Survival time trends for major lymphoid malignancies in Europe and USA

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Rationale

Lymphoid malignancies (LMs) are a group of blood cancers including non-Hodgkin lymphoma (NHL), Hodgkin lymphoma (HL), plasma cell neoplasms and lymphoid leukaemias. Incidence rates in Europe and the USA are generally similar ((30/100000 vs. 35/100000), accounting for approximately 50% of all haematological malignancies (HMs), in both Europe and US [1,2]). The first comparative analyses of population-based European and US survival data including patients diagnosed in the late 1990's, using the HAEMACARE and SEER databases, evidenced remarkable survival differences between European countries [3] and between Europe and US [4,5]. The interpretation of results, however, was complicated by inconsistencies in inclusion and classification (overall or subtype-specific) criteria. The HAEMACARE project [6], implemented on the EUROCARE database [7], promoted the harmonisation and standardisation of HM cancer registry data, and the uniform adoption of updated International Classification of Disease for Oncology (ICD-O) [8] subtype classifications. Furthermore, since the 2000s, innovative effective treatments have became available for many HMs [9-13], but access to these treatments is not uniform across regions and continents, or groups of patients, and survival differences were confirmed also by the last EUROCARE-5 analyses [14,15].

Aims

The aims of our study are:

- To compare survival for LM and its subtypes in Europe and USA, using the two largest databases presently available for epidemiologic and public health research, i.e. US-SEER [16] and HAEMACARE/EUROCARE. Over time changes in survival will be compared between the two continents;
- Survival will be analysed by specific disease subtypes, focussing on LM subtypes benefiting from novel treatments available since late nineties (e.g. rituximab);

- To help elucidate reasons for survival differences, by multivariate models adjusting by registry, sub-geography, age, gender, and disease subtype, taking into consideration the country specific general mortality.

Material and Methods

For our analyses, carried out on individual data, we need information on patient:

- gender
- date of birth and/or age at diagnosis
- date of diagnosis
- vital status
- date of last vital status check
- geographic region/cancer registry
- morphology, coded according to the 3rd edition of ICD-O (ICD-O-3 [8]),

for all adult (≥15 years) patients diagnosed from 1996 to the last available complete incidence year (for EUROCARE orientatively 2007) with LM followed up to the end of 2008, using HMs data recorded in the population-based HAEMACARE/EUROCARE and SEER databases.

In particular, we would like to focus on those HMs for which effective treatments were made available since early 2000s and grouped according to HAEMACARE criteria [6]:

Hodgkin Lymphoma (HL, ICD-O-3 codes: 9650-9655, 9659, 9661-9667)

Non-Hodgkin lymphoma (NHL: 9675, 9690-9698, 9678-9684, 9673, 9687, 9826, 9596, 9671, 9760-9762, 9764-9767, 9689, 9699, 9750-9758, 9833, 9940, 9700-9719, 9827-9831, 9834, 9948) – *to be divided in detailed groups depending on data availability* –

Lymphoid leukaemias, including:

Chronic Lymphocytic Leukaemia and Small B lymphocytic lymphoma (CLL/SBLL: 9670, 9823)

Precursor lymphoblastic leukaemia/lymphoma (LBL/L: 9727-9729, 9835-9837)

Multiple Myeloma/Plamocytoma (MM/P: 9731-9734).

To compare the completeness of morphology codes and to be sure to carry out analyses on comparable data, information on poorly specified tumours (Lymphoid malignancy of unknown type: 9590, 9820, 9832; NHL of unknown type: 9591) should be also provided.

Statistical methods

A unique database will be realised by merging the HAEMACARE/EUROCARE and the US-SEER databases; standardized statistical methods will be used to estimate net survival, i.e. the survival of patients with cancer in the hypothetical situation where the cancer may be assumed to be the only possible cause of death (it can be interpreted as cancer survival after controlling for competing causes of death). The unbiased and non-parametric Pohar-Perme estimator [17] will be considered.

We will focus on both age-specific and age-standardised survival estimates. As regards age at diagnosis, it will be categorised in different groups specific for the analysed haematologic entity.

Survival estimates will be age-standardised using the International Cancer Survival Standards [18].

We will also estimate the excess risks of death (or excess mortality ratios) during 5 years after diagnosis in the framework of regression models (taking into account the possibility to model both linear effects and non-linear and/or timedependent [interaction with time since diagnosis] effects of age using restricted-cubic splines [19,20]) adjusting for age, sex, country.

For the time trends analyses, calendar period will be included as covariate in the regression models.

Several regression models will be tested and the choice of the best model will be based on the likelihood ratio test or the Akaike information criterion for goodness of fit [21], depending on the regression models fitted.

All the analyses will be carried out using the 12th version of STATA Statistical software [22].

Timing

The collaborative analyses on EU and US data will start approximately in March/April 2015. A draft of the paper will be circulated among the EUROCARE Working Group during summer or within mid October 2015.

The Italian team at the Fondazione IRCCS Istituto Nazionale Tumori will carry out the main statistical analyses, the US-SEER team at the Cancer Prevention Institute of California will participate finalizing the study design, collaborating to data checks and results interpretation, and writing article.

Further authors to be involved:

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