HCV infection is a major cause of mortality worldwide. HCV-related deaths also represent a leading cause of mortality in HIV-coinfected individuals. Telaprevir is an NS3/4A protease inhibitor approved for the treatment of chronic HCV genotype 1 infection in adults in combination with pegylated interferon and ribavirin. Telaprevir-based treatment has been shown to increase rates of sustained viral response in HCV genotype-1-monoinfected patients, and studies in HCV–HIV-coinfected patients are ongoing. Drug–drug interactions of telaprevir with antiretroviral drugs were investigated in a series of studies in healthy subjects. This review summarizes the results of interaction studies with low-dose ritonavir, ritonavir-boosted HIV protease inhibitors (atazanavir, darunavir, fosamprenavir and lopinavir), efavirenz, etravirine, rilpivirine, tenofovir disoproxil fumarate and raltegravir.

HCV infection is a serious health challenge [1,2], affecting 170 million people, which is approximately 3% of the global population [3,4]. Worldwide, approximately 4 to 5 million individuals are coinfected with HCV and HIV. HCV prevalence among HIV-infected individuals is particularly high in injection drug users (72–95%), but is also found in heterosexuals (9–27%) and homosexual men (1–12%) [5]. A number of studies demonstrate increased mortality among coinfected individuals treated with HAART [6] and also emphasize the need for earlier and more aggressive HIV and HCV treatment in coinfected individuals [7,8].

Liver-related deaths represent a leading cause of death in patients with HIV, primarily due to HCV coinfection. HCV-associated liver disease is accelerated in HIV-coinfected individuals with a threefold higher progression to cirrhosis compared with individuals with HCV monoinfection [9,10]. Pegylated interferon plus ribavirin (PEG-IFN/RBV) has been the standard HCV treatment in coinfected patients. However, sustained viral response (SVR) is achieved in only approximately 33% of coinfected individuals across HCV genotypes, and the likelihood of SVR is significantly lower in HCV genotype 1/4 infection compared with other genotypes [11].

Hepatitis C therapies that provide better efficacy are therefore widely requested for coinfected patients. Telaprevir has been approved for treatment of chronic HCV genotype-1-infected adult patients in combination with PEG-IFN/RBV [12,13], and is being evaluated for use in coinfected patients. Telaprevir is an inhibitor of the HCV NS3/4A protease. Telaprevir is orally bioavailable [14], is primarily metabolized by cytochrome P450 3A4 (CYP3A4) as well as by non-CYP pathways [15] and is also a potent inhibitor of CYP3A4 [16]. Therefore, doses of drugs that are substrates of CYP3A may need to be adjusted when coadministered with telaprevir. Telaprevir can also inhibit or saturate P-glycoprotein (P-gp) in the gut and doses of drugs that are P-gp substrates may have to be reduced [16].

Efficacy and safety of telaprevir administration in HCV-monoinfected patients was demonstrated in three Phase III studies, which showed significantly improved SVR rates with telaprevir-based regimens for both treatment-naive and -experienced patients [17–19]. The relationship between telaprevir exposure and antiviral efficacy with the approved treatment regimen (750 mg telaprevir every 8 h plus PEG-IFN/RBV) was found to be shallow and non-significant [20].

To guide evaluation of telaprevir-based regimens in HIV–HCV-coinfected patients, a number of studies have been conducted to investigate the potential drug–drug interaction (DDI) between telaprevir and a range of antiretroviral drugs in healthy subjects. The results of these...
studies are discussed in this review. The DDI data are summarized in Table 1.

HIV protease inhibitors

Ritonavir

Telaprevir exposure (maximum plasma concentration \(C_{\text{max}}\), predose plasma concentration and average plasma concentration) after a single oral dose application of 750 mg in the fed state was approximately twice as high when combined with ritonavir (RTV) 100 mg compared with 750 mg telaprevir only [21].

In the multiple-dose administration part of the study, healthy male subjects received adjusted lower doses of telaprevir (750 mg every 12 h) in combination with low-dose RTV (100 mg every 12 h) which was compared with telaprevir 750 mg every 8 h given alone. All drugs were taken with food.

A 2.5-fold increase in telaprevir exposure (area under the concentration time curve [AUC]) was observed on day 14 compared to day 1 in the 750 mg telaprevir alone every 8 h group but a 15% decrease in the 750 mg telaprevir every 12 h/100 mg RTV every 12 h group. RTV has been reported to have a time-dependent inductive/inhibitory effect on P-gp in the intestinal cell lines [22]. The reduction of telaprevir exposure after multiple dosing seen in this study is possibly due to inductive effects of RTV on CYP3A4, P-gp or other transporters, which may play a role in telaprevir disposition [21–23].

