our combined analyses of HCV DAA clinical trials had cirrhosis and HCV/ HIV-1 coinfection, all from the TURQUOISE-I trial of ombitasvir/paritaprevir/ritonavir plus dasabuvir and RBV [2, 3]. We also note that eligible subjects in TURQUOISE-I were to be on a stable antiretroviral treatment regimen with plasma HIV-1 RNA <40 copies/mL [3].

Despite the presence of advanced liver disease and HIV-1 coinfection for all patients in the Merli et al analysis, their results were consistent with those from our analyses, with observations of declines in absolute lymphocyte and CD4+ T-cell levels without an associated change in CD4+ T-cell percentage during treatment with DAAs plus RBV. Although the changes appeared somewhat greater in the authors’ analysis (particularly CD4+), this effect of RBV-containing treatment generally resolved after treatment, consistent with our analyses. The authors reported that 4 patients experienced a bacterial infection between baseline and posttreatment week 4. It would be interesting to understand if these infections were temporally associated with reductions in lymphocyte levels; a temporal association between severe RBV-related lymphopenia and infection was not apparent in our analyses, although the number of cases was small [2]. Fortunately, the infections described by the authors were not reported as opportunistic infections, most were mild, all patients recovered after antibiotic therapy, and no treatment discontinuations due to infection were reported, again consistent with our analyses and those specifically from TURQUOISE-I [3].

One limitation of the Merli et al analysis is the lack of data from a comparator group of patients who received combination DAA regimens without RBV. Because inclusion of RBV is often recommended to improve treatment efficacy, particularly in patients with more advanced HCV disease, the lack of an RBV-free comparator group for this population is understandable. Furthermore, based on our analyses, one can assume that RBV was the primary driver of the reduced lymphocyte and CD4+ T-cell levels observed by the authors.

We agree with the authors that careful monitoring of lymphocyte levels (and CD4+ T-cell levels for patients with HCV/HIV-1 coinfection) may be justified during anti-HCV treatment for some patients at risk of severe infection. However, it is also important for care providers to be aware that the impact of RBV on these laboratory results is transient due to the fixed duration of therapy, and while severe lymphopenia during interferon-based treatment was associated with a risk of severe infection [4], to our knowledge such an association has not been made with interferon-free treatment.

For certain DAA regimens and patient populations, RBV improves treatment efficacy, reducing the rate of virologic failure and thus preventing DAA resistance emergence that may impact subsequent retreatment. Based on our results [2] and those reported by Merli et al and others [1, 3, 5], we believe the risk–benefit balance of RBV is still favorable when it provides a clear efficacy benefit and is not contraindicated, even in patients with advanced liver disease and HIV-1 coinfection.

Notes

Disclaimer. The views expressed in this correspondence are those of the authors and do not necessarily represent official policy of the US Food and Drug Administration.

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