Table S1: Summary Table
Diagnostic testing for liver fibrosis (by biopsy)
Categorical outcomes

PMID	Author	Year	Type of article	Study design	Population	Sample size	Description of Diagnostic Test		Timpoint
							Diagnostic test	Reference standard (Sensitivity threshold)	
20357753	**Liu CH., Liang CC., Liu CJ., Hsu SJ., Lin JW., Chen SI., Hung PH., Tsai HB., Lai MY., Chen PJ., Chen JH., Chen DS., Kao JH.**	2010	Peer-reviewed publication	Cohort study, prospective	HD	279	APRI (≥0.30)	Liver biopsy (F2-F4)	**0 months**
						175			**12-18 months**
					HD	279	APRI (≥0.40)	Liver biopsy (F2-F4)	**0 months**
						175			**12-18 months**
					HD	279	APRI (≥0.60)	Liver biopsy (F2-F4)	**0 months**
						175			**12-18 months**
					HD	279	APRI (≥0.80)	Liver biopsy (F2-F4)	**0 months**
						175			**12-18 months**
					HD	279	APRI (≥0.95)	Liver biopsy (F2-F4)	**0 months**
						175			**12-18 months**
17634962	**Schiavon LL., Schiavon JL., Filho RJ., Sampaio JP., Lanzoni VP., Silva AE., Ferraz ML.**	2007	Peer-reviewed publication	Cross-sectional study	HD	203	APRI (≥0.4)	Liver biopsy (F2-F4)	**nd**
							APRI (≥0.95)	Liver biopsy (F2-F4)	

PMID	Author	Year	Type of article	Study design	Population	Sample size	Description of Diagnostic Test		
							Diagnostic test	Reference standard (Sensitivity threshold)	Timpoint
							APRI (>0.55)	Liver biopsy (F3-F4)	
							APRI (≥1.00)	Liver biopsy (F3-F4)	
19758273	**Schiavon LL., Carvalho-Filho RJ., Narciso-Schiavon JL., Pinheiro SR., Barbosa DV., Lanzoni VP., Ferraz ML., Silva AE.**	2010	Peer-reviewed publication	Cross-sectional study	Transplant	102	APRI (>0.50)	Liver biopsy (F2-F4)	**nd**
							APRI (>1.50)	Liver biopsy (F2-F4)	
ATC-abstract 596	**A. Brar, M. Salifu, M. Rampal, N. Sumrani, D. John, F. Tedla.**	2012	Abstract	Cross-sectional study	HD	26	APRI	Liver biopsy (F2-F4)	**nd**
24353319	**Jiang Y., Huang E., Mehrnia A., Kamgar M., Pham PT., Ogunorunyinka O., Brown I., Danovitch GM., Bunnapradist S.**	2014	Peer-reviewed publication	Cross-sectional study	HD? (Transplant candidates)	210	APRI (≥0.4)	Liver biopsy (F3-F4)	**nd**
							APRI (>0.95)	Liver biopsy (F3-F4)	
21393486	**Liu CH., Liang CC., Huang KW., Liu CJ., Chen SI., Lin JW., Hung PH., Tsai HB., Lai MY., Chen PJ., Chen JH., Chen DS., Kao JH.**	2011	Peer-reviewed publication	Cross-sectional study	HD	304	APRI (1.5)	Liver biopsy (≥F2)	**nd**
							APRI (0.55)	Liver biopsy (≥F2)	**nd**
							APRI (0.5)	Liver biopsy (≥F2)	**nd**
							APRI (1.75)	Liver biopsy (F3)	**nd**
							APRI (0.75)	Liver biopsy (F3)	**nd**

PMID	Author	Year	Type of article	Study design	Population	Sample size	Description of Diagnostic Test		
							Diagnostic test	Reference standard (Sensitivity threshold)	Timpoint
16371924	**Varaut A., Fontaine H., Serpaggi J., Verkarre V., Vallet-Pichard A., Nalpas B., Imbertbismuth F., Lebray P., Pol S.**	2005	Peer-reviewed publication	Cross-sectional study	HD & Transplant	110	Fibrotest (>0.6)	Liver biopsy (F2-F4)	**nd**
							Fibrotest (≥0.2)	Liver biopsy (F2-F4)	
							Fibrotest (>0.6)	Liver biopsy (F3-F4)	
							Fibrotest (≥0.2)	Liver biopsy (F3-F4)	
					HD	50	Fibrotest (>0.6)	Liver biopsy (F2-F4)	
							Fibrotest (≥0.2)	Liver biopsy (F2-F4)	
							Fibrotest (>0.6)	Liver biopsy (F3-F4)	
							Fibrotest (≥0.2)	Liver biopsy (F3-F4)	
					Transplant	60	Fibrotest (>0.6)	Liver biopsy (F2-F4)	
							Fibrotest (≥0.2)	Liver biopsy (F2-F4)	
							Fibrotest (>0.6)	Liver biopsy (F3-F4)	
							Fibrotest (≥0.2)	Liver biopsy (F3-F4)	

PMID	Author	Year	Type of article	Study design	Population	Sample size	Description of Diagnostic Test		
							Diagnostic test	Reference standard (Sensitivity threshold)	Timpoint
20847572	**Canbakan M., Senturk H., Canbakan B., Toptas T., Tabak O., Ozaras R., Tabak F., Balcı H., Sut N., Ozbay G.**	2011	Peer-reviewed publication	Cross-sectional study	HD	33	Fibrotest (>0.19)	Liver biopsy (F2-F4)	**nd**
							Fibrotest (>0.6)	Liver biopsy (F2-F4)	
21393486	**Liu CH., Liang CC., Huang KW., Liu CJ., Chen SI., Lin JW., Hung PH., Tsai HB., Lai MY., Chen PJ., Chen JH., Chen DS., Kao JH.**	2011	Peer-reviewed publication	Cross-sectional study	HD	304	Fibroscan (8.8)	Liver biopsy (F2-F4)	**nd**
							Fibroscan (7.1)	Liver biopsy (F2-F4)	**nd**
							Fibroscan (5.3)	Liver biopsy (F2-F4)	**nd**
							Fibroscan (9.5)	Liver biopsy (F3-4)	**nd**
							Fibroscan (9.6)	Liver biopsy (F3-4)	**nd**
							Fibroscan (8.3)	Liver biopsy (F3-4)	**nd**
ATC-abstract 596	**A. Brar, M. Salifu, M. Rampal, N. Sumrani, D. John, F. Tedla.**	2012	Abstract	Cross-sectional study	HD	26	FIB-4	Liver biopsy (F2-F4)	
20847572	**Canbakan M., Senturk H., Canbakan B., Toptas T., Tabak O., Ozaras R., Tabak F., Balcı H., Sut N., Ozbay G.**	2011	Peer-reviewed publication	Cross-sectional study	HD	33	ActiTest (>0.11)	Liver biopsy (≥A2)	

Table S1: Summary Table
Diagnostic testing for liver fibrosis (by biopsy)
Categorical outcomes

PMID	Author	Year	Outcome	Sensitivity (%)	Specificity (%)	ROC-AUC	Quality
20357753	**Liu CH., Liang CC., Liu CJ., Hsu SJ., Lin JW., Chen SI., Hung PH., Tsai HB., Lai MY., Chen PJ., Chen JH., Chen DS., Kao JH.**	2010	**Fibrosis**	**97**	**23**	**0.83**	**Good**
				76	**55**	**0.71**	
				84	**51**		
				50	**73**		
				61	**90**		
				45	**89**		
				45	**95**		
				33	**95**		
				32	**96**		
				14	**98**		
17634962	**Schiavon LL., Schiavon JL., Filho RJ., Sampaio JP., Lanzoni VP., Silva AE., Ferraz ML.**	2007	**Fibrosis**	**88**	**54**	**0.80**	**Good**
				44	**93**		

PMID	Author	Year	Outcome	Sensitivity (%)	Specificity (%)	ROC-AUC	Quality
				95	69	0.84	
				42	89		
19758273	Schiavon LL., Carvalho-Filho RJ., Narciso-Schiavon JL., Pinheiro SR., Barbosa DV., Lanzoni VP., Ferraz ML., Silva AE.	2010	Fibrosis	85	51	0.73	Good
				25	89		
ATC-abstract 596	A. Brar, M. Salifu, M. Rampal, N. Sumrani, D. John, F. Tedla.	2012	Fibrosis	nd	nd	0.81	Fair
24353319	Jiang Y., Huang E., Mehrnia A., Kamgar M., Pham PT., Ogunorunyinka O., Brown I., Danovitch GM., Bunnapradist S.	2014	Fibrosis	67	56	nd	Good
				27	92		
21393486	Liu CH., Liang CC., Huang KW., Liu CJ., Chen SI., Lin JW., Hung PH., Tsai HB., Lai MY., Chen PJ., Chen JH., Chen DS., Kao JH.	2011	Fibrosis	3	100	nd	Good
			Fibrosis	74	82	0.84 (0.79, 0.88)	
			Fibrosis	79	70	nd	
			Fibrosis	2	99	nd	
			Fibrosis	93	90	0.93 (0.90, 0.97)	

PMID	Author	Year	Outcome	Sensitivity (%)	Specificity (%)	ROC-AUC	Quality
16371924	**Varaut A., Fontaine H., Serpaggi J., Verkarre V., Vallet-Pichard A., Nalpas B., Imbertbismuth F., Lebray P., Pol S.**	2005	**Fibrosis**	**24**	**92**	**0.66**	**Fair**
				84	**45**		
				nd	**nd**	**0.70**	
				nd	**nd**		
				14	**97**	**0.47**	
				71	**52**		
				30	**98**	**0.66**	
				80	**48**		
				69	**88**	**0.71**	
				93	**39**		
				nd	**nd**	**0.72**	
				100	**29**		

PMID	Author	Year	Outcome	Sensitivity (%)	Specificity (%)	ROC-AUC	Quality
20847572	**Canbakan M., Senturk H., Canbakan B., Toptas T., Tabak O., Ozaras R., Tabak F., Balcı H., Sut N., Ozbay G.**	2011	**Fibrosis**	**64**	**32**	**0.46 (0.25, 0.67)**	**Poor**
				13	**84**		
21393486	**Liu CH., Liang CC., Huang KW., Liu CJ., Chen SI., Lin JW., Hung PH., Tsai HB., Lai MY., Chen PJ., Chen JH., Chen DS., Kao JH.**	2011	**Fibrosis**	**30**	**100**	**nd**	**Good**
			Fibrosis	**55**	**96**	**nd**	
			Fibrosis	**93**	**88**	**0.96 (0.94, 0.98)**	
			Fibrosis	**45**	**99**	**nd**	
			Fibrosis	**45**	**99**	**nd**	
			Fibrosis	**95**	**99**	**0.98 (0.97, 1.00)**	
ATC-abstract 596	**A. Brar, M. Salifu, M. Rampal, N. Sumrani, D. John, F. Tedla.**	2012	**Fibrosis**	**nd**	**nd**	**0.54**	**Fair**
20847572	**Canbakan M., Senturk H., Canbakan B., Toptas T., Tabak O., Ozaras R., Tabak F., Balcı H., Sut N., Ozbay G.**	2011	**Activity (Necroinflammation)**	**36**	**40**	**0.36 (0.15, 0.57)**	**Poor**

Table S2: Evidence profile: Diagnostic testing for liver fibrosis (by biopsy)

Diagnostic Test	# of Studies	Total N of Patients	Methodological Quality of Studies	Consistency Across Studies	Directness of the Evidence, including Applicability	Other Considerations	Summary of Findings		
							Quality of Evidence for Outcome	Description of Findings	Importance of Outcome
APRI*	5 studies	995	No limitations (0)	No important inconsistencies (0)	Direct (0)	None (0)	High	F2-F4: AUC 0.73-0.83 (4 studies, transplant/HD) APRI >0.4 Sn 84-88%, Sp 51-54% (2 studies, HD) APRI >0.95 Sn 32-44%, Sp 93-96% (2 studies, HD) † F3-F4: AUC 0.84 (1 study, HD) APRI >0.4 Sn 67%, Sp 56% (1 of 2 studies, HD) ‡ APRI >0.95 Sn 27%, Sp 92% (1 of 2 studies, HD) §	High
Fibroscan ‖	1 study	304	No limitations (0)	NA	Direct (0)	Sparse data (-1)	Moderate	F2-F4: AUC 0.96 (1 study, HD) F3-F4: AUC 0.98 (1 study, HD)	High
Fibrotest ¶	2 studies	143	Some limitations (-1)	No important inconsistencies (0)	Direct (0)	None (0)	Moderate	F2-F4: AUC 0.46-0.47 (2 studies, HD) Fibrotest >0.2 Sn 64-71%, Sp 32-52% (2 studies)** Fibrotest >0.6 Sn 13-14%, Sp 84-97% (2 studies) †† F3-F4: AUC 0.66 (1 study, HD), AUC 0.72 (1 study, Txp)	High
FIB-4 ‡‡	1 study	26	Some limitations (-1)	NA	Direct (0)	Sparse data (-1)	Low	AUC 0.54 (1 study, HD)	High
ActiTest §§	1 study	33	Serious limitations (-2)	NA	Indirect (-1)	Sparse data (-1)	Very Low	Predicting "Activity" (necroinflammation): ActiTest >0.11 Sn 36%, Sp 40%, AUC 0.36	High

Overall summary (and Quality of Overall Evidence):

High quality evidence that APRI accurately diagnoses METAVIR F2-F4, sparse evidence that APRI accurately diagnoses F3-F4.
Sparse, moderate quality evidence that Fibroscan very accurately diagnoses F2-F4 and F3-F4.
Very Low to Moderate evidence that other tests (Fibrotest, FIB-4, ActiTest) do not accurately diagnose liver fibrosis (or necroinflammation).

Studies included in EP: 16371924, 20847572, 21393486, ATC-abstract 596, 20847572

Abbreviations: ALT = alanine aminotransferase, APRI = AST to platelet ratio index, AST = aspartate aminotransferase, AUC = area under the (receiver operating characteristics) curve, F2/F3/F4 = METAVIR scores, FIB4 = Fibrosis-4 test, GGT = γ-glutamyltranspeptidase, HD = hemodialysis, NA = not applicable (single study), Sn = sensitivity, Sp = specificity.

Annotations:

* APRI = (AST level [U/L]/upper limit of normal)/platelet counts (10^9 /liter) x 100
† Transplant population (1 study): APRI >0.50 Sn 85%, Sp 51%; APRI >1.5 Sn 25%, Sp 89%.
‡ 2nd HD study: APRI >0.55 Sn 95%, Sp 69%.
§ 2nd HD study: APRI >1.0 Sn 42%, Sp 89%.
‖ Also known as transient elastography or liver stiffness measurement, based on proprietary ultrasonography.
¶ Proprietary test based on α2-macroglobulin, haptoglobin, apoliprotein A1, GGT, total bilirubin, age and sex.
** In transplant population (1 study): Fibrotest >0.2 Sn 93%, Sp 39%.
†† In transplant population (1 study): Fibrotest >0.6 Sn 69%, Sp 88%; AUC 0.71.
‡‡ FIB4 = age (years) × AST [U/L]/platelet count[10^9/L] × (ALT [U/L])$^{1/2}$
§§ Proprietary test based on α2-macroglobulin, haptoglobin, apoliprotein A1, GGT, total bilirubin, ALT, age and sex.

Table S3: Summary Table
HCV infection as independent predictor of CKD progression

PMID	Author	Year	Type of article	Country	Study design	Registry Name	Population	Sample Size, Total	CKD stage, baseline	Kidney function, baseline	HCV genotypes	Follow-up Time	Predictor	Predictor Definition	Predictor units	# w/Predictor or mean (95%)
													HCV+	nd	nd	100,518
25529816	**Molnar**	2015	Peer-reviewed publication	US	Retrospective cohort study	nd	US veterans with baseline GFR ≥60 mL.min.1.73m2 with and without HCV	1,021,049	CKD 1-2	HCV+: 93 ± 16 HCV-: 87 ± 16	nd	7.8 years (IQR 6.8, 8.4)				
													HCV-			920,531
													HCV+	nd	nd	100,518
													HCV-			920,531
													HCV+	nd	nd	100,518
												8.0 years (IQR 7.1, 8.5)				
													HCV-			920,531
														detectable RNA		
23904290	**Lucas**	2013	Peer-reviewed publication	US	Retrospective cohort study	NA-ACCORD	HIV+ adults	63,023	CKD 0-5	GFR >90 70% GFR 60-89 26% GFR 30-59 3.4% GFR 15-29 0.4%	nd	nd	HCV viremic HCV aviremic HCV-	seropositivte, undetectable RNA		57,854 pt-yr 4769 pt-yr 269,805 pt-yr
														detectable RNA		
										GFR <15 0.7%			HCV viremic HCV aviremic HCV-	seropositivte, undetectable RNA		61 833 pt-yr 5139 pt-yr 287,386 pt-yr
														detectable RNA		
													HCV viremic HCV aviremic HCV-	seropositivte, undetectable RNA		59 892 pt-yr 4952 pt-yr 279 096 pt-yr
														seropositive	**nd**	5,189
20400217	**Lee**	2010	Peer-reviewed publication	Taiwan	Cross-sectional study	Taiwanese National Health Insurance Program	Adults	54,966	CKD 1-5	GFR ≥90: 27.7%	nd	nd	HCV alone			
														seropositive	**nd**	5,189
										GFR 60-89: 57.9%			HCV alone			
														seropositive	**nd**	5,189
										GFR 30-59: 13.7%			HCV alone			
														seropositive	**nd**	5,189
										GFR <0.8%			HCV alone			
21386707	**Hofmann**	2011	Peer-reviewed publication	Sweden	Retrospective cohort study	Swedish Institute for Infectious Diseae Control	HCV and matched controls	43,000	nd	nd	nd	nd				
													MALES			
													HCV-infected	nd	**nd**	25,412
													HCV-infected	nd	**nd**	25,412
													HCV-infected	nd	**nd**	25,412
													HCV-infected	nd	**nd**	25,412
													FEMALES			
													HCV-infected	nd	**nd**	25,412
													HCV-infected	nd	**nd**	25,412

PMID	Author	Year	Type of article	Country	Study design	Registry Name	Population	Sample Size, Total	CKD stage, baseline	Kidney function, baseline	HCV genotypes	Follow-up Time	Predictor	Predictor Definition	Predictor units	# w/Predictor or mean (95%)
													HCV-infected	nd	**nd**	25,412
													HCV-infected	nd	**nd**	25,412
18371161	**Ishizaka**	2008	Peer-reviewed publication	Japan	Cross-sectional study	General Health Screen at Mitsui Memorial Hospital	Working adults	12,535	nd	Hep B - and Hep C -: 70 ± 10 Hep B +: 70 ± 9 Hep C +: 67 ± 13	nd	nd	HCV + HCV - and HBV - HCV + HCV - and HBV - HCV + HCV - and HBV -	HCV Ag + HCV Ag - and HBV Ag - HCV Ag + HCV Ag - and HBV Ag - HCV Ag + HCV Ag - and HBV Ag -	**nd** **nd** **nd** **nd** **nd** **nd**	72 12,333 72 12,333 72 12,333
23311442	**Cao**	2013	Peer-reviewed publication	China	Cross-sectional Study	nd	HIV infected antiretroviral therapy-naïve	538	nd	Non-CKD: 113.54 ± 24.06 CKD: 98.98 ± 34.48	nd	nd	HCV + HCV -	HCV Ab + HCV Ab -	**nd** **nd**	80 444
17592100	**Tsui**	2007	Peer-reviewed	US	Retrospective Cohort Study	Medicare, the Department of Veterans Affairs, and the United States Renal Data System	US Veterans	474,369	HCV+: 9.4% with any stage HCV-: 16.6% with any stage	HCV+ GFR>=60: 83% GFR 30-59: 15% GFR<30: 2% HCV- GFR>=60: 91% GFR 30-59: 8% GFR<30: 2%	nd	3.4y (median 3.6y)	HCV+ HCV- HCV+, eGFR >= 60 HCV-, eGFR >= 61 HCV+, eGFR 30-59 HCV-, eGFR 30-59 HCV+, eGFR <30 HCV-, eGFR <30	seropositive seronegative seropositive seronegative seropositive seronegative seropositive seronegative	nd nd nd nd nd nd nd nd	178,447 pt-yr 1,442,826 pt-yr 163,846 pt-yr 1,219,523 pt-yr 13,295 pt-yr 207,484 pt-yr 1,307 pt-yr 15,819 pt-yr
26526451	**Rogal**	2016	Peer-reviewed	US	Retrospective Cohort Study	HCV Infected Veterans (ERCHIVES)	US Veterans	71,528			1: 33.14%, 2: 4.75%, 3: 5.25%, 4: 0.35%, Mixed: 0.08%, Missing: 56.43%	HCV+: 5.99 (SD 2.84)y HCV-: 4.91 (SD 2.16)y	HCV+ HCV- HCV+ HCV-	nd nd		nd nd
22554802	**Su**	2012	Peer-reviewed	Taiwan	Retrospective Case Control	Taiwan National Health Insurance Research Database	Taiwanese adults	37,746			nd	5.58 (SD 2.04)	HCV+ HCV-			32,648 pt-yr 176,921 pt-yr
26817874	**Hwang**	2016	Peer-reviewed	Taiwan	Retrospective Case Control	Longitudinal Cohort of Diabetes Patients	DM	19,574			nd	12 y	HCV+ HCV-			nd
16524948	**Tsui**	2006	Peer-reviewed publication	US	Cross-sectional	NHANES III	US general population	15029 (366 HCV+)	nd	HCV+: 110 (106-114) HCV-: 100 (99-101)	nd	nd nd	HCV+ HCV- HCV+ HCV- HCV+ HCV-	nd nd nd nd	nd nd nd nd	366 14,663 366 14,663 100,518 920,531
19747988	**Asrani**	2010	Peer-reviewed publication	US	Retrospective cohort study	Conglomerate of health insurance carriers database, NOS	US adults	167,569	CKD 0-5	GFR >60 95% GFR 30-59 5.0% GFR 15-29 0.2% GFR <15 0.1%	nd	nd	HCV+ HCV - HCV+ HCV -	EIA, NAT, gentoype test EIA, NAT, genotype test		13,384 154,185 8,063 80,759
24257691	**Chen**	2014	Peer-reviewed publication	Taiwan	Retrospective cohort study	Taiwan National Health Insurance Research Database	Taiwanese adults (no renal Txp)	9430 HCV+ and 3772	Non-CKD (per ICD-9)	nd	nd	~7 years	HCV +	ICD-9 codes		9,430

