

# **Hepatitis C Virus Recurrence in patients underwent Living Donor Liver Transplantation: efficacy and safety of treatment with combined Sofosbuvir and Daclatasvir**

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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

وَأَنْزَلَ اللَّهُ عَلَيْكَ الْكِتَابَ  
وَالْحِكْمَةَ وَعَلَّمَكَ مَا لَمْ تَكُنْ تَعْلَمُ  
وَكَانَ فَضْلُ اللَّهِ عَلَيْكَ عَظِيمًا

صدق الله العظيم

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# Dedication

**To:**

**The soul of my mother**

**To my father**

*Who gave me too much  
And received too little,*

**My husband and my  
lovely children**

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## List of Abbreviations

<b>AASLD</b>	American association for the study of liver disease
<b>ACR</b>	Acute Cellular Rejection
<b>AFP</b>	Alpha fetoprotein
<b>ALT</b>	Alanine amino transferase
<b>AST</b>	Aspartate amino trasnaminase
<b>ATG</b>	Antithymoglobulin
<b>ASV</b>	Asunaprevir
<b>BMD</b>	Bone mineral density
<b>BOC</b>	Boceprevir
<b>CAD</b>	Coronary artery disease
<b>CIT</b>	Cold Ischemia Time
<b>CLD</b>	Chronic Liver Disease
<b>CMV</b>	Cytomegallo virus
<b>CNI</b> s	Calcineurin Inhibitors
<b>CT</b>	Computed Tomograghy
<b>CTP</b>	Child-Turcotte-Pugh Score

<b>CYP- 3A4</b>	Cytochrome P 3A4
<b>CYP 450</b>	Cytochrome P 450
<b>DAAs</b>	Direct Acting Antivirals
<b>DCV</b>	Daclatasvir
<b>DDLT</b>	Deceased Donor Liver Transplantation
<b>EBV</b>	Epstein Bar Virus
<b>EDHS</b>	Egypt Demographic and Health Survey
<b>ELTR</b>	European Liver Transplant Registry
<b>ESLD</b>	End Stage Liver Disease
<b>GAG</b>	Glycosaminoglycan
<b>GFR</b>	Glomerular filtration rate
<b>GRWR</b>	Graft recipient weight ratio
<b>HALT-C</b>	Hepatitis C antiviral long term treatment against cirrhosis
<b>HBIG</b>	Hepatitis B immunoglobulin
<b>HBV</b>	Hepatitis B Virus
<b>HCC</b>	Hepatocellular Carcinoma
<b>HCV</b>	Hepatitis C Virus

<b>HFL</b>	Hepatic focal lesion
<b>HIV</b>	Human immunodeficiency virus
<b>HLA</b>	Human leucocyte antigen
<b>HPS</b>	Hepatopulmonary Syndrome
<b>IL2</b>	Interleukin 2
<b>INR</b>	International normalized ratio
<b>IRES</b>	Internal Ribosomal Entry Site
<b>LDL</b>	Low Density Lipoprotein
<b>LDLT</b>	Living Donor Liver Transplantation
<b>LTx</b>	Liver Transplantation
<b>MELD</b>	Model for end stage liver disease
<b>MHC</b>	Major histocompatibility complex
<b>MMF</b>	Mycophenol Mofetil
<b>NI</b> s	Nucleoside inhibitors
<b>NODM</b>	New onset diabetes mellitus
<b>NTR</b>	Non Translated Region
<b>ORF</b>	Open Reading Frame
<b>PBC</b>	Primary biliary cirrhosis

<b>PCR</b>	Polymerase Chain Reaction
<b>PEG-INF</b>	Pegylated Interferone
<b>PELD</b>	Pediatric End Stage Liver Disease
<b>PIs</b>	Protease inhibitors
<b>PSC</b>	Primary Sclerosing Cholangitis
<b>PTLD</b>	Post transplant lymphoproliferative disease
<b>RBV</b>	Ribavirin
<b>RdRp</b>	RNA dependant RNA polymerase
<b>SD</b>	Standard deviation
<b>SOC</b>	Standard of care
<b>SOF</b>	Sofosbuvir
<b>SP</b>	Signal Peptidase
<b>SPP</b>	Signal Peptide Peptidase
<b>SVR</b>	Sustained Virological Response
<b>TIPS</b>	Transjugular intrahepatic portosystemic shunts
<b>TPV</b>	Telaprevir
<b>UNOS</b>	United Network For organ Sharing
<b>US</b>	Ultrasound

**UTR**

Untranslated Region

## ABSTRACT

**Background:** Treatment of hepatitis C in the post-liver transplantation patient is a rapidly evolving field. When treating hepatitis C in this setting, the main goals of therapy include: (a) cure of HCV chronic infection in the allograft post-transplant, (b) minimize the risk of developing HCV associated complications in the allograft, such as fibrosingcholestatic hepatitis and allograft failure, and (c) prevent development of hepatic fibrosis and thus preserve the function of the transplanted liver. The Association of sofosbuvir and daclatasvir has been shown to have very high antiviral efficacy when administered, with or without ribavirin, to previously naïve or non-responder patients with chronic HCV infection. Combination with daclatasvir in a LT recipient with severe recurrent cholestatic hepatitis C has been reported, showing a favourable outcome and the lack of drug interactions with calcineurin inhibitors (CNI).

**Aim of the work:** The purpose of this study was to evaluate the virological response, clinical efficacy and safety of the combined sofosbuvir and daclatasvir in living donor liver transplant recipients with recurrent hepatitis C following transplantation and screening for the development of hepatocellular carcinoma during, after end of treatment or during followup.

**Patients and Methods:** This study included 40 patients underwent living donor liver transplantation during the period from January 2015 till December 2015 who started treatment at least 3 months following transplantation. Laboratory studies were done, including CBC, liver function tests, liver enzymes, coagulation profile, sodium, potassium, kidney function tests, thyroid function tests, autoimmune markers (ANA, ASMA, LKM, AMA), HCV antibodies and quantitative HCV RNA by PCR, HBV markers, CMV antibodies, EBV antibodies and tumor markers including AFP, CEA and CA19-9. Imaging studies including, abdominal ultrasonography, Doppler ultrasound, arteriography, venoportography, Fibroscan and Triphasic computed tomography with contrast.

### **Results:**

**Conclusion:** Non interferon-based therapies with oral DAA agents have revolutionized the treatment of HCV recurrence post-transplant. These regimens have consistently demonstrated high SVR rates, shorter treatment courses, and a more favorable side effect profile than interferon based therapies. Although DAA agents are effective even in advanced liver disease, SVR rates seem diminished when compared with patients with minimal liver disease. Further studies are needed to clarify whether DAAs increase HCC incidence and to determine the natural history and baseline post-SVR HCC incidence according to the type of anti-HCV therapy in each specific patient population.

**Key words:** Hepatitis C Virus, Recurrence, Living Donor Liver Transplantation, Sofosbuvir and Daclatasvir.