Overcoming challenges in TB care: from policy to practice

Safety, effectiveness and feasibility of treating Active Hepatitis C with direct-acting antivirals in patients with MDR-TB

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Thanks to Nara Melikyan

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Background

- Hepatotoxicity common adverse during MDR TB treatment (Bastard, Latvia)
  - Hepatitis C is a risk factor (Bastard, Lee)

- Direct-acting antiviral (DAA): safe and effective treatment for hepatitis C
- Theoretically few interactions between MDR-TB drugs and DAAs expected
- No studies assessing safety/effectiveness of DAA and MDR-TB treatment

- Armenia:
  - no prevalence data on hepatitis C
  - Introduction of active screening of MDR-TB patients for Chronic Active Hepatitis C (January 2016- December 2018 supported by MSF
  - DAA treatment available through MSF

Objectives

1. To estimate the prevalence of Chronic Active Hepatitis C among MDR-TB patients.

2. To assess the safety, effectiveness of treating Chronic Active Hepatitis C with DAA in patients with MDR-TB.

3. To assess feasibility of treating Chronic Active Hepatitis C with DAA in patients with MDR-TB

2. To assess the safety and effectiveness of DAA in patients with MDR-TB

Design: a retrospective and prospective cohort study

Population: all MDR-TB patients above 18 years

- diagnosed with Chronic Active Hepatitis C between January 2016 and the end of December 2018
- on TB treatment or who completed TB treatment not more than 24 months ago and started DAA treatment during that time

Treatment success:

- Negative viral load or viral load concentration below 12IU/mL 12 weeks after the end of treatment (SVR12).

Treatment failure:

- Viral load detectable 12 weeks after end of DAA treatment

Methods

Patient assessment and selection by a **multidisciplinary** team:

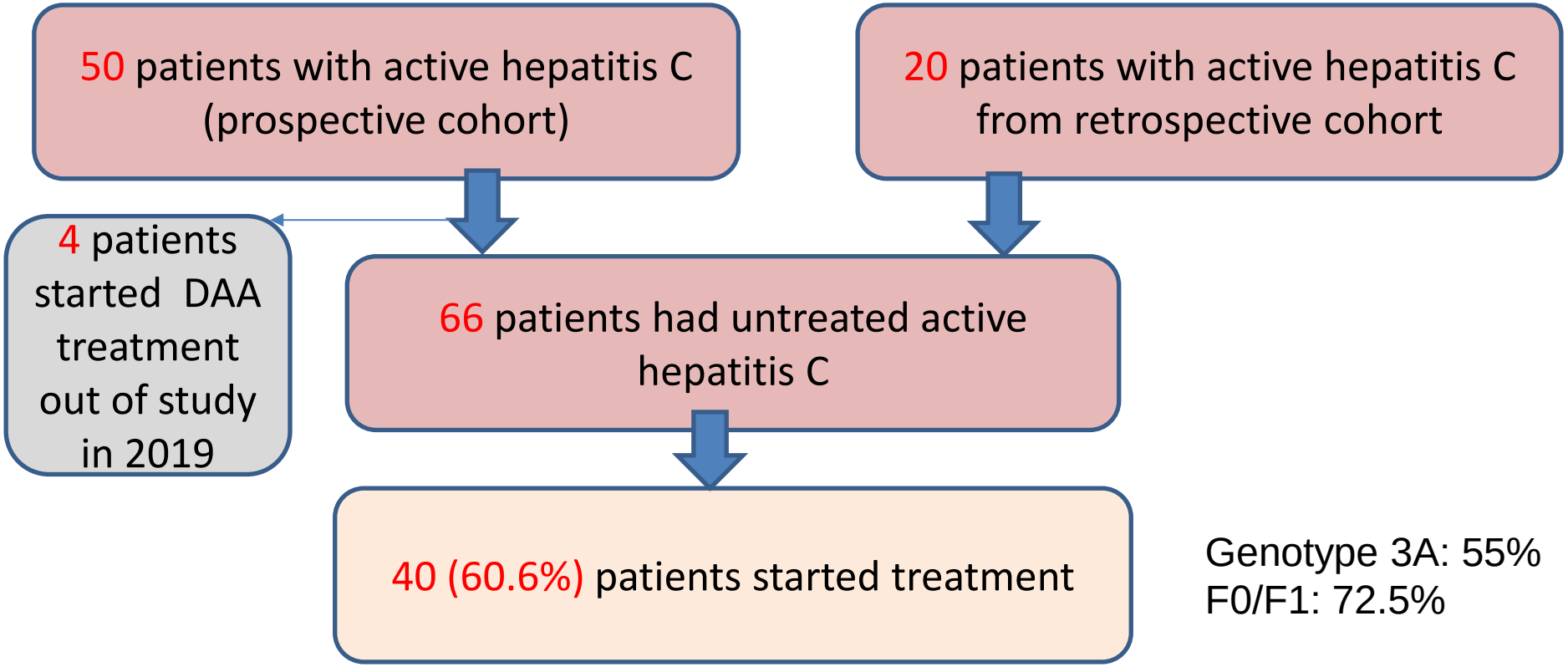
Exclusion of patients with criteria: severe condition, HIV viral load detectable

