CROI 2018
Boston, MA, USA

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TREATMENT OF CHRONIC HEPATITIS C GT1,2,4 IN AFRICA: FINAL RESULTS OF ANRS 12311 TAC TRIAL

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Introduction

- Chronic hepatitis C is increasingly identified as an emerging chronic condition leading to a greater health burden in resource-limited countries[1].
- Once considered as a hidden epidemic, chronic hepatitis C virus (HCV) infection is now more likely to be diagnosed. Its spread is linked to increased drug-use in urban areas of Eastern, Central and West Africa and to nosocomial transmission[2].
- Access to HCV treatment in resource-limited countries has always been a challenge due to technical and financial constraints.
- The recent advent of direct antiviral agents targeting HCV protease or polymerase activities has triggered a major shift in the treatment of HCV genotype 1, 2 and 4. Shorter courses of treatment associated with a higher rate of sustained virological response and a lower rate of side effects make DAA appealing candidates for HCV treatment in resource-limited settings[3].
- Evidence-based medicine data are regularly required by WHO and local governments, whereby recommendations on HCV care and treatment are adapted to Sub-Saharan settings[4].

Objective

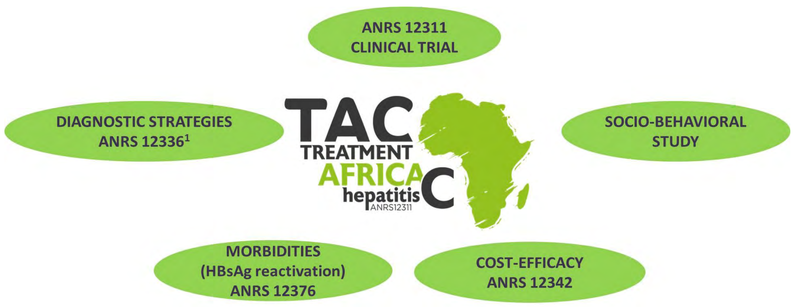
Evaluate the efficacy (sustained virological response 12 weeks after end of treatment) of 12-week course of an interferon-free regimen containing sofosbuvir and weight-based ribavirin (genotype 2), or sofosbuvir and ledipasvir (genotype 1 and 4) in treatment naïve patients infected with HCV genotype 1,2 or 4 in West and Central Africa (Senegal, Cameroon, Côte d'Ivoire)

Methods and Patients

Study Design: International one arm, non randomized, pilot clinical trial
Patients:

- Confirmed G1, G2 or G4 HCV infection, plasma HCV-RNA >12 IU/ml or the detection limit of the participating site, no history of HCV treatment of any kind, on birth control method;
- In case of HIV infection: Confirmed HIV-1 infection, stable HIV treatment for at least 8 weeks, current CD4+ lymphocytes count ≥100/mm^3, current plasma HIV-1 RNA <200 copies/Ml
- Non inclusion: confirmed HBsAg+

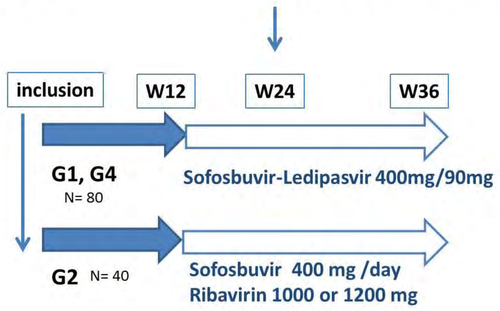
Sample size: Fleming/A Hern's design: target efficacy level = 70%, 1-β=80%, α=5%, thus 40 patients in each group of genotype



Study design

Primary endpoint:
SVR 12

Secondary endpoints
HIV, HCV kinetics, tolerability



SVR12: sustained virological response 12 weeks after end of treatment

Results (1/2)

Table 1: baseline characteristics of included patients

		Genotype 1 n=40	2 n=40	4 n=40	Overall n=120
Male	n (%)	21 (53%)	25 (63%)	19 (48%)	65 (54%)
Age (year)	median (IQR)	59 (51 - 64)	52 (41 - 60)	61 (55 - 63)	58 (49 - 63)
BMI (Kg/m2)	median (IQR)	23.6 (19.9 - 25.9)	24.3 (21.9 - 27.6)	28.0 (24.3 - 31.2)	24.9 (22.0 - 28.4)
Alcohol, Yes, <once a day	n (%)	2 (5%)	8 (20%)	11 (28%)	21 (18%)
HIV infection	n (%)	8 (20%)	12 (30%)	16 (40%)	36 (30%)
Cirrhosis (APRI low >1)	n (%)	9 (23%)	10 (25%)	10 (25%)	29 (24%)
(APRI high >2)	n (%)	3 (8%)	6 (15%)	5 (13%)	14 (12%)
logHCV-RNA (IU/mL) at W0	median (IQR)	5.8 (5.2 - 6.3)	6.0 (5.3 - 6.4)	6.4 (5.8 - 6.7)	6.0 (5.5 - 6.6)
ALAT (IU/L) at W0	median (IQR)	50 (36 - 71)	46 (26 - 89)	49 (39 - 80)	47 (36 - 78)
ALAT grade at W0:					
0	n (%)	23 (58%)	26 (65%)	25 (63%)	74 (62%)
1.25 - 2.50 x ULN	n (%)	15 (38%)	7 (18%)	10 (25%)	32 (27%)
>2.50 - 5.00 x ULN	n (%)	2 (5%)	5 (13%)	4 (10%)	11 (9%)
>5.00 - 10.00 x ULN	n (%)	0	2 (5%)	1 (3%)	3 (3%)
Creatinine (mg/L) at W0	median (IQR)	7 (6 - 10)	9 (8 - 10)	8 (7 - 10)	8 (7 - 10)
Hemoglobine (g/dL) at W0	median (IQR)	13 (12 - 14)	14 (13 - 15)	14 (13 - 14)	14 (12 - 14)

