Rise in ALT after HCV treatment is a highly sensitive screen for treatment failure: a diagnostic accuracy study

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Background

Nucleic acid testing to confirm cure after HCV therapy is expensive and requires technical expertise that is frequently unavailable in settings where disease prevalence is highest.

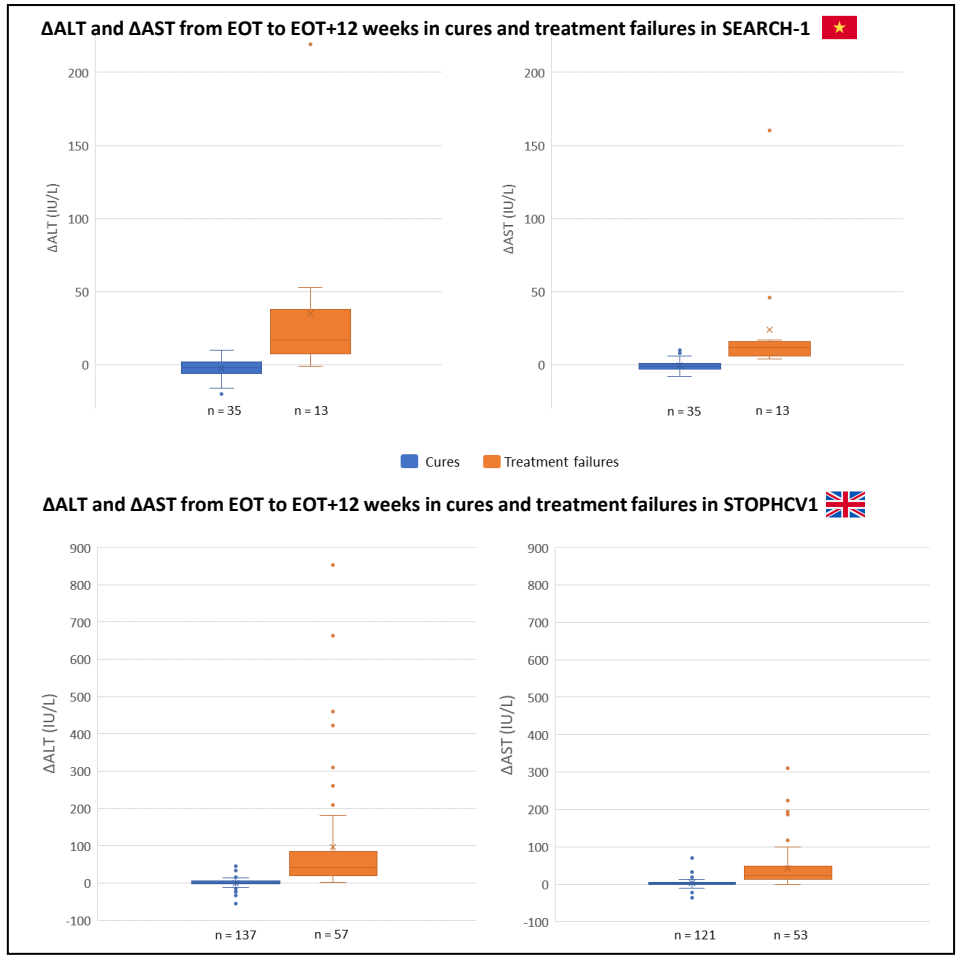
We investigated monitoring levels of ALT and AST in blood to identify treatment success.

Methods

We used data from an HCV trial in Vietnam (n=52) to describe how changes in ALT (ΔALT) and AST (ΔAST) from end of treatment (EOT) to EOT+12 weeks related to cure, defined as HCV RNA < lower limit of quantification 12 weeks after EOT.

In a separate UK trial population (n=202), we then tested the hypothesis that *any* elevation in ALT or AST between EOT and EOT12 is a sensitive marker of treatment failure.

Data



	SEARCH-1	STOPHCV1
N (available data)	48	194
Cures	35	137
Treatment failures	13	57
Median ΔALT (IQR) Cures	-2 IU/L (-5.5, +1.5)	0 IU/L (-2, +5)
Median ΔALT (IQR) Failures	+17 IU/L (+9, +38)	+41 IU/L (+20, +83)
Sensitivity (95% C.I.)	92% (64 – 99.8)	100% (93.7, 100)
Specificity (95% C.I.)	66% (48 - 81)	50.4% (41.7, 59.0)
AUROC (95% C.I.)	0.95 (0.87-1.00)	0.96 (0.94 -0.99)
Median ΔAST (IQR) Cures	-1 IU/L (-3, +1)	+2 IU/L (-1, +5)
Median ΔAST (IQR) Failures	+12 IU/L (+7, +15)	+23 IU/L (+13, +37)
Sensitivity (95% C.I.)	100% (75 - 100)	98.1% (89.9, 99.9)
Specificity (95% C.I.)	66% (48 - 81)	36.4% (27.8, 45.6)
AUROC (95% C.I.)	0.96 (0.91 - 1.00)	0.92 (0.88 - 0.96)

Results

In SEARCH-1, among 48 individuals with data, 13 failed to achieve cure with 4-8 weeks sofosbuvir + daclatasvir.

ΔALT and ΔAST were higher in treatment failures than cures [median ΔALT (IQR):+17 IU/L (+7.5, +38) vs -2 IU/L (-6, +2)] ($p < 0.001$).

12/13 and 13/13 treatment failures had an increase in ALT and AST between EOT and EOT12, compared with 12/35 cures.

In STOPHCV1, 194/202 treated with 4-8wks ombitasvir, paritaprevir, ritonavir +/- dasabuvir had data, of which 57 failed to achieve cure. ΔALT and ΔAST were again higher in treatment failures.

Increase in ALT after EOT (ΔALT>0 IU/L) was
- **100% sensitive (95% C.I. [93.7 - 100])**
- **50% specific (95% C.I. [41.7 - 59.0])**

for detecting treatment failure.

ΔAST>0 IU/L performed similarly.

Interpretation

Rise in ALT after HCV therapy is a highly sensitive screen for treatment failure in patients with mild liver disease.

With standard rates of cure, this approach could half number of HCV RNA tests performed at EOT+12, reducing treatment costs and facilitating decentralisation of care in remote and resource-limited settings.