Online Supplemental Data

Systemic Review and Meta-analyses: Real-World Effectiveness of Direct-acting Antiviral Therapies in Chronic Hepatitis C Genotype 3 in Asia

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Online Supplementary 1: Table S1 SVR12 of DAA therapies in Asia meta-analyses of real-world studies and global clinical trials in HCV GT3 patients

Study		Our study	VALENCE	BOSON	ALLY-3	Other network meta- analysis* (reference 40)
Study setting		Real- world practice	Clinical trial	Clinical trial	Clinical trial	RCTs; single-arm studies; observational cohorts
Patient No.	Total	4230	250	592 (GT2>3)	152	-
	Asian (%)	4230 (100%)	9 (4%)	80 (14%) (GT2>3)	7 (5%)	-
SVR12 by DAA Regimen	SOF+RBV for 16 weeks	-	-	71%	-	-
	SOF+RBV for 24 weeks	93.0%	-	84%	-	87% NC 56% LC
	SOF+RBV+PEG-IFN for 12 weeks	95.4%	-	93%	-	95% NC 78% LC
	DCV+SOF±RBV for 12 or 24 weeks	91.7%	-	-	89%	96% NC 80% LC
	LDV+SOF for 12 weeks	75.0%	-	-	-	-
SVR12 for GT3	Overall:	92.7%	85%	83%	89%	-
	NC LC	98.9% 88.6%	91% 68%	87% 73%	96% 63%	-
	TN TE	94.6% 94.0%	-	86% 78%	90% 86%	-

Note: * This study include regimens other than the five DAA regimens included in our meta-analysis GT, genotype; DAA, Direct-acting antiviral; NC, non-cirrhosis; LC, liver cirrhosis; TN, treatment naïve; TE, treatment experienced; SVR, sustained virological response;

First Author Published Year	Selection score (4 points)	Comparability score (2 points)	Outcome score (3 points)	Total score (9 points)
Abbas 2017	2	1	2	5
Akhter 2016	4	2	2	8
Capileno 2017	3	0	3	6
Farooqi 2016	3	0	0	3
Goel 2017	4	1	3	8
Hlaing 2017	3	1	3	7
Mehta 2016	3	2	3	8
Merta 2017	3	2	3	8
Sarwar 2017	2	0	2	4
Satsangi 2017	3	2	2	7
Shah 2016	2	2	2	6
Sidhu 2017	3	2	3	8
Sood 2017	4	2	1	7
Win 2016	2	0	1	3
Yousaf 2017	3	2	2	7

Online Supplementary 2: Table S2 Quality assessment of the included studies

Note: Quality assessment performed by the developed Newcastle-Ottawa Scale for cohort studies (NOS).

Online Supplementary 3: Table S3 Sensitivity analyses by study setting, sample size and quality assessment score

Study characteristics	Number of studies	N	SVR12 estimate (95%CI)	l ²
Study setting:				
Full-text publication	10	2435	91.7% (88.1% - 94.6%)	84.4%
Sample size:				
> 100 participants	9	3885	92.3% (87.3% - 96.1%)	95.6%
Quality assessment:				
Fair to High-quality studies (score \geq 4)	13	4110	92.2% (88.1% - 95.6%)	93.7%

Note: Quality assessment performed by the Newcastle-Ottawa Scale for cohort studies to evaluate risk of bias; SVR

12, sustained virological response 12 weeks after the end of treatment

Online Supplementary 4: Figure S1 Forest plot for sustained virologic response (SVR 12) in chronic hepatitis C genotype 3 patients treated with DAAs in Asia by regimens

