

Clinical trial finds therapy to be well-tolerated in patients with aggressive brain tumour

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A phase I clinical trial that set out to assess the safety of a new combination therapy for a type of aggressive brain tumour has found the treatment to be well tolerated in patients.

The trial used a treatment combination of ADI-PEG20, pemetrexed and cisplatin, which showed encouraging efficacy in patients with recurrent high-grade gliomas (HGGs), a disease for which little progress has been made over the last few decades.

In the trial, led by Professor Peter Szloserek from Queen Mary University of London and Barts Health NHS Trust, ten patients with heavily pre-treated, recurrent HGG were treated with ADI-PEG20 in combination with standard chemotherapies pemetrexed and cisplatin.

This clinical work built upon pre-[clinical studies](#) performed at Queen Mary's Barts Cancer Institute (funded by Cancer Research UK) and Imperial College London (funded in part by Brain Tumour Research), which identified that ADI-PEG20 can enhance the effects of other standard chemotherapies such as pemetrexed and cisplatin.

Normal cells are able to generate their own supply of the essential amino acid arginine, which is required for a variety of cellular processes. However this capability is lost in many tumour types due to the downregulation of the ASS1 enzyme required for arginine production.

Consequently, tumour cells rely on the arginine supply in the blood stream, a vulnerability that can be exploited therapeutically. ADI-PEG20 works by depleting arginine in the blood, thus 'starving' tumours of this essential amino acid.

Combining the concept of arginine deprivation with pemetrexed and cisplatin has proven efficacious in other cancer types, including treatment-resistant ASS1-deficient mesothelioma or non-[small cell lung cancer](#).

The findings of the trial, published in *Clinical Cancer Research*, are an important step forward for this historically under-funded area of research, for which there is a very [poor prognosis](#) and no recognised standard of care treatment currently.

Sue Farrington Smith, Chief Executive, Brain Tumour Research said: "Poor funding for research has meant options and outcomes for brain [tumour](#) patients haven't improved in line with other forms of cancer where the research is better funded. We must change this. The collaboration of two of our research centres shows that progress can be made and spurs on our efforts to work with the Government and larger [cancer](#) charities to make sure there is a better future for those diagnosed with this devastating disease and their families."

Dr. Peter Hall, first author of the study and the main Specialist Registrar for the trial at Barts Health NHS Trust, said: "This trial represents an important first step in developing a biomarker-led approach to treating recurrent high-grade gliomas, a disease which has lacked funding historically and for which the outlook remains very poor."

As the treatment was shown to be well tolerated in [patients](#), the results of this trial pave the way for a phase II trial to include a larger patient cohort to further assess efficacy, which is currently being developed.

More information: Peter E. Hall et al. A Phase I Study of Pegylated Arginine Deiminase (Pegargiminase), Cisplatin, and Pemetrexed in Argininosuccinate Synthetase 1-Deficient Recurrent High-grade Glioma, *Clinical Cancer Research* (2019). [DOI: 10.1158/1078-0432.CCR-18-3729](https://doi.org/10.1158/1078-0432.CCR-18-3729)

Provided by Queen Mary, University of London

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