

AGORÀ PENITENZIARIA 2018

XIX CONGRESSO NAZIONALE SIMSPE-ONLUS



Roma, 4 – 5 ottobre 2018

Hotel dei Congressi, Roma



DAA nei detenuti F3-F4

Dott.ssa Serena Dell'Isola

UOC Medicina Protetta Malattie Infettive

(Direttore Dott G. Starnini; Dott.ssa A M Ialungo; Dott.ssa E

Rastrelli; Dott ssa E Liguori)

Ospedale Belcolle Viterbo

Roma 4 Ottobre 2018



SISTEMA SANITARIO REGIONALE

**ASL
VITERBO**

Recommendations for Screening and Treatment of HCV Infection in Jails

| RECOMMENDED | RATING |
|---|--------|
| <p>Jails should implement opt-out HCV testing consisting of HCV-antibody testing followed by confirmatory HCV-RNA testing if antibody-positive.</p> <ul style="list-style-type: none">• Chronically infected individuals should receive counseling about HCV infection and be provided linkage to follow-up community healthcare for evaluation of liver disease and treatment upon release.• Chronically infected individuals whose jail sentence is sufficiently long to complete a recommended course of antiviral therapy should receive treatment for chronic HCV infection according to AASLD/IDSA guidance while incarcerated. Upon release, patients should be provided linkage to community healthcare for surveillance for HCV-related complications. | Ila, C |

Recommendations for Screening and Treatment of HCV Infection in Prisons

| RECOMMENDED | RATING |
|--|--------|
| Prisons should implement opt-out HCV testing. Chronically infected individuals should receive antiviral therapy according to AASLD/IDSA guidance while incarcerated. Upon release, patients should be provided linkage to community healthcare for surveillance for HCV-related complications. | Ila, C |
| To prevent HCV reinfection and reduce the risk of progression of HCV-associated liver disease, prisons should provide harm reduction and evidence-based treatment for underlying substance use disorders. | Ila, C |

Recommendation for Continuation of HCV Treatment in Jail and Prison Settings

| RECOMMENDED | RATING |
|--|--------|
| Jails and prisons should facilitate continuation of HCV therapy for individuals on treatment at the time of incarceration. | Ila, C |



HCV (micro-) elimination in certain populations is also feasible in the short-to-medium term



**Decompensated
cirrhotics**



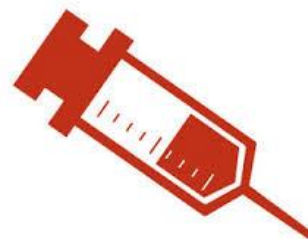
Veterans



**Patients with
haemophilia**



**Transplant
patients**



PWID, prisoners

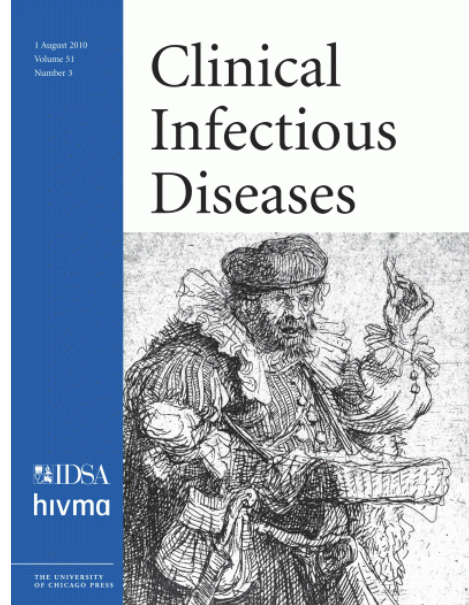


HIV/HCV co-infected

[Clin Infect Dis](#). 2018 Jul 18;67(3):460-463. doi: 10.1093/cid/ciy210.

Demonstration of Near-Elimination of Hepatitis C Virus Among a Prison Population: The Lotus Glen Correctional Centre Hepatitis C Treatment Project.

[Bartlett SR](#)¹, [Fox P](#)², [Cabatingan H](#)³, [Jaros A](#)³, [Gorton C](#)⁴, [Lewis R](#)⁴, [Priscott E](#)⁴, [Dore GJ](#)¹, [Russell DB](#)^{4,5,6}.



Abstract

Micro-elimination of hepatitis C virus (HCV) infection through rapid uptake of government-funded direct-acting antiviral therapy within an Australian prison setting is demonstrated. During a 22-month period, 119 patients initiated treatment for chronic HCV infection, with HCV in-prison viremic prevalence declining from 12% to 1%.

