Recommendation for treatment of hepatitis C virus infection

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I. INTRODUCTION
Treatment of hepatitis C virus (HCV) infection includes treatment-naïve patients and patients with treatment experience, either interferon, peginterferon plus ribavirin or any direct-acting antivirals (DAA). Recommended regimens are those that are favored for most chronic hepatitis C (CHC) patients in a given group, based on optimal efficacy, favored tolerability and adverse effect profiles and duration. Alternative regimens are also effective but relative to recommended regimes because of having potential disadvantages, limitations for use in such populations, or less supporting data than recommended regimens.

The following treatment regimens are listed in order of level of evidence. Some were reimbursed in Turkey. According to unpublished data, until today, in Turkey, sustained virological response (SVR) rate of either a combination of ledipasvir/sofosbuvir or a combination of paritaprevir/ritonavir/ombitasvir with dasabuvir with/without ribavirin is more than 90% in CHC patients with/without cirrhosis.

II. HCV Treatment in G1 Patients
There are several recommended regimens with comparable efficacy. Some were on market in Turkey*

II.A. Treatment in G1 Patients
II.A.1 Treatment-Naive G1 Patients
II.A.1.a Treatment for Patients without Cirrhosis
- A combination of ledipasvir (90 mg/d)/sofosbuvir (400 mg/d) for 12 weeks*.
  - Daily fixed dose combination of ledipasvir (90 mg/d)/sofosbuvir (400 mg/d) for Eight weeks in patients, whose HCV RNA level is <6 million IU/mL
- A combination of paritaprevir (150 mg/d)/ritonavir (100 mg/d)/ombitasvir (25 mg/d) with dasabuvir (500 mg/d) plus weight-based ribavirin for 12 weeks*.
- A combination of daclatasvir (60 mg/d)/sofosbuvir (400 mg/d) for 12 weeks*
- A combination of sofosbuvir (400 mg/d)/velpatasvir (100 mg/d) for 12 weeks

Alternative Regimens
- A combination of elbasvir (50 mg/d)/grazoprevir (100 mg/d) for 12 weeks if no baseline NSSA Resistance-associated substitutions (RAS) for elbasvir.
- A combination of simeprevir (150 mg/d)/sofosbuvir (400 mg/d) for 12 weeks if there were no basal Q80K mutations*
II.A.1.b Treatment for Patients with Compensated Cirrhosis

- A combination of ledipasvir (90 mg/d)/sofosbuvir (400 mg/d) for 12 weeks*
- A combination of paritaprevir (150 mg/d)/ritonavir (100 mg/d)/ombitasvir (25 mg/d) with dasabuvir (500 mg/d) plus weight-based ribavirin for 24 weeks*
- A combination of daclatasvir (60 mg/d)/sofosbuvir (400 mg/d) plus weight-based ribavirin for 12 weeks or without ribavirin for 24 weeks*
- A combination of sofosbuvir (400 mg/d)/velpatasvir (100 mg/d) for 12 weeks

Alternative Regimens

- A combination of elbasvir (50 mg/d)/grazoprevir (100 mg/d) for 12 weeks if no baseline NS5A RAS for elbasvir.
- A combination of simeprevir (150 mg/d)/sofosbuvir (400 mg/d) for 24 weeks if there were no basal Q80K mutations*

II.A.2. Treatment For G1a Patients with Peginterferon/Ribavirin-Experienced

II.A.2.a. Treatment for Patients without Cirrhosis

- A combination of ledipasvir (90 mg/d)/sofosbuvir (400 mg/d) for 12 weeks*.
- A combination of paritaprevir (150 mg/d)/ritonavir (100 mg/d)/ombitasvir (25 mg/d) with dasabuvir (500 mg/d) for 12 weeks*.
- A combination of daclatasvir (60 mg/d)/sofosbuvir (400 mg/d) for 12 weeks*.
- A combination of simeprevir (150 mg/d)/sofosbuvir (400 mg/d) for 12 weeks.
- A combination of elbasvir (50 mg/d)/grazoprevir (100 mg/d) for 12 weeks.
- A combination of sofosbuvir (400 mg/d)/velpatasvir (100 mg/d) for 12 weeks.

Alternative Regimens

- A combination of daclatasvir (60 mg/d)/asunaprevir (400 mg/d) for 24 weeks if no baseline NS5A mutation.

