

Essential reading from the editor's desk

T. Vanuytsel^{1,2}, C. Reenaers³

(1) Gastroenterology and Hepatology, University Hospitals Leuven, KU Leuven, Leuven, Belgium; (2) Translational Research in Gastrointestinal Diseases (TARGID), KU Leuven, Leuven, Belgium; (3) Gastroenterology, University Hospital Liège, Liège, Belgium.

Keywords: hepatitis B; hepatitis C; metabolic-dysfunction associated liver disease; biosimilar; HIPEC.

The prevalence of metabolic dysfunction associated liver disease (MALFD) – previously known as non-alcoholic fatty liver disease (NAFLD) – has increased dramatically in the past few decades and is now the most common cause of chronic liver disease worldwide (1-4). Nevertheless, chronic hepatitis B (HBV) remains an important cause of cirrhosis and hepatocellular carcinoma on a global scale (5). Even if there is still controversy which patients to treat with antiviral therapy (e.g. high DNA levels with normal aminotransferase levels), it is clear that treatment reduces disease progression and improves survival in the presence of active necroinflammation (5,6). In the current edition of the *Acta Gastro-Enterologica Belgica*, Gok Sargin and colleagues have performed a large retrospective cohort study in 469 patients with chronic hepatitis B to evaluate adverse effects of the three approved antivirals: entecavir, tenofovir disoproxil fumarate and tenofovir alafenamide (7). Efficacy in terms of DNA suppression, normalization of aminotransferase levels and HBsAg seroconversion was comparable in the three groups. All treatments were associated with a mild decrease in renal function, but without a difference between the groups. Finally, no differences were observed in terms of metabolic complications including bone mineral density and lipid profiles.

HBV-related acute-on-chronic liver failure is a relatively rare complication of chronic hepatitis B, but is associated with high mortality (8). In a retrospective study including 302 patients, glucocorticoid treatment improved short-term survival (4.6 vs. 11.9% and 16.6 vs. 25.8% mortality after 1 and 2 months respectively), but without an impact on liver function and complications including encephalopathy, kidney failure and GI bleeding (9). Moreover, fungal infection rates increased with corticosteroids.

This study indicates that glucocorticoids can be considered in HBV-related acute-on-chronic liver failure – especially in young individuals and milder subgroups – but that the indication is less established in comparison to e.g. alcoholic acute-on-chronic liver failure.

The treatment of chronic hepatitis C has been revolutionized with the advent of direct-acting antiviral (DAA) therapy (10,11). Kanayama and colleagues from

Japan have analyzed their cohort of 1461 hepatitis C patients treated with DAA therapy (12). They found a higher than expected incidence of malignancies, including lung cancer, and five patients developed auto-immune diseases (rheumatoid arthritis and membranoproliferative glomerulonephritis) after treatment which were considered to be possibly related to treatment. These results call for a close follow-up to monitor efficacy and safety of the treatment which remains a challenge in the chronic hepatitis C population (13).

Outcome of chronic liver disease is not only related to liver function and hepatic complications. Clinicians should take into account the interaction of the liver with other organ systems as well, leading to the concept of e.g. liver-gut axis and more recently the bidirectional liver-muscle axis. It is known that patients with advanced liver disease are more likely to suffer from sarcopenia, i.e. reduced muscle mass and function, which influences their prognosis (14). In this edition, the hepatology group from Cliniques Universitaires Saint-Luc in Brussels have nicely summarized the complex interplay between skeletal muscle and the liver in chronic liver disease and identify novel treatment targets independent of disease etiology (15).

In the past five years biosimilars of monoclonal antibodies have become available for the treatment of chronic inflammatory bowel diseases (IBD). Since 2017 five biosimilars of the anti-TNF monoclonal adalimumab have been approved in Europe. Nevertheless, several uncertainties regarding efficacy remain and the Belgian IBD Research Group (BIRD) have recently published a statement calling for pharmacovigilance and real-world evidence, which was still missing in Belgium (16). In a prospective study in two Belgian IBD centers, the effect of switching adalimumab originator to SB5 biosimilar was evaluated in 110 patients (17). They found that 85% of the patients was willing to switch to biosimilars after adequate information. The adalimumab trough levels decreased in the first 6 months, which remained unexplained in this study, and stayed stable afterwards, but all levels stayed within the predefined target range.

Correspondence to: Tim Vanuytsel, MD, PhD, Herestraat 49, box 701, 3000 Leuven, Belgium. Phone: +32 16 34 19 73. Fax: +32 16 34 44 19. Email: tim.vanuytsel@uzleuven.be

Submission date: 03/12/2022
Acceptance date: 03/12/2022

The authors also observed no changes in disease activity scores or biochemical parameters, suggesting that patients can be switched safely to biosimilars for adalimumab.

Finally, Livin and colleagues describe the outcome of almost 100 patients with cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (HIPEC) for peritoneal carcinomatosis from colorectal cancer (18). The 2 and 5 year recurrence-free survival rates were 34 and 22% respectively. Based on their findings, they suggest that radical surgery and HIPEC should be reserved for patients with an intraoperative peritoneal carcinomatosis index (PCI) of 7 or below.

The entire editorial board wishes you a pleasant reading with these highlighted and many other thought-provoking manuscripts.

