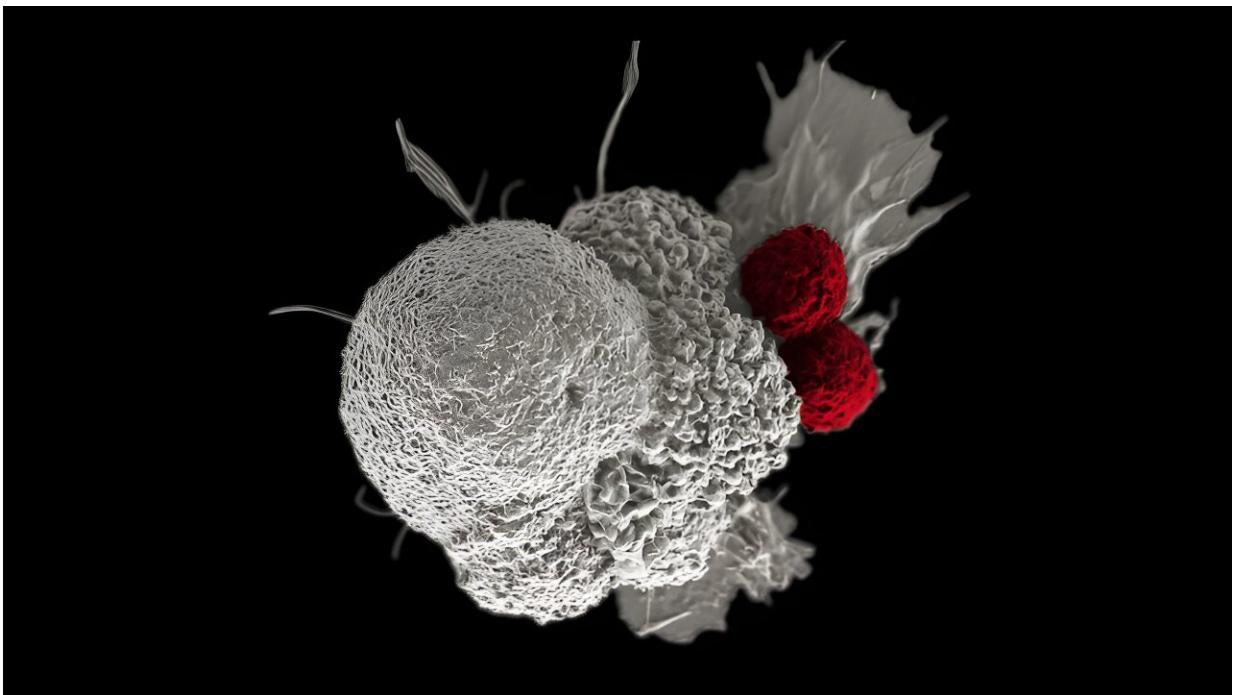


Immunotherapy shows promise as a kinder first-line treatment for advanced head and neck cancers

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Oral squamous cancer cell (white) being attacked by two cytotoxic T cells (red).
Credit: [NIH](#)

Immunotherapy can extend the response of some head and neck tumors to treatment, maintaining the anti-tumor effects and preventing them from growing or spreading for longer, a study reports.

A new trial shows that among patients whose tumors were sensitive to immunotherapy, the treatment could keep their cancer from growing or spreading for longer and with fewer side effects than the previous standard of care therapy.

A personalized approach to immunotherapy

The findings of the KESTREL trial support the need for a personalized approach to immunotherapy treatments, as although these treatments work for a minority of patients, they can bring significant improvements in quality of life for those who respond.

As well as leading to long-lasting responses, the immunotherapy [durvalumab](#), on its own or combined with another immunotherapy called tremelimumab, also led to fewer side effects in people with head and neck cancer which had spread or come back.

Fewer than 2 in 10 people on immunotherapy had severe side effects, compared to around half of the patients on the standard of care regimen.

An international trial

The results from the KESTREL study, led by an international team of researchers including scientists at The Institute of Cancer Research, London, offer hope for the development of kinder first-line treatments for this hard-to-treat cancer.

The study was published in [Annals of Oncology](#).

Overall, the trial did not meet its primary endpoint of improving overall survival (OS) versus the standard of care regimen of chemotherapy plus cetuximab in patients whose tumors expressed high levels of the PD-L1

protein. Nonetheless, it provided important insights into the use of immunotherapy as part of first-line treatment for relapsed and/or metastatic head and neck cancer.

