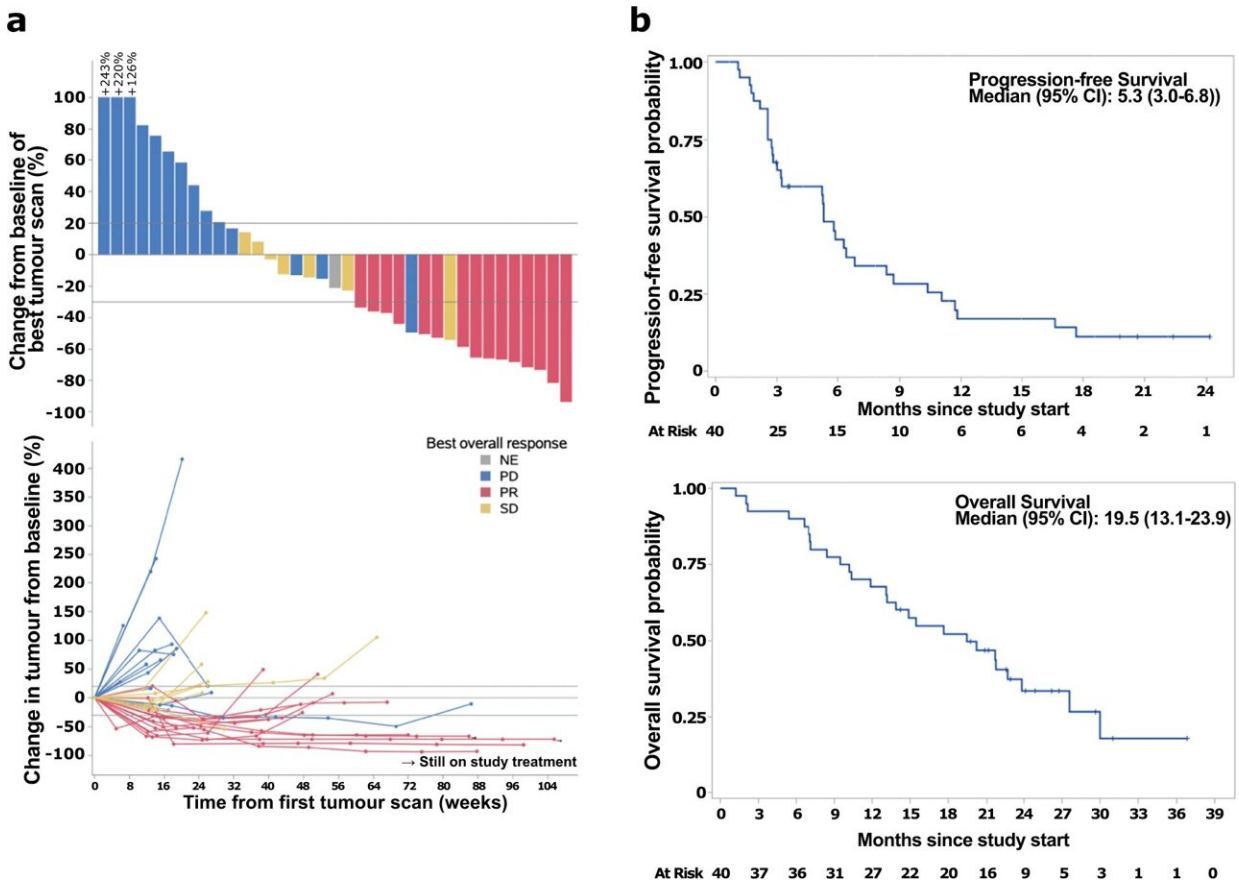
Dual immunotherapy shows promise to treat recurrent or metastatic nasopharyngeal cancer

June 7 2023



Details on patient response and outcome data. **a** Extent and depth of response in trial cohort showing best tumor scan (Top) and changes in tumor size over time (Bottom). Not evaluable (NE) in gray, progressive disease (PD) in blue, partial response (PR) in red and stable disease (SD) in yellow. *n* = 40. **b** Progression-free (Top) and overall (Bottom) survivals of trial cohort. *n* = 40. Source data are

provided as a Source Data file. Credit: *Nature Communications* (2023). DOI: 10.1038/s41467-023-38407-7

A team led by the National Cancer Centre Singapore (NCCS) with members from Singapore General Hospital, A*STAR's Institute of Molecular and Cell Biology (IMCB) and Genome Institute of Singapore (GIS), National University of Singapore's Cancer Science Institute of Singapore and National Taiwan University, have evaluated that the dual immunotherapy, PD-1 immune checkpoint inhibitor nivolumab and CTLA-4 targeting drug ipilimumab, is effective in treating recurrent or metastatic nasopharyngeal carcinoma (NPC).