PMID	Author	Year	Type of article	Country	Study design	Registry Name	Population	Sample Size, Total	CKD stage, baseline	Kidney function, baseline	HCV genotypes	Follow-up Time	Predictor	Predictor Definition	Predictor units	# w/Predictor or mean (95%)
													HCV-			37,720 (matched)
25826420	**Mocroft**	2015	Peer-reviewed publication	Europe, U	Prospective cohort study	nd	HIV+	17,594	Healthy (not CKD)	median: 104	nd	103,185 person-years	HCV +	nd		2,262
													HCV -	nd		11,386
21185632	**Butt**	2011	Peer-reviewed publication	US	Retrospective cohort study	ERCHIVES	HCV infected patients, HCV-uninfected controls	43,139	Healthy (not CKD 3-5)	HCV+: 99 (22.6)	nd	HCV+: 3.15 (1.4) y	HCV +	anti-HCV Ab + or HCV RNA +		18,002
										HCV-: 92 (22.2)		HCV-: 3.00 (1.3) y	HCV -	anti-HCV Ab - or HCV RNA -		25,137
22994610	**Bickel**	2015	Peer-reviewed publication	Germany	Prospective cohort study	nd	HIV+	9198	Not ESRD	nd	nd	5 years max	HCV +			1008
													HCV -			4330 (+3860 unknown)

Table S3: Summary Table
HCV infection as independent predictor of CKD progression

PMID	Author	Year	Outcome	Outcome Definition	Cases (# w/Outcome)	Rate	Adjustments (reject if none)	Metric (HR, OR, RR, beta, change)	Estimate (95% CI)	Comparison	P_value	Risk of bias
25529816	**Molnar**	2015	GFR<60 incidence	the presence of two consecutive eGFR values of <60 mL/min/1.73 m2 at least 90 days apart with the added stipulation that the decrease in eGFR should be at least 25% from the baseline eGFR	11,271 95,837	16.7 (16.4,17.0)/1000 pt/yr 14.9 (14.8,15.0)/1000 pt-yr	age, gender, race/ethnicity, baseline GFR, ,comorbidities, SBP, DBP, BMI, socio-demographic parameters	HR	1.15 (1.12, 1.17)	vs. HCV-	nd	**LOW**
			GFR loss >5 mL/min/1.73m2/year	Rapid deterioration was defined as slopes of < –5 mL/min/1.73 m2/year (i.e., loss of eGFR of >5 mL/min/1.73 m2) /year).	nd nd	nd nd	age, gender, race/ethnicity, baseline GFR, ,comorbidities, SBP, DBP, BMI, socio-demographic parameters	OR	1.22 (1.19, 1.26)	vs. HCV-	nd	
			ESRD	initiation of renal replacement therapy or preemptive transplant	904 2479	1.2 (1.1, 1.3)/1000 pt-yr 0.36 (0.34, 0.37)/1000 pt-yr	age, gender, race/ethnicity, baseline GFR, ,comorbidities, SBP, DBP, BMI, socio-demographic parameters	HR	1.98 (1.81, 2.16)	vs. HCV-	nd	
23904290	**Lucas**	2013	CKD 3	GFR<60 for >=90 d	1666 122 5090	28.8 (27.5, 30.2)/1000 pt-yr 25.6 (21.4, 30.6)/1000 pt-yr 18.9 (18.4, 19.4)/1000 pt-yr	Age, sex, race, history of injection drug use, hepatitis B surface antigen positivity, baseline glomerular filtration rate, and time-updated covariates including calendar year, CD4 cell count, HIV RNA, antiretroviral therapy use, tenofovir use, indinavir use, lopinavir/ritonavir use, atazanavir use, hypertension, and diabetes.	HR	1.36 (1.26, 1.46) 1.19 (0.98, 1.45)	vs. HCV- vs. HCV-	nd nd	**LOW**
			CKD 5	GFR<15 for >=90 d	376 23 699	6.1 (5.5, 6.7)/1000 pt-yr 4.4 (2.9, 6.7)/1000 pt-yr 2.4 (2.3, 2.6)/1000 pt-yr	Age, sex, race, history of injection drug use, hepatitis B surface antigen positivity, baseline glomerular filtration rate, and time-updated covariates including calendar year, CD4 cell count, HIV RNA, antiretroviral therapy use, tenofovir use, indinavir use, lopinavir/ritonavir use, atazanavir use, hypertension, and diabetes.	HR	1.95 (1.64, 2.31) 1.69 (1.07, 2.65)	vs. HCV- vs. HCV-	nd nd	
			CKD decline	≥25% GFR decline from baseline to a GFR < 60 mL/min/1.73 m2 that persisted for at least 90 days among subjects with baseline GFR ≥ 30 mL/min/1.73 m2.	984 76 2885	16.4 (15.4, 17.5)/1000 pt-yr 15.4 (12.3, 19.2)/1000 pt-yr 10.3 (9.9, 10.7)/1000 pt-yr	Age, sex, race, history of injection drug use, hepatitis B surface antigen positivity, baseline glomerular filtration rate, and time-updated covariates including calendar year, CD4 cell count, HIV RNA, antiretroviral therapy use, tenofovir use, indinavir use, lopinavir/ritonavir use, atazanavir use, hypertension, and diabetes.	HR	1.31 (1.19, 1.44) 1.31 (1.02, 1.68)	vs. HCV- vs. HCV-	nd nd	
20400217	**Lee**	2010	CKD	determined by eGFR and proteinuria based on the K/DOQI definition	nd	nd	age, sex, educational status, BMA, albumin, Hb, cholesterol, uric acid, HTN, and DM	OR	1.26 (1.17, 1.38)	vs. HBV or HBV/HCV	<0.001	**HIGH**
			CKD	defined using GFR estimated using the 6-variable MDRD Study equation	nd	nd	age, sex, educational status, BMA, albumin, Hb, cholesterol, uric acid, HTN, and DM	OR	1.23 (1.14, 1.34)	vs. HBV or HBV/HCV	<0.001	
			proteinuria	presence of urine protein of at least grade 1+ in repeated measures	nd	nd	age, sex, educational status, BMA, albumin, Hb, cholesterol, uric acid, HTN, and DM	OR	1.14 (1.003, 1.300)	vs. HBV or HBV/HCV	0.04	
			low GFR	eGFR <60 mL/min/1.73 m2	nd	nd	age, sex, educational status, BMA, albumin, Hb, cholesterol, uric acid, HTN, and DM	OR	1.30 (1.20, 1.42)	vs. HBV or HBV/HCV	<0.001	
21386707	**Hofmann**	2011										**HIGH**
			glomerular diseases	risk of hospitalization for glomerular disease; ICD-9 codes: 580–583, ICD-10 codes: N00–N08	104	nd	age, sex, and interaction between HCV status and sex	HR	2.9 (2.0, 4.3)	vs. no HCV infection	nd	
			renal failure	risk of hospitalization for renal failure; ICD-9 codes: 584–586, ICD-10 codes: N17–N19	245	nd	age, sex, and interaction between HCV status and sex	HR	4.6 (3.7, 5.8)	vs. no HCV infection	nd	
			other kidney diseases	risk of hospitalization for other kidney diseases; ICD-9 codes: 587–589 and 593, ICD-10 codes:N25–N28	30	nd	age, sex, and interaction between HCV status and sex	HR	2.9 (1.4, 6.0)	vs. no HCV infection	nd	
			all noncancer kidney diseases combined	risk of hospitalization for combination of above	349	nd	age, sex, and interaction between HCV status and sex	HR	3.9 (3.2, 4.8)	vs. no HCV infection	nd	
			glomerular diseases	risk of hospitalization for glomerular disease; ICD-9 codes: 580–583, ICD-10 codes: N00–N08	34	nd	age, sex, and interaction between HCV status and sex	HR	5.1 (3.0, 8.8)	vs. no HCV infection	nd	
			renal failure	risk of hospitalization for renal failure; ICD-9 codes: 584–586, ICD-10 codes: N17–N19	59	nd	age, sex, and interaction between HCV status and sex	HR	7.2 (4.9, 10.6)	vs. no HCV infection	nd	

PMID	Author	Year	Outcome	Outcome Definition	Cases (# w/Outcome)	Rate	Adjustments (reject if none)	Metric (HR, OR, RR, beta, change)	Estimate (95% CI)	Comparison	P_value	Risk of bias
			other kidney diseases	risk of hospitalization for other kidney diseases; ICD-9 codes: 587–589 and 593, ICD-10 codes:N25–N28	4	nd	age, sex, and interaction between HCV status and sex	HR	10.0 (2.7, 37.2)	vs. no HCV infection	nd	
			all noncancer kidney diseases combined	risk of hospitalization for combination of above	94	nd	age, sex, and interaction between HCV status and sex	HR	5.8 (4.2, 7.9)	vs. no HCV infection	nd	
18371161	**Ishizaka**	2008	Low eGFR	eGFR<60 mL/min/1.73 m2	22 1887	31% 15%	age, sex, SBP, and FPG	OR	1.63 (0.95, 2.80)	vs. HCV - and HBV -	0.077	**HIGH**
			Albuminuria	UAER of 330 mg/g	14 1157	19% 9%	age, sex, SBP, and FPG	OR	2.00 (1.06, 3.76)	vs. HCV - and HBV -	0.034	
			CKD	eGFR<60 mL/min/1.73 m2, or UAER of 330 mg/g	nd nd	nd nd	age, sex, SBP, and FPG	OR	1.83 (1.10, 3.05)	vs. HCV - and HBV -	0.02	
23311442	**Cao**	2013	CKD	GFR < 60 mL/min per 1.73 m2 and/or isolated proteinuria (>= 1 + on urine dipstick) for 3 months	20 64	25% 14%	age, HIV viral load	OR	2.074 (1.036, 4.149)	vs. HCV -	0.011	**HIGH**
17592100	**Tsui**	2007	ESRD	onset of chronic dialysis or renal transplantation	760 4393 106 308 228 1039 426 3046	4.26 (3.97-4.57)/1000 pt-yr 3.05 (2.96-3.14)/1000 pt-yr 0.65 (0.54-0.78)/1000 pt-yr 0.25 (0.23-0.28)/1000/ pt-yr 17.15 (15.06-19.53)/1000 pt-yr 5.01 (4.71-5.32)/1000 pt-yr 326.03 (296.49-358.50)/1000 pt-yr 192.55 (185.83-199.51)/1000 pt-yr	age, sex, race/ethnicity, diabetes mellitus, hypertension, human immunodeficiency virus infection, congestive heart failure, coronary heart disease, peripheral vascular disease, chronic obstructive pulmonary disease, cerebrovascular disease, substance abuse, and baseline eGFR, also stratified by age	HR HR HR HR	1.68 (1.54-1.82) 2.74 (2.13-3.51) 2.57 (2.20-3.01) 1.28 (1.15-1.44)	vs. HCV- vs. HCV- vs. HCV- vs. HCV-	nd nd nd nd	**LOW**
26526451	**Rogal**	2016	CKD 3-5		nd	nd	baseline GFR with FIB-4 included as a time-varying covariate	HR	0.86 (0.79, 0.92)	HCV+ vs. HCV-	<0.0001	**LOW**
			Progressive CKD	decline in eGFR of >= 30 from baseline	nd	nd	baseline GFR with FIB-4 included as a time-varying covariate	HR	0.93 (0.86, 1.00)	HCV+ vs. HCV-	0.06	
22554802	**Su**	2012	ESRD		77 196		age, sex, occupation, urbanization, and Charlson Comorbidity Index score results also stratified by age, sex, and followup interval	HR	1.53 (1.17, 2.01)	vs. HCV-	0.002	**LOW**
26817874	**Hwang**	2016	ESRD		nd	nd	sex, age at index date and various comorbidities including hypertension, CAD, hyperlipidemia, HBV infection, gout and liver cirrhosis	HR	1.47 (1.11-1.93)	vs. HCV-	<0.05	**LOW**
16524948	**Tsui**	2006	GFR<60 prevalence	eGFR <60	366 14,663	2.0 (1.1,3.6) % 4.3 (3.7,4.9) %	age, gender, race/ethnicity, educational status, smoking status, DM,and HTN	OR	0.89 (0.49, 1.62)	vs. HCV-	0.7	**LOW**
			Albuminuria prevalence	Albuminuria	366 14,663	nd nd	age, gender, race/ethnicity, educational status, smoking status, DM,and HTN	OR	1.22 (1.19, 1.26)	vs. HCV-	nd	
19747988	**Asrani**	2010	CKD prevalence (baseline)	GFR<60 (single measurement)	13,384 154,185	5.3% 5.1%	Age, sex, cirrhosis, DM, HTN, CHF, PVD, CAD, COPD, HIV, drug/alcohol abuse, depression	OR	0.90 (0.36, 2.27)	vs. HCV-	0.7	**LOW**
			Progression to CKD	GFR <60 without baseline CKD	8,063 80,759	3.8% 3.5%	Age, sex, cirrhosis, DM, HTN, CHF, PVD, CAD, COPD, HIV, drug/alcohol abuse, depression	OR	0.92 (0.79, 1.08)	vs. HCV-		
24257691	**Chen**	2014	CKD, incident	ICD-9 code	367	3.9% (5.46/1000 person-yr)	age per year, sex, comorbidities, geographic region, urbanization level, enrollee category, and number of medical visits in 1 year before study entry	HR	1.28 (1.12, 1.46)	vs HCV-	<0.001	**LOW**

PMID	Author	Year	Outcome	Outcome Definition	Cases (# w/Outcome)	Rate	Adjustments (reject if none)	Metric (HR, OR, RR, beta, change)	Estimate (95% CI)	Comparison	P_value	Risk of bias
					960	2.5% (3.43/1000 person-yr)						
25826420	**Mocroft**	2015	CKD	eGFR <= 60 mL/min per 1.73 m2 (>3mo)	89	13.9%	age, sex, HIV risk, eGFR, nadir CD4 <200, HTN, prior CVD, diabetes	OR [exp(beta)]	1.40 (nd)	vs. HCV -	nd (at least <0.10)	**HIGH**
					391	61.0%						
21185632	**Butt**	2011	CKD 3-5	eGFR < 60 mL/min per 1.73 m2 for >=2 times	3,140	17.4%	age, sex, race, eGFR, HTN, smoking, COPD, diabetes, dyslipidemia, anemia, alcohol abuse, drug abuse, decompensated liver disease, ACEi/ARB use	HR	1.30 (1.23, 1.37)	vs. HCV -	< 0.0001	**LOW**
					3,738	14.9%						
22994610	**Bickel**	2015	ESRD	Initiation of RRT	~13	nd	race (black), intravenous drug use (sex, AIDS, HBV coinfection were NS)		0.84 (0.24, 2.86)	vs. HCV -	0.79	**UNCLEAR**
					~22	nd						

Table S4: Evidence profile: HCV infection as independent predictor of CKD progression

Outcome	# of Studies and Study Design*	Total N of Participants	Methodological Quality of Studies	Consistency Across Studies	Directness of the Evidence, including Applicability	Other Considerations	Summary of Findings		
							Quality of Evidence for Outcome	Description of Findings	Importance of Outcome
ESRD	6 retrospective, 1 prospective cohorts	Cohorts: 9198-1,021,049	No limitations (0)	No important inconsistencies (0)†	Direct (0)	None	High (Moderate for HIV coinfection)	No HIV coinfection: All studies (6 of 6 analyses in 5 studies) found significantly higher rates of ESRD in HCV+ (vs. HCV-). ES range 1.47-7.2 (women)/4.6 (men). HIV coinfection: Inconsistent: One study found no significant association between HCV coinfection and RRT (ES 0.84) One found significant association with CKD 5 (ES 1.95)	Critical
CKD	10 retrospective, 1 prospective cohorts	Cohorts: 538-1,021,049	No limitations (0)	Some inconsistencies (-1)	Direct (0)	None	Moderate	No HIV coinfection: Most studies(5 of 7) found significantly higher CKD incidence in HCV+ (vs. HCV-). ES range 0.86-1.83. One study found significantly *lower* risk of CKD in patients with *newly acquired* HCV. HIV coinfection: All studies (3 of 3) found significantly higher CKD incidence in HCV+ coinfection (vs. HCV-). ES range 1.36-2.07.	High
Decline in Kidney Function	3 retrospective cohorts	Cohorts: 63,023-1,021,049	No limitations (0)	Some inconsistencies (-1)	Direct (0)	None	Moderate	No HIV coinfection: 2 studies had conflicting findings with significant association between HCV+ and GFR loss >5 mL/min (OR 1.22) in 1 study, and no association with GFR loss ≥30 mL/min (HR 0.93) in 1 study. HIV coinfection: 1 study significant association between HCV+ and GFR decline ≥25% to <60 mL/min (HR 1.31).	High
Total N	15 retrospective, 1 prospective cohorts	Cohorts: 538-1,021,049							

Association of HCV+ status and CKD:

People with HCV infection are at increased risk of CKD and ESRD compared to people without HCV infection. Among people with HIV, coinfection with HCV increases the risk for CKD, but it remains unclear whether it also increases the risk for ESRD.

Quality of Overall Evidence:

Moderate

Studies included in EP: 25529816, 23904290, 20400217, 21386707, 18371161, 23311442, 17592100, 26526451, 22554802, 26817874, 16524948, 19747988, 24257691, 25826420, 21185632, 22994610

Abbreviations: CKD: chronic kidney disease; DAA: direct-acting antivirals; GFR: glomerular filtration rate; RCT: randomized controlled trial; SVR: sustained virological response

Annotations:

* Limited to largest studies with the addition of smaller studies of HIV population and from otherwise unrepresented countries.

† For general population. Two studies of HIV population were inconsistent with each other.

Table S5: Summary table
Treatment with direct-acting antiviral regimens in chronic HCV-infected CKD patients
Categorical outcomes

PMID	Author	Year	Type of article	Study design	Sample size	CKD stage	Kidney function	Viral HCV RNA	HCV genotype	Outcome	Definition
26456905	**Roth D., Nelson DR., Bruchfeld A., Liapakis A., Silva M., Monsour H., Martin P., Pol S., Londoño MC., Hassanein T., Zamor PJ., Zuckerman E., Wan S., Jackson B., Nguyen BY., Robertson M., Barr E., Wahl J., Greaves W.** See Bruchfeld 2017 below for 2ndary analysis in placebo group	2015	Peer-reviewed publication	RCT	226	CKD 4: 18.7%, CKD 5: 81.3% (CKD 5 nonD: 23.8%; CKD 5 D: 76.2%)	nd	≤800,000 IU/mL: 42.6% >800,000 IU/mL: 57.4%	1a: 51.9%; 1b: 47.7%; 1: 0.4%	Serious AEs	any
										SVR12	**nd**
										SVR4	nd
										Relapse (viral)	**nd**
										Acute kidney injury	SCr >2.5x baseline value
										Discontinuation due to AEs	**nd**
										Discontinuation	nd
										Death	**nd**
26583882	**Nazario HE., Ndungu M., Modi AA.**	2015	Peer-reviewed publication	Single arm (cohort), prospective	17	CKD Stage 5 nonD: 12%; CKD 5 HD: 88%	GFR <30 mL/min with no dialysis: 12% HD: 88%	>800,000 IU/mL: 76%	1a: 76%	**SVR0**	**undetectable hepatitis C viral load at the completion of 12 weeks of therapy**
										SVR12	nd
AASLD 2015 109	**Almarzooqi S; Klair JS; Karkada JG; Maan R; Cerocchi O; Kowgier M; Harrell SM; Rhodes K; Janssen HL; Feld JJ; Duarte-Rojo A**	2015	Abstract	nRCS, retrospective	456	CKD 1-2	CrCl: 0.83 (0.16)	nd	1: 78%; 2: 13%; 3; 7%	**Liver cirrhosis**	**nd**
										Acute kidney injury	SCr ↑≥50%
AASLD 2015 115	**Dumortier J, Bailly F, Pageaux GP, Vallet-Pichard A, Radenne S, Habersetzer F, Gagnieu MC, Grange JD, Minello A, Kamar N, Alric L, Leroy V**	2015	Abstract	Single arm (cohort), retrospective	50	CKD 3-5; CKD 5 HD: 70%; KTR: 34%; Transplant candidate: 54%	nd	nd	1a: 14%; 1b: 42%; 2: 12%; 3: 10%; 4: 18%; 5: 4%	**Serious AEs**	**Severe anemia**
										Discontinuation due to AEs	nd
										SVR12	**nd**
										Relapse (viral)	nd
										Discontinuation	**nd**
26923436; ILC 2(	**Saxena V; Koraishy FM; Sise M; Lim JK; Chung RT; Liapakis A; Nelson DR; Schmidt M; Fried MW; Terrault N**	2015	Abstract	Single arm (cohort), retrospective	1890	CKD 3: 12.2%; CKD Stage 5: 86.8%	nd	nd	1: 71%; 2: 17%; 3: 9%	SVR12 in eGFR >60	nd
										SVR12 in eGFR <=30	
										SVR12 in eGFR 31-45	
										SVR12 in eGFR 46-60	
										Death in eGFR >60	**nd**
										Death in eGFR <=30	
										Death in eGFR 31-45	
										Death in eGFR 46-60	
										Discontinuation due to AEs in eGFR >60	nd
										Discontinuation due to AEs in eGFR <=30	
										Discontinuation due to AEs in eGFR 31-45	
										Discontinuation due to AEs in eGFR 46-60	
										Discontinuation in eGFR >60	**nd**
										Discontinuation in eGFR <=30	
										Discontinuation in eGFR 31-45	
										Discontinuation in eGFR 46-60	
										Kidney Function, categorical in eGFR >60	Acute kidney injury
										Kidney Function, categorical in eGFR <=30	
										Kidney Function, categorical in eGFR 31-45	

