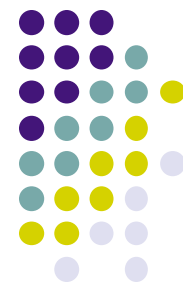


# Hepatitis C and CKD: News from KDIGO



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Novosibirsk | September 23<sup>rd</sup>, 2017

# Acknowledgement

**This slide deck was developed based on the draft public-review version of the KDIGO guideline on Hepatitis C in CKD.**

**It is based on a set of slides kindly shared by Dr Michel Jadoul.**

# KDIGO Guidelines on HCV in CKD

OFFICIAL JOURNAL OF THE INTERNATIONAL SOCIETY OF NEPHROLOGY



**kidney**  
INTERNATIONAL



KDIGO 2008

**First global comprehensive  
guidelines on Hepatitis C  
Virus in nephrology**

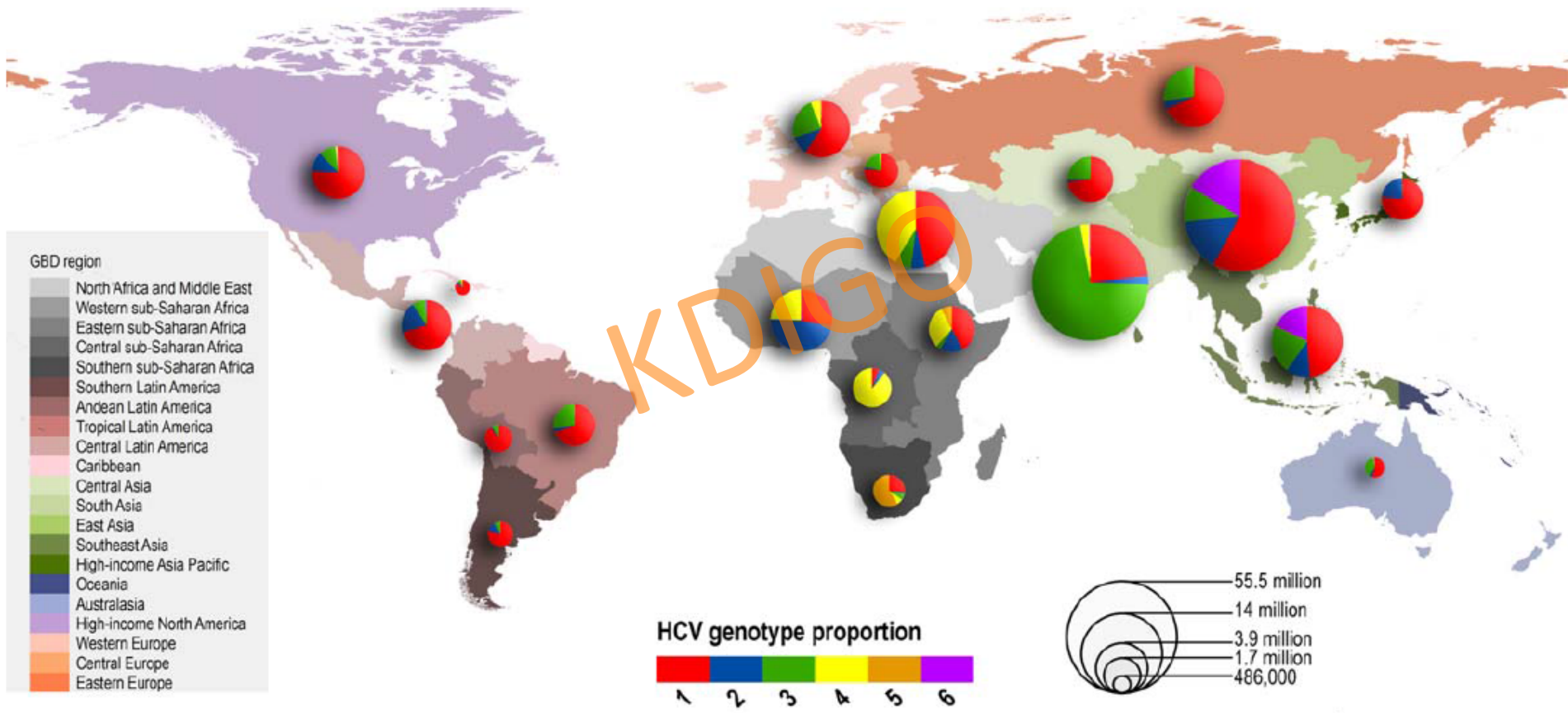
KDIGO Clinical Practice Guidelines for the Prevention, Diagnosis, Evaluation,  
and Treatment of Hepatitis C in Chronic Kidney Disease

VOLUME 73 | SUPPLEMENT 109 | APRIL 2008

Supplement to Kidney International

<http://www.kidney-international.org>

# Global HCV Genotype Distribution



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# Evolution in HCV Therapy: SVRs