Alternatively, telaprevir itself is a strong inhibitor of CYP3A [13] and autoinhibition of CYP3A may also explain the lack of a significant effect of RTV on telaprevir exposure after multiple-dose administration of telaprevir when CYP3A is already maximally inhibited. Thus, although RTV increased telaprevir exposure when given as a single dose, this was not sustained after repeated dosage of the combination of 750 mg telaprevir every 12 h (1,500 mg per day) and 100 mg RTV every 12 h.

Coadministration of telaprevir with RTV was well tolerated with generalized pruritus, headache, rash, nausea and diarrhoea as the most frequent drug-related adverse events. No serious adverse events and no clinically significant changes in laboratory values or vital signs were reported [21].

Atazanavir/ritonavir

A combination of 300 mg atazanavir (ATV)/100 mg RTV once daily and 750 mg telaprevir every 8 h were coadministered in healthy subjects [24]. ATV/RTV coadministration decreased telaprevir steady-state plasma concentrations compared with telaprevir alone. Telaprevir \(C_{\text{max}}\), minimum plasma concentration (\(C_{\text{min}}\)) and AUC\(_{\text{ss}}\) were decreased by 21%, 15% and 20%, respectively (Figure 1). The effect of ATV on telaprevir exposure is considered to be modest; the relationship between telaprevir exposure and antiviral

Table 1. Summary of clinical drug interaction studies of telaprevir with antiretroviral agents

<table>
<thead>
<tr>
<th>Coadministered drug</th>
<th>Coadministered drug</th>
<th>Number of individuals(^a)</th>
<th>AUC, LS means ratio (90% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Coadministered drug</td>
</tr>
<tr>
<td>HIV protease inhibitors</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lopinavir/ritonavir</td>
<td>400/100 mg twice daily</td>
<td>750 mg every 8 h</td>
<td>12</td>
</tr>
<tr>
<td>Atazanavir/ritonavir</td>
<td>300/100 mg once daily</td>
<td>750 mg every 8 h</td>
<td>14</td>
</tr>
<tr>
<td>Darunavir/ritonavir</td>
<td>600/100 mg twice daily</td>
<td>750 mg every 8 h</td>
<td>11</td>
</tr>
<tr>
<td>Fosamprenavir/ritonavir</td>
<td>700/100 mg twice daily</td>
<td>750 mg every 8 h</td>
<td>20</td>
</tr>
<tr>
<td>Reverse transcriptase inhibitors</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TDF</td>
<td>300 mg once daily</td>
<td>750 mg every 8 h</td>
<td>16</td>
</tr>
<tr>
<td>EFV</td>
<td>600 mg once daily</td>
<td>750 mg every 8 h</td>
<td>21</td>
</tr>
<tr>
<td>EFV and TDF</td>
<td>600 mg once daily EFV and 300 mg once daily TDF</td>
<td>1,125 mg every 8 h</td>
<td>15</td>
</tr>
<tr>
<td>EFV and TDF</td>
<td>600 mg once daily EFV and 300 mg once daily TDF</td>
<td>1,500 mg every 12 h</td>
<td>16</td>
</tr>
<tr>
<td>Etravirine</td>
<td>200 mg twice daily</td>
<td>750 mg every 8 h</td>
<td>15</td>
</tr>
<tr>
<td>Rilpivirine</td>
<td>25 mg once daily</td>
<td>750 mg every 8 h</td>
<td>16</td>
</tr>
<tr>
<td>HIV integrase inhibitors</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Raltegravir</td>
<td>400 mg twice daily</td>
<td>750 mg every 8 h</td>
<td>20</td>
</tr>
</tbody>
</table>

\(^a\)The number of individuals differs depending on the respective calculated ratio. \(^b\)Ratio (telaprevir 1,125 mg every 8 h with tenofovir disoproxil fumarate [TDF] and efavirenz [EFV])/(telaprevir 750 mg every 8 h alone). \(^c\)Least square (LS) mean ratio based on average concentration at steady-state \(C_{\text{ss}}\) instead of the area under the concentration–time curve (AUC), ratio (telaprevir 1,500 mg every 12 h with TDF and EFV)/(telaprevir 750 mg every 8 h alone). \(^\uparrow\), upwards increase in exposure; \(^\downarrow\), decrease in exposure; **, no change in exposure.
efficacy has been shown to be shallow and non-significant [20].

