[7] Buster EH, Flink HJ, Cakaloglu Y, Simon K, Trojan J, Tabak F, et al. Sustained HBeAg and HBsAg loss after long-term follow-up of HBeAg positive patients treated with peginterferon alpha-2b. Gastroenterology 2008;135:459–467.
[8] Chien RN, Yeh CT, Tsai SL, Chu CM, Liaw YF. Determinants for sustained HBeAg response to lamivudine therapy. Hepatology (Baltimore, Md.) 2003;38:1267–1273.
[9] Buti M, Cotrina M, Valdes A, Jardi R, Rodriguez-Frias F, Esteban R. Is hepatitis B virus subtype testing useful in predicting virological response and resistance to lamivudine? J Hepatol 2002;36:445–446.
[10] Lurie Y, Manns MP, Gish RG, Chang TT, Yurdaydin C, Lai CL, et al. The efficacy of entecavir is similar regardless of disease-related baseline subgroups in treatment of nucleoside-naive, HBeAg(+) and HBeAg(−) patients with chronic hepatitis B. J Hepatol 2005;42:184.
[11] Yuen MF, Wong DK, Sablon E, Yuan HJ, Sum SM, Hui CK, et al. Hepatitis B virus genotypes B and C do not affect the antiviral response to lamivudine. Antivir Ther 2003;8:531–534.
[12] Buster EH, Hansen BE, Verhey E, De Man RA, Janssen HL. HBV genotype is an important predictor of sustained off-treatment response to both peginterferon alpha-2b and entecavir in HBeAg positive chronic hepatitis B. Hepatology (Baltimore, MD) 2008;48:716A.

Erik H.C.J. Buster
Harry L.A. Janssen
Department of Gastroenterology and Hepatology, Erasmus MC, University Medical Center Rotterdam, 's Gravendijkwal 230, 3015, CE Rotterdam, The Netherlands
Tel.: +31 10 4635942; fax: +31 10 4365916
E-mail address: h.janssen@erasmusmc.nl (H.L.A. Jans)

HBV genotype must be included in treatment algorithm

Reply to Buster and Janssen:
We thank Drs. Buster and Janssen for their appreciative comments on our review article recently published in the Journal. We entirely share their views on the important role of HBV genotype in a modern treatment algorithm of patients with chronic HBV infection irrespective of the medicament used, even though, as the authors also reiterated, its effects are indisputably evident only in interferon-treated patients. We also think that a correct algorithm must include histology as an additional variable and that future trials must be powered to detect the effects of other factors, such as age, ALT, and HBV DNA.

We apologize for not citing their abstracts on the role of HBV genotype as predictor of sustained off treatment responses in HBeAg positive patients, but the criteria we set for our review were such that we considered for analysis only full papers reporting randomized clinical trials with any information provided on HBV genotypes, baseline characteristics of study subjects, response to antiviral therapy, and interaction with the type of therapy. Finally, we fully support Buster and Janssen's recommendation that HBV genotyping should be part of a diagnostic work-up at least in all tertiary referral centers where specialized treatment is actually instituted.

Conflict of interest

The authors declare that they do not have anything to disclose regarding funding or conflict of interest with respect to this Letter.

Mario U. Mondelli[1,*]
Sara Raimondi[2]
Savino Bruno[3]
Patrick Maisonneuve[2]
[1]*Research Laboratories, Department of Infectious Diseases, Fondazione IRCCS Policlinico San Matteo, University of Pavia, Pavia, Italy*
[2]*Division of Epidemiology and Biostatistics, European Institute of Oncology, Milan, Italy*
[3]*Liver Unit, Department of Medicine, Azienda Ospedaliera Fatebenefratelli e Oftalmico, Milan, Italy*
[*]*Address: S.C. di Infettivologia Molecolare, Dipartimento di Malattie Infettive, Fondazione IRCCS Policlinico San Matteo, p.le Golgi 19, 27100 Pavia, Italy*
Tel.: +39 0382 502639; fax: +39 0382 526450
E-mail addresses: .mario.mondelli@unipv.it, m.mondelli@smatteo.pv.it (M.U. Mondelli)

mTOR inhibitors and sorafenib for recurrent heptocellular carcinoma after orthotopic liver transplantation

To the Editor:
With interest we read the recent publication of the Milan group by Bhoori et al., describing a patient with a late recurrent hepatocellular carcinoma (HCC) after orthotopic liver transplantation who was successfully treated with a combination of everolimus and sorafenib after initial failure of sorafenib [1]. In general, the prognosis of recurrent HCC after orthotopic liver transplantation is fatal, especially in those patients presenting with early recurrence [2]. The majority of these patients present with metastatic disease and treatment options are very limited [3].

Sorafenib, a tyrosine kinase-inhibitor with anti-proliferative and anti-angiogenic activity, is currently the only approved systemic treatment in patients with advanced Barcelona Clinic Liver Cancer (BCLC) stage HCC [4]. It inhibits downstream signaling of VEGFR-2 and -3, Flt-3, PDGFR, and FGFR-1 and blocks the Ras-Raf-MEK-ERK cascade by targeting the serine–threonine kinase Raf. Rapamycin and its analogues, e.g. sirolimus and everolimus, inhibit *mammalian target of rapamycin* (mTOR),