**ASBTRACT ESH 2021**

Title:

**Treatment-free remission - establishing a global registry**

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Background:

After the early groundbreaking reports demonstrating the feasibility of treatment-free remission (TFR) in CML, multiple clinical trials have been conducted to identify the most effective clinical pathway leading to a successful discontinuation of tyrosine kinase inhibitor (TKI) treatment. Factors such as rapidity of initial molecular response, duration and level of deep molecular response (DMR), 1$^{st}$ versus later generation TKIs, transcript type, and haplotype of killer-cell immunoglobulin-like receptors have all been suggested to influence the duration of TFR. Available data, however, is still mainly based on clinical trials with relatively small patient numbers. Thus, robust predictive models still remain to be identified. Furthermore, there have been reports on single cases of CML disease progression in association with TKI-stopping attempts, a concern of foremost clinical importance. Although this progression risk has been deemed as small, it has not yet been sufficiently addressed in published studies. Today a large majority of TKI-stopping attempts are being conducted outside controlled prospective studies. To be able to accumulate large enough data to effectively elucidate important TFR issues a broad international collaborative approach, involving multiple population-based CML registries, is therefore needed.

Objectives:

To address these issues the international CML foundation (iCMLf) has announced a project to establish and maintain a *Global Treatment-Free Remission Registry*. The two main objectives of the registry are to (1) construct a clinical prediction model and (2) continue assessing the safety of TFR.

Methods:

During the fall of 2021 we plan to conduct a comprehensive survey aimed at key clinical and academic individuals to identify already available prospectively and retrospectively collected clinical and laboratory data, as well as data from clinical trials. Furthermore, we will identify the legal frameworks, including national laws and regulations, that need to be addressed in order to generate a prospective global TFR cohort.

The initial survey will then be used to include collaborating countries and/or organizations, ultimately to generate a global registry utilizing competences from all over the world to conduct sound TFR research. The initial survey also serves to identify a reasonable “minimal clinical dataset” with a trade-off between temporal-data resolution, the possibility to study variables agnostically and to have homogeneity between variables between included countries and/or organizations. As a part of the registry, we also intend to maintain a virtual tissue database, with information on tissue sampling point, necessary clinical information and access policies to allow for analysis of samples with the intent to identify clinically actionable biomarkers of TFR success or failure.

Already existing prospective cohorts may be combined in order to, in a data-driven method, conduct exploratory analysis with the aim of identifying variables that should be included in a prospective cohort.

Results:

A outline of the suggested database is depicted in Figure 1.

Conclusions:

In order to answer the main outstanding questions related to TFR, in particular those related to predictive factors and safety issues, the formation of the global joint registry initiative appears highly warranted. With initial surveying of the global community, the details of a collaborative registry can be identified.

Figure 1. Schematic drawing of a global TFR registry.