

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

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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. Agestandardized 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

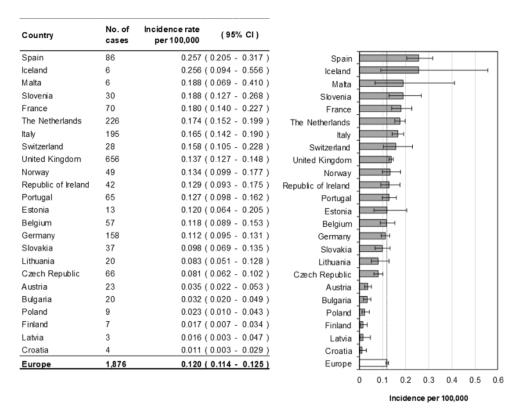
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Acute promyelocytic leukemia (APL) is a rare, highly treatable form of acute myeloid leukemia (1). The paucity of studies conducted in Central and South America hint towards a higher prevalence of APL among descendants of Spaniards, as compared to 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%



**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 underregistration 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.

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## **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/).

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