Best Practice & Research Clinical Haematology 29 (2016) 100–110

Contents lists available at ScienceDirect

Best Practice & Research Clinical Haematology

journal homepage: www.elsevier.com/locate/beha

Present and future of personalized medicine in CLL

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Keywords:
Chronic lymphocytic leukaemia
Personalized medicine
Next-generation sequencing
Prognostic factors
Predictive factors

A B S T R A C T

Medicine has been 'personalized' (i.e. centred in persons) since its foundation. Recently, however, the term 'personalized medicine' (or, better, 'precision medicine') has been introduced to define 'a form of medicine that uses information about a person's genes, proteins, and environment to prevent, diagnose, and treat disease'. This concept has gained momentum thanks to next-generation-sequencing (NGS) techniques that allow identification of molecular characteristics unique to the patient and to the tumour. It is hoped that NGS will not only contribute to a better understanding of chronic lymphocytic leukaemia (CLL), but will identify disease subsets that could benefit from specific treatment interventions. Recent advances in diagnosis (e.g. high-resolution immunophenotyping, markers of genetic abnormalities), prognosis (e.g. biomarkers), response predictors [e.g. del(17p)/*TP53* mutations even at subclonal level], treatment (e.g. BCR signalling inhibitors, BCL2 antagonists, CAR-T cells) and methods to evaluate minimal residual disease constitute good examples of tools facilitating 'personalized' management of patients with CLL.

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http://dx.doi.org/10.1016/j.beha.2016.08.009
1521-6926/© 2016 Published by Elsevier Ltd.

Introduction

Chronic lymphocytic leukaemia (CLL) is a common disorder characterized by the accumulation of neoplastic $CD5^+$ B lymphocytes with a characteristic immunophenotype ($CD19^+$, $CD20^{weak}$, $CD23^+$) in blood, bone marrow and lymphoid tissues. The median age of patients at diagnosis is approximately 70 years. The incidence of CLL is approximately 4/100,000 people per year, and this increases markedly with age up to more than 20/100,000 per year in people aged >70 years. Despite significant progress in its management, CLL remains an incurable disease [1,2]. Continued improvement in understanding of the clinical and biological heterogeneity of CLL, and the development of non-cytotoxic targeted therapies are driving the management of this form of leukaemia based on an individualized, personalized approach [3,4].

What is personalized medicine?

Personalized medicine does not have a unique definition. The National Cancer Institute defines personalized medicine as 'a form of medicine that uses information about a person's genes, proteins, and environment to prevent, diagnose, and treat disease' [5]. Other terms such as 'individualized medicine', 'precision medicine', 'sequential medicine', 'stratified medicine' and 'genomic medicine' have been coined to describe what, in practical terms, is comparable, if not the same, to personalized medicine [6]. It can be argued that medicine has been 'personalized' (i.e. centred in people) since its foundation, as classically underlined by the maxim 'there are no diseases but people suffering from a given disease'. Currently, there is increasing confidence that modern techniques to study the immunophenotype, genetics, epigenetics, pharmacogenetics and all corresponding present and future 'omics', along with new and non-cytotoxic treatments will allow identification of the 'right treatment for the right patient'; one of the objectives of personalized medicine. Indeed, personalized medicine should be considered as part of, if not equivalent to, comprehensive patient management (Fig. 1). Readers interested in the history, development and conceptual aspects of personalized medicine are

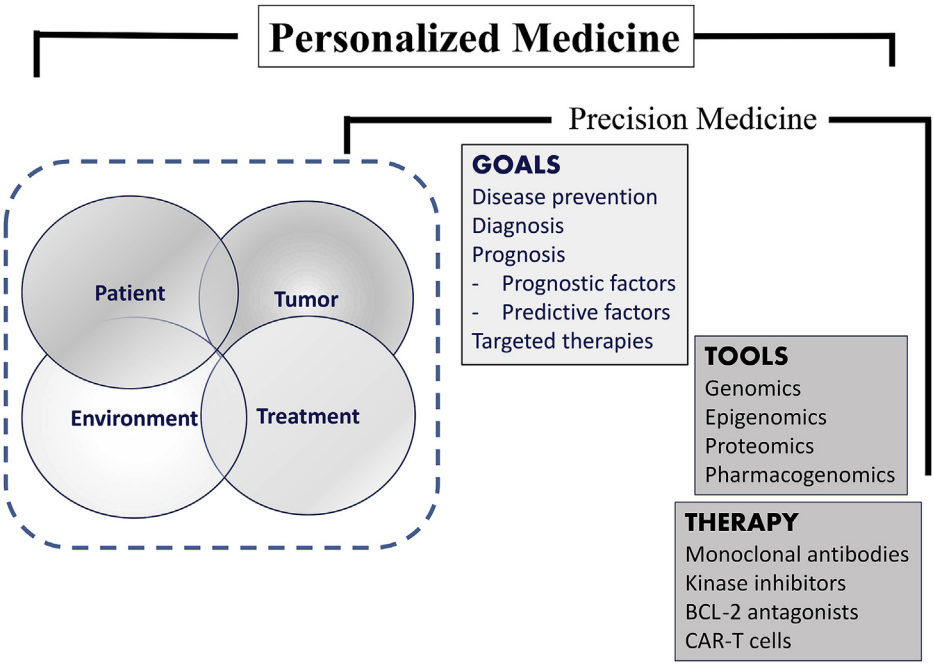

Fig. 1. Comprehensive, personalized and precision medicine.

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