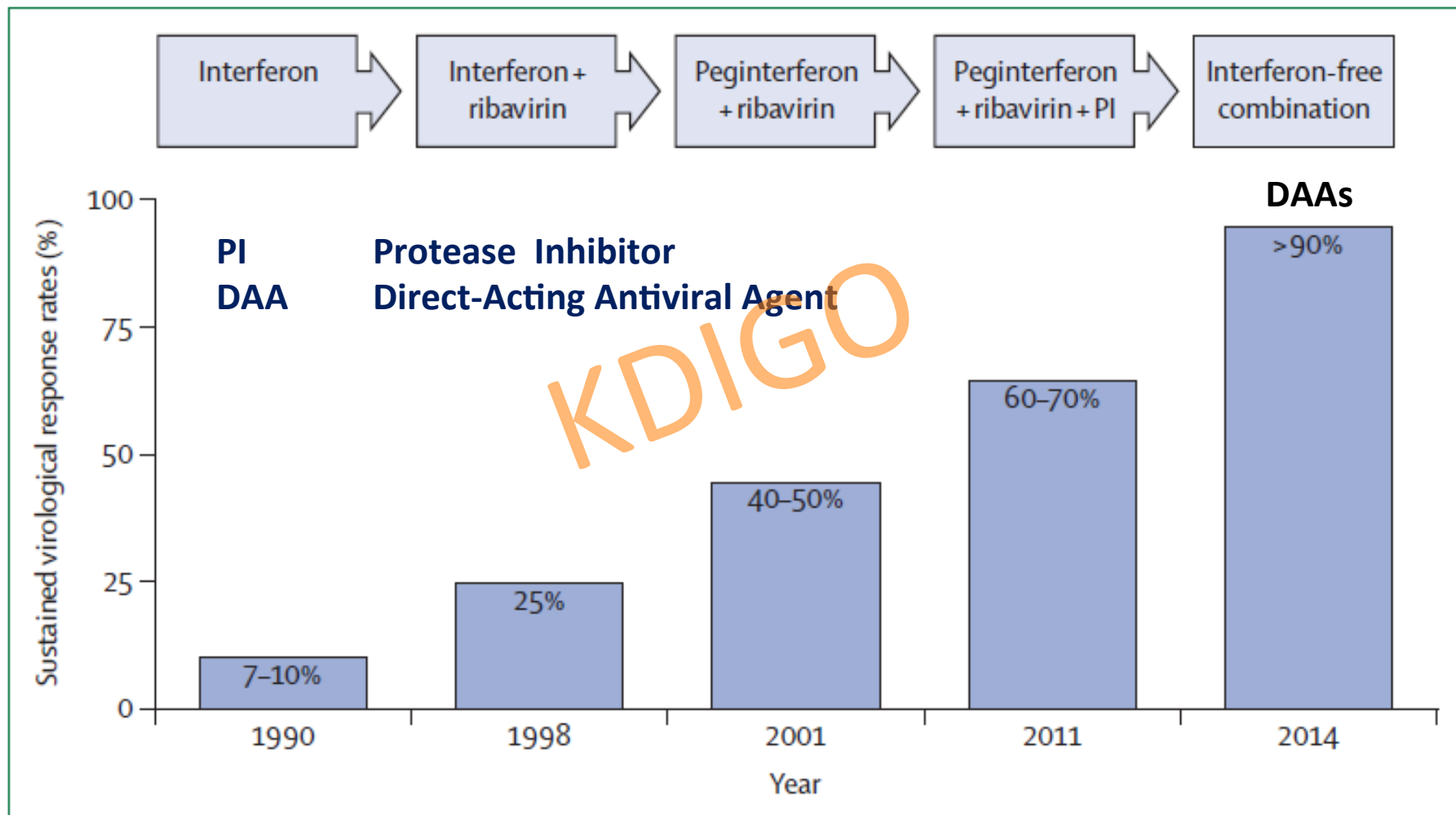
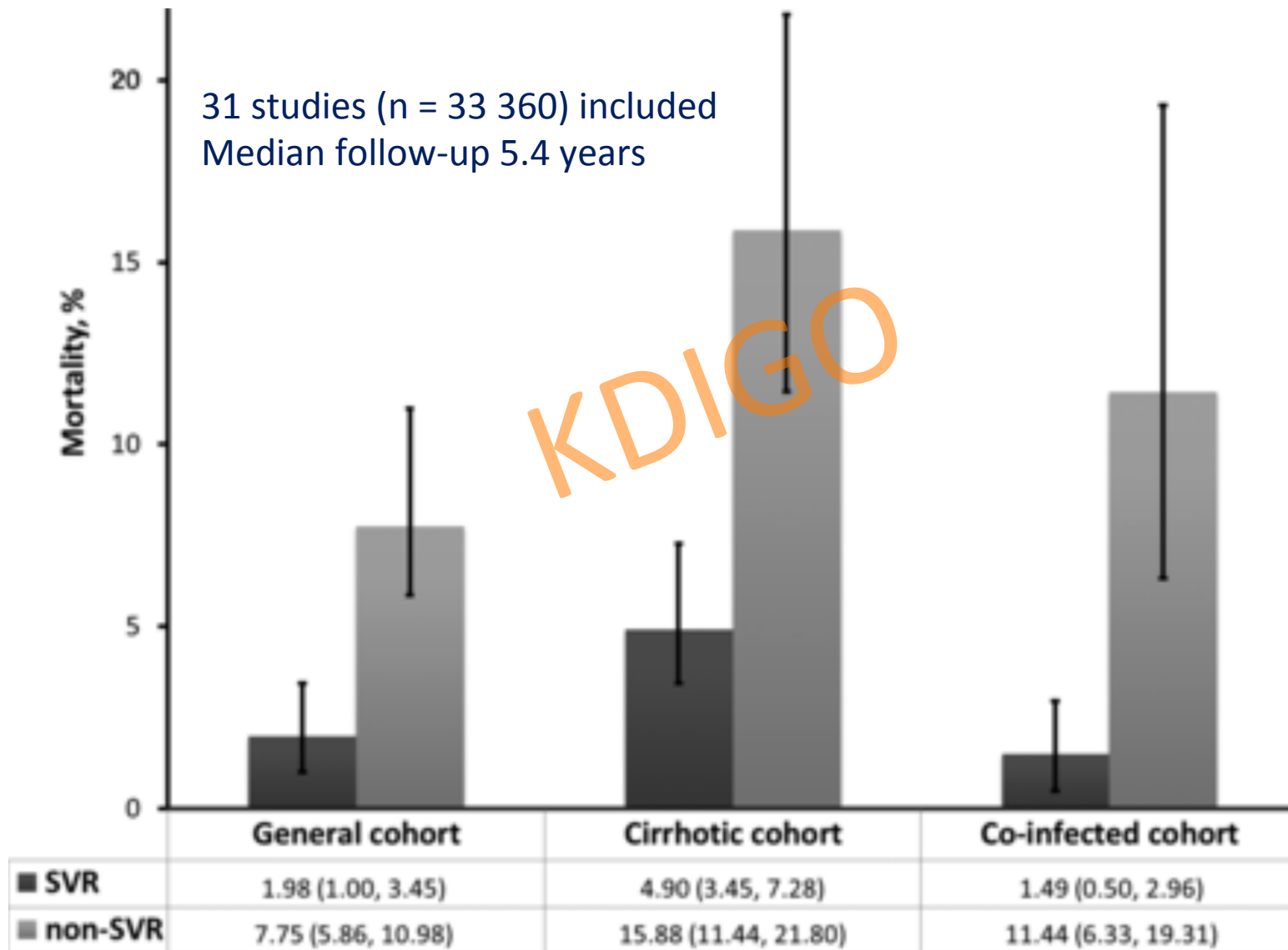


Figure 1: Changes in standard of care for HCV, and improvements in numbers of sustained virological responses

# SVR in HCV and Long-Term Outcomes





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**KDIGO 2017 CLINICAL PRACTICE GUIDELINE  
ON THE PREVENTION, DIAGNOSIS, EVALUATION AND  
TREATMENT OF HEPATITIS C IN CKD**

**DRAFT VERSION: NOT FOR CIRCULATION**

**PUBLIC REVIEW DRAFT  
FEBRUARY 2017**

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# **KDIGO 2017 CLINICAL PRACTICE GUIDELINE ON THE PREVENTION, DIAGNOSIS, EVALUATION AND TREATMENT OF HEPATITIS C IN CKD**

**DRAFT VERSION: NOT FOR CIRCULATION**

- Chapter 1      Detection and Evaluation of HCV in CKD**
- Chapter 2      Treatment of HCV Infection in Patients with CKD**
- Chapter 3      Preventing HCV Transmission in HD Units**
- Chapter 4      Management of HCV-Infected Patients before and  
after Kidney Transplantation**
- Chapter 5      Diagnosis and Management of Kidney Diseases  
Associated with HCV Infection**

# Chapter 1: Detection and Evaluation of HCV in CKD

## HCV Screening of Patients with CKD

- 1.1.1 We recommend screening all patients for HCV infection at the time of initial evaluation of CKD. (1C)
- 1.1.1.1 We recommend using immunoassay followed by nucleic acid testing (NAT). (1A)
- 1.1.2 We recommend screening all patients upon initiation of in-center hemodialysis or upon transferring to another dialysis facility or modality for HCV infection. (1A)
- 1.1.2.1 We recommend using NAT, or immunoassay followed by NAT. (1A)
- 1.1.3 We suggest screening all patients upon initiation of peritoneal dialysis or home hemodialysis for HCV infection. (2D)
- 1.1.4 We recommend screening all patients for HCV infection at the time of evaluation for kidney transplantation. (1A)

