

Modeling the HepQuant STAT Test for Pre-screening NASH Subjects to Enrich Study Populations for the desired Stage of Disease



Steve M. Helmke and Gregory T. Everson
HepQuant, LLC, Greenwood Village, CO

Background

HepQuant STAT is a simple “drink and draw” blood-based clearance test that quantifies hepatic impairment from early through late stages of disease. Hepatic impairment may distinguish NASH from benign steatosis. F3/F4 NASH is a particular focus of drug development as reversal of F3/F4 NASH could improve patients’ clinical outcome. Drug trials in NASH are hampered by unacceptably high rates of screen failure for NASH or F3/F4 NASH.

Objective

To model the use of STAT as a pre-screening tool to enhance subject enrollment, reduce the number of risky procedures, and lower costs.

Subjects

There were 50 healthy controls (30 lean, 16 overweight, 4 obese) with normal liver blood tests and 39 NASH subjects (8 F1/F2, 9 F3, 13 compensated F4, and 9 with decompensated F4) that were included in this analysis.

Methods

The HepQuant STAT liver diagnostic test kit is simple to administer, requires no specialized bedside equipment, and involves administration of 40 mg of d4-cholate orally and one timed 3 to 5 mL blood sample at 60 minutes post-dose. Cholates are quantified by LC/MS and STAT is calculated from the d4-cholate concentration at the 60 min timepoint. STAT estimates the disease severity index, DSI. The optimum STAT cutoffs for diagnosing NASH and identifying F3/compensated F4 NASH were defined by Youden Indexes in ROC curve analyses.

Results: STAT as a Pre-screen for Enriching a Study Population for NASH Patients

The optimum STAT cutoff of $>0.65 \mu\text{M}$ had a sensitivity 69% and specificity 98% for diagnosing NASH. In this model, a pharmaceutical company wishes to enroll 400 biopsy-diagnosed NASH patients in a clinical trial, the target population is adults with obesity and/or T2DM, and the estimated prevalence of NASH in the target population is 30%.

	STAT Tests		Liver Bx		Subjects Enrolled		Bx Complications		Total Costs\$
	N	Cost \$400/test	N	Cost \$5000/Bx	N	Yield (% of Bxs)	N	Cost \$50000/comp	
No STAT	0	\$0	1333	\$6,665,000	400	30%	8	\$400,000	\$7,065,000
STAT	1932	\$772,800	427	\$2,135,000	400	94%	2.6	\$130,000	\$3,037,800
Savings:			906			64%	5.4		\$4,027,200

Results: STAT as a Pre-screen for Enriching F3/compensated F4 NASH Patients

A STAT range of $0.81 - 2.50 \mu\text{M}$ could identify NASH F3/compensated F4 patients with sensitivity 59% and specificity 88%. In this model, a pharmaceutical company wishes to enroll 400 patients of this stage in a clinical trial, the target population is adults with obesity and/or T2DM, and the estimated prevalence of F3/compensated F4 NASH in the target population is 30%.

	STAT Tests		Liver Bx		Subjects Enrolled		Bx Complications		Total Costs\$
	N	Cost \$400/test	N	Cost \$5000/Bx	N	Yield (% of Bxs)	N	Cost \$50000/comp	
No STAT	0	\$0	1333	\$6,665,000	400	30%	8	\$400,000	\$7,065,000
STAT	2260	\$904,000	589	\$2,945,000	400	68%	3.5	\$175,000	\$4,024,000
Savings:			744			38%	4.5		\$3,041,000

Conclusions

HepQuant STAT may be an effective tool for use during pre-screen to enrich a study population for either subjects with NASH or subjects with F3/F4 NASH. Our results suggest that STAT Pre-Screen could reduce the number of liver biopsies, lower cost, limit risk to the subject, and enhance patient tolerability.