Telaprevir increased the exposure to ATV, as expressed by AUC<sub>24 h</sub>, by 17% (Figure 2). This can be explained by the ATV C<sub>min</sub> increase of 85%, which likely reflects reduced systemic elimination of ATV due to telaprevir inhibition of CYP3A. However, there was no significant effect on ATV absorption, as indicated by the small change in ATV C<sub>max</sub> (15% decrease).

### Darunavir/ritonavir

To study interactions between darunavir (DRV)/RTV and telaprevir, healthy subjects received 600 mg DRV/100 mg RTV twice daily and 750 mg telaprevir every 8 h [24]. Steady-state concentrations of telaprevir decreased after coadministration of DRV/RTV and telaprevir: telaprevir C<sub>max</sub><sup>T</sup>, C<sub>max</sub><sup>R</sup>, and AUC<sub>8 h</sub> were decreased by 32%, 36% and 35%, respectively (Figure 1). DRV concentrations were decreased in the presence of telaprevir: C<sub>min</sub> decreased by 42%, C<sub>max</sub> decreased by 40% and AUC<sub>12 h</sub> decreased by 40% (Figure 2).

### Fosamprenavir/ritonavir

Interactions between fosamprenavir (fAPV)/RTV and telaprevir were studied in healthy subjects receiving 700 mg fAPV/100 mg RTV twice daily and 750 mg telaprevir every 8 h [24]. Telaprevir concentrations at steady-state decreased by 30% for C<sub>max</sub><sup>T</sup> by 33% for C<sub>min</sub><sup>T</sup> and by 32% for AUC<sub>12 h</sub> (Figure 1). Amprenavir (APV) concentrations were also lowered in the presence of telaprevir: APV C<sub>max</sub><sup>T</sup>, C<sub>max</sub><sup>R</sup> and AUC<sub>12 h</sub> decreased by 56%, 35% and 47%, respectively (Figure 2).

### Lopinavir/ritonavir

Coadministration of 400 mg lopinavir (LPV)/100 mg RTV twice daily and 750 mg telaprevir every 8 h in healthy subjects [24] decreased steady-state plasma concentrations of telaprevir relative to telaprevir administered alone: C<sub>max</sub><sup>T</sup> was decreased by 53%, C<sub>min</sub><sup>T</sup> was decreased by 52% and AUC<sub>12 h</sub> was decreased by 54% (Figure 1). Telaprevir did not affect the exposure to LPV (expressed by C<sub>max</sub><sup>T</sup> and AUC<sub>12 h</sub>; Figure 2); however, the C<sub>min</sub> of LPV was increased by 14% after coadministration with telaprevir.

### Summary of telaprevir interactions with ritonavir-boosted protease inhibitors

The variable degrees of reduction in exposure to telaprevir as well as to some of the HIV protease inhibitors administered together with RTV during coadministration were unexpected as all of these agents are both substrates and inhibitors of CYP3A, although various non-overlapping metabolic pathways are involved as well. Similar unexpected findings were recently reported for the HCV protease inhibitor boceprevir, which is also a substrate and strong inhibitor of CYP3A [25]. Mean reductions in the AUC of ATV, LPV and DRV by 34–44% were observed during combination with boceprevir. Coadministration of RTV-boosted ATV with boceprevir did not alter the exposure of boceprevir, but coadministration of boceprevir with LPV/RTV or RTV-boosted DRV decreased the exposure of boceprevir by 45% and 32%, respectively [26].

These findings can possibly be explained by the complex interplay between metabolic interactions and competition of telaprevir and the HIV protease inhibitors for plasma protein binding sites. Telaprevir is only moderately (59–76%) bound to plasma proteins (to both albumin and α-acid glycoprotein) and protein displacement has been shown to occur both in vitro and in vivo. An increase in the free fraction of R-methadone was observed in an in vivo DDI study with telaprevir [27], and in an in vitro study, it was shown that warfarin increased the free fraction of telaprevir [28]. Since all of the HIV protease inhibitors are highly bound to plasma proteins (85–99%), with varying contributions of albumin and α-acid glycoprotein, competition for binding sites could occur [29–32]. DRV and APV have been reported to primarily bind to α-acid glycoprotein, while ATV and LPV are bound to both α-acid glycoprotein and albumin [30–32]. Since α-acid glycoprotein is present in plasma at much lower concentrations than albumin [32], the potential for protein displacement may be higher for DRV and APV compared with ATV and LPV. This could explain the differences in the magnitude of the observed interactions with these drugs during coadministration of telaprevir. However, other mechanisms, such as the effect on drug transporters may also be involved. Based on the modest effect of ATV/RTV on telaprevir exposure (see above) and the limited effect on exposure to ATV, the combination of ATV/RTV with telaprevir was selected for further clinical evaluation in patients with HIV–HCV-coinfection.