References

- FRANCQUE S., LANTHIER N., VERBEKE L., REYNAERT H., VAN STEENKISTE C., VONGHIA L., et al. The Belgian Association for Study of the Liver Guidance Document on the Management of Adult and Paediatric Non-Alcoholic Fatty Liver Disease. *Acta Gastroenterol Belg*, 2018,**81**(1):55-81.
- ESLAM M., SANYAL A. J., GEORGE J., INTERNATIONAL CONSENSUS P. MAFLD: A Consensus-Driven Proposed Nomenclature for Metabolic Associated Fatty Liver Disease. *Gastroenterology*, 2020,**158**(7):1999-2014 e1.
- KAZE E., DESCAMPS O. S., HENRION J. The changing pattern of cirrhosis in Belgium: a study based on two cohorts prospectively collected 15 years apart. *Acta Gastroenterol Belg*, 2020,**83**(4):559-563.
- BINET Q., LOUMAYE A., PREUMONT V., THISSEN J.-P., HERMANS M. P., LANTHIER N. Non-invasive screening, staging and management of metabolic dysfunction associated fatty liver disease (MAFLD) in type 2 diabetes mellitus patients: what do we know so far? *Acta Gastroenterol Belg*, 2022,**85**(2):346-357.
- EUROPEAN ASSOCIATION FOR THE STUDY OF THE LIVER. ELECTRONIC ADDRESS E. E. E., EUROPEAN ASSOCIATION FOR THE STUDY OF THE L. EASL 2017 Clinical Practice Guidelines on the management of hepatitis B virus infection. *J Hepatol*, 2017,**67**(2):370-398.
- KOC O. M., VERBEEK J., KOEK G. H., BIELEN R., BUSSCHOTS D., GAMIL M., et al. A long-term study of liver-related events in Caucasian hepatitis B patients with normal ALT values and high viremia. *Acta Gastroenterol Belg*, 2022,**85**(1):56-61.
- GOK SARGIN Z., CELIK U., DUSUNCELI I., USTUNDAG Y. Comparison of the Side Effects of Antivirals in Chronic Hepatitis B Patients: A Single-Center Experience. *Acta Gastroenterol Belg*, 2022,**85**(4):587-592.
- WU T., LI J., SHAO L., XIN J., JIANG L., ZHOU Q., et al. Development of diagnostic criteria and a prognostic score for hepatitis B virus-related acute-on-chronic liver failure. *Gut*, 2018,**67**(12):2181-2191.
- SHI P., ZHU W. T., LIANG A., WAN J., FU J. W., WU X. P. Efficacy and predictive factors of glucocorticoid therapy for patients with hepatitis B virus-related acute-on-chronic liver failure. *Acta Gastroenterol Belg*, 2022,**85**(4):593-600.
- GUNTIPALLI P., PAKALA R., KUMARI GARA S., AHMED F., BHATNAGAR A., ENDAYA CORONEL M. K., et al. Worldwide prevalence, genotype distribution and management of hepatitis C. *Acta Gastroenterol Belg*, 2021,**84**(4):637-656.
- BOURGEOIS S., MULKAY J. P., COOL M., VERHELST X., ROBAEYS G., LASSER L., et al. Comorbidities and concomitant medications in patients with chronic hepatitis C virus infection receiving second-generation direct-acting antiviral regimens in Belgium: an observational study. *Acta Gastroenterol Belg*, 2021,**84**(1):33-41.
- KANAYAMA Y., SATO K., SAITO S., UENO T., SHIMADA Y., KOHGA T., et al. Prognosis and incidence of immunological and oncological complications after direct-acting antiviral therapy for chronic hepatitis C. *Acta Gastroenterol Belg*, 2022,**85**(4):601-609.
- KEYMEULEN H., VAN DE VELDE H., DEGROOTE H., GEERTS A., VAN VLIJBERGHE H., VERHELST X. Patients with chronic hepatitis C virus infection are at high risk of being lost to follow-up. Focused interventions can increase linkage to care. *Acta Gastroenterol Belg*, 2020,**83**(1):94.
- HOU J. C., ZHANG Y. M., QIANG Z., ZHU L. Y., ZHENG H., SHEN Z. Y. The psoas muscle depletion index is related to the degree of cirrhosis and skeletal muscle loss in patients with end-stage liver disease. *Acta Gastroenterol Belg*, 2022,**85**(3):453-462.
- HENIN G., LANTHIER N., DAHLQVIST G. Pathophysiological changes of the liver-muscle axis in end-stage liver disease: what is the right target? *Acta Gastroenterol Belg*, 2022,**85**(4):611-624.
- SOMERS M., BOSSUYT P., FERRANTE M., PEETERS H., BAERT F. Belgian IBD Research Group [BIRD] Position Statement 2019 on the Use of Adalimumab Biosimilars in Inflammatory Bowel Diseases. *Journal of Crohn's & Colitis*, 2020,**14**(5):680-685.
- DEPREZ N., DE SOMER T., BAERT D., DECEUNINCK M., HUYS I., MATTENS V., et al. Evaluation of the safety and effectiveness after switch from adalimumab originator to biosimilar SB5 in patients with inflammatory bowel disease in a real-life setting. *Acta Gastroenterol Belg*, 2022,**85**(4):557-564.
- LIVIN M., LEONARD D., BACHMANN R., REMUE C. B., S. COTTE, E. VAN DEN EYNDE, M., DE CUYPER A., SINAPI I., et al. Cytoreductive surgery and hyperthermic intraperitoneal chemotherapy for peritoneal carcinomatosis from colorectal cancer: a 13 years-retrospective monocentric study. *Acta Gastroenterol Belg*, 2022,**85**(4):573-579.