



The evolving landscape of PBC: new therapies and future directions

An expert discussion with **Kris Kowdley & David Jones**



Current therapeutic landscape for PBC:



- Patients should receive UDCA as first-line therapy.
- It is important to assess the response to UDCA, when patients do not respond, starting second-line therapy should be considered.
- OCA is currently the only licensed therapy in the second-line setting. Elafibranor and seladelpar have recently completed phase III trials and their approvals are expected in the near future.
- Importance of identifying the right therapy for individual patients to improve outcomes.

Recent studies and implications in real world:



- ELATIVE and RESPONSE trials, assessing respectively elafibranor and seladelpar, have demonstrated significant improvements in ALP and bilirubin levels.
- Important aspects of these trials:
 - › Focus on achieving normalization of ALP levels
 - › Beneficial effects on symptoms (like itch and fatigue)
 - › Favorable safety profile

Challenges in adopting new medications:



- Primary challenges are achieving regulatory approval and demonstrating effectiveness in terms of survival.
- Future complexity in treatment selection and guidelines for clinicians due to the availability of multiple therapies.
- Need for guidance to facilitate appropriate therapy individualization.

Upcoming trials and emerging therapies:



- Novel trials focusing on symptom control, particularly itch and fatigue will lead to additional tools for patient management.
- Exploration of combination therapies (PPAR agonists and FXR agonists, which appear to be synergistic) to enhance treatment efficacy.
- Future direction towards reevaluating primary therapy in higher risk patients to achieve better disease control from early stages.



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ALP = alkaline phosphatase; OCA = obeticholic acid; UDCA = ursodeoxycholic acid