# Chapter 1: Detection and Evaluation of HCV in CKD

## Follow-up HCV Screening of in-Center HD Patients

- 1.2.1 We recommend screening in-center hemodialysis patients for HCV every 6 months. (1B)
  - 1.2.1.1 Report any new HCV infection identified in a hemodialysis patient to the appropriate public health authority. (Not Graded)
  - 1.2.1.2 If a new HCV infection is identified in a hemodialysis facility, we recommend all patients within the facility who were NAT negative be tested for HCV infection and the frequency of subsequent HCV testing for these patients be increased. (1A)
  - 1.2.1.3 We recommend hemodialysis patients with resolved HCV infection undergo repeat testing every 6 months using NAT. (1B)
- 1.2.2 We suggest patients have serum alanine aminotransferase (ALT) level checked upon initiation of in-center hemodialysis or upon transfer to another facility or modality.  
We suggest NAT-negative hemodialysis patients have serum alanine aminotransferase (ALT) level checked monthly. (2B)

# Chapter 1: Detection and Evaluation of HCV in CKD

## Liver Testing in Patients with CKD and HCV Infection

- 1.3.1 We recommend HCV-infected patients with CKD be assessed for liver fibrosis. (1A)
- 1.3.2 We recommend an initial non-invasive evaluation of liver fibrosis. (1B)
- 1.3.3 When the cause of liver disease is uncertain or non-invasive testing results are discordant, consider liver biopsy. (Not Graded)
- 1.3.4 We recommend assessment of portal hypertension in CKD patients with suspected advanced fibrosis (F3-4). (1A)

# Chapter 1: Detection and Evaluation of HCV in CKD

## Liver Testing in Patients with CKD and HCV Infection

- 1.3.1 We recommend HCV-infected patients with CKD be assessed for liver fibrosis. (1A)
- 1.3.2 We recommend an initial non-invasive evaluation of liver fibrosis. (1B)
- 1.3.3 When the cause of liver disease is uncertain or non-invasive testing results are discordant, consider liver biopsy. (Not Graded)
- 1.3.4 We recommend assessment of portal hypertension in CKD patients with suspected advanced fibrosis (F3-4). (1A)

# Chapter 1: Detection and Evaluation of HCV in CKD

## Other Testing of Patients with HCV Infection

- 1.4.1 We recommend that all patients be assessed for kidney disease at the time of HCV diagnosis. (1A)
  - 1.4.1.1 Screen for kidney disease with urinalysis and estimated glomerular filtration rate (eGFR). (Not Graded)
- 1.4.2 If there is no evidence of kidney disease at initial evaluation, patients who remain NAT positive should undergo repeat screening for kidney disease. (Not Graded)
- 1.4.3 We recommend that all CKD patients with a history of HCV infection, whether NAT positive or not, be followed regularly to assess for progression of kidney disease. (1A)
- 1.4.4 We recommend that all CKD patients with a history of HCV infection, whether NAT positive or not, be screened and, if appropriate, vaccinated for HAV and HBV, and screened for HIV. (1A)

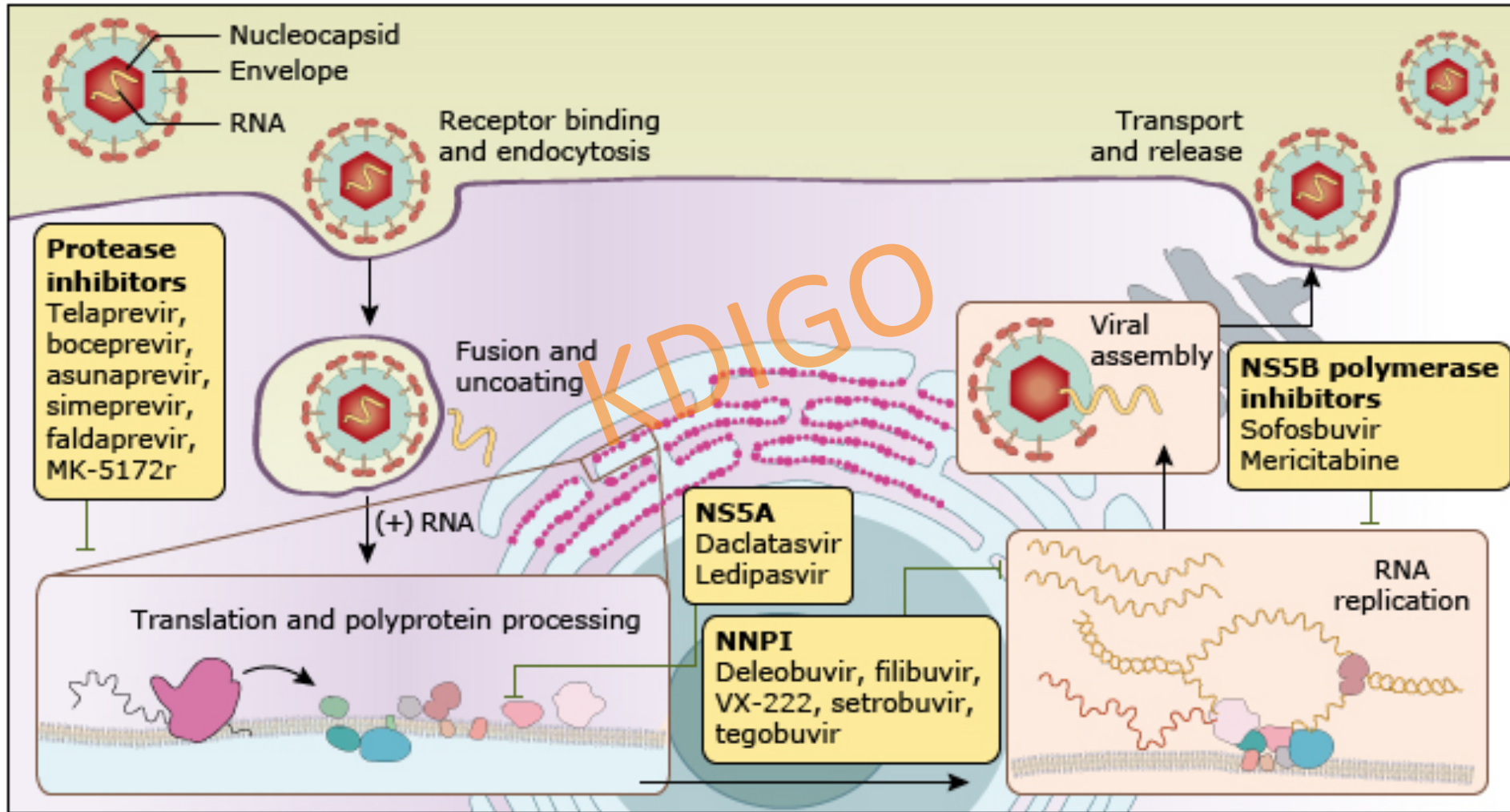


# **KDIGO 2017 CLINICAL PRACTICE GUIDELINE ON THE PREVENTION, DIAGNOSIS, EVALUATION AND TREATMENT OF HEPATITIS C IN CKD**

