ASSESSING THE IMPACT OF DIRECT-ACTING ANTIVIRALS ON HEPATITIS C COMPLICATIONS:

A SYSTEMATIC REVIEW AND META-ANALYSIS

TAN, Quan Rui [1]; LIM, Phei Ching, Lim [2]; LOW, Wei Yang [1]; LEE, Chong Yew [3]; YEW, Kuo Chao [4]

 1 - Ministry of Health (MOH) Holdings Pte Ltd, Singapore; 2 - Pharmacy Department, Hospital Pulau Pinang, Georgetown, Penang, Malaysia; 3
 - School of Pharmaceutical Sciences, Universiti Sains Malaysia, Minden, Penang, Malaysia; 4 - Department of Gastroenterology and Hepatology, Tan Tock Seng Hospital, Singapore

Introduction

Globally, 1.5 million new patients get infected with Hepatitis C Virus (HCV) per year.¹ Yet, the breakthrough of Direct-acting Antivirals (DAAs) has allowed WHO's target to eliminate HCV by 2030 become realistic.¹ While there are obvious improvements in clinical and biochemical liver function following DAA therapy, especially in decompensated cirrhosis, there is currently insufficient evidence to assess the treatment's overall benefits, particularly in terms of

Results

 Overall, DAA treatment lowered HCC recurrence (RR 0.71, 95%CI 0.55 – 0.92), all-cause mortality (RR 0.43, 95%CI 0.23-0.78) and liver decompensation (RR 0.52, 95%CI 0.33-0.83) significantly

 DAAs reduced HCC occurrence significantly in non-cirrhosis (RR 0.80, 95%CI 0.69-0.92) and cirrhosis (RR 0.39, 95%CI 0.24-0.64) but not in decompensated cirrhosis

• Meta-regression analysis showed that male gender (r = -0.036; 95%

preventing the need for liver transplantation or reducing mortality. There is also insufficient understanding of which particular patient cohorts will benefit most from DAA therapy.

Objectives

- .. To synthesise existing evidence on the impact of DAAs on 5 outcomes – Hepatocarcinoma (HCC) occurrence and recurrence, all-cause mortality, liver decompensation and liver transplant (LT).
- 2. To outline the patient cohorts that would benefit most from DAA therapy, using subgroup analyses.

Materials and Methods

MEDLINE, EMBASE and Cochrane were sourced for papers from March 1993 to March 2022. Subsequently, data was extracted and processed by 2 reviewers, before analysis using the the randomeffects model. Inclusion criteria were:

- Randomised controlled trials (RCTs), cohort and case-control studies
- English language publications only

CI -0.0455, -0.0266; p<0.0001) in DAA treatment groups and and patients with genotype 1 in untreated group (r = 0.0263; 95% CI 0.0206, 0.0320; p<0.001) showed significant contribution to all-cause mortality.

