Scoring system predicts head and neck cancer patient response to immunotherapy

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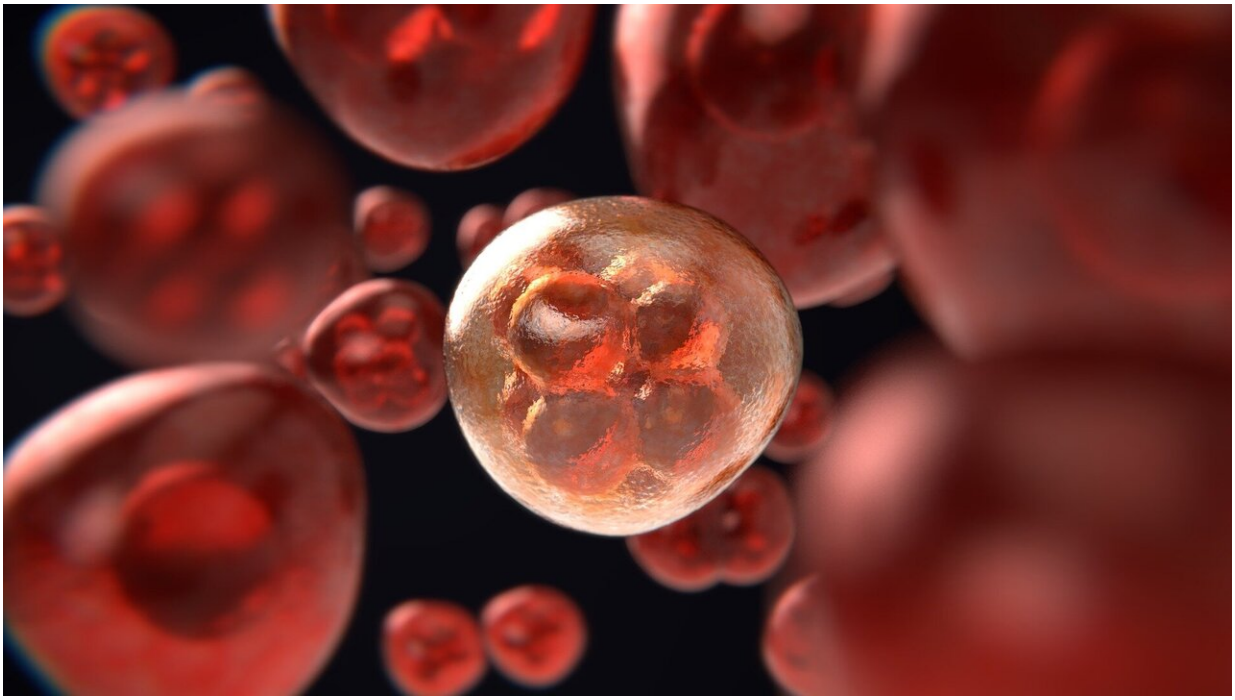

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A prognostic scoring system that is cheap, efficient and reliable can predict how patients with relapsed and/or metastatic head and neck cancer will respond to immunotherapy, new research has shown.

The system, developed by a team led by researchers at The Institute of Cancer Research, London and our partner hospital The Royal Marsden

NHS Foundation Trust, could also provide on-treatment feedback about how well the immunotherapy is working.

Its development is described in a new study published in the *Journal for ImmunoTherapy of Cancer*—the first study to date to define reliable biomarkers for monitoring patient response and chance of survival when treated with a type of immunotherapy drug called immune checkpoint inhibitors.

A biomarker is a characteristic that can be measured by doctors and tells them something about a disease in a specific patient, often using a blood test or biopsies. In this study, the researchers measured three values, in particular—the relative levels of neutrophils and lymphocyte blood cells, levels of fibrinogen and lactate dehydrogenase.

The researchers measured the levels of these factors in 100 patients with relapsed and/or metastatic head and neck squamous cell carcinoma (HNSCC), and found that two factors—the neutrophil-to-lymphocyte ratio (NLR) and fibrinogen—can accurately reveal whether a patient is at higher or lower risk of disease progression and death.

