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ORIGINAL RESEARCH

Safety and efficacy of dendritic cell-based immunotherapy (DCVAC/LuCa) combined with carboplatin/pemetrexed for patients with advanced non-squamous non-small-cell lung cancer without oncogenic drivers

R. Zhong[†], X. Ling[†], S. Cao, J. Xu, B. Zhang, X. Zhang, H. Wang, B. Han[*‡] & H. Zhong[*‡]

Department of Pulmonary Medicine, Shanghai Chest Hospital, Shanghai Jiaotong University, Shanghai, China

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Background: Our prospective, open-label, single-arm phase II study investigated the safety and efficacy of DCVAC/LuCa (dendritic cell vaccines for lung cancer) combined with standard carboplatin/pemetrexed in advanced non-squamous (nsq) non-small-cell lung cancer (NSCLC).

Patients and methods: Eligible patients had stage IV nsq NSCLC without oncogenic drivers and had not received prior systemic cancer therapy. Treatment consisted of carboplatin/pemetrexed for up to 6 cycles followed by 21 cycles of pemetrexed maintenance or until progression or intolerance. Non-progression patients after two cycles of chemotherapy started to receive DCVAC/LuCa subcutaneously (s.c.) on day 15 of cycle 3, and thereafter q3w (day 15 of chemotherapy cycles) for up to 15 doses. Dosing of DCVAC/LuCa s.c. varied among patients depending on the baseline number of leucocytes but remained constant for each single patient. Safety was assessed by adverse events (AEs), treatment-related adverse events (TRAEs), serious adverse events (SAEs), and adverse events of special interest (AESIs). Efficacy was measured by overall survival (OS), progression-free survival (PFS), time to progression (TTP), and objective response rate (ORR).

Results: Sixty-one patients were enrolled. In the safety population ($n = 60$), eight patients (13.33%) had grade 3 or greater TRAEs, and six patients (10.0%) showed SAEs which were not related to leukapheresis or DC vaccination. Six grade 1 AEs were considered to be related to leukapheresis. No AESIs or DCVAC/LuCa-induced AEs were observed. The 2-year survival rate in the modified intention-to-treat population ($n = 44$) was 52.57%. Median OS was not reached. Median PFS was 8.0 months, median TTP was 10.2 months, and the ORR was 31.82%.

Conclusion: In treatment-naïve stage IV nsq NSCLC patients without oncogenic drivers, the combination of carboplatin/pemetrexed and DCVAC/LuCa was well tolerated and showed promising efficacy. Therefore, a study to prove our immunotherapeutic concept in a randomized phase III trial is planned.

Key words: DCVAC/LuCa, dendritic cell vaccination, non-small-cell lung cancer

INTRODUCTION

Lung cancer was the leading cause of cancer deaths and the second most diagnosed cancer throughout the world in 2020.[1] For many years, standard first-line therapy for patients with advanced non-small-cell lung cancer (NSCLC) without genetic variants has been platinum-based doublet therapy with or without the option of maintenance therapy. Immune checkpoint inhibitors (ICIs) were also approved in first-line therapy for programmed cell death-ligand 1 (PD-L1) expression-positive population,[2] changing significantly the treatment algorithm of NSCLC. The outcome of therapies still indicates the need for developing more effective therapies.[3]

DCVAC/LuCa, a dendritic cell (DC) vaccination, is a self-activated cellular immunotherapy, which works in a completely different mechanism from ICIs. It consists of autologous DC pulsed *ex vivo* with killed NSCLC H522 cell lines. Several clinical trials have tested DC vaccination in various cancer types, especially in those with immunogenic nature such as melanoma and prostate cancer, demonstrating the feasibility of applying DC vaccination in some certain malignancies.[4,5] Some phase I studies have shown a

*Correspondence to: Prof. Hua Zhong, Department of Pulmonary Medicine, Shanghai Chest Hospital, Shanghai Jiaotong University, 200030 Shanghai, China. Tel: +86-021-22200000

E-mail: eddiedong8@hotmail.com (H. Zhong).

*Prof. Baohui Han, Department of Pulmonary Medicine, Shanghai Chest Hospital, Shanghai Jiaotong University, 200030 Shanghai, China. Tel: +86-021-22200000

E-mail: 18930858216@163.com (B. Han).