Study	SVR12 Total	Events per 100 observations	SVR12(%)	95% CI	Weight
Subgroup = SOF+RBV Yousaf et al 2017 Satsangi et al 2017 Shah et al 2016 Sood et al 2017 Hlaing et al 2017 Sidhu et al 2017 Akhter et al 2017 Akhter et al 2017 Capileno et al 2017 Goel et al 2017 Random effects mode Heterogeneity: $J^2 = 89.3\%$	840 847 75 76 57 59 390 405 46 50 453 499 47 55 148 175 128 153 17 21 2201 2340		98.7 96.6 96.3 92.0 90.8 85.5 84.6 83.7 81.0	[98.3; 99.6] [92.9; 99.8] [88.5; 99.1] [94.0; 97.7] [81.2; 96.8] [87.9; 93.0] [73.8; 92.4] [78.5; 89.2] [77.0; 88.7] [60.0; 92.3] [87.9; 96.1]	4.7% 2.1% 3.1% 5.3% 4.0% 5.8% 4.7% 5.6% 5.5% 3.8% 44.6%
Subgroup = SOF+RBV Win et al 2016 Hlaing et al 2017 Satsangi et al 2017 Yousaf et al 2017 Goel et al 2017 Sood et al 2017 Sidhu et al 2017 Abbas et al 2017 Random effects mode Heterogeneity: $J^2 = 81.9\%$	73 73 65 66 29 29 515 528 38 39 175 184 386 432 56 66 1 1337 1417		98.5 100.0 97.5 97.4 95.1 89.4 84.8	[95.0; 100.0] [91.9; 99.7] [88.3; 100.0] [95.8; 98.6] [86.8; 99.5] [91.0; 97.4] [86.1; 91.9] [74.3; 91.6] [90.9; 97.7]	1.3% 2.1% 1.3% 5.2% 2.1% 4.9% 5.8% 4.9% 27.6%
Subgroup = DCV+SOF Goel et al 2017 Hlaing et al 2017 Merat et al 2017 Random effects mode Heterogeneity: $J^2 = 0\%$, p	92 100 5 5 40 44 I 137 149		→ 100.0 90.9	[85.0; 95.9] [56.6; 100.0] [78.8; 96.4] [86.0; 95.1]	4.8% 1.2% 4.0% 10.0%
Subgroup = LDV+SOF Hlaing et al 2017 Random effects mode Heterogeneity: not applica	9 12 I 9 12			[46.8; 91.1] [44.8; 91.7]	3.3% 3.3%
Subgroup = Combined Mehta et al 2016 Farooqi et al 2016 Sarwar et al 2017 Random effects mode Heterogeneity: l^2 = 38.8%	62 67 40 47 165 198 267 312	g-IFN 12/24wk	85.1 83.3	[83.7; 96.8] [72.3; 92.6] [77.5; 87.9] [79.4; 91.0]	4.3% 4.6% 5.6% 14.5%
Random effects mode Heterogeneity: <i>I</i> ² = 83.4%		50 60 70 80 90 SVR12 (%)	92.6	[89.8; 94.7]	100.0%

Online Supplementary 5: Figure S2 Forest plot for sustained virologic response (SVR 12) in chronic hepatitis C genotype 3 patients treated with DAAs in Asia by treatment history

Study	SVR12 Total	Events per 100 observations	SVR12(%) 95% CI Weight
Subgroup = Treatment Yousaf et al 2017 Satsangi et al 2017 Shah et al 2016 Sood et al 2017 Hlaing et al 2017 Sidhu et al 2017 Mehta et al 2016 Merat et al 2016 Random effects mode Heterogeneity: l^2 = 76.7%	485 490 85 86 57 59 565 589 111 119 802 863 46 50 16 19 25 30 2192 2305		99.0 [97.6; 99.6] 7.4% 98.8 [93.7; 99.8] 4.3% 96.6 [88.5; 99.1] 5.8% 95.9 [94.0; 97.2] 8.6% 93.3 [87.3; 96.6] 7.8% 92.9 [91.0; 94.5] 8.8% 92.0 [81.2; 96.8] 6.9% 84.2 [62.4; 94.5] 6.3% 83.3 [66.4; 92.7] 7.1% 94.6 [91.3; 96.7] 63.0%
Subgroup = Treatment Yousaf et al 2017 Satsangi et al 2017 Hlaing et al 2017 Merat et al 2017 Mehta et al 2016 Akhter et al 2016 Sidhu et al 2017 Random effects mode Heterogeneity: $I^2 = 92.5\%$	870 885 19 19 14 14 24 25 16 17 22 25 47 68 1 1012 1053		98.3 [97.2; 99.0] 8.4% 100.0 [83.2; 100.0] 2.8% 100.0 [78.5; 100.0] 2.8% 96.0 [80.5; 99.3] 4.2% 94.1 [73.0; 99.0] 4.2% 88.0 [70.0; 95.8] 6.4% 69.1 [57.4; 78.8] 8.3% 94.0 [77.5; 98.6] 37.0%
Random effects mode Heterogeneity: <i>I</i> ² = 87.1%		60 70 80 90 1 SVR12 (%)	9 4.2 [90.3; 96.6] 100.0%

Online Supplementary 6: Figure S3 Forest plot for sustained virologic response (SVR 12) in chronic hepatitis C genotype 3 patients treated with DAAs in Asia by cirrhosis status and treatment history

