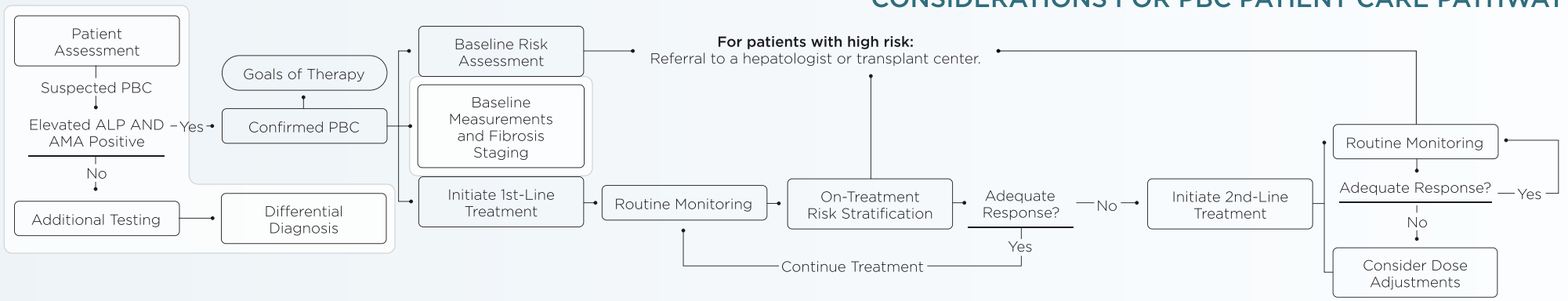
CONSIDERATIONS FOR PBC PATIENT CARE PATHWAY



OVERVIEW

- This document is for educational purposes only and provides a non-exhaustive description of potential care options in PBC.
- The content of this document is based on information from approved product prescribing information, published guidelines, and peer-reviewed literature.
- HCPs should exercise their independent clinical judgment when managing patients with PBC.
- This educational tool does not promote the use of any particular treatment option.
- If requested, this material is available through a Medical Information Request Form (MIRF).

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Liver biopsies are rarely needed to diagnose PBC but may be recommended in AMA-negative patients with the absence of PBC-specific autoantibodies, or to rule out concomitant AIH, NASH or other liver diseases.[1-3]

Evidence of portal hypertension include ascites, gastroesophageal varices or persistent thrombocytopenia.[9]

Noninvasive imaging tests (TE, MRE) can identify patients with advanced fibrosis and at risk of hepatic decompensation.[10]

LSM by VCTE, in combination with established biochemical criteria of therapeutic response or prognostic score, improves outcome prediction in PBC.[11]

This educational resource was developed and is provided by Intercept Pharmaceuticals, Inc.
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PATIENT ASSESSMENT & BASELINE MEASUREMENTS

- ☐ History, physical examination[1-3]

Patient with suspected PBC:

- ☐ Chronic cholestasis with abnormalities in serum biochemistry (elevated ALP/GGT/AST/ALT)[1-3]
- ☐ Symptoms including fatigue, pruritus, abdominal pain, sicca, arthralgias (joint stiffness), excoriations, hyperpigmentation[1-4]
- ☐ Diagnosis of autoimmune conditions (e.g., Sjögren syndrome, CREST, thyroid disease, Celiac disease, scleroderma, and Raynaud disease)[1-4]

Laboratory testing for consideration

The following testing is not all required routinely (or in all patients) for diagnosing PBC, but may be used in AMA-negative cases and at initial assessment to rule out other causes for symptoms and/or achieve baseline measurements.

- ☐ Complete Blood Count (CBC)*
  - ☐ Platelets[1-4]
  - ☐ Hemoglobin (Hgb)[1-3]
- ☐ Comprehensive Metabolic Panel (CMP)* → liver function/enzymes
  - ☐ Albumin[1-3]
  - ☐ Total bilirubin[2-4]
  - ☐ Direct bilirubin[2-4]
  - ☐ Liver enzymes (**ALP,** ALT, AST), GGT[1-4]
- ☐ Antibody test
  - ☐ **AMA**[1-4]
  - ☐ If AMA-negative → ANA[4] (anti-sp100, anti-gp210)[1-4]
- ☐ Immunoglobulin test
  - ☐ IgM[1-4] ☐ IgG[1-3]
- ☐ Blood clotting tests: INR[2,3]
- ☐ Lipid panel[1-3]:
  - ☐ LDL ☐ Cholesterol
  - ☐ HDL ☐ Triglycerides
- ☐ Vitamin A, D[1-3]
- ☐ Thyroid-stimulating hormone (TSH)[1-3]
- ☐ Bone mineral density (BMD)[1-4]
- ☐ Abdominal ultrasound[2-4]
  - ☐ Exclude mechanical bile duct obstruction, mass lesions, and abnormalities of the gallbladder[3]
  - ☐ Spleen length > 12 cm indicative of splenomegaly[36]
  - ☐ Portal vein diameter > 12 mm via doppler ultrasound is indicative of portal hypertension[37]
- ☐ Assess fibrosis/liver stiffness[3-5]
  - ☐ Transient elastography
  - ☐ Serology: FIB-4, APRI
- ☐ Upper endoscopy (stage for varices; for patients with cirrhosis; consider in patients with advanced fibrosis based on clinical judgment)[1,3]
- ☐ Liver biopsy[1-3]
- ☐ Screen for hepatitis A, B and C[38-42]
  - ☐ HAV: total antibody[45]
  - ☐ HBV: test all adults with the triple panel (HBsAg, anti-HBc total, and anti-HBs)[40,43]
    - ☐ Offer to vaccinate all appropriate adults for HBV when HBV triple panel negative, if appropriate[40]
    - ☐ If HB surface antigen positive, evaluate HBV DNA quantity and hepatitis delta total antibody[43]
    - ☐ Treat individuals who are HBV DNA positive, if appropriate[43]
    - ☐ Stage liver disease and start surveillance for liver cancer and other forms of liver disease, if appropriate[43]
  - ☐ HCV: FDA-approved anti-HCV test[41]
- ☐ HCC surveillance[1-3]: AFP, DCP, AFP-L3% levels[6], GALAD Score[7]
- ☐ Assess for Celiac Disease (e.g., anti-trans-glutaminase assay, biopsy of small intestine)[8]