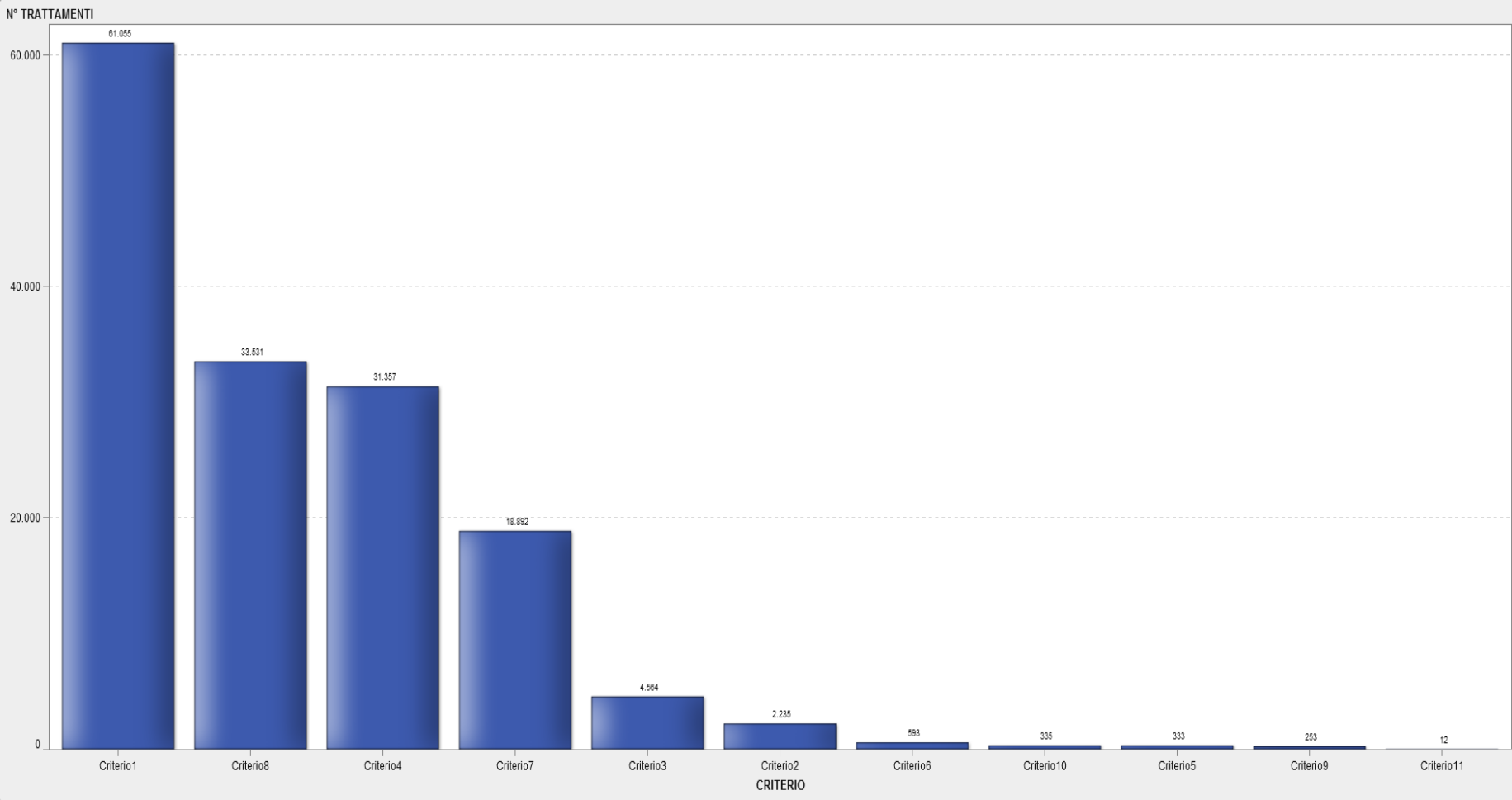
| 2- Scheda Eleggibilità e Dati Clinici (EDC) | | | |
|---|------------------------|---|---|
| Di seguito sono riportate le tipologie (vedi i criteri) dei pazienti candidabili al trattamento con medicinali ad azione antivirale diretta di seconda generazione (DAAs) nell'ordine progressivo di priorità in base all'urgenza clinica definito dalla Commissione Tecnico Scientifica dell'AIFA secondo le indicazioni del Tavolo tecnico AIFA sull'Epatite C. | | | testo fisso |
| E | Tipologia di paziente: | Paziente con cirrosi in classe di Child A o B e/o con HCC con risposta completa a terapie resettive chirurgiche o loco-regionali non candidabili a trapianto epatico nei quali la malattia epatica sia determinante per la prognosi | Criterio 1 |
| | | Epatite ricorrente HCV-RNA positiva del fegato trapiantato in paziente stabile clinicamente e con livelli ottimali di immunosoppressione | Criterio 2 <i>La sicurezza e l'efficacia di ZEPATIER non sono state stabilite nei soggetti sottoposti a trapianto di fegato (blocca)</i> |
| | | Epatite cronica con gravi manifestazioni extra-epatiche HCV-correlate (sindrome crioglobulinemica con danno d'organo, sindromi linfoproliferative a cellule B, insufficienza renale) | Criterio 3 |
| | | Epatite cronica con fibrosi METAVIR F3 (o corrispondente Ishak) | Criterio 4 |
| | | In lista per trapianto di fegato con cirrosi MELD <25 e/o con HCC all'interno dei criteri di Milano con la possibilità di una attesa in lista di almeno 2 mesi | Criterio 5 |
| | | Epatite cronica dopo trapianto di organo solido (non fegato) o di midollo in paziente stabile clinicamente e con livelli ottimali di immunosoppressione | Criterio 6 <i>Vedi la nota RCP per il criterio 2 (blocca)</i> |
| | | Epatite cronica con fibrosi METAVIR F2 (o corrispondente Ishak) e/o comorbidità a rischio di progressione del danno epatico [coinfezione HBV, coinfezione HIV, malattie croniche di fegato non virali, diabete mellito in trattamento farmacologico, obesità (body mass index ≥ 30 kg/m ²), emoglobinopatie e coagulopatie congenite] | Criterio 7 |
| | | Epatite cronica con fibrosi METAVIR F0-F1 (o corrispondente Ishak) e/o comorbidità a rischio di progressione del danno epatico [coinfezione HBV, coinfezione HIV, malattie croniche di fegato non virali, diabete mellito in trattamento farmacologico, obesità (body mass index ≥ 30 kg/m ²), emoglobinopatie e coagulopatie congenite] | Criterio 8 |
| | | Operatori sanitari infetti | Criterio 9 |
| | | Epatite cronica o cirrosi epatica in pazienti con insufficienza renale cronica in trattamento emodialitico | Criterio 10 |
| | | Epatite cronica nel paziente in lista d'attesa per trapianto di organo solido (non fegato) o di midollo | Criterio 11 |

