Brief Report

Stem Cell INVESTIGATION

Incidence of acute promyelocytic leukemia across Europe: results of RARECAREnet—a population-based study

Avinash G. Dinmohamed[1,2,3,4], Otto Visser[5]

[1]Department of Research and Development, Netherlands Comprehensive Cancer Organisation (IKNL), Utrecht, The Netherlands; [2]Department of Public Health, Erasmus University Medical Center, Rotterdam, The Netherlands; [3]Amsterdam UMC, Vrije Universiteit Amsterdam, Department of Hematology, Cancer Center Amsterdam, Amsterdam, The Netherlands; [4]Amsterdam UMC, University of Amsterdam, Department of Hematology, Cancer Center Amsterdam, Amsterdam, The Netherlands; [5]Department of Registration, Netherlands Comprehensive Cancer Organisation (IKNL), Utrecht, The Netherlands

Correspondence to: Avinash G. Dinmohamed. Department of Research and Development, Netherlands Comprehensive Cancer Organisation (IKNL), Utrecht, The Netherlands. Email: a.dinmohamed@iknl.nl.

Abstract: The scarcity of studies performed over the past decades in Central and South America provided clues that the prevalence of acute promyelocytic leukemia (APL)—a rare and distinct subtype of acute myeloid leukemia—might be higher among descendants of Spaniards, as compared to other ethnic groups. Currently, a comprehensive apprehension on APL incidence across Europe has yet been established. Therefore, we conducted a population-based study to assess the incidence of APL across Europe. We selected all patients diagnosed with APL in Europe from the RARECAREnet database that holds data from 94 cancer registries across 27 European countries on rare malignancies diagnosed during 2000–2007. Age-standardized incidence rates (ASRs) with 95% confidence intervals (CIs) were calculated for the European pool per 100,000 person-years. Also, crude incidence rates with 95% CIs were calculated per 100,000 person-years by country. Overall, 1,876 patients with APL (48% male and 24% aged ≥65 years) were included in our analytic cohort. The overall ASR of APL was 0.112 (95% CI, 0.107–0.117) in Europe. The incidence of APL varied considerably across Europe, with the highest incidence in Spain (0.257; 95% CI, 0.205–0.317), as compared to the European average. Altogether, these finding adds additional support to the hypothesis that APL might be more prevalent among individuals with Spanish ancestry. Future research is warranted to specifically explore etiologic factors of APL across different genetic and environmental backgrounds.

Keywords: Acute promyelocytic leukemia (APL); incidence; epidemiology; registry

Received: 04 September 2019; Accepted: 08 October 2019; Published: 26 November 2019.
doi: 10.21037/sci.2019.10.03
View this article at: http://dx.doi.org/10.21037/sci.2019.10.03

Acute promyelocytic leukemia (APL) is a rare, highly treatable form of acute myeloid leukemia (1). The paucity of studies conducted in Central and South America hint towards a higher prevalence of APL among descendants of Spaniards, as compared to other ethnic groups (2-4). At present, a comprehensive study that delineates potential disparities in APL incidence across Europe has yet been reported.

Therefore, we conducted a population-based study to assess APL incidence across Europe using the RARECAREnet database that holds data from 94 cancer registries across 27 European countries on rare malignancies diagnosed during 2000–2007 (5). To account for completeness and quality, only the pool of 83 cancer registries across 24 European countries that provided data for all cancer types is considered.

Age-standardized incidence rates (ASRs) with 95% confidence intervals (CIs) were calculated per 100,000 person-years for the overall cohort and by sex. These rates were standardized as per the European standard population to account for differences in age structure across countries. Furthermore, crude incidence rates with 95%

Country	No. of cases	Incidence rate per 100,000	(95% CI)
Spain	86	0.257	(0.205 - 0.317)
Iceland	6	0.256	(0.094 - 0.556)
Malta	6	0.188	(0.069 - 0.410)
Slovenia	30	0.188	(0.127 - 0.268)
France	70	0.180	(0.140 - 0.227)
The Netherlands	226	0.174	(0.152 - 0.199)
Italy	195	0.165	(0.142 - 0.190)
Switzerland	28	0.158	(0.105 - 0.228)
United Kingdom	656	0.137	(0.127 - 0.148)
Norway	49	0.134	(0.099 - 0.177)
Republic of Ireland	42	0.129	(0.093 - 0.175)
Portugal	65	0.127	(0.098 - 0.162)
Estonia	13	0.120	(0.064 - 0.205)
Belgium	57	0.118	(0.089 - 0.153)
Germany	158	0.112	(0.095 - 0.131)
Slovakia	37	0.098	(0.069 - 0.135)
Lithuania	20	0.083	(0.051 - 0.128)
Czech Republic	66	0.081	(0.062 - 0.102)
Austria	23	0.035	(0.022 - 0.053)
Bulgaria	20	0.032	(0.020 - 0.049)
Poland	9	0.023	(0.010 - 0.043)
Finland	7	0.017	(0.007 - 0.034)
Latvia	3	0.016	(0.003 - 0.047)
Croatia	4	0.011	(0.003 - 0.029)
Europe	**1,876**	**0.120**	**(0.114 - 0.125)**

