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EXPERT CONSENSUS CRITERIA AND PRACTICAL RECOMMENDATIONS FOR PBC CARE IN THE COVID-19 ERA AND BEYOND

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Background: Primary biliary cholangitis (PBC) is a chronic autoimmune cholestatic liver disease that can progress to liver fibrosis and cirrhosis, and requires timely diagnosis, optimal treatment, and risk stratification. Several guidelines for the management of PBC have been published, including the American Association for the Study of Liver Disease (AASLD) and European Association for the Study of the Liver (EASL) Clinical Practice Guidelines, which include goals for standards of PBC care. However, recent audits have identified deficiencies in real-world PBC care. In addition, the global coronavirus (COVID-19) pandemic has generally reduced access to care, diminished healthcare resources and accelerated the use of remote patient management. There is therefore a need for simple, actionable guidance that physicians can implement in order to maintain standards of care in PBC in the new environment.
Aims: A working group of ten PBC specialists from Europe and Canada were convened by Intercept Pharmaceuticals in January 2020 with the aim of defining key criteria for the care of patients with PBC.
Methods: Following the outbreak of the COVID-19 pandemic, based on these criteria, a smaller working group of six PBC specialists developed practical recommendations to assist physicians in maintaining standards of care and to guide remote management of patients.
Results: The working group defined five key criteria for care in PBC, encompassing PBC diagnosis, initiation of first line therapy with ursodeoxycholic acid (UDCA), risk stratification on UDCA, symptom management, and initiation of 2L therapy. The group developed 21 practical recommendations for the management of patients with PBC in the COVID-19 environment including modality, frequency and timing of investigations and monitoring. (**Figure 1**).
Conclusions: The delivery of PBC care during the COVID-19 pandemic carries significant challenges. These consensus criteria and practical recommendations provide guidance for the management of PBC during the pandemic era and beyond.

Key Criteria for Care in PBC	Practical Recommendations
Elevated ALP and positive AMA are sufficient for the diagnosis of PBC and, in the correct clinical context, biopsy is rarely needed • Ultrasound is sufficient to exclude obstruction; MRCP is not necessary in the majority of patients • ALT is often elevated as PBC is an inflammatory disease; overlap with AIH is rare	• Diagnosis of PBC can be made either face-to-face or in a remote consultation and should not be delayed until a face-to-face consultation is possible • The AMA test with an elevated ALP reading (> 1 xULN) is conclusive, regardless of the degree of abnormality of ALP • Isolated positive AMA with normal ALP is not diagnostic of PBC but suggests potential future risk. Regular ALP monitoring is suggested. • The diagnosis of PBC and initiation of UDCA therapy should not be delayed by the absence of other investigations or suspicion of AIH overlap
Initiation of first-line therapy with UDCA UDCA at 13–15 mg/kg/day is recommended for first-line use in all patients with PBC; it should be started at diagnosis and continued life-long • Higher doses are not indicated	• UDCA should be initiated at diagnosis and can be safely initiated through remote consultation • In case of suspected PBC–AIH overlap, UDCA initiation should not be delayed and steroids should be initiated later if overlap is confirmed • Patients at high risk of progression to end-stage liver disease (e.g. with advanced fibrosis, liver cirrhosis, abnormal bilirubin, reduced albumin, or low platelet count) or those with significant symptom burden need rapid review within 3 months and regular follow-ups. • Consider opportunities to educate patients on PBC, via digital or printed materials, and reassure them about medication (e.g. that UDCA is not immunosuppressive and about the importance of adherence to treatment)
Patients at greatest risk of disease progression and/or advanced disease stage should be referred to experienced PBC centers, and such patients include those with: • Decompensated cirrhosis (Child-Pugh B or C) • Signs of clinically significant portal hypertension e.g. platelets < 150 x 10^3/μL • Bilirubin > 2 xULN • ALT > 5 xULN	• Risk stratification should be performed at diagnosis (age and stage) and every 12 months on UDCA therapy (ALP and bilirubin) • Blood tests to stage fibrosis (e.g. APRI) and assess for portal hypertension (e.g. platelet count) are sufficient to stage the disease until patients can access elastography and/or ultrasound • Patients should have an ultrasound scan and/or transient elastography within 3 to 6 months of diagnosis in order to confirm stage of disease. Patients with compensated cirrhosis should be reviewed every 6 months. • Treatment response to UDCA should be assessed as early as 6 month, but no later than 12 months, and this can be done either at a virtual or face-to-face visit • All patients with PBC should have a management plan which is shared with the patient and their PCP with predefined frequency and format of consultations, based on patient risk and disease stage
Management of symptoms Symptoms, particularly pruritus and fatigue, are an important part of living with PBC and should be carefully evaluated • There are effective interventions for pruritus that patients should be offered	• Fatigue and pruritus should be assessed in the first patient consultation • Use patient self-assessment and remote consultations to assess symptoms • Pruritus should be assessed (e.g. VAS scores) and treatment (e.g. emollients, bile sequestrants) offered, which can be done via remote consultations
Initiation of second-line therapy • Second-line therapy should be considered in patients with ongoing ALP > 1.5 xULN and/or abnormal bilirubin despite 12 months of UDCA therapy	• Assess adherence to UDCA, prior to initiating second-line therapy • When initiating second-line therapy, take the time during consultation to educate the patient on the expectations of treatment and reinforce the importance of ongoing monitoring • Pruritus should be managed prior to commencing OCALIVA (obeticholic acid) • Categorize the patient according to the management plan – with pre-defined frequency and format of consultations, based on patient risk and disease stage • Assess response to second-line treatment using a range of biochemical parameters (e.g. ALP, GGT, bilirubin, and transaminases) and fibrosis measures

Funding Agencies: NoneIntercept Pharmaceutical