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DIFFERENTIAL DIAGNOSIS

The diagnosis of PBC should be suspected in **adult patients with chronic liver test abnormalities, after exclusion of other causes of liver disease,**[1,3] including, but not limited to:

- ☐ Cholestatic drug reaction[1,3]
- ☐ Biliary obstruction[1-3]
- ☐ Sarcoidosis[1,3]
- ☐ Autoimmune Hepatitis (AIH)[1-3]
- ☐ Primary sclerosing cholangitis (PSC)[1-3]
- ☐ Progressive familial intrahepatic cholestasis[3]
- ☐ Nonalcoholic steatohepatitis (NASH)[1-3]
- ☐ Benign recurrent intrahepatic cholestasis[3]
- ☐ Infiltrative liver diseases[3]
- ☐ IgG4-associated cholangitis[3]

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*Key considerations for PBC diagnosis and management, not comprehensive of all measures included in laboratory testing.

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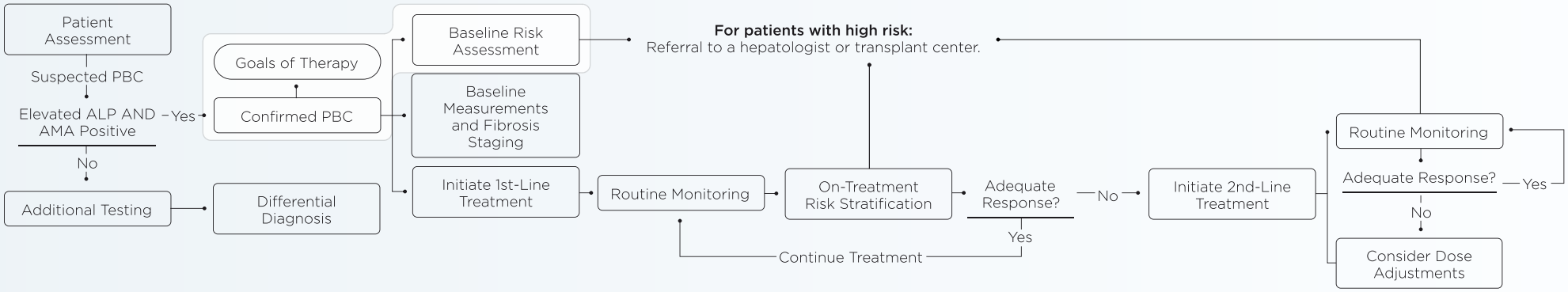

DIAGNOSIS OF PBC

The diagnosis of PBC should be suspected in adult patients with chronic cholestasis after exclusion of other causes of liver disease.[1,3] While the available guidelines differ slightly in recommendations for patients with suspected PBC who are AMA-negative, **the guidelines listed below agree that a PBC diagnosis can be established in patients with[1,3]:**

☐ AMA positive* AND elevated ALP with exclusion of other causes of liver disease

*AMA positive immunofluorescent assay titer of >1:40 or EIA > 25 units.[2,3]

Note: AMA positivity alone is not sufficient to make the diagnosis of PBC.[1-3] Guidelines recommend following up with these patients every 6-12 months with repeat liver enzyme panels.[2]

Additional scenarios and considerations for diagnosing PBC based on available guidelines

☐ AASLD GUIDELINES[1]

The diagnosis of PBC can be established when two of the following three criteria are met:

- Biochemical evidence of cholestasis based on elevated ALP
- Presence of AMA, or other PBC-specific auto-antibodies, including sp100 or gp210, if AMA is negative
- Histologic evidence of nonsuppurative destructive cholangitis and destruction of interlobular bile ducts

☐ ACG/CLDF GUIDELINES[2]

The following scenarios support a PBC diagnosis:

- Scenario 1: Chronic elevation of ALP; positive AMA in the absence of other liver and systemic diseases
- Scenario 2: Chronic elevation of ALP; negative AMA and antinuclear antibodies (ANA) tests but a liver biopsy that shows destructive cholangitis and destruction of interlobular bile ducts
- Scenario 3: Chronic elevation of ALP; negative AMA but positive PBC-specific ANA tests (sp100, gp210; these tests not widely available in the US)

☐ EASL GUIDELINES[3]

Diagnosis of PBC can be based on:

- Elevated ALP and the presence of AMA with no likelihood of systemic disease
- AMA-negative with cholestasis and specific ANA immunofluorescence (nuclear dots or perinuclear rims) or ELISA results (sp100, gp210)

Confirmed PBC

Stage disease

Baseline Measurements | Initiate 1st-Line Treatment | Baseline Risk Assessment

GOALS OF PBC THERAPY

The treatment goals of PBC are aimed to **prevent progression to advanced liver disease and to alleviate symptoms.[1-4,12]**

- ☐ Slow disease progression[1-4]
- ☐ Prevent progression to cirrhosis or complications in patients who already have cirrhosis (decompensation, HCC)[1-4]
- ☐ Symptom management[1-4]
- ☐ Normalization of ALP[2,4,12]
- ☐ Stabilization/reduction of bilirubin[4,12]
- ☐ Decrease hospitalization due to liver related complications
- ☐ Increase transplant-free survival[1,2]

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BASELINE RISK ASSESSMENT

Pre-treatment Risk Assessment

Assessing baseline risk ensures patients receive timely follow-up and allows for a personalized treatment approach.

