Baseline liver stiffness and alanine transaminase predicts reduction in liver stiffness in people with chronic hepatitis B on tenofovir alafenamide

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Background

- 296 million people are chronically infected with hepatitis B (CHB).
- CHB is a leading cause of cirrhosis and hepatocellular carcinoma.
- Suppressive therapy with nucleos(t)ide (NUC) analogue therapy, such as tenofovir alafenamide (TAF), reduces the risk of cirrhosis and cancer.
- Transient elastography measures liver stiffness and is used to monitor liver fibrosis in CHB.

Aim

- Evaluate correlates with improvement in liver fibrosis with NUC treatment

Method

- TEMUL (Tenofovir Alafenamide for HBV – A Longitudinal Study) is a prospective study at the University of Maryland, Baltimore with the aim of measuring change in fibrosis with 2 years of treatment with tenofovir alafenamide (TAF).
- Inclusion criteria:
  - Adults with chronic hepatitis B infection eligible to receive NUC therapy according to standard-of-care
- Exclusion criteria:
  - Any contraindications to TAF
  - Pregnant or breastfeeding
  - HIV coinfection
- Eligible subjects were either:
  - Already taking a NUC and switched to TAF (SWITCH group)

  or
  - Off NUC at baseline (NO NUC group) – either treatment naïve or prior NUC treatment.
- Statistical analysis: Comparison of baseline characteristics by unpaired t-test of non-parametric Mann-Whitney U test. Correlates of change in liver stiffness was evaluated with multiple linear regression. P-value of <0.05 was considered statistically significant.

Results

- Since 2017, 60 have completed the study.
- 19 had advanced fibrosis (≥F2). Fibrosis improved by at least stage in 14 with no change in 5.
- Baseline ALT was higher in the NO NUC group .
- Liver stiffness decreased in the NO NUC group only (6.5 kPa to 5.3, p=0.02).
- Baseline liver stiffness and ALT correlated with reduction in liver stiffness (figures 1a and b).
- The effect of baseline liver stiffness and ALT on reduction in liver stiffness was differed in the Switch and No NUC groups, but this interaction was only statistically significant for baseline liver stiffness (figure 2).

Table 1 – Baseline characteristics

(ALT – alanine transaminase; sAg – hepatitis B surface antigen; eAg – hepatitis B e-antigen; CAP – controlled attenuated parameter, measure of hepatic steatosis)

Characteristic		Switch (N=29)	No NUC (N=31)	*P*
Sex N(%)	Male	19	21	0.9
	Female	10	10	
Mean Age (SD)		47.6 (12.5)	48 (10.4)	0.9
Mean ALT, U/L (SD)		30 (15)	53 (43)	0.007*
Mean baseline sAg titer, IU/ml (SD)		19425 (38084)	8794 (17882)	0.7
eAg, N(%)	Positive	12	8	0.2
	Negative	17	23	
Mean baseline liver stiffness, kPA (SD)		6.3 (2.8)	6.5 (2.5)	0.7
Baseline Fibrosis Score, N (%)	F1	20 (69)	21 (68)	0.2
	F2	4 (14)	1 (3)	
	F3	2 (7)	7(23)	
	F4	3 (10)	2 (6)	
Mean change in FibroScan, kPA (SD)		-0.2 (2.3)	-1.2 (2.7)	0.1
Mean baseline CAP score, dB/m (SD)		231 (48)	225 (47)	0.6

Figure 1: Correlations with reduction in liver stiffness (a) baseline liver stiffness, (b) baseline ALT

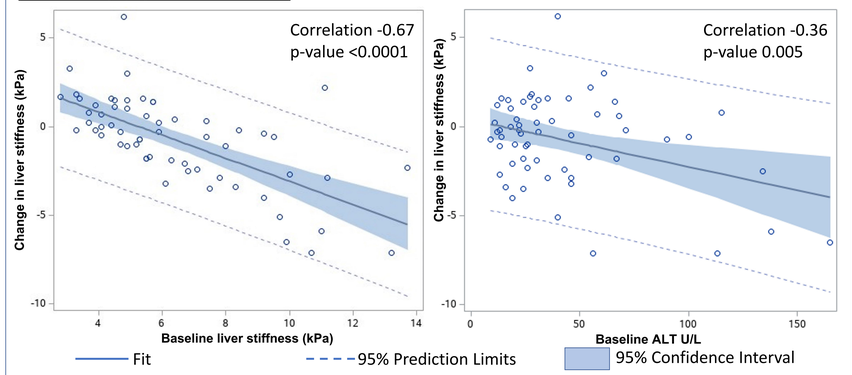
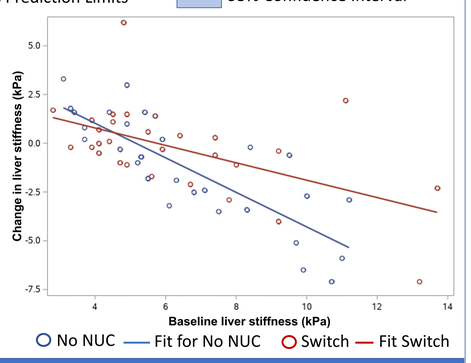


Figure 2: Effect of baseline liver stiffness was modified by NUC status at baseline

P-value for interaction = 0.02
Switch Correlation = -0.544, P=0.002
No NUC correlation = -0.8, p=<0.001.



Conclusion

- After 2 years of treatment with TAF, liver stiffness improved in people with elevated ALT and liver stiffness.
- Reduction in liver stiffness correlated with baseline liver stiffness and ALT, with a greater effect seen in people that were not on NUC therapy at baseline.
- This reflects overestimation of liver fibrosis due to inflammation at NUC initiation or resumption.
- Liver fibrosis measurement should be repeated after initiating NUC, especially in people with elevated ALT, to guide ongoing CHB care.

Conflicts of interest: Dr Tang received research funding from Gilead Sciences paid to her institution.