Which of these best describes your role in primary biliary cholangitis (PBC) care?

Please select a profile to continue

I treat new and stable patients and make my own treatment decisions

I see patients for follow-up appointments and coordinate care with the primary managing physician

I currently do not see patients with PBC

Navigating Cholestasis

DRSC-US-000153
July 2024

IPSEN

How do you manage patients with primary biliary cholangitis (PBC)?

- In this activity, you will answer questions about the management of a fictional patient with PBC
- Once you answer a question, more information about the possible answers will appear and you will then be able to move on to the next question
- The patient pathway and the information provided is based on guidance from the 2023 expert consensus document from Kowdley et al. This is not medical advice. There may be other appropriate steps based on patient need

Kowdley KV et al. *Am J Gastroenterol* 2023;118:232–242.

How do you manage patients with primary biliary cholangitis (PBC)?

Your patient has just been diagnosed with PBC. What would you do next?

Patient diagnosed with PBC

Select an answer to learn more

- **A** Start 1L treatment
- **B** Watch and wait
- **C** Determine how advanced their disease is (fibrosis staging)

See the PBC management algorithm

1L, first-line.

How do you manage patients with primary biliary cholangitis (PBC)?

Your patient has just been diagnosed with PBC. What would you do next?

Patient diagnosed with PBC

- **Fibrosis stage** should be established at baseline to predict prognosis and identify patients at risk of decompensation
- Measurement of liver stiffness by TE or MRE is recommended for fibrosis staging.
  - Patients with TE ≥10 kPa or MRE ≥4.3 kPa can be considered as having advanced fibrosis and at increased risk of future hepatic decompensation

The recommendations provided above are based on those from Kowdley et al, 2023. They do not represent an exhaustive list of management options.

See the PBC management algorithm

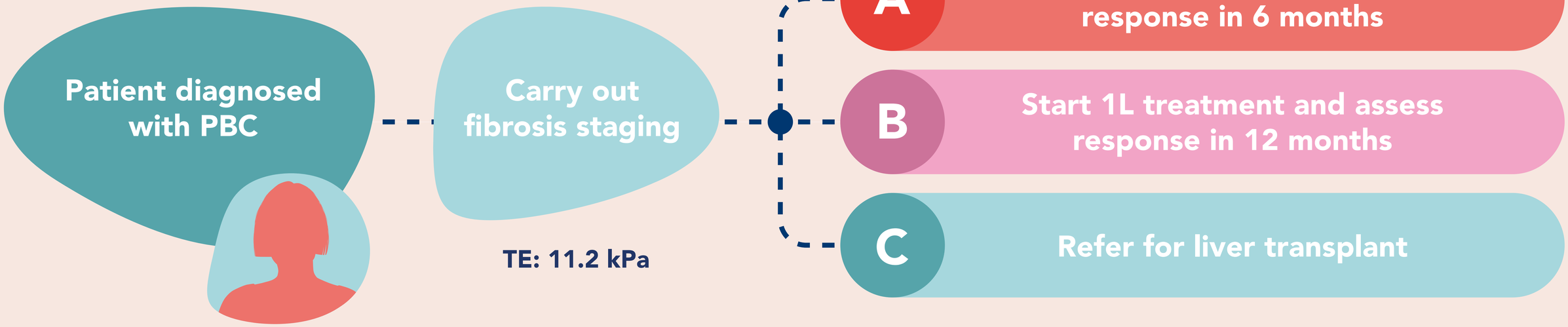
kPa, kilopascal; MRE, magnetic resonance elastography; TE, transient elastography.

Kowdley KV et al. *Am J Gastroenterol* 2023;118:232–242.

How do you manage patients with primary biliary cholangitis (PBC)?

Your patient has a transient elastography (TE) result of 11.2 kPa, suggesting they have a more advanced fibrosis stage. What would you do next?