II.A.2.b. Treatment for G1a Patients with Compensated Cirrhosis

- A combination of ledipasvir (90 mg/d)/sofosbuvir (400 mg/d) plus weight-based ribavirin for 12 weeks or without ribavirin for 24 weeks*.
- A combination of paritaprevir (150 mg/d)/ritonavir (100 mg/d)/ombitasvir (25 mg/d) with dasabuvir (500 mg/d) plus weight-based ribavirin for 24 weeks*.
- A combination of daclatasvir (60 mg/d)/sofosbuvir (400 mg/d) plus weight-based ribavirin for 12 weeks or without ribavirin for 24 weeks*.
- A combination of sofosbuvir (400 mg/d)/velpatasvir (100 mg/d) for 12 weeks.

Alternative Regimens

- A combination of elbasvir (50 mg/d)/grazoprevir (100 mg/d) for 12 weeks if no baseline NS5A RAS for elbasvir.
- A combination of simeprevir (150 mg/d)/sofosbuvir (400 mg/d) plus weight-based ribavirin for 12 weeks or without ribavirin for 24 weeks*.
- A combination of elbasvir (50 mg/d)/grazoprevir (100 mg/d) for 12 weeks.
- A combination of sofosbuvir (400 mg/d)/velpatasvir (100 mg/d) for 12 weeks.

II.B. Treatment for Patients Infected with Genotype 1b

II.B.1. Treatment-Naive G1b

II.B.1.a. Treatment for Patients without Cirrhosis

- A combination of ledipasvir (90 mg/d)/sofosbuvir (400 mg/d) for 12 weeks*.
  - Daily fixed dose combination of ledipasvir (90 mg/d)/sofosbuvir (400 mg/d) for eight weeks in patients, whose HCV RNA level is <6 million IU/mL.
- A combination of paritaprevir (150 mg/d)/ritonavir (100 mg/d)/ombitasvir (25 mg/d) with dasabuvir (500 mg/d) for 12 weeks*.
- A combination of daclatasvir (60 mg/d)/sofosbuvir (400 mg/d) for 12 weeks*.
- A combination of simeprevir (150 mg/d)/sofosbuvir (400 mg/d) for 12 weeks.
- A combination of elbasvir (50 mg/d)/grazoprevir (100 mg/d) for 12 weeks.
- A combination of sofosbuvir (400 mg/d)/velpatasvir (100 mg/d) for 12 weeks.

Alternative Regimens

- A combination of daclatasvir (60 mg/d)/asunaprevir (400 mg/d) for 24 weeks if no baseline NS5A mutation.

II.B.1.b. Treatment for Patients with Compensated Cirrhosis

- A combination of ledipasvir (90 mg/d)/sofosbuvir (400 mg/d) for 12 weeks*.
- A combination of paritaprevir (150 mg/d)/ritonavir (100 mg/d)/ombitasvir (25 mg/d) with dasabuvir (500 mg/d) for 12 weeks*.
- A combination of daclatasvir (60 mg/d)/sofosbuvir (400 mg/d) for 12 weeks*.
- A combination of simeprevir (150 mg/d)/sofosbuvir (400 mg/d) plus weight-based ribavirin for 12 weeks or without ribavirin for 24 weeks*.
- A combination of elbasvir (50 mg/d)/grazoprevir (100 mg/d) for 12 weeks.
- A combination of sofosbuvir (400 mg/d)/velpatasvir (100 mg/d) for 12 weeks.

Alternative Regimens

- A combination of daclatasvir (60 mg/d) and asunaprevir (400 mg/d) for 24 weeks if no baseline NS5A mutation.

II.B.2. Treatment for G1b Patients with Peginterferon/Ribavirin-Experienced

II.B.2.a. Treatment for Patients without Cirrhosis

- A combination of ledipasvir (90 mg/d)/sofosbuvir (400 mg/d) for 12 weeks*.
- A combination of paritaprevir (150 mg/d)/ritonavir (100 mg/d)/ombitasvir (25 mg/d) with dasabuvir (500 mg/d) for 12 weeks*.
- A combination of daclatasvir (60 mg/d)/sofosbuvir (400 mg/d) for 12 weeks*.
- A combination of simeprevir (150 mg/d)/sofosbuvir (400 mg/d) plus weight-based ribavirin for 12 weeks or without ribavirin for 24 weeks*.
- A combination of elbasvir (50 mg/d)/grazoprevir (100 mg/d) for 12 weeks.
- A combination of sofosbuvir (400 mg/d)/velpatasvir (100 mg/d) for 12 weeks.

