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Livdelzi (Seladelpar) A Recent Approved Drug Used for the Treatment of Primary Biliary Cholangitis

Mr. Aniket Vinod Kulkarni, Prof Harale M. V., Dr. Bhosale M. P
Dharmaraj Shaikshanik Pratishthan College of Pharmacy, Walki, Ahilyanagar

Abstract: *Seladelpar (Livdelzi) is a recently approved drug for the treatment of primary biliary cholangitis (PBC), a chronic autoimmune liver disease.primary biliary cholangitis (PBC), a progressive autoimmune liver disease characterized by the destruction of bile ducts, leading to liver damage and cirrhosis. Its unique mechanism of action and favorable safety profile make it a valuable addition to the management of this chronic liver disease. These review provides overview of progressive autoimmune liver disease it's treatment aspects clinical manifestations and complete activity of recently approved drug selandelpar (Livdelzi).*

Keywords: *Seladelpar (Livdelzi)*

I. INTRODUCTION

Primary Biliary Cholangitis (PBC) is a chronic autoimmune cholestatic liver disease.
Characterized by progressive destruction of intrahepatic bile ducts.
Leads to cholestasis, fibrosis, cirrhosis, and liver failure if untreated.
Livdelzi (Seladelpar) is a recently approved drug offering a new therapeutic option.
The pathophysiology of Primary Biliary Cholangitis (PBC) involves a complex interplay of immune-mediated mechanisms, leading to progressive destruction of the intrahepatic bile ducts. Here's a simplified overview:
1. Autoimmune response:
- Abnormal immune response targets the bile ducts
- Activated T-cells and autoantibodies (e.g., AMA) attack the bile ducts2. Bile duct damage:
- Inflammation and apoptosis (cell death) of cholangiocytes (bile ductcells)
- Progressive destruction of small to medium-sized bile ducts3. Cholestasis:
- Reduced bile flow and accumulation of toxic bile acids- Liver damage and inflammation
4. Fibrosis:
- Activation of hepatic stellate cells, leading to collagen deposition
- Progressive scarring and cirrhosis
5. Immune dysregulation:
- Imbalance of regulatory T-cells and effector T-cells- Abnormal cytokine production (e.g., increased IL-12, IL-17)
6. Environmental and genetic factors:
- Triggers (e.g., infections, xenobiotics) may initiate the autoimmune response
- Genetic predisposition (e.g., HLA-DR8, HLA-DQB1) This complex interplay leads to the characteristic features of PBC:- Chronic cholestasis
- Bile duct destruction
- Liver inflammation and fibrosis- Cirrhosis and liver failure (if left untreated)
Symptoms:-
The symptoms of Primary Biliary Cholangitis (PBC) can vary in severity and may progress gradually over time. Here are the common symptoms:

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-Early symptoms:
1. Fatigue (most common)
2. Pruritus (itching, often worse at night)3. Abdominal pain or discomfort
4. Nausea and vomiting
5. Diarrhea or constipation

-As the disease progresses:
1. Jaundice (yellowing of skin and eyes)2. Dark urine and pale stools
3. Weight loss

4. Loss of appetite
5. Swelling in the legs and feet (edema)
-Advanced symptoms:
1. Cirrhosis and liver failure
2. Portal hypertension (high blood pressure in the liver)
3. Varices (enlarged veins) in the esophagus or stomach
4. Ascites (fluid accumulation in the abdomen)
5. Hepatic encephalopathy (brain dysfunction due to liver disease)

-Other symptoms:
1. Osteoporosis (bone loss)
2. Vitamin deficiencies (A, D, E, K)3. Skin hyperpigmentation
4. Hair loss