†These authors contributed equally to this work and should be considered co-first authors.

‡These authors contributed equally to this work and should be considered co-corresponding authors.

good toleration of DC vaccination in NSCLC patients.[6-8] However, the role of DC vaccines in improving the prognosis of advanced lung cancer patients has to be determined.[9,10] DC vaccine can activate cytotoxic $CD8^+$ T cells and target the tumor-associated antigens (TAAs) expressed by the patient's cancer cells and released under the effect of chemotherapy, to generate immune responses aiming for cancer-cell elimination.[11,12] The immunosuppressive microenvironment produced by tumors, which widely exists in advanced NSCLCs, is a drawback to the effectiveness of DC vaccination.[13,14] Considering that the changes brought by chemotherapy to the tumor cells might improve the effectiveness of DC vaccination, combining DCVAC/LuCa with chemotherapy can be a promising regimen for the treatment of advanced NSCLC without genetic variants.[15,16]

Our phase II clinical trial combines the regimen of DCVAC/LuCa therapy with chemotherapy for stage IV non-squamous (nsq) NSCLC assessing efficacy and safety.

PATIENTS AND METHODS

Trial design and patients

This study was an open-label, single-arm, phase II study carried out in the Department of Pulmonary Medicine, Shanghai Chest Hospital. The trial was approved by the institutional review board of Shanghai Chest Hospital. Written informed consent was provided by all study patients. Enrolled in this study were patients with stage IV, nsq NSCLC confirmed by histological or cytological tests, with an Eastern Cooperative Oncology Group score of 0-1 and had not been treated with systemic therapy for NSCLC before. Exclusion criteria included: active or untreated central nervous system metastasis, primary immunodeficiency, preexisting medical condition requiring long-term chronic steroid or immunosuppressive therapy, human immunodeficiency virus positivity, hepatitis B and/or C infection, syphilis, other malignant tumors, significant co-morbidities, severe hypersensitivity to pemetrexed, carboplatin, and the components of DCVAC/LuCa. The full eligibility criteria are described in the Supplementary Appendix, Supplementary Table S1 available at https://doi.org/10.1016/j.esmoop.2021.100334. This study is registered with ClinicalTrials.gov, number NCT 02669719.

Procedures

The peripheral blood mononuclear cells were obtained from the patients using the COBE Spectra (Terumo BCT, Inc., USA) blood cell separator within 1 week after enrolment. Adherent mononuclear cells were selected and cultivated in CellGro RPMI 1640 (Lonza, Switzerland) media containing 20 ng/ml granulocyte—macrophage colony-stimulating factor and 2500 U/ml interleukin-4 (IL-4). Immature DCs were obtained after 5 days. Killed tumor cell lines H522 were cultured, treated with a high hydrostatic pressure (HHP) of 200 MPa, frozen in aliquots of 20×10^6 cells per vial in 1 ml of cryopreservation medium, and then mixed at 1 : 1 ratio. The mixed cells were subsequently used for pulsing of immature DCs in a ratio of 5 : 1 (DCs to tumor cells).[17] Finally, DCs pulsed with tumor cells were matured by Toll-like receptor-3ligand, poly (I : C) (Supplementary Figure S1, available at https://doi.org/10.1016/j.esmoop.2021.100334). The final product was cryopreserved at a defined minimum dose of 5×10^6 DCs per vial in 1 ml of cryopreservation medium under -50°C.

Pemetrexed 500 mg/m^2 and carboplatin at a target area under curve 5 (the maximum dose is $5 \times 150 = 750$ mg) were given to the patients intravenously every 3 weeks. Patients who had not experienced disease progression or chemotherapy intolerance started to receive the DCVAC/LuCa treatment on day 15 ($\pm$3 days) of chemotherapy cycle 3. DCVAC/LuCa was then administrated on day 15 ($\pm$3 days) of every chemotherapy cycle until the maximum number of 15 doses, by subcutaneous (s.c.) injection into the lymph node area (Figure 1A). The induction part of therapy consisted of 4-6 cycles of carboplatin/pemetrexed followed by intravenous pemetrexed 500 mg/m^2 every 3 weeks as maintenance chemotherapy up to 21 cycles. Maintenance was discontinued in case of disease progression or inacceptable toxicity. The DCVAC/LuCa treatment started on day 15 ($\pm$3 days) of chemotherapy cycle 3 and was then administrated on day 15 ($\pm$3 days) of every chemotherapy cycle until the maximum number of 15 doses, by s.c. injection into the lymph node area (Figure 1A). The individual dose of DCVAC/LuCa was unchanged, but varied among patients depending on their baseline leukocyte level. Each dose of DCVAC/LuCa contained a median number of 8.48×10^6 [95% confidence interval (CI) 8.46-8.49 $\times$ 10^6] DCs. The combination therapy was discontinued in case of progression.