Select an answer to learn more

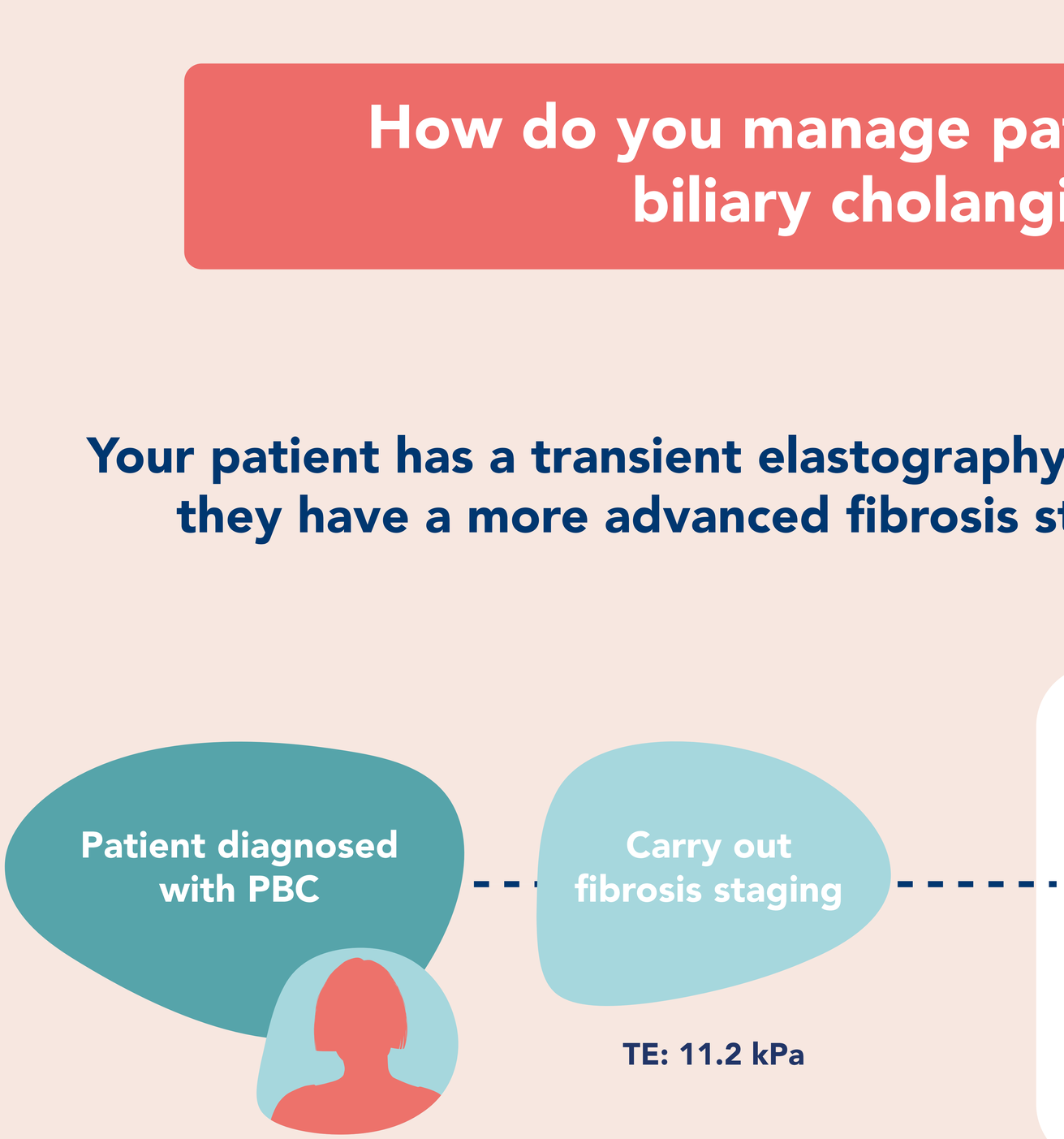


See the PBC management algorithm

1L, first-line; kPa, kilopascal.

How do you manage patients with primary biliary cholangitis (PBC)?

Your patient has a transient elastography (TE) result of 11.2 kPa, suggesting they have a more advanced fibrosis stage. What would you do next?



- Response to 1L treatment has historically been assessed after 12 months, however, there is growing evidence that it can be reliably predicted as **early as 6 months** after treatment initiation
- Patients with a **lower stage of fibrosis** (VCTE or TE <10 kPa; MRE <4.3 kPa) may continue 1L treatment for 12 months before measuring for a response
- Patients with more **advanced fibrosis**, **compensated liver disease**, and **no signs of portal hypertension** should be **assessed for response at 6 months**

The recommendations provided above are based on those from Kowdley et al, 2023. They do not represent an exhaustive list of management options.

