Successful treatment of patients on opiate replacement therapy utilising partial directly observed therapy of DAAs in community pharmacies

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INTRODUCTION

Directly observed therapy (DOT) is established as a means of ensuring compliance with medication in a number of different therapeutic areas.

In Glasgow, opiate replacement therapy (ORT) is prescribed as DOT when patients are still injecting, or in the early stages of recovery, lending a unique opportunity to co-administer direct acting antivirals (DAAs), and treat patients historically considered more difficult to treat.

We have previously demonstrated the efficacy of this model with once daily DAAs[1]. Changes to national guidelines in 2016 led to first line use of a twice daily (BD) regimen for patients with genotype 1 and 4 HCV infection. This required a switch to partial DOT (pDOT), where the second of the BD doses is given away with the patient.

We report results from our experience with pDOT of ombitasvir/ paritaprevir/ ritonavir +/- dasabuvir +/- ribavirin (3D/2D).

AIM

We sought to examine the effectiveness of using pDOT to dispense 3D/2D to patients on daily supervised methadone.

METHODS:

Data

Patients starting on a 3D/2D regimen prior to 31/09/2016 in Glasgow treatment centres were identified from the Scottish HCV database.

Data on age, genotype, presence of cirrhosis, prior treatment, PWID status, intended and actual treatment duration and SVR12 were collected.

Data were linked with pharmacy records to identify the location and frequency of dispensing of DAAs. Patients receiving treatment in an institution (prison or hospital) were excluded.

Categorical variables were compared using Fisher's exact test, continuous by Student's t-test.

Treatment

Per local protocol:

- GT1a patients received 3D/RBV for 12 weeks
- GT1b patients received 3D for 12 weeks
- GT4 patients received 2D/RBV for 12 weeks

Patients with Child's A cirrhosis had to have all 3 of:

- AFP <20, Platelets ≥90, Alb ≥35

otherwise they received an alternative regimen.

Dispensing

All patients received DAAs via their community pharmacy, with dispensing according to ORT status:

- DOT ORT patients received pDOT dispensed DAAs
- Weekly ORT patients received weekly dispensed DAAs
- Non ORT patients received fortnightly dispensed DAAs
- pDOT patients received their am dose under supervision, and were given their pm dose to take away. Most pharmacies close on a Sunday and patients received their Saturday evening and both Sunday doses to take away.

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RESULTS

Patients:

Of 173 patients, 31 (17.9%) received pDOT (table 1).

- Patients receiving pDOT were
  - Younger
  - More likely to report a history of injecting drug use
  - Equally likely to have cirrhosis
- 135 (78%) of patients received their DAA weekly
- 7 (4%) patients, not on methadone, received their DAAs fortnightly

Table 1. Patient characteristics

	pDOT (N=31)	Non DOT (N=142)	p
Mean Age (±SD)	45.5 (7.3)	50.4 (8.3)	0.0028
History of IVDU (%)	30 (96.8)	99 (69.7)	0.001
Cirrhosis (%)	5 (16.2)	25 (17.6)	1.0
Mean LSM (kPA) (SD)	7.7 (3.6)	10.3 (10.4)	0.10
GT1a (%)	31 (100)	130* (91.5)	0.12
		*10 (7%) GT1b, 2 (1.4%) GT4	

Safety:

12/173 (6.9%) patients prematurely discontinued treatment, with similar rates in pDOT vs. non DOT patients (table 2).

4 patients discontinued treatment due to AEs felt related to treatment

- 2 hyperbilirubinaemia (without transaminitis, resolving on discontinuation)
- 2 due to mood disturbance and lethargy

Table 2. Premature discontinuation

	pDOT (N=31)	Non DOT (N=142)	p
Premature discontinuation (%)	2 (6.5)	10 (7.0)	1.0
Discontinuation due to: Treatment related AEs (%)	0 (0)	4 (2.8)	1.0
Non compliance (%)	2 (6.5)	4 (2.8)	0.29
Drug/Alcohol Relapse (%)	0 (0)	2 (1.4)	1.0

SVR:

To date 151/160 (94.3%) patients attending for SVR12 bloods have achieved SVR, with comparable rates between pDOT and non DOT patients (table 3).

- Of the 9 patients failing therapy:
  - 4 discontinued prematurely due to AEs
  - 4 discontinued prematurely due to non compliance
  - 1 completed 12 weeks but had documented missed doses (non DOT arm)

Table 3. SVR

	pDOT (N=29)	Non DOT (N=131)	p
SVR (%)	28/29 (96.6)	123/131 (93.9)	1.0

CONCLUSIONS

- DOT of DAAs with ORT allows patients who are still injecting or in the early stages of recovery to be treated safely and effectively with DAAs.
- Patients on daily supervised ORT demonstrate low rates of discontinuation, and achieve high SVR rates with 3D/2D±RBV using pDOT.
- The requirement for patients to take a second daily dose of a BD DAA regimen did not impact on SVR rates, suggesting good compliance.

References: 1. Introduction of Directly Observed Community Pharmacy Dispensing of Directing Acting Antivirals Achieves High Sustained Viral Response Rates in a Difficult to Treat Cohort. Marra F et al, Journal of Hepatology, Vol. 64, Issue 2, S766