Farmaci antivirali per HCV

| Genotipo | Regimi Pangenotipici | | | Regimi Genotipo dipendenti |
|------------|----------------------|---------|--------------|----------------------------|
| | SOF/VEL | GLE/PIB | SOF/VEL/VOX* | GZR/EBR |
| Genotipo 1 | Si | Si | Si | Si |
| Genotipo 2 | Si | Si | Si | No |
| Genotipo 3 | Si | Si | Si | No |
| Genotipo 4 | Si | Si | Si | Si |
| Genotipo 5 | Si | Si | Si | No |
| Genotipo 6 | Si | Si | Si | No |

*Solo nel ritrattamento di pazienti con fallimento a DAA

Trattamenti avviati per criterio



| Criterio | N trattamenti |
|----------|---------------|
| 1 | 61.055 |
| 8 | 33.531 |
| 4 | 31.357 |
| 7 | 18.892 |
| 3 | 4.564 |
| 2 | 2.235 |
| 6 | 593 |
| 10 | 335 |
| 5 | 333 |
| 9 | 253 |
| 11 | 12 |



Regression of liver stiffness in patients with HCV-related compensated cirrhosis after viral eradication by DAAs

Mauro Viganò¹, Giuseppina Brancaccio², Sara Labanca¹, Marco Cantone², Vincenzo Occhipinti¹, Giovanni Battista Gaeta², Mariagrazia Rumi¹

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INTRODUCTION

Transient elastography (TE) is a non-invasive and reproducible tool for staging hepatic fibrosis in patients with chronic liver diseases.

Regression of liver stiffness (LS) by TE in patients with chronic HCV infection after sustained virological response (SVR) has been reported.

AIMS OF THE STUDY

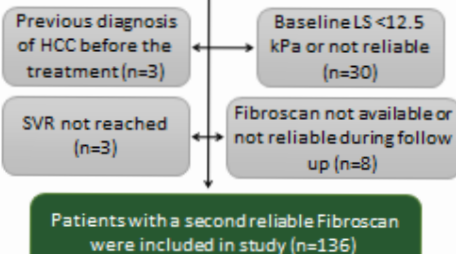
-To evaluate LS changes in patients with HCV-related compensated cirrhosis who achieved SVR by direct antiviral agents (DAAs)

-To evaluate the rate of cirrhosis regression defined as a reduction of LS <12.5 Kpa

-To identify predictors of cirrhosis regression

PATIENTS & METHODS

Patients with HCV-related compensated cirrhosis consecutively treated with DAAs between March 2015 and July 2016 (n=180)



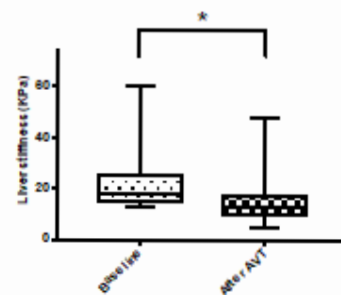
Each patient was evaluated with a complete biochemical profile and with TE (Fibroscan®) performed at baseline and 26 months after end of antiviral treatment.

Table 1. Baseline characteristics of the patients

| | |
|---|----------------|
| Age, years* | 70 (39 – 85) |
| Male, no. | 71 (52%) |
| Baseline LS (KPa)* | 18 (12.6 – 60) |
| Time of TE re-evaluation** | 12 (6 – 15) |
| PLT (x 10 ³ /mm ³)** | 132 ± 59 |
| Serum bilirubin (mg/dl)** | 1 ± 0.7 |
| INR** | 1.1 ± 0.3 |
| AST (U/L)** | 90 ± 50 |
| ALT (U/L)** | 100 ± 65 |
| γGT (U/L)** | 89 ± 81 |
| aFP (ng/ml)** | 24 ± 33 |
| APRI >2, no. | 54 (40%) |
| Fib4 >3.25, no. | 95 (70%) |
| Oesophageal varices, no. | 36 (26%) |
| BMI >25 kg/m ² , no. | 30 (22%) |
| Diabetes, no. | 11 (8%) |

*Median (range); **Mean ± SD; *months after EOT

Figure 1: LS changes after antiviral therapy



-LS reduced in 121/136 patients (89%) after a median time of 12 (6–15) months after EOT

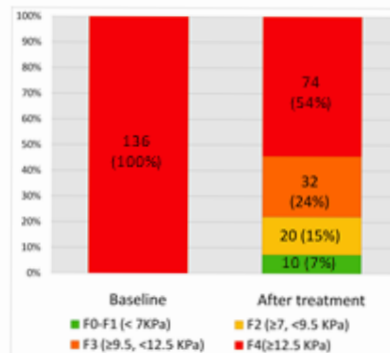
-Median LS reduction of 6 (1–32) kPa (p<0.0001*)