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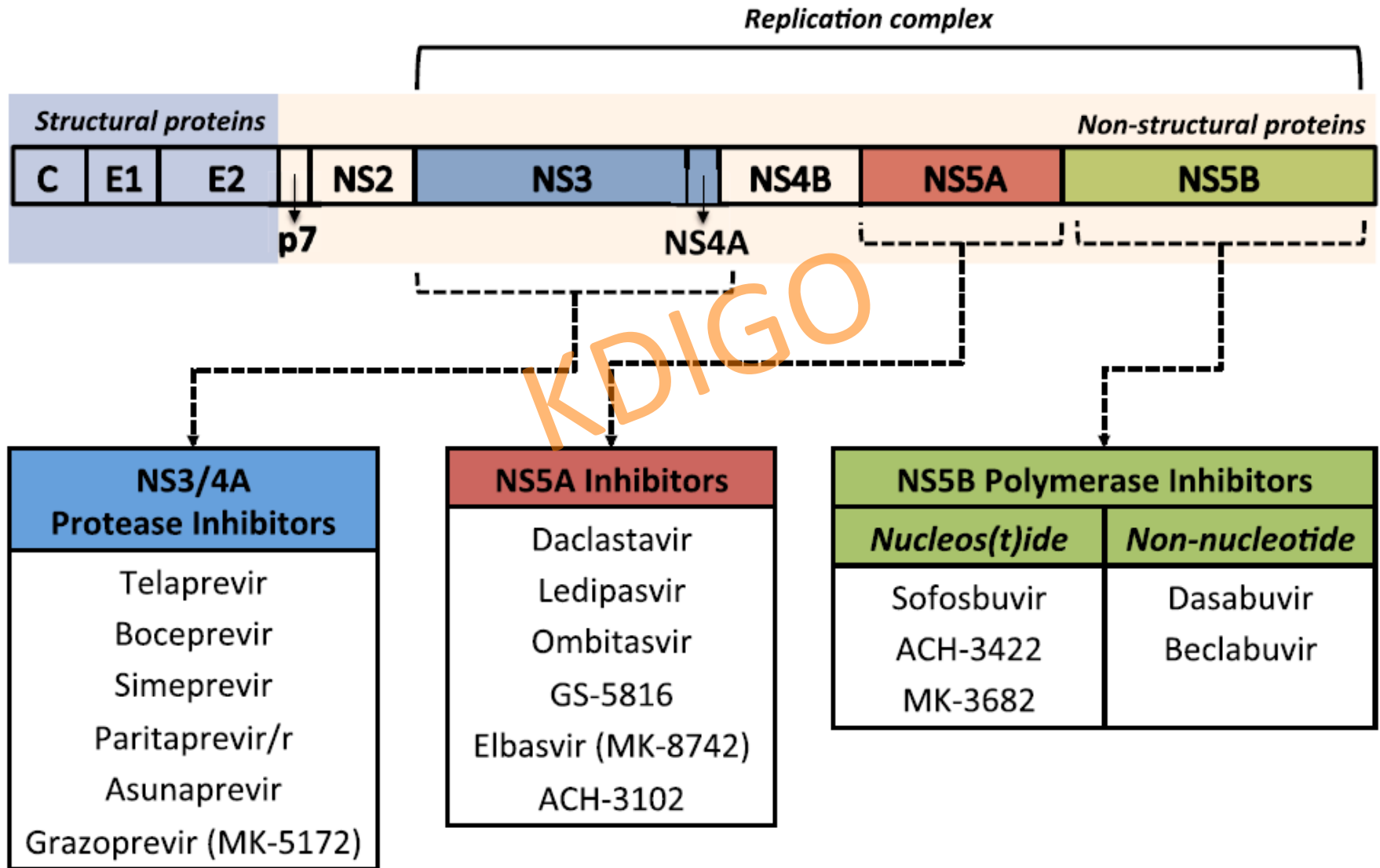
# DAA for HCV: Site of Action



NS5A: nonstructural protein 5A; NS5B: nonstructural protein 5B; NNPI: non-nucleoside polymerase inhibitor



# DAA for HCV: Molecular Targets



# DAA for HCV: Summary by Class

	- PREVIR	-ASVIR	-BUVIR	
Site of Action	NS3 Protease inhibitors	NS5A inhibitors	Nucleos(t)ide NS5B Polymerase inhibitors	Non-nucleoside NS5B Polymerase inhibitors
Potency	High <u>1<sup>st</sup> generation</u> variable genotypes  <u>2<sup>nd</sup> generation</u> Increasingly pangenotypic	High Increasingly pangenotypic	Moderate-High  Pangenotypic	Variable  Variable among HCV genotypes
Barriers to resistance	Low  1a < 1b	Low  1a < 1b	High  1a = 1b	Very low  1a < 1b
Drug interaction potential	High	Low to moderate	Minimal	Variable

NS5A: nonstructural protein 5A; NS5B: nonstructural protein 5B; NNPI: non-nucleoside polymerase inhibitor

# Use of DAAs in CKD and ESRD

Stage of CKD	SOF	SOF/LDV	SIM	PTV/OMB DSB	DAC
Stage 1 GFR > 90 ml/min	Y	Y	Y	Y	Y
Stage 2 (mild) GFR 60–89 ml/min	Y	Y	Y	Y	Y
Stage 3 (moderate) GFR 30–59 ml/min	Y	Y	Y	Y	Y
Stage 4 (severe) GFR 15–29 ml/min	N	N	Y	Y	Y
Stage 5 (renal failure) GFR < 15 ml/min or dialysis	N	N	N	N	Y

CKD, chronic kidney disease; LDV, ledipasvir; SOF, sofosbuvir.

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# Chapter 2: Treatment of HCV Infection in CKD

- 2.1 We recommend that all CKD patients infected with HCV be evaluated for antiviral therapy. (1A)
  - 2.1.1 We recommend an interferon-free regimen. (1A)
  - 2.1.2 We recommend choice of specific regimen be based on HCV genotype (and subtype), viral load, drug-drug interactions, eGFR category, stage of hepatic fibrosis, kidney and liver transplant candidacy, and comorbidities. (1A)
  - 2.1.3 Treat kidney transplant candidates in collaboration with the transplant center to optimize timing of therapy. (Not Graded)

# Chapter 2: Treatment of HCV Infection in CKD

- 2.2 We recommend that patients with eGFR > 30 ml/min/1.73 m<sup>2</sup> be treated with any licensed DAA-based regimen. (1A)

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# AASLD: HCV Treatment in CKD 1-3

## Recommended Dosage Adjustments for Patients with Mild to Moderate Renal Impairment

RECOMMENDED

RATING 

For patients with mild to moderate renal impairment (eGFR 30 mL/min-80 mL/min), no dosage adjustment is required when using daclatasvir (60 mg\*), fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg), fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg), or fixed-dose combination of paritaprevir (150 mg)/ritonavir (100 mg)/ombitasvir (25 mg) with (or without for HCV genotype 4 infection) twice-daily dosed dasabuvir (250 mg), simeprevir (150 mg), or sofosbuvir (400 mg) to treat or retreat HCV infection in patients with appropriate genotypes.

