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REPLY:

We read with interest the letter from Dai and coworkers related to the potential reflux-related complications of esophageal stents. However, the complications the authors described were related to long-term esophageal stents used to treat benign or malign strictures of the esophagus, which is not the case. In fact, the stents used to control acute esophageal variceal bleeding are specifically designed for this severe complication and are removable stents, which can remain in place from 6 to 14 days. Moreover, they were also used to treat esophageal tears caused by a previous balloon tamponade.[1,2]

As stated by the authors, all patients developing acute variceal bleeding are placed in a slightly upright position to avoid aspiration of the gastric content, which, unfortunately, occurred in one patient in the stent group. However, this adverse event could be attributed to the presence of hematemesis, upper endoscopy, placement of the stent, etc. As mentioned in the article, aspiration was more frequent in the group of patients treated by esophageal balloon tamponade than in those receiving esophageal metal stents.

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Interferon Lambda 4 Variant rs12979860 Is not Associated With RAV NS5A Y93H in Hepatitis C Virus Genotype 3a

TO THE EDITOR:

Peiffer et al. recently reported[1] an association between the host interferon lambda 4 (*INFL4*) single-nucleotide polymorphism (SNP), rs12979860, and the NS5A resistance-associated variant (RAV) Y93H in hepatitis C virus (HCV) genotype 1b (HCVg1b). This observation is intriguing because it directly links innate immunity to HCV viral drug resistance for the first time. A small cohort of (51) HCV genotype 3 (HCVg3) patients was included in the analysis; this

TABLE 1. Prevalence of Y93H RAV in HCVg3a-Infected Patients (n=496) Stratified by rs12979860 *IFNL4* SNP

	Y93H: Consensus Level n/N (%)	Y93H: All Types n/N (%)
INFL4 C/C	12/184 (6.5)	25/184 (13.5)
INFL4 non C/C	11/312 (3.5)	30/312 (9.6)

subgroup analysis was underpowered and no association was observed in HCVg3. The association was also not observed in 259 patients with HCV subtype 1a.

HCVg3 infections are more difficult to treat with direct-acting antivirals. The reason for this is unknown, but could be explained by a distinct pattern of RAVs and an increase in the prevalence of "favorable" *IFNL4* SNPs in this genotype. Here, we used a large cohort of 496 HCVg3a-infected patients (from the BOSON clinical study[2]) and report no significant association ($P > 0.05$) between the treatment-beneficial C/C genotype of *INFL4* and RAV site Y93H in the *NS5A* gene.

Using next-generation sequencing,[3] baseline viral sequences from 556 BOSON patients chronically infected with either HCVg2 or HCVg3 were obtained. The *INFL4* SNP rs12979860 was also genotyped. The cohort (total of 556) was composed of 49 (8.8%) HCVg2- and 507 (91.2%) HCVg3-infected patients, of which 496 (89.2%) were subtype 3a.

Substitutions in the quasi-species at Y93 (Y93H) were only observed in HCVg3a-infected patients; therefore, the analysis was done on this subset of the data. The Y93H RAV was present in 11.1% (55 of 496) of the genotype 3a–infected patients; in 4.7% (23 of 496), Y93H was as the majority variant. There was no significant association between the presence of H (either as the consensus level or at any level of detection) and the beneficial C/C genotype of *INFL4* ($P > 0.05$; Table 1). Overall, our data support the Peiffer et al. hypothesis that the association between INFL4 and Y93H is specific to HCV genotype 1b.

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REPLY:

Interesting data were presented by Pedergnana et al. to add to the picture of the association between the host interferon lambda 4 (*IFNL4*) genotype and the presence of the NS5A resistance-associated variant (RAV), Y93H, in hepatitis C virus (HCV)-infected patients. Recently, we and other groups observed a highly significant correlation between the presence of