Alternative Regimens

- A combination of daclatasvir (60 mg/d) and asunaprevir (400 mg/d) for 24 weeks if no baseline NS5A mutation.

II.B.2.b. Treatment for G1b Patients with Compensated Cirrhosis

- A combination of ledipasvir (90 mg/d)/sofosbuvir (400 mg/d) for 12 weeks*.
- A combination of paritaprevir (150 mg/d)/ritonavir (100 mg/d)/ombitasvir (25 mg/d) with dasabuvir (500 mg/d) for 12 weeks*.
- A combination of daclatasvir (60 mg/d)/sofosbuvir (400 mg/d) for 12 weeks*.
- A combination of simeprevir (150 mg/d)/sofosbuvir (400 mg/d) plus weight-based ribavirin for 12 weeks or without ribavirin for 24 weeks*.
- A combination of elbasvir (50 mg/d)/grazoprevir (100 mg/d) for 12 weeks.
- A combination of sofosbuvir (400 mg/d)/velpatasvir (100 mg/d) for 12 weeks.

Alternative Regimens

- A combination of daclatasvir (60 mg/d) and asunaprevir (400 mg/d) for 24 weeks if no baseline NS5A mutation.
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- A combination of simeprevir (150 mg/d)/sofosbuvir (400 mg/d) for 12 weeks*
- A combination of elbasvir (50 mg/d)/grazoprevir (100 mg/d) for 12 weeks
- A combination of sofosbuvir (400 mg/d)/velpatasvir (100 mg/d) for 12 weeks

II.B.2.b. Treatment for Patients with Compensated Cirrhosis
- A combination of ledipasvir (90 mg/d)/sofosbuvir (400 mg/d) plus weight-based ribavirin for 12 weeks or without ribavirin for 24 weeks*.
- A combination of paritaprevir (150 mg/d)/ritonavir (100 mg/d)/ombitasvir (25 mg/d) with dasabuvir (500 mg/d) for 12 weeks*
- A combination of elbasvir (50 mg/d)/grazoprevir (100 mg/d) for 12 weeks
- A combination of daclatasvir (60 mg/d)/sofosbuvir (400 mg/d) plus weight-based ribavirin for 12 weeks or without ribavirin for 24 weeks*
- A combination of simeprevir (150 mg/d)/sofosbuvir (400 mg/d) plus weight-based ribavirin for 12 weeks or without ribavirin for 24 weeks*
- A combination of sofosbuvir (400 mg/d)/velpatasvir (100 mg/d) for 12 weeks

II.C. Treatment for G1 Patients with DAA experience

II.C.1. Treatment for G1 Patients with Sofosbuvir+PegIFN+Ribavirin-Experienced

II.C.1.a. Treatment for Patients without Cirrhosis
- A combination of ledipasvir (90 mg/d)/sofosbuvir (400 mg/d) plus for 12 weeks*

II.C.1.b. Treatment for Patients with Compensated Cirrhosis
- A combination of ledipasvir (90 mg/d)/sofosbuvir (400 mg/d) plus weight-based ribavirin for 24 weeks*.

II.C.2. Treatment for G1 Patients with NS3 Protease Inhibitor+Peginterferon+Ribavirin-Experienced

II.C.2.a. Treatment for Patients without Cirrhosis
- A combination of ledipasvir (90 mg/d)/sofosbuvir (400 mg/d) plus weight-based ribavirin for 12 weeks*

II.C.2.b. Treatment for Patients with Compensated Cirrhosis
- A combination of ledipasvir (90 mg/d)/sofosbuvir (400 mg/d) for 12 weeks*.
- A combination of daclatasvir (60 mg/d)/sofosbuvir (400 mg/d) plus weight-based ribavirin for 12 weeks or without ribavirin for 24 weeks*
- A combination of simeprevir (150 mg/d)/sofosbuvir (400 mg/d) plus weight-based ribavirin for 12 weeks or without ribavirin for 24 weeks*
- A combination of sofosbuvir (400 mg/d)/velpatasvir (100 mg/d) for 12 weeks

Alternative Regimens
- A combination of elbasvir (50 mg/d)/grazoprevir (100 mg/d) plus weight-based ribavirin for 16 weeks for patients with baseline NSSA RASs for elbasvir

II.C.2.b. Treatment for Patients with Compensated Cirrhosis
- A combination of ledipasvir (90 mg/d)/sofosbuvir (400 mg/d) plus weight-based ribavirin for 12 weeks or without ribavirin for 24 weeks*.