These results, published *Nature Communications*, introduce a new approach in treating NPC.

NPC is often diagnosed at a late stage where patients present with metastatic disease and have increased chance of recurrence. The current, standard treatment for this group of patients is chemotherapy. Recent results of combination therapy targeting PD-1 and CTLA-4 in other tumor types, such as malignant melanoma and renal cell carcinoma, have been successful, prompting the investigation of similar drug combinations to treat metastatic and recurrent NPC. This is the first time this combination has been studied in NPC, globally.

The NCCS-led research team initiated a single-arm, phase 2 trial to evaluate the safety and efficacy of combination nivolumab and ipilimumab in 40 patients with metastatic and/or recurrent Epstein-Barr virus (EBV)-associated NPC in 2017. EBV is a virus associated with NPC but it is unclear why only some individuals, particularly Southern Chinese, develop NPC while over 90% of the world's population is infected with EBV.

The age range of patients recruited to trial was between 23 and 73 years, with a median of 53 years, and the majority were male (82.5%), which reflects the predominance of NPC incidence in the male population. Patients, who had failed prior chemotherapy, received nivolumab every two weeks, and ipilimumab every six weeks, until disease progression or development of toxicities.

Trial results were measured based on the patients' best overall response rate (BOR), partial response (PR) to the therapy, progression free survival (PFS) and overall survival (OS). Results of the trial showed that the cohort of patients had a BOR of 38% and PR of 37.5% with median PFS of 5.3 months and 19.5 months of OS. This is comparable to historical response rates and survival benefits conferred by chemotherapy, as second line treatment.

The research team also analyzed both blood and tumor samples from the patients. There was better response and PFS in patients with low pre-treatment plasma EBV DNA levels suggesting the possibility that this could be used to select patients more likely to benefit from the dual immunotherapy. The team also performed complex genetic analysis, including whole-exome sequencing and multiplex immunohistochemistry, but did not find genetic biomarkers to predict treatment response before the start of treatment.

However, they found that during treatment, gene expression between patients who had PR to treatment compared to those who did not was significantly different. This suggests = that to identify patients who would respond, future studies should focus on obtaining data after the start of treatment rather than before. They were able to identify that these differences lay in PD-1 and CTLA-4 expressing CD8 gene subpopulations, and could potentially predict response to this combined therapy and be targeted for better treatment outcomes in the future.

"We are encouraged that this trial has shown efficacy in treating metastatic and, or, recurrent NPC by achieving good responses and increased overall survival in a significant proportion of patients," said Associate Professor Darren Lim, Senior Consultant, Department of Lung, Head & Neck and Genitourinary Medical Oncology, Division of Medical Oncology, NCCS and lead author of this study.

"We are validating these findings in a larger patient group and hope to determine which subset of patients would benefit most from this combination treatment."

"The findings of this study offer new options to NPC patients who currently have limited treatment options outside chemotherapy. If this new combination treatment's efficacy is confirmed on the larger cohort that we are testing on, it would provide a possible alternative therapy for a uniquely Asian-endemic cancer," said Professor Gopal Iyer, senior author of the study and Head and Senior Consultant, Department of Head and Neck Surgery, Division of Surgery and Surgical Oncology, Singapore General Hospital and NCCS.

More information: Darren Wan-Teck Lim et al, Clinical efficacy and biomarker analysis of dual PD-1/CTLA-4 blockade in recurrent/metastatic EBV-associated nasopharyngeal carcinoma, *Nature Communications* (2023). DOI: 10.1038/s41467-023-38407-7

Provided by SingHealth