Diarrhea                | 17 (23.9)   | 9 (26.5)         | 8 (21.6)          | 0.632   |
| Skin rash               | 3 (4.2)     | 1 (2.9)          | 2 (5.4)           | 0.606   |
| Insomnia                | 2 (2.8)     | 1 (2.9)          | 1 (2.7)           | 0.952   |
| Dizziness               | 4 (5.6)     | 1 (2.9)          | 3 (8.1)           | 0.346   |
| Nausea                  | 1 (1.4)     | 0                | 1 (2.9)           | 0.334   |
| Depression              | 2 (2.8)     | 0                | 2 (5.4)           | 0.169   |
| PLT decrease            | 4 (5.6)     | 1 (2.9)          | 3 (8.1)           | 0.346   |
| WBC decrease            | 6 (8.5)     | 0                | 6 (16.2)          | 0.014   |
| ALT increase            | 11 (15.5)   | 3 (8.8)          | 8 (21.6)          | 0.137   |
| Creatine increase       | 4 (5.6)     | 1 (2.9)          | 3 (8.1)           | 0.346   |

Data are presented as n (%). PLT, platelet; WBC, white blood cell; ALT, alanine transferase; ABT, albuvirtide; NRTI, nucleotide reverse transcriptase inhibitor.

2.2 (1.6–2.7) lg copies/mL of HIV-1 RNA from baseline. Furthermore, 55.6% (5/9) of patients achieved viral load suppression (HIV-1 RNA <50 copies/mL) at week 7. The phase III multicenter, open-label, randomized, controlled TALENT trial was conducted in patients infected with HIV-1 who failed ART. A non-inferiority endpoint was reached, with 80% and 66% of individuals showing HIV-1 RNA load <50 copies/mL at week 48 in the ABT group and the NRTI group, respectively, which is consistent with our report (13).

The safety of antiretroviral agents is a fundamental aspect in the treatment of patients with HIV. While some adverse events were observed in our study cohort, ABT + LPV/r was generally well-tolerated by most patients, which is consistent with previous studies (11-13). Data from the TALENT study indicated that the more common adverse events were rash, gastrointestinal abnormalities, headache, dizziness, hematuria, increased cholesterol and triglyceride levels. However, there was no significant difference between the NRTI group and the ABT group (13). Our laboratory data revealed that ABT + LPV/r and NRTIs + LPV/r had similar effects on renal and liver health, and the related adverse events were mild in severity.

There are several limitations to this current investigation. First, the size of the study cohort was small, and this is due to the exceptional use of ABT, which is not yet recommended by guidelines. Furthermore, the study was a short-term study and a longer follow-up period would be helpful in evaluating the safety of ABT + LPV/r. For example, lactic acidosis, lipoatrophy, peripheral neuropathy, hepatic steatosis, cardiomyopathy, pancreatitis, bone marrow suppression, and lactic acidosis, which are clinical presentations of NRTI toxicity (21,22), should be assessed. It remains unknown whether ABT + LPV/r could introduce new mutation sites and viral resurgence, and long-term studies should be conducted. Additionally, these results may not be applicable to all patients who change HIV treatment. The good renal function in our study population meant that no other drugs, except for ABT, NRTIs, and LPV/r, were adopted in this study. Therefore, further research is required to determine the drug interactions of ABT, so as to safely expand the use of ABT + LPV/r.

Conclusions

In conclusion, ABT (320 mg/day) + LPV/r (400/100 mg/day) could effectively achieve a virological suppression in a 12-week treatment period and is well tolerated. A two-drug regimen could provide a simpler and safer treatment option, with less drug-drug interaction than regimens involving 3–4 drugs. The long half-life of ABT is easier to adhere to than that of daily medications. The results herein suggested that conversion to ABT + LPV/r may be an effective strategy for treatment-experienced individuals with poor...
adherence to or resistance to ART drugs. ARTs should be carefully analyzed before conversion, and a genotype resistance assessment should be performed.

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Footnote

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Data Sharing Statement: Available at https://atm.amegroups.com/article/view/10.21037/atm-22-4369/dss

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This study was approved by the Ethics Committee of Biomedical Research, West China Hospital of Sichuan University (No. 2020-450). Given the study used routinely collected clinical data in an anonymized format, the requirement for written consent was waived.

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