value, p > 0.05; except for activity impairment: −8.1%, p = 0.0194). In contrast, cirrhotic patients treated with IFN-containing regimens showed substantial decline in PRoS (decline by 3.4–16.0%, all p < 0.005). Nevertheless, by follow-up week 12, no decrement in PRoS from baseline was observed in cirrhosics regardless of the treatment regimen. Furthermore, in HCV-cirrhosis who achieved SVR-12, significant improvements (compared to baseline) were observed in total CLDQ-HCV and FACTIT-T scores [+6.8% to +12.0%, p < 0.05 (FUSION); +4.0% to +5.7%, p < 0.05, (NEUTRINO)]. During treatment, changes in PRO scores were similar between cirrhosics and non-cirrhosics for both treatment regimens (all p > 0.05). Moreover, improvements in PRoS associated with SVR-12 relative to baseline were similar between cirrhosics and non-cirrhosics except for fatigue [FUSION: +12.0% of maximum in cirrhosis vs. +3.4% in non-cirrhosics (p = 0.029)].

Conclusions: During treatment, HCV-cirrhosis have similar PRO scores to non-cirrhotic patients. After achieving SVR-12, cirrhosics also show similar PRO improvement to non-cirrhosics.

P1115 IMPAIRED IL28B GENE INDUCTION AND EXPRESSION OF IFN-LAMBDA4 ARE CLOSELY ASSOCIATED WITH A NON-RESPONSE TO INTERFERON-BASED THERAPY IN CHRONIC HEPATITIS C PATIENTS

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Background and Aims: The mechanisms responsible for poor response influenced by IL28B unfavorable SNPs and IFN4 are unknown. The aim is to evaluate the effect of IFN4 expression on IL28B induction or treatment outcome in chronic hepatitis C (CHC) patients.

Methods:

1. The effects of IFN4 overexpression on ISG and IL28B inductions were assessed in Huh751, Huh751/HCV 1b-replicon, 293T cells and immortalized B lymphocytes.
2. IFN4 expressions were analyzed in liver samples and PBMC obtained from 11 of 22 CHC patients with ss469415590-[AG]. IFN4 expression was associated with IFN-treatment response (p < 0.001). In these 11 patients, 8 (73%) became non-responder, whereas only 23% of IFN4-undetected patients became non-responder (3/11). In PBMC samples, ex-vivo induction of IL28B by IFN4-poly(I:C) was significantly lower in non-responders (n = 18) than in relapsers (n = 14, p = 0.04) or viral responders (n = 32, p = 0.004). IFN4 mRNA was detectable in non-stimulated PBMC obtained form 7 of 23 patients with ss469415590-[AG]-allele and 5 in IFN4-poly(I:C) stimulated PBMC, but not in patients with favorable genotype. IL28B induction levels were lower in IFN4-detectable patients (p = 0.04).

Conclusions: Induction of IL28B expression by IFN4-based stimulation is closely associated with the treatment outcome and may be suppressed by IFN4 expression.

P1116 BOCEPREVIR REAL-LIFE TREATMENT (brit) STUDY – PRACTICALITIES OF USING BOCEPREVIR-BASED TRIPLE THERAPY IN THE UNITED KINGDOM AND EARLY RESPONSES TO TREATMENT-WEEK 12 RESULTS

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Background and Aims: Boceprevir and other direct-acting antivirals (DAAs) have changed treatment, and the need for sensitive viral assays and quick PCR turnaround times has become more important. We explored whether these issues affected patient care in real life and evaluated early on-treatment efficacy.

Methods: Retrospective, multicentre, national cohort study. We evaluated HCV G1 mono-infected and HIV/HCV co-infected patients that started boceprevir up until March 2013. PCR assay, turnaround times and viral loads at treatment weeks (TW) 4, 8 and 12 were assessed using descriptive analysis.

Results: We analysed data from 9 centres (n = 123). PCR assays used had a lower limit of detection from 10–25 IU/ml, and turnaround times varied from 0–17 days (mean 4.01) with a lead-in period of 4–10 weeks (mean 4.56). 67% achieved ≥1 log10 drop after the pegylated interferon/ribavirin (PR) lead-in, irrespective of cirrhosis, prior treatment status or HCV G1 subtype. Some patients with <1 log10 drop at TW4 and <3 log10 drop at TW8 discontinued treatment. 87% were undetectable at TW12. All co-infected and cirrhotic patients who received at least one dose of boceprevir were <100IU/ml by TW12. The label-specified week 12 futility rule was applied to all patients.

Conclusions: PCR turnaround times were consistent with those achieved in the pivotal trials. These additional considerations did not adversely affect the addition of boceprevir to treatment regimens. Good early efficacy was demonstrated in all patient types. TW4 and TW8 responses influenced decisions to introduce or discontinue boceprevir from an HCV treatment regimen.

