Medical Xpress

Combination immunotherapy drugs herald new hope for melanoma patients with long term survival rates

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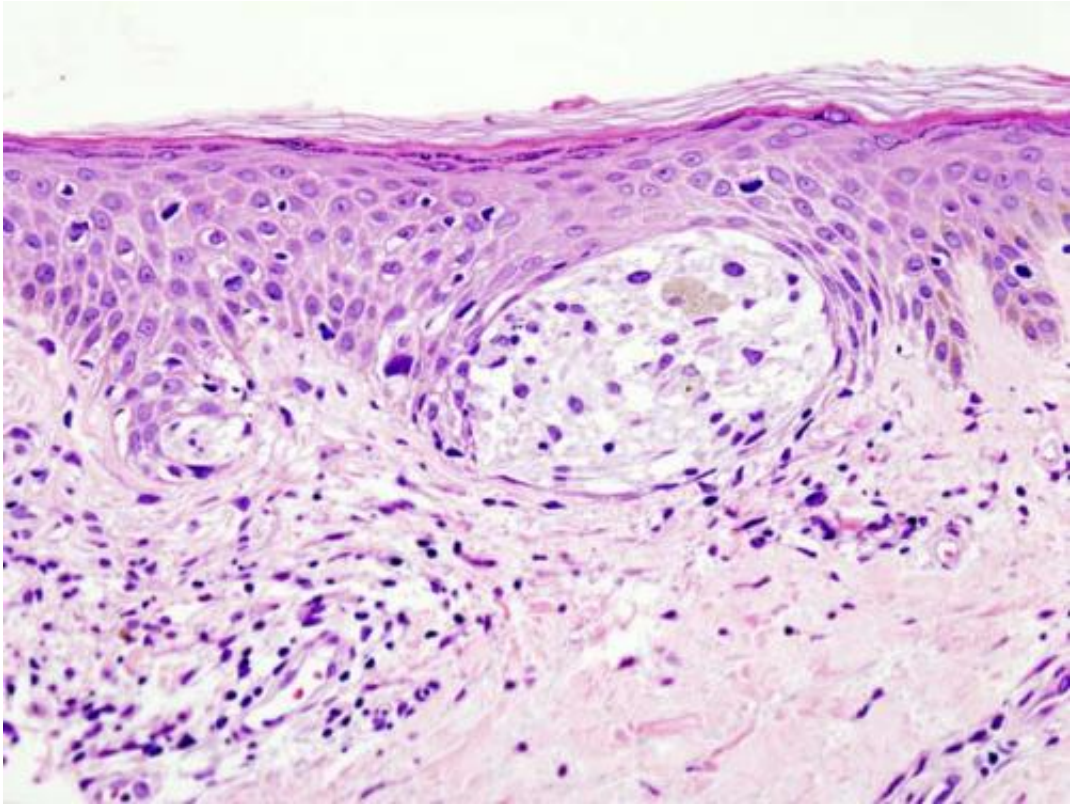

Melanoma in skin biopsy with H&E stain—this case may represent superficial spreading melanoma. Credit: Wikipedia/CC BY-SA 3.0

A combination of two immunotherapy drugs, ipilimumab and nivolumab, has stopped or reversed the progression of advanced

melanoma for five years or more in one in two patients, according to a study led by The Royal Marsden NHS Foundation Trust.

Just 10 years ago, only 1 in 20 patients with advanced melanoma would survive for five years- with many living for just six to nine months. The results from the Checkmate 067 trial, due to be presented today (Saturday 28 September) at the 2019 ESMO Annual Meeting in Barcelona, Spain, and simultaneously published in *The New England Journal of Medicine*, represent the longest phase three trial follow-up for checkpoint inhibitor combination therapy.

Professor James Larkin, Consultant Medical Oncologist at The Royal Marsden NHS Foundation Trust and Professor at the Institute of Cancer Research (ICR), who presented the results, said: "In the past, metastatic melanoma was regarded as untreatable. Oncologists considered melanoma different to other cancers—it couldn't be treated once it had spread. This is the first time we can say that the chances of being a long-term survivor of advanced melanoma are now over 50 per cent, which is a huge milestone."

The trial saw 945 patients with advanced melanoma randomised into three groups: 314 patients received the 'double-hit' of nivolumab plus ipilimumab; 316 patients received nivolumab plus a placebo; and 315 patients received ipilimumab plus placebo. Each nivolumab arm was compared to ipilimumab by itself, and was administered until the disease progressed or until any side-effects became unacceptable.

The five-year overall survival rate for the combination of nivolumab plus ipilimumab was 52%, with 74% of those patients treatment-free after five years. The overall survival for nivolumab was 44%, and 26% for ipilimumab.

Prof Larkin says: "By giving these drugs together you are effectively

taking two brakes off the immune system rather than one so that the immune system is able to recognise tumours it wasn't previously recognising and react to that and destroy them."

Importantly, for those patients who stopped treatment because of side-effects such as fatigue, skin rashes and diarrhoea, the outcome was just as good as it was for those who were on the combination for longer. One of the key points about immunotherapies is that the immune system can be re-educated even with a short duration of treatment. This is in contrast to other treatments like chemotherapy which can require a full course to be as effective.

Pamela Smith, 67, joined the Checkmate 067 trial in January 2014 soon after finding out that her melanoma had spread.

Pamela said: "It was inoperable, so the trial was my only option. I'd been having treatment every two weeks for about four months when I developed diarrhoea that was so bad I had to come off treatment. Amazingly, the first scan and every scan since has shown that in that relatively short time, it worked. My tumour shrank to less than half its original size and it hasn't changed in five years. I've not had any treatment since and I feel brilliant. At every appointment at The Royal Marsden, they ask how I feel on a scale of 1 to 100 and I answer 100. I feel well and very lucky to be alive, and to be able to spend time with my eight grandchildren."

More information: 'Five-Year Survival with Combined Nivolumab and Ipilimumab in Advanced Melanoma' is published today Saturday 28 September 2019 at 7:30 UK BST in The *New England Journal of Medicine*.