### Safety of coadministration of telaprevir and ritonavir-boosted HIV protease inhibitors

The type of adverse events observed during coadministration of telaprevir and HIV protease inhibitors ATV/RTV, LPV/RTV, DRV/RTV or fAPV/RTV in these healthy volunteer studies was consistent with the safety profile of the individual drugs. Events related to hyperbilirubinemia were observed during treatments including ATV/RTV (that is, increased blood bilirubin and ocular icterus).

### Pharmacokinetic interactions between telaprevir and reverse transcriptase inhibitors

DDIs between telaprevir and the nucleotide reverse transcriptase inhibitor tenofovir disoproxil fumarate (TDF), and the non-nucleoside reverse transcriptase inhibitors (NNRTIs) efavirenz (EFV), etravirine (ETR) and rilpivirine (RPV) were investigated.
Figure 1. Pharmacokinetic profiles of telaprevir alone and in combination with HIV protease inhibitors

**Figure 2.** Pharmacokinetic profiles of HIV protease inhibitors alone and in combination with telaprevir
Tenofovir disoproxil fumarate

TDF is a widely used nucleotide reverse transcriptase inhibitor for the treatment of HIV infections, in combination with other antiretroviral agents. TDF is a prodrug of tenofovir and is administered at 300 mg once daily, which is equivalent to 136 mg of tenofovir. Although tenofovir is largely excreted unchanged into the urine, previous trials [33,34] have shown drug interactions with CYP3A4 substrates and/or inhibitors such as HIV protease inhibitors. As telaprevir is a CYP3A4 substrate and inhibitor, interaction with tenofovir was studied in healthy subjects [35]. Subjects received 300 mg TDF once daily and 750 mg telaprevir every 8 h. The exposure to telaprevir, as expressed by C_{\text{min}}, C_{\text{max}} and AUC_{0-24}, was not affected by coadministration of TDF. Steady-state plasma concentrations of tenofovir were higher after coadministration of TDF with telaprevir than after intake of TDF alone: tenofovir C_{\text{min}}, C_{\text{max}} and AUC_{0-24} increased by 41%, 30% and 30%, respectively. Renal clearance of tenofovir (total amount of tenofovir excreted in urine over 24 h divided by the plasma AUC_{0-24}) was decreased by 36% when TDF was administered in combination with telaprevir, compared with TDF administration alone [35].

Increased exposure to tenofovir during coadministration of telaprevir may be explained by the effect of telaprevir on uptake and efflux transporters, which have been shown to play a role in the pharmacokinetics of tenofovir. TDF (but not tenofovir) is a substrate of P-gp and inhibition of intestinal P-gp has been proposed as a mechanism for increased tenofovir exposure during combination with HIV protease inhibitors [33]. Telaprevir has been shown to increase the exposure to orally administered digoxin (a P-gp probe substrate), and reduced efflux of TDF during absorption may contribute to increase exposure to tenofovir during combination with telaprevir. Based on in vitro studies, several drug transporters have been shown to play a role in the active renal tubular secretion of tenofovir. Tenofovir is transported from the blood into the proximal tubule cells by the human organic anion transporters hOAT1 and hOAT3, and subsequently eliminated from these cells into urine by the MRP4 efflux pump. Neither hOCT1, hOCT2, MRP2 nor P-gp are involved in active tubular secretion of tenofovir [36].

These results suggest that TDF and telaprevir can be coadministered without dose adjustments but with increased clinical and/or laboratory monitoring for adverse events related to increased tenofovir exposure.

Efavirenz

EFV is an HIV-1-specific NNRTI indicated to treat HIV-1 infection. EFV is metabolized by CYP3A4 and is also an inducer of CYP3A4 [37]. Therefore, it has the potential to decrease concentrations of telaprevir. As telaprevir can inhibit CYP3A4, it was hypothesized that coadministration of telaprevir and EFV could result in changed exposure of both telaprevir and EFV.