Outcome measures

We assessed the safety of DCVAC/LuCa with pemetrexed and carboplatin by analyses of reported adverse events (AEs) (according to the National Cancer Institute's Common Terminology Criteria for Adverse Events, version 4.03), treatment-related adverse events (TRAEs), serious adverse events (SAEs), and adverse events of special interest (AESI). TRAEs were defined as AEs associated with the study therapy including the application of DCVAC/LuCa and chemotherapy as well as leukapheresis. AESIs were defined as events associated with the study therapy, including systemic allergic reactions, transmission of an infectious agent related to DCVAC/LuCa or leukapheresis, and autoimmunity events. Overall survival (OS), progression-free survival (PFS), objective response rate (ORR), and time to progression (TTP) analyses were mainly based on the modified intention-to-treat (mITT) population. We defined mITT population as patients whose tumors were evaluated as stable disease (SD) or objective response [including complete response (CR) and partial response (PR) according to RECIST 1.1] after two cycles of induction chemotherapy and received the third cycle of chemotherapy with the first dose of DCVAC/LuCa. Safety was assessed in the safety population, which included all patients who received any study treatment.

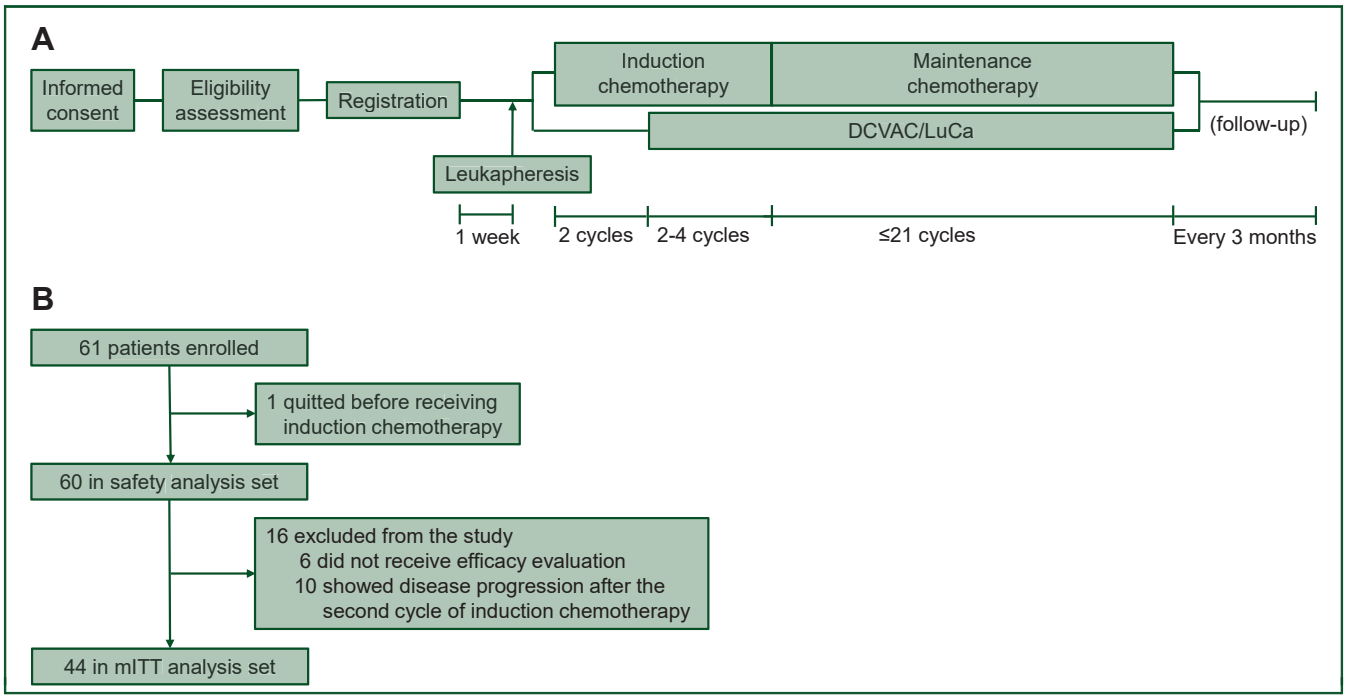

Figure 1. Study design and participant flow chart.
(A) Study design of the evaluation of efficacy and safety of DCVAC/LuCa with chemotherapy for patients with stage IV NSCLC. (B) Participant flow chart. DCVAC/LuCa, dendritic cell vaccines for lung cancer; mITT, modified intention-to-treat; NSCLC, non-small-cell lung cancer.

Endpoints of efficacy included OS, as well as 1-year survival rate and 2-year survival rate. We also analyzed PFS, defined as the time from receiving the first dose of study therapy to the time point of tumor progression, as well as 1-year PFS rate and 2-year PFS rate. Other efficacy endpoints consisted of TTP, defined as the time from randomization to time of tumor progression, and ORR, defined as the proportion of patients who had CR or PR (according to the RECIST 1.1).

Statistical analyses

A target sample size of 38 assessable patients was set. It could provide the trial with 50% power to detect an increase in median OS from a baseline of 12 months (chemotherapy) according to previous studies[18] to 20 months (DCVAC/LuCa plus chemotherapy), with a two-sided significance level of $\alpha = 0.10$. Sample size calculation was based on assuming an accrual time of 24 months with an additional 24 months of follow-up and was done by PASS (version 13.0.13) (NCSS, USA).