PMID	Author	Year	Type of article	Study design	Sample size	CKD stage	Kidney function	Viral HCV RNA	HCV genotype	Outcome	Definition
										Kidney Function, categorical in eGFR 46-60	
										Kidney Function, categorical in eGFR >60	Renal or Urinary System
										Kidney Function, categorical in eGFR <=30	
										Kidney Function, categorical in eGFR 31-45	
										Kidney Function, categorical in eGFR 46-60	
ILC 2015 P0802	**Nazario HE, Ndungu M, Modi A**	2015	Abstract	Single arm (cohort), unclear	12	CKD 3-5: 8.3%; CKD 5 HD: 91.7%	nd	nd	1a: 83%; 1b: 17%	Discontinuation	nd
										Serious AEs	Anemia requiring blood
										SVR12	nd
ILC 2015 P0878,	**Czul F; Schiff E; Peyton A; Levy C; Hernandez M; Jeffers L; O'Brien C; Martin P; Bhamidimarri KR**	2015	Abstract	Single arm (cohort), prospective	28	CKD 4-5 HD	nd	nd	1a: 56%; 1b: 36%; 2: 4%; 3: 4%	SVR12	nd
										Serious AEs	Hepatic encephalopathy
										Serious AEs	Uncontrolled diarrhea
26976799	**Pockros PJ., Reddy KR., Mantry PS., Cohen E., Bennett M., Sulkowski MS., Bernstein DE., Cohen DE., Shulman NS., Wang D., Khatri A., Abunimeh M., Podsadecki T., Lawitz E.**	2016	Peer-reviewed publication	Single arm (cohort), unclear	20	CKD 5 (all): 70%; CKD 4: 30%	GFR: median 10.9 mL/min/1.73m2 (range 5.4, 29.9); CrCl: median 18.1 mL/min (range 8.9, 63.1); SCr: median 6.2 mg/dL (range 2.2, 10.8)	median 6.6 (range 5.5, 7.6) log10 IU/mL	1a: 65%; 1b: 35%	SVR12	nd
										SVR4	nd
										Death	nd
										Discontinuation due to AEs	nd
										Relapse (viral)	nd
										Serious AEs	treatment-emergent AEs
26872889	**Toyoda H., Kumada T., Tada T., Takaguchi K., Ishikawa T., Tsuji K., Zeniya M., Iio E., Tanaka Y.**	2016	Peer-reviewed publication	Single arm (cohort), prospective	28	CKD HD	GFR: 6.9 (2.4) mL/min/1.73m2; SCr: 7.16 (1.90) mg/dL	5.89 (0.91) log10 IU/mL	1b: 100%	SVR 12	nd
										SVR	nd
										Discontinuation due to AEs	nd
										Relapse (viral)	nd
27098678	**Miyazaki R., Miyagi K.**	2016	Peer-reviewed publication	Case series/report	10	CKD HD	nd	4.5 (0.97) log10 IU/mL	nd	SVR12	nd
										Discontinuation due to AEs	nd
26768604	**Suda G., Kudo M., Nagasaka A., Furuya K., Yamamoto Y., Kobayashi T., Shinada K., Tateyama M., Konno J., Tsukuda Y., Yamasaki K., Kimura M., Umemura M., Izumi T., Tsunematsu S., Sato F., Terashita K., Nakai M., Horimoto H., Sho T., Natsuizaka M., Morikawa K., Ogawa K., Sakamoto N.**	2016	Peer-reviewed publication	Single arm (cohort), prospective	34	CKD HD	nd	median 5.7 (range 2.9, 6.8) log10 IU/mL	1a: 4.8%; 1b: 90.5%	SVR 12	nd
										Relapse (viral)	nd
										Hepatocellular carcinoma (HCC)	nd
										Serious AEs	nd
27771774	**Morisawa, N. and Koshima, Y. and Satoh, J. I. and Maruyama, Y. and Kuriyama, S. and Yokoo, T. and Amemiya, M.**	2016	Peer-reviewed publication	Single arm (cohort), retrospective	29	CKD 3-5D	eGFR: 45.8 (15.9) SCr: 1.82 (2.69)	6.0 (3.7, 6.7) log10IU/mL	1b: 100%	SVR12	nd
										SVR24	nd
										Discontinuation	overall discontinuations
27602542	**Nakamura, Y. and Imamura, M. and Kawakami, Y. and Teraoka, Y. and Daijo, K. and Honda, F. and Morio, K. and Kobayashi, T. and Nakahara, T. and Nagaoki, Y. and Kawaoka, T. and Tsuge, M. and Hiramatsu, A. and Aikata, H. and Hayes, C. N. and Miki, D. and Ochi, H. and Chayama, K.**	2017	Peer-reviewed publication	Single arm (cohort), prospective	147	CKD 1-5D	eGFR: 69 (17, 128) mL/min/1/73m2 GFR >=50: 85.7% GFR <50: 14.3% SCr: 0.70 (0.39, 2.33)	nd	nd	SVR	timepoint unclear
										Discontinuations due to AEs	timepoint unclear nd
ASN TH-PO1143	**Sise M.E., G.L. Hundemer, G. Ortiz, E. Backman, D.Chute, J.Brancale, R.I. Thadhani, R.T. Chung.**	2016	Abstract	Single arm (cohort), prospective	107	CKD 3-5D	SCr: 1.26 (0.37) mg/dL	nd	nd	SVR	nd
AASLD 909	**Bernstein DE, et al**	2016	Abstract	Multiple pooled prospective studies	82 1479 1172	eGFR <60 ml/min eGFR 60-90 ml/min eGFR >90 ml/min	nd nd nd	nd nd nd	1: 100% 1: 100% 1: 100%	Factors associated with >10ml/min increase in eGFR	**Mutlivariate analysis**
AASLD 950	**Miyase S, et al**	2016	Abstract	Single arm (cohort), prospective	16	CKD HD	nd	nd	1b: 100%	SVR 12 Discontinue due to AEs	nd
AASLD 1967	**Suda G, et al**	2016	Abstract	Single arm (cohort), prospective	29	CKD HD	nd	nd	nd	SVR 12 Discontinue due to AEs	nd

PMID	Author	Year	Type of article	Study design	Sample size	CKD stage	Kidney function	Viral HCV RNA	HCV genotype	Outcome	Definition
AASLD 1982	**Panziani FR et al**	2016	Abstract	Single arm (cohort), prospective	10	CKD HD	nd	513,330 IU/mL	1a:10%, 1b:80%, 4:10%	SVR 12	nd
27943523	**Goki S., Atsushi Nagasaka, Yoshiya Yamamoto, Ken Furuya, Kenichi Kumagai, Mineo Kudo, Katsumi Terashita, Tomoe Kobayashi, Izumi Tsunematsu, Junichi Yoshida,10 Takashi Meguro,11 Megumi Kimura,1 Jun Ito,1 Machiko Umemura,1, Takaaki Izumi,1 Seiji Tsunematsu,1 Fumiyuki Sato,1 Yoko Tsukuda,1,2 Masato Nakai,1, Takuya Sho,1 Mitsuteru Natsuizaka,1 Kenichi Morikawa,1 Koji Ogawa,1 Naoya Sakamoto1, for the NORTE Study Group**	2017	Peer-reviewed publication	Single arm (cohort), prospective	322	CKD 1-5D	eGFR 70 (10, 121) mL/min/1.73 m2	6.1 (2.6, 7.8) log10 IU/mL	1: 100%	SVR12	overall SVR
											overall SVR in patients with
											overall SVR in patients with
											overall SVR in patients with
											overall SVR in patients with
											overall SVR in patients with
										SVR24	overall end of treatment (ETR)
											overall ETR in patients with CKD
											overall ETR in patients with CKD
											overall ETR in patients with CKD
											overall ETR in patients with CKD
											overall ETR in patients with CKD
										Discontinuations due to AEs	did not complete 24 weeks of
29020583	**Gane E, et al**	2017	Peer-reviewed publication	Single arm (cohort), prospective	104	CKD 4: 13%, CKD 5: 87%	nd	5.9 (3.4-7.5) log10	1: 52% (1a: 22%, 1b: 28%, non1a/1b: 2%),	SVR12	
										SVR24	
										Discontinuations due to AEs	
29270489	**Agarwal SK, et al**	2017	Peer-reviewed publication	Single arm (cohort), prospective	62	CKD HD	nd	nd	1: 64.5%, 2: 1.6%, 3: 29%, 4: 3.2%, 6: 1.6%	SVR12	
28882857	**Sise ME, et al**	2017	Peer-reviewed publication	Single arm (cohort), retrospective	98	CKD 1-3	SCr 1.3 (0.3) mg/dL	4.4 (5.8) log10 IU/ml	1: 73% (1a: 55%, 1b: 18%), 2:14%, 3: 7%, 4: 5%	SVR12	
							eGFR 60 (20) ml/min			Discontinuation due to AEs	
										Serious adverse events	
28576451	**Bruchfeld A, et al** This study includes the placebo group from Roth 2015 26456905 who received deferred treatment after the trial was completed.	2017	Peer-reviewed publication	RCT	113	CKD 4: 19%, CKD 5: 81%	nd	≤800,000 IU/mL: 42%	1a: 52%; 1b: 47%; 1other: 1%	SVR12	**nd**
										Serious adverse events	
										Discontinuation due to AEs	
										Patient survival	

Table S5: Summary table
Treatment with direct-acting antiviral regimens in chronic HCV-infected CKD patients
Categorical outcomes

PMID	Author	Year	Arm	Dose	Duration	Timepoint	Frequency/Rate	Relative effect	p-value	Quality
26456905	**Roth D., Nelson DR., Bruchfeld A., Liapakis A., Silva M., Monsour H., Martin P., Pol S., Londoño MC., Hassanein T., Zamor PJ., Zuckerman E., Wan S., Jackson B., Nguyen BY., Robertson M., Barr E., Wahl J., Greaves W.**	2015	**grazoprevir + elbasvir (immediate treatment)**	**100 mg OD + 50 mg OD**	**12 weeks**	**12 weeks**	**16/111 (14.4%)**	**nd**	**nd**	Good
	See Bruchfeld 2017 below for 2ndary analysis in placebo group		placebo	NA	12-28 weeks		19/113 (16.8%)			
			grazoprevir + elbasvir (immediate treatment)	**100 mg OD + 50 mg OD**	**12 weeks**	**12 weeks post-Tx**	**115/122 (94.3%)**	**nd**	**nd**	
			placebo	NA	12-28 weeks		nd			
			grazoprevir + elbasvir (immediate treatment)	**100 mg OD + 50 mg OD**	**12 weeks**	**4 weeks post-Tx**	**118/118 (100%)**	**nd**	**nd**	
			placebo	NA	12-28 weeks		1/113 (0.9%)			
			grazoprevir + elbasvir (immediate treatment)	**100 mg OD + 50 mg OD**	**12 weeks**	**12 weeks**	**1/116 (0.9%)**	**nd**	**nd**	
			placebo	NA	12-28 weeks		nd			
			grazoprevir + elbasvir (immediate treatment)	**100 mg OD + 50 mg OD**	**12 weeks**	**12 weeks**	**1/111 (1.2%)**	**nd**	**nd**	
			placebo	NA	12-28 weeks		0/113 (0%)			
			grazoprevir + elbasvir (immediate treatment)	**100 mg OD + 50 mg OD**	**12 weeks**	**12 weeks**	**0/111 (0%)**	**nd**	**nd**	
			placebo	NA	12-28 weeks		5/113 (4.4%)			
			grazoprevir + elbasvir (immediate treatment)	**100 mg OD + 50 mg OD**	**12 weeks**	**12 weeks**	**6/111 (5.4%)**	**nd**	**nd**	
			placebo	NA	12-28 weeks		6/113 (5.3%)			
			grazoprevir + elbasvir (immediate treatment)	**100 mg OD + 50 mg OD**	**12 weeks**	**12 weeks**	**1/111 (0.8%)**	**nd**	**nd**	
			placebo	NA	12-28 weeks		3/113 (2.7%)			
26583882	**Nazario HE., Ndungu M., Modi AA.**	2015	**sofosbuvir + simeprevir**	**400 mg OD + 150 mg OD**	**12 weeks**	**0 (Completion of treatment)**	**16/17 (94%)**			Good
						12 weeks	**17/17 (100%)**			
AASLD 2015 109	**Almarzooqi S; Klair JS; Karkada JG; Maan R; Cerocchi O; Kowgier M; Harrell SM; Rhodes K; Janssen HL; Feld JJ; Duarte-Rojo A**	2015	**Sofosbuvir + peg-interferon + Ribavirin**	**nd**	**nd**	**nd**	**33/76 (44%)**	**nd**	**0.001**	Good
			Non-IFN/RBV treatments (combined)	nd	nd	nd	nd (60%)			
			Sofosbuvir + peg-interferon + Ribavirin	**nd**	**nd**	**nd**	**4/76 (5%)**	**nd**	**nd**	
			Boceprevir + Telaprevir	nd	nd	nd	16/224 (7%)			
AASLD 2015 115	**Dumortier J, Bailly F, Pageaux GP, Vallet-Pichard A, Radenne S, Habersetzer F, Gagnieu MC, Grange JD, Minello A, Kamar N, Alric L, Leroy V**	2015	**sofosbuvir-based therapy**	**nd**	**12-24 weeks**	**nd**	**0/50 (0%)**	**nd**	**nd**	Poor
						nd	**0/50 (0%)**	**nd**	**nd**	
						12 weeks	**24/26 (92%)**	**nd**	**nd**	
						12 weeks	**2/50 (4%)**	**nd**	**nd**	
						nd	**0/50 (0%)**	**nd**	**nd**	
26923436; ILC 2(	**Saxena V; Koraishy FM; Sise M; Lim JK; Chung RT; Liapakis A; Nelson DR; Schmidt M; Fried MW; Terrault N**	2015	**sofosbuvir-based therapy**	**nd**	**nd**	**nd**	**1075/1284 (84%)**	**nd**	**nd**	Fair
							11/13 (85%)	**nd**	**nd**	
							30/37 (81%)	**nd**	**nd**	
							108/123 (88%)	**nd**	**nd**	
						nd	**10/1641 (0.6%)**	**nd**	**nd**	
							1/18 (6%)	**nd**	**nd**	
							0/63 (0%)	**nd**	**nd**	
							2/168 (1%)	**nd**	**nd**	
						nd	**33/1641 (2%)**	**nd**	**nd**	
							1/18 (6%)	**nd**	**nd**	
							3/63 (5%)	**nd**	**nd**	
							3/168 (2%)	**nd**	**nd**	
						nd	**66/1641 (4%)**	**nd**	**nd**	
							2/18 (9%)	**nd**	**nd**	
							5/63 (8%)	**nd**	**nd**	
							7/168 (4%)	**nd**	**nd**	
						nd	**16/1641 (1%)**	**nd**	**nd**	
							5/18 (25%)	**nd**	**nd**	
							8/63 (13%)	**nd**	**nd**	

PMID	Author	Year	Arm	Dose	Duration	Timepoint	Frequency/Rate	Relative effect	p-value	Quality
							3/168 (2%)	nd	nd	
						nd	82/1641 (5%)	nd	nd	
							5/18 (25%)	nd	nd	
							8/63 (13%)	nd	nd	
							13/168 (8%)	nd	nd	
ILC 2015 P0802	Nazario HE, Ndungu M, Modi A	2015	sofosbuvir + simeprevir	400 mg OD + 150 mg OD	12 weeks	nd	0/12 (0%)	nd	nd	Poor
						nd	1/12	nd	nd	
						12 weeks	5/5 (100%)	nd	nd	
ILC 2015 P0878,	Czul F; Schiff E; Peyton A; Levy C; Hernandez M; Jeffers L; O'Brien C; Martin P; Bhamidimarri KR	2015	sofosbuvir + simeprevir	150 mg OD + 200 mg OD	12 weeks	12 weeks	19/21 (90%)	nd	nd	Good
						12 weeks	1/21 (5%)	nd	nd	
						12 weeks	1/21 (5%)	nd	nd	
26976799	Pockros PJ., Reddy KR., Mantry PS., Cohen E., Bennett M., Sulkowski MS., Bernstein DE., Cohen DE., Shulman NS., Wang D., Khatri A., Abunimeh M., Podsadecki T., Lawitz E.	2016	ombitasvir + paritaprevir + ritonavir + dasabuvir ± ribavirin	25 mg OD + 150 mg OD + 100 mg OD + 250 mg BID + 200 mg OD	12 weeks	12 weeks	18/20 (90%)	nd	nd	Fair
						4 weeks	18/20 (90%)	nd	nd	
						12 weeks	1/20 (5%)	nd	nd	
						12 weeks	0/20 (0%)	nd	nd	
						12 weeks	1/20 (5%)	nd	nd	
						30 days	4/20 (20%)	nd	nd	
26872889	Toyoda H., Kumada T., Tada T., Takaguchi K., Ishikawa T., Tsuji K., Zeniya M., Iio E., Tanaka Y.	2016	daclatasvir + asunaprevir	60 mg OD + 100 mg BID	24 weeks	12 weeks	28/28 (100%)	nd	nd	Fair
						2 weeks	14/28 (50%)	nd	nd	
						4 weeks	25/28 (89.3%)	nd	nd	
						8 weeks	28/28 (100%)	nd	nd	
						0 weeks post-treatment	1/28 (3.6%)	nd	nd	
						12 weeks	0/28 (0%)	nd	nd	
27098678	Miyazaki R., Miyagi K.	2016	daclatasvir + asunaprevir	60 mg OD + 100 mg BID	24 weeks	12 weeks	10/10 (100%)	nd	nd	Poor
						12 weeks	0/10 (0%)	nd	nd	
26768604	Suda G., Kudo M., Nagasaka A., Furuya K., Yamamoto Y., Kobayashi T., Shinada K., Tateyama M., Konno J., Tsukuda Y., Yamasaki K., Kimura M., Umemura M., Izumi T., Tsunematsu S., Sato F., Terashita K., Nakai M., Horimoto H., Sho T., Natsuizaka M., Morikawa K., Ogawa K., Sakamoto N.	2016	daclatavir + asunaprevir	100 mg PO BID + 60 mg PO BID	24 weeks	12 weeks	20/21 (95%)	nd	nd	Poor
						12 weeks	1/21 (5%)	nd	nd	
						24 weeks	1/21 (5%)	nd	nd	
						24 weeks	1/21 (5%)	nd	nd	
27771774	Morisawa, N. and Koshima, Y. and Satoh, J. I. and Maruyama, Y. and Kuriyama, S. and Yokoo, T. and Amemiya, M.	2016	daclatasvir + asunaprevir	nd	nd	12 weeks	27/29 (93.1%)	nd	nd	Fair
						24 weeks	27/29 (93.1%)	nd	nd	
						48 weeks	3/29 (10.3%)	nd	nd	
27602542	Nakamura, Y. and Imamura, M. and Kawakami, Y. and Teraoka, Y. and Daijo, K. and Honda, F. and Morio, K. and Kobayashi, T. and Nakahara, T. and Nagaoki, Y. and Kawaoka, T. and Tsuge, M. and Hiramatsu, A. and Aikata, H. and Hayes, C. N. and Miki, D. and Ochi, H. and Chayama, K.	2017	daclatasvir + asunaprevir (GFR >=50)	60 mg OD + 200 mg BID	24 weeks	nd	119*126 (94.4%)	nd	nd	Fair
			daclatasvir + asunaprevir (GFR <50)				20/21 (95.2%)	nd	nd	
			dacaltasvir + asunaprevir	60 mg OD + 200 mg BID	24 weeks	24 weeks	2/147 (1.3%)	nd	nd	
ASN TH-PO1143	Sise M.E., G.L. Hundemer, G. Ortiz, E. Backman, D.Chute, J.Brancale, R.I. Thadhani, R.T. Chung.	2016	sofosbuvir + simeprevir (42%) sofosbuvir + ledipasvir (24%) sofosbuvir + ribavirin (34%)	nd	nd	12 weeks	81%	nd	nd	Poor
AASLD 909	Bernstein DE, et al	2016	ombitasvir + paritaprevir + ritonavir + dasabuvir ± ribavirin	25 mg OD + 150 mg OD + 100 mg	nd	nd		Baseline proteinuria OR 1.647 (1.320-2.054) Baseline diabetes OR 1.512 (1.059-2.161) Baseline BMI OR 0.948 (0.926-0.971(African American race OR 0.596 (0.384-0.923)	<0.001 0.023 <0.001 0.021	Poor
AASLD 950	Miyase S, et al	2016	daclatasvir + asunaprevir	nd	nd	12 weeks	100%	nd	nd	Poor
							6%	nd	nd	
AASLD 1967	Suda G, et al	2016	daclatasvir + asunaprevir	nd	nd	12 weeks	97%	nd	nd	Poor
							7%	nd	nd	

PMID	Author	Year	Arm	Dose	Duration	Timepoint	Frequency/Rate	Relative effect	p-value	Quality
AASLD 1982	**Panziani FR et al**	2016	**ombitasvir + paritaprevir + ritonavir + dasabuvir ± ribavirin**	**25 mg OD + 150 mg OD + 100 mg OD + 250 mg BID + 200 mg OD**	**nd**	12-24 weeks	**100%**	nd	nd	Poor
27943523	**Goki S., Atsushi Nagasaka, Yoshiya Yamamoto, Ken Furuya, Kenichi Kumagai, Mineo Kudo, Katsumi Terashita, Tomoe Kobayashi, Izumi Tsunematsu, Junichi Yoshida,10 Takashi Meguro,11 Megumi Kimura,1 Jun Ito,1 Machiko Umemura,1, Takaaki Izumi,1 Seiji Tsunematsu,1 Fumiyuki Sato,1 Yoko Tsukuda,1,2 Masato Nakai,1, Takuya Sho,1 Mitsuteru Natsuizaka,1 Kenichi Morikawa,1 Koji Ogawa,1 Naoya Sakamoto1, for the NORTE Study Group**	2017	**asunaprevir + daclatasvir**	**100 mg PO BID + 60 mg PO BID**	**24 weeks**	12 weeks	**289/322 (89.9%)**	nd	nd	Good
			asunaprevir + daclatasvir	**101 mg PO BID + 60 mg PO BID**	**24 weeks**	12 weeks	**8/8 (100%)**	nd	nd	
			asunaprevir + daclatasvir	**102 mg PO BID + 60 mg PO BID**	**24 weeks**	12 weeks	**16/16 (100%)**	nd	nd	
			asunaprevir + daclatasvir	**103 mg PO BID + 60 mg PO BID**	**24 weeks**	12 weeks	**63/71 (88.7%)**	nd	nd	
			asunaprevir + daclatasvir	**104 mg PO BID + 60 mg PO BID**	**24 weeks**	12 weeks	**137/159 (86.2%)**	nd	nd	
			asunaprevir + daclatasvir	**104 mg PO BID + 60 mg PO BID**	**24 weeks**	12 weeks	**65/68 (95.6%)**	nd	nd	
			asunaprevir + daclatasvir	**100 mg PO BID + 60 mg PO BID**	**24 weeks**	24 weeks	**95%**	nd	nd	
			asunaprevir + daclatasvir	**101 mg PO BID + 60 mg PO BID**	**24 weeks**	24 weeks	**100%**	nd	nd	
			asunaprevir + daclatasvir	**102 mg PO BID + 60 mg PO BID**	**24 weeks**	24 weeks	**100%**	nd	nd	
			asunaprevir + daclatasvir	**103 mg PO BID + 60 mg PO BID**	**24 weeks**	24 weeks	**95.80%**	nd	nd	
			asunaprevir + daclatasvir	**104 mg PO BID + 60 mg PO BID**	**24 weeks**	24 weeks	**93.70%**	nd	nd	
			asunaprevir + daclatasvir	**104 mg PO BID + 60 mg PO BID**	**24 weeks**	24 weeks	**95.60%**	nd	nd	
			asunaprevir + daclatasvir	**101 mg PO BID + 60 mg PO BID**	**25 weeks**	24 weeks	**27/322 (8.4%)**	nd	nd	
29020583	**Gane E, et al**	2017	**glecaprevir + pibrentasvir**				**102/104 (98%)**	nd	nd	Good
			glecaprevir + pibrentasvir				**100/104 (96%)**	nd	nd	
			glecaprevir + pibrentasvir				**25/104 (24%)**	nd	nd	
			glecaprevir + pibrentasvir				**5/104 (5%)**	nd	nd	
29270489	**Agarwal SK, et al**	2017	**Sofosbuvir + ribavirin**				**39/41 (95%)**	nd	nd	Fair
			Sofosbuvir + daclatasvir				**20/21 (95%)**	nd	nd	
28882857	**Sise ME, et al**	2017	**Sofosbuvir-based treatment**				**79/98 (81%)**	nd	nd	Fair
			Sofosbuvir-based treatment				**8/98 (8%)**	nd	nd	
			Sofosbuvir-based treatment				**17/98 (17%)**	nd	nd	
28576451	**Bruchfeld A, et al** This study includes the placebo group from Roth 2015 26456905 who received deferred treatment after the trial was completed.	2017	**grazoprevir + elbasvir (deferred treatment)**	**100 mg OD + 50 mg OD**	**12 weeks**	**12 weeks post-Tx**	**97/102 (95.1%)**	**nd**	**nd**	Good
			grazoprevir + elbasvir (deferred treatment)	**100 mg OD + 50 mg OD**	**12 weeks**	**12 weeks post-Tx**	**19/113 (16.8%)**	**nd**	**nd**	
			grazoprevir + elbasvir (deferred treatment)	**100 mg OD + 50 mg OD**	**12 weeks**	**12 weeks post-Tx**	**5/113 (4.4%)**	**nd**	**nd**	
			grazoprevir + elbasvir (deferred treatment)	**100 mg OD + 50 mg OD**	**12 weeks**	**12 weeks post-Tx**	**110/113 (97.3%)**	**nd**	**nd**	