Pharmacokinetic interactions between EFV and telaprevir were investigated in healthy subjects [38]. Subjects received 600 mg EFV once daily and 750 mg telaprevir every 8 h. Coadministration of EFV with telaprevir decreased the C_{\text{min}} of telaprevir by 47% and the telaprevir exposure (AUC_{0-24}) by 26%. The C_{\text{max}} of telaprevir was unaffected. The pharmacokinetic parameters of EFV were similar in the presence or absence of telaprevir [38].

Overall, this study demonstrates that there was a significant effect of the CYP3A4 inducer EFV on the pharmacokinetics of telaprevir, and therefore dosage adjustment strategies of telaprevir were evaluated in a subsequent study.

Tenofovir disoproxil fumarate and efavirenz coadministration

Based on the previously described findings with TDF and EFV, a follow-up study examined the effect of EFV on telaprevir pharmacokinetics with the dosing schedule of telaprevir changed to either 1,125 mg every 8 h or 1,500 mg every 12 h to compensate for the decreased telaprevir concentrations seen with EFV coadministration [24]. Because EFV and TDF are frequently coadministered in HIV-infected subjects, and because of the previously observed 30% increase in tenofovir exposure when coadministered with telaprevir, this study was designed to investigate the effect of coadministration of all three drugs on their pharmacokinetic parameters.

Healthy subjects received a telaprevir dosage of 1,125 mg every 8 h or 1,500 mg every 12 h coadministered with EFV (600 mg once daily) and TDF (300 mg once daily). Telaprevir plasma concentrations at steady-state were compared with those achieved with telaprevir alone at 750 mg every 8 h and were decreased in both combination dosage regimens. When telaprevir was given at 1,125 mg every 8 h in addition to EFV plus TDF, C_{\text{min}}, C_{\text{max}} and AUC_{0-24} of telaprevir were 25%, 14% and 18% lower, respectively. When telaprevir was given at 1,500 mg every 12 h in addition to EFV plus TDF, C_{\text{max}} and average concentration at steady state of telaprevir were 48% and 20% lower, respectively, while C_{\text{min}} was not changed significantly.

Telaprevir coadministration decreased EFV plasma concentrations at steady-state in a similar amount in both combination-dosing regimens: EFV C_{\text{max}} was decreased by 24%, C_{\text{min}} by 10% and AUC_{0-24} by 18%, respectively, when EFV and TDF were administered in the presence of telaprevir 1,125 mg every 8 h, and by 20%, 11% and 15%, respectively, in the presence of telaprevir 1,500 mg every 12 h.
By contrast, telaprevir coadministration increased plasma concentrations of tenofovir at steady state with both combination-dosing regimens showing a similar effect: tenofovir $C_{\text{min}}$ was increased by 17%, $C_{\text{max}}$ by 22% and AUC$_{24\text{h}}$ by 10% when EFV and TDF were administered in the presence of telaprevir 1,125 mg every 8 h, and by 6%, 24% and 10%, respectively, in the presence of telaprevir at 1,500 mg every 12 h.

Telaprevir alone or in combinations with TDF and EFV, was generally safe and well tolerated in this study in healthy subjects [24]. These results suggested that during coadministration of telaprevir, EFV and TDF, the dosage of telaprevir should be increased from 750 mg every 8 h to 1,125 mg every 8 h. EFV and TDF can be administered without dose adjustment. The combination of EFV and TDF with the 1,125 every 8 h dose of telaprevir is being tested in ongoing studies in patients with HIV–HCV coinfection.

Etravirine
ETR is a substrate and weak inducer of CYP3A, a substrate and weak inhibitor of CYP2C9 and CYP2C19, and a weak inhibitor of P-glycoprotein [39]. Therefore, a study was designed to determine the pharmacokinetic effects of ETR and telaprevir on each other at steady-state under fed conditions [40]. This study had separate study panels addressing the DDIs with ETR or RPV (see below) and telaprevir in a crossover design.

Subjects received ETR 200 mg twice daily as reference and ETR 200 mg twice plus telaprevir 750 mg every 8 h as test treatment to evaluate ETR exposure. Exposure to ETR was not affected by concomitant application of telaprevir at steady-state. Exposure to telaprevir was evaluated by comparing telaprevir 750 mg every 8 h as reference to telaprevir 750 mg every 8 h plus 25 mg ETR twice daily as test treatment. Telaprevir exposure was not affected by concomitant application of RPV at steady state [40].