See the PBC management algorithm

1L, first-line; kPa, kilopascal; MRE, magnetic resonance elastography, VCTE, vibration-controlled transient elastography.

Kowdley KV et al. *Am J Gastroenterol* 2023;118:232–242.

How do you manage patients with primary biliary cholangitis (PBC)?

You initiate 1L treatment and assess response at 6 months. What threshold would you use to determine a potential response?

Select an answer to learn more

Carry out fibrosis staging

TE: 11.2 kPa

Initiate 1L treatment and assess response at 6 months

- **A** ALP <1.9 x ULN and bilirubin <1.0 x ULN
- **B** ALP <1.5 x ULN and bilirubin <1.0 x ULN
- **C** ALP normalization and bilirubin ≤0.6 mg/dL

See the PBC management algorithm

1L, first-line; ALP, alkaline phosphatase; kPa, kilopascal; TE, transient elastography; ULN, upper limit of normal.

How do you manage patients with primary biliary cholangitis (PBC)?

You initiate 1L treatment and assess response at 6 months. What threshold would you use to determine a potential response?

Carry out fibrosis staging

TE: 11.2 kPa

Initiate 1L treatment and assess response at 6 months

- A study from the Global PBC Study Group proposed that an ALP cut-off of **1.9 x ULN** could be used to determine response at **6 months**, with a negative predictive value of 90%
- A more stringent ALP cut-off of **1.5 x ULN** may be used if assessing response at **12 months**, alongside normal bilirubin
- Recent data also suggests there may be additional survival benefit in achieving **normalization of ALP and a bilirubin level ≤0.6 mg/dL**

The recommendations provided above are based on those from Kowdley et al, 2023. They do not represent an exhaustive list of management options.

See the PBC management algorithm

1L, first-line; ALP, alkaline phosphatase; kPa, kilopascal; TE, transient elastography; ULN, upper limit of normal.
Kowdley KV et al. *Am J Gastroenterol* 2023;118:232–242.

How do you manage patients with primary biliary cholangitis (PBC)?

You determine that your patient is non-responsive to 1L treatment at 6 months. They have no signs of decompensated liver disease or clinically significant portal hypertension. What do you do next?

Select an answer to learn more

Carry out fibrosis staging

TE: 11.2 kPa

Initiate 1L treatment and assess response at 6 months

ALP: 2.1 x ULN; bilirubin: 0.9 x ULN

- **A** Discuss clinical trials
- **B** Refer for liver transplant
- **C** Initiate 2L treatment

See the PBC management algorithm

1L, first-line; 2L, second-line; ALP, alkaline phosphatase; kPa, kilopascal; TE, transient elastography; ULN, upper limit of normal.

How do you manage patients with primary biliary cholangitis (PBC)?

You determine that your patient is non-responsive to 1L treatment at 6 months. They have no signs of decompensated liver disease or clinically significant portal hypertension. What do you do next?

Carry out fibrosis staging

TE: 11.2 kPa

Initiate 1L treatment and assess response at 6 months

ALP: 2.1 x ULN; bilirubin: 0.9 x ULN

- **Guideline-recommended 2L options, including clinical trials**, should be discussed with patients who are non-responsive or intolerant to 1L treatment
- A referral for a liver transplant may be appropriate for patients with decompensated cirrhosis or portal hypertension, or for those significantly affected by severe pruritus or fatigue

The recommendations provided above are based on those from Kowdley et al, 2023. They do not represent an exhaustive list of management options.

See the PBC management algorithm

1L, first-line; 2L, second-line; ALP, alkaline phosphatase; kPa, kilopascal; TE, transient elastography; ULN, upper limit of normal.

Kowdley KV et al. *Am J Gastroenterol* 2023;118:232–242.

How do you manage patients with primary biliary cholangitis (PBC)?

