Treatment of Patients with Primary Biliary Cholangitis with Seladelpar for 52 Weeks Improves Predicted Transplant-free Survival

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BACKGROUND

o Primary biliary cholangitis (PBC) is a chronic cholestatic liver disease characterized by destruction of small intrahepatic bile ducts.[1]
o Patients with an incomplete response to ursodeoxycholic acid (UDCA) are at risk of progressing to end stage liver disease, thus new treatment options are still needed.
o The GLOBE score is a validated prognostic tool that can be used to estimate transplant-free survival.[2]
o Seladelpar is a peroxisome proliferator-activated receptor delta (PPAR δ) agonist in development as therapy in patients who are inadequate responders or intolerant to UDCA.

AIM

o **To evaluate the predicted changes in transplant-free survival associated with treatment with seladelpar based on the GLOBE score.**

METHODS

o **110 patients** from an ongoing Phase 2 trial of seladelpar with an incomplete response or an intolerance to UDCA were evaluated.
o Patients received seladelpar at a dose of either 2 mg, 5 mg, or 10 mg per day (pooled).
o After 12 weeks of treatment, dose escalation was an option for those with 2 mg or 5 mg based on ALP response and safety.
o Changes in liver biochemistry were compared from baseline to 52 weeks (Paired t-test or Wilcoxon signed-rank test).
o The GLOBE score was calculated at baseline, 26 weeks, and 52 weeks to estimate transplant-free survival at 3, 5, 10, and 15 years for each subject and estimates were compared with Wilcoxon signed-rank test.
o GLOBE score changes were assessed based on baseline treatment assignment.

RESULTS

Table 1. Baseline characteristics

	Total cohort n = 110
Age, *years*	58.1 (9.0)
Female, n (%)	105 (95.5)
UDCA, n (%)	103 (93.6)
Rotterdam disease stage, n (%)	
Mild	92 (83.6)
Moderately advanced	18 (16.4)
Advanced	0 (0)
Baseline seladelpar dose, n (%)	
2 mg	11 (10.0)
5 mg	49 (44.5)
10 mg	50 (45.5)
GLOBE score[a]	0.44 (0.63)

Data presented as mean (SD) or n (%)
[a]*GLOBE score was available for 104 patients due to platelet count availability.*

Changes in biochemical parameters from GLOBE score

o There was a significant reduction in ALP and the GLOBE score
o Meanwhile, platelet count and albumin increased significantly from baseline to 52 weeks

Table 2. Improvement in biochemical parameters and GLOBE score after 52 weeks of treatment with seladelpar

	Baseline n = 110	Week 52[a] n = 44	P[b]
ALP, U/L	260 (211-382)	139 (110-199)	<0.001
Bilirubin, μmol/L	11.6 (9.6-14.2)	10.8 (8.3-14.3)	0.54
Albumin, g/L	41 (38-42)	42 (38-44)	0.01
Platelet count, ×10⁹/L	221 (175-297)	238 (183-321)	<0.001
GLOBE score[c]	0.42 (-0.09-0.89)	-0.02 (-0.53-0.63)	<0.001

Data presented as median (25th-75th percentile).
[a]*A total of 44 patients had a total follow-up of 52 weeks (weeks 51-55).*
[b]*Differences in ALP, bilirubin, albumin, and GLOBE score were assessed with the Wilcoxon signed-rank test, while differences in platelet count were assessed with a paired t-test.*
[c]*Globe score was available for 104 patients at baseline and 43 patients at week 52 due to platelet count availability.*

Changes in GLOBE score and predicted transplant-free survival

Figure 1. Improvement in GLOBE score over 52 weeks of treatment with seladelpar
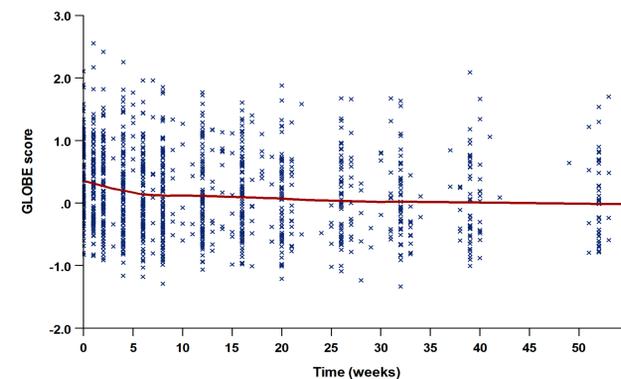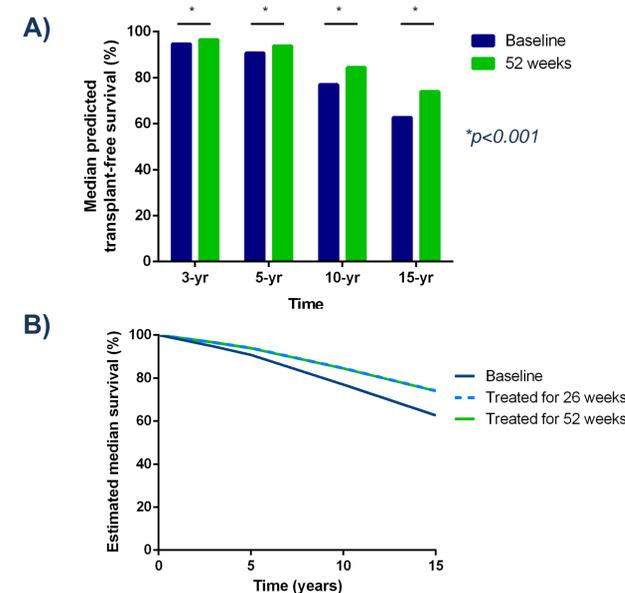

Figure 2. Improvement in predicted transplant-free survival at 3, 5, 10, and 15 years after 52 weeks of treatment with seladelpar


3-year survival = 0.9652^e^globe score; 5-year survival = 0.9385^e^globe score; 10-year survival = 0.8429^e^globe score; 15-year survival = 0.7361^e^globe score

CONCLUSIONS

o Treatment of patients with an incomplete response or an intolerance to UDCA for 52 weeks with seladelpar leads to an improvement in ALP, albumin, platelet count, and GLOBE score.

o The predicted survival at 3, 5, 10, and 15 years was significantly improved after treatment for 52 weeks.

o **Estimates of transplant-free survival assessed by the GLOBE score improve after 26 weeks of treatment and are maintained at 52 weeks.**

Figure 3. Improvement in GLOBE score stratified according to baseline treatment assignment
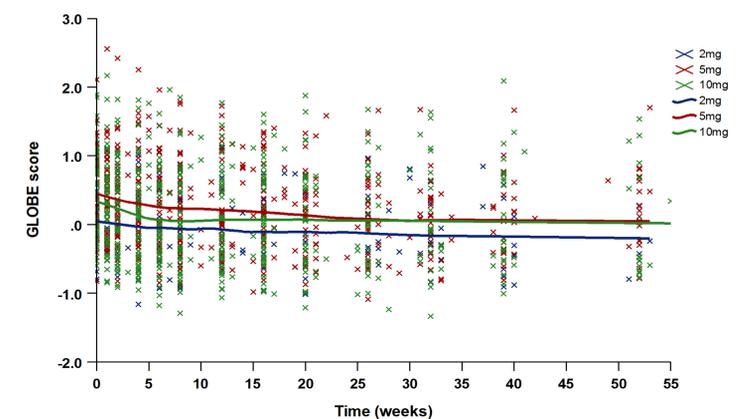
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