to examine adverse events rather than efficacy of treatments—something we addressed in the paper.

One of the interesting subgroup analyses (admittedly post hoc) in PRECISION showed that celecoxib was especially effective among rheumatoid arthritis patients taking steroids. This result was similar to that seen in a prior analysis of the results of the VIGOR trial, which included previously unreported data showing that the GI significant safety benefits of rofecoxib over naproxen in rheumatoid arthritis were limited to patients also taking steroids.[6,7]

Finally, the dose of celecoxib taken by most patients in PRECISION was lower than in many earlier studies. As always, the aim of NSAID treatment should be to use the lowest doses with the durations limited to the time needed to control symptoms, which is especially true in osteoarthritis where symptoms are often intermittent.

ACKNOWLEDGEMENTS

The authors' declarations of personal and financial interests are unchanged from those in the original article.[4]

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LINKED CONTENT

This article is linked to Yeomans et al and Laine papers. To view these articles visit https://doi.org/10.1111/apt.14610 and https://doi.org/10.1111/apt.14642.

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DOI: 10.1111/apt.14644

Editorial: grey zone, a new area of interest in chronic hepatitis B

Chronic hepatitis B virus (HBV) infection is a major health problem worldwide. One of the main issues in the management of this disease is to decide which patient will benefit from antiviral treatment. In 2017, the European Association for the Study of the Liver (EASL) published a new version of their Clinical Practice Guidelines (CPG) on the management of HBV infection and defined 5 phases in the natural history of HBV: hepatitis B e-antigen (HBeAg)-positive chronic infection, HBeAg-positive chronic hepatitis, HBeAg-negative chronic infection, HBeAg-negative chronic hepatitis and HBsAg-negative phase.[1] Generally, patients within chronic hepatitis phases need to be treated.[2]

Most patients fall into one of these phases, but some individuals fall into an indeterminate area, and treatment decision needs to be individualised.[1,2] In a recent issue of AP&T, a study by Bonacci and colleagues describes what happen in patients falling in one of this indeterminate areas.[3] They described a "Grey Zone" (GZ) between HBeAg-negative chronic infection (formerly called inactive carriers [IC]) and HBeAg-negative chronic hepatitis, since HBV-DNA and ALT levels may fluctuate over time making difficult a precise classification of the patient clinical situation. They defined 3 GZ categories based on HBV-DNA and ALT levels and compared clinical and virological outcomes with patients in the HBeAg-negative chronic infection phase or IC. Most patients show a stable disease with 45% of the GZ patients transitioning to the IC phase. Only 6.3% of them progressed to HBeAg-negative chronic hepatitis phase (requiring

treatment according to EASL CPG[1]), none developed fibrosis progression or cirrhosis, and only 1 patient developed an hepatocellular carcinoma (HCC) without cirrhosis.[3]

These excellent outcomes after a long-term follow-up in patients of this "GZ new category" are encouraging, since this scenario is frequently seen in clinical practice.[4] Olivieri et al report similar results in a recent study and defined this group with HBV-DNA ≤20.000 IU/mL as low-viraemic active carriers (LV-AC).[5] In this report, 43.5% of LV-AC became IC, 54.3% remained stable in this phase and only one patient (2.2%) progressed to the chronic hepatitis phase. No major liver-related events were reported during the study.[5]

In both studies, most patients had mild disease at baseline. There are no baseline factors helping in predict outcomes. Bonacci et al found higher HBsAg levels in GZ than in IC, and Olivieri et al propose a cut-off value of 1000 IU/mL to predict virological outcomes in patients with HBV DNA <20.000 IU/mL.[3,5] Also, HBsAg levels <100-1000 IU/mL where proposed for defining IC with good long-term outcomes.[6,7]

This study helps us in characterising a common clinical condition with uncertain outcome until now. Most GZ patients have a benign natural history with good long-term prognosis. This result may help clinicians in deciding which of these patients may need invasive assessments of liver disease and who may benefit from antiviral therapy. Therefore, this group of GZ patients appears to have good long-term prognosis and treatment is not required. Since this is a dynamic condition, clinical and virological long-term follow-up is recommended for GZ patients as in IC, despite its benign outcome.[1,8]

ACKNOWLEDGEMENTS

Declaration of personal interests: None.

FUNDING INFORMATION

None.

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LINKED CONTENT

This article is linked to Bonacci et al paper. To view this article visit https://doi.org/10.1111/apt.14613.

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DOI: 10.1111/apt.14646

Editorial: genotype 3 HCV—who still needs ribavirin in a pan-genotypic era?

Chronic hepatitis C virus (HCV) treatment has become simpler and more effective with the use of direct acting anti-virals (DAAs). Clinical trial data of the newest agents show that HCV cure occurs in most treated patients. However, treatment efficacy rates in specific patient groups with genotype 3 (GT3) HCV infection, such as those with prior treatment experience, cirrhosis or baseline resistance-associated substitutions (RAS) remain suboptimal, especially when compared to other genotypes.

von Felden et al retrospectively assessed the real-world experience of 12 weeks of sofosbuvir/velpatasvir (SOF/VEL) with or