I, A


# Chapter 2: Treatment of HCV Infection in CKD

- 2.3** We recommend that patients with eGFR < 30 ml/min/1.73 m<sup>2</sup> be treated with DAA based regimens, preferentially ribavirin-free (1B), as follows:
- 2.3.1** We recommend for HCV genotype 1 subtype A the use of grazoprevir/elbasvir (1A) and for HCV genotype 1 subtype B, grazoprevir/elbasvir (1A) or the “PROD” regimen (the combination of ritonavir-boosted paritaprevir, ombitasvir and dasabuvir) (1B) for 12 weeks.
- 2.3.2** We suggest for HCV genotype 4 the use of grazoprevir/elbasvir or the “2D” regimen (the combination of ritonavir-boosted paritaprevir, ombitasvir regimen) for 12 weeks. (2D)
- 2.3.3** Treat patients with HCV genotypes 2, 3, 5, and 6 on a case-by-case basis. (*Not Graded*)  
*Grz/Elb and PROD regimens not active on these genotypes*

# AASLD: HCV Treatment in CKD 5, 5D

Recommended Regimens by evidence level and alphabetically for:

**Patients with Severe Renal Impairment, Including Severe Renal Impairment (eGFR <30 mL/min) or End-Stage Renal Disease (ESRD)**

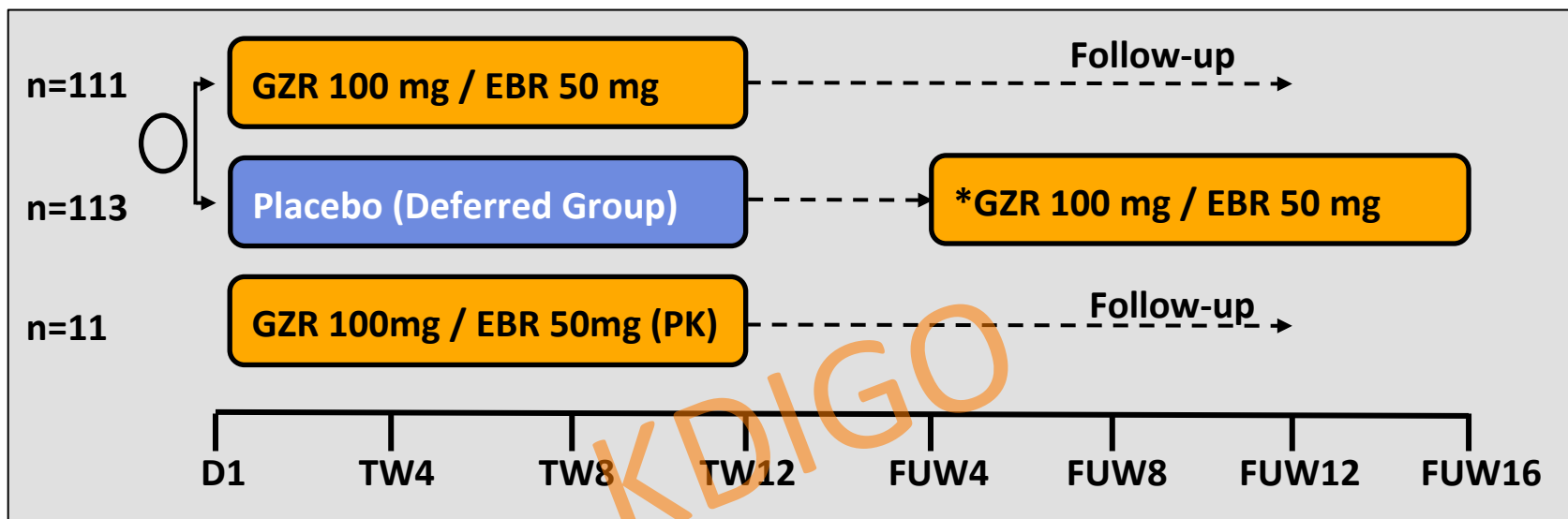
RECOMMENDED	DURATION	RATING 
For patients with genotype 1a, or 1b, or 4 infection and eGFR below 30 mL/min, for whom treatment has been elected, daily fixed-dose combination of elbasvir (50 mg)/grazoprevir (100 mg) <b>(C-SURFER regimen, LANCET 2015)</b>	12 weeks	I, B
For patients with genotype 1b infection and eGFR below 30 mL/min, for whom treatment has been elected, daily fixed-dose combination of paritaprevir (150 mg)/ritonavir (100 mg)/ombitasvir (25 mg) plus twice-daily dosed dasabuvir (250 mg) <b>(PROD regimen, J Virology 2017)</b>	12 weeks	IIb, B
For patients with HCV genotype 2, 3, 5, or 6 infection and eGFR below 30 mL/min, for whom the urgency to treat is high, PEG-IFN and dose-adjusted ribavirin** (200 mg daily)	-	IIb, B

\* The dose of daclatasvir may need to increase or decrease when used concomitantly with cytochrome P450 3A/4 inducers and inhibitors, respectively. Please refer to the prescribing information and the section on [HIV/HCV coinfection](#) for patients on antiretroviral therapy.

\*\* Caution is recommended in this group, owing to the potential for hemolytic anemia due to impaired renal clearance in this population, and ribavirin should be restricted to those with a baseline hemoglobin concentration above 10 g/dL.