You initiate 2L treatment and monitor the patient's ALP and bilirubin every 3–6 months

Carry out fibrosis staging

TE: 11.2 kPa

Initiate 1L treatment and assess response at 6 months

ALP: 2.1 x ULN; bilirubin: 0.9 x ULN

Initiate 2L treatment and monitor response every 3–6 months

Continue to see the full PBC management algorithm from the expert consensus document

1L, first-line; 2L, second-line; ALP, alkaline phosphatase; kPa, kilopascal; TE, transient elastography; ULN, upper limit of normal.

How do you manage patients with primary biliary cholangitis (PBC)?

Evidence-based algorithm for the management of PBC from the 2023 expert consensus document

Establish diagnosis of PBC

Stage via TE or MRE

Start 1L treatment

- For 6 months if VCTE ≥ 10 kPa, compensated liver disease, and no signs of portal hypertension
- For 12 months if TE < 10 kPa, MRE <4.3 kPa

Adequate response to 1L treatment?
- Target at 6 months: ALP <1.9 x ULN, bilirubin <1.0 x ULN
- Target at 12 months: ALP <1.5 x ULN, bilirubin <1.0 x ULN

No / Yes

Continue 1L treatment
- Monitor ALP and bilirubin every 3–6 months

Intolerance to 1L treatment

Clinically significant portal hypertension, liver decompensation or CPC-B/C?

No / Yes

Start 2L treatment

Intolerance to 2L treatment

Adequate response to 2L treatment
Target: ALP <1.5 x ULN, bilirubin <1.0 x ULN

No / Yes

Consider another 2L therapeutic agent

Continue 2L treatment
- Monitor ALP and bilirubin every 3–6 months

Consider liver transplant

Adapted from Kowdley et al, 2023. See manuscript for the full algorithm.

1L, first-line; 2L, second-line; ALP, alkaline phosphatase; CPC-B/C, Child-Pugh class B/C; kPa, kilopascal; MRE, magnetic resonance elastography; TE, transient elastography; ULN, upper limit of normal; VTCE, vibration-controlled transient elastography

Kowdley KV et al. *Am J Gastroenterol* 2023;118:232–242.

How do you manage patients with primary biliary cholangitis (PBC)?

Scan the QR code to see a full version of the PBC management algorithm

What do a patient's test results tell you about their symptoms?

In this exercise, you'll be shown two patient profiles* followed by a series of statements

Can you guess which patient made the statement based on their laboratory results alone?

*Fictional patient profiles. Reviewed by Professor Gideon Hirschfield for medical accuracy.

Patient A and patient B are both living with PBC*

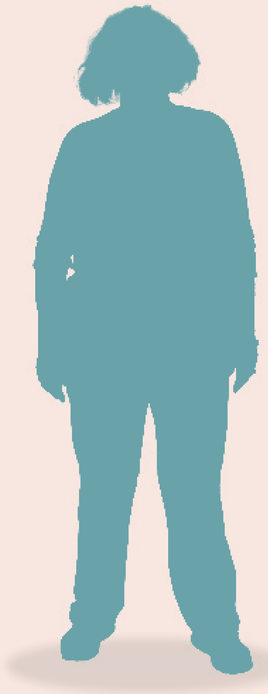
A

- ◯ Female
- ◯ 50 years old (diagnosed 2 years ago)
- ◯ Weight: 143 lb (65 kg)
- ◯ Height: 1.62 m
- ◯ ALP: 1.6 x ULN (208.7 IU/L)
- ◯ Bilirubin: 1.0 mg/dL
- ◯ Albumin: 5.2 g/dL
- ◯ Receiving first-line treatment