Study	SVR12 Total	Events per 100 observations	SVR12(%) 95% CI Weight
Subgroup = Non-cirrho Satsangi et al 2017 Yousaf et al 2017 Mehta et al 2016 Shah et al 2016 Sidhu et al 2017 Random effects model Heterogeneity: $J^2 = 17.2\%$	61 61 485 490 23 23 44 45 685 705 1298 1324		100.0 [94.1; 100.0] 4.0% 99.0 [97.6; 99.6] 6.8% 100.0 [85.7; 100.0] 4.0% 97.8 [88.4; 99.6] 5.1% 97.2 [95.7; 98.2] 7.2% 98.0 [96.6; 98.8] 27.0%
Subgroup = Cirrhotic T Satsangi et al 2017 Shah et al 2016 Mehta et al 2016 Merat et al 2017 Sidhu et al 2017 Random effects model Heterogeneity: $I^2 = 10.4\%$	24 25 13 14 23 27 16 19 126 158 202 243		96.0[80.5; 99.3]5.1%92.9[68.5; 98.7]5.1%85.2[67.5; 94.1]6.5%84.2[62.4; 94.5]6.3%79.7[72.8; 85.3]7.2%83.1[76.2; 88.3]30.2%
Subgroup = Non-cirrho Yousaf et al 2017 Satsangi et al 2017 Mehta et al 2016 Sidhu et al 2017 Random effects model Heterogeneity: $J^2 = 94.8\%$	870 885 9 9 2 2 20 31 901 927		98.3 [97.2; 99.0] 7.1% 100.0 [70.1; 100.0] 3.9% 100.0 [34.2; 100.0] 3.7% 64.5 [46.9; 78.9] 6.9% 91.1 [47.8; 99.1] 21.6%
Subgroup = Cirrhotic T Merat et al 2017 Satsangi et al 2017 Mehta et al 2016 Sidhu et al 2017 Random effects model Heterogeneity: $J^2 = 82.4\%$	24 25 10 10 14 15 18 37 66 87	d	96.0 [80.5; 99.3] 5.1% 100.0 [72.2; 100.0] 3.9% 93.3 [70.2; 98.8] 5.1% 48.6 [33.4; 64.1] 7.0% 88.2 [49.0; 98.3] 21.1%
Random effects model Heterogeneity: <i>I</i> ² = 91.7%,) 50 60 70 80 90 10 SVR12 (%)	93.3 [85.9; 96.9] 100.0%

Online Supplementary 7: Figure S4 Forest plot for sustained virologic response (SVR 12) in chronic hepatitis C genotype 3 patients treated with DAAs in Asia by country

Study	SVR12 Total	Events per 100 observations	SVR12(%) 9	5% CI Weight
Country = India Satsangi et al 2017 Shah et al 2016 Sood et al 2017 Mehta et al 2016 Goel et al 2017 Sidhu et al 2017 Random effects mode Heterogeneity: l^2 = 79.1%			96.6 [88.5; 95.9 [94.0; 92.5 [83.7;	
Country = Pakistan Yousaf et al 2017 Akhter et al 2016 Farooqi et al 2016 Capileno et al 2017 Sarwar et al 2017 Abbas et al 2017 Random effects model Heterogeneity: $l^2 = 97\%$, p			98.5 [97.8; 85.5 [73.8; 85.1 [72.3; 83.7 [77.0; 83.3 [77.5; 82.6 [77.3; 87.6 [75.3;	92.4] 5.9% 92.6] 5.6% 88.7] 7.0% 87.9] 7.1% 86.8] 7.2%
Country = Myanmar Win et al 2016 Hlaing et al 2017 Random effects model Heterogeneity: l^2 = 86.3%			100.0 [95.0; 94.0 [88.6; 97.9 [88.5;	96.9 6.8%
Country = Iran Merat et al 2017 Random effects mode Heterogeneity: not applicat			90.9 [78.8; 90.9 [80.3;	
Random effects model Heterogeneity: <i>I</i> ² = 93.2%		70 80 90 10 SVR12 (%)	92.7 [88.9 ;	95.8] 100.0%

Online Supplementary 8: Supplemental List 1: List of Asian countries and areas included in literature search based on PubMed MeSH term for Asia

Asia Countries and Asia Areas

Asia, Central

- Kazakhstan
- Kyrgyzstan
- Tajikistan
- Turkmenistan
- Uzbekistan

Asia, Northern

• Siberia

Asia, Southeastern

- Borneo
- Brunei
- Cambodia
- Indonesia
- Laos
- Malaysia
- Mekong Valley
- Myanmar
- Philippines
- Singapore
- Thailand
- Timor-Leste
- Vietnam

Asia, Western

- Bangladesh
- Bhutan
- India
- Afghanistan
- Bahrain
- Iran
- Iraq
- Israel
- Jordan
- Kuwait
- Lebanon
- Oman
- Qatar
- Saudi Arabia
- Syria
- Turkey
- United Arab Emirates
- Yemen
- Nepal
- Pakistan
- Sri Lanka

Far East

- China
- Japan
- Korea
- Mongolia
- Taiwan