

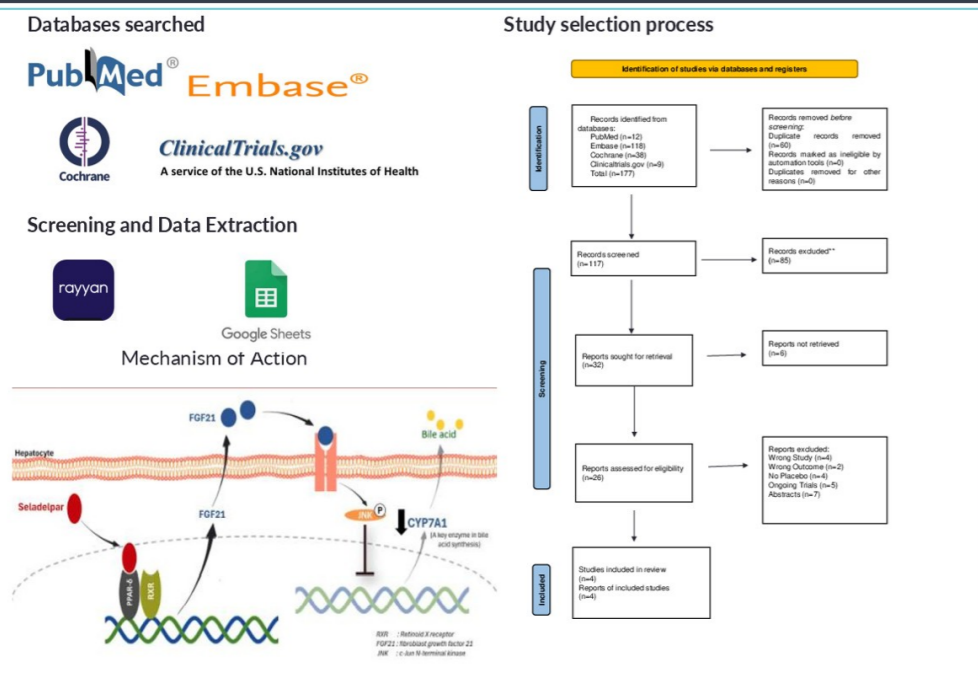


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PURPOSE / OBJECTIVES

- Primary Biliary Cholangitis (PBC) is a chronic autoimmune liver disease marked by progressive bile duct destruction, leading to cholestasis, fibrosis, and potentially cirrhosis or liver failure.
- Ursodeoxycholic acid (UDCA) is the standard therapy, but ~40% of patients respond inadequately.
- Seladelpar, a selective PPAR- δ agonist, shows promise by improving liver biochemistry (e.g., ALP levels) and offering anti-inflammatory, antifibrotic, and choleric benefits.

MATERIAL & METHODS



RESULTS

- A total of 428 patients from four studies were included; 94.6% were female, with a mean age of 48 years (range 18-75).
- Primary Outcome: Seladelpar significantly reduced serum ALP levels (Mean Difference [MD] -42.56; 95% CI: -50.83 to -34.29), indicating improvement in cholestasis.
- Secondary Outcomes: No significant changes were observed in total bilirubin levels (MD -0.08; 95% CI: -0.18 to 0.02) or in pruritus scores ≥ 4 (MD 0.46; 95% CI: -2.76 to 3.68).
- Safety Profile: Increased risk of abdominal pain (Risk Ratio [RR] 2.56; 95% CI: 1.10-6.00) and nausea (RR 1.51; 95% CI: 0.78-2.93) was noted. No significant differences were seen in joint pain, upper respiratory tract infections, overall adverse events, or serious adverse events.

SUMMARY / CONCLUSION

Seladelpar effectively reduces ALP levels in UDCA-refractory PBC, though its impact on bilirubin and pruritus remains unclear. Some adverse events like abdominal pain and headache decreased, but no major differences were seen in overall or serious adverse events. Further randomized trials with standardized dosing are needed to validate safety, efficacy, and effects on pruritus and bilirubin.

Salient Points

- Primary biliary cholangitis (PBC) is a chronic autoimmune liver disease, predominantly affecting middle-aged women, often presenting initially with fatigue and pruritus.
- Seladelpar, a selective PPAR- δ agonist, is studied as a treatment for PBC, especially in patients who do not respond to ursodeoxycholic acid (UDCA).
- A meta-analysis of 4 studies (n=428, 94.6% female, mean age 48) evaluates Seladelpar's efficacy and safety.
- Significant reduction in serum ALP levels observed with Seladelpar (MD -42.56, 95% CI -50.83 to -34.29), suggesting potential benefit in disease activity.
- No significant improvement in total bilirubin levels or pruritus scores, indicating limited symptomatic relief.
- Adverse effects: Increased risk of abdominal pain (RR 2.56) and nausea (RR 1.51); no significant differences in serious adverse events or other common side effects.
- Clinical takeaway: Seladelpar may offer biochemical improvement in PBC but lacks evidence for symptom relief and has potential tolerability issues.
- Further large-scale trials are essential to confirm long-term safety and to assess clinical outcomes beyond biochemical markers.

Efficacy Outcomes:

Outcome	Effect Size	95% CI	Interpretation
ALP Reduction	MD -42.56	-50.83 to -34.29	Significant Reduction
Total Bilirubin Level reduction	MD -0.08	-0.18 to 0.02	Not statistically significant
Pruritus Score ≥ 4	MD 0.46	-2.76 to 3.68	No meaningful change

Safety Outcomes:

Adverse Events	Relative Risk (RR)	95% CI	P-Value	Heterogeneity	Interpretation
Any Adverse Events	0.94	0.83-1.07	0.33	40%	No significant difference
Serious Adverse Events	0.91	0.39-2.14	0.83	0%	No significant difference
Abdominal Pain	2.56	1.10-6.00	0.03	0%	Increased risk
Pruritus	0.62	0.27-1.40	0.25	49%	No significant difference
Nausea	1.51	0.78-2.93	0.22	0%	No significant difference
Headache	3.84	1.34-11.00	0.01	0%	Increased
Arthralgia	0.93	0.46-1.87	0.83	0%	No significant difference
Asthenia	1.46	0.15-14.57	0.75	56%	No significant difference
Dizziness	0.28	0.06-1.24	0.09	0%	No significant difference
Fatigue	0.55	0.26-1.18	0.13	10%	No significant difference
URTI (Upper Resp. Tract)	0.87	0.11-6.64	0.89	75%	No significant difference
UTI	2.18	0.25-19.22	0.48	61%	No significant difference