B

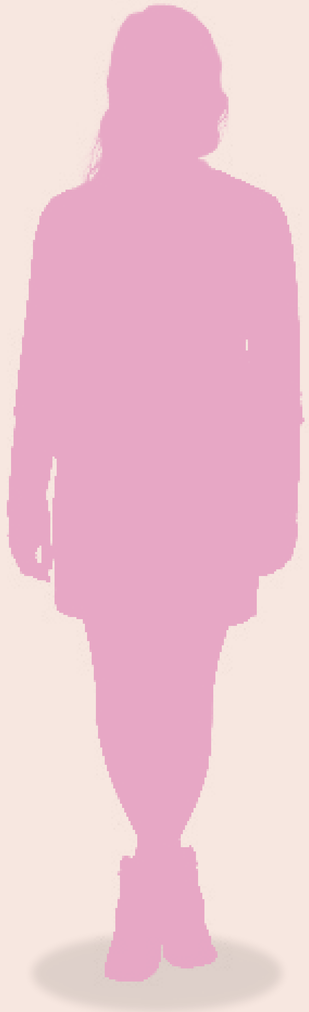
- ◯ Female
- ◯ 62 years old (diagnosed 8 years ago)
- ◯ Weight: 176 lb (80 kg)
- ◯ Height: 1.67 m
- ◯ ALP: 2.8 x ULN (360 IU/L)
- ◯ Bilirubin: 1.1 mg/dL
- ◯ Albumin: 5.8 g/dL
- ◯ Non-responder to first-line treatment
- ◯ Receiving second-line treatment

Lorem ipsum dolor sit amet, consectetuer adipiscing elit, sed diam



*Fictional patient profiles. Reviewed by Professor Gideon Hirschfield for medical accuracy.
ALP, alkaline phosphatase; primary biliary cholangitis; ULN, upper limit of normal.

When scoring the impact of fatigue, which patient do you think gave a score of 8/10?*



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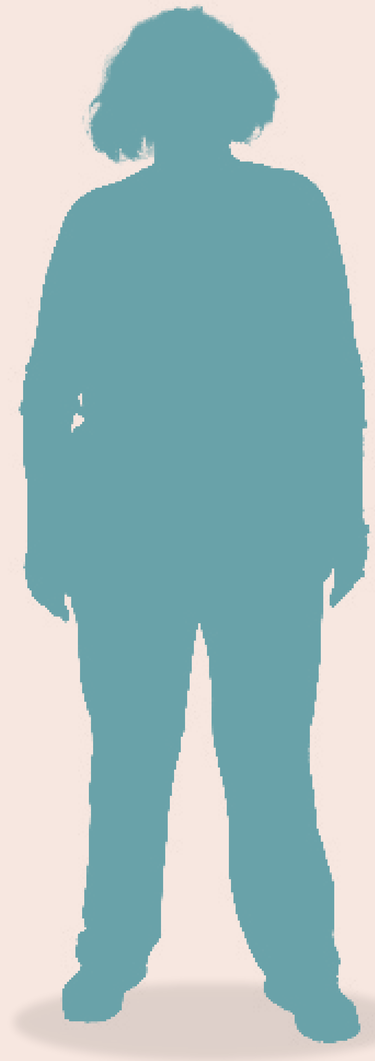

Click on a patient to choose your answer

*Fictional patient profiles. Reviewed by Professor Gideon Hirschfield for medical accuracy.
ALP, alkaline phosphatase; ULN, upper limit of normal.

When scoring the impact of fatigue, which patient do you think gave a score of 8/10?*

"Despite my doctor saying that my test results are OK and my treatment is working, I feel exhausted all the time and my life is becoming unrecognizable."

Not actual patient.
Image of a model used for illustrative purposes only.

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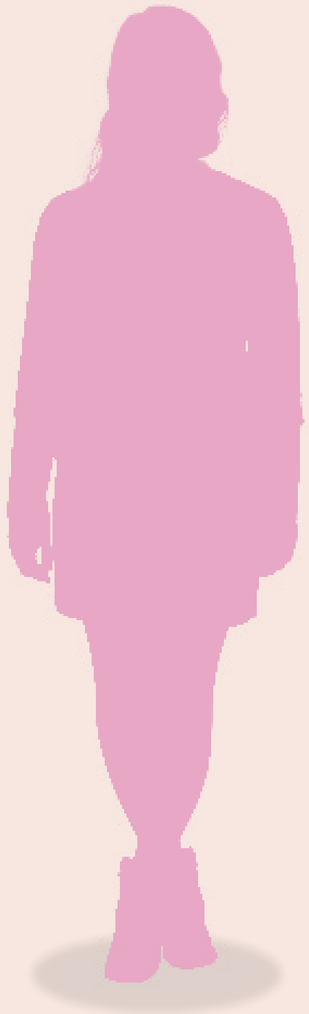
***Fictional patient profiles. Reviewed by Professor Gideon Hirschfield for medical accuracy.**
ALP, alkaline phosphatase; ULN, upper limit of normal.

