Evaluation of a Blood-Based microRNA Clinical Assay for Guiding Immunosuppressive Management in Liver Transplant Recipients

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Introduction

- Liver transplant recipients require lifelong immunosuppression, which is associated with infection, malignancy, nephrotoxicity, metabolic complications, and reduced quality of life. Current monitoring relies on liver enzymes and biopsy, which typically detect rejection only after liver injury has occurred.
- HepatoTrack is a circulating microRNA assay previously shown to have strong clinical performance for detection of acute cellular rejection (ACR) in liver transplant recipients and may identify rejection-associated molecular signals before clinical injury becomes apparent.
- This study evaluated the utility of HepatoTrack for guiding immunosuppression minimization and identifying patients at risk for rejection during withdrawal.

Methods

HepatoTrack™ Clinical Assay

- **Sample**: 100 µL serum or plasma
- **Method**: RT-qPCR analysis
- **Analytes**: miR-122 and miR-885; miR-23a serves as the endogenous reference and cel-miR-39 as the exogenous control.
- **Test Score**: HepatoTrack prediction scores (HPS) for acute cellular rejection (ACR) were generated using a predefined proprietary algorithm.
- **Previously Published ACR Diagnostic Performance (*n*=37):** Sensitivity 92.9%, specificity 73.9%, PPV 68.4%, NPV 94.4% (Wang et al., 2026).
- **Current Study: Additional evaluation in two independent cohorts: A-WISH and OPTIMAL.**

Cohort 1: the A-WISH Study (*n*=22)

- Biopsy-confirmed rejection status was available for evaluation of HepatoTrack diagnostic performance.

Cohort 2: the OPTIMAL Study (*n*=60)

Patients (*n*=60) were categorized according to their response to immunosuppression withdrawal (ISW).

- **Tolerant patients** (*n*=10) were those who successfully discontinued immunosuppression and maintained stable graft function without clinical or histologic evidence of rejection.
- **Non-tolerant by biopsy patients** (*n*=8) remained off immunosuppression but demonstrated subclinical rejection or histologic abnormalities on protocol biopsy.
- **Failed after ISW patients** (*n*=7) initially completed IS withdrawal but subsequently required reinstitution of immunosuppression due to clinically manifest rejection or graft dysfunction.
- **Failed ISW patients** (*n*=35) were unable to complete the withdrawal protocol because of rejection, abnormal liver tests, or other clinical indications requiring resumption or escalation of immunosuppression.

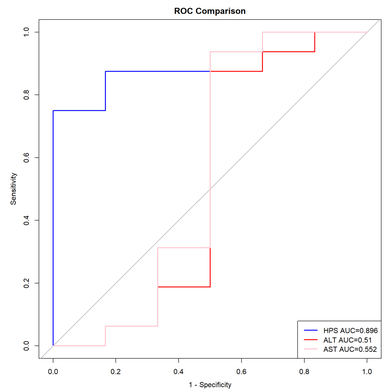
Results

Cohort 1

Clinical Performance of HepatoTrack in Cohort 1

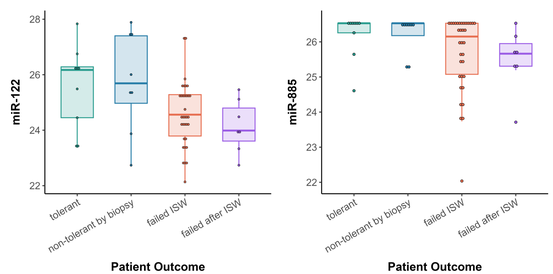
	LB Confirmed ACR	LB Confirmed non-ACR
Predicted ACR	14	1
Predicted non-ACR	2	5

Patient Number (n)	22
Accuracy	86.4%
Sensitivity	87.5%
Specificity	83.3%
Pos Pred Value (PPV)	93.3%
Neg Pred Value (NPV)	71.4%