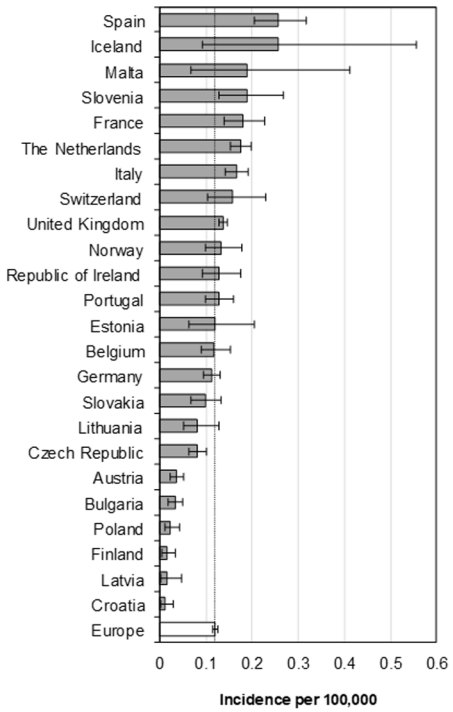

Figure 1 Incidence of APL across Europe, 2000–2007. Crude incidence rates are presented per 100,000 person-years. The error bars represent the 95% CI of the incidence estimates. The dotted line represents the European average. APL, acute promyelocytic leukemia; CI, confidence interval.

CIs were calculated per 100,000 person-years for the overall cohort and four age groups, and by country.

Our analytic cohort included 1,876 patients with APL, of whom 48% were male and 24% aged ≥65 years. The overall ASR of APL was 0.112 (95% CI, 0.107–0.117) in Europe, with similar ASRs between males (0.111; 95% CI, 0.103–0.118) and females (0.114; 95% CI, 0.107–0.122). The age-specific incidence rates of APL were 0.034 (95% CI, 0.028–0.042), 0.077 (95% CI, 0.066–0.090), 0.138 (95% CI, 0.130–0.146), and 0.181 (95% CI, 0.165–0.198) in the age groups 0–14, 15–24, 25–64, and ≥65 years, respectively. The incidence of APL varied markedly across Europe, with the highest incidence in Spain (0.257; 95% CI, 0.205–0.317; *Figure 1*). Of note, particular country-specific estimates should be interpreted with caution, as small sample sizes increase the wideness of 95% CIs and made it expedient to compute rates without age standardization. Furthermore, aspects related to under-registration and/or under-diagnosis of cases might plague particular registries and/or countries, particularly in Austria, Bulgaria, Poland, Finland, Latvia, and Croatia.

Collectively, the incidence of APL was the highest in Spain, as compared to the European average. This finding adds further support to the hypothesis that APL might be more prevalent among individuals with Spanish ancestry. Notwithstanding this finding, environmental factors might also influence susceptibility to APL. Therefore, forthcoming studies are warranted to specifically investigate etiologic factors of APL across different genetic and environmental backgrounds.

Acknowledgments

The authors would like to thank all members of the RARECAREnet working group for contributing data to the RARECAREnet database.

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects

of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The current study was performed with publicly available data from the RARECAREnet database (http://www.rarecarenet.eu/).

References

1. Cicconi L, Lo-Coco F. Current management of newly diagnosed acute promyelocytic leukemia. Ann Oncol 2016;27:1474-81.
2. Douer D, Preston-Martin S, Chang E, et al. High frequency of acute promyelocytic leukemia among Latinos with acute myeloid leukemia. Blood 1996;87:308-13.
3. Otero JC, Santillana S, Fereyros G. High frequency of acute promyelocytic leukemia among Latinos with acute myeloid leukemia. Blood 1996;88:377.
4. Swords R, Sznol J, Elias R, et al. Acute leukemia in adult Hispanic Americans: a large-population study. Blood Cancer J 2016;6:e484.
5. Gatta G, Capocaccia R, Botta L, et al. Burden and centralised treatment in Europe of rare tumours: results of RARECAREnet-a population-based study. Lancet Oncol 2017;18:1022-39.

doi: 10.21037/sci.2019.10.03
Cite this article as: Dinmohamed AG, Visser O. Incidence of acute promyelocytic leukemia across Europe: results of RARECAREnet—a population-based study. Stem Cell Investig 2019;6:37.