Table S5: Summary table
Treatment with direct-acting antiviral regimens in chronic HCV-infected CKD patients
Continuous outcomes

PMID	Author	Year	Type of article	Study design	Sample size	CKD stage	Kidney function	Viral HCV RNA	HCV genotype	Outcome	Definition
AASLD 2015 1158	**Dumortier J, Bailly F, Pageaux GP, Vallet-Pichard A, Radenne S, Habersetzer F, Gagnieu MC, Grange JD, Minello A, Kamar N, Alric L, Leroy V**	2015	Abstract	Single arm (cohort), retrospective	50	CKD 3-5; CKD 5 HD: 70%; KTR: 34%; Transplant candidate: 54%	nd	nd	1a: 14%; 1b: 42%; 2: 12%; 3: 10%; 4: 18%; 5: 4%	**GFR**	**GFR in nonHD patients, ml/min**
ASN TH-PO1143	**M.E. Sise, G.L. Hundemer, G. Ortiz, E. Backman, D.Chute, J.Brancale, R.I. Thadhani, R.T. Chung.**	2016	Abstract	Single arm (cohort), prospective	107	CKD 3-5D	SCr: 1.26 (0.37) mg/dL	nd	nd	SCr	average creatinine 12 weeks after therapy
ASN PUB204	**J. Pagan, A.A. Armstrong, V. Blumer, R.J. Echeverri, M. Del Pilar Hernandez, F.E. Pedraza, M.A. LadinoAvellaneda, D. Roth**	2016	Abstract	Single arm (cohort), retrospective	397	nd	SCr: 1.4 mg/dL eGFR: 53 mL/min	nd	nd	**SCr** **GFR**	**SCr after DAA therapy** **eGFR after DAA therapy**
AASLD 889	Reddy KR et. al.	2016	Abstract	Single arm (cohort), prospecdtive	32 1657	eGFR 30-60 ml/min eGFR >60 ml/min	eGFR 56 (45-59) ml/min eGFR 100 (61-364) ml/min	3,344,605 IU/mL 4,030,364 IU/mL	nd	eGFR eGFR	eGFR 12 weeks after DAA therapy eGFR 12 weeks after DAA therapy
29020583	Gane E, et al	2017	Peer-reviewed publicatio	Single arm (cohort), prospective	104	CKD 4-5 (18%)	eGFR	nd	nd	eGFR	eGFR 12 weeks after DAA therapy
28882857	Sise ME, et al	2017	Peer-reviewed publicatio	Single arm (cohort), retrospective	98	CKD 1-3	SCr: 1.3 (0.3) mg/dL eGFR: 60 (20) mL/min	4.4 (5.8) log10 IU/ml	1: 73% (1a: 55%, 1b: 18%), 2:14%, 3: 7%, 4: 5%	eGFR	eGFR 6 months after DAA therapy

Table S5: Summary table
Treatment with direct-acting antiviral regimens in chronic HCV-infected CKD patients
Continuous outcomes

PMID	Author	Year	Arm	Dose	Duration	N	Baseline Value	Timepoint	Value	Change	p-value	Quality
AASLD 2015 1158	**Dumortier J, Bailly F, Pageaux GP, Vallet-Pichard A, Radenne S, Habersetzer F, Gagnieu MC, Grange JD, Minello A, Kamar N, Alric L, Leroy V**	2015	**sofosbuvir-based therapy**	**nd**	**12-24 weeks**	**12**	**29.6 (6.2)**	**24 weeks**	**27.9 (6.5)**	**-1.7**	**NS**	Poor
ASN TH-PO1143	**M.E. Sise, G.L. Hundemer, G. Ortiz, E. Backman, D.Chute, J.Brancale, R.I. Thadhani, R.T. Chung.**	2016	**sofosbuvir + simeprevir (42%)**									
			sofosbuvir + ledipasvir (24%)									
			sofosbuvir + ribavirin (34%)	**nd**	**nd**	**107**	**1.26 (0.37)**	**12 weeks**	**1.24 (0.8)**	**-0.02**	**nd**	Poor
ASN PUB204	**J. Pagan, A.A. Armstrong, V. Blumer, R.J. Echeverri, M. Del Pilar Hernandez, F.E. Pedraza, M.A. LadinoAvellaneda, D. Roth**	2016	**sofosbuvir (390/396:98.5%), ribavirin (201/396:50.8%), ledipasvir (195/396:49.2%), simeprivir (155/396:39.1%) or daclastavir (8/396:2%)**	**nd**	**nd**	**397**	**1.4**	**12 weeks**	**1.2**	**-0.2**	**0.001**	Poor
			sofosbuvir (390/396:98.5%), ribavirin (201/396:50.8%),	**nd**	**nd**	**397**	**53**	**12 weeks**	**64**	**11**	**0.001**	
AASLD 889	Reddy KR et. al.	2016	elbasvir/grazoprevir (39% with ribavirin)	50/100mg	8-18 weeks	32	eGFR 56 (45-59) ml/min	12 weeks	eGFR 59 (38-78) ml/min	3	nd	Poor
			elbasvir/grazoprevir (39% with ribavirin)	50/100mg	8-18 weeks	1657	eGFR 100 (61-364) ml/min	12 weeks	eGFR 100 (48-364) ml/min	0	nd	
29020583	Gane E, et al	2017	glecaprevir + pibrentasvir	300/120mg	12 weeks	19	eGFR 20.6	12 weeks	eGFR 20.2	-0.4	nd	Good
28882857	Sise ME, et al	2017	Sofosbuvir-based therapy	multiple	12 weeks	98	eGFR 60 (20) ml/min	6 months	unclear			

Table S6: Evidence profile: Treatment with direct-acting antiviral regimens in chronic HCV-infected CKD patients

Outcome	# of Studies and Study Design	Total N of Patients on Treatment	Methodological Quality of Studies	Consistency Across Studies	Directness of the Evidence, including Applicability	Other Considerations	Summary of Findings		
							Quality of Evidence for Outcome	Description of Findings	Importance of Outcome
Death	1 RCT 1 prospective 1 retrospective 1 cohort	495	Some limitations (-1)‡	No important inconsistencies (0)	Direct (0)	Sparse (-1)	Low	Inconclusive if DAA lowers mortality	Critical
Sustained virological response	1 RCT 14 prospective 4 retrospective 2 cohort 1 case series	1597	Some limitations (-1)§	No important inconsistencies (0)	Direct (0)	None (0)	Moderate	SVR12: 81-100% across DAA regimens* (SVR12: 0% in placebo arm)	High
Discontinuation due to adverse events	1 RCT 8 prospective 3 retrospective 1 cohort 1 case series	1516	Some limitations (-1)¶	Important inconsistencies (-1)‖	Direct (0)	None (0)	Low	0-8%†	High
Serious adverse events	1 RCT 5 prospective 2 retrospective 2 cohort	789	Some limitations (-1)**	Important inconsistencies (-1)‖	Some uncertainty about directness of evidence (-1)‡‡	None (0)	Very low	Sofosbuvir-based and Daclatasvir + Asunaprevir (4 studies) 0-8% Grazoprevir + Elbasvir and Ombitasvir + Paritaprevir + Ritonavir + Dasabuvir +/- Ribavirin (2 studies): 14-20% (none attributed to DAA) Glecaprevir + Pibrentasvir (1 study): 24% (none attributed to DAA)	Moderate
Hepatocellular carcinoma	1 prospective	34	Serious limitations (-2)††	NA	Direct (0)	Sparse (-1)	Very low	Daclatasvir + Asunaprevir 1/21 patients at 24 weeks (1 study)	Moderate
Kidney function, continuous	2 prospective 2 retrospective	2243	Serious limitations (-2)††	NA	Direct (0)	Sparse (-1)	Very low	No significant change in eGFR with Sofosbuvir-based or Grazoprevir + Elbasvir in patients with CKD stages 1-5	Moderate
Total N		3252							

Balance of Potential Benefits and Harms:
DAAs yield very high rates of SVR 12 with low rates of discontinuation due to adverse events or serious adverse events attributable to DAAs

Quality of Overall Evidence:
Low

Studies included in EP: 26456905, 26583882, AASLD 2015 1099, AASLD 2015 1158, 26923436; ILC 2015 LP08, ILC 2015 P0802, ILC 2015 P0878, AASLD 2015 2256, 26976799, 26872889, 27098678, 26768604, 27771774, 27602542, ASN TH-PO1143, AASLD 909, AASLD 950, AASLD 1967, AASLD 1982, 27943523, 29020583, 29270489, 28882857, 28576451, ASN PUB204, AASLD 889

Abbreviations: CKD: chronic kidney disease; DAA: direct-acting antivirals; GFR: glomerular filtration rate; RCT: randomized controlled trial; SVR: sustained virological response

Annotations:

* Sofosbuvir-based 81-100% SVR (8 studies), Daclatasvir + Asunaprevir 90-100% (8 studies), Grazoprevir + Elbasvir 94-95% (2 studies), Ombitasvir + Paritaprevir + Ritonavir + Dasabuvir +/- Ribavirin 90-100% (2 studies), Glecaprevir + Pibrentasvir 98% (1 study)

† Sofosbuvir-based 0-8%% SVR (3 studies), Daclatasvir + Asunaprevir 0-4% (6 studies), Grazoprevir + Elbasvir 0-4% (2 studies), Ombitasvir + Paritaprevir + Ritonavir + Dasabuvir +/- Ribavirin 0% (1 study), Glecaprevir + Pibrentasvir 5% (1 study)

‡ 2 good quality; 2 fair quality

§ 7 good quality; 7 fair quality; 8 poor quality

‖ Mix of CKD 1-5 both dialysis and non-dialysis patients

¶ 5 good quality; 5 fair quality; 3 poor quality

**5 good quality; 2 fair quality; 3 poor quality

†† 1 poor quality study

‡‡ Inconsistent definitions

Table S7: Summary Table
Treatment with direct-acting antiviral regimens in kidney transplant recipients with chronic HCV infection
Categorical outcomes

PMID	Author	Year	Type of article	Study design	Sample size	CKD stage	Kidney function	Viral HCV RNA	HCV genotype	Outcome
26587971	**Kamar N., Marion O., Rostaing L., Cointault O., Ribes D., Lavayssière L., Esposito L., Del Bello A., Métivier S., Barange K., Izopet J., Alric L.**	2015	Peer-reviewed publication	Single arm (cohort), unclear	25	KTR	GFR: 64 (21) ml/min; SCr: 117 (57) µmol/L	6.33 (0.6) log IU/mL	1a: 16%; 1b: 60%; 2: 8%; 3: 4%; 4: 12%	**Kidney Graft Failure/Loss** **SVR12** **SVR24**
26604182	**Sawinski D., Kaur N., Ajeti A., Trofe-Clark J., Lim M., Bleicher M., Goral S., Forde KA., Bloom RD.**	2015	Peer-reviewed publication	Retrospective cohort	20	KTR	SCr: 1.39 (range 0.74-2.24)	median 6.5 log copies/mL (IQR 6.3-7)	1a: 30%; 1b: 30%; 1: 25%; 2: 15%	**SVR12** **Discontinuation due to AEs** **Acute kidney injury**
AASLD 2015 1148	**Bhamidimarri KR., Roth D., Guerra G., Levy C., Martin P.**	2015	Abstract	Single arm (cohort), prospective	14	KTR	GFR: 60 ml/min	3.4 million IU	1a: 79%; 1b: 21%	**SVR12**
ATC 2015 3034	**Sharfuddin A, Taber T, Mujtaba M, Yaqub M, Mishler D, Kwo P, Vuppalanchi R**	2015	Abstract	Single arm (cohort), prospective	12	KTR	SCr: 1.9 (0.6); proteinuria: 2.2 (2.2)	25.6 (38.0) million IU/mL	1a: 91.7%	**SVR12** **Relapse (viral)** **Relapse (viral)** **Discontinuation** **Serious AEs**
27842383	**Colombo M., Aghemo A., Liu H., Dvory-Sobol H., Hyland RH., Yun C., Brainard D.M., McHutchison J.G., Bourlière M., Peck-Radosavljevic M., Manns M., Pol S.**	2017	Peer-reviewed publication	RCT	114	KTR	GFR: median 56 mL/min/1.73m2 (range 35, 135)	median 6.3 (range 4.5, 7.6) log10 IU/mL	1: 2% 1a:15% 1b: 75% 4: 9%	**SVR12** **SVR24** **Discontinuation due to AEs** **Serious AEs** **Deaths**
27495770	**Eisenberger, U. and Guberina, H. and Willuweit, K. and Bienholz, A. and Kribben, A. and Gerken, G. and Witzke, O. and Herzer, K.**	2016	Peer-reviewed publication	Retrospective cohort	15	KTR	GFR: median 77.9 ml/min/1.73m2 (36.4, 124) SCr: median 1.22 mg/dL (range 0.77, 2.04)	median 1.2 x 10^6 (range 3007, 9.3 x 10^6) log 10 IU/mL	1a: 27% 1b: 67% 4: 7%	**SVR12** **Mid to Moderate Adverse Events**
0	**Kirushnan B, M.A. Shujauddin, K. Arumugam, R. Ravichandran**	2016	Peer-reviewed publication	Retrospective cohort	20	KTR	SCr: 1.41 (0.54) mg%	median 3,394,705 IU/ml	1: 60% 2: 0% 3: 30% 4: 5% 1a and 2: 5%	**SVR12**

PMID	Author	Year	Type of article	Study design	Sample size	CKD stage	Kidney function	Viral HCV RNA	HCV genotype	Outcome
ASN TH-PO770	**Gonzalez Corvillo C., MA Gentil Govantes, A. Sanchez Fructuoso, A. Mazuecos.**	2016	Abstract	Prospective and retrospective cohort	110 (119 with 9 combined liver-kidney transplant)	KTR	nd	nd	1a: 13.8% 1b: 68.1% 2: 4.3% 3: 7.8% 4: 6%	**SVR** **Discontinuation due to AEs** **Deaths**
ASN TH-PO772	**Prasad N., M. Ranjan Patel, A. Jaiswal, D. Bhadauria, R.K. Sharma, A. Gupta**	2016	Abstract	Prospective cohort	22	KTR	nd	range 96425-24175475 copes logIU/mL	1: 27.2% 2: 4.5% 3: 63.6% 4: 4.5%	**SVR12** **SVR24**
ASN TH-PO774	**Kusnir J.E., A. Dejman, K. Bhamidimarri, F.E. Pedraza, M.A. LadinoAvellaneda, D. Roth**	2016	Abstract	Prospective cohort	21	KTR	nd	nd	nd	**SVR 12**
28009781	**Lubetzky M, et al**	2017	Peer-reviewed publilcation	Retrospective cohort	31	KTR	SCr: 1.3 (0.4) mg/dL GFR: 64.2 (16.5) mL/min/BSA	nd	nd	**SVR12** **Patient survival** **Graft survival**
28239909	**Morales AL, et al**	2017	Peer-reviewed publication	Retrospective cohort	32	KTR	nd	nd	1a: 62.5%, 1b: 28.1%; 2: 3.1%; 3: 3.1%; 4: 3.1%	**SVR12** Patient survival
28703905	**Taneja S, et al**	2017	Peer-reviwed publication	Prospective cohort	47	KTR	eGFR 67.8 ml/min	7.38 x10^6 IU/ml	1: 68%, 2: 2%, 3: 21%, 4: 9%	SVR12 Treatment discontinuation
28504842	**Saxena V, et al**	2017	Peer-reviewed publication	Retrospective cohort	60	KTR	eGFR 58.5 ml/min (7.4-156.4)	6.3 x 10^6 IU/ml	1a: 48%, 1b: 37%; 2: 2%; 3: 3%; 4: 3%; 5: 0%; 6: 2%	SVR12 Acute rejection Treatment discontinuation Patient survival
28332729	**Bhamidimarri KR, et al**	2017	Peer-reviewed publication	Prospective cohort	25	KTR	Scr 1.3 mg/dL	nd	1a: 68%; 1b: 24%; 2: 4%; 3: 4%	SVR12 Acute rejection
28039098	**Fernandez I, et al**	2017	Peer-reviewed publication	Retrospective cohort	103	KTR	SCr 1.7mg/dL (0.6-8.8)	6.6 x 10^6 IU/ml	1a: 8%, 1b: 74%; 2: 0%; 3: 6%; 4: 8%; 5: 2%; 6: 0%	SVR12 Acute rejection
Journal of Hepatology 2017 vol. 66 | S63–S94 (and ASN 2017 poster SA-PO496)	**Reau, et al**	2017	Conference poster	Prospective cohort	20	KTR	eGFR <60 ml/min 55%; >=90 10%	>6 x 10^6 IU/ml 20%	1a: 30%; 1b: 55%; 3: 10%; 4: 5%	SVR12 Patient survival Graft survival Discontinuation due to AEs Serious AEs

Table S7: Summary Table
Treatment with direct-acting antiviral regimens in kidney transplant recipients with chronic HCV infection
Categorical outcomes

PMID	Author	Year	Definition	Arm	Duration	Timepoint	Frequency/Rate	Relative effect	p-value	Quality	Dose
26587971	Kamar N., Marion O., Rostaing L., Cointault O., Ribes D., Lavayssière L., Esposito L., Del Bello A., Métivier S., Barange K., Izopet J., Alric L.	2015		sofosbuvir + daclatasvir/simeprevir + peg-IFN	nd	nd	0/25 (0%)	ND	ND	Poor	400 mg OD + 60/150 mg OD + 135 mg QW
				sofosbuvir + daclatasvir/simeprevir + peg-IFN	nd	12 weeks	25/25 (100%)	ND	ND		
				sofosbuvir + daclatasvir/simeprevir + peg-IFN	nd	24 weeks	8/8 (100%)	ND	ND		
26604182	Sawinski D., Kaur N., Ajeti A., Trofe-Clark J., Lim M., Bleicher M., Goral S., Forde KA., Bloom RD.	2015		HCV therapy + Immunosuppression	12 weeks	12 weeks	20/20 (100%)	ND	ND	Good	nd
				HCV therapy + Immunosuppression	12 weeks	37 weeks	0/20 (0%)	ND	ND		
			SCr ↑0.25 mg/dL	HCV therapy + Immunosuppression	12 weeks	37 weeks	4/20 (20%)	ND	ND		
AASLD 2015 1148	Bhamidimarri KR., Roth D., Guerra G., Levy C., Martin P.	2015		sofosbuvir/ledipasvir	nd	12 weeks	1/1 (100%)	ND	ND	Fair	nd
ATC 2015 3034	Sharfuddin A, Taber T, Mujtaba M, Yaqub M, Mishler D, Kwo P, Vuppalanchi R	2015		sofosbuvir-based therapy	12-24 weeks	12 weeks	2/3 (67%)	ND	ND	Poor	
				sofosbuvir-based therapy	12-24 weeks	4 weeks	1/9 (11%)	ND	ND		
				sofosbuvir-based therapy	12-24 weeks	12 weeks	1/3 (33%)	ND	ND		
				sofosbuvir-based therapy	12-24 weeks	12 weeks	1/3 (33%)	ND	ND		
			anemia	sofosbuvir-based therapy	12-24 weeks	nd	5/12 (42%)	ND	ND		
27842383	Colombo M., Aghemo A., Liu H., Dvory-Sobol H., Hyland RH., Yun C., Brainard D.M., McHutchison J.G., Bourlière M., Peck-Radosavljevic M., Manns M., Pol S.	2017		ledipasvir + sofosbuvir for 12 weeks	12 weeks	12 weeks	57/57 (100%)	ND	ND	Good	90mg + 400 mg OD
				ledipasvir + sofosbuvir for 24 weeks	24 weeks		57/57 (100%)	ND	ND		90mg + 400 mg OD
				ledipasvir + sofosbuvir for 12 weeks	12 weeks	24 weeks	NA	ND	ND		90mg + 400 mg OD
				ledipasvir + sofosbuvir for 24 weeks	24 weeks		57/57 (100%)	ND	ND		90mg + 400 mg OD
				ledipasvir + sofosbuvir for 12 weeks	12 weeks	30 days after the last dose	1/57 (2%)	ND	ND		90mg + 400 mg OD
				ledipasvir + sofosbuvir for 24 weeks	24 weeks		0/57 (0%)	ND	ND		90mg + 400 mg OD
			treatment-related searious adverse events	ledipasvir + sofosbuvir for 12 weeks	12 weeks	30 days after the last dose	1/57 (2%)	ND	ND		90mg + 400 mg OD
				ledipasvir + sofosbuvir for 24 weeks	24 weeks		2/57 (4%)	ND	ND		90mg + 400 mg OD
			all serious adverse events	ledipasvir + sofosbuvir for 12 weeks	12 weeks	30 days after the last dose	5/57 (9%)	ND	ND		90mg + 400 mg OD
				ledipasvir + sofosbuvir for 24 weeks	24 weeks		8/57 (14%)	ND	ND		90mg + 400 mg OD
				ledipasvir + sofosbuvir for 12 weeks	12 weeks	30 days after the last dose	0/57 (0%)	ND	ND		90mg + 400 mg OD
				ledipasvir + sofosbuvir for 24 weeks	24 weeks		0/57 (0%)	ND	ND		90mg + 400 mg OD
27495770	Eisenberger, U. and Guberina, H. and Willuweit, K. and Bienholz, A. and Kribben, A. and Gerken, G. and Witzke, O. and Herzer, K.	2016		ledipasvir + sofosbuvir for 8 weeks	8 weeks	12 weeks	3/3 (100%)	ND	ND	Fair	90mg + 400 mg OD
				ledipasvir + sofosbuvir for 12 weeks	12 weeks	12 weeks	12/12 (100%)	ND	ND		90mg + 400 mg OD
			fatigue, headache, nausea, hypertension	all patients	8 or 12 weeks	up to 12 weeks after treatment	5/15 (33%)	ND	ND		90mg + 400 mg OD
0	Kirushnan B, M.A. Shujauddin, K. Arumugam, R. Ravichandran	2016		sofosbuvir + ribavirin		12 weeks	10/13 (77%)	ND	ND	Fair	400 mg + dose adjusted

