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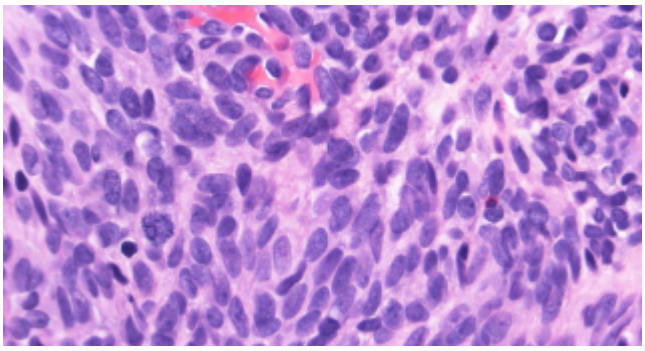

[7]

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Genetic test could pick out ?ultra high risk? bone marrow cancer patients

Date:
11 March 2020

A new genetic test could help doctors pick out patients with the bone marrow cancer multiple myeloma who are at ?ultra high risk? of their cancer progressing aggressively early on.

Genetic test could pick out ?ultra high risk? bone marrow cancer patients

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https://shared-d7-royalmarsden-publicne-live.s3-eu-west-1.amazonaws.com/files_brc/s3fs-public/styles/lead_image/public/Genetic%20test%20for%20myeloma.jpg?itok=clVc

Researchers showed that patients whose tumours display particular genetic patterns have a much poorer survival than average and are unlikely to benefit from a drug called lenalidomide on its own.

Picking out patients whose tumours have high-risk genetic features could therefore help clinicians realise sooner if they?re unlikely to respond to treatment, enabling them to find alternative options as early as possible.

Scientists at **The Institute of Cancer Research, London** **[8]** (ICR), studied 329 patients from the phase III Myeloma XI trial, which looked at the effectiveness of a range of targeted drugs, including lenalidomide, in people with newly diagnosed with multiple myeloma.

Their study was published in the journal [9]***Leukemia*** *[9]* and was funded by Myeloma UK and the NIHR Biomedical Research Centre at **The Royal Marsden NHS Foundation Trust** **[10]** and the ICR, with further support from Cancer Research UK and through a Jacquelin Forbes-Nixon Fellowship.

Patterns of abnormal gene activity

Researchers looked for people at ultra-high risk by analysing patterns of abnormal gene activity and genetic mutations of their tumours ? with the aim of finding out if these ?signatures? could provide clues as to how aggressive their cancer is, how quickly it spreads and if it is likely to respond to treatment with lenalidomide on its own.

One quarter of the patients, 81 in total, had tumours with the so-called SKY92 signature ? a pattern of gene activity involving 92 genes linked to high-risk status.

On average patients with myeloma tumours carrying the SKY92 high-risk gene expression signature had an up to 3-fold increased risk of their cancer returning early. Those with heavily genetically mutated ? so called ?double-hit? cancers ? had a 2-fold increased risk of death.

Combining information about these two risk features, which had before been regarded as an ?either or? test, improved the researcher?s ability to predict disease outcome.

11-fold increased risk of death

Around 10 per cent of the total patient group had both the SKY92 signature and double-hit genetic features. People in this group were at ultra high risk of early, aggressive disease relapse, with all cancers in this group progressing within 4 years with current standard therapies ? as opposed to much longer responses in other groups. Patients with ultra high risk disease had an 11-fold increased risk of death compared with other patients.

The ICR researchers found that patients in this ultra high risk group were highly unlikely to benefit from lenalidomide as ongoing or maintenance therapy ? a treatment that can help very efficiently to keep myeloma from coming back after it has responded to initial therapy in

tumours with only few or no genetic high risk features.

The researchers believe people with ultra-high risk myeloma have a high unmet need for new treatment approaches, including cocktails of novel immunotherapy drugs in combination with chemotherapy. The researchers will be testing this in a new clinical trial, OPTIMUM.

Next, the researchers plan to combine the insights from this study with the ongoing OPTIMUM trial, which will look at 470 patients, in order to find alternative treatment options for people with high-risk myeloma.

'Not all patients with myloma are the same'

Study leader Dr Martin Kaiser [11], Team Leader in Myeloma Molecular Therapy at The Institute of Cancer Research, London, and Consultant Haematologist at The Royal Marsden NHS Foundation Trust, said:

> *?Our study shows that people whose tumours have an ?ultra high risk? combination of genetic features have particularly aggressive disease which doesn?t respond sufficiently to standard treatment to keep their cancer at bay.*
>
> *?Testing for high-risk genetic features could help target myeloma treatment, focusing on the specific needs of each patient. Not all patients with myeloma are the same, and we know that by better understanding their cancer?s genetic and molecular features, we can tailor their treatment much more effectively.*
>
> *?The next step is to combine our results for this study with the ongoing OPTIMUM trial, which will provide us with more information on how to tailor treatment for patients at ultra high risk based on genetic information.?*

Personalising treatment

Professor Paul Workman [12], Chief Executive of The Institute of Cancer Research, London, said:

> *?This exciting new research shows how it is possible to use genetic information to divide patients with bone marrow cancer into many different disease sub-types, and to plan treatment accordingly.*
>
> *It will be exciting to see whether targeting these highest-risk patients with an intensive new treatment can improve survival.?*

Our research: Uncommon Cancers [13]

Improving diagnosis, treatment and outcomes of patients with uncommon cancers including cancers of childhood and adolescence

Find out more [13]

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