When scoring the impact of fatigue, which patient do you think gave a score of 8/10?

Please click back and choose another answer

Not actual patient.
Image of a model used for illustrative purposes only.

Which patient do you think went on to receive a liver transplant?*



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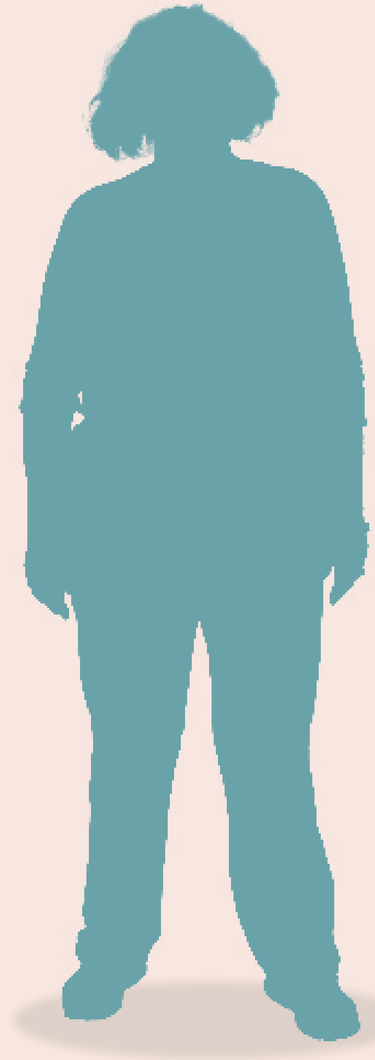

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- ○ Non-responder to first-line treatment
- ○ Receiving second-line treatment

"My doctor says none of the treatments have worked, and now I must receive a transplant; I am very afraid."

Not actual patient.
Image of a model used for illustrative purposes only.

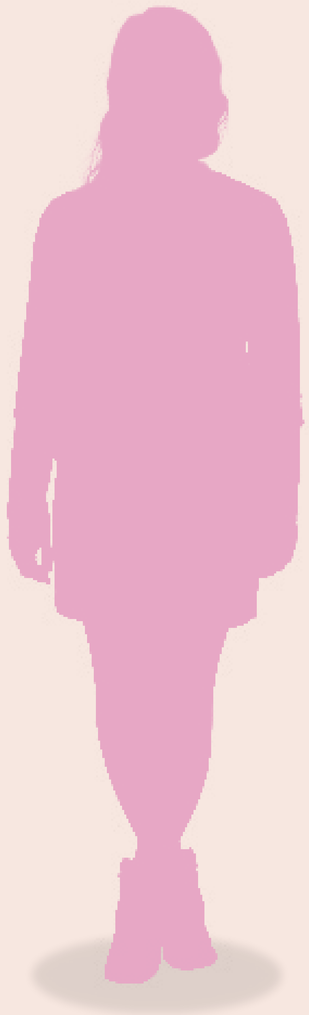
***Fictional patient profiles. Reviewed by Professor Gideon Hirschfield for medical accuracy.**
ALP, alkaline phosphatase; ULN, upper limit of normal.

Which patient do you think went on to receive a liver transplant?

Please click back and choose another answer

Not actual patient.
Image of a model used for illustrative purposes only.

Which patient do you think no longer takes their granddaughter swimming due to their pruritus?*



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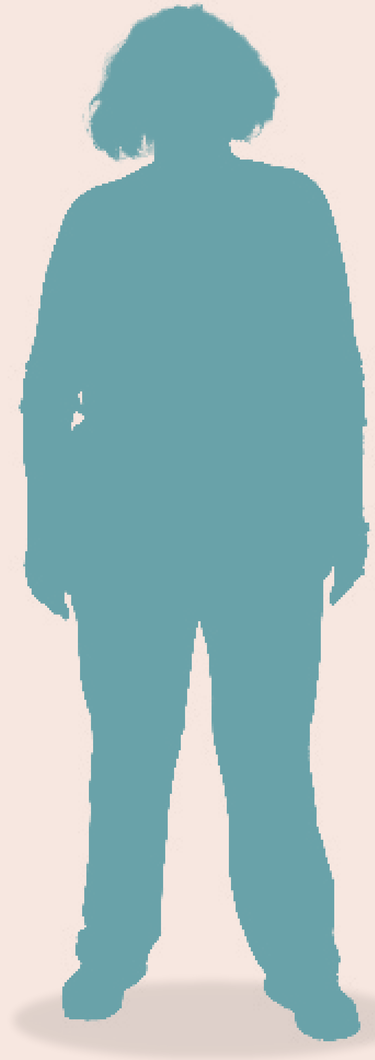