5. Memory problems or cognitive impairment
The diagnosis of Primary Biliary Cholangitis (PBC):-
Involves a combination of clinical evaluation, laboratory tests, and imaging studies. Here's a step-by-step approach:
1. Clinical evaluation:
- Medical history: fatigue, pruritus, jaundice, and abdominal pain- Physical examination: jaundice, hepatomegaly, and splenomegaly
2. Laboratory tests:
- Liver function tests (LFTs): elevated alkaline phosphatase, gammaglutamyl transferase, and bilirubin - Autoantibodies:
- Antimitochondrial antibodies (AMA): positive in 90-95% of PBCpatients
- Antinuclear antibodies (ANA): positive in 20-50%
- *Immunoglobulins*: elevated IgM levels
3. Imaging studies:
- Ultrasound: evaluates liver size, shape, and texture
- Magnetic Resonance Cholangiopancreatography (MRCP)*: assesses bile ducts and liver parenchyma 4. Liver biopsy:
- Histological examination: characteristic features include
chronicnonsuppurative cholangitis, bile duct damage, and fibrosis 5. Diagnostic criteria: - 2 of 3 criteria:
1. AMA positivity
2. Cholestatic LFTs
3. Histological evidence of PBC
Mechanism of action:-
Seladelpar, a PPARδ agonist, exerts its therapeutic effects in primary biliary cholangitis (PBC) through several mechanisms:
● Anti-inflammatory effects:
Reduces inflammation in the liver by inhibiting pro-inflammatory cytokines and increasing anti-inflammatory cytokines.

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● Antifibrotic effects:
Decreases liver fibrosis by reducing collagen deposition and promoting collagen breakdown.
● Immunomodulation:
Modulates the immune response, reducing autoantibody production and T- cell activation.
● Bile acid metabolism:
Regulates bile acid synthesis, reducing toxic bile acid accumulation.
● Cellular protection:
Protects cholangiocytes (bile duct cells) from apoptosis (cell death) and promotes their survival.
● PPARδ activation:
Activates PPARδ receptors, leading to increased expression of genes involved in lipid metabolism, inflammation, and fibrosis.
Pharmacokinetics:-
The pharmacokinetics of seladelpar, a PPARδ agonist, are as follows:
Absorption:-
- Oral bioavailability: 73%
- Peak plasma concentration (Cmax): 1-2 hours after administration Distribution:-
- Volume of distribution (Vd): 245 L- Protein binding: 99% (primarily to albumin)
Metabolism:-
- Metabolized by CYP2C8 and CYP3A4 enzymes- Major metabolites: glucuronide and sulfate conjugates
Elimination:-
- Half-life (t1/2): 20-25 hours
- Clearance (CL): 1.3 L/h
- Excretion: primarily in feces (90%), with minimal renal excretion (10%) Steady-state:-
- Reached within 7-10 days of once-daily administration- Accumulation ratio: 1.3-1.5
Food effects:-
- Food does not significantly affect seladelpar absorptionAdverse effect of selandelpar:-THeadache — one of the most common complaints.
Abdominal pain (stomach pain) — very common. Nausea — common.
Abdominal distension (bloating) — common. Dizziness — common.
Less Common Adverse Effects (Infrequent but reported)
Dyspepsia (indigestion)
Rash or skin reactions (including pruritus related or unrelated to PBC) Cough
Hair loss (alopecia)
Anemia (low red blood cell count)
Serum creatinine elevation (lab measure of kidney function)
Contraindications:-
1. Hypersensitivity to seladelpar or its components
2. Severe hepatic impairment (Child-Pugh Class C)
Use in special populations: Tab-1

Sr. no	Special cases	Description
1	Pregnancy	Not recommended due to unknown effects on the fetus. No adequate and well-controlled studies in pregnant women. Use only if potential benefit justifies potential risk.
2	Lactation	Unknown whether seladelpar is excreted in human milk. Caution advised; consider interrupting breastfeeding or discontinuing seladelpar.
3	Pediatric patients	No significant differences in safety or efficacy observed . Dose adjustment not necessary based on age alone.

