# Unexpectedly **High Fatality Rate** in Globally Collected Spontaneous Reports of **Progressive Multifocal Leukoencephalopathy** with **Alemtuzumab**

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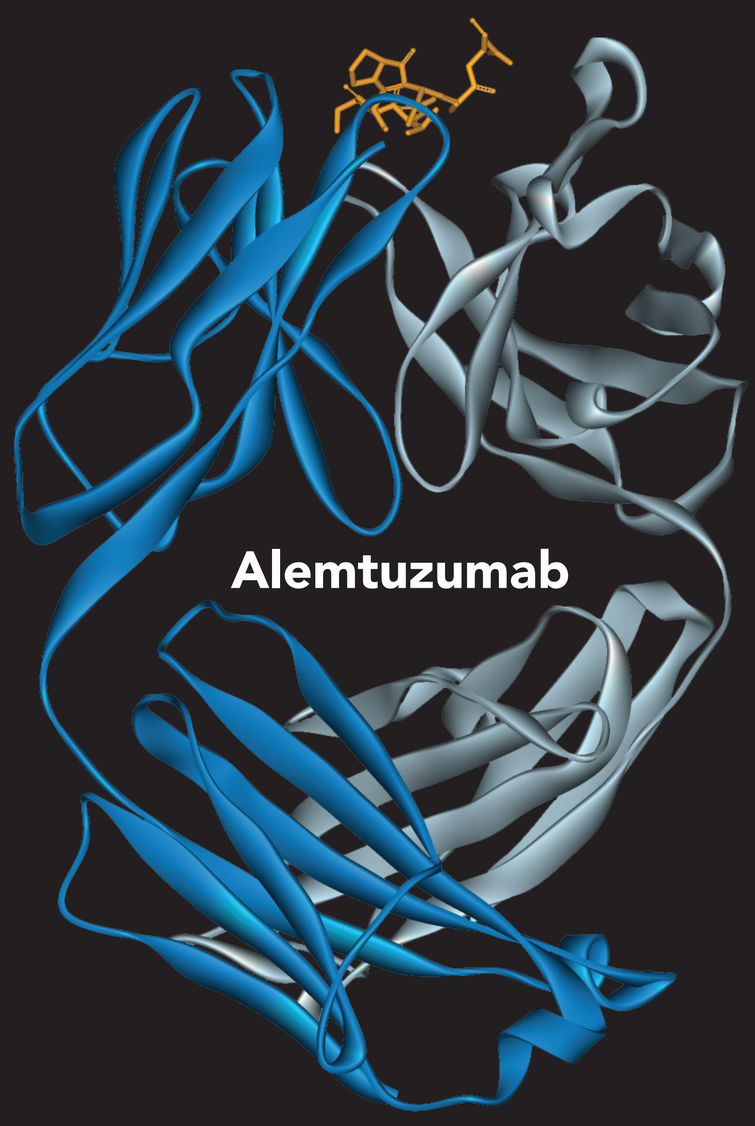
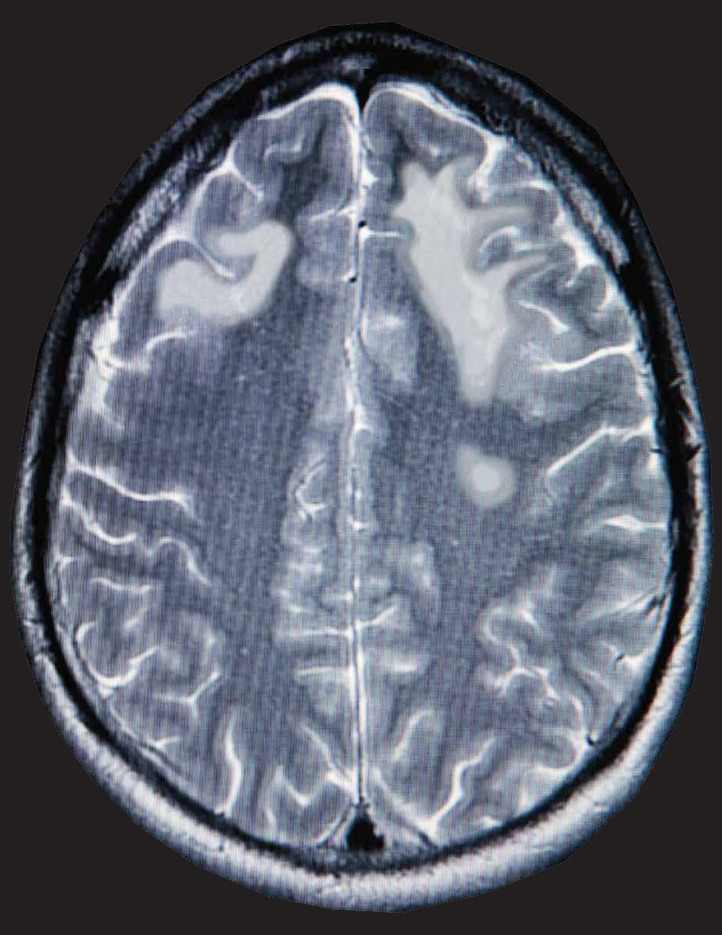
## Introduction

Alemtuzumab is an immunomodulating monoclonal antibody (mAb) targeting the CD52 antigen of lymphocytes. Its indications are B-cell chronic lymphocytic leukaemia and relapsing-remitting multiple sclerosis, but uses include other immunosuppressive and antineoplastic conditions. Like several other mAbs, alemtuzumab has been associated with progressive multifocal leukoencephalopathy (PML), a rare but serious demyelinating disease induced by JC virus infection [1]. The characteristics of alemtuzumab-associated PML, including its fatality rate, are largely unknown.