No new or clinically significant safety issues were identified for ETR, RPV or telaprevir in this study. RPV has been shown to prolong the QTc interval at supratherapeutic doses (≥75 mg once daily), but not at the recommended therapeutic dose of 25 mg once daily [42], and the observed increased exposure to RPV during combination with telaprevir is not considered to be clinically relevant. The results of this study suggest that RPV and telaprevir can be administered together without dose adjustment [40].

HIV integrase inhibitor: raltegravir
The HIV integrase inhibitor raltegravir (RAL) is glucuronidated via UGT1A1 and is a substrate of P-gp and therefore had the potential to interact with telaprevir. This was investigated in a study in healthy subjects receiving telaprevir 750 mg every 8 h alone for 6 days and RAL 400 mg twice daily alone for 4 days followed by coadministration of telaprevir 750 mg every 8 h and RAL 400 mg twice daily [43].

Coadministration of RAL did not influence the exposure to telaprevir. Coadministration of telaprevir did moderately increase the exposure to RAL. The RAL $C_{\text{min}}$, $C_{\text{max}}$ and AUC$_{24\text{h}}$ increased by 78%, 26% and 31%, respectively. Exposure to glucuronidated RAL was similarly increased with a least square mean ratio (90% CI) for the AUC of RAL versus glucuronidated RAL of 1.05 (0.95, 1.15). The increase in exposure to RAL was possibly due to inhibition of intestinal P-gp by telaprevir as no influence on UGT1A1 glucuronidation activity was found based on the parent/metabolite ratio.

The effect of telaprevir on RAL was not considered clinically relevant and both drugs can be administered without dose adjustment [43].

Conclusions
Pharmacokinetics and safety of coadministration of telaprevir and respective anti-HIV treatment were investigated in healthy subjects. Mutual DDIs were observed.

Coadministration of telaprevir and the RTV-boosted protease inhibitors ATV, DRV, fAPV or LPV reduced the exposure to telaprevir after repeated doses to some degree, with the least effect on telaprevir observed during combination with ATV/RTV. Telaprevir did not significantly influence exposure to ATV or LPV but decreased the exposure to DRV and APV. Given these data, the combination of telaprevir-based treatment and ATV/RTV therapy was investigated in a pilot study in HIV–HCV-coinfected patients.
patients [44]. Interim data from this study suggest that telaprevir and ATV/RTV can be coadministered without dose modification [44], but larger confirmatory studies in this population are necessary. Appropriate doses for combination treatment with the other studied RTV-boosted HIV protease inhibitors have not yet been established. Further studies to investigate the mechanism of these interactions are ongoing.

Exposure to telaprevir was not affected during coadministration with the reverse transcriptase inhibitor TDF, and exposure to tenofovir was only modestly increased similar to the effect seen with HIV protease inhibitors. No dose adjustment is necessary, but increased monitoring is warranted. Coadministration of EFV resulted in reduced exposure to telaprevir, but higher telaprevir doses (1,125 mg every 8 h) were able to largely offset the interaction with EFV. Therefore, the combination of telaprevir (1,125 mg every 8 h) plus PEG-IFN/RBV with EFV plus TDF/emtricitabine was also investigated in HIV–HCV-coinfected patients [44]. Interim results suggest that this higher telaprevir dose is adequate in this setting [44]. Coadministration of telaprevir with the NNRTI ETR showed no relevant changes in exposure to telaprevir and ETR. RPV exposure was increased when given in combination with telaprevir but a dose adjustment is not considered necessary.

The effect of telaprevir on RAL was not considered clinically relevant and both drugs can be administered without dose adjustment. Administration of telaprevir and coadministration of telaprevir with antiretroviral medications was generally well tolerated in healthy subjects.

In conclusion, a number of DDI studies of telaprevir and antiretrovirals have been conducted in preparation of further clinical evaluation of telaprevir-based therapy in HIV–HCV-coinfected patients. The results of these studies have guided the selection of antiretrovirals for further clinical evaluation in combination with telaprevir-based therapy. While the mechanisms involved in the interactions between telaprevir and different antiretroviral therapies is not known, we are investigating the involvement of drug transporters and protein-binding displacement as possible mechanisms. Further clinical evaluation is warranted to establish the safety and efficacy of telaprevir-based therapy in this population.

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Disclosure statement

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