Individualizing Care

Management Beyond Medical Therapy

Laura Cristoferi, MD[a], Alessandra Nardi, PhD[b], Pietro Invernizzi, MD, PhD[a], George Mells, MRCP, PhD[c], Marco Carbone, MD, PhD[a,d,*]

KEYWORDS

• Primary biliary cholangitis • Precision medicine • Risk-stratification
• Autoimmune liver disease • Individualized care • Novel therapies • Omics

KEY POINTS

- The forthcoming availability of several novel drugs in primary biliary cholangitis (PBC) coupled with the rise of high-throughput omics technologies prompt changing the paradigm of the management of the disease.
- Precision medicine (PM), through the application of omics-based approaches, should enable identifying disease variants, stratifying patients according to disease trajectory, risk of disease progression, and likelihood of response to different therapeutic options in PBC.
- The development of PM needs specific interventions, such as sequencing more genomes, creating bigger biobanks, and linking biological information to health data in electronic medical record.
- The authors envisage that a diagnostic work-up of PBC patients will include information on genetic variants and molecular signature that may define a particular subtype of disease and provide an estimate of treatment response and survival.

Primary biliary cholangitis (PBC) is a chronic, autoimmune liver disease characterized by nonsuppurative granulomatous cholangitis, causing progressive duct destruction and portal fibrosis that progresses slowly to biliary cirrhosis. A substantial proportion of cases eventually develops cirrhosis with attendant complications, such as portal hypertension, chronic liver failure, or hepatocellular cancer (HCC). PBC, therefore, remains a leading indication for liver transplantation (LT).

Advances over the past several years have improved the ability to individualize care in PBC. This is prescient: individualizing care is the aim of precision medicine (PM),

The authors have nothing to disclose.

[a] Division of Gastroenterology and Hepatology, Department of Medicine and Surgery, University of Milan Bicocca, Piazza dell'Ateneo Nuovo, 1, 20126 Milan, Italy; [b] Department of Mathematics, Tor Vergata University of Rome, Via della Ricerca Scientifica 1, Rome, Italy; [c] Academic Department of Medical Genetics, University of Cambridge, Hills Road 1, Cambridge, UK; [d] Academic Department of Medical Genetics, University of Cambridge, Cambridge, UK
* Corresponding author. Division of Gastroenterology and Hepatology, Department of Medicine and Surgery, University of Milan Bicocca, Piazza dell'Ateneo Nuovo, 1, 20126 Milan, Italy.
E-mail address: marco.carbone@unimib.it

Clin Liver Dis 22 (2018) 545–561
https://doi.org/10.1016/j.cld.2018.03.006
liver.theclinics.com

described as “an emerging approach for disease treatment and prevention that takes into account individual variability in genes, environment, and lifestyle for each person.”[1] The aim of PM is to enable health care workers and biomedical researchers to more accurately predict which treatment and prevention strategies for a particular disease will work in which groups of patients. It contrasts with a 1-size-fits-all approach, in which disease treatment and prevention strategies are developed for the average patient, with less consideration for interindividual variation.[1]

PM relies on biomarkers (or panels of biomarkers) that accurately predict key outcomes, such as treatment response or disease progression (Fig. 1). Biomarkers may be measurements in blood, urine, saliva, or other biofluids—but the concept also encompasses features on imaging and histology. Omics-based approaches, coupled with computational and bioinformatics methods, provide an unprecedented opportunity to accelerate biomarker discovery. Such approaches include genetic analysis (genome-wide genotyping of common to rare variants, exome sequencing, and whole-genome sequencing) and a plethora of approaches for profiling the epigenome, transcriptome, proteome, and metabolome (Fig. 2). PM is applicable to PBC, as it is to other chronic inflammatory conditions, especially now with the current and forthcoming availability of more efficacious medications.

The clinical features and investigations that already enable individualizing the care of PBC patients are reviewed—and how emerging biomedical technologies might improve the ability to individualize management of PBC patients in the future is speculated on. The premise throughout is that individualized care for PBC, current or future, should achieve the following major objectives:

- Identification of disease variants that may require different management, such as PBC with autoimmune features or the premature ductopenic variant
- Stratification of patients according to different disease trajectories that might require different forms of surveillance, such as portal hypertensive progression; hepatocellular failure-type progression, or progression to HCC

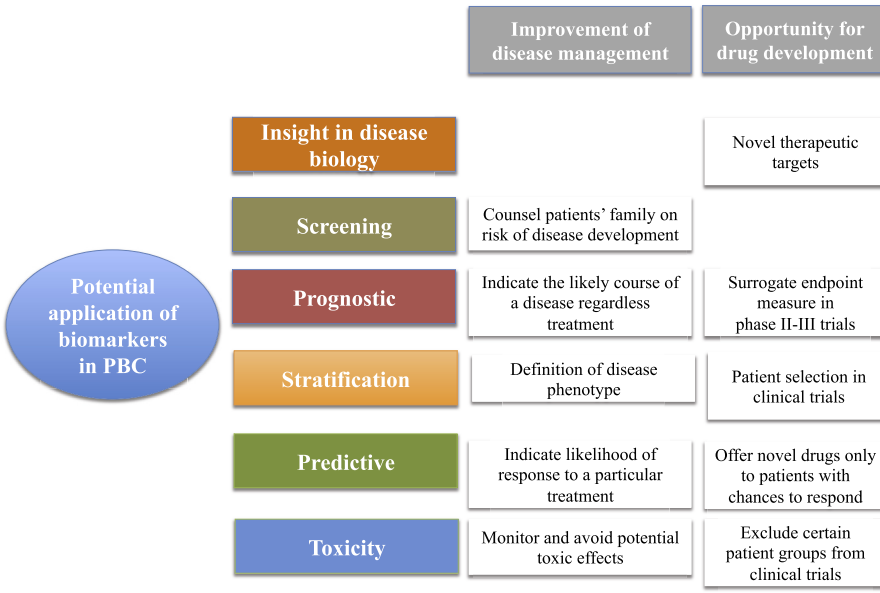

Fig. 1. Potential application of biomarkers in PBC.