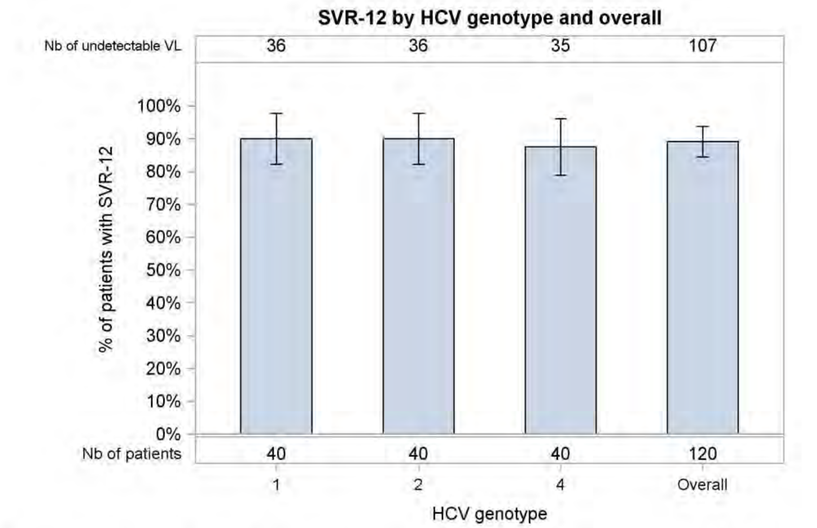
Table 2: characteristics of HIV+ patients

HIV patients		Genotype 1 n=6	2 n=12	4 n=16	Overall n=36
WHO stage					
1	n (%)	4 (50)	6 (50)	8 (50)	18 (50)
2	n (%)	3 (38)	2 (17)	2 (13)	7 (19)
3	n (%)	1 (8)	1 (8)	5 (31)	7 (19)
4	n (%)	0	3 (25)	1 (6)	4 (11)
CD4 (/mm3)	median (IQR)	593 (398 - 864)	647 (391 - 738)	669 (453 - 874)	624 (422 - 844)
HIV viral load (cp/mL) <50 cp/mL	n (%)	7 (88)	9 (75)	14 (88)	30 (83)
Ongoing ARV treatment					
ABC-3TC-EFV	n (%)	0	1 (8)	0	1 (3)
ABC-3TC-LPV/r	n (%)	0	1 (8)	0	1 (3)
TDF-3TC-LPV/r	n (%)	1 (13)	0	1 (6)	2 (6)
TDF-3TC-NEVIRAPINE	n (%)	0	2 (17)	6 (38)	8 (22)
TDF-3TC -ATV/r	n (%)	1 (8)	0	0	1 (3)
TDF-3TC-EFV	n (%)	6 (75)	8 (67)	9 (56)	23 (64)
Time on ARV (months)	median (IQR)	25 (21 - 56)	30 (5 - 46)	21 (7 - 61)	25 (7 - 54)

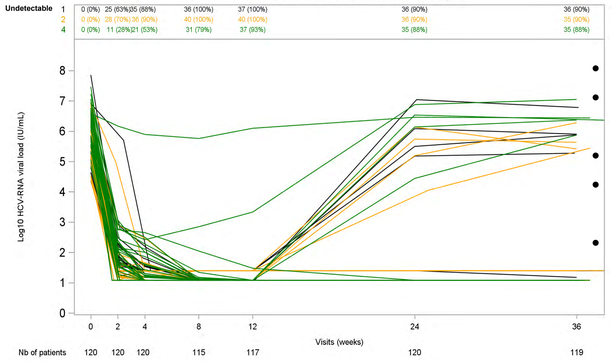
Table 3: adherence at week 12 based on pill count

	Genotype 1 n=40	2 n=40	4 n=40
sofosbuvir	-	94% (79% - 100%)	-
ribavirin	-	97% (92% - 100%)	-
sofosbuvir/ledispavir	100% (94% - 100%)	-	83% (71% - 98%)

Results (2/2)



% of undetectable 90% CI	**90.0% [82.2 - 97.8]**	**90.0% [82.2 - 97.8]**	**87.5% [78.9 – 96.1]**	**89.2% [84.5 – 93.8]**



- 13 patients failed treatment
- Resistance genotyping on-going
- No impact of HIV, adherence
- Trend of impact of cirrhosis status
- No safety concern, even in patients on ribavirin

Conclusions

- **SOF-based HCV treatment in Sub-saharan Africa was safe, well-tolerated, and efficient, including in HIV-coinfected patients**
- **These results support the need for scaling-up of HCV treatment in the African continent.**

References

(1) Global Burden of Diseases, JAMA Oncol 2017; (2) Lemoine, J Hepatol 2014; (3) Hill, Science 2014. (4) Global Hepatitis report, WHO 2017

Acknowledgements

- ANRS sponsored the Trial
- IMEA and PACCI ensured monitoring and statiistical analysis
- Gilead Sciences provided sofosbuvir and sofosbuvir/ledipasvir for free
- Mylan provided ribavirin at reduced price