II.D. Treatment of Patients with Decompensated Cirrhosis
Protease inhibitors treatment should not be used in decompensated patients. From baseline to post-treatment week 12, DAA therapy improves clinical and biochemical parameters including Child-Turcotte-Pugh (CTP) and Model for End-Stage Liver Disease (MELD) scores. Severity of underlying liver disease has an effect on the treatment success. MELD score can be used as a predictor of improvement. MELD score ≥18 may be less likely to improve and may indicate that it’s better to undertake liver transplantation (LT) instead of antiviral treatment. Ribavirin should be started with low initial dose (600 mg) and the dose should be titrated according to patients tolerance.

II.D.1a Treatment of Patients with Decompensated Cirrhosis Infected with Genotype 1
- A combination of ledipasvir (90 mg/d)/sofosbuvir (400 mg/d) plus weight-based ribavirin for 12 weeks or without ribavirin for 24 weeks*.
- A combination of daclatasvir (60 mg/d)/sofosbuvir (400 mg/d) plus weight-based ribavirin for 12 weeks or without ribavirin for 24 weeks*
- A combination of sofosbuvir (400 mg/d)/velpatasvir (100 mg/d) plus weight-based ribavirin for 12 weeks or without ribavirin for 24 weeks

II.D.1b Treatment of Patients with Decompensated Cirrhosis Infected with Genotype 1 in whom Prior Sofosbuvir- or NS5A-Based Treatment Failed
- A combination of ledipasvir (90 mg/d)/sofosbuvir (400 mg/d) plus weight-based ribavirin for 24 weeks*.
- A combination of daclatasvir (60 mg/d)/sofosbuvir (400 mg/d) plus weight-based ribavirin for 24 weeks*
- A combination of sofosbuvir (400 mg/d)/velpatasvir (100 mg/d) plus weight-based ribavirin for 24 weeks

III. TREATMENT FOR PATIENTS INFECTED WITH GENOTYPE 2

III.A. Treatment for Treatment-Naive Genotype 2 Patients

III.A.1.a. Treatment for G2 Patients without Cirrhosis
- A combination of daclatasvir (60 mg/d)/sofosbuvir (400 mg/d) for 12 weeks*
- A combination of sofosbuvir (400 mg/d)/velpatasvir (100 mg/d) for 12 weeks

Alternative Regimens
- A combination of sofosbuvir (400 mg/d) with weight-based ribavirin for 12 weeks*

III.A.1.b. Treatment for G2 Patients with Compensated Cirrhosis
- A combination of daclatasvir (60 mg/d)/sofosbuvir (400 mg/d) for 12 weeks*.
• A combination of sofosbuvir (400 mg/d)/velpatasvir (100 mg/d) for 12 weeks

Alternative Regimens
• A combination of sofosbuvir (400 mg/d) with weight-based ribavirin for 16-20 weeks*

III.B. Treatment for Peginterferon/Ribavirin-Experienced Genotype 2 Patients

III.B.1.a. Treatment for G2 Patients without Cirrhosis
• A combination of daclatasvir (60 mg/d)/sofosbuvir (400 mg/d) for 12 weeks*
• A combination of sofosbuvir (400 mg/d)/velpatasvir (100 mg/d) for 12 weeks

Alternative Regimens
• A combination of sofosbuvir (400 mg/d) with weight-based ribavirin for 12 weeks*

III.B.1.b. Treatment for Patients with Compensated Cirrhosis
• A combination of daclatasvir (60 mg/d)/sofosbuvir (400 mg/d) plus weight-based ribavirin for 12 weeks or without ribavirin for 24 weeks*
• A combination of sofosbuvir (400 mg/d)/velpatasvir (100 mg/d) plus weight-based ribavirin for 12 weeks

Alternative Regimens
• A combination of sofosbuvir (400 mg/d) with weight-based ribavirin for 16-20 weeks*