	Urtanty			C	antra l				1
Study	, (A)	Experii Events		Events	ontrol Total	Risk Ratio	RR	95%-CI	Weight
Warzy	szyńska (2	017) 8	3 19	21	32		0.64	[0.36; 1.15]	8.4%
-	(2017)	19		41	89			[0.29; 0.73]	10.8%
	eux (2017)			42	45	-+-		[0.84; 1.13]	18.2%
-	to (2017)	1	23	1	23 -			[0.07; 15.04]	0.7%
	bo (2018)	28		38	102			[0.49; 1.10]	12.0%
i	(2018)	58		58	59	+		[0.91; 1.03]	19.4%
-	(RFA) (20	(19) 3	3 14		14			0.09; 0.70]	3.8%
1	(TACE) (2		8 8	8	8			[0.18; 0.92]	5.6%
Singa	I (2019)	128	304	288	489		0.71	[0.61; 0.83]	18.1%
Tse (2	2021)	5	5 99	5	72		0.73	[0.22; 2.42]	2.9%
	om effects	-	742		933		0.71	[0.55; 0.92]	100.0%
Helero	geneity: /	= 74%, τ ² = 0.065	n, p < 0	.01		0.1 0.5 1 2 10			
						Favors DAA Disfavors DAA			
	(B)	Experir	mental	C	ontrol				
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	g (2016)	14 2	406 89	13 3	261 89			0 [0.33; 1.45]	
lkeda (2 Zanetto	2017) (2017)	23	23	3	23			[0.11; 3.89] [0.22; 4.45]	
	o (2017)	5	102	18	102			0.17; 0.89]	
Hill (20		11	196	17	182	- .		0.29; 1.25]	
Huang		18	62	49	87			2 [0.34; 0.79]	
Mettke		2	158	3	184			[0.13; 4.59]	
Carrat		129		89	2551	· · · ·		[0.39; 0.66]	
Hanafy		0	160	18	80	I		[0.00; 0.22]	
Butt (20		62	1836		10417	+		[0.12; 0.19]	
Rando	m effects	model	10376		13976		0.43	[0.23; 0.78]	100.0%
		$87\%, \tau^2 = 0.4574$		01			1		
	100		1507423		0.		000		
						Favors DAA Disfavors DAA	•		
a t 1	(C)	•	mental		ontrol			05% 01	
Study		Events	lotal	Events	lotal	Risk Ratio	RR	95%-CI	weight
Cheun	ig (2016)	72	406	73	261	֥	0.63	[0.48; 0.84]	16.6%
1	bo (2018)	6			102			[0.17; 1.07]	8.5%
Hill (20		19			182			[0.23; 0.61]	13.8%
	(2019)	74						[0.53; 1.21]	14.9%
Park (2		109			18177			[0.60; 0.93]	17.3%
Butt (2		9			10417			[0.09; 0.35]	11.4%
Park (2		119			19874			[0.50; 0.75]	17.5%
-									100.001
	om effects	-	27166		51564		0.52	[0.33; 0.83]	100.0%
Hetero	geneity: /* =	= 73%, τ ² = 0.1857	, p < 0.	01			0		
					(0.1 0.5 1 2 1 Favors DAA Disfavors DAA	0		
		Experi	mental		ontrol	Tavois DAA DISIAVOIS DAA			
Study	(D)	•		Events		Risk Ratio	RR	95%-CI	Weight
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	(2019)	21	4521	14				[0.39; 1.52]	14.6%
Park (2		25			17238			2 [0.46; 1.12]	
Butt (2		1	1836		10417	<u>}</u>		[0.10; 6.58]	1.5%
Park (2	2021)	39	7748	109	18564		0.86	[0.60; 1.23]	50.0%
1									1
Rande	om effecte	model	20815	8	48548	<u>.</u>	0.80	10 69 . 0 931	100 0%
	om effects geneity: / ² =	$model = 0\%, \tau^2 = 0, p = 0$	20815		48548		0.80	[0.69; 0.92]	100.0%

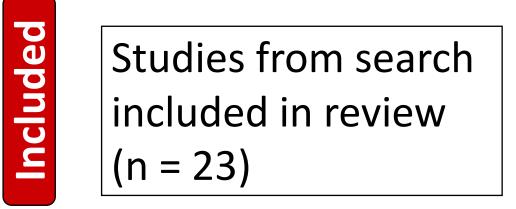
Studies must have 2 arms involving a no-treatment control
 Search terms: Direct-acting antiviral, Hepatitis C, liver cirrhosis, liver fibrosis or end stage liver disease, carcinoma, hepatocellular, mortality, liver failure, and decompensation

Identification of studies via databases and registers

Records identified from: Databases (n = 1497)	Records removed <i>befo</i> Duplicate records rer 363)
	Records excluded
Records screened	Reviews or laborator
(n = 1134)	(n=491)
↓	Reports excluded (n =
Reports assessed for	DAA not an intervent
eligibility (n = 643)	Outcomes reported
_	aim (n = 339)

Catabases and registersStuords removed before screening:
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A not an intervention (n = 26)
utcomes reported were not ourStu

Lack of control group (n = 233)



Identification

creening

Conference abstracts (n = 21)	
Severe bias (n=1)	

0.1 0.5 1 2 10 Favors DAA Disfavors DAA

Fig 2: Forest Plots showing significant effect of DAAs on A) overall HCC recurrence B) Overall all-cause mortality HCC C) Overall liver decompensation D) HCC occurrence in non-cirrhosis patients

Fig 1: Data extraction of 23 final papers were done using PRISMA method

Conclusion

• DAA therapy is beneficial in reducing HCC recurrence, all-cause mortality and liver decompensation.

The study findings indicate that initiating DAA treatment early could be advantageous even for non-cirrhotic patients, challenging the prevailing rationale of some countries using justification for prescribing or reimbursing DAAs based on fibrosis severity.^{2,3}
Active screening and early treatment of HCV shall be considered for better outcomes.

References

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