What can we learn from cancer registries?

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In this issue of Haematologica, Maya Schulpen and colleagues report their population-based study of non-Hodgkin lymphoma (NHL) patients in the Netherlands focused on the examination of survival outcomes among a cohort comprising 5,600 children, adolescents, and young adults (AYA). Individuals were diagnosed with Burkitt lymphoma (BL), diffuse large B-cell lymphoma (DLBCL), T-cell lymphoblastic lymphoma (T-LBL) and anaplastic large cell lymphoma (ALCL) between the years 1990 and 2015.[1]

All data was sourced from the nationwide population-based Netherlands Cancer Registry (NCR). The analysis addresses a critical and relevant topic elucidating trends in survival and disparities between pediatric and AYA NHL patients. Further, it initiates to bridge the knowledge gap concerning the relevance of patient age at the time of diagnosis to survival outcomes.

Two major aspects contribute to the relevance of the analysis: firstly, the data acquisition employed a population-based approach within a prototypical Western Europe country. Although not explicitly presented in the paper, these data can be reasonably regarded as representative of Western countries. The second important aspect is that the data for all age groups were provided from the same registry data base and thus, following identical procedures of data collection, quality control and data analysis. Analyses like these underline the high value of national cancer registries covering all age groups.

In the context of this specific paper, the authors presented a constant improvement of survival for all analyzed NHL entities comparing children and adolescents with young adults. This favorable trajectory is notably prominent, with the exception of a relatively small cohort of young adults with ALCL wherein survival rates did not increase between 1990-99 and 2000-09, but in the following period until 2015. Results like these are of major relevance and impact for patients and their families, healthcare professionals, heath insurances, politics etc. In addition, there is a high value of publishing such expansive data providing patient characteristics and treatment for more than 5,600 patients. These data will serve as comparator for many subsequent studies.

Results of the analyses of cancer registry data for non-Hodgkin lymphoma patients

The most frequent histological subtypes of NHL in children and adolescents are analyzed in the current study. Specifically, in BL survival rates are reported to be comparatively lower amongst young adults compared to children and adolescents; however, a relevant improvement over time, especially in the AYA cohort, was reported. A similar trend is observed for T-LBL patients with substantial variation in survival according to age at diagnosis. Interestingly, there are no or only minor survival differences for DLBCL and ALCL comparing the different age groups. From the perspective of a pediatrician, an intriguing commonality emerges between BL and T-LBL on one hand and DLBCL and ALCL on the other: the rescue chance for patients with refractory or relapsed disease (r/r). Despite all efforts, there is still almost no second chance for r/r BL and r/r T-LBL, while survival for r/r DLBCL and ALCL reaches more than 50%. To what extent does this knowledge and empirical evidence contribute to the observed variations in survival rates among different age cohorts?

Limitations of cancer registry data analyses

Why?

The main scientific limitation inherent to studies based on cancer registry data is the restricted availability of data resources to comprehensively address the question “Why?”. While the current study has revealed several statistically significant differences, the existent dataset proves to be insufficient to explain the underlying reasons for these differences or to explain the absence of distinctions among other cohorts. More extensive datasets are needed in cancer registries, to go into the details of questions reaching further, e.g., data on predisposition, diagnostics, treatment, treatment-related toxicities and cause of deaths. Adherence to data protection guidelines

and additionally, the supplementary documentational requirements mandated by treating institutions and the concurrent requests for extensive documentation for a cancer registry represent another significant reason limiting the available datasets in conventional cancer registry studies. Consequently, studies such as the currently discussed are constrained as e.g., differences in treatment or treatment intensity can not be adequately taken into account. This leads to certain inaccuracies that need to be studied in subsequent projects. The strength of cancer registry studies might be to describe and raise questions.

The reported survival differences in NHL patients according to age are probably multifactorial. Both, cancer registry data analyses and translational studies on well-defined patient cohorts with access to biological samples are needed to study how aspects like

- patient characteristics like age and sex,[2] weight, body surface area, predisposition
- biology of the tumor, molecular characteristics[3]
- treatment intensity and treatment tolerability
- treatment compliance
- country of residence[4]
- participation in a clinical trial
- access to new drugs
- supportive care
- psychosocial conditions and family support

and others contribute to these differences.

There is another hot topic that is touched on in the current manuscript: the highly relevant discrepancies and extensive delays in drug development for children and adolescents compared to adults. Rituximab has emerged as game changer for mature B-cell lymphoma.[5] Rituximab was approved for adults in the late 90th, while approval for children and adolescents with advanced B-NHL was given in 2021. Research efforts such as the current study, underscore the need for smarter approaches of drug development for vulnerable patient populations to allow access to new drugs.[6,7]

Disclosures

No conflicts of interest to disclose.

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