PMID	Author	Year	Definition	Arm	Duration	Timepoint	Frequency/Rate	Relative effect	p-value	Quality	Dose
ASN TH-PO770	Gonzalez Corvillo C., MA Gentil Govantes, A. Sanchez Fructuoso, A. Mazuecos.	2016		sofosbuvir(91%) + ledipasvir (55%) sofosbuvir (91%) + simeprevir (14%) sofosbuvir (91%) + daclatasvir (13%)	nd	nd	110/110 (100%)	ND	ND	Poor	nd
			neurotoxicity caused by the interaction between 3D and tacrolimus and anemia caused by Ribavirin	sofosbuvir(91%) + ledipasvir (55%) sofosbuvir (91%) + simeprevir (14%) sofosbuvir (91%) + daclatasvir (13%)	nd	nd	2/119 (1.6%)	ND	ND		nd
				sofosbuvir(91%) + ledipasvir (55%) sofosbuvir (91%) + simeprevir (14%) sofosbuvir (91%) + daclatasvir (13%)	nd	nd	110/110 (100%)	ND	ND		nd
ASN TH-PO772	Prasad N., M. Ranjan Patel, A. Jaiswal, D. Bhadauria, R.K. Sharma, A. Gupta	2016		sofosbuvir + ribavirin (63.6%) sofosbuvir + ribavirin + daclatasvir (22.7%) sofosbivir + ribavirin + ledipasvir (13.6%)	24 weeks	12 weeks	22/22 (100%)	ND	ND	Poor	nd
				sofosbuvir + ribavirin (63.6%) sofosbuvir + ribavirin + daclatasvir (22.7%) sofosbivir + ribavirin + ledipasvir (13.6%)	12 weeks minimum	24 weeks	22/22 (100%)	ND	ND		nd
ASN TH-PO774	Kusnir J.E., A. Dejman, K. Bhamidimarri, F.E. Pedraza, M.A. LadinoAvellaneda, D. Roth	2016		sofosbuvir + ledipasvir + ribavirin (61.9%) sofosbuvir + ledipasvir (23.8%) sofosbuvir + daclatasvir (4.8%) sofosbuvir + simeprevir (4.8%) sofosbuvir + ribavirin (4.8%)	12 weeks	12 weeks	21/21 (100%)	ND	ND	Poor	nd
28009781	Lubetzky M, et al	2017		DAAs, most commonly sofosbuvir + ledipasvir (67.7%)	12 weeks	12 weeks	30/31 (97%)	ND	ND	Fair	nd
				DAAs, most commonly sofosbuvir + ledipasvir (67.7%)	12 weeks	nd	31/31 (100%)	ND	ND		nd
				DAAs, most commonly sofosbuvir + ledipasvir (67.7%)	12 weeks	nd	31/31 (100%)	ND	ND		nd
28239909	Morales AL, et al	2017		Sofosbuvir+ledipasvir	8 weeks (9%); 12 weeks (66%), 24 weeks (25%)	12 weeks	27/32 (84%)	ND	ND	Fair	nd
				Sofosbuvir+ledipasvir		12 weeks	28/32 (87%)	ND	nd		nd
28703905	Taneja S, et al	2017		Sofosbuvir+ribavirin	24 weeks	12 weeks	12/14 (86%)	ND	nd	Fair	mult
				Sofosbuvir+ ledipasvir +/- ribavirin	12 weeks	12 weeks	22/22 (100%)	ND	nd		mult
				Sofosbuvir + daclatasvir +/- ribavirin	12 weeks	12 weeks	12/12 (100%)	ND	nd		mult
				Sofosbuvir+ribavirin	24 weeks	12 weeks	2/14 (14%)	ND	nd		mult
				Sofosbuvir+ ledipasvir +/- ribavirin	12 weeks	12 weeks	0/22 (0%)	ND	nd		mult
				Sofosbuvir + daclatasvir +/- ribavirin	12 weeks	12 weeks	0/12 (0%)	ND	nd		mult
28504842	Saxena V, et al	2017		DAA, most commonly sofosbuvir+ ledipasvir +/- ribavirin (80%) but also sofosbuvir + daclatasvir +/- ribavirin (4%) and PrOD regimen (16%)	12 weeks	12 weeks	52/58 (90%)	ND	nd	Fair	mult
			biopsy proven	DAA, most commonly sofosbuvir+ ledipasvir +/- ribavirin (80%) but also sofosbuvir + daclatasvir +/- ribavirin (4%) and PrOD regimen (16%)	12 weeks	12 weeks	2/58 (3%)	ND	nd		mult
				DAA, most commonly sofosbuvir+ ledipasvir +/- ribavirin (80%) but also sofosbuvir + daclatasvir +/- ribavirin (4%) and PrOD regimen (16%)	12 weeks	12 weeks	4/60 (7%)	ND	nd		mult
				DAA, most commonly sofosbuvir+ ledipasvir +/- ribavirin (80%) but also sofosbuvir + daclatasvir +/- ribavirin (4%) and PrOD regimen (16%)	12 weeks	12 weeks	60/60 (100%)	ND	nd		mult
28332729	Bhamidimarri KR, et al	2017		Sofosbuvir+ ledipasvir +/- ribavirin (96%)	12 weeks	12 weeks	24/25 (96%)	ND	nd	Fair	mult
			biopsy proven	Sofosbuvir+ ledipasvir +/- ribavirin (96%)	12 weeks	12 weeks	4/25 (16%)	ND	nd		mult
28039098	Fernandez I, et al	2017		DAA, most commonly sofosbuvir+ ledipasvir +/- ribavirin (57%) but also sofosbuvir + daclatasvir +/- ribavirin (17%) and PrOD regimen (10%)	12 weeks	12 weeks	101/103 (98%)	ND	nd	Good	mult
				DAA, most commonly sofosbuvir+ ledipasvir +/- ribavirin (57%) but also sofosbuvir + daclatasvir +/- ribavirin (17%) and PrOD regimen (10%)	12 weeks	12 weeks	4/103 (4%)	ND	nd		mult
Journal of Hepatology 2017 vol. 66 | S63–S94 (and ASN 2017 poster SA-PO496)	Reau, et al	2017		Glecaprevir + Pibrentasvir	12 weeks	12 weeks	20/20 (100%)	ND	nd	Good	300+120 mg
				Glecaprevir + Pibrentasvir	12 weeks	24 weeks	20/20 (100%)	ND	nd		300+120 mg
				Glecaprevir + Pibrentasvir	12 weeks	24 weeks	20/20 (100%)	ND	nd		300+120 mg
				Glecaprevir + Pibrentasvir	12 weeks		0/20 (0%)	ND	nd		300+120 mg
			None attributable to GP	Glecaprevir + Pibrentasvir	12 weeks		3/20 (15%)	ND	nd		300+120 mg

Table S7: Summary Table
Treatment with direct-acting antiviral regimens in kidney transplant recipients with chronic HCV infection
Continuous outcomes

PMID	Author	Year	Type of article	Study design	Sample size	CKD stage	Kidney function	Viral HCV RNA	HCV genotype	Outcome	Definition
26587971	**Kamar N., Marion O., Rostaing L., Cointault O., Ribes D., Lavayssière L., Esposito L., Del Bello A., Métivier S., Barange K., Izopet J., Alric L.**	2015	Peer-reviewed publication	Single arm (cohort), unclear	25	KTR	GFR: 64 (21) ml/min; SCr: 117 (57) µmol/L	6.33 (0.6) log IU/mL	1a: 16%; 1b: 60%; 2: 8%; 3: 4%; 4: 12%	**Kidney Function, continuous** **Kidney Function, continuous**	**SCr, µmol/L** **GFR, ml/min**
ATC 2015 3034	**Sharfuddin A, Taber T, Mujtaba M, Yaqub M, Mishler D, Kwo P, Vuppalanchi R**	2015	Abstract	Single arm (cohort), prospective	12	KTR	SCr: 1.9 (0.6); proteinuria: 2.2 (2.2)	25.6 (38.0) million IU/mL	1a: 91.7%	**Proteinuria, continuous**	**proteinuria, g/day**
27842383, EASL 2016 Barcelona	**Colombo M., Aghemo A., Liu H., Dvory-Sobol H., Hyland RH., Yun C., Brainard D.M., McHutchison J.G., Bourlière M., Peck-Radosavljevic M., Manns M., Pol S.**	2017	Peer-reviewed publication	OL, pjase 2 RCT	114	KTR	GFR: median 56 mL/min/1.73m2 (range 35, 135)	median 6.3 (range 4.5, 7.6) log10 IU/mL	1: 2% 1a:15% 1b: 75% 4: 9%	**Kidney Function, continuous**	**change in mean GFR over time**
27495770	**Eisenberger, U. and Guberina, H. and Willuweit, K. and Bienholz, A. and Kribben, A. and Gerken, G. and Witzke, O. and Herzer, K.**	2016	Peer-reviewed publication	Retrospective cohort	15	KTR	GFR: median 77.9 ml/min/1.73m2 (36.4, 124) SCr: median 1.22 mg/dL (range 0.77, 2.04)	median 1.2 x 10^6 (range 3007, 9.3 x 10^6) log 10 IU/mL	1a: 27% 1b: 67% 4: 7%	**Kidney Function, continuous**	**median GFR over time**
27495759	**Sawinski D, Patel N, Appolo B, Bloom RD**	2016	Peer-reviewed publication	Retrospective	43	KTR	SCr: median 1.49 mg/dL	median 6.6 (range 6.2,6.9) log10 IU/mL	1: 83.3%; 2: 16.7%	**Kidney Function, continuous** **Days spent on waitlist for donor**	**median serum creatinine** **median number of total days**
ASN TH-PO775	**M. Lubetzky, M. Ajaimy, L. Kamal, M. Coco, E. Akalin, G. De Boccardo.**	2016	Abstract	Retrospective cohort	31	KTR	SCr: 1.3 (0.4) mg/dL GFR: 64.2 (16.5) mL/min/BSA	nd	nd	**Kidney Function, continuous** **Kidney Function, continuous** **Proteinuria, continuous**	**change in SCr after therapy, mg/dL** **change in GFR by MDRD after therapy, mL/min/BSA** **change in proteinuria after therapy, mg/g**
ASN TH-PO777	**M.R. Goetsch, R. Franco, A. Tamhane, M. Varshney, A. Kapil, E. Turner Overton, G. Towns**	2016	Abstract	Retrospective cohort	16	KTR	nd	nd	nd	**Kidney Function, continuous** **Kidney Function, continuous** **Kidney Function, continuous**	**change in median protinuria/creatinine (P/C) ratios** **absolute mean decrease in P/C ratios** **absolute median percent decrease in P/C ratios**

Table S7: Summary Table
Treatment with direct-acting antiviral regimens in kidney transplant recipients with chronic HCV infection
Continuous outcomes

PMID	Author	Year	Arm	Dose	Duration	N	Baseline Value	Timepoint	Value	Change	p-value	Quality
26587971	Kamar N., Marion O., Rostaing L., Cointault O., Ribes D., Lavayssière L., Esposito L., Del Bello A., Métivier S., Barange K., Izopet J., Alric L.	2015	sofosbuvir + daclatasvir/simeprevir + peg-IFN	400 mg OD + 60/150 mg OD + 135 mg QW	nd	25	117 (57)	12 weeks	126 (69)	nd	nd	Poor
						25	61 (21)	12 weeks	59 (20)	nd	nd	
ATC 2015 3034	Sharfuddin A, Taber T, Mujtaba M, Yaqub M, Mishler D, Kwo P, Vuppalanchi R	2015	sofosbuvir-based therapy	nd	12-24 weeks	12	2.2 (2.2)	24 weeks	1.7 (1.9)	nd	nd	Poor
27842383, EASL 2016 Barcelona	Colombo M., Aghemo A., Liu H., Dvory-Sobol H., Hyland RH., Yun C., Brainard D.M., McHutchison J.G., Bourlière M., Peck-Radosavljevic M., Manns M., Pol S.	2017	ledipasvir + sofosbuvir for 12 weeks	90mg + 400 mg OD	12 weeks	57	59.1 (20.51)	12 weeks	57 (21.23)	-1.6 (7.62)	nd	Good
			ledipasvir + sofosbuvir for 24 weeks	90mg + 400 mg OD	24 weeks	57	63.5 (20.26)		61.9 (18.66)	-2.0 (8.97)		
			ledipasvir + sofosbuvir for 12 weeks	90mg + 400 mg OD	12 weeks	57	59.1 (20.51)	24 weeks	NA	NA	nd	
			ledipasvir + sofosbuvir for 24 weeks	90mg + 400 mg OD	24 weeks	57	63.5 (20.26)		60.6 (19.76)	-2.7 (10.00)		
27495770	Eisenberger, U. and Guberina, H. and Willuweit, K. and Bienholz, A. and Kribben, A. and Gerken, G. and Witzke, O. and Herzer, K.	2016	ledipasvir + sofosbuvir for 8/12 weeks	90mg + 400 mg OD	8/12 weeks	15	77.9 (36.4, 124)	EOT (8 or 12 weeks)	69.1 (32.5, 120.5)	nd	0.99	Poor
27495759	Sawinski D, Patel N, Appolo B, Bloom RD	2016	LDV+SOF: ledipasvir/sofosbuvir	nd	12 weeks	24	1.46 mg/dL	12 weeks	1.49 mg/dL	nd	nd	Fair
			LDV+SOF+RBV: ledipasvir/sofobuvir with ribavirin	nd	12 weeks	24	1.46 mg/dL	12 weeks	1.49 mg/dL	nd	nd	
			SOF+RBV: sofosbuvir/ribavirin	nd	12 weeks	24	1.46 mg/dL	12 weeks	1.49 mg/dL	nd	nd	
			SOF+SIM: sofosbuvir/simeprevir	nd	12 weeks	24	1.46 mg/dL	12 weeks	1.49 mg/dL	nd	nd	
			HCV+ donor	nd	485 (IQR 228,783)		nd	nd	nd	nd	0.02	
			HCV- donor	nd	969 (IQR 452,2008)		nd	nd	nd	nd		
ASN TH-PO775	M. Lubetzky, M. Ajaimy, L. Kamal, M. Coco, E. Akalin, G. De Boccardo.	2016	DAAs, most commonly sofosbuvir + ledipasvir (67.7%)	nd	12 weeks	31	1.3 mg/dL	12 weeks	1.4 mg/dL	0.1	0.25	Fair
			DAAs, most commonly sofosbuvir + ledipasvir (67.7%)	nd	12 weeks	31	64.2 mL/min/BSA	12 weeks	58.9 mL/min/BSA	-5.3	0.22	
			DAAs, most commonly sofosbuvir + ledipasvir (67.7%)	nd	12 weeks	31	0.66 mg/g	12 weeks	1.1 mg/g	0.44	0.1	
ASN TH-PO777	M.R. Goetsch, R. Franco, A. Tamhane, M. Varshney, A. Kapil, E. Turner Overton, G. Towns	2016	DAA treatment	nd	nd	14	0.176 (0.165, 0.385)	nd	0.107 (0.081, 0.151)	-0.069	0.001	Poor
			DAA treatment	nd	nd	14	nd	nd	nd	0.118	nd	
			DAA treatment	nd	nd	14	nd	nd	nd	0.5	nd	

Table S8: Evidence profile: Treatment with direct-acting antiviral regimens in kidney transplant recipients with chronic HCV infection

Outcome	# of Studies and Study Design	Total N of Patients on Treatment	Methodological Quality of Studies	Consistency Across Studies	Directness of the Evidence, including Applicability	Other Considerations	Summary of Findings		
							Quality of Evidence for Outcome	Description of Findings	Importance of Outcome
Mortality	1 RCT 2 prospective 3 retrospective	367	Some limitations (-1)[A]	No important inconsistencies (0)	Direct (0)	Limited follow-up [B] (-1)	Low	Mortality 0% 12-24 weeks post-treatment (13% in one uncontrolled study)	Critical
Kidney failure / graft loss	1 prospective 2 retrospective	76	Some limitations (-1)[C]	No important inconsistencies (0)	Direct (0)	Sparse (-1)	Low	Graft loss rates 0% 12-24 weeks post-treatment	Critical
Sustained virological response	1 RCT 8 prospective 8 retrospective	558	Some limitations (-1)[D]	No important inconsistencies (0)	Direct (0)	None (0)	Moderate	SVR12 in 537/558 (96%) across DAA regimens	High
Discontinuation due to adverse events	1 RCT 4 prospective 2 retrospective	293	Some limitations (-1)[E]	Some inconsistency (-1)	Direct (0)	None (0)	Low	10/293 (3.4%) across DAA regimens (range 0-14% [F])	High
Serious adverse events	1 RCT 2 prospective	89	Some limitations (-1)[G]	No important inconsistencies (0)	Indirect (-1)[H]	Sparse (-1)	Low	None attributable to DAA	Moderate
Kidney function, continuous	1 RCT (different durations) 5 retrospective 1 cohort	272	Some limitations (-1) [I]	Some inconsistency (-1)	Direct (0)	Sparse (-1)	Very Low	No to small change in SCr or eGFR (0-5 mL/min in 6 months)	Moderate
Proteinuria, continuous	1 prospective 2 retrospective	69	Serious limitations (-2) [J]	Some inconsistency (-1)	Direct (0)	Sparse (-1)	Very low	Variable changes in proteinuria (from -23% to + 39-67%)	Moderate
Total N		691							

Balance of Benefit and Harms:

DAAs yield very high rates of SVR 12 with low rates of discontinuation due to adverse events. DAA treatment has minimal impact on kidney function and variable effect on proteinuria.

Quality of Overall Evidence:

Low

Studies included in EP: 26587971, 26604182, AASLD 2015 1148, ATC 2015 3034, 27842383, 27495770, ASN TH-PO770, ASN TH-PO772, ASN TH-PO774, 28009781, 28239909, 28703905, 28504842, 28332729, 28039098, 27495759, ASN TH-PO777, Journal of Hepatology 2017 vol. 66 | S63–S94/ASN 2017 Poster SA-PO496, Kirushman 2016

Abbreviations: DAA: direct-acting antivirals; GFR: glomerular filtration rate; RCT: randomized controlled trial; SCr: serum creatinine; SVR: sustained virological response

Annotations:
A. 2 good quality, 3 fair quality, 1 poor quality.
B. Mostly 3 months after treatment.
C. 1 good quality, 1 fair quality, 1 poor quality.
D. 4 good quality, 8 fair quality, 5 poor quality.
E. 3 good quality, 2 fair quality; 2 poor quality.
F. Among studies with at least 10 participants.
G. 2 good, 1 poor.
H. Reporting and attribution of adverse events were unclear and inconsistent.
I. 1 good quality, 2 fair quality; 4 poor quality.
J. 1 fair quality, 2 poor quality.

Table S9: Summary Table
Isolation of HCV patients receiving hemodialysis
Categorical outcomes

PMID	Author	Year	Country	Type of article	Study design	Sample size	CKD stage	Blood transfusions	HD vintage	Outcome	Definition	Arm
19147995	**Agarwal SK., Dash SC., Gupta S., Pandey RM.**	2009	India	Peer-reviewed publication	Pre-post design	1285	CKD HD	6.6 (3.9)	nd	**HCV seroconversion**	**nd**	**Isolation for HCV+, 2003-2006** No isolation for HCV+, 1995-1998
7753458	**Blumberg A., Zehnder C., Burckhardt JJ.**	1995	Switzerland	Peer-reviewed publication	Pre-post design	131	CKD HD	nd	2 weeks-284 months	**HCV seroconversion**	**nd**	**Isolation for HCV+** No isolation for HCV+
16903625	**Karkar A., Abdelrahman M., Ghacha R., Malik TQ.**	2006	Saudi Arabia	Peer-reviewed publication	Pre-post design	265	CKD HD	nd	4-21 years	**HCV seroconversion**	**nd**	**Isolation for HCV+** No isolation for HCV+
										HCV (antibody) positivity	**nd**	**Isolation for HCV+** No isolation for HCV+
16685138	**Gallego E., López A., Pérez J., Llamas F., Lorenzo I., López E., Illescas ML., Andrés E., Olivas E., Gómez-Roldan C.**	2006	Spain	Peer-reviewed publication	Pre-post design	282	CKD HD	nd	nd	**HCV seroconversion**	**nd**	**Strict/complete isolation for HCV+** Isolation for HCV+
										HCV (antibody) positivity	**nd**	**Strict/complete isolation for HCV+** Isolation for HCV+
17382087	**Shebeb AM., Kotkat AM., Abd El Reheim SM., Farghaly AG., Fetohy EM.**	2006	Egypt	Peer-reviewed publication	nRCS, unclear	101	CKD HD	nd	2.3 (1.4)	**HCV seroconversion**	**nd**	Intervention program + no isolation **No intervention program + isolation** No intervention program + no isolation Intervention program + no isolation **No intervention program + isolation** No intervention program + no isolation Intervention program + no isolation **No intervention program + isolation** No intervention program + no isolation
15469615	**Shamshirsaz AA., Kamgar M., Bekheirnia MR., Ayazi F., Hashemi SR., Bouzari N., Habibzadeh MR., Pourzahedgilani N., Broumand V., Shamshirsaz AH., Moradi M., Borghei M., Haghighi NN., Broumand B.**	2004	Iran	Peer-reviewed publication	RCT	442	CKD HD	24%	21.6 month	**HCV (RNA) positivity**	**incidence of HC**	**dedicated HD machine** **nondedicated HD machine** **dedicated HD machine** **nondedicated HD machine**

Table S9: Summary Table
Isolation of HCV patients receiving hemodialysis
Categorical outcomes