Descriptive statistics were used to analyze demographic and baseline characteristics, safety, and efficacy data. The safety assessments were done from the start of treatment to 30 days after the last dose of treatment (DCVAC/LuCa or chemotherapy). Complications occurring within 24 hours after leukapheresis were also reported. The numbers and percentages of patients who experienced AEs, TRAEs, and SAEs were summarized. We assessed and calculated median OS, PFS, and TTP with two-sided 95% CI by the Kaplan–Meier method. We did the statistical analyses with SAS (version 9.4) (SAS, USA) and R (version 4.0.3) (R studio, USA).

RESULTS

Patients

We enrolled 61 patients from January 2016 to March 2018. Patients' follow-up was continued until March 2020. After excluding one patient who refused receiving any therapy, the safety population included 60 patients (98.4%). Among them, 44 patients (72.1%) who showed SD or PR after two cycles of induction chemotherapy started to receive the combination therapy of DCVAC/LuCa with chemotherapy and were allowed in the mITT population for efficacy analysis (Figure 1B).

Baseline characteristics of the patients are listed in Table 1. Among the 60 patients in the safety population, 57 patients (95%) had adenocarcinoma. The median age of patients was 59 years (range, 32-78 years). All the 44 patients in the mITT population had adenocarcinoma. The median age of them was 63 years (range, 37-78 years). One of them had received local radiotherapy for bone metastasis before the study treatment (Table 1).

Safety

All the 60 patients experienced at least one TRAE of any grade, while only 8 (13.33%) of them had grade $\geq$3 TRAEs. The most common any-grade TRAEs which occurred in $>$10% of the assessed patients were constipation, anorexia, fatigue, elevated aspartate aminotransferase, decreased hemoglobin, abdominal discomfort, elevated alanine aminotransferase, decreased white blood cell count, anemia, decreased red blood cell count, decreased platelet count, decreased neutrophil count, and elevated γ-glutamyl transferase. Details are shown in Table 2. Grade $\geq$3 events

Table 1. Baseline characteristics

	Safety population (n = 60)	mITT population (n = 44)
Age, median years (range)	59 (32-78)	63 (37-78)
Gender, *n* (%)		
Male	35 (58.33)	21 (47.73)
Female	25 (41.67)	23 (52.27)
ECOG PS, *n* (%)		
0	2 (3.33)	2 (4.55)
1	58 (96.67)	42 (95.45)
Smoking history, *n* (%)		
Smoker	18 (30.00)	11 (25.00)
Nonsmoker	39 (65.00)	31 (70.45)
Ex-smoker	3 (5.00)	2 (4.55)
Histology, *n* (%)		
Adenocarcinoma	57 (95.00)	44 (100.00)
Others	3 (5.00)	0 (0.00)
Prior treatment history, *n* (%)		
Chemotherapy	0 (0)	0 (0.00)
Radiotherapy	2 (3.33)	1 (2.27)