Click on a patient to choose your answer

*Fictional patient profiles. Reviewed by Professor Gideon Hirschfield for medical accuracy.
ALP, alkaline phosphatase; ULN, upper limit of normal.

Which patient do you think no longer takes their granddaughter swimming due to their pruritus?*

"Until recently, I would rest beforehand so I could still take my granddaughter swimming, but now my skin is so itchy, I can't face anything that might make it worse."

Not actual patient.
Image of a model used for illustrative purposes only.

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- ○ 50 years old (diagnosed 2 years ago)
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ALP, alkaline phosphatase; ULN, upper limit of normal.

Which patient do you think no longer takes their granddaughter swimming due to their pruritus?

Please click back and choose another answer

Not actual patient.
Image of a model used for illustrative purposes only.

So, what do a patient's test results tell you about their symptoms?

- The severity of PBC symptoms, such as fatigue and pruritus, does not always correlate with the severity and stage of disease.[1–3]
- This means it can be hard to understand the impact of PBC on a patient's quality of life from their laboratory results alone

PBC, primary biliary cholangitis.

1. Cauch-Dudek K et al. *Gut* 1998;43:705–710; 2. Newton JL et al. *J Hepatol* 2006;44:776–783; 3. Hirschfield G, et al. *Gut* 2018;67:1568–1594.

Do you discuss symptoms and their impact with patients?

Patient survey results show that:*

~1/3 of patients do not feel comfortable raising queries about their symptoms with their healthcare professional (HCP)

"Did not think anything could be done to help"

Reported as the reason they did not raise symptoms with their HCP by **35% of patients with itch** and **22% with fatigue.**

"Not enough time in appointments"

Reported as the reason they did not raise symptoms with their HCP by **12% of patients with itch** and **20% with fatigue.**

*Results from a questionnaire completed by 227 patients living with PBC in the UK. 196 patients experienced fatigue and 142 patients experienced itch. Of the patients experiencing fatigue and itch, 69% and 68% felt comfortable raising queries about their symptoms with clinicians. 138 patients said they were asked about their symptoms by clinicians in the previous 12 months. Mitchell C et al. *Gut* 2022;71(Suppl 3):Abstract P13.

What is primary biliary cholangitis (PBC)?

What is primary biliary cholangitis (PBC)?

PBC is a rare, progressive autoimmune disease of the liver:[1,2]

- Estimated to affect 4.3 people per 100,000 per year in the US[3]
- Characterized by T-cell mediated destruction of bile ducts[1]
- Commonly causing symptoms of fatigue and pruritus[1,4]
- That can lead to liver fibrosis, cirrhosis, and end-stage liver disease[1]

1. Galoosian A et al. *J Clin Transl Hepatol* 2020;8:49–60; 2. Hirschfield G, et al. *Gut* 2018;67:1568–1594; 3. Lu M et al. *Clin Gastroenterol Hepatol* 2018;16:1342–1350;
4. Dahlqvist G et al. *Hepatology* 2017;65:152–163.

What is primary biliary cholangitis (PBC)?

PBC affects more women than men[1–4]

Most prevalent in women **over 40 years of age**[3–6]

1. Lu M et al. *Clin Gastroenterol Hepatol* 2018;16:1342–1350; 2. Gershwin ME et al. *Hepatology* 2005;42:1194–1202; 3. Hirschfield G, et al. *Gut* 2018;67:1568–1594;
4. Kim WR et al. *Gastroenterol* 2000;119:1631–1636; 5. Dahlqvist G et al. *Hepatology* 2017;65:152–163; 6. Kim KA et al. *Ailment Pharmacol Ther* 2016;43:154–162.