The study compared the effectiveness of durvalumab with or without tremelimumab to the current standard of care known as the EXTREME regimen—a combination of two different chemotherapies plus the targeted drug cetuximab.

KESTREL involved 823 patients with head and neck squamous cell carcinoma of the mouth or throat who had not received prior treatment. They were randomly assigned to one of three [treatment options](#): durvalumab with tremelimumab, durvalumab alone, or the EXTREME regimen.

The researchers analyzed how long patients lived overall, how long the response to treatment lasted, and how safe the treatments were.

Because durvalumab helps the [immune system](#) to find and attack cancer cells by blocking a protein called PD-L1, researchers also looked at PD-L1 levels in patients, in case it could help them predict who would be most likely to benefit from the immunotherapy.

Providing longer-lasting benefits than standard treatment

Around half of the patients who had initially responded to durvalumab or durvalumab plus tremelimumab (49.3 and 48.1 percent, respectively) remained in response—meaning their tumors were not growing or spreading—after a year, compared to around one in ten (9.8 percent) for those who had responded to the EXTREME regimen. This finding suggests that, for the minority of patients who respond to treatment,

immunotherapy could provide longer-lasting benefits than the current standard.

Patients who received durvalumab on its own or plus tremelimumab did not live longer than those on the EXTREME regimen. The [median overall survival](#) for durvalumab with or without tremilimumab was 10.9 months, compared with a median of 11.2 months for EXTREME—indicating no significant difference in survival outcomes in patients with high levels of PD-L1, or all randomized patients.

However, researchers noted that some patients in the EXTREME group received additional immunotherapy after the study—due to other immunotherapy approvals, such as the approval of pembrolizumab and nivolumab as second-line treatment—which may have affected the outcomes and allowed these people to live longer.

Researchers also found that durvalumab and durvalumab plus tremelimumab, which are given as a drip into a vein every four weeks, had fewer serious side effects compared to the EXTREME regimen.

Only 8.9 and 19.1 percent of all randomized patients who had durvalumab or durvalumab plus tremelimumab, respectively, experienced severe side effects, compared to 53.1 percent of patients who received the EXTREME regimen.

Some of the side effects included infections, blood and lymphatic system disorders such as low white blood cell count and low platelet count, and gastrointestinal side effects such as nausea, vomiting and diarrhea.

Further research to ensure more benefit from immunotherapy

Since immunotherapy showed promise by having longer-lasting responses and fewer side effects compared to the EXTREME regimen, the KESTREL findings highlight the need for further investigation into the potential of immunotherapy options for head and [neck cancer](#).

At the ICR's Centre for Translational Immunotherapy, clinicians and scientists are working together to realize the full potential of immunotherapy, so it can benefit many more [cancer](#) patients.

Professor Kevin Harrington, Professor of Biological Cancer Therapies at The Institute of Cancer Research, London, and Consultant Clinical Oncologist at The Royal Marsden NHS Foundation Trust, who was involved in the KESTREL trial, said,

"Immunotherapy holds great potential as a kinder treatment option in head and neck cancers, potentially sparing patients from the need for harsh chemotherapy regimens. Even though patients on immunotherapy in this study lived for a similar amount of time as those on the current standard, those on immunotherapy faced fewer [severe side effects](#) and, for those who responded, they had longer-lasting responses to treatment.

"This study looked at how well immunotherapies worked for patients whose tumors are already sensitive to treatment, however we know that many patients are not yet able to benefit. There is an urgent need to understand better how immunotherapies work, and the underlying biology that determines which patients can benefit. This is a [major focus](#) for our lab at the ICR. With further research we hope to unlock the potential of [immunotherapy](#) so that more patients can benefit from a better quality of life and, in some cases, the chance of a cure."

More information: A. Psyrri et al, Durvalumab with or without tremelimumab versus the EXTREME regimen as first-line treatment for recurrent or metastatic squamous cell carcinoma of the head and neck:

KESTREL, a randomized, open-label, phase III study, *Annals of Oncology* (2022). [DOI: 10.1016/j.annonc.2022.12.008](https://doi.org/10.1016/j.annonc.2022.12.008)

Provided by Institute of Cancer Research

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