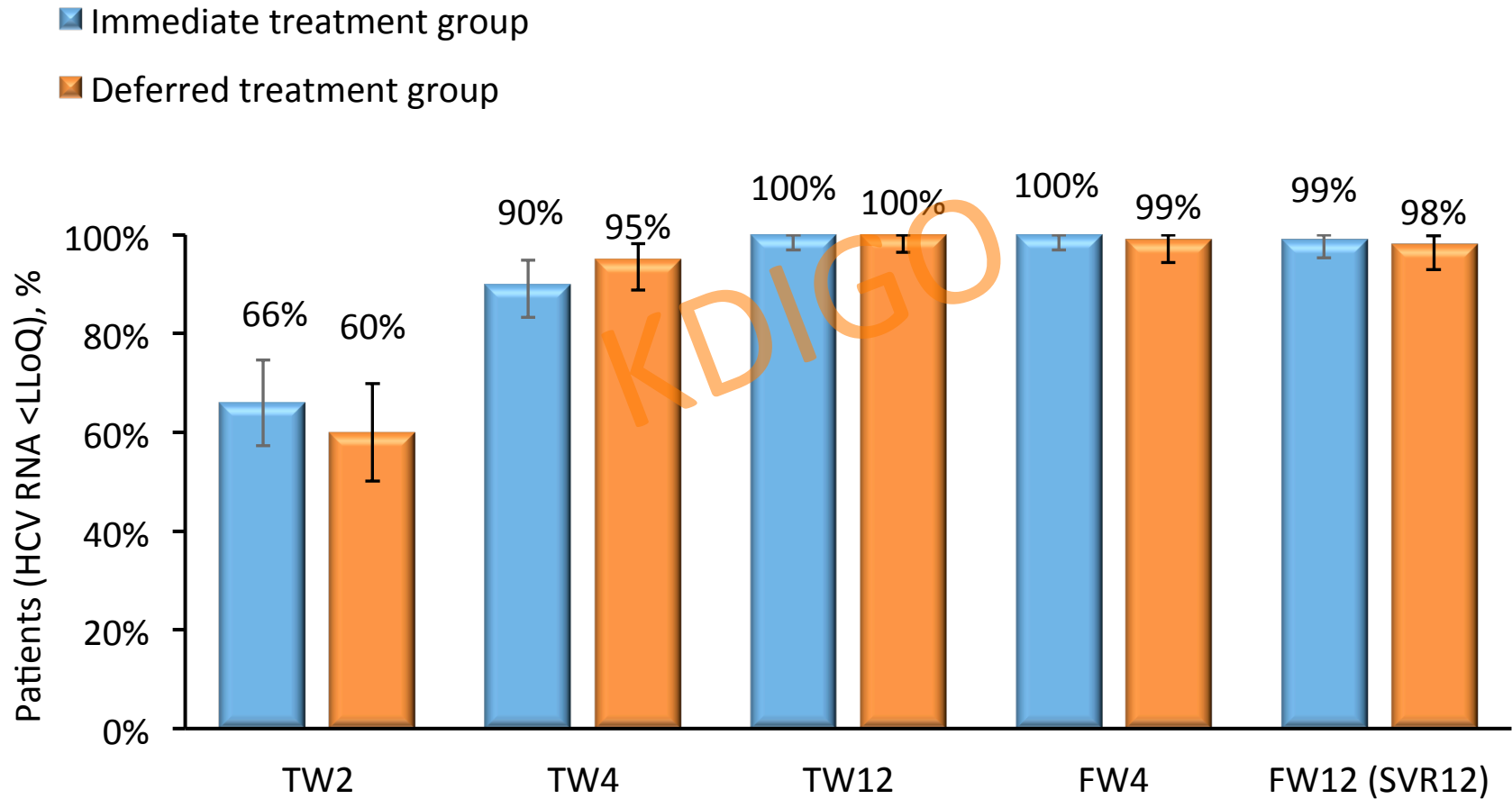
# C-SURFER in CKD 4-5/ESRD



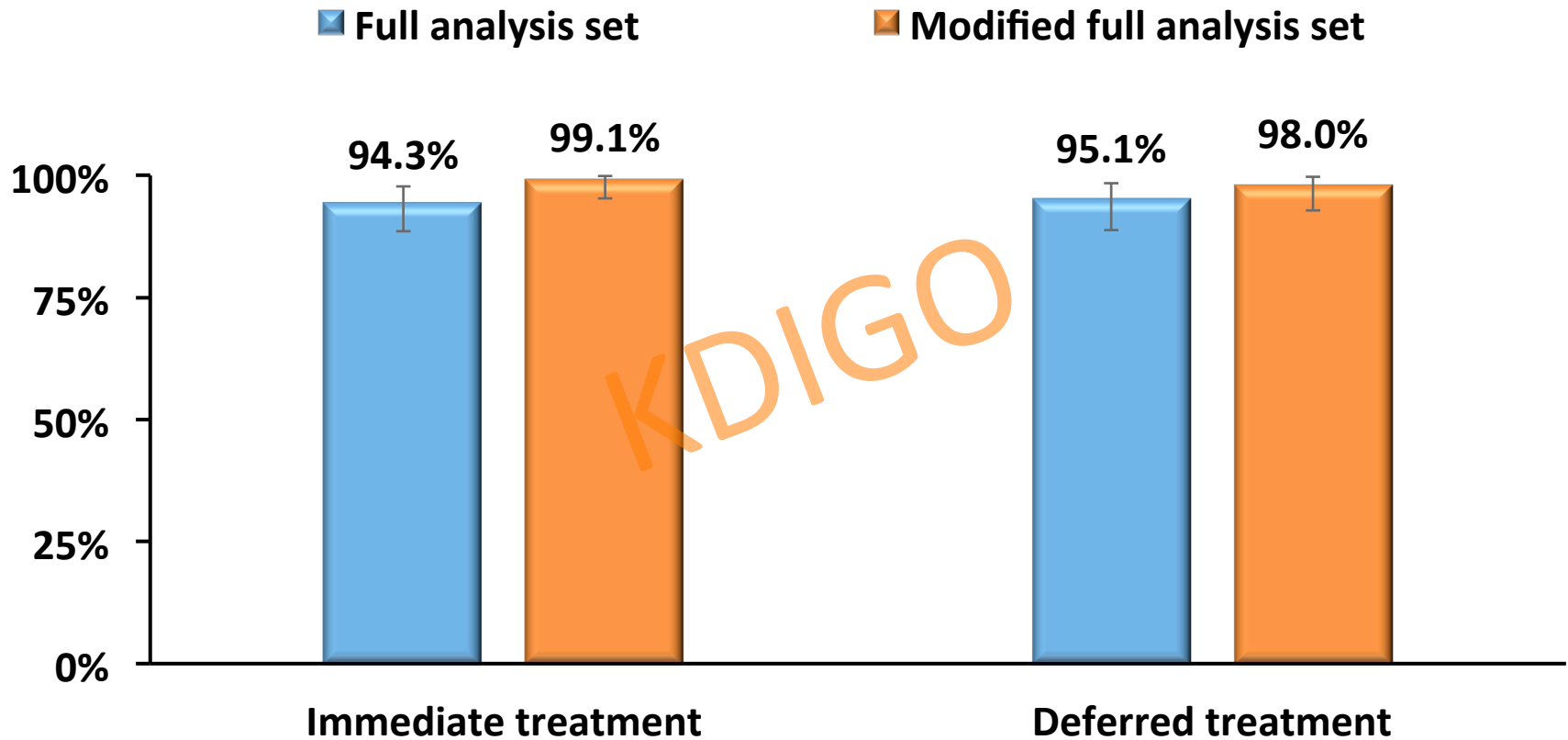
GZR: Grazoprevir EBR: Elbasvir

- **Primary efficacy outcome was a comparison of sustained virological response at 12 weeks (SVR12) after the end of therapy**
- HCV Genotype 1 infection ( 52% 1a, 48% 1b). No Liver biopsy required.
- Treatment-naïve and treatment-experienced patients:
  - CKD stage 4/5
  - Hemodialysis-Dependent (76%)
- All HBV and HIV negative.

# C-SURFER in CKD 4-5/ESRD: Virologic Response on Treatment



# C-SURFER in CKD 4-5/ESRD: Cure Rates



# C-SURFER in CKD 4-5/ESRD: Adverse Event Rates

	GZR/EBR (ITG) (n = 111)	GZR/EBR (DTG) (n = 102)	Placebo (DTG) (n = 113)	Difference in % Estimate ITG vs placebo (95% CI)
AEs, <sup>a</sup> n (%)	84 (75.7)	61 (59.8)	95 (84.1)	-8.3 (-18.9, 2.2)
Headache	19 (17.1)	7 (6.9)	19 (16.8)	0.3 (-9.6, 10.4)
Nausea	17 (15.3)	10 (9.8)	18 (15.9)	-0.6 (-10.3, 9.1)
Fatigue	11 (9.9)	9 (8.8)	17 (15.0)	-5.1 (-14.1, 3.7)
Insomnia	7 (6.3)	2 (2.0)	12 (10.6)	-4.3 (-12.2, 3.2)
Dizziness	6 (5.4)	5 (4.9)	18 (15.9)	<b>-10.5 (-19.1, -2.6)</b>
Diarrhea	6 (5.4)	5 (4.9)	15 (13.3)	<b>-7.8 (-16.1, -0.2)</b>
Serious AEs, n (%)	16 <sup>b</sup> (14.4)	13 <sup>c</sup> (12.7)	19 (16.8)	-2.4 (-12.1, 7.3)
Discontinued due to AE, n (%)	0 (0)	3 (2.9)	5 (4.4)	-4.4 (10.0, -1.0)
Deaths, n (%)	1 (0.9)	0 (0)	3 (2.7)	-1.8 (-6.7, 2.5)

