MADRID 2026 ESMO congress

LBA52

Personalized neoantigen vaccine combined with precision critical lesion radiotherapy (CLERT) in advanced solid tumors: Updated results from the iNATURE phase II trial

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Background

Despite promising outcomes in the adjuvant setting, personalized neoantigen peptide vaccines (PPVax) have shown limited efficacy in advanced disease. We examined whether PPVax combined with critical-lesion immuno-preserving radiotherapy (CLERT) improves progression-free survival (PFS) in refractory solid tumors.

Methods

This is iNATURE study, GCOG0028 (NCT06314087), a randomized, phase II trial in metastatic solid tumors progressing after ≥1 line of treatment. Whole exosome sequencing was performed for immunogenic mutations, validated by RNA sequencing; neoantigens were validated by 3 AI algorithms. PPVax (BXP-001) were made individually and given as 5 priming doses (month 1) plus 4 monthly boosters. Patients were stratified by tumor type and randomized 1:1 to PPVax or placebo; all received CLERT, which was stereotactically designed targeting to the critical lesions. Neoantigen-specific immune responses were assessed by ELISpot and ELISA. CTCAE v5.0 and NIH/NCI PROMIS Quality of Life were recorded.

Results

A total of 114 patients were screened for tumor genomic mutations, of whom 106 had neoantigens; 40 were eligible and signed written consent. Thirty-five patients were eventually randomized (PPVax, n=16; placebo, n=19), including 26 (74.3%) lung cancer, 4 (11.4%) colorectal cancer, and 5 other solid tumors. Patients had a median of 3 lines of systemic therapy. Median PFS was 10.3 mo (95% CI, 6.2–not reached) and 3.1 mo (95% CI, 2.0–6.4) for PPVax and placebo arms, respectively (p=0.0045), without significant differences across cancer type (p=0.651). The hazard ratio of PPVax over placebo was 0.29 (95% CI, 0.12–0.71; p=0.007). PPVax induced neoantigen-specific T-cell responses in 83.3% of evaluable patients and antibody responses in 100%. In the PPVax arm, 2/16 patients experienced >30% shrinkage of liver or mediastinal metastases. There was no grade ≥3 PPVax-related AE neither arm. QOL did not change significantly in both arms.

Conclusions

In combination with CLERT, PPVax improved PFS significantly, with 7 mo extension without serious toxicity in patients with solid tumors refractory to multi-lines' treatment. A multicenter validation study is underway.

Clinical trial identification

NCT06314087, ChiCTR2300078055, GCOG0028.

Legal entity responsible for the study

The University of Hong Kong–Shenzhen Hospital, acting as the coordinating and sponsoring institution for the study.

Funding

The National Natural Science Foundation of China (NSFC82303769) Shenzhen Medical Research Fund (D2402020), Alice Ho Miu Ling Nethersole Charity Foundation, Shenzhen Science and Technology Program (No. KQTD20180411185028798), Shenzhen Fundamental Research Program (No. JCYJ2020109150427184 (2020N384)), the Shenzhen Key Laboratory for cancer metastasis and personalized therapy (ZDSYS20210623091811035) We acknowledge the support of P&PMed Biotechnology Co. Ltd. (Shanghai, China. http://www.pnp-med.com/), BayVax Biotech Limited and YuceBio Technology Co., Ltd for the neoantigen screening and neoantigen vaccine preparation.

Disclosure

All authors have declared no conflicts of interest.

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