PMID	Author	Year	Definition	Timepoint	Frequency/Rate	Relative effect	p-value	Quality
19147995	**Agarwal SK., Dash SC., Gupta S., Pandey RM.**	2009	**separate room, separate machine**	**3 years**	**2.7%**	**nd**	**<0.001**	Fair
			shared room, shared machine		36.2%			
7753458	**Blumberg A., Zehnder C., Burckhardt JJ.**	1995	**separate machine, same room**	**1992+**	**7/<131 (unclear)**	**nd**	**nd**	Poor
			nd	nd	0/nd (unclear)			
16903625	**Karkar A., Abdelrahman M., Ghacha R., Malik TQ.**	2006	**separate rooms, separate machines**	**2005**	**0/265 (0%)**	**nd**	**nd**	Poor
				2004	**0/265 (0%)**	**nd**	**nd**	
				2003	**nd/265 (0.2%)**	**nd**	**nd**	
				2002	**1/265 (0.3%)**	**nd**	**nd**	
			nd	2001	7/265 (2.6%)	**nd**	**nd**	
				2000	6/265 (2.3%)	**nd**	**nd**	
				1999	6/265 (2.1%)	**nd**	**nd**	
				1998	7/265 (2.7%)	**nd**	**nd**	
			separate rooms, separate machines	**2005**	**77/265 (29%)**	**nd**	**nd**	
				2004	**85/265 (32%)**	**nd**	**nd**	
				2003	**90/265 (34%)**	**nd**	**nd**	
				2002	**117/265 (44%)**	**nd**	**nd**	
			nd	2001	151/265 (57%)	**nd**	**nd**	
				2000	130/265 (49%)	**nd**	**nd**	
				1999	148/265 (56%)	**nd**	**nd**	
				1998	154/265 (58%)	**nd**	**nd**	
				1996-2003	**0/171 (0%)**	**nd**	**nd**	
16685138	**Gallego E., López A., Pérez J., Llamas F., Lorenzo I., López E., Illescas ML., Andrés E., Olivas E., Gómez-Roldan C.**	2006	**separate room, separate staff, separate machine**					Fair
			separate machines, shared room	1993	2/144 (1.4%)	nd	nd	
			separate room, separate staff, separate machine	**2003**	**10/161 (6.2%)**	**nd**	**nd**	
				2003	**14/175 (8.0%)**	**nd**	**nd**	
				2001	**13/183 (7.1%)**	**nd**	**nd**	
				2000	**17/172 (10%)**	**nd**	**nd**	
				1999	**18/150 (12%)**	**nd**	**nd**	
				1998	**23/161 (14.3%)**	**nd**	**nd**	
				1997	**26/169 (15.4%)**	**nd**	**nd**	
				1996	**31/171 (18.1%)**	**nd**	**nd**	
			separate machines, shared room	1995	34/157 (21.7%)	nd	nd	
				1994	38/146 (26.0%)	nd	nd	
				1993	37/144 (25.7%)	nd	nd	
				1992	37/121 (30.6%)	nd	nd	
17382087	**Shebeb AM., Kotkat AM., Abd El Reheim SM., Farghaly AG., Fetohy EM.**	2006	Health Education Program (HEP)	**6 month**	1/10 (10%)	nd	nd	Poor
			isolation of seropositive patients		**11/45 (24%)**	**nd**	**nd**	
			nd		2/19 (11%)	nd	nd	
			Health Education Program (HEP)	**6-12 month**	1/18	nd	nd	
			isolation of seropositive patients		**3/32**	**nd**	**nd**	
			nd		5/24	nd	nd	
			Health Education Program (HEP)	**6-18 months**	0/15	nd	nd	
			isolation of seropositive patients		**3/30**	**OR 0.65 (0.23, 1.80)**	**nd**	
			nd		2/12	nd	nd	
15469615	**Shamshirsaz AA., Kamgar M., Bekheirnia MR., Ayazi F., Hashemi SR., Bouzari N., Habibzadeh MR., Pourzahedgilani N., Broumand V., Shamshirsaz AH., Moradi M., Borghei M., Haghighi NN., Broumand B.**	2004	**The only difference between two groups of HD cente**	**9 months**	**4/254 (1.6%)**	**nd**	**0.05**	Good
					9/192 (4.7%)	**nd**		
			The only difference between two groups of HD cente	**18 months**	**2/160 (1.3%)**	**nd**	**<0.05**	
					7/121 (5.8%)	**nd**		

Table S10: Evidence profile: Isolation of HCV patients receiving hemodialysis

Outcome	# of Studies and Study Design	Total N of Patients	Methodological Quality of Studies	Consistency Across Studies	Directness of the Evidence, including Applicability	Other Considerations	Summary of Findings		
							Quality of Evidence for Outcome	Description of Findings	Importance of Outcome
HCV seroconversion	4 Pre-post design, 1 nRCS	2064	Important Limitations* (-2)	No Important Inconsistencies† (0)	Some uncertainty about directness of evidence‡ (-1)	None	Very Low	Large reductions in rates of seroconversion in most studies, to 0% in 2 studies	High
HCV positivity	1 RCT 2 Pre-post design 1 cohort	1072	RCT: none Observational: Important Limitations* (-2)	No Important Inconsistencies§ (0)	Some uncertainty about directness of evidence‡ (-1)	None	Low	Significantly lower event rate with dedicated HD machines (1.3% vs. 5.8%) 1 study with reduction post-isolation, but rate was already falling annually without isolation 2 studies with rate falling by about half	Moderate
Total N		2543							

Balance of Potential Benefits and Harms:
Introduction of isolation associated with reduction in HCV seroconversion and HCV positivity; however, unclear if this was the primary cause of the improvement.

Quality of Overall Evidence:
Very Low

Studies included in EP: 19147995,7753458, 16903625, 16685138, 17382087, 15469615

Abbreviations: HCV = hepatitis C virus, HD = hemodialysis, nRCS = nonrandomized comparative study, RCT = randomized controlled trial.

Annotations:

***** Some studies did not incorporate or report the comparability of the baseline characteristics and co-interventions between groups in the study design and/or data analysis. Some studies did not report the compliance with the interventions. Mostly based on pre-post studies, where other factors may have changed also.

† HCV seroconversion rate was higher in the non-isolation group in most studies, while was slightly higher in the NRCS. There was great heterogeneity in measures for isolation.

‡ Mostly limited to developing countries (Iran, Egypt, India, Macedonia, Saudi Arabia, Turkey; also Spain and Switzerland).

§ HCV (antibody) positive rate was consistently higher in the non-isolation group, although it might reflect the decreased prevalence in the general population in the pre-post design.

Table S11: Summary table
Transplantation vs. waitlist among patients with HCV infection
Categorical outcomes

PMID	Author	Year	Type of article	Study design	Database	Sample size	CKD stage	Kidney function	HCV+	HCV genotype	Outcome	Definition	Arm
21546575	Roth D, Gaynor JJ, Reddy R, Ciancio G, Sageshima J, Kupin W, Guerra G, Chen L, Burke GW	2011	Peer-reviewed publication	nRCS	United Network Organ Sharing	175	nd	nd	nd	nd	Patient survival	relative risk of the impact of kidney transplantation on the HR of death	KTx No KTx (candidates)
												relative risk of the impact of kidney transplantation on the HR of death from infection; relative	KTx No KTx (candidates)
												relative risk of the impact of kidney transplantation on the HR od death from CV event	KTx No KTx (candidates)
25340605	Scalea JR, Barth RN, Munivenkatappa R, Philosophe B, Cooper M, Whitlow V, LaMattina JC	2015	Peer-reviewed publication	nRCS	nd	1679	nd	nd	nd	nd	Graft survival	hazards ratio of multivariate analysis of variables associated with graft failure	Longer waitlist time Shorter waitlist time
15636622	Bloom RD, Sayer G, Kosunarty F, Constantinescu S, Abt, Reddy KR	2005	Peer-reviewed publication	nRCS	nd	315	nd	nd	100%	nd	Patient survival	Kaplan Meier	KTx No KTx (candidates)
9100052	Knoll GA, Tankersley MR, Lee JY, Julian BA, Curtis JJ	1997	Peer-reviewed publication	nRCS	United Network for Organ Sharing	58	nd	nd	100%	nd	Patient survival	Kaplan Meier	KTx No KTx (candidates)
9573555	Pereira BJ, Natov SN, Bouthot BA, Murthy BV, Ruthazer R, Schmid CH, Levey AS	1998	Peer-reviewed publication	nRCS	New England Organ Bank	287	nd	nd	100%	nd	Patient survival	relative risk of death	KTx No KTx (candidates)
													KTx No KTx (candidates)
													KTx No KTx (candidates)
													KTx No KTx (candidates)

Table S11: Summary table
Transplantation vs. waitlist among patients with HCV infection
Categorical outcomes

PMID	Author	Year	Timepoint	Frequency/Rate	Relative effect	p-value	Adjusted for
21546575	Roth D, Gaynor JJ, Reddy R, Ciancio G, Sageshima J, Kupin W, Guerra G, Chen L, Burke GW	2011	0-6 mo post-txp	nd	2.51 (1.12, 5.66)	0.03	simultaneous panceas-kidney transplant listing, age 55 years, and white race
			>6-≤84 mo post-txp	nd	0.32 (0.17, 0.62)	0.0007	simultaneous panceas-kidney transplant listing, age 55 years, and white race
			>84 mo post txp	nd	0.74 (0.19, 2.92)	0.66	simultaneous panceas-kidney transplant listing, age 55 years, and white race
			0-6 mo post-txp	nd	26.62 (5.01, 141.3)	0.0001	simultaneous panceas-kidney transplant listing
			>6 months post -txp	nd	1.69 (0.31, 9.14)	0.54	simultaneous panceas-kidney transplant listing
			overall post-txp effect	nd	0.20 (0.08, 0.47)	0.0002	simultaneous panceas-kidney transplant listing, age 55 years, and white race
25340605	Scalea JR, Barth RN, Munivenkatappa R, Philosophe B, Cooper M, Whitlow V, LaMattina JC	2015	7.8 years	nd	1.05 (1.01, 1.10)	0.02	DGF, Donor age, R-D-, R+D+, R+D-, Retransplant, Pretransplant, History of receipient DM, Recipient race
15636622	Bloom RD, Sayer G, Kosunarty F, Constantinescu S, Abt, Reddy KR	2005	96 months	~80% ~50%	nd	0.003	nd
9100052	Knoll GA, Tankersley MR, Lee JY, Julian BA, Curtis JJ	1997	48 months	~85% ~70%	nd	0.043	nd
9573555	Pereira BJ, Natov SN, Bouthot BA, Murthy BV, Ruthazer R, Schmid CH, Levey AS	1998	0-3 months post-tx	nd nd	4.75 (2.76, 8.17)	nd	nd
			4-6 months post-tx	nd nd	1.76 (0.75, 4.13)	nd	nd
			7-47 months post-tx	nd nd	0.31 (0.18, 0.54)	nd	nd
			>48 months post-tx	nd nd	0.84 (0.51, 1.37)	nd	nd

Table S12: Evidence profile: Transplantation vs. waitlist among patients with HCV infection

Outcome	# of Studies and Study Design	Total N of Patients	Methodological Quality of Studies	Consistency Across Studies	Directness of the Evidence, including Applicability	Other Considerations	Summary of Findings		
							Quality of Evidence for Outcome	Description of Findings	Importance of Outcome
Death	4 retrospective	835	Serious limitations (-1)*	No important inconsistencies (0)	Direct (0)	None (0)	Moderate	Better long-term survival with kidney transplant	Critical
Graft loss	1 retrospective	1679	No limitations (0)	N/A	Indirect (-1)	Sparse (-1)	Low	Better graft survival with short waitlist time than long waitlist time.	Critical
Total N		2514							

Balance of Potential Benefits and Harms:
Kidney transplantation results in improved patient and graft survival than remaining on the waitlist.

Quality of Overall Evidence:
Moderate

Studies included in EP: 21546575, 25340605, 15636622, 9100052, 9573555

Annotations:
***** Mostly unadjusted analyses.
† Study comparison was of short vs. long waitlist time.

Table S13: Summary table HCV infection as predictor of death among kidney transplant recipients

PMID	Author	Year	Type of article	Country	Study design	Registry Name	Population	Sample Size, Total	CKD stage, baseline	Kidney function, baseline	HCV genotypes	Follow-up Time	Predictor	Predictor Definition	Predictor units	# w/Predictor or mean (95%)	Outcome	Outcome Definition
	Fontaine	2013	Abstract	France	Retrospective Case Control	Cristal database	KTx	25,830	CKD 5T			15 y	HCV+ HBV+ and HCV+	nd coinfection		983 76	Mortality	
23400903	**Soliman**	2013	Peer-reviewed	Egypt	Retrospective cohort study	nd	KTx, HCV genotype 4	411	CKD 5T	nd	genotype 4 100%	8 years	HCV + HCV -	HCV Ab + one year after transplantation HCV Ab - one year after transplantation		137 274	Mortality	nd
25098499	**Xia**	2014	Peer-reviewed	US	Retrospective cohort study	Donor kidney mate analysis	KTx	7036	CKD 5T			10 years max	HCV + (D-/R+) HCV - (D-/R-)			3518 3518	Mortality	
	Heo	2015	Abstract	US	Retrospective cohort study	OPTN	KTx	35,557	CKD 5T			10 years max	HCV + HCV -			2024 33533	Mortality	
22994610	**Ridruejo**	2010	Peer-reviewed	Argentina	Retrospective cohort study	none	KTx	542	CKD 5T			Long-term (unclear)	HCV + HCV -			180 362	Mortality	

Table S13: Summary table HCV infection as predictor of death among kidney transplant recipients

PMID	Author	Year	Cases (# w/Outcome)	Rate	Adjustments (reject if none)	Metric (HR, OR, RR, beta, change)	Estimate (95% CI)	Comparison	P_value	Risk of Bias
	Fontaine	2013	64	nd	"confounding factors"	HR	1.8 (1.6, 2.2)	vs. HCV-	<0.0001	LOW
			59	nd		HR	3.2 (1.9, 5.2)	vs. not coinfected	<0.0001	
23400903	**Soliman**	2013	43	31%	Univariate. Excluded from multivariate model (with age, diabetes, sex, HD time, HTN, CMV, proteinuria)	HR	1.01 (0.97, 1.06)	vs. HCV -	0.5	HIGH
			101	37%			Univariate; Excluded from multivariate model.			
25098499	**Xia**	2014	nd	nd	recipient risk factors	HR	1.24 (1.06, 1.45)	vs HCV- (matched to donor kidney mate)	nd	LOW
			nd	nd						
	Heo	2015	nd	nd	not reported	HR	1.60 (1.40, 1.82)	vs. HCV -	nd	LOW
22994610	**Ridruejo**	2010	46	26%	age >49 y, HBsAg, cadaveric donor, pancreas transplant, IS triple therapy	HR	1.64 (1.05, 2.55)	vs. HCV -	0.027	LOW
			48	13%						

Table S13: Summary Table
HCV infection as predictor of graft loss among kidney transplant recipients

PMID	Author	Year	Type of article	Country	Study design	Registry Name	Population	Sample Size, Total	CKD stage, baseline	Kidney function, baseline	HCV genotypes	Follow-up Time	Predictor	Predictor Definition	Predictor units
	Fontaine	2013	Abstract	France	Retrospective Case Control	Cristal database	KTx	25,830				15 y	HCV+ HBV+ and HCV+		
16244496	**Mitwalli**	2006	Peer-reviewed	Saudi Arabia	Retrospective cohort study	nd	KTx	448	CKD 5T	nd	nd	5.85 (2.7)	HCV + HCV -	2nd and 3rd generation ELISA tests for HCV Ab, Ampiclor HCV amplification kit for HCV RNA	
26900309	**Molmenti**	2015	Peer-reviewed publication	US	Retrospective cohort study	UNOS	KTx	88,284	CKD 5T	nd, all received KTx	nd	nd	HCV + HCV - HCV + HCV -		
25098499	**Xia**	2014	Peer reviewed	US	Retrospective cohort study	Donor kidney mate analysis	KTx	7036	CKD 5T			10 years max	HCV + (D-/R+) HCV - (D-/R-)		
	Heo	2015	Abstract	US	Retrospective cohort study	OPTN	KTx	35,557	CKD 5T			10 years max	HCV + HCV -		
	Kassis	2014	Abstract	US	Retrospective cohort study	UNOS/OPTN	KTx	61,775	CKD 5T			14 years max	HCV + HCV -		
22994610	**Ridruejo**	2010	Peer-reviewed	Argentina	Retrospective cohort study	none	KTx	542	CKD 5T			6 months	HCV + HCV -		

Table S13: Summary Table
HCV infection as predictor of graft loss among kidney transplant recipients

PMID	Author	Year	# w/Predictor or mean (95%)	Outcome	Outcome Definition	Cases (# w/Outcome)	Rate	Adjustments (reject if none)	Metric (HR, OR, RR, beta, change)	Estimate (95% CI)	Comparison	P_value	Risk of Bias
	Fontaine	2013	983	Graft loss		53	nd	"confounding factors"	HR	1.3 (1.2, 1.6)	vs. HCV-	<0.0001	LOW
			76			54	nd		HR	1.8 (1.2, 2.7)	vs. not coinfected	<0.01	
16244496	**Mitwalli**	2006	286	Graft failure	nd	119	41.6%	age, sex, type of donor, hypertension	HR	4.37 (1.81, 4.77)	vs. HCV -	nd	LOW
			162			106	65.4%						
26900309	**Molmenti**	2015	799	graft failure (live donor recipient)	nd	nd	nd	donor age, donor BMI, donor gender, donor ethnicity, HLA mismatch level, donor preoperative creatinine, and donor hepatitis C antibodyrecipient drug-treated hypertension and Hep B SAg	HR	1.56 (1.33, 1.83)	vs. HCV-	<0.05	LOW
			23,544			nd	nd						
			4076	graft failure (deceased donor recipient)	nd	nd	nd	donor age, donor BMI, donor gender, donor ethnicity, HLA mismatch level, donor terminal laboratory creatinine, donor hepatitis C antibody, donor history of diabetes, donor history of hypertension, donor cause of death, and donor cardiac arrest postbrain death, recipient drug-treated hypertension and hepatitis B surface antigen	HR	1.44 (1.34, 1.54)	vs. HCV-	<0.05	
			49241			nd	nd						
25098499	**Xia**	2014	3518	Graft loss		nd	nd	recipient risk factors	HR	1.24 (1.04, 1.47)	vs HCV- (matched to donor kidney mate)	nd	LOW
			3518			nd	nd						
	Heo	2015	2024	Graft failure		nd	nd	not reported	HR	1.32 (1.15, 1.52	vs. HCV -	nd	LOW
			33533										
	Kassis	2014	3334	Graft failure		nd	nd	not reported	HR	1.34 (1.31, 1.37)	vs. HCV-	<0.001	
			58441										
22994610	**Ridruejo**	2010	180	Graft failure		36	20%	age >49 y, cadaveric donor, IS triple therapy	HR	2.65 (1.19, 3.23)	vs. HCV -	0.008	LOW
			362			31	9%						

Table S14: Evidence profile: HCV infection as predictor of death and graft loss among kidney transplant recipients

Outcome	# of Studies and Study Design	Total N of Participants	Methodological Quality of Studies	Consistency Across Studies	Directness of the Evidence, including Applicability	Other Considerations	Summary of Findings		
							Quality of Evidence for Outcome	Description of Findings	Importance of Outcome
Death	5 retrospective cohorts	Cohorts: 411-35,557	No limitations (0)	No important inconsistencies (0)	Direct (0)	None	High	4 of 5 studies found significant association between HCV+ status and mortality among KTx recipients (HR 1.01-1.8). The study with a nonsignificant finding was restricted to HCV genotype 4 (in Egypt). 1 study found that HCV/HBV coinfection was associated with a higher death rate (HR 3.2).	Critical
Graft Loss	7 retrospective cohorts	Cohorts: 448-61,775	No limitations (0)	No important inconsistencies (0)	Direct (0)	None	High	All 7 studies found statistically significant associations between HCV+ status and increased risk of graft loss (ES 1.3-4.37). 1 study found similarly increased risk in patients with live or deceased donor kidneys. 1 study found that HCV/HBV coinfection was associated with a higher rate of graft loss (HR 1.8).	Critical
Total N	8 retrospective cohorts	Cohorts: 411-61,775							

Association of HCV+ status and CKD:
Kidney transplant recipients with HCV infection are at higher risk of death and graft loss than similar patients without HCV.