ECOG PS, Eastern Cooperative Oncology Group performance status; mITT, modified intention-to-treat.

reported by more than one patient were anemia [4 (7%)], leukopenia [3 (5%)], and a decreased neutrophil count [2 (3%)]. SAEs were reported in six patients (10%) (Supplementary Table S2, available at https://doi.org/10.1016/j.esmoop.2021.100334). Dose reduction due to any AE occurred in one of the 60 treated patients. Dose interruption due to any AE occurred in 12% (5/60) of patients. No AEs led to discontinuation of the study therapy. No AESIs were observed in the whole population. The complete data of all the assessed AEs and TRAEs are listed in Supplementary Tables S3 and S4, available at https://doi.org/10.1016/j.esmoop.2021.100334.

Efficacy

A summary of clinical endpoints is shown in Table 3. The median follow-up for overall survival was 23.1 months. In the mITT population, the percentage of patients who were alive was 72.73% at 1 year and 52.57% at 2 years. The median PFS was 8.0 months (95% CI 5.4-11.9 months). The median OS was not reached. Kaplan—Meier curves for OS and PFS are shown in Figure 2A and B. The median TTP was 10.2 months (95% CI 3.6-15.7 months). The ORR was 31.82%. Fourteen (31.82%) of the 44 patients achieved a PR, and 30 (68.18%) had SD. Among the 34 patients who showed SD at the end of the first two cycles of induction chemotherapy, 8 (23.53%) reached PR during the combination therapy. The subgroup analysis found that patients who received DCVAC/LuCa with $>8.95 \times 10^6$ DCs per dose showed significantly better OS than those who received DCVAC/LuCa with $\leq 8.95 \times 10^6$ DCs per dose ($P = 0.0038$), while the difference in PFS was not statistically significant (Figure 2C and D).

DISCUSSION

In recent years, DC vaccination, a self-activated cellular immunotherapy, has shown its value in treating some malignancies after the Food and Drug Administration approval of cancer vaccine sipuleucel-T.[4,5,19] But the exploration of applying DC-based immunotherapy in advanced NSCLC is still in the preliminary stage.

An early phase I trial applying DC vaccines (DCs loaded with autologous tumor lysate) as second- or third-line treatment in patients with advanced NSCLC revealed good toleration but limited efficacy, even though over half of the participants showed activated T-cell response.[8] Notably, DC vaccination resulted in obvious control of initial metastatic lesion in two patients, despite the fact that they developed new metastatic sites elsewhere. We could learn from the experience that antigenic heterogeneity between different lesions, antigenic changes before the time of DC vaccine injection, and the refractory and bulky tumor burden after resistance to conventional therapy probably restrained the vaccination-induced immune responses from reaching an ideal efficiency. Optimizing the production of DC vaccines, bringing forward the timing of application, or trying combination therapy which has the potential to improve DC-induced immune response might be reasonable solutions.

Conventional production processes of DC vaccines involve TAAs after a comprehensive and individualized TAA selection.[20] However, we enforced DCs with killed human adenocarcinoma cell lines during manufacturing, with the ability to recognize full antigens of human adenocarcinoma cells. Our procedure increased the possibility of provoking a stronger tumor-directed immune response, and was at the same time more practical as individualized antigen selection was no longer necessary. Moreover, for enforcing DCs, we used a pretreatment of NSCLC cell lines with an HHP of 200 MPa. HHP is so far the optimum method for generating tumor vaccines, which inactivates tumor cells effectively, is non-toxic, does not wreck the immunogenicity of the tumor cells, and can comply with Good Manufacturing Practices and legal requirements.[21] Besides, the high preparation efficiency, producing 15 doses of DCVAC after one leukapheresis, is also a progress making the therapy more practical compared to other known DC vaccines such as sipuleucel-T.