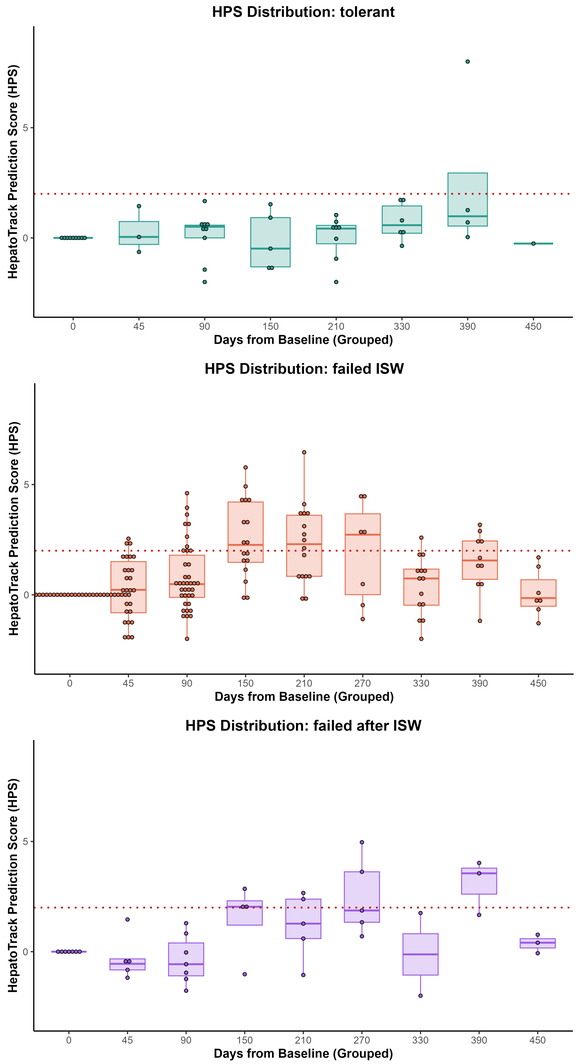


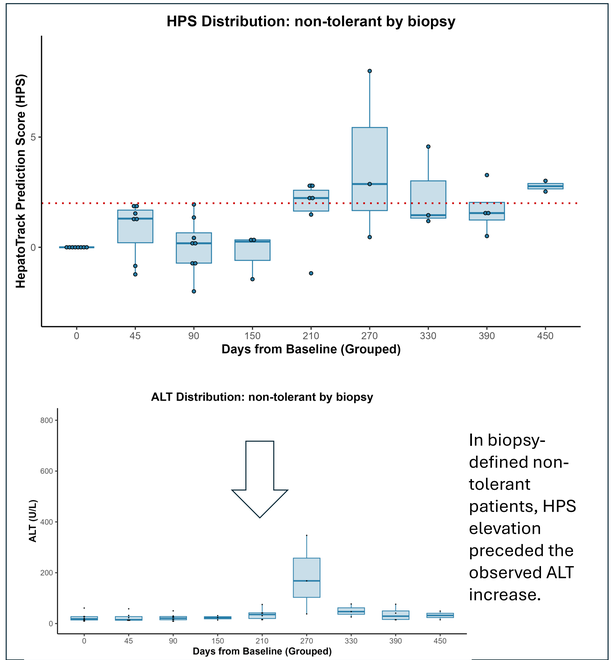
Cohort 2

Baseline miR-122 and miR-885 Levels Associated with Immunosuppression Withdrawal Outcome



Longitudinal Distribution of HepatoTrack Prediction Scores Across Immunosuppression Withdrawal Outcome Groups





In biopsy-defined non-tolerant patients, HPS elevation preceded the observed ALT increase.

Conclusion

HepatoTrack demonstrated strong ACR diagnostic performance in an additional independent cohort and showed potential for earlier detection of alloimmune activity during immunosuppression withdrawal.

Literature

1. Wang Y, et al. Diagnostics. 2026;16(14):2152. Analytical and clinical validation of a serum microRNA RT-qPCR assay for detection of acute cellular rejection in liver transplant recipients. doi:10.3390/diagnostics16142152.
2. Shaked A., et al. An ectopically expressed serum miRNA signature is prognostic, diagnostic, and biologically related to liver allograft rejection. Hepatology. 2017;65:269–280. doi: 10.1002/hep.28786.

Acknowledgement

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