Quality of Overall Evidence:
High

Studies included in EP: 23400903, 16244496, 26900309, 25098499, 22994610, AASLD-850 2013, ATC Abstracts 2015, Kassis 2014

Abbreviations: CKD: chronic kidney disease; DAA: direct-acting antivirals; GFR: glomerular filtration rate; RCT: randomized controlled trial; SVR: sustained virological response

Table S15: Summary Table
Clinical outcomes of HCV-positive kidney transplant recipients from HCV-positive donors
Categorical outcomes

PMID	Author	Year	Publication	Study design	Database	Sample size	CKD stage	Kidney function	HCV+	HCV genotype	Outcome	Arm
ATC 2013 C1264	**Jawa P et al**	2013	Abstract	nRCS, retrospective	Einstein Medical Center Philadelphia	163	nd	nd	nd	nd	**Death**	**D+/R+**
												D-/R+
												D+/R+
												D-/R+
												D+/R+
												D-/R+
											Graft loss	**D+/R+**
												D-/R+
												D+/R+
												D-/R+
												D+/R+
												D-/R+
AST 2015 P-53	**Limkemann A et al.**	2015	Abstract	nRCS, retrospective	OPTN	1841	nd	nd	37.6% donors 0% recipients	nd	**Death**	**D+/R-**
												D-/R-
											Graft loss	**D+/R-**
												D-/R-
20353475	**Kucirka LM et al.**	2010	Journal	nRCS, retrospective	UNOS	6830	nd		29.3% donors 100% recipients	nd	**Death**	**D+/R+**
22560841	**Kucirka LM et al.**	2012				6250						D-/R+
											Graft loss	**D+/R+**
												D-/R+
22283142	**Singh N et al.**	2012	Journal	nRCS, retrospective	UWisconsin Abdominal Transplant	2169	nd	nd	7.1% donors	nd	**Death**	**D+/R+**
												D-/R+
												D+/R-
												D-/R-
											Graft loss	**D+/R+**
												D-/R+
												D+/R-
												D-/R-

PMID	Author	Year	Publication	Study design	Database	Sample size	CKD stage	Kidney function	HCV+	HCV genotype	Outcome	Arm
											Acute rejection	**D+/R+**
												D-/R+
												D+/R-
												D-/R-
20977636	**Morales JM et al.**	2010	Journal	nRCS, prospective	Madrid/Barcelona transplant centers	545	nd	nd	34.6% donors 100% recipients		**Death**	**D+/R+**
												D-/R+
											Graft loss	**D+/R+**
												D-/R+
											Acute rejection	**D+/R+**
												D-/R+
											Delayed graft function	**D+/R+**
												D-/R+
ATC 2015 1678	**Myint T et al**	2015	Abstract	nRCS, retrospective	SRTR	12,841	nd	nd	100% donors	nd	**Death**	**D+/R+ ≤50 yo**
												D-/R+ ≤50 yo
												D+/R+ >50 yo
												D-/R+ >50 yo
												D+/R-
												D-/R-
25340605	**Scalea JR et al**	2015	Journal	nRCS, retrospective	Baltimore transplant center	1679	nd	nd	nd	nd	**Death**	**D+/R+**
												D-/R+
												D-/R-
											Graft loss	**D+/R+**
												D-/R+
												D-/R-

Table S15: Summary Table
Clinical outcomes of HCV-positive kidney transplant recipients from HCV-positive donors
Categorical outcomes

PMID	Author	Year	Timepoint	Frequency/Rate	Relative effect	p-value	Quality	Notes
ATC 2013 C1264	**Jawa P et al**	2013	**1 year**	**7/106 (6.7%)**	**nd**	**>0.05 (overall)**		Time since transplant, not waitlist
				9/57 (16%)				
			3 years	**25/106 (24%)**		**nd**		
				15/57 (26%)				
			5 years	**43/106 (41%)**		**nd**		
				23/57 (41%)				
			1 year	**4/102 (3.9%)**	**nd**	**>0.05 (overall)**		
				6/57 (11%)				
			3 years	**21/106 (20%)**		**nd**		
				11/57 (19%)				
			5 years	**41/106 (39%)**		**nd**		
				14/57 (24%)				
AST 2015 P-53	**Limkemann A et al.**	2015	**5 years**	**nd/692 (31%)**	**nd**	**<0.001**		Time since transplant, not waitlist; D+ on waitlist for 3 years less than D-
				nd/1149 (25%)				
			5 years	**nd/692 (53%)**	**nd**	**<0.001**		
				nd/1149 (37%)				
20353475	**Kucirka LM et al.**	2010	**nd**	**613/1804 (34.0%) [smaller subset]**	**adjHR 1.29 (1.15, 1.45)**	**<0.001**		Adjusted for wait time
22560841	**Kucirka LM et al.**	2012		1467/4446 (33.0%) [smaller subset]				
			nd	**774/1804 (42.9%) [smaller subset]**	**adjHR 1.18 (1.04, 1.32)**	**0.007**		
				1881/4446 (42.3%) [smaller subset]				
22283142	**Singh N et al.**	2012	**6.0 years (mean)**	**38/95 (40%) (52% per survival curve)**	**adjHR 2.1 (1.4, 2.9)**	**<0.01**		Multivariate, but not adjusted for wait time
				13/59 (22%) (30% per survival curve)	NS (no further data)	NS		
				93/118 (79%) (77% per survival curve)	**adjHR 2.5 (1.9, 3.2)**	**<0.01**		
				446/1897 (24%) (35% per survival curve)	REF			
			6.0 years (mean)	**63/95 (66%) (77% per survival curve)**	**adjHR 1.8 (1.4, 2.5)**	**<0.01**		
				36/59 (61%) (76% per survival curve)	adjHR 2.0 (1.4, 2.8)	<0.01		
				103/108 (87%) (84% per survival curve)	**adjHR 2.1 (1.6, 2.6)**	**<0.01**		
				723/1897 (38%) (52% per survival curve)	REF			

PMID	Author	Year	Timepoint	Frequency/Rate	Relative effect	p-value	Quality	Notes
			6.0 years (mean)	**61%**	**NS (no further data)**	**NS**		
				72%	adjHR 1.9 (1.4, 2.7)	<0.05		
				53%	**NS (no further data)**	**NS**		
				44%	REF			
20977636	**Morales JM et al.**	2010	**6.2 years (mean)**	**33/162 (20%)**	**OR 0.71 (0.41, 1.22)**	**0.22**		Time on dialysis tested, NS
				53/306 (17%)				
			6.2 years (mean)	**68/162 (42%)**	1.25 (0.90, 1.73)	**0.18**		
				112/306 (37%)				
			6.2 years (mean)	**nd/162 (42%)**	**nd**	**0.57**		
				nd/306 (37%)				
			6.2 years (mean)	**nd/162 (54%)**	**nd**	**0.26**		
				nd/306 (48%)				
ATC 2015 1678	**Myint T et al**	2015	nd	**nd**	**adjHR 0.88 (0.72, 1.08) vs. waitlist w/o Txp (implied)**	**NS**		Comparison with waitlist w/o Txp
				nd	adjHR 0.69 (0.53, 0.90)	<0.05		
				nd	**adjHR 0.66 (0.57, 0.77)**	**<0.05**		
				nd	adjHR 0.67 (0.55, 0.81)	<0.05		
				nd	adjHR 1.13 (0.92, 1.40)	NS		
				nd	adjHR 0.55 (0.50, 0.60)	<0.05		
25340605	**Scalea JR et al**	2015	**7.8 years (mean)**	**nd/195 (51% 10 year)**	**nd**	**nd**		multivariate
				nd/66 (59% 10 year)	nd	nd		
				nd/1418 (46% 10 year)	nd	nd		
			7.8 years (mean)	**nd/195 (53% 10 year)**	**0.78 (0.57, 1.08)**	**0.10**		
				nd/66 (72% 10 year)	**1.67 (1.10, 2.52)**	**0.02**		
				nd/1418 (64% 10 year)	**REF**			

Table S15: Summary Table
Clinical outcomes of HCV-positive kidney transplant recipients from HCV-positive donors
Continuous outcomes

PMID	Author	Year	Publication	Study design	Database	Sample size	CKD stage	Kidney function	HCV+	HCV genotype	Outcome	Definition	Arm
22283142	**Singh N et al.**	2012	Journal	nRCS, retrospective	UWisconsin Abdominal Transplant	2169	nd	nd	7.1% donors	nd	**Patient survival**	**median in years**	**D+/R+** **D+/R-** D-/R+ D-/R-
											Graft survival	**median in years**	**D+/R+** **D+/R-** D-/R+ D-/R-
25340605	**Scalea JR et al.**	2015	Journal	nRCS, retrospective	Baltimore transplant center	1679	nd	nd	nd	nd	**Waitlist time**	**mean (SD) in days**	**HCV+ donors** HCV- donors D-/R-
AST 2015 P-53	**Limkemann A et al.**	2015	Abstract	nRCS, retrospective	OPTN	1841	nd	nd	37.6% donors 0% recipients	nd	**Waitlist time**	mean (SD) in days	**D+/R-** **D-/R-**

Table S15: Summary Table
Clinical outcomes of HCV-positive kidney transplant recipients from HCV-positive donors
Continuous outcomes

PMID	Author	Year	N	Timepoint	Value	Change	p-value	Quality
			25	**10 years**	**5.3**	**nd**	**nd**	
22283142	**Singh N et al.**	2012						Good
			23		**9.3**	**nd**	**nd**	
			15		15.5	nd	nd	
			362		16	nd	nd	
			11	**10 years**	**4.4**	**nd**	**nd**	
			17		**5.2**	**nd**	**nd**	
			5		4.8	nd	nd	
			290		9.5	nd	nd	
25340605	**Scalea JR et al.**	2015	**195**	**Txp**		**nd**	**nd**	
					318 (458)			Good
			66		570 (838)	nd	**nd**	
			1418		613 (819)	nd	**nd**	
AST 2015 P-53			**692**	**Txp**	**450 (461)**		**<0.001**	Fair
	Limkemann A et al.	2015						
			1149		**1490 (880)**			

Table S16: Summary Table
Induction and immunosuppression in kidney transplant recipients with HCV infection
Categorical outcomes

PMID	Author	Year	Publication	Study design	Sample size	CKD Stage	Kidney function	Viral HCV RNA	HCV genotype	Outcome	Definition
18551066	**Luan FL et al. (Immunosuppression)**	2008	Journal	nRCS, retrospective	3708	KTR	nd	nd	nd	**Death**	**Death**
18551066	**Luan FL et al. (Induction)**	2008	Journal	nRCS, retrospective	3708	KTR	nd	nd	nd	**Death**	**nd**
										Kidney Graft Failure/Loss	**nd**
ATC 2012 1001	**Sureshkumar KK et al.**	2012	Abstract	nRCS, retrospective	1676	KTR	nd	nd	nd	**Death**	**Survival**
										Kidney Graft Failure/Loss	**Graft Survival**
ATC 2013 B1097	**Aull M et al.**	2013	Abstract	nRCS, retrospective	634	KTR	nd	nd	nd	**Kidney Graft Failure/Loss**	**Graft Survival**

PMID	Author	Year	Publication	Study design	Sample size	CKD Stage	Kidney function	Viral HCV RNA	HCV genotype	Outcome	Definition
ATC 2013 oral 179	**Linatoc J et al.**	2013	Abstract	nRCS, retrospective	79	KTR	nd	nd	nd	**Death**	**Survival**
										Kidney Graft Failure/Loss	**Graft Survival**

Table S16: Summary Table
Induction and immunosuppression in kidney transplant recipients with HCV infection
Categorical outcomes

PMID	Author	Year	Arm	Dose	Duration	Timepoint	Frequency/Rate	Relative effect	p-value
18551066	**Luan FL et al. (Immunosuppression)**	2008	**tacrolimus**	**nd**	**nd**	**nd**	**nd**	**adj HR 1.03 (0.79, 1.35)**	**0.83**
			cyclosporin A	**nd**	**nd**	**nd**	**nd**	**adj HR 1.12 (0.88, 1.44)**	**0.37**
			mycophenolate mofetil	**nd**	**nd**	**nd**	**nd**	**adj HR 0.77 (0.64, 0.92)**	**0.005**
			sirolimus/everolimus	**nd**	**nd**	**nd**	**nd**	**adj HR 1.13 (0.83, 1.55)**	**0.43**
			steroid	**nd**	**nd**	**nd**	**nd**	**adj HR 1.16 (0.79, 1.71)**	**0.44**
			no immunosuppression	nd	nd	nd	nd		
18551066	**Luan FL et al. (Induction)**	2008	**depleting antibodies**	**nd**	**nd**	**nd**	**nd**	**adj HR 0.75 (0.61, 0.90)**	**0.003**
			nondepleting antibodies	**nd**	**nd**	**nd**	**nd**	**adj HR 0.82 (0.69, 0.98)**	**0.03**
			no immunosuppression	**nd**	**nd**	**nd**	**nd**	**adj HR 0.79 (0.64, 0.98)**	**0.03**
			no induction	nd	nd	nd	nd		
			depleting antibodies	**nd**	**nd**	**nd**	**nd**	**adj HR 1.14 (0.92, 1.42)**	**0.42**
			no induction	nd	nd	nd	nd		
ATC 2012 1001	**Sureshkumar KK et al.**	2012	**rabbit-antithymocyte globulin or alemtuzumab**	**nd**	**nd**	**nd**	**nd**	**HR 1.00 (0.76, 1.33)**	**0.97**
			basiliximab or daclizumab	nd	nd	nd	nd		
			rabbit-antithymocyte globulin or alemtuzumab	**nd**	**nd**	**nd**	**nd**	**HR 1.12 (0.93, 1.36)**	**0.24**
			basiliximab or daclizumab	nd	nd	nd	nd		
ATC 2013 B1097	**Aull M et al.**	2013	**rATG induction + tacrolimus + mycophenolate + rapid steroid taper**	**nd**	**nd**	**234 weeks**	**22/31 (72%)**		

PMID	Author	Year	Arm	Dose	Duration	Timepoint	Frequency/Rate	Relative effect	p-value
ATC 2013 oral 179	**Linatoc J et al.**	2013	**thymoglobulin**	**nd**	**nd**	**52 weeks**	**34/40 (85%)**	**nd**	**nd**
			no induction	nd	nd	52 weeks	37/39 (94.9%)		
			thymoglobulin	**nd**	**nd**	**156 weeks**	**28/40 (69.7%)**	**nd**	**nd**
			no induction	nd	nd	156 weeks	32/39 (82.1%)		
			thymoglobulin	**nd**	**nd**	**260 weeks**	**25/40 (61.7%)**	**nd**	**0.005**
			no induction	nd	nd	260 weeks	32/39 (79.5%)		
			thymoglobulin	**nd**	**nd**	**52 weeks**	**36/40 (92%)**	**nd**	**nd**
			no induction	nd	nd	52 weeks	37/39 (94.7%)		
			thymoglobulin	**nd**	**nd**	**156 weeks**	**33/40 (83.3%)**	**nd**	**nd**
			no induction	nd	nd	156 weeks	31/39 (80.4%)		
			thymoglobulin	**nd**	**nd**	**260 weeks**	**23/40 (58.1%)**	**nd**	**0.005**
			no induction	nd	nd	260 weeks	30/39 (77.4%)		

Table S17: Summary Table
HCV treatment of HCV-associated glomerular disease
Categorical outcomes

PMID	Author	Year	Type of article	Study design	Sample size	CKD stage	Kidney function	GN description	Viral HCV RNA	HCV genotype	Outcome
18711294	**Abbas G., Hussain S., Shafi T.**	2008	Peer-reviewed publication	Single arm (cohort), unclear	30	nd	SCr: 1.44 mg/dL (range 0.70, 4.60); proteinuria: 4.83 g (range 1.60, 9.07)	Membranoproliferative glomerulonephritis in 25/30 (83%), membranous glomerulonephritis (MGN) in 3/30 (10%), mesangioproliferative glomerulonephritis (MesGN) in 2/30 (7%)	nd	3: 100%	**SVR24** **Serious AEs**
26567178, ILC 2015 LP08	**Saadoun D., Thibault V., Si Ahmed SN., Alric L., Mallet M., Guillaud C., Izzedine H., Plaisier A., Fontaine H., Costopoulos M., Le Garff-Tavernier M., Hezode C., Pol S., Musset L., Poynard T., Cacoub P.**	2015	Peer-reviewed publication	Single arm (cohort), prospective	24	CKD 1-3	GFR: median 77.3 mL/min/1.73m2 (44-90); SCr: median 89 µmol/L (80-163); proteinuria: 1.09 g/d (0.6, 2.4)	HCV-cryoglobulinemia vasculitis; 5 (21%) patients had renal involvement	5.9 log10 IU/mL (4.5-6.3)	1a: 25%; 1b: 25%; 2: 8%; 3: 25%; 4: 13%; 5: 4%	**Death** **Discontinuation due to AEs** **Relapse (viral)** **SVR12** **Serious AEs**
EULAR 2013 OPO212	**Roccatello D., Sciascia S., Baldovino S., Rossi D.**	2012	Abstract	Single arm (cohort), prospective	27	Type II mixed cryoglobulinemia syndrome with manifestations, including renal involvement (diffuse membranoproliferative glomerulonephritis in 15 cases), peripheral neuropathy (26 cases) and large	SCr: 2.2 (1.9); proteinuria: 2.3 (2.1)	Diffuse membranoproliferative glomerulonephritis (15 cases), peripheral neuropathy (26 cases), large skin ulcers (9 case, in 7 necrotizing)	nd	nd	**Relapse (viral)**
22147661; 26255249	**De Vita S., Quartuccio L., Isola M., Mazzaro C., Scaini P., Lenzi M., Campanini M., Naclerio C., Tavoni A., Pietrogrande M., Ferri C., Mascia MT., Masolini P., Zabotti A., Maset M., Roccatello D., Zignego AL., Pioltelli P., Gabrielli A., Filippini D., Perrella O., Migliaresi S., Galli M., Bombardieri S., Monti G.; Quartuccio L., Zuliani F., Corazza L., Scaini P., Zani R., Lenzi M., Tavoni A., Sebastiani M., Baldovino S., Urraro T., Saccardo F., Sbreglia C., Mazzaro C., Pioltelli P., Fraticelli P., Filippini D., Gabrielli A., Perrella O., Scarpato S., Roccatello D., Zignego AL., Ferri C., Bombardieri S., Pietrogrande M., Monti G., Galli M., De Vita S.**	2012; 2015	Peer-reviewed publication	RCT	59	CKD 1-3	SCr: 1.4 mg/dL (range 0.7, 2.8); Proteinuria: 2.0 g/24h (range 0.6, 7.9)	Severe cryoglobulinemic vasculitis	nd	nd	**Death** **Discontinuation due to AEs** **Discontinuation** **Relapse** **Serious AEs**
26474537	**Sise ME., Bloom AK., Wisocky J., Lin MV., Gustafson JL., Lundquist AL., Steele D., Thiim M., Williams WW., Hashemi N., Kim AY., Thadhani R., Chung RT.**	2016	Peer-reviewed publication	nRCS, retrospective	22	CKD 1-2: 58%; CKD 3A: 25%; CKD 3B: 8%; CKD 4-5: 8%	GFR: 79 mL/min/1.73m2 (range 43, 115); SCr: 0.97 mg/dL (0.70, 2.47)	Mixed cryoglobulinemia	nd	1a: 45.5%; 1b: 13.6%; 2: 18.2%; 3: 9.1%; 4: 4.5%	**SVR12** **Discontinuation due to AEs** **Relapse (viral)** **Serious AEs**
22147444	**Sneller MC., Hu Z., Langford CA.**	2012	Peer-reviewed publication	RCT	24	CKD 1-3	CrCl: >30 mL/min	Hepatitis C-associated cryoglobulinemic vasculitis	median 5.50 log10 copies/mL	1: 83.3%; 2: 16.7%	**Relapse** **Serious AEs**
25890508	**Mazzaro C., Panarello G., Mauro E., Gattei V., Pozzato G.**	2015	Peer-reviewed publication	Single arm (cohort), retrospective	10	CKD 3	CrCl: 47 (10) mL/min; SCr: 1.6 (0.3) mg/mL; Proteinuria: 4.0 (0.7) g/24h	HCV-positive cryoglobulinemic glomerulonephritis.	15.0 x 10^6 copies/mL (17.5 x 10^6)	1b: 50%; 2: 20%; 3: 30%	**SVR** **Discontinuation due to AEs** **Relapse (viral)**
17075881	**Saadoun D., Resche-Rigon M., Thibault V., Piette JC., Cacoub P.**	2006	Peer-reviewed publication	Single arm (cohort), prospective	72	nd	GFR ≤70: 22%	Mixed cryoglobulinemia vasculitis	5.87 (0.65) log copies/mL	1: 61.1%	**Early SVR** **SVR26** **SVR0** **SVR total** **Death** **Discontinuation due to AEs** **Serious AEs**
22153224	**Mazzaro**	2011	Peer-reviewed publication	Single arm (cohort), retrospective	86	nd	nd	Mixed cryoglobulinemia vasculitis	nd	1a: 7%, 1b: 42%, 2: 39%, 3: 11%, 4: 1%	**SVR** **Relapse (viral)** **Discontinuation due to AEs**

PMID	Author	Year	Type of article	Study design	Sample size	CKD stage	Kidney function	GN description	Viral HCV RNA	HCV genotype	Outcome
26853322	**Gragnani**	2016	Peer-reviewed publication	Single arm (cohort), prospective	17	CKD 3: 17.6%	CrCl: 100.0 (39.6) ml/min, Proteinuria: 13.8 (29.0) mg/dl	Mixed cryoglobulinemia vasculitis	1.77 (1.85) x 10^6 IU/ml	1a: 12%, 1b: 65%, 2: 6%, 3: 17%	**Serious AEs**
											SVR12
27483451	**Gragnani**	2016	Peer-reviewed publication	nRCS, prospective	44	nd	nd	Mixed cryoglobulinemia	2.9 (3.6) IU/mL x 10^6	1a: 4.5%; 1b: 47.7%, 2: 29.5%; 3: 11.3%, 4: 6.8%	**SVR24**
											SVR4
											Discontinuations due to AEs

Table S17: Summary Table
HCV treatment of HCV-associated glomerular disease
Categorical outcomes