The combination therapy of DCVAC/LuCa combined with standard carboplatin/pemetrexed as first-line treatment in advanced nsq NSCLC is applied in our trial, with a two-cycle chemotherapy period implemented before the first dose of DCVAC/LuCa. Patients who did not show disease progression after the two cycles started to receive the DC vaccination combination therapy. It is very challenging to induce antitumor immune responses in late stages in the settings of a profound tumor-induced immune suppression. Adding chemotherapy to DC vaccines could better activate patients' immune response based on multiple mechanisms.[15,16] Applying chemotherapy first could help get in control of the metastatic disease and reduce the tumor burden, and that effect should be promoted by DC vaccination. Vice versa the positive effects that chemotherapy might bring to patients' response to DC vaccine should also be realized. Therefore, applying DCVAC/LuCa to patients who did not show disease progression after two cycles of chemo was considered the optimal way. Patients who received at least

Table 2. Common treatment-related adverse events

TRAEs	Any grade *n* (%)	Grade 1 *n* (%)	Grade 2 *n* (%)	Grade 3 *n* (%)	Grade 4 *n* (%)
Constipation	38 (63.33)	38 (63.33)	0 (0)	0 (0)	0 (0)
Anorexia	37 (61.67)	37 (61.67)	0 (0)	0 (0)	0 (0)
Fatigue	36 (60.00)	36 (60.00)	0 (0)	0 (0)	0 (0)
Aspartate aminotransferase increased	13 (21.67)	13 (21.67)	0 (0)	0 (0)	0 (0)
Hemoglobin decreased	13 (21.67)	11 (18.33)	1 (1.67)	1 (1.67)	0 (0)
Abdominal discomfort	13 (21.67)	13 (21.67)	0 (0)	0 (0)	0 (0)
Alanine aminotransferase increased	12 (20.00)	12 (20.00)	0 (0)	0 (0)	0 (0)
White blood cell count decreased	12 (20.00)	10 (16.67)	3 (5.00)	3 (5.00)	0 (0)
Anemia	12 (20.00)	9 (15.00)	1 (1.67)	4 (6.67)	0 (0)
Red blood cell count decreased	7 (11.67)	7 (11.67)	0 (0)	0 (0)	0 (0)
Platelet count decreased	6 (10.00)	5 (8.33)	3 (5.00)	1 (1.67)	0 (0)
Neutrophil count decreased	6 (10.00)	5 (8.33)	1 (1.67)	2 (3.33)	0 (0)
GGT increased	6 (10.00)	4 (6.67)	2 (3.33)	0 (0)	0 (0)

Safety analysis set. TRAEs are defined as adverse events that might be associated with the study therapy, including the application of DCVAC/LuCa and chemotherapy and the procedure of leukapheresis. TRAEs are graded with the National Cancer Institute's Common Terminology Criteria for Adverse Events, version 4.03. Events are listed in order of descending frequency in the total population. The highest grade is recorded if a patient had experienced TRAEs more than once.
GGT, γ-glutamyl transferase; TRAE, treatment-related adverse event.

Table 3. Summary of endpoints

	mITT population
OS	
Median OS, months (95% CI)	Not reached
1-year survival rate	72.73%
2-year survival rate	52.57%
PFS	
Median PFS, months (95% CI)	8.0 (5.4-11.9)
1-year PFS rate	30.16%
2-year PFS rate	9.05%
Best overall response, *n* (%)	
Complete response	0 (0)
Partial response	14 (31.82)
Stable disease	30 (68.18)
Progressive disease	0 (0)
ORR	31.82%
Median TTP, months (95% CI)	10.2 (3.6-15.7)

CI, confidence interval; mITT, modified intent-to-treat; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; TTP, time to progression.

one dose of DC vaccine formed the mITT population for efficacy evaluation, in order to analyze the therapeutic effect brought by DCVAC/LuCa. The modification of the efficacy population avoided also possible ineffectiveness of the combination therapy in patients' resistant to chemotherapy.