P1117 SIMEPREVIR REDUCES TIME WITH PEGINTERFERON/RIBAVIRIN-INDUCED SYMPTOMS AND QUALITY-OF-LIFE IMPAIRMENTS: 72-WEEK RESULTS FROM THREE PHASE III STUDIES

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Background and Aims: QUEST-1, QUEST-2 and PROMISE phase 3, double-blind, randomised, controlled studies evaluated simeprevir (SMV, TMC435) 150 mg, a one pill, once-daily, oral HCV, NS3/4A protease inhibitor, plus peginterferon/ribavirin (PR) in HCV genotype 1 patients. We report 72-wk analyses evaluating impact of treatment on symptoms, functioning and quality of life (QoL) using patient-reported outcome (PRO) data.

Methods: Treatment-naïve (QUEST-1, n = 394: QUEST-2, n = 391) and prior relapser (PROMISE, n = 393) patients received SMV (12wks) + PR (24/48wks: response-guided therapy), or placebo (PBO, 12wks) + PR (48wks). Patients completed these PRO throughout the studies: Fatigue Severity Scale (FSS), Center for Epidemiologic Studies Depression Scale (CES-D), Work Productivity and Activity Impairment (WPAI:HePC) and EuroQol (EQ-5D).

Results: Mean PRO scores worsened comparably in both treatment groups from baseline at 4–24wks, then returned to baseline after 24wks in the SMV/PR group and after 48wks in the PBO/PR group. AUC72 (area-under-curve from baseline to 72wks) significantly favoured SMV/PR over PBO/PR for all PRO endpoints except absenteeism and CES-D. No treatment differences were observed in proportion of patients experiencing clinically important worsening...
relative to baseline for any PRO endpoint: however SMV/PR was associated with significantly shorter duration of worsening for all PROs except absenteeism (all three studies) and CES-D (QUEST-1) (Table 1). Mean improvement in FSS scores from baseline to 72wks for SMV/PR were clinically relevant and significant in all three studies.

Conclusions: Adding SMV to PR reduces time with fatigue, depressive symptoms and impaired functioning and QoL without increasing severity of these problems during treatment.

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P1118

NO EFFECT OF FALDAPREVIR ON RENAL FUNCTION IN TREATMENT-NAÏVE PATIENTS WITH CHRONIC HCV GENOTYPE-1 INFECTION: POOLED DATA FROM TWO PHASE III TRIALS


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Background and Aims: With an aging HCV-infected population, the effect of direct-acting antivirals on renal function is increasingly important. STARTVerso1 and 2 assessed the HCV NS3/4A inhibitor faldaprevir plus pegylated interferon α-2a and ribavirin (PR) in treatment-naïve patients with chronic HCV genotype-1 infection. This analysis assessed the effects of faldaprevir on renal function.

Methods: Patients (N = 1309) received PR plus: placebo for 24 weeks (W); faldaprevir 120 mg QD for 12W or 24W; or faldaprevir 240 mg QD for 12W. Patients with serum creatinine >1.5× upper limit of normal or baseline creatinine clearance (CrCL) ≤50 mL/min were excluded. Serum creatinine level and CrCL, calculated using the Cockcroft–Gault method, were assessed during treatment.

Results: Mean baseline creatinine levels and CrCL were similar (76.1–76.5 µmol/L and 106–110 mL/min, respectively) between treatment arms. No time-dependent changes in creatinine or CrCL rates were observed between W2 and W12 in any arm (Table). However, maximum reductions [Mean(SD)] in creatinine levels from baseline with placebo and faldaprevir treatment were −10.6(7.3) µmol/L (faldaprevir 120 mg) and −9.5(8.5) µmol/L (faldaprevir 240 mg) versus −10.5(7.0) µmol/L with placebo. CrCL remained constant irrespective of treatment (<5 mL/min [5%] difference in all arms). Mean(SD) maximum reductions in minimum CrCL from baseline with faldaprevir were −7(13) mL/min (faldaprevir 120 mg) and −11(17) mL/min (faldaprevir 240 mg) versus −11(15) mL/min with placebo.

Conclusions: No differences in serum creatinine and CrCL for placebo- and faldaprevir-treated patients suggest that faldaprevir does not affect renal function.

Table: Difference in serum creatinine from baseline

<table>
<thead>
<tr>
<th>Week</th>
<th>PR + Placebo</th>
<th>PR + Faldaprevir</th>
</tr>
</thead>
<tbody>
<tr>
<td>Week 2</td>
<td>−2.3 (7.2)</td>
<td>−3.3 (8.2)</td>
</tr>
<tr>
<td>Week 4</td>
<td>−3.3 (7.0)</td>
<td>−3.9 (7.5)</td>
</tr>
<tr>
<td>Week 8</td>
<td>−3.3 (7.3)</td>
<td>−3.7 (8.1)</td>
</tr>
<tr>
<td>Week 12</td>
<td>−3.3 (8.2)</td>
<td>−3.8 (9.0)</td>
</tr>
</tbody>
</table>

*1 µmol/L = 0.0113 mg/dL.
**High SD associated with one patient with acute renal failure (not related to FDV treatment) following 8 weeks of untreated diarrhoea and vomiting while receiving diuretics.