**Progressive Multifocal Leukoencephalopathy (PML)**



## Aim

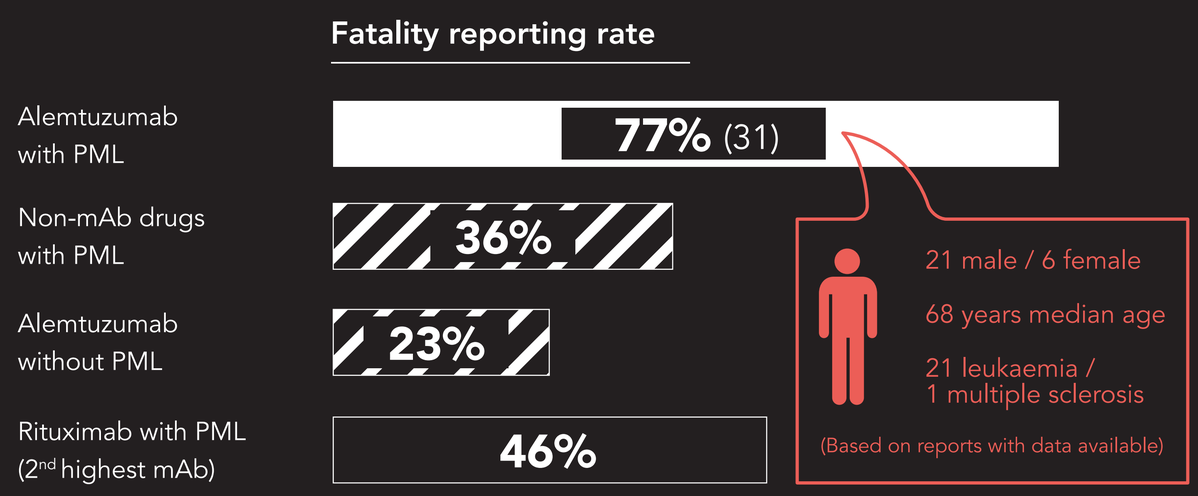
To identify and describe the most prominent characteristics of globally collected spontaneous reports on alemtuzumab with PML.

## Methods

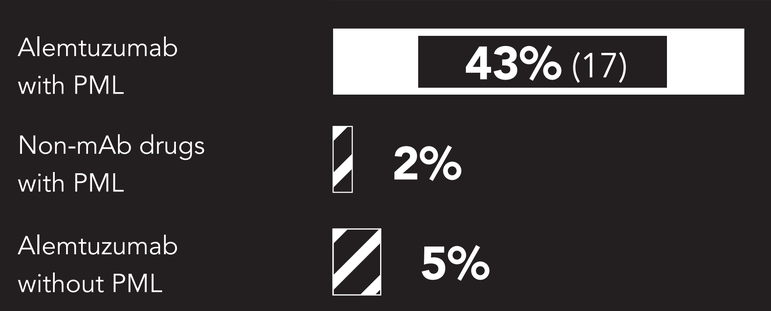
Data were taken from VigiBase, the WHO global database of individual case safety reports, as of 15 September 2016, after exclusion of suspected duplicates [2] and reports with HIV/AIDS treatment. Alemtuzumab reports with PML were compared to (a) PML reports for non-mAb drugs, and (b) alemtuzumab reports with suspected reactions other than PML, with respect to reporting rates of numerous different characteristics including patient age and sex, fatality, and co-reported drugs and adverse reactions. Analysis was performed with vigiPoint, a method that identifies reporting characteristics deviating significantly between a foreground of reports and a suitable reference group of reports, in terms of log odds ratios [3].

## Results

**Fatality reporting rate**




**Co-reporting with rituximab**




## Conclusion

In VigiBase, the proportion of fatal cases in alemtuzumab-associated PML is high both in absolute and relative terms. The typical patient is male, above middle age, and treated for leukaemia. Concurrent use of alemtuzumab and rituximab may synergistically add to the PML risk, although this hypothesis warrants independent verification. These results refer to reporting patterns, and causality has not been assessed. Fatality rates in spontaneous reports are expected to be inflated due to differential under-reporting.

## References

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## Disclosure

The authors are indebted to the national centres that contribute data to the WHO Programme for International Drug Monitoring. However, the opinions and conclusions in this study are not necessarily those of the various centres, nor of WHO.

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