RESULTS

Table 2. Predictors of cirrhosis regression

| Clinical characteristics | Cirrhosis regression (n=62) | Not cirrhosis regression (n=74) | p |
|---|-----------------------------|---------------------------------|----------|
| Age (years)** | 66 ± 13 | 68 ± 11 | 0.1692 |
| Male, no. | 34 (55%) | 37 (50%) | 0.6082 |
| Baseline LS (kPa)** | 16.3 ± 0.6 | 25.9 ± 1.2 | <0.0001* |
| Time of TE re-evaluation, months* | 11.5 (6 – 15) | 12 (6 – 15) | 0.5729 |
| PLT (x 10 ³ /mm ³)** | 149 ± 7 | 119 ± 7 | 0.0029* |
| Serum bilirubin (mg/dl)** | 0.84 ± 0.05 | 1.22 ± 0.11 | 0.0029* |
| AST (U/L)** | 80 ± 6 | 98 ± 6 | 0.0357* |
| ALT (U/L)** | 96 ± 7 | 104 ± 9 | 0.5040 |
| γGT (U/L)** | 90 ± 11 | 87 ± 9 | 0.8232 |
| aFP (ng/ml)** | 15 ± 4 | 29 ± 5 | 0.0513 |
| APRI >2, no. | 15 (24%) | 37 (50%) | 0.0026* |
| Fib4 >3.25, no. | 34 (55%) | 61 (82%) | 0.0007* |
| Oesophageal varices, no. | 8 (13%) | 28 (38%) | 0.0016* |
| BMI >25 kg/m ² , no. | 22 (35%) | 38 (51%) | 0.0830 |
| Diabetes, no. | 6 (10%) | 13 (18%) | 0.2208 |

Figure 2: cirrhosis regression



Among 40 patients with baseline LS >23 kPa, only 3 (8%) patients achieved cirrhosis regression

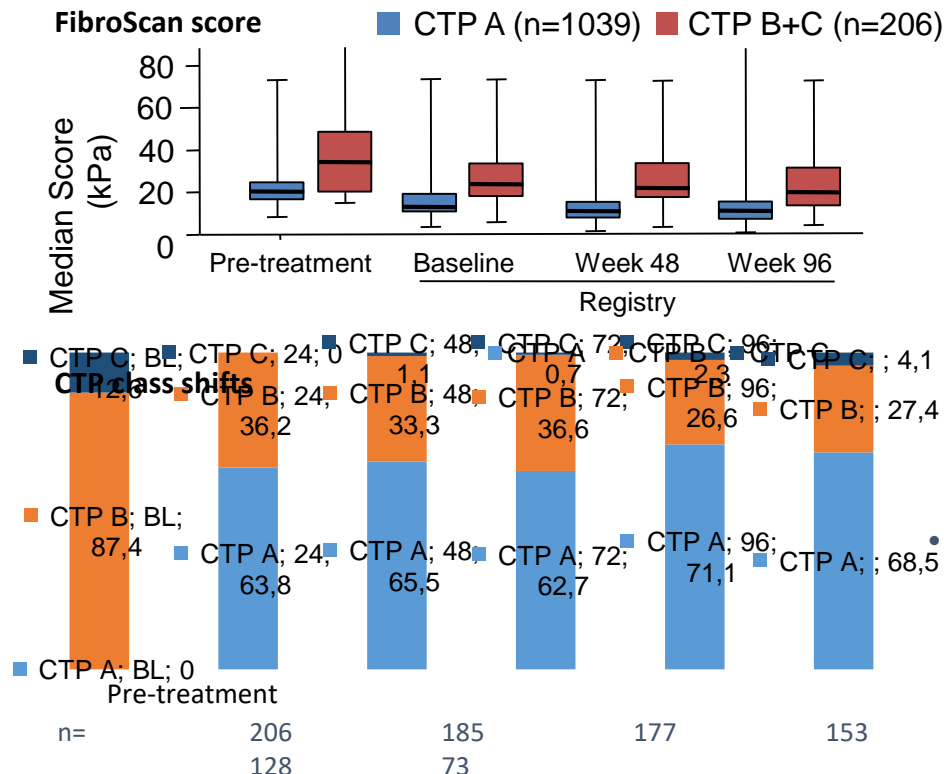
CONCLUSIONS

- Significant reduction of LS was observed in patients with HCV-related compensated cirrhosis successfully treated with DAAs
- 46% of patients showed cirrhosis regression
- Patients with most advanced liver disease have less probability to achieve cirrhosis regression
- LS value >23 kPa at baseline identifies patients with a low probability of cirrhosis regression (NPV=92%) whereas the PPV of LS ≤23 kPa is low (61%)
- Long-term follow-up studies may better define the clinical impact of LS reduction in HCV-cirrhotic patients after SVR

Disclosures: Mauro Viganò - Speaking and Teaching: Gilead Sciences, Roche, BMS; Giovanni Battista Gaeta - Advisory Committees or Review Panels: Janssen; Board Membership: Merck; Speaking and Teaching: BMS, Gilead, Bristol, Abbvie; Maria Grazia Rumi - Advisory Committees or Review Panels: Abbvie, Speaking and Teaching: Abbvie, MSD, Gilead