IV. TREATMENT FOR PATIENTS INFECTED WITH GENOTYPE 3

IV.A. Treatment for Treatment-Naïve Patients

IV.A.1.a Treatment for Patients without Cirrhosis
• A combination of daclatasvir (60 mg/d)/sofosbuvir (400 mg/d) for 12 weeks*
• A combination of sofosbuvir (400 mg/d)/velpatasvir (100 mg/d) for 12 weeks

Alternative Regimens
• A combination of sofosbuvir (400 mg/d) with weight-based ribavirin for 16-20 weeks*

IV.A.1.b. Treatment for Patients with Compensated Cirrhosis
• A combination of daclatasvir (60 mg/d)/sofosbuvir (400 mg/d) plus weight-based ribavirin for 12 weeks or without ribavirin for 24 weeks*
• A combination of sofosbuvir (400 mg/d)/velpatasvir (100 mg/d) plus weight-based ribavirin for 12 weeks

IV.B. Treatment for Peginterferon/Ribavirin-Experienced Genotype 3 Patients

IV.B.1.a Treatment for Patients without Cirrhosis
• A combination of daclatasvir (60 mg/d)/sofosbuvir (400 mg/d) plus weight-based ribavirin for 12 weeks*
• A combination of sofosbuvir (400 mg/d)/velpatasvir (100 mg/d) plus weight-based ribavirin for 12 weeks

IV.B.1.b Treatment for Patients with Compensated Cirrhosis
• A combination of daclatasvir (60 mg/d)/sofosbuvir (400 mg/d) plus weight-based ribavirin for 24 weeks*
• A combination of sofosbuvir (400 mg/d)/velpatasvir (100 mg/d) plus weight-based ribavirin for 12 weeks

V. TREATMENT FOR PATIENTS INFECTED WITH GENOTYPE 5 OR 6

V.A. Treatment for Treatment-Naïve Patients

V.A.1. Treatment for Patients without Cirrhosis or with Compensated Cirrhosis
• A combination of ledipasvir (90 mg/d)/sofosbuvir (400 mg/d) for 12 weeks*
• A combination of paritaprevir (150 mg/d)/ritonavir (100 mg/d)/ombitasvir (25 mg/d) with weight-based ribavirin for 12 weeks*
• A combination of daclatasvir (60 mg/d)/sofosbuvir (400 mg/d) for 12 weeks*
• A combination of sofosbuvir (400 mg/d)/velpatasvir (100 mg/d) for 12 weeks
• A combination of elbasvir (50 mg/d)/grazoprevir (100 mg/d) for 12 weeks

VI. Treatment for Peginterferon/Ribavirin-Experienced Patients

VI.A. Treatment for Treatment-Naïve Patients

VI.A.1. Treatment for Patients without Cirrhosis or with Compensated Cirrhosis
• A combination of ledipasvir (90 mg/d)/sofosbuvir (400 mg/d) plus weight-based ribavirin for 12 weeks or without ribavirin for 24 weeks*
• A combination of paritaprevir (150 mg/d)/ritonavir (100 mg/d)/ombitasvir (25 mg/d) with weight-based ribavirin for 12 weeks*
• A combination of daclatasvir (60 mg/d)/sofosbuvir (400 mg/d) plus weight-based ribavirin for 12 weeks or without ribavirin for 24 weeks*
• A combination of sofosbuvir (400 mg/d)/velpatasvir (100 mg/d) plus weight-based ribavirin for 12 weeks
• A combination of elbasvir (50 mg/d)/grazoprevir (100 mg/d) plus weight-based ribavirin for 12 weeks
VI.B. Treatment for Treatment-Peginterferon/Ribavirin-Experienced Patients

VI.B.1. Treatment for Patients without Cirrhosis or with Compensated Cirrhosis

- A combination of ledipasvir (90 mg/d)/sofosbuvir (400 mg/d) weight-based ribavirin for 12 weeks*
- A combination of daclatasvir (60 mg/d)/sofosbuvir (400 mg/d) weight-based ribavirin for 12 weeks or without ribavirin for 24 weeks*
- A combination of sofosbuvir (400 mg/d)/velpatasvir (100 mg/d) for 12 weeks

VII. SPECIAL PATIENT POPULATIONS

VII.A. Hepatitis C Treatment after Liver Transplantation

Antiviral treatment for recurrent HCV infection post LT should be started preferably three months after the transplantation. CHC recipients should be treated and followed by gastroenterologist and hepatologist in Transplantation Center.

