High-dose (PEG)interferon therapy in treatment-naïve, interleukin-28B rs12979860 CT/TT genotype 1 chronic hepatitis C

Dear Editor,

Interleukin-28B (IL28B) rs12979860 CT/TT genotype 1 chronic hepatitis C patients exhibit a less-pronounced viral decline during the peginterferon and ribavirin lead-in-phase preceding the starting of a triple combination regimen based on boceprevir compared with IL28B rs12979860 CC genotype 1 patients [1,2]. A greater than 1 log HCV-RNA drop after a 4-week peginterferon/ribavirin lead-in period is commonly achieved in rs12979860 CC patients leading to higher sustained virological response (SVR) rates with short 24 week treatment duration, while rs12979860 CT/TT patients achieve this less often and more frequently require 48-week treatments to maximise SVR rates [3]. We examined whether high-dose (PEG)interferon induction therapy ameliorates 1st and 2nd phase viral kinetics in treatment-naïve rs12979860 CT/TT genotype 1 patients.

We identified 15 rs12979860 CT/TT treatment-naïve genotype 1 mono-infected patients who were treated in 3 pilot studies in our centre with different induction schemes (group A, n = 4: interferon alpha-2a 9 MU/d, group B, n = 4: peginterferon alpha-2a 360 µg/w and group C, n = 7: combined regimen interferon-alpha-2a 4.5 MU/d plus peginterferon alpha-2a 180 µg/w).

The 1st and 2nd phase viral decline patterns during the first 4 weeks in the pilot groups were compared with a historical control group, consisting of 126 genotype 1 treatment-naïve rs12979860 CT/TT HCV patients who were treated with peginterferon alpha-2a 180 µg/w prior to randomisation in study arms as previously published [4]. Patients in the 3 pilot groups and historical control group all received a similar dose of oral ribavirin of 1000 or 1200 mg for bodyweight below or above 75 kg, respectively.

HCV-RNA levels of both pilot studies and historical control group had been determined centrally at Erasmus MC University Medical Center Rotterdam (Cobas Amplicor HCV Monitor Version 2.0, Roche Diagnostics, Branchburg, NJ) and were available at days 0, 1, 4 and 7 followed by weekly determinations until week 4 in all patients. Statistical analysis was performed using SPSS® 20.0 statistical software (SPSS Inc., Chicago, IL, USA) with 2-sided tests and a type I error of 0.05. Baseline characteristics sex, age, body mass index, mean ribavirin dosage per body weight, baseline viraemia, fibrosis stage, alanine aminotransferase, platelet and neutrophil count were comparable across groups. A greater number of patients in the control group exhibited the rs12979860 TT genotype compared with the pilot study groups.

A trend towards greater viral decline was observed 24 h after the start of therapy in groups A and C containing short-acting interferon, although not statistically significant when compared with the control group. Within the next days of treatment, the viral decline patterns in rs12979860 CT/TT treatment-naïve patients in all 3 high-dose pilot groups became identical to the values observed in the control group. The mean HCV-RNA log10 declines at day 4 were 0.97, 0.59 and 0.72 in groups A, B and C, respectively, versus 0.80 in the control group (p = 0.62, 0.52, 0.76). The HCV-RNA log10 declines at week 4 were 2.16, 1.10 and 2.22 in groups A, B and C, respectively, versus 2.37 in controls (p = 0.74, 0.04, 0.75). The second phase mean log10 decline/day between day 7 and week 4 did not differ across groups (Fig. 1).

Our analysis is the first detailed analysis of the 1st and 2nd phase viral kinetics in treatment-naïve genotype 1 IL28B rs12979860 CT/TT patients who were treated with (PEG)interferon dose-intensified regimes in combination with oral ribavirin. Our study shows that the suboptimal viral response of treatment-naïve genotype 1 chronic hepatitis C patients with the rs12979860 CT/TT genotype is not amenable for improvement with any of the 3 high-dose induction schemes studied. Our data suggest that rs12979860 CT/TT status but not a higher than the current standard dose of (PEG)interferon is the main determinant of the observed response.
to exogenously administered interferon in treatment-naive geno-
type 1 patients.