LOW RISK

- ☐ No/early fibrosis[4]
- ☐ Mild ALP (<1.5x ULN)[2,4] **AND**
- ☐ Normal bilirubin[4] **AND**
- ☐ Normal albumin[4]

EMERGING DATA

- ☐ Total bilirubin ≤ 0.6x ULN[12]

INTERMEDIATE-HIGH RISK

- ☐ Age at diagnosis < 45[4]
- ☐ ALP > 1.5x ULN[4]
- ☐ Abnormal bilirubin[4]
- ☐ Low albumin[4]
- ☐ Advanced baseline fibrosis (F3-F4)[4,13]
- ☐ Early cirrhosis (Child-Pugh A)[4]

CONSIDER REFERRAL TO A HEPATOLOGIST OR TRANSPLANT CENTER FOR FURTHER ASSESSMENT

- ☐ Decompensated cirrhosis (Child-Pugh B or C)[4] **OR**
- ☐ Bilirubin > 2x ULN[4] **OR**
- ☐ Severe uncontrolled pruritus[4]

Emerging data from peer-reviewed, primary research literature; not incorporated in guidelines

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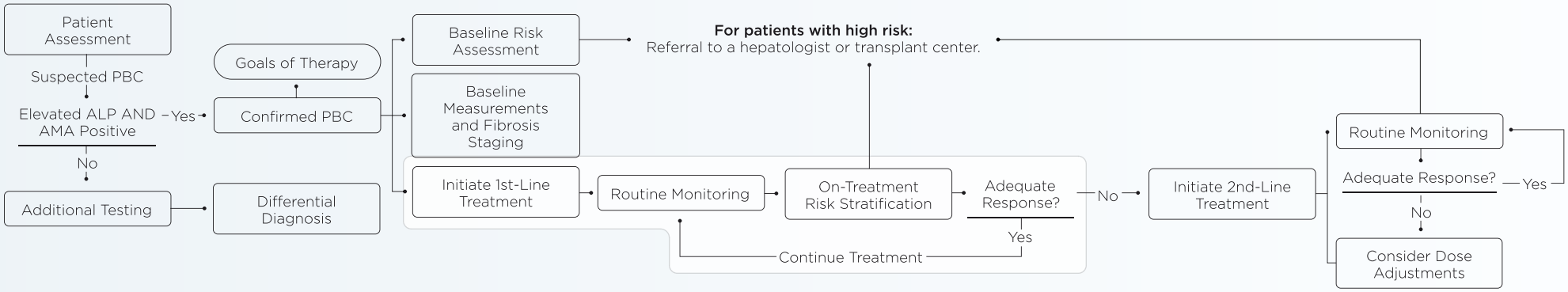

INITIATION OF FIRST-LINE TREATMENT CONSIDERATIONS

Initiate 1st-line treatment

- ☐ Ursodeoxycholic acid (UDCA) 13-15 mg/kg/day[1-3,14]
  - ☐ 2-4 divided doses with food[14]

Per discretion of provider:

- ☐ 2 divided doses[1]
- ☐ Once daily (may improve compliance)[1]

Routinely monitor for biochemical response, tolerability, and progression of PBC[14]

- ☐ Every month for 3 months after initiating therapy and every 6 months thereafter[14]

Per discretion of provider:

- ☐ 6 months after initiating therapy[2,3]
- ☐ 3-6 months indefinitely[1]
- ☐ 1 year after initiating therapy[1]

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Binary criteria and definition of response[1,2]

TORONTO
ALP 1.67x ULN

PARIS II
ALP 1.5x ULN
AST 1.5x ULN
Total bilirubin 1 mg/dL

RISK SCORING SYSTEMS[1-3]

- ☐ GLOBE Score
- ☐ UK-PBC Score
- ☐ Mayo PBC Score

Response achieved

On-Treatment Risk Stratification

No response → Initiate 2nd-Line treatment

Ongoing Routine Monitoring Assessments

Routine follow-up assessments should look for[1-3,14]

- ☐ Abdominal discomfort[14]
- ☐ Abdominal pain[14]
- ☐ Hair loss[1,3,14]
- ☐ Diarrhea[1-3,14]
- ☐ Nausea[14]
- ☐ Pruritus[14]
- ☐ Rash[14]
- ☐ Increased GGT, ALP, AST, ALT, bilirubin[14]
- ☐ Complete biliary obstruction[14]

Per discretion of provider:

- ☐ Weight gain[1,3]
- ☐ Progression of liver stiffness/fibrosis[1]

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Discontinuing treatment should be considered in patients with increased GGT, ALP, AST, ALT, bilirubin.[14]

Tolerating treatment?

Yes → Continue Treatment

No → Discontinue UDCA and evaluate for 2nd-Line

Fibrosis stage (as assessed by VCTE or MRE) can guide the decision of whether response to UDCA and subsequent second-line treatment need should be assessed at 6 months or 12 months.[10]

Contraindicated in patients with[14]:

- complete biliary obstruction
- known hypersensitivity or intolerance to ursodiol or any components of the formulation

Patients with the following should receive appropriate specific treatment[14]:

- Variceal bleeding
- Hepatic encephalopathy
- Ascites
- In need of an urgent liver transplant

To report suspected adverse reactions,
contact Intercept Pharmaceuticals, Inc. or the FDA:

1-844-782-ICPT

fda.gov/medwatch

1-800-FDA-1088

The content of this page is based on information from UDCA PI[14] and published guidelines.[1-3]

