### Supplementary Table II: Severe adverse events

<table>
<thead>
<tr>
<th>Category</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiovascular*</td>
<td>11</td>
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<tr>
<td>Anemia</td>
<td>10</td>
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<tr>
<td>Hepatocellular carcinoma</td>
<td>8</td>
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<tr>
<td>Infectious</td>
<td>7</td>
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<tr>
<td>Neurological</td>
<td>6</td>
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<tr>
<td>Decompensation of cirrhosis</td>
<td>4</td>
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<tr>
<td>Cutaneous</td>
<td>3</td>
</tr>
<tr>
<td>Extra-hepatic malignancy</td>
<td>3</td>
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<tr>
<td>Fatigue</td>
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<tr>
<td>Psychiatric</td>
<td>3</td>
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<tr>
<td>Renal failure</td>
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<tr>
<td>Hypoglycemia</td>
<td>1</td>
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<tr>
<td>Thyroid dysfunction</td>
<td>2</td>
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<tr>
<td>Hemorrhagic proctitis</td>
<td>1</td>
</tr>
<tr>
<td>Increase in creatine phosphokinase</td>
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</tbody>
</table>

* Summarized case histories of patients with cardiovascular SAEs.

**Patient N°223** was a 55 year-old man with type 1 diabetes, essential sinus tachycardia treated with atenolol (50 mg/d), and Child A cirrhosis. Two months after starting CHC.
treatment with sofosbuvir and daclatasvir, he briefly lost consciousness when getting up in
the morning and fell down, causing an ankle fracture. Sinus bradycardia and orthostatic
hypotension were identified, atenolol was stopped and antivirals were continued for the
planned duration of 24 weeks.

Patient N°271 was a 68 years-old man with a prosthetic aortic valve, treated with fluindione,
esomeprazole, low-dose aspirin ezetimib, simvastatin and atenolol, and CHC with moderate
fibrosis. Four weeks after starting treatment with sofosbuvir and ribavirin, he developed
atypical chest pain. The EKG showed sinus bradycardia and left bundle branch block.
Acoronarography did not show and significant lesions. Hb had decreased by 2.2 g/dL.
Ribavirin was reduced from 800 to 400 mg/d until the end (12 weeks) of treatment, and there
was no further chest pain.

Patient N°573 was a 58 year-old man with no previous medical history or drug intake, and
CHC with moderate fibrosis. Sixteen weeks after starting CHC treatment with sofosbuvir and
ledipasvir, he developed rapid atrial fibrillation. Antiviral drugs were stopped. The patient
was treated with rivaroxaban and atenolol and returned in sinus rhythm after cardioversion,
without relapse.

Patient N°675 was a 65 year-old woman with no specific medical history or drug intake and
CHC with moderate fibrosis. Four days after starting treatment with sofosbuvir and
simeprevir she developed palpitations and malaise. The EKG showed ventricular
extrasystoles. The daily dose of sofosbuvir was reduced by 50%, and cibenzolin and low-dose
aspirin were added. Palpitations persisted during the 12 weeks of treatment and were not
recorded 6 months later.

Patient N°863 was a 59 year-old man with a past history of nephrotic syndrome, arterial
hypertension, chronic interstitial lung disease, and CHC with moderate fibrosis, treated with
olmesartan and perindopril. After 4 weeks of treatment with sofosbuvir and ribavirin, he
developed effort angina. Hb had decreased to 8.7 g/dL and serum creatinine increased to 160
µM. The dose of ribavirin was reduced from 1200 to 600 mg/day to the end (12 weeks) of
treatment, with no relapse in pain.

**Patient N°210** was a 60 year old-woman with type 2 diabetes and Child B cirrhosis. Eight
weeks after starting treatment with sofosbuvir and daclatasvir, the patient developed acute
dyspnea. Severe pulmonary hypertension was diagnosed, antiviral treatment was stopped.
The patient gradually improved and was hospitalized for two months and continued treatment
with sildenafil, bosentan and epoprostenol.

**Patient N°647** was a 63 year-old woman with arterial hypertension, resected pulmonary
adenocarcinoma, and Child A cirrhosis. After 16 weeks of treatment with sofosbuvir and
daclatasvir, she gradually developed dyspnea. Pulmonary arterial hypertension was
diagnosed and treated with sildenafil and bosentan, and antiviral treatment was stopped.
Hepatocellular carcinoma occurred two months later and the patient died (cerebral
metastasis) 8 months after the end of antiviral treatment.

**Patient N°940** was a 56 year-old man with aortic valvular stenosis and Child A cirrhosis.
After 2 weeks of treatment with sofosbuvir, ledipasvir and ribavirin, he developed exertional
dyspnea. Hb had decreased by 3.3 g/dL, and echocardiography showed aortic stenosis. The
dose of Ribavirin was reduced from 1000 to 400 mg/d until the end of treatment (12 weeks).
An aortic valve prosthesis was successfully implanted one month after the end of treatment.

**Patient N°1223** was a 73 year-old man with arterial hypertension, coronary heart disease,
lower limbs arterial disease, Child A cirrhosis and past hepatocellular carcinoma. One
month after 12 weeks of treatment with sofosbuvir and daclatasvir, the patient died from
pulmonary edema complicating heart failure.

**Patient N° 874** was a 56 year-old man with HIV infection and Child B cirrhosis. After 8
weeks of treatment with sofosbuvir, ledipasvir and ribavirin (total duration: 12 weeks), he
developed right leg thrombosis that was successfully treated with subcutaneous heparin.

Patient N°1105 was a 79 year-old woman with arterial hypertension, atrial fibrillation and Child A cirrhosis. She was being treated with flecaïnide, which was stopped before the onset of antiviral treatment. A few days after stopping flecaïnide, atrial fibrillation relapsed complicated by an embolic stroke. The patient was given acenocoumarol. She was then treated with sofosbuvir and simeprevir (12 weeks) with no further complications.

All these patients achieved an SVR, except patient N°1223 who died one month after the end of treatment.