PMID	Author	Year	Definition	Arm	Dose	Timepoint	Duration	Frequency/Rate	Relative effect	p-value	Quality
18711294	Abbas G., Hussain S., Shafi T.	2008	nd	IFN + RBV	3 MU TIW + 200-1000 mg OD	24 weeks	≥6 months	4/8 (50%)			
			severe anemia			nd		7/27 (26%)			Poor
26567178, ILC 2015 LP08	Saadoun D., Thibault V., Si Ahmed SN., Alric L., Mallet M., Guillaud C., Izzedine H., Plaisier A., Fontaine H., Costopoulos M., Le Garff-Tavernier M., Hezode C., Pol S., Musset L., Poynard T., Cacoub P.	2015		sofosbuvir + ribavirin	400 mg OD + 200-1400 mg OD	24 weeks	24 weeks	2/24 (8%)			
			nd								Good
			nd			24 weeks		2/24 (8%)			
			nd			12 weeks		4/24 (17%)			
			nd			12 weeks		18/24 (74%)			
			nd			24 weeks		2/24 (8%)			
EULAR 2013 OPO212	Roccatello D., Sciascia S., Baldovino S., Rossi D.	2012	nd	rituximab	375 mg/m2 on days 1, 8, 15, 22 and then 2 months later	124 weeks	nd	9/27 (33%)			
											Fair
22147661; 26255249	De Vita S., Quartuccio L., Isola M., Mazzaro C., Scaini P., Lenzi M., Campanini M., Naclerio C., Tavoni A., Pietrogrande M., Ferri C., Mascia MT., Masolini P., Zabotti A., Maset M., Roccatello D., Zignego AL., Pioltelli P., Gabrielli A., Filippini D., Perrella O., Migliaresi S., Galli M., Bombardieri S., Monti G.; Quartuccio L., Zuliani F., Corazza L., Scaini P., Zani R., Lenzi M., Tavoni A., Sebastiani M., Baldovino S., Urraro T., Saccardo F., Sbreglia C., Mazzaro C., Pioltelli P., Fraticelli P., Filippini D., Gabrielli A., Perrella O., Scarpato S., Roccatello D., Zignego AL., Ferri C., Bombardieri S., Pietrogrande M., Monti G., Galli M., De Vita S.	2012; 2015	nd	rituximab	1 g IV days 0 and 14	24 months	24 months	2/28 (7.1%)			
											Fair
				rituximab	1 g IV days 0 and 14	72.6 months	24 months	5/30 (20%)			
				control	NA		24 months	1/29 (3.4%)			
			nd	rituximab	1 g IV days 0 and 14	24 months	24 months	2/28 (7.1%)			
				control	NA		24 months	3/29 (10.3%)			
			nd	rituximab	1 g IV days 0 and 14	24 months	24 months	11/28 (39.2%)			
				control	NA		24 months	28/29 (96.5%)			
			nd	rituximab	1 g IV days 0 and 14	72.6 months	24 months	17/30 (56.7%)			
			nd	rituximab	1 g IV days 0 and 14	24 months	24 months	5/28 (17.9%)			
				control	NA		24 months	3/29 (10.3%)			
26474537	Sise ME., Bloom AK., Wisocky J., Lin MV., Gustafson JL., Lundquist AL, Steele D., Thiim M., Williams WW., Hashemi N., Kim AY., Thadhani R., Chung RT.	2016	nd	sofosbuvir-based therapy (SOF/SIM: 67%; SOF/RBV 12 weeks: 17%; SOF/RBV 24 weeks: 17%)	SOF: 400 mg OD; SIM: 150 mg OD; RBV: 400-1200 mg OD	12 weeks	SOF: 12-24 weeks; SIM: 12 weeks; RBV: 12-24 weeks	10/12 (83.3%)			
											Poor
				peg-IFN + RBV	180 µg QW + 800 mg OD		24-52 weeks	1/10 (10%)			
			due to severe AEs	sofosbuvir-based therapy (SOF/SIM: 67%; SOF/RBV 12 weeks: 17%; SOF/RBV 24 weeks: 17%)	SOF: 400 mg OD; SIM: 150 mg OD; RBV: 400-1200 mg OD	12-24 weeks	SOF: 12-24 weeks; SIM: 12 weeks; RBV: 12-24 weeks	1/12 (8.3%)			
				peg-IFN + RBV	180 µg QW + 800 mg OD	24-52 weeks	24-52 weeks	5/10 (50%)			
			nd	sofosbuvir-based therapy (SOF/SIM: 67%; SOF/RBV 12 weeks: 17%; SOF/RBV 24 weeks: 17%)	SOF: 400 mg OD; SIM: 150 mg OD; RBV: 400-1200 mg OD	12 weeks	SOF: 12-24 weeks; SIM: 12 weeks; RBV: 12-24 weeks	2/12 (16.6%)			
				peg-IFN + RBV	180 µg QW + 800 mg OD		24-52 weeks	nd/10 (nd)			
			nd	sofosbuvir-based therapy (SOF/SIM: 67%; SOF/RBV 12 weeks: 17%; SOF/RBV 24 weeks: 17%)	SOF: 400 mg OD; SIM: 150 mg OD; RBV: 400-1200 mg OD	12-24 weeks	SOF: 12-24 weeks; SIM: 12 weeks; RBV: 12-24 weeks	2/12 (16.6%)			
				peg-IFN + RBV	180 µg QW + 800 mg OD	24-52 weeks	24-52 weeks	5/10 (50%)			
22147444	Sneller MC., Hu Z., Langford CA.	2012	nd	rituximab	375 mg/m2 on days 1, 8, 15, and 22	12 months	12 months	4/12 (33.3%)			Good
				control	NA			no remissions			
			nd	rituximab	375 mg/m2 on days 1, 8, 15, and 22	12 months	12 months	1/12 (8.3%)			
				control	NA			0/12 (0%)			
25890508	Mazzaro C., Panarello G., Mauro E., Gattei V., Pozzato G.	2015	nd	peg-IFN + RBV	1.5 µg/kg QW + 800-1200 mg OD	4 months	24-48 weeks	6/10 (60%)			
											Good
						36 months		4/10 (40%)			
			nd			4 months		1/10 (10%)			
			nd			36 months		2/10 (20%)			
17075881	Saadoun D., Resche-Rigon M., Thibault V., Piette JC., Cacoub P.	2006	An early virologic response was defined as the absence of detectable serum HCV RNA 3 months after starting antiviral treatment.	IFN + RBV	3 MU TIW + 600-1200 mg OD	3 months	≥6 months	16/32 (50%)			
											Good
				peg-IFN + RBV	1.5 µg/kg OD + 600-1200 mg OD		≥6 months	25/40 (62.5%)			
			A sustained virologic response was defined as the absence of detectable serum HCV RNA 6 months after stopping antiviral treatment.	IFN + RBV	3 MU TIW + 600-1200 mg OD	12 months	≥6 months	19/32 (59.3%)			
				peg-IFN + RBV	1.5 µg/kg OD + 600-1200 mg OD		≥6 months	30/40 (75%)			
				IFN + RBV	3 MU TIW + 600-1200 mg OD	16.63 months (end of therapy)	≥6 months	20/32 (62.5%)			
				peg-IFN + RBV	1.5 µg/kg OD + 600-1200 mg OD		≥6 months	30/40 (75%)			
				IFN + RBV	3 MU TIW + 600-1200 mg OD	39.7 months (end of follow-up)	≥6 months	17/32 (53.1%)			
				peg-IFN + RBV	1.5 µg/kg OD + 600-1200 mg OD		≥6 months	25/40 (62.5%)			
				IFN + RBV	3 MU TIW + 600-1200 mg OD	16.63 months (end of therapy)	≥6 months	6/32 (18.8%)	nd	0.98	
				peg-IFN + RBV	1.5 µg/kg OD + 600-1200 mg OD		≥6 months	2/40 (5%)			
				IFN + RBV	3 MU TIW + 600-1200 mg OD	39.7 months (end of follow-up)	≥6 months	0/32 (0%)			
				peg-IFN + RBV	1.5 µg/kg OD + 600-1200 mg OD		≥6 months	0/40 (0%)			
				IFN + RBV	3 MU TIW + 600-1200 mg OD	39.7 months (end of follow-up)	≥6 months	nd/32 (53.1%)			
				peg-IFN + RBV	1.5 µg/kg OD + 600-1200 mg OD		≥6 months	nd/40 (55%)			
22153224	Mazzaro	2011		peg-IFN + RBV	1.5 meg/kg qW + 800-1200 mg qD	>=17.6 or 23.2 months (end of follow-up)	24 or 48 weeks	43/85 (50.6%)			Fair
				peg-IFN + RBV	1.5 meg/kg qW + 800-1200 mg qD	>=17.6 or 23.2 months (end of follow-up)	24 or 48 weeks	19/86 (22.1%)			
				peg-IFN + RBV	1.5 meg/kg qW + 800-1200 mg qD	24 or 48 weeks (end of therapy)	24 or 48 weeks	5/86 (5.8%)			

PMID	Author	Year	Definition	Arm	Dose	Timepoint	Duration	Frequency/Rate	Relative effect	p-value	Quality
26853322	Gragnani	2016		DAA + RBV	(1) ombitasvir, paritaprevir+ ritonavir (once daily dose of 25-mg ombitasvir, 150-mg paritaprevir, and 100- mg ritonavir) and dasabuvir (250 mg twice daily) for 12 or 24 weeks; (2) ombitasvir, paritaprevir+ ritonavir (once daily dose of 25-mg ombitasvir, 150-mg paritaprevir, and 100- mg ritonavir) and dasabuvir (250 mg twice daily) and ribavirin (800-1200 mg daily, weight based dose) for 12 or 24 weeks; (3) sofosbuvir (400 mg once daily) plus daclatasvir (60 mg once daily); (4) sofosbuvir (400 mg once daily) plus ribavirin (800-1200 daily, weight-based dose).	8 weeks (on treatment)	12 or 24 weeks	1/17 (5.9%)			Fair
			nd	sofosbuvir-based combinations	sofosbuvir 400 mg, simeprevir 150 mg, ledipasvir 90 mg, daclatasvir 30 mg, and ribavirin 800-1200 mg daily in a weight-based dose	24 weeks	12 weeks	44/44 (100%)	nd	nd	
27483451	Gragnani	2016									Good
			nd				24 weeks	44/44 (100%)	nd	nd	
			nd				4 weeks	44/44 (100%)	nd	nd	
			nd				24 weeks	0/44 (0%)	nd	nd	

Table S17: Summary Table
HCV treatment of HCV-associated glomerular disease
Continuous outcomes

PMID	Author	Year	Type of article	Study design	Sample size	CKD stage	Kidney function	GN description	Viral HCV RNA	HCV genotype	Outcome	Definition
18711294	**Abbas G., H**	2008	Peer-reviewed publicat	Single arm (cohort), unclear	30	nd	SCr: 1.44 mg/dL (range 0	Membranoproliferative	nd	3: 100%	**Kidney Function, continuous** **Proteinuria, continuous**	**SCr, mg/dL** **proteinuria, g/2**
20439619	**Saadoun D.**	2010	Peer-reviewed publicat	nRCS, prospective	31 (kidney involven	nd	GFR: 58.0 (7.4) mL/min; S	HCV-MC	5.8 log copies/mL (0.7)	1: 67.7%; 2: 9.6%; 3: 1	**Kidney Function, continuous** **Kidney Function, continuous** **Proteinuria, continuous**	**creatininemia, µ** **GFR, mL/min** **proteinuria, g/2**
26567178; ILC 20	**Saadoun D.**	2015	Peer-reviewed publicat	Single arm (cohort), prospective	24	CKD 1-3	GFR: median 77.3 mL/mi	HCV-cryoglobulinemia v	5.9 log10 IU/mL (4.5-6.	1a: 25%; 1b: 25%; 2: 8	**Kidney Function, continuous** **QoL Physical status** **QoL mental status** **Kidney Function, continuous** **Proteinuria, continuous**	**median SCr, µm** **physical status** **mental status** **median GFR, mL** **median proteinu**
EULAR 2013 OPO	**Roccatello**	2012	Abstract	Single arm (cohort), prospective	27	Type II mixed cry	SCr: 2.2 (1.9); proteinuria	diffuse membranoprolif	nd	nd	**Kidney Function, continuous** **Proteinuria, continuous**	**SCr, mg/dL** **proteinuria, g/2**
22147661; 26255	**De Vita S.,**	2012; 20	Peer-reviewed publicat	RCT	59	CKD 1-3	SCr: 1.4 mg/dL (range 0.7	Severe cryoglobulinemic	nd	nd	**Kidney Function, continuous** **Proteinuria, continuous** **QoL Pain** **QoL Paresthesia**	**SCr, mg/dL** **g/24 h** **VAS score for pa** **VAS score for pa**
25890508	**Mazzaro C.**	2015	Peer-reviewed publicat	Single arm (cohort), retrospective	10	CKD 3	CrCl: 47 (10) mL/min; SCr	HCV-positive cryoglobul	15.0 x 10^6 copies/mL (	1b: 50%; 2: 20%; 3: 30	**Kidney Function, continuous** **Kidney Function, continuous** **Proteinuria, continuous**	**SCr, mg/mL** **CrCl, mL/min** **g/24 h**
ACR 2012 1547	**Roccatello**	2012	Abstract	Single arm (cohort), prospective	27	nd	SCr: 2.2 (1.9) mg/dL; Prot	Mixed cryoglobulinemia	nd	nd	**Kidney function, continuous** **Proteinuria, continuous**	**SCr, mg/dL** **g/24 h**
22153224	**Mazzaro**	2011	Peer-reviewed publicat	Single arm (cohort), retrospective	86	nd	nd	Mixed cryoglobulinemia	nd	1a: 7%, 1b: 42%, 2: 39	**Rheumatoid factor** **Cryocrit** **C4 level**	**U/L** **%** **mg/mL**
26853322	**Gragnani**	2016	Peer-reviewed publicat	Single arm (cohort), prospective	17	CKD 3: 17.6%	CrCl: 100.0 (39.6) ml/min	Mixed cryoglobulinemia	1.77 (1.85) x 10^6 IU/m	1a: 12%, 1b: 65%, 2: 6	**Rheumatoid factor** **Cryocrit**	**IU/mL** **%**

PMID	Author	Year	Type of article	Study design	Sample size	CKD stage	Kidney function	GN description	Viral HCV RNA	HCV genotype	Outcome	Definition
											C4 level	mg/dL
											C3 Level	mg/dL
27483451	**Gragnani**	2016	Peer-reviewed publicat	nRCS, prospective	44	nd	nd	Mixed cryoglobulinemia	2.9 (3.6) IU/mL x 10^6	1a: 4.5%; 1b: 47.7%, 2:	**Liver cirrhosis**	**Mode for End-S**

Table S17: Summary Table
HCV treatment of HCV-associated glo
Continuous outcomes

PMID	Author	Year	Arm	Dose	Duration	N	Baseline Value	Timepoint	Value	Change from baseline	p-value	Quality
18711294	Abbas G., H	2008	IFN + RBV	3 MU TI\	≥6 months	30	1.44 (0.70, 4.60)	24 weeks	1.39 0.80, 2.60)	nd	0.678	Poor
			4 hours			30	4.83 (1.60, 9.07)	24 weeks	1.19 (0.50, 2.50)	nd	<0.001	
20439619	Saadoun D.	2010	rituximab + peg-IFN + RBV	375 mg/	52 weeks	21	217.5 (47.4)	24 weeks	136.9 (27.1)	nd	0.03	Fair
			peg-IFN + RBV	2a: 180 µ	48 weeks	10	150.0 (30.6)		169.2 (44.2)	nd	0.28	
			rituximab + peg-IFN + RBV	375 mg/	52 weeks	21	42.8 (5.8)	24 weeks	57.6 (4.5)	nd	0.01	
			peg-IFN + RBV	2a: 180 µ	48 weeks	10	58.0 (7.4)		59.5 (9.9)	nd	0.41	
			rituximab + peg-IFN + RBV	375 mg/	52 weeks	21	3.5 (0.9)	24 weeks	0.35 (0.1)	nd	<0.001	
			peg-IFN + RBV	2a: 180 µ	48 weeks	10	3.1 (0.9)		1.2 (0.5)	nd	0.046	
26567178; ILC 20	Saadoun D.	2015	sofosbuvir + ribavirin	400 mg (	24 weeks	24	89 (80, 163)	24 weeks	85 (78, 146)	nd	nd	Good
						24	nd	24 weeks	nd	+10%	nd	
						24	nd	36 weeks	nd	+14%	nd	
						24	nd	24 weeks	nd	+4%	nd	
						24	nd	36 weeks	nd	+7%	nd	
			./min/1.73 m2			24	77.3 (44, 90)	24 weeks	66.7 (48, 87)	nd	nd	
			ıria, g/24 hours			24	1.09 (0.6, 2.4)	24 weeks	0.17 (0.25, 0.07)	nd	nd	
EULAR 2013 OPO	Roccatello	2012	rituximab	375 mg/	nd	27	2.2 (1.9)	216 weeks	1.6 (1.2)	nd	≤0.05	Fair
			4 hours			27	2.3 (2.1)	216 weeks	0.9 (1.9)	nd	≤0.05	
22147661; 26255	De Vita S.,	2012; 20	rituximab	1 g IV da	24 months	28	1.6 (0.7, 2.8)	1 month	1.2 (0.8, 6.0)	nd	nd	Fair
			control	NA	24 months	29	1.2 (0.7, 2.3)		1.2 (1.0, 2.0)	nd	nd	
			rituximab	1 g IV da	24 months	28	1.6 (0.7, 2.8)	2 months	1.6 (0.8, 6.0)	nd	nd	
			control	NA	24 months	29	1.2 (0.7, 2.3)		1.5 (0.8, 2.4)	nd	nd	
			rituximab	1 g IV da	24 months	28	2.0 (0.6, ,7.9)	1 month	0.6 (0.5, 7.8)	nd	nd	
			control	NA	24 months	29	2.0 (0.9, 6.8)		2.1 (0.9, 7.0)	nd	nd	
			rituximab	1 g IV da	24 months	28	2.0 (0.6, ,7.9)	2 months	0.9 (0.5, 4.5)	nd	nd	
			control	NA	24 months	29	2.0 (0.9, 6.8)		1.85 (1.0, 11.0)	nd	nd	
			rituximab	1 g IV da	24 months	28	70 (10, 100)	1 month	52 (0, 100)	nd	nd	
			control	NA	24 months	29	88 (30, 100)		82 (20,100)	nd	nd	
			rituximab	1 g IV da	24 months	28	70 (10, 100)	2 months	40 (0, 81)	nd	nd	
			control	NA	24 months	29	88 (30, 100)		90 (0, 100)	nd	nd	
			rituximab	1 g IV da	24 months	28	89 (30, 100)	1 month	63 (30, 100)	nd	nd	
			control	NA	24 months	29	90 (10, 100)		70 (10, 100)	nd	nd	
			rituximab	1 g IV da	24 months	28	89 (30, 100)	2 months	44 (10, 100)	nd	nd	
			control	NA	24 months	29	90 (10, 100)		80.5 (10, 100)	nd	nd	
25890508	Mazzaro C.	2015	peg-IFN + RBV	1.5 µg/k	24-48 weeks	10	1.6 (0.3)	4 months	1.6 (0.6)	nd	nd	Good
								36 months	1.7 (0.9)	nd	nd	
						10	47 (10)	4 months	46 (16)	nd	nd	
								36 months	42 (14)	nd	nd	
						10	4.0 (0.7)	4 months	2.9 (1.7)	nd	nd	
								36 months	2.9 (2.4)	nd	nd	
ACR 2012 1547	Roccatello	2012	rituximab	375 mg/	3 months	27	2.2 (1.9)	3 months	1.6 (1.2)	nd	≤0.05	ND
						27	2.3 (2.1)	3 months	0.9 (1.9)	nd	≤0.05	
22153224	Mazzaro	2011	peg-IFN + RBV	1.5 mg/	24 or 48 week	86	211 (320)	24 or 48 weeks (end of therapy)	175 (324)	nd	nd	Fair
								>=17.6 or 23.2 months (end of follow-up)	197 (348)	nd	nd	
			peg-IFN + RBV	1.5 mg/	24 or 48 week	86	5.6 (6.0)	24 or 48 weeks (end of therapy)	2.4 (4.5)	nd	nd	
								>=17.6 or 23.2 months (end of follow-up)	3.8 (4.2)	nd	nd	
			peg-IFN + RBV	1.5 mg/	24 or 48 week	86	9.8 (5.9)	24 or 48 weeks (end of therapy)	11.5 (7.7)	nd	nd	
								>=17.6 or 23.2 months (end of follow-up)	12.3 (8.8)	nd	nd	
26853322	Gragnani	2016	DAA + RBV	(1) ombi	12 or 24 week	17	626.6 (216.8)	8 weeks (on treatment)	137.7 (30.3)	nd	nd	Fair
			DAA + RBV	(1) ombi	12 or 24 week	17	60.2 (11.0)	8 weeks (on treatment)	13.4 (3.1)	nd	nd	

PMID	Author	Year	Arm	Dose	Duration	N	Baseline Value	Timepoint	Value	Change from baseline	p-value	Quality
			DAA + RBV	(1) ombi	12 or 24 week	17	0.087 (0.010)	8 weeks (on treatment)	0.094 (0.009)	nd	nd	
			DAA + RBV	(1) ombi	12 or 24 week	17	0.71 (0.02)	8 weeks (on treatment)	0.88 (0.03)	nd	nd	
27483451	Gragnani	2016	sofosbuvir-based combinatior	sofosbu	24 weeks	44	9.9 (2.5)	12 weeks	8.8 (2.7)	nd	nd	Good
								24 weeks	7.3 (1.9)	nd	nd	

Table S18: Evidence profile: HCV treatment of HCV-associated glomerular disease

Outcome	# of Studies and Study Design	Total N of Patients on Treatment	Methodological Quality of Studies	Consistency Across Studies	Directness of the Evidence, including Applicability	Other Considerations	Summary of Findings		
							Quality of Evidence for Outcome	Description of Findings	Importance of Outcome
Survival	1 RCT 2 cohort (pro)	155	Some limitations (-1)*	Consistent (0)	Direct (0)	Sparse (-1)	Low	Range of survival was 83%-92% Survival was 89% at 40 months for interferon+ribavirin Survival was 92% at 40 months for sofosbuvir+ribavirin Survival was 83% at 73 months for rituximab	Critical
Sustained virological response	1 RCT 13 cohort (4 pro, 9 ret)	654	Some limitations (-1)‡	Consistent (0)	Direct (0)	None (0)	Moderate	SVR 12 or 24:74-100% with DAA treatment (5 studies) 10-63% with PEG-IFN +RBV (4 studies) 50-53% with IFN + RBV (2 studies)	High
Serious adverse events	2 RCT 5 cohort (3 pro, 1 ret, 1 unclear)	248	Some limitations (-1)¶	Important inconsistencies (-1)†	Direct (0)	None (0)	Low	6-17% with Sofosbuvir-based treatment (3 studies) 26-55% with IFN + RBV or PEG-IFN +RBV (4 studies) 8-18% with rituximab (2 studies) 0-10% in placebo arms (2 studies)	High
Discontinuation due to adverse events	2 RCT 12 cohort (5 pro, 5 ret)	362	Some limitations (-1)‖	Important inconsistencies (-1)†	Direct (0)	None (0)	Low	0-8% with Sofosbuvir-based treatment (2 studies) 0-10% with IFN + RBV or PEG-IFN +RBV (4 studies) 7% with rituximab (1 study)	High
Kidney function, continuous	1 RCT 1 nRCS 5 cohort (3 pro, 1 ret, 1 unclear)	208	Some limitations (-1)‡‡	Important inconsistencies (-1)†	Direct (0)	None (0)	Low	Range of decreased serum creatinine for interferon 0-0.1mg/dl Range of decreased serum creatinine for rituximab 0.4-0.9mg/dl Decreased serum creatinine for sofosbuvir+ribavirin 0.04mg/dl	Moderate
Quality of Life	1 RCT 1 cohort (pro)	73	Some limitations (-1)‡‡	Important inconsistencies (-1)†	Direct (0)	None (0)	Low	Increased quality of life (physical, mental status) with sofosbuvir+ribavirin (1 study) Increased quality of life (pain, paresthesia) with rituximab (1 study)	High
Proteinuria, continuous	1 RCT 1 nRCS 5 cohort (3 pro, 1 ret, 1 unclear)	208	Some limitations (-1)‡‡	Important inconsistencies (-1)†	Direct (0)	None (0)	Low	Range of decreased proteinuria for interferon 28-75% Range of decreased proteinuria for rituximab 61-90% Decreased proteinuria for sofosbuvir+ribavirin 84%	Moderate
Cryocrit, Continuous	2 cohort (1 pro, 1 ret)	103	Some limitations (-1)‡‡	Important inconsistencies (-1)†	Direct (0)	None (0)	Low	77% decrease in cryocrit with DAA treatment† (1 study) 32% decrease in cryocrit with PEG-IFN (1 study)	Moderate

Total N	702	

Balance of Potential Benefits and Harms:	**Quality of Overall Evidence:**
Decreased proteinuria for all interventions, improvement in renal function, cryocrit and quality of life for sofosbuvir and rituximab; SVR rates high for DAAs and interferon-based treatment with low rates of discontinuation for all agents, despite high serious adverse event rates with interferon-based treatments. Survival rates good but no untreated group for comparison.	Low

Studies included in EP: 18711294, 26567178, ILC 2015 LP08, EULAR 2013 OPO212, 22147661; 26255249, 26474537, 22147444, 25890508, 17075881, 22153224, 26853322, 27483451, 20439619

Abbreviations: DAA = direct acting antiviral; ESRD: end stage renal disease; GN: glomerulonephritis; HCV: hepatitis C; nRCS: non-randomized controlled study; pro = prospective (single-group cohort), RCT: randomized controlled trial; ret = retrospective (single-group cohort), SVR: sustained virologic response

Annotations:
* 1 good quality; 2 fair quality
† Heterogeneous treatment and inconsistent reporting of outcomes
‡ 4 good quality; 2 fair quality; 9 poor quality
§ Wide range of sample sizes and duration of follow-up
‖ 4 good quality; 3 fair quality; 7 poor quality
¶ 3 good quality; 2 fair quality; 2 poor quality
** 3 good quality; 3 fair quality; 1 poor quality
†† 1 fair quality; 6 poor quality
‡‡ 2 good quality; 4 fair quality; 1 poor quality