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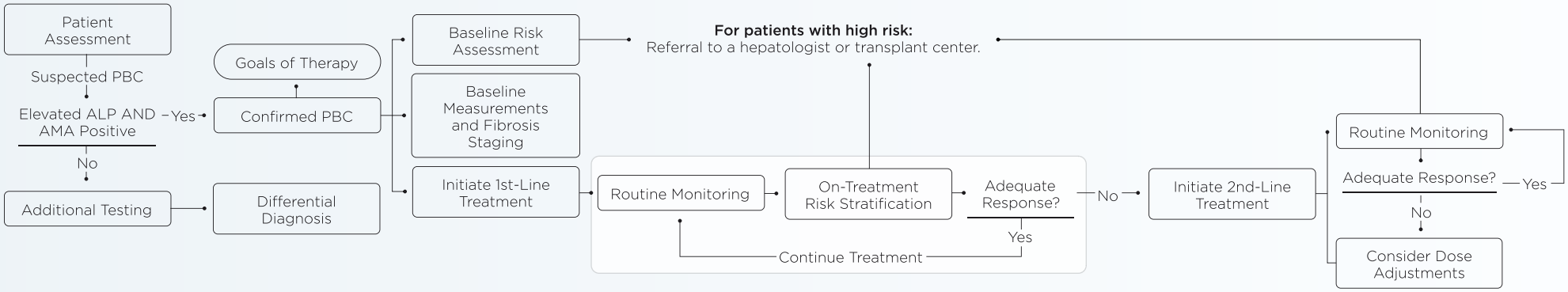

ROUTINE MONITORING ASSESSMENTS FOR FIRST-LINE TREATMENT

Routine follow-up assessments should look for[1-3,14]

- ☐ Weight gain[1,3]
- ☐ Hair loss[1,3,14]
- ☐ Pruritus[14]
- ☐ Ascites[14]
- ☐ Jaundice[14]
- ☐ Variceal bleeding[14]
- ☐ Increased GGT, ALP, AST, ALT, bilirubin[14]
- ☐ Progression of liver stiffness/fibrosis[1]
- ☐ Cirrhosis[1]
- ☐ Portal hypertension[2]
- ☐ Hepatic encephalopathy[14]
- ☐ HCC[1,3]
- ☐ Bone disease/osteoporosis[1,2]
- ☐ Sicca syndrome[2]
- ☐ Dyslipidemia[2]

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All chronic liver disease patients[2]

- ☐ Immunizations against Hepatitis A and B
- ☐ Optimize body weight
- ☐ Minimize alcohol consumption
  - ☐ Counsel on alcohol abstinence[1]

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Laboratory testing for consideration when conducting ongoing monitoring and assessments[1-6]

- ☐ Complete Blood Count (CBC)*
  - ☐ Platelets[1-4]
  - ☐ Hemoglobin (Hgb)[1-3]
- ☐ Comprehensive Metabolic Panel (CMP)* → liver function/enzymes
  - ☐ Albumin[1-3]
  - ☐ Total bilirubin[2-4]
  - ☐ Direct bilirubin[2-4]
  - ☐ Liver enzymes (**ALP,** ALT, AST), GGT[1-4]
- ☐ Lipid panel[1-3]:
  - ☐ LDL
  - ☐ HDL
  - ☐ Cholesterol
  - ☐ Triglycerides
- ☐ Blood clotting tests: INR[2,3]
- ☐ Thyroid-stimulating hormone (TSH)[1-3]
- ☐ Vitamin A, D[1-3]
- ☐ Bone mineral density (BMD) (every 2 years)[1-4]
- ☐ Abdominal ultrasound: monitor for ascites[2-4]
- ☐ Assess fibrosis/liver stiffness[3-5]
  - ☐ Transient elastography
  - ☐ Serology: FIB-4, APRI
- ☐ Cholangiography with MRCP[2]
- ☐ Upper endoscopy (stage for varices; for patients with cirrhosis)[1,3]
- ☐ Liver biopsy[1-3]
- ☐ Screen for HCC[1]
- ☐ HCC surveillance: AFP, DCP, AFP-L3% levels (surveillance every 6 months with ultrasound and AFP in patients with advanced fibrosis and men with PBC), GALAD score[1-4,6,7]

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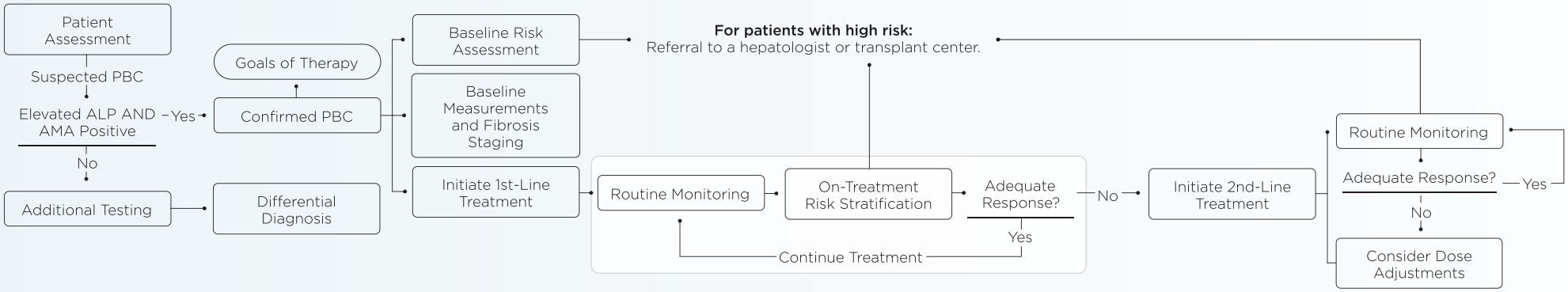

RESPONSE AND ON-TREATMENT RISK STRATIFICATION

Despite treatment with UDCA, PBC can remain a progressive disease and has a risk of liver-related complications and death. The risk of developing end-stage complications and potential need for additional treatments should be assessed in all patients.[3]

Assess risk of progression based on response to treatment[1,2,4,10,13]

LOW RISK[4]/ADEQUATE RESPONSE TO UDCA

- ☐ ALP (<1.5x ULN)[4] **AND**
- ☐ Normal bilirubin[4] **AND**
- ☐ No/early fibrosis[4]