The result of the study, which was largely funded by the National Institute for Health Research (NIHR) Biomedical Research Centre at the ICR and The Royal Marsden, with support from the CRIS Cancer Foundation, could help clinicians with key monitoring decisions in the clinic, such as when to request a CT scan for a patient. They might also allow scientists and clinicians to select patients with advanced cancer who are eligible for clinical trials.

Searching for biomarkers

Pembrolizumab and nivolumab are immune checkpoint inhibitor drugs targeting the protein PD-1, and are known to improve overall survival in

HNSCC patients.

The global KEYNOTE-048 trial, led in the UK by the ICR and The Royal Marsden, established pembrolizumab as a first-line treatment for relapsed and metastatic head and neck cancer. The ICR and The Royal Marsden also played a leading role in the UK arm of the Checkmate-141 trial, which showed the effectiveness of nivolumab in head and neck cancer.

But only around 20 percent of HNSCC patients receiving first- or second-line immunotherapy actually respond to it, and new biomarkers are urgently needed that effectively predict whether they will.

To search for new biomarkers, the researchers analyzed blood samples from the 100 patients with relapsed and/or metastatic HNSCC who were treated with immune checkpoint inhibitors, 54 percent of whom had received it as a first-line treatment.

The team found that low levels of on-treatment NLR in patients' blood, below a ratio of four, correlated with a better response to immunotherapy. Similarly, an on-treatment fibrinogen level below four nanograms per milliliter was linked to both a better response and improved overall survival. However, the researchers found no association between LDH and response or HNSCC survival.

They developed a simple three-point scoring system: zero for low levels of both NLR and fibrinogen, one for increased levels of either one of these biomarkers, and two for patients in whom both biomarkers are above the threshold level. Patients with a score of zero had significantly improved progression-free and overall survival and patients with a score of one had better overall survival.

The researchers determined specific cut-off points for the scoring

system based on a powerful statistic test and validated the results—an important step to ensure it can work for different cohorts of patients.

First on-treatment score

Although NLR has been previously described as a prognostic or predictive biomarker for response to immunotherapy, this study marks the first time that fibrinogen has been established as one.

Fibrinogen is a good indicator of a patient's immune status since it directly links to molecules that mediate immune activation and suppression in the body. Fibrinogen level is requested when a patient receives immunotherapy, making it an accessible option for a prognostic biomarker, along with NLR, which is easy to calculate.

Study lead author Dr. Pablo Nenclares, Ph.D. student at the ICR and Clinical Research Fellow in the Head and Neck Unit at The Royal Marsden, said:

"Because the majority of HNSCC patients receiving immunotherapy don't respond to it, their cancer is still likely to progress, leaving a large subset of patients who require other treatment options. We recognized there is room for improvement in assessing and selecting patients for immunotherapy to improve their prognosis.

"Both NLR and fibrinogen correlate well with immune status and can be measured with cheap, simple tests, making them reliable biomarkers for informing this scoring system for potential use in a clinical or research setting."

Study leader Professor Kevin Harrington, professor of biological cancer therapies at the ICR and clinical consultant at The Royal Marsden, said: "Our scoring system is a new way of predicting whether patients with a

type of head and neck cancer are likely to respond to immunotherapy, and can also be used during treatment to reflect the effects of immunotherapy on their tumor.

"It will give clinicians a clearer idea of whether patients will benefit from immunotherapy or not, and can help to inform individualized treatment plans. It's likely that the scoring system could be prognostic and predictive of other cancer types too, which will be a key next step to explore in collaboration with other research groups and organizations."

More information: Pablo Nenclares et al, On-treatment immune prognostic score for patients with relapsed and/or metastatic head and neck squamous cell carcinoma treated with immunotherapy, *Journal for ImmunoTherapy of Cancer* (2021). DOI: 10.1136/jitc-2021-002718

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