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4	Geriatric patients	No significant differences in safety or efficacy observed. Dose adjustment not necessary based on age alone.
5	Hepatic impairment	Severe hepatic impairment (Child-Pugh Class C): contraindicated. Moderate hepatic impairment (Child-Pugh Class B): use with caution. Mild hepatic impairment (Child-Pugh Class A): no dose adjustment needed.
6	Renal impairment	No significant differences in pharmacokinetics or safety observed. Dose adjustment not necessary based on renal function alone.

Warnings and Precautions

Fractures: Fractures occurred in 4% of LIVDELZI-treated patients compared to no placebo-treated patients. Consider the risk of fracture in the care of patients treated with LIVDELZI and monitor bone health according to current standards of care.

Liver Test Abnormalities: LIVDELZI has been associated with dose-related increases in serum transaminase (AST and ALT) levels > 3 x ULN in patients receiving 50 mg and 200 mg once daily (5x and 20x higher than the recommended dosage of 10 mg once daily). Perform baseline clinical and laboratory testing when starting

LIVDELZI and monitor thereafter according to routine patient management. Interrupt treatment if the liver tests (ALT, AST, total bilirubin, and/or ALP) worsen, or if the patient develops signs and symptoms of clinical hepatitis (eg, jaundice, right upper quadrant pain, eosinophilia). Consider permanent discontinuation if liver tests worsen after restarting LIVDELZI.

Biliary Obstruction: Avoid use of LIVDELZI in patients with complete biliary obstruction. If biliary obstruction is suspected, interrupt LIVDELZI and treat as clinically indicated.

Drug Interactions

● OAT3 Inhibitors and Strong CYP2C9 Inhibitors: Avoid coadministration with LIVDELZI due to increased LIVDELZI exposure.

● Rifampin: Monitor biochemical response (e.g., ALP and bilirubin) when patients initiate rifampin during LIVDELZI treatment. Coadministration may result in delayed or suboptimal biochemical response of LIVDELZI.

● Dual Moderate CYP2C9 and Moderate-to-Strong CYP3A4 Inhibitors and BCRP Inhibitors (eg, cyclosporine): Monitor closely for adverse effects.

Concomitant administration with LIVDELZI may increase LIVDELZI exposure.

● CYP2C9 Poor Metabolizers Using Moderate-to-Strong CYP3A4 Inhibitors: Monitor more frequently for adverse reactions as concomitant use of a moderate-to-strong CYP3A4 inhibitor in patients who are

● CYP2C9 poor metabolizers may increase LIVDELZI exposure and risk of LIVDELZI adverse reactions.

● Bile Acid Sequestrants: Administer LIVDELZI at least 4 hours before or 4 hours after taking a bile acid sequestrant, or at as great an interval as possible.

II. CONCLUSION

In conclusion, seladelpar is a novel PPARδ agonist approved for the treatment of primary biliary cholangitis (PBC). It has shown efficacy in reducing liver enzymes, improving liver function, and slowing disease progression. Seladelpar's pharmacokinetics and pharmacodynamics demonstrate a favorable profile, with a good safety and tolerability record. However, potential adverse effects, such as fatigue, headache, and increased liver enzymes, should be monitored. Special populations, including pregnant or lactating women, pediatric patients, and those with severe hepatic impairment, require cautious use or avoidance. Overall, seladelpar offers a new treatment option for PBC patients, and its benefits and risks should be carefully considered by healthcare providers to ensure optimal patient outcomes.