EMERGING DATA

- ☐ Total bilirubin ≤ 0.6x ULN[12] **OR**
- ☐ Total bilirubin > 0.6x-1x ULN **AND** ALP normalization (< 1x ULN)[12]

Continue 1st-Line treatment and assess response every 3-6 months[1]

INTERMEDIATE-HIGH RISK[4]/INTOLERANCE OR INADEQUATE RESPONSE TO UDCA[1] (based on established criteria)

- ☐ According to available predictive models (UK-PBC, GLOBE PBC)[2]
- ☐ Increasing fibrosis[2,4]/cirrhosis[1,2,4]

OR ALP:

- ☐ ALP > 1.5x ULN 12 months after initiating UDCA[3,4]
- ☐ Persistently elevated serum ALP after 12 months of therapy with UDCA[2]
- ☐ ALP remains > 1.67x ULN 24 months after initiating UDCA[3]

OR BILIRUBIN:

- ☐ Rising bilirubin/levels > ULN[4]
- ☐ Lack of normalization of bilirubin after 12 months of therapy with UDCA[1,2]

OR ALBUMIN:

- ☐ Albumin < LLN[4]

EMERGING DATA

- ☐ ALP > 1.0x ULN at 12 months[12]
- ☐ Total bilirubin > 0.6x-1x ULN at 12 months[12]
- ☐ GGT ≥ 3.2x ULN at 12 months[15]
- ☐ ALP > 1.9x ULN 6 months after initiating UDCA[32]

CONSIDER REFERRAL FOR FURTHER ASSESSMENT

- ☐ Decompensated cirrhosis (Child-Pugh B or C, ascites, variceal bleeding)[4] **OR**
- ☐ Compensated cirrhosis and portal hypertension[4] **OR**
- ☐ Bilirubin > 2x ULN[4] **OR**
- ☐ Severe pruritus[4]
- ☐ AST or ALT > 5x ULN[4]

Evaluate risk-benefit of 2nd-Line treatment

Yes → Initiate 2nd-Line treatment

No → Referral to a hepatologist or transplant center further assessment

Emerging data from peer-reviewed, primary research literature; not incorporated in guidelines

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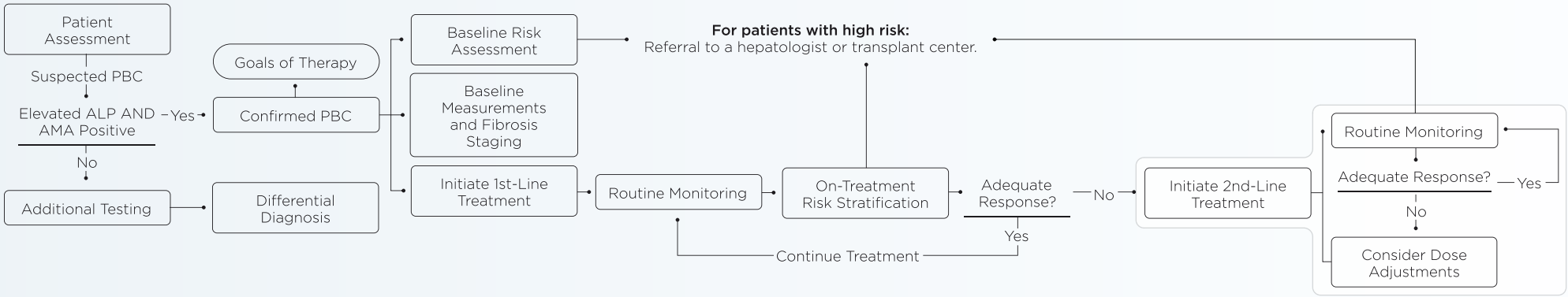

SECOND-LINE TREATMENT CONSIDERATIONS

Options for 2nd-line treatment[10]

- ☐ Obeticholic acid (only FDA-approved 2nd-line treatment for PBC)
- ☐ Fibrates (not FDA-approved for PBC; use off-label)
- ☐ Clinical trials

Initiate 2nd-line treatment

- ☐ Obeticholic acid (5 mg daily)[1-3,16] for the first 3 months
- ☐ **If no response to the above is achieved after monitoring,** increase to maximum dose of obeticholic acid (10 mg daily)[1-3,16]

Routinely monitor for biochemical response, tolerability, and progression of PBC[16]

- ☐ 3 months after initiating therapy[16]

Per discretion of provider:

- ☐ Every 3 months ☐ Every 6 months ☐ Annually

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Closely monitor patients with[16]:

- ☐ Compensated cirrhosis
- ☐ Concomitant hepatic disease (e.g., AIH, ALD)
- ☐ Severe intercurrent illness

For:

- ☐ New evidence of portal hypertension (e.g., ascites, gastroesophageal varices, persistent thrombocytopenia)
- ☐ Increases above the upper limit of normal in total bilirubin, direct bilirubin, or prothrombin time

Response achieved?

No → Initiate 2nd-line treatment

Yes → Intolerance occurs

If there is intolerance due to pruritus,[16] consider:

- ☐ Bile acid-binding resins
- ☐ Antihistamines
- ☐ Reduce dosage to
  - ☐ 5 mg every other day (if intolerant to 5 mg daily)
  - ☐ 5 mg daily (if intolerant to 10 mg daily)
- ☐ Interrupt treatment for up to 2 weeks; restart at reduced dosage

Pruritus managed?

