MedicalXpress

Study picks out children with incurable brain cancer who could benefit from adult therapy

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Children with incurable brain tumours could benefit from potentially life-extending treatment if genetic testing was used to personalise therapy as it is in many adults, major new research reports.

Scientists analysed the DNA of children taking an adult cancer drug on a clinical trial deemed to have 'failed', and found that many with particular genetic traits had actually responded well to treatment.

Some of these children survived more than a year longer than others on the trial.

The international study—led by a team at The Institute of Cancer Research, London, and involving 51 centres in 14 countries—found that children whose tumours had mutations in the MAPK network of genes benefited from Avastin (bevacizumab) alongside standard treatment.

In these children, Avastin also appeared to cause immune cells to flood in to help destroy their tumours—raising the possibility that they could be good candidates for future immunotherapy.

Children's aggressive, or 'high grade', brain tumours are currently treated as one disease, but a recent genetic analysis by the same team at The Institute of Cancer Research (ICR) showed they were actually at least 10 different diseases.

The new research shows the benefits of testing children for genetic

mutations in their tumours to make sure they receive the treatment most likely to work.

Increasingly, treatment of adult cancers is shaped by genetic testing, but children's cancer continues to lag behind.

The new independent academic study—published today (Monday) in the prestigious journal *Cancer Cell* and funded by Roche—analysed genetic, molecular and immunology data from the HERBY phase II clinical trial after it had been completed.

The researchers will now look to confirm the findings in a clinical trial set up specifically to test the effectiveness of Avastin in children with these mutations. If successful, it would open up a whole new treatment option for a disease with very few effective therapies.

This trial compared Avastin combined with standard treatment of temozolomide and radiotherapy with standard treatment alone in 121 children aged three to 18 with high-grade brain tumours.

The trial found that, overall, children did not benefit from the addition of adult cancer drug Avastin—a drug that works by blocking a tumour's blood supply and drawing the immune system to the cancer.

But looking deeper into the genetics of the tumours revealed that children taking Avastin whose tumours had mutations in the MAPK network of genes—around 10-15 per cent of the total—survived up to 16 months longer than other patients.

These children also saw many more immune cells called killer T cells flock to the site of their tumours—in some cases because their cancers had more mutations overall and so were easier for the immune system to pick apart from healthy cells.

Children with these tumours could potentially be considered for future clinical trials of immunotherapies, which tend to work best in patients whose cancers have already sparked some immune reaction.

Children with tumours that were driven by mutations in the histone H3F3FA gene did not benefit from Avastin, with an average survival of only 7.9 months, and there were very few immune cells present in and around the tumour.

Researchers at the ICR—a research institute and charity—believe that testing for mutations could help direct treatment so some children are picked out for Avastin, and others spared treatment that is very unlikely to work for them.

Although rare, aggressive childhood brain tumours are the biggest cause of cancer-related death under 19 years of age because survival rates are so poor—children with these tumours are only expected to live an average of nine to 15 months.

Study leader Professor Chris Jones, Professor of Childhood Brain Tumour Biology at The Institute of Cancer Research, London, said: "We will never see progress in treatment of children's brain cancers while we continue to lump everyone with these cancers together in one group. Children deserve better.

"Our research has previously shown that children's brain cancer is really 10 different diseases, and our new study found these genetic differences can have a major impact on how children respond to drugs. We are building up evidence that genetic testing in children with cancer can have real benefits for selecting the best treatment.

"The next step is to confirm our findings in a clinical trial where only children with these specific mutations receive Avastin. If that is

successful, we can open up a promising new option for paediatric brain cancer by turning an established drug for adult cancers into a targeted treatment for children."

Professor Paul Workman, Chief Executive of The Institute of Cancer Research, London, said: "We've seen dramatic progress in the treatment of adult cancers, through advances such as the introduction of targeted therapies and more recently immunotherapies. But that progress hasn't yet been matched in children.

"This exciting research is giving us the tools to personalise treatment for children with brain cancer. It's vital that we take advantage of advances in research by improving children's access to genetic testing and clinical trials, so every child has the best possible chance of receiving a drug that may work for them."

Provided by Institute of Cancer Research

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