Primary biliary cholangitis: an update on treatment

Gerri Mortimore, Senior Lecturer at the University of Derby, provides an updated clinical review on therapeutic options in light of the latest guidance

Primary biliary cholangitis (PBC), previously known as primary biliary cirrhosis, is a chronic but progressive disease that, over many years, causes damage to bile ducts, leading to cholestasis and, in some patients, cirrhosis. The rate at which PBC progresses varies from person to person, but significant damage takes decades to occur. It predominately affects women aged 40–60 years with a female to male ratio of 9:1, but can affect anyone from the age of 20. There is no cure for PBC other than liver transplant, but medications can be given to slow down disease progression and for the treatment of symptoms. Health professionals should monitor for complications, including the development of osteoporosis, vitamin deficiencies and liver cirrhosis, which carries the associated complications of portal hypertension, varices and ascites

Ursodeoxycholic acid (UDCA) The primary drug of choice for the treatment of PBC is ursodeoxycholic acid (UDCA), due to its anticholestatic effects that can slow disease progression. However, it is more effective if given in the early stages of PBC. UCDA is sold as Ursofalk (Dr Falk, Bourne End) and Ursodiol (Watson Pharma Private, Salcette Goa, India). The usual dose is between 13–15 mg/kg daily. This provides a 90% improvement in ALP and GGT within the first 9–12 months (Lindor et al, 2009). The degree of biochemical response correlates with long-term prognosis; patients with ALP < 3x ULN, AST < 2x ULN and bilirubin ≤ x1 mg/dl after 1 year of UDCA had a 90%

transplant-free survival (Poupon, 2010). However, a systematic review by Gong et al (2007) revealed that UDCA does not reduce mortality in PBC patients. UDCA has been shown to be safe to take. However, a small number of patients are intolerant of the drug, as it can cause gastrointestinal upset, mainly in the form of diarrhoea, but also less commonly nausea and vomiting and thinning of the hair (Lindor, 2009). If patients do complain of gastrointestinal upset, then UDCA can be commenced at smaller doses, and then increased if tolerated until the patient's maximum tolerated level is reached. The use of obeticholic acid, sold as Ocaliva (Intercept, New York), has been approved for PBC in guidelines from EASL (Hirschfield et al, 2017). Monotherapy is suggested for patients who are intolerant to UDCA, while dual therapy is recommended for those with an inadequate response to UDCA.

Obeticholic acid (OBA) Since the original publication of the article this update is based on, new PBC treatment and management guidelines have been published by the British Society of Gastroenterology (BSG) in conjunction with UK PBC (Hirschfield et al, 2018). These UK guidelines

acknowledge recommendations produced by the European Association for the Study of the Liver (EASL) in 2017. One of the major changes in the management of PBC was the launch of a second line drug treatment option called obeticholic acid (OCA), which has been licensed and endorsed by the National Institute for Health and Care Excellence (NICE) (2017a), and acts by helping to reduce bile acid production and increase the flow of bile acids out of the liver. Patients who have failed to respond to UDCA, or are intolerant of the drug, can now have this medication prescribed either as dual therapy with UDCA, or as monotherapy. For an adult, the recommended prescribed dose is 5 mg once daily (OD) for 6 months, increasing to 10 mg OD if required and tolerated. However, this drug has known common side effects (Table 1), as well as the risk of serious liver injury in patients with moderate or severe hepatic impairment. The Medicines and Healthcare products Regulatory Agency, (MHRA) acknowledges this severe risk, recommending dose adjustment according to liver function tests, which is also the recommendation in the UK guidelines (Hirschfield et al, 2018). All patients defined as suboptimal responders to first line treatment with UDCA should be referred to specialist liver centres for assessment and suitability for second line treatment and initiation of close monitoring of liver function tests and side effects, such as itching, which can be a symptom of PBC and side effect of OCA. NICE (2017a) and BSG/UKPBC guidelines (Hirschfield et al, 2018) recommend that clinicians should monitor the response of OCA after 12 months of treatment and only continue with the treatment if there is clinical benefit. Compared to UDCA, OCA is expensive costing approximately £2384 per pack of 30 tablets. The cost does vary according to local procurement costs and patient access schemes with the Department of Health. NICE acknowledged the cost effectiveness of dual therapy with UDCA increased both life expectancy and quality of life (NICE 2017b). Transplantation Patients should be considered for transplantation either if their total bilirubin approaches 100 or if they score highly on a test used by clinicians to indicate the severity of liver disease. This would include a Model for End-stage Liver Disease (MELD) score greater than 12 or a United Kingdom model for End-stage Liver Disease (UKELD) score greater than 49. Patients with intractable pruritus can also be offered liver transplantation. Unfortunately, PBC recurs in around 20% of transplanted patients with associated symptoms of pruritis and fatigue (Poupon, 2010), although transplanted patients can still complain of fatigue (Hirschfield et al, 2017)

Box 1. Common side effects of obeticholic acid (OBA) • Constipation • Dizziness • Palpitations • Peripheral oedema • Fatigue • Increased temperature • Skin reactions (including pruritis) • Gastrointestinal discomfort • Oropharyngeal pain

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