Yes → Routinely monitor for biochemical response, tolerability, and progression of PBC[16]

No

Discontinue treatment in patients who[16]:

- Develop evidence of hepatic decompensation
- Have compensated cirrhosis and develop evidence of portal hypertension
- Experience clinically significant hepatic adverse reactions
- Develop complete biliary obstruction
- Have persistent, intolerable pruritus

Refer to a hepatologist or transplant center

Obeticholic acid is contraindicated in patients with[16]:

- decompensated cirrhosis (e.g., Child-Pugh Class B or C) or prior decompensation event
- compensated cirrhosis who have evidence of portal hypertension (e.g., ascites, gastroesophageal varices, persistent thrombocytopenia)
- complete biliary obstruction

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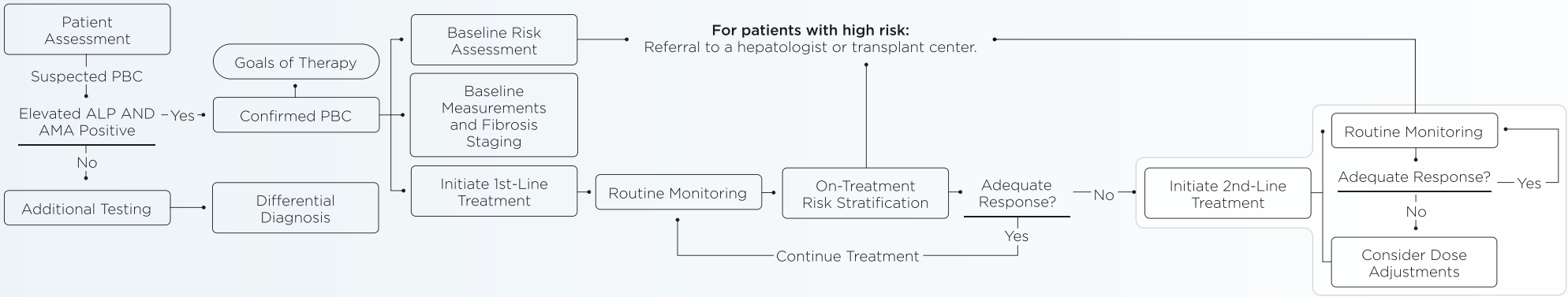

ROUTINE MONITORING ASSESSMENTS FOR SECOND-LINE TREATMENT

Patients with cirrhosis (even if not advanced) on obeticholic acid should be carefully monitored for evidence of liver decompensation or portal hypertension.[9]

Routine follow-up assessments should look for[1-3,14]

- ☐ Pruritus[14]
- ☐ Ascites[14]
- ☐ Jaundice[14]
- ☐ Variceal bleeding[14]
- ☐ Reduction in HDL-C[16]
- ☐ Progression of liver stiffness/fibrosis[1]
- ☐ Cirrhosis[1]
- ☐ Portal hypertension[2]
- ☐ Hepatic encephalopathy[14]
- ☐ HCC[1,3]
- ☐ Bone disease/osteoporosis[1,2]
- ☐ Sicca syndrome[2]
- ☐ Dyslipidemia[2]

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All chronic liver disease patients[2]

- ☐ Immunizations against Hepatitis A and B
- ☐ Optimize body weight
- ☐ Minimize alcohol consumption
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Laboratory testing for consideration when conducting ongoing monitoring and assessments[1-6]

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  - ☐ Platelets[1-4]
  - ☐ Hemoglobin (Hgb)[1-3]
- ☐ Comprehensive Metabolic Panel (CMP)* → liver function/enzymes
  - ☐ Albumin[1-3]
  - ☐ Total bilirubin[2-4]
  - ☐ Direct bilirubin[2-4]
  - ☐ Liver enzymes (**ALP,** ALT, AST), GGT[1-4]
- ☐ Lipid panel[1-3]:
  - ☐ LDL
  - ☐ HDL
  - ☐ Cholesterol
  - ☐ Triglycerides
- ☐ Blood clotting tests: INR[2,3]
- ☐ Thyroid-stimulating hormone (TSH)[1-3]
- ☐ Vitamin A, D[1-3]
- ☐ Bone mineral density (BMD) (every 2 years)[1-4]
- ☐ Abdominal ultrasound: monitor for ascites[2-4]
- ☐ Assess fibrosis/liver stiffness[3-5]
  - ☐ Transient elastography
  - ☐ Serology: FIB-4, APRI
- ☐ Cholangiography with MRCP[2]
- ☐ Upper endoscopy (stage for varices; for patients with cirrhosis)[1,3]
- ☐ Liver biopsy[1-3]
- ☐ Screen for HCC[1]
- ☐ HCC surveillance: AFP, DCP, AFP-L3% levels (surveillance every 6 months with ultrasound and AFP in patients with advanced fibrosis and men with PBC), GALAD score[1-4,6,7]

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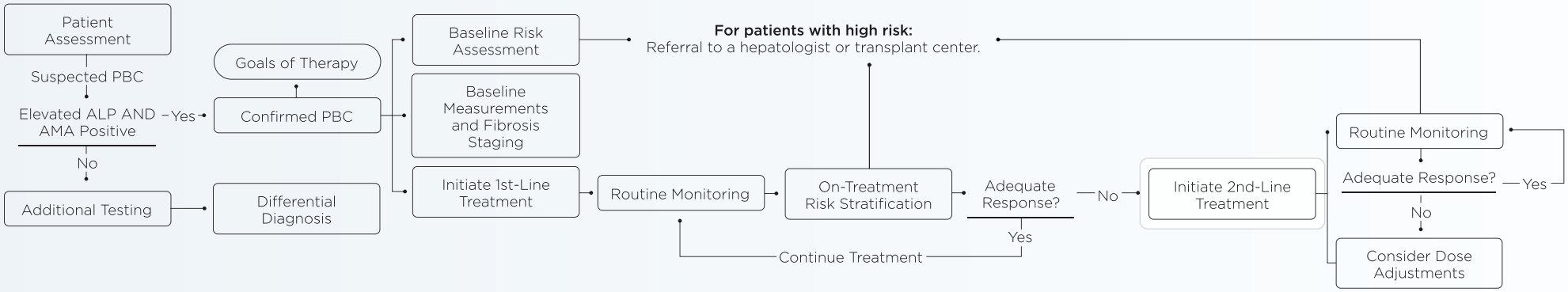