# Chapter 2: Treatment of HCV Infection in CKD

## Transplantation

- 2.4 We recommend that all kidney transplant recipients infected with HCV be evaluated for treatment. (1B)
- 2.4.1 We recommend treatment with a DAA-based regimen. (1A)
- 2.4.2 We recommend the choice of regimen be based on HCV genotype (and subtype), viral load, drug-drug interactions, eGFR category, stage of hepatic fibrosis, liver transplant candidacy, and comorbidities. (1A)
- 2.4.3 We recommend that treatment with interferon be avoided. (1A)

# RCT: Ledipasvir-Sofosbuvir in Transplant Response Rates

Table 2. Response During and After Treatment

Variable	Ledipasvir-Sofosbuvir		Total (n = 114)
	12 wk (n = 57)	24 wk (n = 57)	
<b>HCV RNA level less than the LLOQ during treatment, n/N (%)</b>			
Baseline	0/57 (0)	0/57 (0)	0/114 (0)
Week 1	9/57 (16)	7/57 (12)	16/114 (14)
Week 2	31/57 (54)	33/57 (58)	64/114 (56)
Week 4	50/57 (88)	52/57 (91)	102/114 (89)
Week 8	56/56 (100)*	57/57 (100)	113/113 (100)
Week 12	56/56 (100)*	57/57 (100)	113/113 (100)
Week 16	NA	57/57 (100)	57/57 (100)
Week 20	NA	57/57 (100)	57/57 (100)
Week 24	NA	57/57 (100)	57/57 (100)
<b>HCV RNA level less than the LLOQ after end of treatment, n/N (% [95% CI])</b>			
SVR4	57/57 (100 [94-100])	57/57 (100 [94-100])	114/114 (100 [97-100])
SVR12	57/57 (100 [94-100])	57/57 (100 [94-100])	114/114 (100 [97-100])
<b>Overall virologic failure (relapse), n/N (%)</b>	0/0 (0)	0/0 (0)	0/0 (0)

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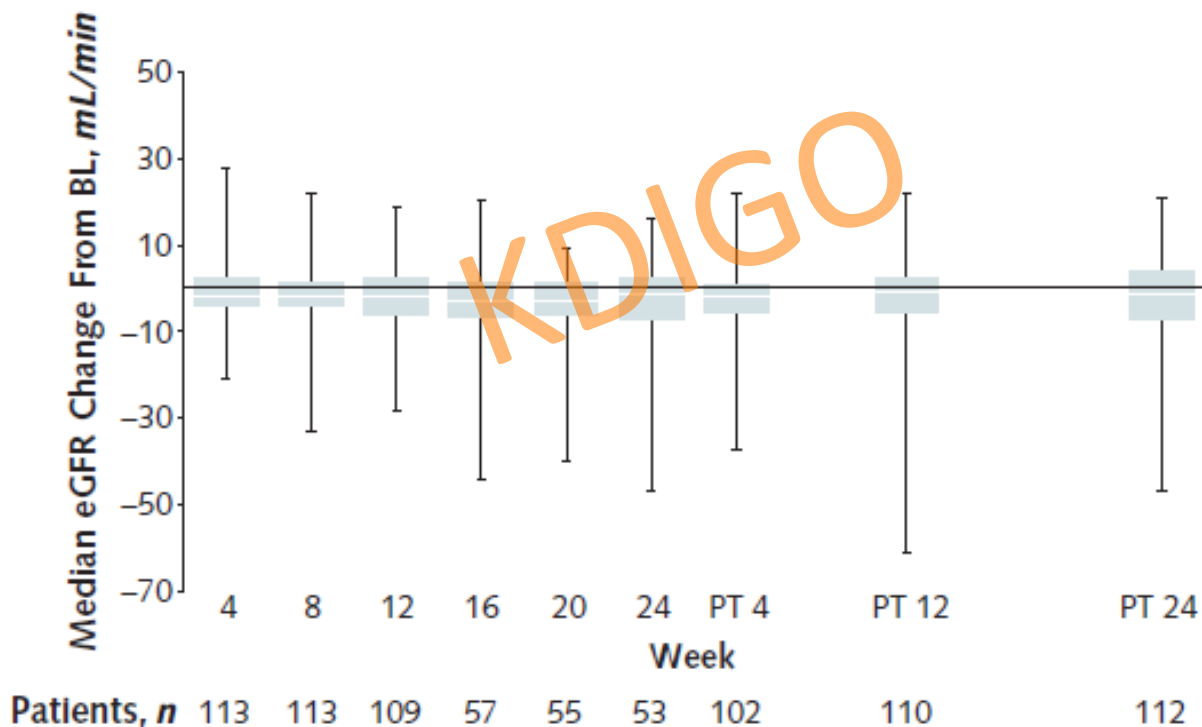
HCV = hepatitis C virus; LLOQ = lower limit of quantification; NA = not available; SVR4 = sustained virologic response at 4 wk; SVR12 = sustained virologic response at 12 wk.

\* Excluding 1 patient in the 12-wk group who discontinued study treatment early at week 4 because of a serious adverse event. This patient achieved SVR12.

- HCV Genotype 1 or 4 infection
- Median of 10 years after kidney transplantation, Cirrhosis 15%
- Median creatinine clearance by CG: 56 ml/min
- Regimens: Tacrolimus 47%, Cyclosporin A 39%, MMF 61%, Steroids 98%

# RCT: Ledipasvir-Sofosbuvir in Transplant Changes in GFR

**Figure 1.** Median change in eGFR by Cockcroft-Gault equation.



The horizontal line is the median value, the box is interquartile range, and the whiskers show overall range. BL = baseline; eGFR = estimated glomerular filtration rate; PT = posttreatment.

# Chapter 2: Treatment of HCV Infection in CKD

## Transplantation

- 2.5 We recommend pre-treatment assessment for drug-drug interactions between the DAA-based regimen and other concomitant medications including immunosuppressive drugs in kidney transplant recipients. (1A)
- 2.5.1 We recommend that calcineurin inhibitor levels be monitored during and after DAA treatment. (1B)



# Drug-Drug Interactions: Immunosuppressive Medications

**Table 1.** Drug interactions with currently available direct acting antiviral agent

	SOF	SOF/LDV	SIM	PTV/OMB DSV	DCV
Tacrolimus	NI	NI	NI	I, reduce TAC to 0.5 1–2 weeks	NI
Cyclosporine	NI	NI	I, C	I, reduce CYA to 20%	NI
Sirolimus/everolimus	NI	NI	NI	I, no data	NI
Mycophenolate/mycophenolic acid	NI	NI	NI	I, reduce MMF by 50%	NI
Azathioprine	NI	NI	NI	NI	NI

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C, contraindicated; CYA, cyclosporin; I, interaction; NI, no interaction demonstrated or expected; LDV, ledipasvir; MMF, mycophenolate mofetil; PTV/OMB DSB, paritaprevir/ombitasvir, Dasabuvir; SIM, simeprevir; SOF, sofosbuvir; TAC, tacrolimus.

# Drug-Drug Interactions: Immunosuppressive Medications

Table 1. Drug-drug interactions between HCV DAAs and immunosuppressants

	SOF	SOF/ LDV	SOF/ VEL	3D	GZR/ EBR	DCV	SIM
Azathioprine	◆	◆	◆	◆	◆	◆	◆
Cyclosporine	◆	◆	◆	■	●	◆	●
Etanercept	◆	◆	◆	◆	■	◆	◆
Everolimus	◆	■	■	●	■	■	■
Mycophenolate	◆	◆	◆	■	◆	◆	◆
Sirolimus	◆	◆	◆	■	■	◆	■
Tacrolimus	◆	◆	◆	■	■	◆	■

SOF, sofosbuvir; SOF/LDV, sofosbuvir plus ledipasvir; SOF/VEL, sofosbuvir plus velpatasvir; 3D, ritonavir-boosted paritaprevir, plus ombitasvir and dasabuvir; GZR/EBR, grazoprevir plus elbasvir; DCV, daclatasvir; SIM, simeprevir.