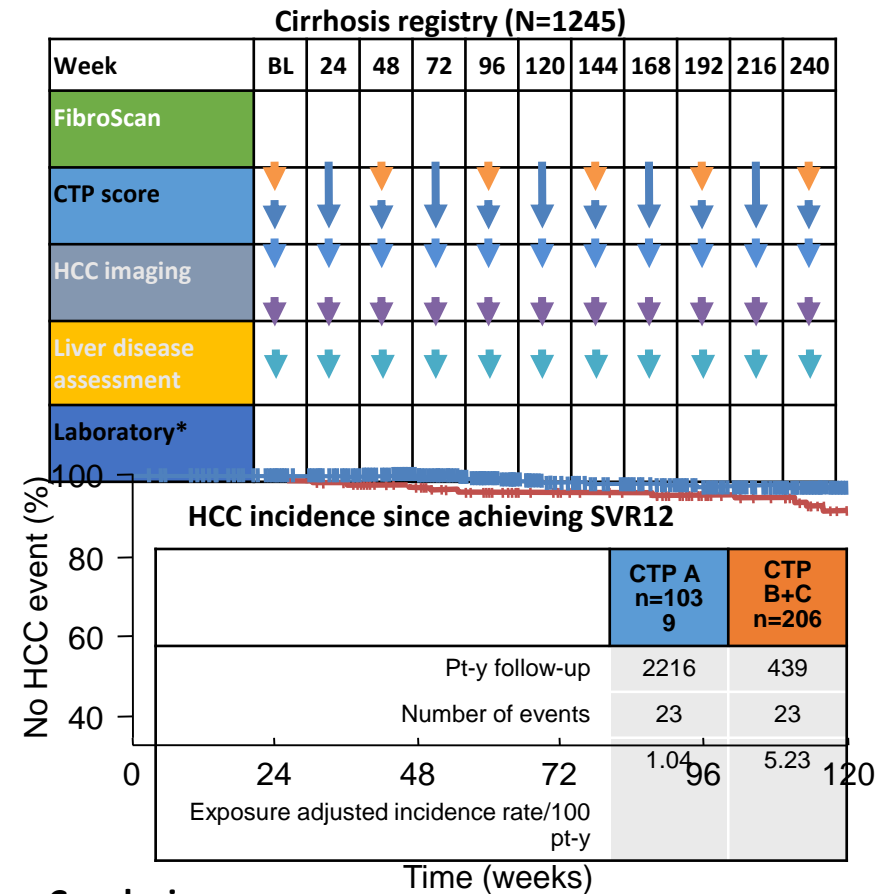
Long-term follow-up of patients with CHC and compensated or decompensated cirrhosis following SOF-based regimens

- Long-term virological and clinical outcomes in patients with cirrhosis who achieve SVR after DAA treatment are being evaluated in the DALTON cirrhosis registry study
- Objective:** to evaluate clinical progression or liver disease reversal after SVR and SVR durability



*Includes haematology, chemistry, lipids, HbA1C, coagulation, HCV RNA, markers of fibrosis and biomarkers. Other assessments: quality of life survey, DNA, endoscopy and optional biopsy

Mangia A, et al. ILC 2018, #GS-018



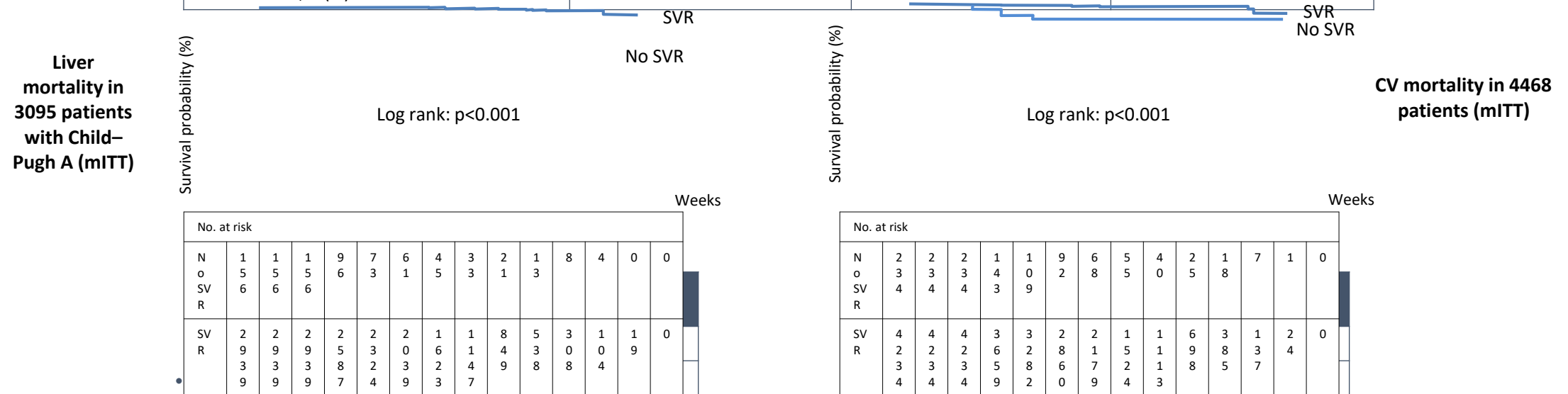
Conclusions

- SVR maintained in >99.9% of patients
- Improvements in fibrosis scores maintained
- Most patients show CTP improvement
- HCC decreased, in keeping with prior literature

Disease outcomes after DAA-induced SVR: Data from the RESIST-HCV Cohort

- Cohort: 4468 patients treated with DAAs (March 2015–Dec 2016), followed for a median of 73 weeks

| 63 patients died during the follow-up | Chronic hepatitis 991 (22.2%) | Child–Pugh A cirrhosis 3095 (69.2%) | Child–Pugh B cirrhosis 383 (8.8%) |
|---------------------------------------|----------------------------------|--|--------------------------------------|
| Overall death, n (%) | 7 (0.7) | 32 (1.0) | 24 (6.3) |
| Liver-related death, n (%) | 0 | 17 (0.5) | 14 (3.7) |
| Cardiovascular death, n (%) | 5 (0.5) | 6 (0.2) | 8 (2.1) |
| Other causes, n (%) | 2 (0.2) | 9 (0.3) | 2 (0.5) |



Conclusions:

- Patients with Child–Pugh A cirrhosis and SVR to DAAs have a better outcome than non-SVR patients
- Patients with Child–Pugh B cirrhosis retain significant risk of liver events and death even after HCV eradication
- Deaths linked to CV diseases seem to be reduced after viral eradication regardless of fibrosis stage

