Individualized modeling in CLL: the perspective of the clinicians.

The remarkable clinical heterogeneity of CLL has prompted several initiatives towards the development of prognostic models aiming to stratify patients into subgroups with distinct outcome. However, despite progress, the resultant prognostic models, mostly based on Cox regression analysis, have not been adopted in everyday clinical practice, mainly due to failure to provide sufficiently accurate predictions on a per patient basis.

We presented at ASH 2015 the results of a novel approach where we developed prognostic indices in CLL based not only on Cox regression analysis but also on alternative statistical methods, namely an ensemble learning algorithm based on decision trees (Adaboost). Our aim was to evaluate the accuracy of these prognostic models. In particular, within a cohort of 789 early stage CLL patients and with a median follow up of 8.5 years (0-40.5 years, >5 years for non-treated patients) we identified 3 risk groups: (i) high risk (HR): time-to-first-treatment (TTFT) <2 years; (ii) intermediate risk (IR): TTFT≥2 years and <5 years; and, (iii) low risk (LR): no need for treatment within 5 years from diagnosis. The developed prognostic indices concerned TTFT and were based on parameters such as gender, age, CD38 expression cytogenetic and immunogenetic profile which were available for all patients. We then evaluated the actual accuracy of each index based on the number of patients successfully assigned to their true risk group.

In a further step, we gave the same clinico-biological parameters used for the development of the prognostic models to 7 trained hematologists and asked them to assign each patient included in the study to one of the 3 risk groups; finally we compared the accuracy of the physicians choices to the outcome of the prognostic indices.

We now aim to expand the number of trained hematologists who voluntarily would agree to stratify the patients of the same cohort in the three mentioned groups based on their personal experience. In the link below you may find instructions regarding how you could participate in this study.

Instructions

Thank you for participating in this ERIC project. Please follow the instructions below:

In this excel file there are included 789 Binet A CLL patients along with their respective demographic (gender, age at diagnosis), immunogenetic (Germline Identity (GI) of IGHV gene and stereotyped subset assignment), FISH and immunophenotypic (CD38 expression) features . Each line corresponds to one patient and each column corresponds to one feature.

Please assign each patient to one of the 3 groups defined in **column L** based on the number list below:

- **1** stands for early need for treatment within two years from diagnosis **(HR)**
- **2** stands for need for treatment between the second and the fifth year from diagnosis **(IR)**
- **3** stands for no need for treatment within the 5 years from diagnosis **(LR).**

Please assign each patient to each risk group only once. You may download the excel file in order to assign the patients whenever you may have the time. Once you have completed the assignment, please send the file to Panagiotis Baliakas (see mail-address below). Try to not be influenced by the results of the analysis that were presented at ASH 2015. Deadline for the submission is the 30th of April.

For any clarification please contact Panagiotis Baliakas (email: panagiotis.baliakas@igp.uu.se)

Thank you for your participation in this ERIC project aiming in improving prognostication in CLL.