## Colour legend

- ◆ No clinically significant interaction expected.
- Potential interaction which may require a dosage adjustment, altered timing of administration or additional monitoring.
- These drugs should not be co-administered.

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# **KDIGO 2017 CLINICAL PRACTICE GUIDELINE ON THE PREVENTION, DIAGNOSIS, EVALUATION AND TREATMENT OF HEPATITIS C IN CKD**

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# Chapter 3: Preventing HCV Transmission in HD Units

- 3.1 We recommend that hemodialysis facilities adhere to standard infection-control procedures including hygienic precautions that effectively prevent transfer of blood and blood-contaminated fluids between patients to prevent transmission of blood-borne pathogens (1A) 3.1.1 We recommend regular observational audits of infection control procedures in hemodialysis units. (1C)**
- 3.1.2 We recommend not using dedicated dialysis machines for HCV-infected patients. (1D)**
- 3.1.3 We suggest not isolating HCV-infected hemodialysis patients. (2C)**
- 3.1.4 We suggest that the dialyzers of HCV-infected patients can be reused if there is adherence to standard infection-control procedures. (2D)**

# Chapter 3: Preventing HCV Transmission in HD Units

- 3.2 We recommend hemodialysis centers examine and track all HCV test results to identify new cases of HCV infections in their patients. (1B)**
- 3.2.1 We recommend aggressive measures be taken to improve hand hygiene (and proper glove use), injection safety, and environmental cleaning and disinfection when a new case of HCV is identified that is likely to be dialysis-related. (1A)**
- 3.3 Strategies to prevent HCV transmission within hemodialysis units should prioritize adherence to standard infection control practices and should not primarily rely upon the treatment of HCV-infected patients. (Not Graded)**



# **KDIGO 2017 CLINICAL PRACTICE GUIDELINE ON THE PREVENTION, DIAGNOSIS, EVALUATION AND TREATMENT OF HEPATITIS C IN CKD**

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# Chapter 4: Management of HCV Infected Patients Before and After Kidney Transplantation

- 4.1 We recommend kidney transplantation as the best therapeutic option for patients with end-stage renal disease (ESRD) irrespective of presence of HCV infection. (1A)**
- 4.2 We suggest that all HCV-infected kidney-transplant candidates be evaluated for severity of liver disease and, if indicated, portal hypertension prior to acceptance for an isolated kidney or combined kidney-liver transplantation. (2D)**
- 4.2.1 We recommend that HCV-infected patients with compensated cirrhosis (without portal hypertension) undergo isolated kidney transplantation. (1B)**
- 4.2.2 We recommend to refer HCV-infected patients with decompensated cirrhosis for combined liver-kidney transplantation (1B) and to defer HCV treatment until after transplantation. (1D)**

# Chapter 4: Management of HCV Infected Patients Before and After Kidney Transplantation

- 4.3** Timing of HCV treatment in relation to kidney transplantation (before vs. after) should be based on donor type (living vs. deceased donor), waitlist times by donor type, center-specific policies for using or not kidneys from HCV-infected deceased donors, HCV genotype, and severity of liver fibrosis. *(Not Graded)*
- 4.3.1** For all HCV-infected patients who are candidates for kidney transplantation, we recommend they be considered for antiviral therapy, either before or after transplantation. *(1A)*
- 4.3.2** For HCV-infected kidney-transplant candidates with a living kidney donor, we suggest they can be considered for treatment before or after transplantation according to HCV genotype and anticipated timing of transplantation. *(2D)*
- 4.3.3** We suggest that, if receiving a kidney from a HCV-positive donor improves the chances for transplantation, the HCV RNA-positive patient can undergo transplantation with a HCV-positive kidney and be treated for HCV infection after transplantation. *(2D)*



# Chapter 4: Management of HCV Infected Patients Before and After Kidney Transplantation

- 4.4.1 We recommend all kidney donors be screened for HCV infection with both immunoassay and NAT (if NAT is available). (1A)
- 4.4.2 We recommend that transplantation of kidneys from HCV RNA-positive donors be directed to recipients with positive NAT. (1A)
- 4.4.3 After the assessment of liver fibrosis, potential HCV-positive living kidney donors who do not have cirrhosis should undergo HCV treatment before donation; they can be accepted for donation if they achieve SVR and remain otherwise eligible to be a donor. (*Not Graded*)

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4.5 We suggest that all conventional current induction and maintenance immunosuppressive regimens can be considered for use in HCV-infected kidney transplant recipients. (2C)

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4.6 *Management of HCV-related complications in kidney transplant recipients (not shown)*



# **KDIGO 2017 CLINICAL PRACTICE GUIDELINE ON THE PREVENTION, DIAGNOSIS, EVALUATION AND TREATMENT OF HEPATITIS C IN CKD**

**DRAFT VERSION: NOT FOR CIRCULATION**

- Chapter 1**      **Detection and Evaluation of HCV in CKD**
- Chapter 2**      **Treatment of HCV Infection in Patients with CKD**
- Chapter 3**      **Preventing HCV Transmission in HD Units**
- Chapter 4**      **Management of HCV-Infected Patients before and  
after Kidney Transplantation**
- Chapter 5**      **Diagnosis and Management of Kidney Diseases  
Associated with HCV Infection**

# Chapter 5: Diagnosis and Management of Kidney Diseases Associated with HCV Infection

- 5.1 We recommend that a kidney biopsy be performed in HCV-infected patients with clinical evidence of glomerular disease. (1B)
- 5.2 We recommend that patients with HCV-associated glomerular disease be treated for HCV. (1A)
  - 5.2.1 We recommend that patients with HCV-related glomerular disease showing stable kidney function and/or non-nephrotic proteinuria be treated initially with DAA. (1B)
  - 5.2.2 We recommend that patients with cryoglobulinemic flare, nephrotic syndrome, or progressive kidney failure be treated with both DAA and immunosuppressive agents and/or plasma-exchange. (1B)
  - 5.2.3 We recommend immunosuppressive therapy in patients with histologically active HCV-associated glomerular disease who do not respond to antiviral therapy, particularly those with cryoglobulinemic kidney disease. (1A)
    - 5.2.3.1 We recommend rituximab as the first-line immunosuppressive treatment. (1B)

# Summary

- Therapy for Hepatitis C Virus infection in CKD/ESRD patients and transplant recipients has been revolutionized towards a cure with newer agents and regimens.
- Many regimens are well tolerated but caution should be exercised given:
  - Need to verify genotype for appropriate regimen
  - Need to avoid certain drugs in CKD 4-5/ESRD (eg. Sofosbuvir)
  - Need to check for drug-drug interactions, especially in transplant patients
- Transplantation in context of Hepatitis C infection, donor and/or recipient, requires deliberation and careful considerations.
- Coordination with hepatologists and infectious disease specialists is critical for successful and safe therapy.
- Upcoming KDIGO guidelines offer a comprehensive up-to-date summary and reference on Hepatitis C infection in renal patients.

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