

Melanoma breakthrough: New treatment saving lives

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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

In what is being hailed as one of the biggest breakthroughs in melanoma treatment since the advent of immunotherapy, a new study has revealed that drug treatment before surgery is effective in preventing deadly spread of the disease.

The study, published today in the prestigious journal *Nature Medicine*, pooled data from six clinical trials where drug therapy was given before surgery, known as neoadjuvant therapy.

Researchers found that giving Stage III patients a short course of pre-operative targeted immunotherapy was effective, and the stronger a patient's response to that treatment in the first six to nine weeks, the greater the likelihood their [disease](#) would not recur after surgery. Remarkably, in the 75% of patients who responded well to dual immunotherapy given before surgery, only 3% saw their tumors return after surgery, suggesting that 97% will likely be cured.

"The neoadjuvant approach is a new way of dealing with melanoma and is a game changer for stage III patients with bulky disease that has spread to their lymph nodes," said Professor Georgina Long AO, Melanoma Institute Australia (MIA) Co-Medical Director and study senior author.

"We have flipped the 'surgery-then-drugs' rationale on its head. By using our arsenal of ground-breaking new treatments before surgical removal of the tumors, this approach is proving effective in stopping melanoma in its tracks and preventing its recurrence and spread to distant organs."

Data from the study suggests that immunotherapy may work more effectively when given before, rather than after surgery, due to the presence of the bulky tumor provoking an immune response. The concept is similar to sniffer dogs being trained by exposure to illegal drugs—if they know what they're searching for, the more effective they are at detection.

In addition to training the immune system to work more effectively against melanoma, neoadjuvant therapy also enables a clinician to assess early on if a patient is responding to a particular treatment and decide on

an alternative plan if needed. It can also make surgery less complex.

Associate Professor Alex Menzies, MIA Oncologist and study first author, said; "Although [neoadjuvant therapy](#) for Stage III patients is not currently an approved standard of treatment, we anticipate that this will ultimately change following the very promising clinical trial results."

The currently approved schedule is first to surgically remove the melanoma tumors, and then give targeted therapy or immunotherapy post-operatively (known as adjuvant therapy). This approach halves the risk of melanoma recurrence. However it's impossible to tell on an individual level whether the [drug treatment](#) is working.

"This study shows that giving drug [therapy](#) before [surgery](#) reduces risk of recurrence even further, preventing spread to vital organs like the brain and liver and saving more lives. We can also now tell whether the drugs are working for an individual patient, so we can direct subsequent treatment and follow-up accordingly," Associate Professor Menzies said.

Professor Long added: "This early marker of a patient's response to treatment should be considered a new benchmark for rapid drug development in melanoma. It is also a great platform to help fast track laboratory research to understand why some patients do not respond to treatment."

Melanoma Institute Australia has been instrumental in trialing neoadjuvant [drug therapy](#) and is a foundation member of the International Neoadjuvant Melanoma Consortium (INMC).

This study is the first large analysis of immunotherapy in the neoadjuvant setting in any cancer, results of which should pave the way for the use of immunotherapy pre-operatively in many other cancer types. Australia has the highest melanoma rates in the world with one

person diagnosed every 30 minutes, and it is estimated 1300 people will die from the disease in Australia this year.

This latest research has focused on patients with earlier stage melanoma (stage III), and how to prevent their disease from progressing to advanced melanoma. The study will also assist with the transition of [drug](#) development into the [neoadjuvant](#) setting rather than the increasingly complex and inefficient metastatic setting.

"Treatment for advanced melanoma patients, where their disease has metastasised and spread to distant organs, has come a long way in the last decade," said Professor Richard Scolyer, MIA Co-Medical Director. "It is exciting that patients with earlier stage disease are now also benefiting from research breakthroughs. If we can prevent these patients from progressing to Stage IV or metastatic disease, then we will be even closer to achieving our goal of zero deaths from [melanoma](#)."

More information: Pathological response and survival with neoadjuvant therapy in melanoma: a pooled analysis from the International Neoadjuvant Melanoma Consortium (INMC). *Nature Medicine*. [DOI: 10.1038/s41591-020-01188-3](https://doi.org/10.1038/s41591-020-01188-3) , www.nature.com/articles/s41591-020-01188-3

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