Comment on: Viral infections in pediatric brain tumor patients treated with targeted therapies

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Dear Dr. Newburger,

We have read with great enthusiasm the article titled **Viral infections in pediatric brain tumor patients treated with targeted therapies** by Lisa Mayr et al [1]. We commend the authors' efforts in collating epidemiologic data and investigating infectious outcomes between pediatric patients being treated with targeted therapy versus conventional therapies. It was a pleasure to read such a well-written paper. We concur with the conclusion that patients receiving targeted therapies are made more susceptible to developing viral infections than those receiving conventional treatment. However, we would like to draw attention to some key points regarding the study following a thorough appraisal.

To begin with, the retrospective nature of the study adds several unavoidable biases such as recollection bias and incorrect data retrieval, which may have been mitigated had the investigators included current cases at the time. The study is also limited in its single-centered scope making it difficult to generalize the findings to this particular pediatric demographic. Moreover, the comparison between the two subsets of brain tumor patients is also subject to several partialities. For instance, it is noted that those receiving targeted therapies were managed in an outpatient setting and by extension, exposed to greater environmental stressors than those being managed on conventional chemotherapy. As a result, a greater proportion of virological infections were reported in children receiving targeted therapy than those being managed conventionally. Further, due to the lack of available data correlating disease severity with treatment option, the possibility that patients receiving conventional chemotherapy simply had a lower disease grade than those on targeted therapies and vice versa exists. Knowing this is pertinent as the body's ability to fight off infections is greatly influenced by the grade of cancer and hence degree of inflammation [2]. Next, it remains to be seen what the baseline nutritional status of the participants was as nutrition and metabolism are known to have a bearing on immune status and hence infectious susceptibility [3]. Finally, the deduction that patients treated with bevacizumab or mTOR (mechanistic target of rapamycin) inhibitors suffered more infections than those treated with other targeted therapeutic drugs cannot be made with certainty as not enough patients were treated with drugs other than bevacizumab or mTOR inhibitors for a fair and accurate comparison.

In conclusion, multi-centered prospective studies are required to better lay claims regarding infectious outcomes and attention to potential influencers of immunity must be given to minimize bias in future studies.

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