The major purpose of our trial was to evaluate the safety of this vaccination combination therapy. Seen tolerability is consistent with previous reports[22,23] and the data published for other cancer types,[24,25] with no new or unexpected adverse reactions, suggesting that the strategy is well tolerated in a selected Chinese population. The most common TRAEs observed, including constipation, decreased appetite and fatigue, were mild and considered to be related to chemotherapy, or antacids, or anti-nausea drugs. We observed no grade $\geq$3 AEs related to leukapheresis or vaccination. For the three patients who experienced grade $\geq$3 AEs and died, none of their deaths were related to DCVAC/LuCa, chemotherapy, or leukapheresis. Six grade 1 TRAEs were considered associated with leukapheresis, consisting of decreased platelet count, decreased red blood cell count, lower extremities discomfort, upper extremities discomfort, numb lips, and localized rash, respectively, occurring in five patients. We specifically analyzed a group of AEs as AESIs, including systemic allergic reactions, transmission of an infectious agent related to DCVAC/LuCa or leukapheresis, and autoimmunity events. These AESIs were considered the most representative events helping us better focus on noteworthy side-effects which might be induced by DC vaccination rather than chemotherapy. No AESIs were observed in the whole population.

Measuring efficacy data in the mITT population, the ORR was 31.82%, which did not show significant improvement compared to conservative chemotherapy with angiogenesis drugs.[26] However, the survival data implied potential clinical value of the tested therapy, as the 2-year survival rate was 52.57% and the median OS was not reached as of 24 months after the first application of chemotherapy. These data seem to be promising compared to the results of a multicenter retrospective study applying DC vaccination monotherapy to 260 patients with advanced NSCLC, in which the median OS was 13.8 months from the time of receiving the first DC dose.[27] Therefore, we believe that combining vaccination and chemotherapy is more effective than DC vaccination alone. We also believe that combining vaccination with DCVAC/LuCa and chemotherapy is superior to anti-angiogenesis drugs in advanced nsq NSCLC, coming along with a median OS ranging from 12.3 to 22.8 months.[26,28-30] However, to make a reliable comparison, a randomized controlled trial using these strategies is critical.

Recently, some clinical trials exploring the application value of DCVAC/LuCa in advanced NSCLC reached decent outcomes both in tolerability and efficacy. A phase I/II trial conducted in Europe, the study design of which was similar to ours, investigating DCVAC/LuCa combined with chemotherapy treating stage IV NSCLC, reported its data recently.[23] The median OS was 15.5 months in the DCVAC/LuCa plus chemotherapy arm, compared to 11.8 months in the chemotherapy arm. The difference between the OS results in our trials might be caused by the heterogeneity of