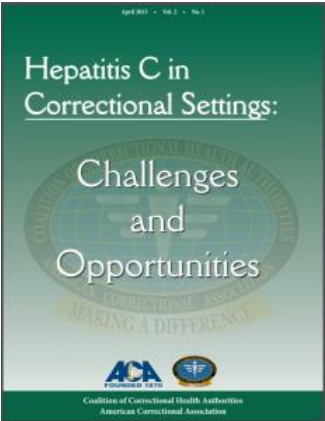
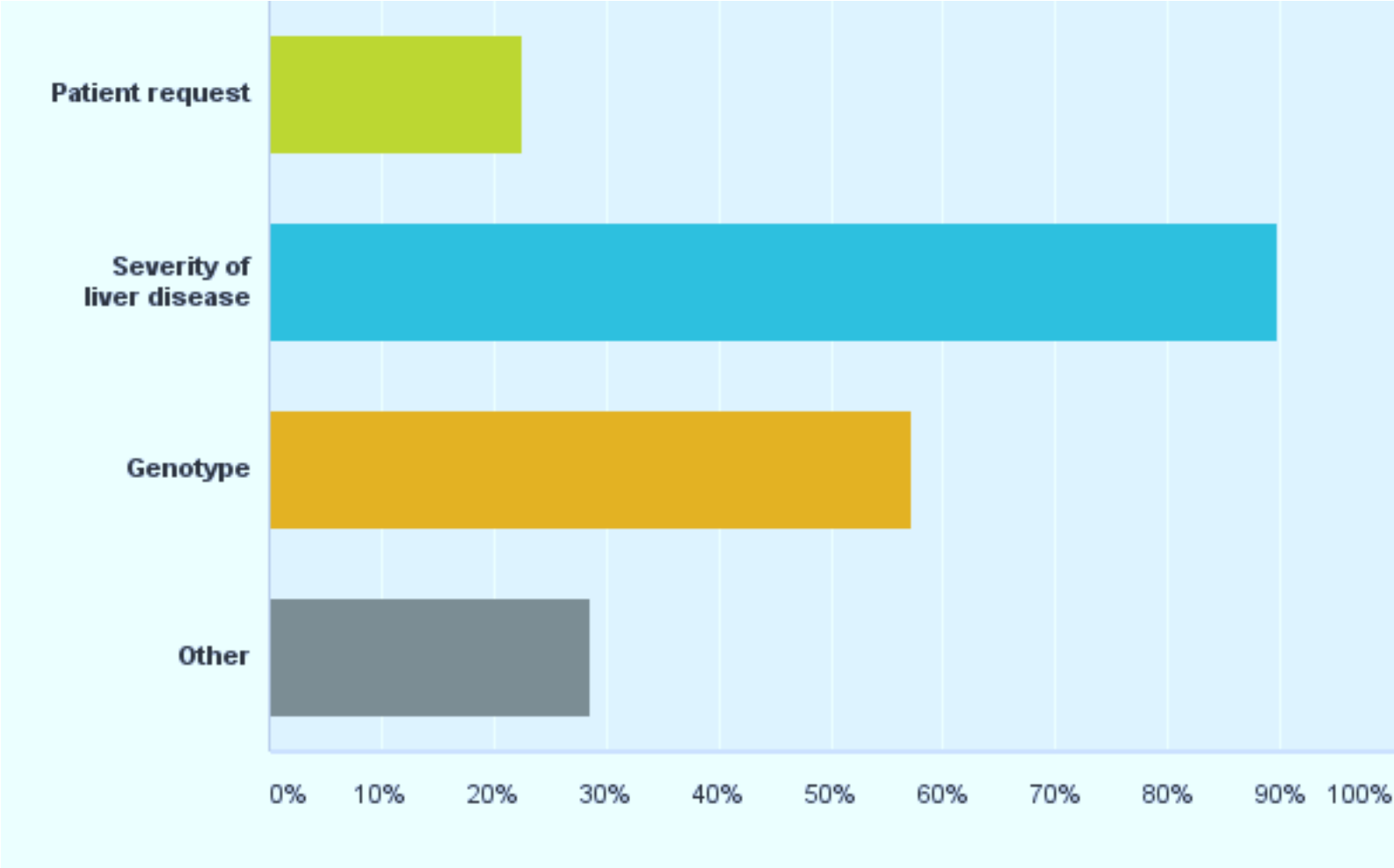
PLoS One. 2018 Feb 13;13(2):e0192763. doi: 10.1371/journal.pone.0192763. eCollection 2018.
Capacity of non-invasive hepatic fibrosis algorithms to replace transient elastography to exclude cirrhosis in people with hepatitis C virus infection: A multi-centre observational study.
 Kelly ML^{1,2,3}, Riordan SM^{4,5}, Bopage R², Lloyd AR^{1,3,6}, Post JJ^{1,2,3,4}.

| Algorithm | Indices utilised | | | | | | | |
|--------------|------------------|-----|-----|---------|-----|----------------|-----|-------------------|
| | Age | AST | ALT | ALT/AST | GGT | Platelet count | INR | Total cholesterol |
| APRI | | x | | | | x | | |
| CDS | | | x | | | x | x | |
| FIB-4 | x | x | x | | | x | | |
| Forns' Index | x | | | | x | x | | x |
| GUCI | | x | | | | x | x | |
| King's Score | x | x | | | | x | x | |
| Lok Index | | x | x | | | x | x | |

APRI = AST to Platelet Ratio Index, CDS = Cirrhosis discriminant score, FIB-4 = Fibrosis-4 score, Forns' = Forns' Index, GUCI = Göteborg University Cirrhosis Index, King's = King's Score, LOK = Lok Index. AST = aspartate aminotransferase, ALT = alanine aminotransferase level, GGT = γ-glutamyl transpeptidase, INR = international normalised ratio