Presentation of primary biliary cholangitis (PBC) can range from asymptomatic to a host of symptoms[1]

Click on the bubbles to see the symptoms

Common symptoms

Other reported symptoms

Concurrent rheumatologic or autoimmune disease are common with PBC[2]

~60% of patients with PBC are asymptomatic at the time of diagnosis[3]

PBC, primary biliary cholangitis.

1. Galoosian A et al. *J Clin Transl Hepatol* 2020;8:49–60; 2. Liu Y et al. *Can J Gastroenterol Hepatol* 2021;5557814; 3. Prince MI et al. *Gut* 2004;53:865–870.

Common symptoms

Fatigue[1]

Joint pain and stiffness[2]

Pruritus[1]

PBC, primary biliary cholangitis.

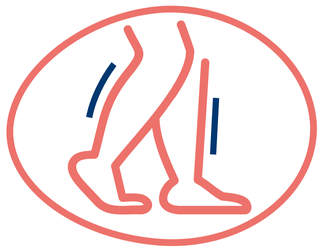
1. Liu Y et al. *Can J Gastroenterol Hepatol* 2021;5557814; 2. Prince MI et al. *Gut* 2004;53:865–870.

1. Dahlqvist G et al. *Hepatology* 2017;65:152–163; 2. Selmi C et al. *Hepatology* 2007;46:1836–1843.

Other reported symptoms

Jaundice[1]

Abdominal discomfort[2]



Restless legs[3]

Cognitive impairment[4]

PBC, primary biliary cholangitis.

1. Dahlqvist G et al. *Hepatology* 2017;65:152–16; 2. Laurin JM et al. *J Gastroenterol* 1994;89:1840–1843;
3. Anderson K et al. *Liver Int* 2013;33:239–243; 4. Newton JL et al. *Hepatology* 2008;48:541–549.

In PBC, T-cell mediated injury against intralobular biliary epithelial cells (BECs) causes progressive destruction of the bile ducts[1,2]

- Apoptosis of BECs leads to the aberrant expression of autoantigens[3,4]
- Recognition of autoantigens by antimitochondrial antibodies results in formation of an immune complex[4,5]
- Further activating the immune system and leading to persistent and widespread BEC damage[4,5]

PBC, primary biliary cholangitis.

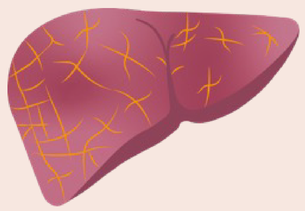
1. Van Den Oord JJ et al. *Liver* 1984;4:264–274; 2. Jones D et al. *Clin Exp Immunol* 1997;107:562–568;
3. Harada K et al. *Hepatology* 1997; 26(6):1399–1405; 4. Lleo A et al. *Hepatology* 2009;49:871–879; 5. Lleo A et al. *Hepatology* 2010;52:987–998.

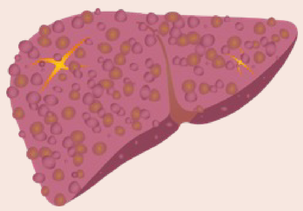
Bile ducts are integral to the regulation of bile acid metabolism in the liver.[1] Their destruction leads to the build-up of bile and other toxins in the liver (cholestasis)[2]

Biliary epithelial cells undergo apoptosis[3] → Causing bile acid to build up within the liver **(cholestasis)**[2] → Cholestasis contributes to **chronic granulomatous inflammation**[2]

↓

Which can lead to **fibrosis**[2] ← And the development of **cirrhosis and portal hypertension**[2] ← Eventually, patients may progress to **end-stage liver disease** (requiring transplantation) or **premature death**[4]





Progression to fibrosis and cirrhosis among PBC patients is becoming less common due to increasing awareness and understanding of the natural history, as well as earlier diagnosis and prompt treatment[2]

PBC, primary biliary cholangitis.

1. Mattner J. *Int J Mol Sci* 2016;17:1864; 2. Galoosian A et al. *J Clin Transl Hepatol* 2020;8:49–60;
3. Lleo A et al. *Hepatology* 2009;49:871–879; 4. Lammers W et al. *Ann Hepatol* 2014;13:316–326.