The drug-drug interaction between DAAs and calcineurin inhibitors is complex and unpredictable. Clinicians should be alert this interaction when antiviral treatment with DAAs is initiated. Calcineurin inhibitors such as tacrolimus levels should be monitored during therapy.

VII.A.1. Treatment for Treatment-naive and -Experienced Genotype 1,4,5,6 Transplanted Patients

VII.A.1.a. Treatment for Patients without Cirrhosis or with Compensated Cirrhosis
- A combination of ledipasvir (90 mg/d)/sofosbuvir (400 mg/d) weight-based ribavirin for 12 weeks
- A combination of daclatasvir (60 mg/d)/sofosbuvir (400 mg/d) weight-based ribavirin for 12 weeks or without ribavirin for 24 weeks
- A combination of sofosbuvir (400 mg/d)/velpatasvir (100 mg/d) for 12 weeks

VII.A.2. Treatment for Treatment-naive and -Experienced Genotype 2 or 3 Transplanted Patients
- A combination of daclatasvir (60 mg/d)/sofosbuvir (400 mg/d) plus weight-based ribavirin for 12 weeks in G2 recipients, for 24 weeks in G3 recipients
- A combination of ledipasvir (90 mg/d)/sofosbuvir (400 mg/d) plus weight-based ribavirin for 12 weeks or without ribavirin for 24 weeks
- A combination of sofosbuvir (400 mg/d)/velpatasvir (100 mg/d) plus weight-based ribavirin for 12 weeks or without ribavirin for 24 weeks

VII.B. Patients with HBV Co-Infections

Hepatitis C virus reactivations have been reported in HCV and HBV co-infected patients during or after DAA therapy. Thus, all CHC patients initiating DAA therapy for HCV infection should be assessed for HBV markers. If patients have not experienced for HBV infection, HBV vaccination is recommended. Serum HBV DNA assay should be recommended in patients with HBsAg-positive. Patients meeting treatment criteria for chronic hepatitis B (CHB) infection, antiviral treatment for HBV is recommended at the same time DAA therapy is started. Patients with low or undetectable serum HBV DNA levels can receive HBV prophylaxis or be monitored of serum HBV DNA levels at regular intervals. HBV-experienced patients should be subsequently monitored (serum HBV DNA assay) for HBV reactivation during and after DAA therapy.

Hepatitis C virus and HBV co-infected patients should be treated as well as patients with chronic HCV monoinfection.

VII.C. Patients with HIV Co-Infections

Liver-related morbidity and mortality and overall mortality are more common in HCV and HIV (Human immunodeficiency virus)-co-infected patients than HCV-monoinfected patients. HIV infection is associated with advance hepatic fibrosis and cirrhosis in co-infected patients. The treatment of CHC patients with HIV co-infections is not different than other CHC patients. The adverse events of antiviral therapy for HCV infection is similar to those observed with HCV monoinfection. The most important point in these co-infected patients is to pay attention to drug-drug interactions that can occur between DAAs and antiretroviral agents. Therefore, for every patient to candidate receiving these treatments, the drug interactions, adverse effects and dose adjustments should be investigated. Physicians should be collaborated with the HIV expert. The presence of HIV co-infection is not a contraindication for LT.

VII.D. Patients with Chronic Kidney Disease

VII.D.1. HCV infection is associated with chronic kidney disease (CKD). Patients with a glomerular filtration rate (GFR) of ≥30 mL/min/1.73m² should be treated as same as CHC patients without CKD. No dose adjustment is required.

VII.D.2. Patients with CKD stage 4 or 5 (GFR <30 mL/min/1.73m² with/without on dialysis) should be treated if they cannot have renal transplantation. Patients who do not have live donors, but are in the waiting lists for cadaveric transplantations are eligible for CHC treatment because of the long-waiting intervals. These treatments should be administered by experienced centers.