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REFERENCES

[1]. Webb GJ, Siminovitch KA, Hirschfield GM. The immunogenetics of primary biliary cirrhosis: a comprehensive review. J Autoimmun. 2015;64:42–52. [PMC free article] [PubMed] [Google Scholar]
[2]. Trivedi PJ, Hirschfield GM. Recent advances in clinical practice: epidemiology of autoimmune liver diseases. Gut. 2021;70:1989–2003. [PubMed] [Google Scholar]
[3]. Lleo A, Wang GQ, Gershwin ME, Hirschfield GM. Primary biliary cholangitis. Lancet. 2020;396:1915–26. [PubMed] [Google Scholar]
[4]. Gulamhusein AF, Hansen BE. Beyond biochemical responses, use of histologic staging to predict outcomes of patients with primary biliary cholangitis. Clin Gastroenterol Hepatol. 2020;18:1033–5. [PubMed] [Google Scholar]
[5]. Lindor KD, Bowlus CL, Boyer J, Levy C, Mayo M. Primary biliary cholangitis: 2018 practice guidance from the American Association for the Study of Liver Diseases. Hepatology. 2019;69:394–419. [PubMed] [Google Scholar]
[6]. Hirschfield GM, Beuers U, Corpechot C, Invernizzi P, Jones D, Marzioni M, et al.. European Association for the Study of the Liver. EASL clinical practice guidelines: the diagnosis and management of patients with primary biliary cholangitis. J Hepatol. 2017;67:145–72. [PubMed] [Google Scholar]
[7]. Hirschfield GM, Dyson JK, Alexander GJM, Chapman MH, Collier J, Hübscher S, et al.. The British Society of Gastroenterology/UK-PBC primary biliary cholangitis treatment and management guidelines. Gut. 2018;67:1568–94. [PMC free article] [PubMed] [Google Scholar]
[8]. Nevens F. PBC-transplantation and disease recurrence. Best Pract ResClin Gastroenterol. 2018;34-35:107–111. [PubMed] [Google Scholar]
[9]. Kumagi T, Guindi M, Fischer SE, Arenovich T, Abdalian R, Coltescu C, et al.. Baseline ductopenia and treatment response predict long-term histological progression in primary biliary cirrhosis. Am J Gastroenterol. 2010;105:2186–94. [PubMed] [Google Scholar]
[10]. Carbone M, Sharp SJ, Flack S, Paximadas D, Spiess K, Adgey C, et al.. The UK- PBC risk scores: derivation and validation of a scoring system for long-term prediction of end-stage liver disease in primary biliary cholangitis. Hepatology. 2016;63:930–50. [PMC free article]
[11]. Floreani A, Franceschet I, Cazzagon N, Spinazze A, Buja A, Furlan P, et al. Extrahepatic autoimmune conditions associated with primary biliary cirrhosis. Clin Rev Allergy Immunol (2015) 48:192–7. doi: 10.1007/s12016-014-8427-xPubMed Abstract | CrossRef Full Text | Google Scholar
[12]. Raszeja-Wyszomirska J, Miazgowski T. Osteoporosis in primary biliary cirrhosis of the liver. Prz Gastroenterol (2014) 9:82–7. doi: 10.5114/pg. 2014.42502 PubMed Abstract | CrossRef Full Text | Google Scholar
[13]. Sorokin A, Brown JL, Thompson. Primary biliary cirrhosis PD. Hyperlipidemia, and atherosclerotic risk: a systematic review. Atherosclerosis (2007) 194:293–9. doi: 10.1016/j.atherosclerosis. 2006.11.036 PubMed Abstract | CrossRef Full Text | Google Scholar
[14]. Ninomiya M, Kondo Y, Funayama R, Nagashima T, Kogure T, Kakazu E, et al. Distinct microRNAs expression profile in primary biliary cirrhosis and evaluation of miR 505-3p and miR197-3p as novel biomarkers. PloS One (2013) 8:e66086. doi: 10.1371/journal.pone.0066086 PubMed Abstract | CrossRef Full Text | Google Scholar
[15]. Deng C, Hu C, Wang L, Zhang S, Li P, Wu Z, et al. Serological comparative proteomics analysis of mitochondrial autoantibody-negative and - positive primary biliary cirrhosis. Electrophoresis (2015) 36:1588–95. doi: 10.1002/elps.201400342