<https://doi.org/10.1371/journal.pone.0192763.t001>

Hepatitis C Viral Infection Treatment Decision Factors



Sorveglianza dei pazienti con fibrosi avanzata o cirrosi che ottengono la SVR

I pazienti con fibrosi avanzata o cirrosi epatica che ottengono la SVR devono continuare ad essere seguiti presso centro specialistico, in cooperazione con i Medici di Medicina Generale

- Nei pazienti con fibrosi F3-F4 METAVIR, con cirrosi clinicamente evidente e/o con valori di Fibroscan >10 KPa al basale pre-terapia antivirale è consigliato effettuare una sorveglianza per lo sviluppo di HCC mediante l'esecuzione della ecografia del fegato, associata o meno al dosaggio plasmatico dei livelli di Alfa-Fetoproteina, a cadenza semestrale.
- In tutti i pazienti con cirrosi epatica e in coloro che presentano un valore di Fibroscan >20 KPa e/o un valore di piastrine <150.000 elementi/mm³ al basale pre-terapia antivirale, è fortemente consigliata l'esecuzione di una esofago-gastrosopia per valutare l'eventuale presenza di varici esofagee. Il trattamento e il monitoraggio delle varici non differiscono da quanto suggerito per i pazienti con cirrosi, secondo le indicazioni di Baveno VI.
- Benché lo sviluppo di scompenso clinico della malattia epatica dopo l'ottenimento della SVR sia un evento raro, è ragionevole associare allo screening per HCC anche un monitoraggio della funzione di sintesi epatica, mediante l'esecuzione degli esami di laboratorio e la valutazione clinica che consentano di calcolare i punteggi di Child-Pugh e di MELD.

Ambulatorio epatologico per la popolazione detenuta (UOC Medicina Protetta-Malattie Infettive)

Dal 2015 ad oggi sono stati trattati 100 pazienti (98 maschi e due femmine)

L'80% dei soggetti trattati presentava un grado di fibrosi elevato: 30% F3- 40% F4-10% cirrosi epatica clinica ecografica

Per il trattamento dei soggetti con fibrosi bassa (F0-F2) si è preferito il trattamento con i regimi antivirali ad 8 settimane

1 drop out per rilascio dall'istituto penitenziario ed interruzione volontaria di terapia (etilista cronico)

1 drop out per evasione dagli arresti domiciliari

1 fallimento a terapia con sofosbuvir ledispavir (GT3-F3)

1 fallimento a terapia con sofosbuvir daclatasvir (cirrosi epatica child B-GT3)

BIOPSIA O FIBROSCAN NEL PAZIENTE DETENUTO: ESPERIENZA E RIFLESSIONE

La biopsia epatica rimane il gold standard per la definizione diagnostica del danno epatico in questa popolazione dove cofattori di danno epatico (alcol, farmaci, steatosi, HBV occulto) influiscono in modo significativo sul monitoraggio successivo alla terapia antivirale

La possibilità, secondo gli 11 criteri AIFA, di trattare tutti i soggetti con epatopatia cronica HCV relata dovrebbe far entrare lo stato detentivo un criterio in cui definire il grado di fibrosi, in assenza di biopsia epatica, anche con i metodi indiretti (Fib-4, Apri test etc..).

Caratteristiche peculiari di questa popolazione è la possibilità di intervento sanitario spesso possibile solo in questo setting con risvolti nella salute individuale ed a livello epidemiologico