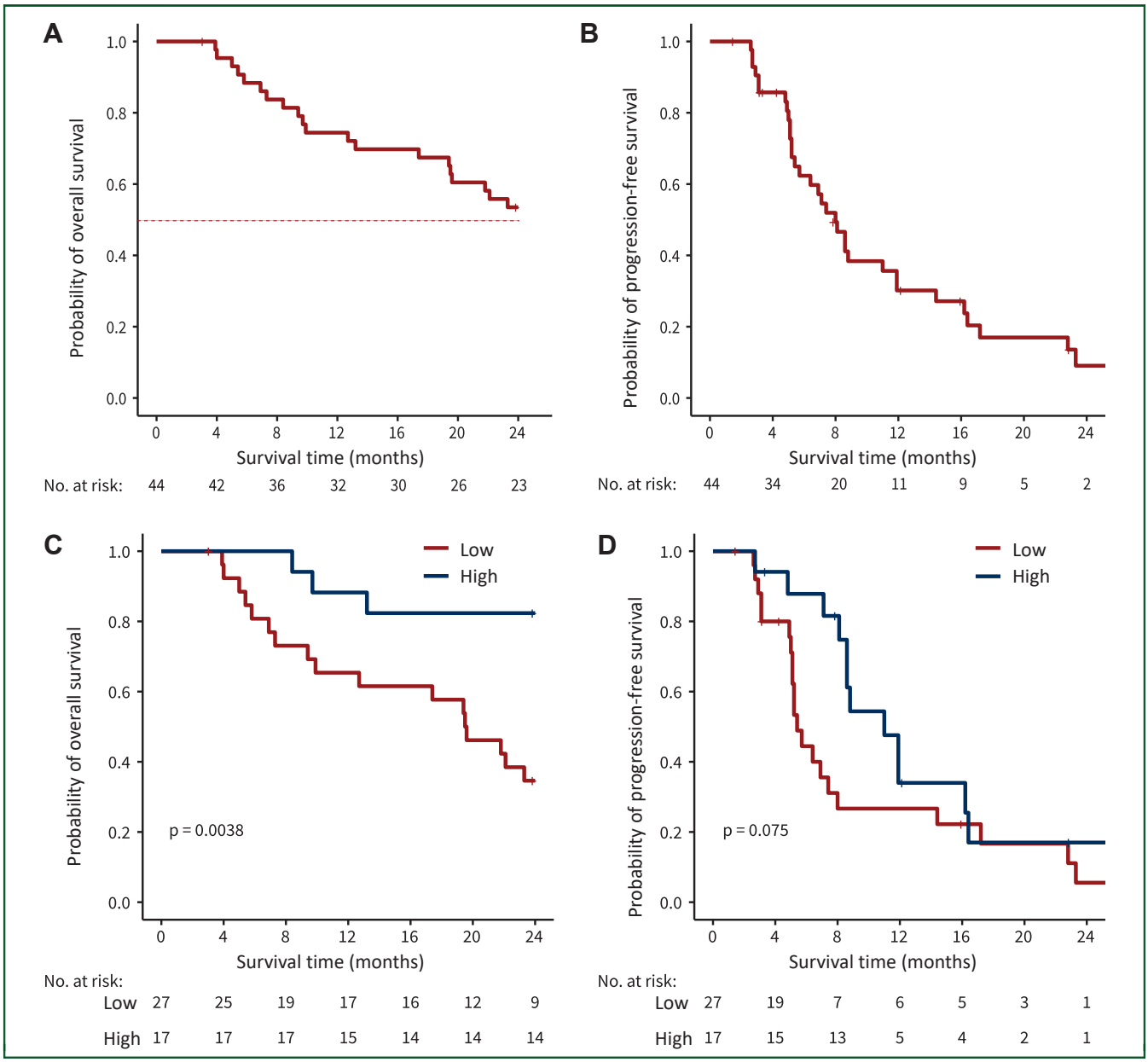

Figure 2. Kaplan-Meier analysis.
(A, B) Overall survival and progression-free survival curve of the mITT population. (C, D) Comparison of overall survival and progression-free survival between patients who received DCVAC/LuCa with $>8.95 \times 10^6$ DCs per dose and those who received DCVAC/LuCa with $\leq 8.95 \times 10^6$ DCs per dose.
DC, dendritic cell; DCVAC/LuCa, dendritic cell vaccines for lung cancer; mITT, modified intention-to-treat.

population and the small sample size. Future larger-scale clinical trials are in need to validate the efficacy results. Another interesting study combining DCVAC/LuCa, chemotherapy, and traditional Chinese medicine in patients with stage IIIb or IV NSCLC also showed promising efficacy outcomes, as the median OS was not reached until 22.3 months.[31] Noteworthy, ICIs in advanced NSCLC show a long-term survival benefit. For example, the CA209-003 trial in this patient group using nivolumab resulted in a 3-year survival rate of 18.4% and a 5-year survival rate of 15.6%.[32] KEYNOTE 001 also showed good OS rates at 2, 3, and 4 years with 49%, 37%, and 31%, respectively.[33] The OS data of our study are also promising, though median OS has not been reached so far. Another approach, using a checkpoint inhibitor blocking the binding of PD-L1, promotes the antigen of dendritic cells and activates the T cells;[34] the combination with DC vaccine could also be clinically attractive.

An important limitation of our study was that we could not analyze the separate role of DCVAC/LuCa in our combination, how DCVAC/LuCa influences patients' immune response to lung cancer, or finding an appropriate biomarker associated with patients' prognosis. Detailed studies covering the investigation of changes in tumor immune microenvironment and immune-related markers after treatment should be conducted in the future. Since our

study was a single-arm, single-center trial, a randomized controlled trial in a larger scale comparing our combination with conventional standard therapies needs to be carried out. Lastly, due to the limited follow-up time so far, OS results were still immature, calling for a longer follow-up result of this study.

In conclusion, in our study, DCVAC/LuCa with concurrent pemetrexed and carboplatin showed synergetic efficacy and remarkable potential in improving patients' survival, with no serious or unexpected adverse reactions emerging, indicating it is safe and feasible in a selected Chinese population. Although the OS data are premature, the combination therapy of DCVAC/LuCa with concurrent pemetrexed and carboplatin might be a promising strategy for the treatment of advanced nsq NSCLC without oncogenic drivers.

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DISCLOSURE

The authors have declared no conflicts of interest.

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