ADDITIONAL PRURITUS MANAGEMENT

Strategies to manage pruritus in obeticholic acid-treated patients

Topical treatments and lifestyle interventions

- ☐ Moisturizers[1,3,33]
- ☐ Cooling agents[33]
- ☐ Antihistamines[1-3,33]
- ☐ Diphenhydramine[33]
- ☐ Oatmeal extract[3,33]
- ☐ Taking cool showers/showering in the morning[3,33]
- ☐ Using clear/gentle soaps and laundry detergents[33]
- ☐ Application of cold packs or fabric strips soaked in cold water[1,33]
- ☐ Avoidance of wool and other potentially irritating fabrics[1,33]
- ☐ Wearing loose-fitting clothing[1,33]
- ☐ Primrose oil[44]

Prescription medications

- ☐ Tobacco cessation[33]
- ☐ Bile acid-binding resin[1,3,33]
- ☐ Cholestyramine[1-3,33]
- ☐ Colestipol[1,33]
- ☐ Rifampicin[1-3,33]
- ☐ Antihistamines[1,33]
- ☐ Hydroxyzine[33]
- ☐ Opioid antagonists[1,3,33]
- ☐ Naltrexone[1,3,33]
- ☐ Naloxone[33]
- ☐ Gabapentin[3,33]
- ☐ Selective serotonin reuptake inhibitors (SSRIs)[1-3,33]

Other therapies*

- ☐ Ultraviolet light therapy[1,3,33]
- ☐ Nasobiliary drainage[1-3,33]
- ☐ Albumin dialysis[1,2,33]
- ☐ Plasmapheresis[1,2,33]

*These physical interventions are available as salvage therapies.

If steps to manage pruritus are not successful[16]:

- ☐ Reduce dosage to
  - ☐ 5 mg QOD (for patients intolerant to 5 mg QD)
  - ☐ 5 mg QD (for patients intolerant to 10 mg QD)
- ☐ Interrupt treatment for up to 2 weeks; restart at reduced dosage
- ☐ If reducing dosage or dose interruption, titrate the dosage based on biochemical response and tolerability
- ☐ Discontinue treatment in patients who continue to experience persistent, intolerable pruritus despite management strategies

Fibrates are discouraged in patients with decompensated liver disease.[9,17]

Fenofibrate is contraindicated in patients with[17]:

- Known hypersensitivity to fenofibrate
- Liver disease
- Severe renal dysfunction
- Preexisting gallbladder disease
- Breastfeeding

If fibrates are used, the following monitoring should be considered[17]:

- Kidney function (uric acid, BUN, creatinine clearance)
- Hepatic function
- CPK
- Platelets, WBC
- Lipid panel: total cholesterol, HDL, LDL, triglycerides