VII.D.2.a. Treatment for Patients with Genotype 1a
- A combination of paritaprevir (150 mg/d)/ritonavir (100 mg/d)/ombitasvir (25 mg/d)/dasabuvir (600 mg/d) with ribavirin (200 mg/d) for 12 weeks
- A combination of elbasvir (50 mg/d)/grazoprevir (100 mg/d) for 12 weeks

VII.D.2.b. Treatment for Patients with Genotype 1b
- A combination of paritaprevir (150 mg/d)/ritonavir (100 mg/d)/ombitasvir (25 mg/d)/dasabuvir (600 mg/d) for 12 weeks
• A combination of elbasvir (50 mg/d)/grazoprevir (100 mg/d) for 12 weeks
• A combination of daclatasvir (60 mg/d)/asunaprevir (400 mg/d) for 24 weeks

VII.D.2.c. Treatment for Patients with Genotype 4
• A combination of paritaprevir (150 mg/d)/ritonavir (100 mg/d)/ombitasvir (25 mg/d)/ dasabuvir (600 mg/d) with ribavirin (200 mg/d) for 12 weeks
• A combination of elbasvir (50 mg/d)/grazoprevir (100 mg/d) for 12 weeks

VII.D.2.d. Treatment for Patients with Genotype 2
• A combination of peginterferon and ribavirin (200 mg/d) for 24 weeks

Alternative Regimens
• A combination of daclatasvir (60 mg/d)/sofosbuvir (400 mg/d) for 12 weeks
• A combination of sofosbuvir (400 mg/d)/velpatasvir (100 mg/d) for 12 weeks

VII.D.2.d. Treatment for Patients with Genotype 3
• A combination of peginterferon and ribavirin (200 mg/d) for 24-48 weeks

Alternative Regimens
• A combination of daclatasvir (60 mg/d)/sofosbuvir (400 mg/d) with ribavirin (200 mg/d) for 12 weeks
• A combination of sofosbuvir (400 mg/d)/velpatasvir (100 mg/d) ribavirin (200 mg/d) for 12 weeks

VII.E. Treatment-Naïve and -Experienced Kidney Transplant Recipients

VII.E.1 Treatment-Naïve and -Experienced Kidney Transplant Recipients with G1 G4, G5, or G6, without Cirrhosis or with Compensated Cirrhosis
• A combination of ledipasvir (90 mg/d)/sofosbuvir (400 mg/d) for 12 weeks
• A combination of daclatasvir (60 mg/d)/sofosbuvir (400 mg/d) for 12 weeks
• A combination of sofosbuvir (400 mg/d)/velpatasvir (100 mg/d) for 12 weeks

VII.E.2 Treatment-Naïve and -Experienced Kidney Transplant Patients with G2, or G3 without Cirrhosis or with Compensated cirrhosis
• A combination of daclatasvir (60 mg/d)/sofosbuvir (400 mg/d) for 12 weeks
• A combination of sofosbuvir (400 mg/d)/velpatasvir (100 mg/d) for 12 weeks

VIII. ACUTE HEPATITIS C TREATMENT
Acute HCV infection spontaneously clears in 20% to 50% of infected individuals. It occurs within six months of the estimated time of acute infection. In past, antiviral treatment with interferons was initiated as early as possible in order to prevent chronicity of acute infection. Currently, there is no consensus regarding when to start DAAs or treatment duration in the treatment of patients with acute HCV infection. Since high efficacy and safety profile of DAAs, it seems to be that no rush is necessary to initiate treatment early. Antiviral therapy is not recommended in spontaneous seroconversion period. The appropriate time frame to initiate treatment should be at the start of serum ALT elevation. The same treatment approaches for CHC which is described above is recommended.

The treatment duration should be extended, up to 12 weeks in patients with HIV co-infection or in patients with high viral load (HCV RNA level >1 million IU/mL).

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REFERENCES
18. Pol S, Bourliere M, Lucier S, et al. Safety and efficacy of daclatasvir-
17. Gane EJ, Shiffman ML, Etzkorn K, et al. Sofosbuvir/Velpatasvir in
15. Feld JJ, Kowdley KV, Coakley E, et al. Treatment of HCV with ABT-450/r-
10. Feld JJ, Kowdley KV, Coakley E, et al. Treatment of HCV with ABT-450/r-
8. Waked I, Shiha G, Qaqish RB, et al. Ombitasvir, paritaprevir, and rito-
7. Hézode C, Asselah T, Qaqish RB, et al. Ombitasvir, paritaprevir, and rito-
5. Nelson DR, Cooper JN, Lalezari JP, et al. All-oral 12-week treatment with 