Conflict of interest
None declared.

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En bloc resection of a 9 cm giant gastro-duodenal lipoma by endoscopic submucosal dissection

Dear Editor,

Lipomas can generally be removed by endoscopic or surgical
treatment methods, but there is no consensus among treatment
options [1]. Here we present a case of endoscopic treatment of a
symptomatic lipoma found in the gastro-duodenal area, success-
fully removed by en bloc resection using endoscopic submucosal
dissection (ESD).

A 77-year old male patient presented with nausea, vomiting
and dyspepsia. Complete blood count and biochemical labora-
tory findings were normal. Endoscopic examination revealed a
mass lesion with a normal mucosal lining, which was thought to
be subepithelial, originating from the duodenum extending to
the antrum–lesser curvature, interfering with the pyloric function
(Fig. 1a). By endoscopic ultrasound, a hyperechoic mass originating
from the submucosa was seen. Endoscopic submucosal dissection
was performed under mild-anaesthesia. Because lesion was in a
submucosal localization, it was not marked. First the lesion was
elevated at the duodenal site by injecting a mixture solution of
sodium hyaluronate (HA) (Adant, Meiji-Seika Kaisha, Tokyo, Japan)
25 mg/2.5 ml, diluted with saline for 0.4%), indigo carmine, and
diluted epinephrine (1:10 000) using a 23-gauge sclerotherapy
needle. Then a lateral incision was done using a Dual Knife (KD
650Q, Olympus, Tokyo, Japan) at the duodenal site. The lesion was
removed en bloc with lateral incision and submucosal dissection
from the duodenum to the antrum using IT Knife2 (KD 611L, Olym-
pus, Tokyo, Japan) (Fig. 1b and c). The procedure lasted 93 min.
Histopathologically the lesion was reported as a lipoma with an
intact capsule (Fig. 1d). No complication was seen during or after
the procedure and the patient was discharged three days later. Six
months later, no residual tissue was seen on control endoscopic
examination and on follow-up it was noted that all the complaints
of the patient had resolved after ESD.

Gastrointestinal lipomas are benign composed of adipose tissue
covered with a capsule, slow-growing, submucosal lesions which
usually occur as a single lesion [2]. Most of the lipomas of the
gastrointestinal system are found incidentally during endoscopy
and usually located in colon and gastric antrum [3]. Lipomas of
the gastrointestinal system larger than 2 cm in size may cause
bleeding, abdominal pain, intestinal obstruction or intussusception
[1]. Our patient had also similar complaints and his complaints
resolved after ESD. Small lipomas with narrow stalk, <2 cm have
been successfully carried out to endoscopic procedures such as
polypectomy, endoscopic mucosal resection or unroofing tech-
niques [1,4]. The management of large lipomas with wide stalk,
>2 cm is controversial and there is no standard treatment approach
to them. For en bloc and complete resection, ESD may be an effective
treatment option in large lipomas [1,5].

The reasons why we preferred ESD to other techniques were
as follows: First, the lesion was localized in the gastro-duodenal
area, and had a wide stalk. It was our belief that it would be hard
to remove this large lesion en bloc with conventional techniques
as the localization included the duodenum, the pylorus and the gastric
area. Although endoscopic manoeuvrability is limited in duode-
num and pylorus, and the intestinal wall is thinner which may
increase rate of complications, only a small portion of the lesion
was located in the duodenum. Second, surgical treatment for com-
plete resection could have more complications in elder patients
and third; we performed 245 successful ESD procedures in our clinic
so far and we are experienced in the procedure.

Additionally, to our knowledge, there are no other reports of
gastro-duodenal lipomas over 9 cm removed by ESD. We think
that ESD, a minimally invasive technique compared to surgical