References

[1]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(1):394-419.
[2]Younossi Z, Bernstein D, Shiffman ML, et al. Diagnosis and management of primary biliary cholangitis. *Am J Gastroenterol.* 2019;114(1):48-63.
[3]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;67:145-172.
[4]Hirschfield GM, Chazouillères O, Cortez-Pinto H, et al. A consensus integrated care pathway for patients with primary biliary cholangitis: a guideline-based approach to clinical care of patients. *Expert Rev Gastroenterol Hepatol.* 2021;15(8):929-939.
[5]Cristoferi L, Calvaruso V, Overi D, et al. Accuracy of transient elastography in assessing fibrosis at diagnosis in naïve patients with primary biliary cholangitis: a dual cut-off approach. *Hepatology.* 2021;74(3):1496-1508.
[6]Marrero JA, Kulik LM, Sirlin CB, et al. Diagnosis, staging, and management of hepatocellular carcinoma: 2018 practice guidance by the American Association for the Study of Liver Diseases. *Hepatology.* 2018;68(2):723-750.
[7]Piratvisuth T, Tanwandee T, Thongsawat S, et al. Multimarker panels for detection of early stage hepatocellular carcinoma: a prospective, multicenter, case-control study. *Hepatol Commun.* 2022;6(4):679-691.
[8]Callichurn K, Cvetkovic L, Therrien A, Vincent C, Hétu PO, Bouin M. Prevalence of celiac disease in patients with primary biliary cholangitis. *J Can Assoc Gastroenterol.* 2021;4(1):44-47.
[9]Lindor KD, Bowlus CL, Boyer J, Levy C, Mayo M. Primary biliary cholangitis: 2021 practice guidance update from the American Association for the Study of Liver Diseases [published online ahead of print, 2021 Aug 24]. *Hepatology.* 2021;10.1002/hep.32117.
[10]Kowdley KV, Bowlus CL, Levy C, et al. Application of the latest advances in evidence-based medicine in primary biliary cholangitis. *Am J Gastroenterol.* 2022;00:1-11.
[11]Corpechot C, Carrat F, Gaouar F, et al. Liver stiffness measurement by vibration-controlled transient elastography improves outcome prediction in primary biliary cholangitis. *J Hepatol.* 2022;77(6):1545-1553.
[12]Murillo Perez CF, Harms MH, Lindor KD, et al. Goals of treatment for improved survival in primary biliary cholangitis: treatment target should be bilirubin within the normal range and normalization of alkaline phosphatase. *Am J Gastroenterol.* 2020;115(7):1066-1074.
[13]Murillo Perez CF, Hirschfield GM, Corpechot C, et al. Fibrosis stage is an independent predictor of outcome in primary biliary cholangitis despite biochemical treatment response. *Aliment Pharmacol Ther.* 2019;50(10):1127-1136.
[14]URSO® 250, URSO® FORTE (ursodiol) [Full Prescribing Information]. Allergan, Inc. Madison, NJ.
[15]Gerussi A, Bernasconi DP, O'Donnell SE, et al. Measurement of gamma glutamyl transferase to determine risk of liver transplantation or death in patients with primary biliary cholangitis. *Clin Gastroenterol Hepatol.* 2021;19(8):1688-1697.e14.
[16]OCALIVA® (obeticholic acid) [Full Prescribing Information]. Intercept Pharmaceuticals, Inc. New York, NY.
[17]Sidhu G, Tripp J. Fenofibrate. In: StatPearls. Treasure Island (FL): StatPearls Publishing; June 28, 2021.
[18]Critical values. October 24, 2022. Accessed May 31, 2023. Available at: https://files.labcorp.com/labcorp-d8/2022-12/Panic_%28Critical%29_Values_10-24-2022.pdf.
[19]Prothrombin Time Sample Report. Accessed April 11, 2023. Available at: https://www.labcorp.com/tests/005199/prothrombin-time-pt.
[20]Prothrombin Time, Serial Sample Report. Accessed May 31, 2023. Available at: https://files.labcorp.com/testmenu-d8/sample_reports/485199.pdf.
[21]Alkaline phosphatase. Accessed May 31, 2023. Available at: https://www.labcorp.com/tests/001107/alkaline-phosphatase.
[22]New ALT reference intervals for children and adults. LabCorp. Accessed May 31, 2023. Available at https://www.labcorp.com/assets/5286.
[23]Aspartate Aminotransferase (AST) Sample Report. Accessed April 11, 2023. Available at: https://www.labcorp.com/tests/001123/aspartate-aminotransferase-ast-sgot.
[24]Hepatic Function Panel Sample Report. Accessed June 1, 2023. Available at: https://files.labcorp.com/testmenu-d8/sample_reports/322755.pdf.
[25]Bilirubin, Direct. Accessed April 25, 2023. Available at: https://www.labcorp.com/tests/001222/bilirubin-direct.
[26]Albumin. Accessed June 1, 2023. Available at: https://www.labcorp.com/tests/001081/albumin.
[27]ANA 12 Sample Report. Accessed June 1, 2023. Available at: https://files.labcorp.com/testmenu-d8/sample_reports/520188.pdf.
[28]PBC Profile Sample Report. Accessed June 1, 2023. Available at: https://files.labcorp.com/testmenu-d8/sample_reports/520192.pdf.
[29]Kasarala G, Tillmann HL. Standard liver tests. Clin Liver Dis. 2016;8(1):13-18.
[30]UK-PBC Score Calculator. Accessed April 28, 2023. Available at: https://www.mdapp.co/uk-pbc-risk-score-calculator-360/
[31]The Global PBC Study Group. The GLOBE score for patients with primary biliary cholangitis (PBC). Accessed April 25, 2023. Available at: https://www.globalpbc.com/globe
[32]Mayo Clinic. The updated natural history model for primary biliary cholangitis. Mayo Calculator. Accessed at: https://www.mayoclinic.org/medical-professionals/transplant-medicine/calculators/the-updated-natural-history-model-for-primary-biliary-cholangitis/itt-20434724
[33]Murillo Perez CF, Ioannou S, Hassanally I, et al. Early identification of insufficient biochemical response to ursodeoxycholic acid in patients with primary biliary cholangitis. Poster 1266 presented at: 2021 AASLD The Liver Meeting; November 12-15, 2021; Virtual.
[34]Pate J, Gutierrez JA, Frenette CT, et al. Practical strategies for pruritus management in the obeticholic acid-treated patient with PBC: proceedings from the 2018 expert panel. *BMJ Open Gastroenterol.* 2019;6(1):e000256.
[35]Iluz-Freundlich D, Uhanova J, Van Iderstine MG, Minuk GY. The impact of primary biliary cholangitis on non-alcoholic fatty liver disease. *Eur J Gastroenterol Hepatol.* 2020;33:565-570.
[36]Chapman J, Goyal A, Azevado Am. Splenomegaly. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing. June 26, 2023. Accessed October 19, 2023. https://www.ncbi.nlm.nih.gov/books/NBK430907/
[37]Augustine A, John R, Simon B, Chandramohan A, Keshava SN, Eapen A. Imaging approach to portal hypertension. *J Gastrointestinal Abdominal Radiol.* 2023;6:123-137.
[38]Centers for Disease Control and Prevention. Hepatitis A questions and answers for health professionals. September 27, 2023. Accessed October 18, 2023. https://www.cdc.gov/hepatitis/hav/havfaq.htm#general
[39]Ramirez JC, Ackerman K, Strain SC, Ahmed ST, de los Santos M, Sear D. Hepatitis A and B screening and vaccination rates among patients with chronic liver disease. *Hum Vaccin Immunother.* 2016;12(1):64-69.
[40]Centers for Disease Control and Prevention. Screening and testing recommendations for chronic hepatitis B virus infection (HBV). March 28, 2022. Accessed October 18, 2023. https://www.cdc.gov/hepatitis/hbv/testingchronic.htm
[41]Centers for Disease Control and Prevention. Testing recommendations for hepatitis C virus infection. July 13, 2023. Accessed October 18, 2023.
[42]Del Poggio P, Mazzoleni M. Screening in liver disease. *World J Gastroenterol.* 2006;12(33):5272-5280.
[43]HBV Primary Care Workgroup. Hepatitis B management: guidance for the primary care provider. February 25, 2020. Accessed October 19, 2023. https://www.hepatitisb.uw.edu/page/primary-care-workgroup/guidance
[44]Thuluvath, PF, Triger DR, Manku MS, et al. Evening primrose oil in the treatment of severe refractory biliary pruritus. *Inpharma Weekly.* 1991;778:15.
[45]Immunize.org. Hepatitis A: Questions and Answers. September 11, 2023. Accessed December 4, 2023. https://www.immunize.org/wp-content/uploads/catg.d/p4204.pdf.

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