FATTORE TEMPO

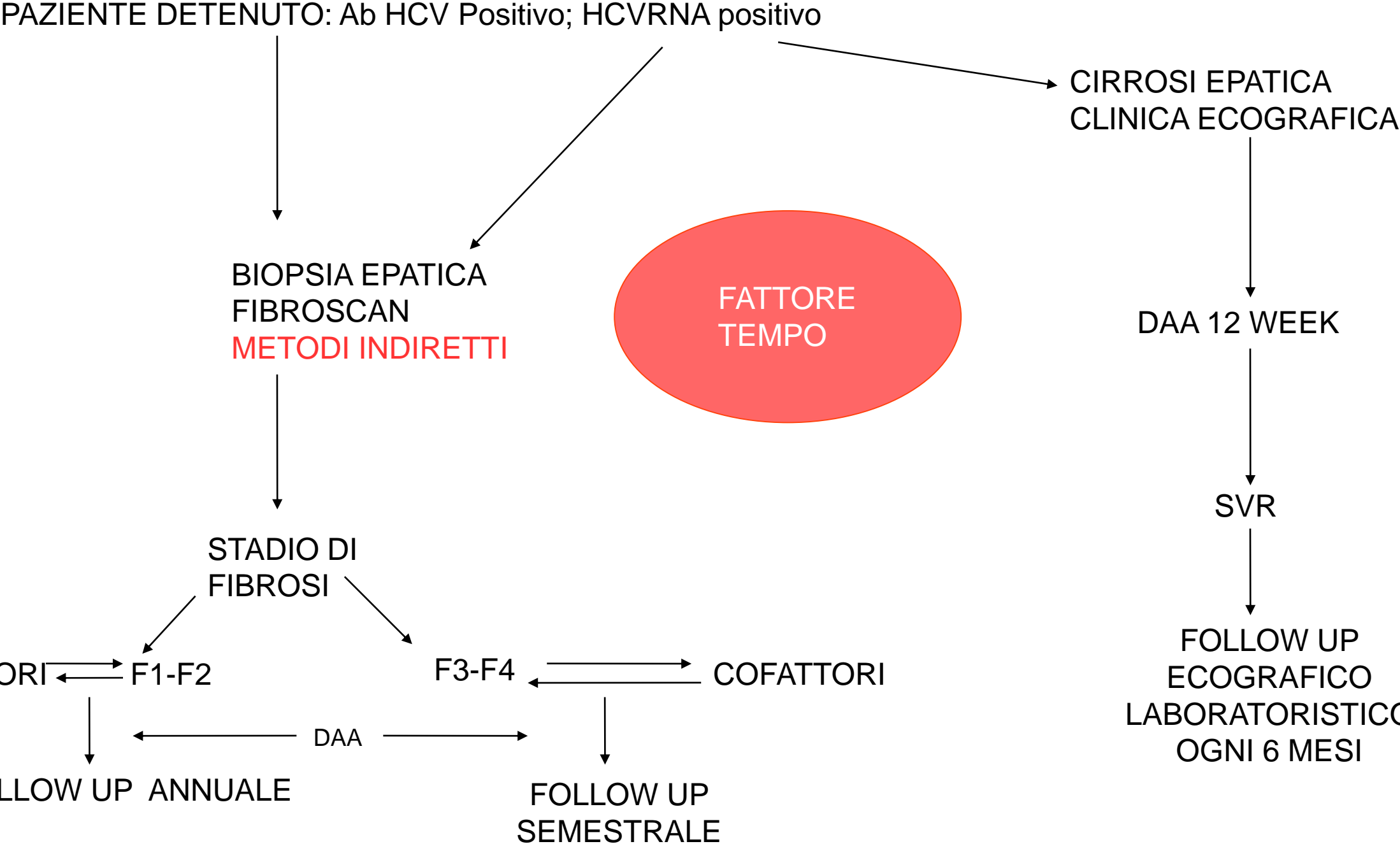


ORIZZONTE DETENTIVO

TRASFERIMENTI

SCHEDA AIFA

RIMBORSO REGIONALE



Treatment with direct-acting antivirals in a multicenter cohort of HCV-infected inmates in Italy.

Pontali E, Fiore V, Ialungo AM, Ranieri R, Mollaretti O, Barbarini G, Marri D, Prestileo T, Dell'Isola S, Rastrelli E, Leo G, Starnini G, Babudieri S, Madeddu G; Gruppo Infettivologi Penitenziari.

Abstract

BACKGROUND:

People who are incarcerated have a significantly higher prevalence of HCV infection than the general population. Given their high-risk behavior, they represent a reservoir of HCV infection for the whole community.

METHODS:

We evaluated all HCV-infected people who were incarcerated in 25 Italian prisons starting direct-acting antivirals (DAAs) treatment between May 2015 and October 2016. We collected information on demographic characteristics, liver disease, HCV-related aspects, anti-HCV treatment, HIV or HBV co-infection.

RESULTS:

We enrolled 142 incarcerated people treated with DAAs. They were mostly Italians (93.7%) and males (98.6%). Median age was 50 years and 108/142 (76.1%) were cirrhotic patients. Prevalent genotypes were 1a (35.9%) and 3 (35.9%). Two patients were HBV co-infected, twenty-one patients (14.8%) were HIV co-infected and almost all (95.2%) received antiretroviral therapy. 118/142 (83.1%) DAAs-based regimens included sofosbuvir. Treatment completion rate was 94.4%. There were eight (5.6%) discontinuations, one (0.7%) due to an adverse reaction, one due to death (0.7%) and six (5.6%) due to release from prison. SVR12 was achieved in 90.8%. Four patients relapsed but no breakthrough occurred.

CONCLUSIONS:

Our study shows that in Italian penitentiary settings DAAs treatment is feasible and effective. This intervention is crucial for reducing HCV circulation with possible benefits to the general population.

J Viral Hepat. 2018 Sep 5. doi:
10.1111/jvh.12998

A systematic review on models of care effectiveness and barriers to Hepatitis C treatment in prison settings in the EU/EEA.

Vroling H, Oordt-Speets AM, Madeddu G, Babudieri S, Monarca R, O'Moore E, Vonk Noordegraaf-Schouten M, Wolff H, Montanari M, Hedrich D, Tavoschi L

Summary

Hepatitis C prevalence in prison populations is much higher than in the community. Effective hepatitis C treatment within this population does not only have a direct individual health benefit, but may lead to substantial community dividend. We reviewed available evidence on hepatitis C treatment in prison settings, with a focus on the European Union/European Economic Area. A systematic review of the literature (PubMed, EMBASE, Cochrane library) was performed and complemented with searches for conference abstracts and grey literature. Thirty-four publications were included reporting on the effectiveness, acceptability and economic aspects of hepatitis C virus treatment models of care to achieve treatment completion and sustained viral response in prison settings. Available evidence shows that hepatitis C treatment in prison settings is feasible and the introduction of direct-acting antivirals will most likely result in increased treatment completion and better clinical outcomes for the prison population, given the caveats of affordability and the need for increased funding for prison health, with the resulting benefits accruing mostly in the community.

TAKE HOME MESSAGE

S stadiazione in tempi brevi con test rapidi (sierologici e molecolari) e metodi indiretti per la valutazione della fibrosi

P prescrizione del regime terapeutico più adeguato alle caratteristiche cliniche ed all'orizzonte detentivo

E eliminazione dei fattori che possono ritardare inizio terapia e dei fattori che ne possono determinare l'interruzione

S sorveglianza dei pazienti con fibrosi avanzata che ottengono svr

Microelimination
HCV free prison

Salute
individuale

Salute pubblica

GRAZIE PER L'ATTENZIONE

....e grazie a Dott.ssa Annamaria Ialungo
Dott.ssa Elisabetta Liguori
Dott.ssa Elena Rastrelli

Al Direttore della UOC Medicina Protetta-Malattie Infettive
Dott Giulio Starnini