Treatment administration: DAA 7 days via directly observed treatment, then self administered treatment for ambulatory patients

Monitoring:

- Baseline: Hepatitis C and B, HIV test and CD4, Clinical and biological evaluations, fibroscan, If advanced disease ultrasound and gastroscopy
- Monthly monitoring of clinical, blood count, liver enzymes
- Monitoring for adverse events of clinical interest and serious adverse events
- Viral load 3 months after end of DAA (Sustained Viral Response SVR 12)

Results: patient inclusion



Genotype 3A: 55%
F0/F1: 72.5%

Characteristics of patients starting DAA

Characteristics, N=40	n	(%)
Age in years (median, IQR)	49.5 (41.4-55.5)	
BMI <18.5	7	(17.5)
Male	38	(95.0)
History of incarceration (past or present)	23	(57.5)
Health worker (past or present)	0	(0)
Alcohol abuse	19	(47.5)
IV drug use (past or present)	18	(45.0)
Comorbidities		
– HIV positive	7	(17.5)
– HBsAg positive	0	(0)
– Anti-HBc-total positive (N=38)	15	(42.1)

Results: HCV treatment regimens

Drugs	Duration	n (%)
Daclatasvir 60mg/sofosbuvir 400 mg	12 weeks	28 (70.0%)
Daclatasvir 90mg*/sofosbuvir 400 mg	12 weeks	5 (12.5%)
Ledispavir 90mg/sofosbuvir 400mg	12 weeks	5 (12.5%)
Daclatasvir 60mg/sofosbuvir 400 mg/ribavirin 1000mg	24 weeks	2 (5.0%)

*dose of daclatasvir was increased to 90 mg for 5 patients whose ART regimen contains evafirenz or nevirapine

Results: DAA and MDR TB treatment

Median time to start DAA after diagnosis of chronic active hepatitis C:

- 5.9 months (IQR: 1.8-13.5, ranges: 0.4-25.9)

DAA received during DRTB treatment: 28/40 (70%)

- median time to start DAA treatment after DR TB start: 5.4 months (IQR: 2.2-12.4, ranges: 0.3-21.4 months)

DAA initiated during last month of DR TB treatment: 2 (5.0%) patients

DAA initiation after completion of DRTB treatment: 10 (25.0%)

- median time to start DAA after DR TB completion was 12.5 months (IQR: 4.8-20.1, ranges: 0.1-23.0)

Results: DAA treatment outcome

40 patients started DAA

1 patient lost to follow up (disappeared after one week of HCV treatment)

39 completed course of DAA

2 patients died:
- Cancer
- HIV disease progression

3 patients left the country:

34 reached 12 weeks after end of treatment visit

Sustained Viral Response (SVR) at 12 weeks post DAA treatment:
32/34(94%) treatment success
2/34 (6%) treatment failure

2 treatment failure patients:
- male, genotype 3a, stage F0-F1 fibrosis
- received 12 weeks sofosbuvir/daclatasvir
- 1 patient was HIV positive which was well controlled

Results: adverse events during DAA treatment (n=39)

Adverse event term	n (%)	AE maximum grade
Any SAE/AE	6 (15.4)	
SAE/AE possibly related to DAA*	2 (5.2)	
SAE/AE leading to temporary DAA discontinuation	1 (2.6)	
SAE/AE leading to permanent DAA discontinuation	0 (0.0)	
Common AEs		
Anemia	1 (2.6)	2
Dizziness	1 (2.6)	1
Hyperbilirubinemia*	1 (2.6)	1
Peripheral neuropathy	1 (2.6)	1
Platelets Decreased	1 (2.6)	1
Common SAEs		
Allergic reaction*	1 (2.6)	3

Conclusion and discussion

High prevalence of HCV co-infection among MDR TB patients in Armenia:

- 29% HCV antibody positive , 19.4% active hepatitis C) with predominate genotypes 1b and 3a.

This is a **first report of concomitant use of direct acting antivirals with DRTB drugs:**

- high rates of sustained viral suppression among those tested (94.1%).
- The combination of DAAs with anti-tuberculosis drugs did not cause any safety concerns.

Feasibility:

- Integrated HCV/MDR-TB care feasible: no increased workload for the TB doctors, helped by hepatologist

Challenges

- Organization of medical examinations for smear-positive patients and imprisoned patients outside of TB facility
- Identification of private lab and private clinic for performance of needed investigations, which created huge extra costs for mission

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- MSF staff in Armenia and in the head quarters