Dendritic-cell vaccine (DCVAC/LuCa) combined with the 1st line chemotherapy in patients with NSCLC: final analysis of phase 2, open label, randomized, multicenter trial

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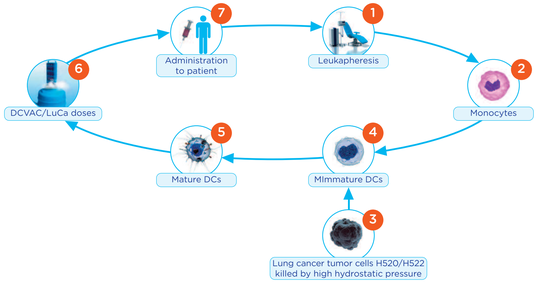
Background:

Immunotherapy for induction of tumor cell specific immune responses destroying tumor cells has emerged as a promising treatment modality in lung cancer. DCVAC can present tumor antigens to elicit a durable immune response. We hypothesized that adding DCVAC to the standard of care chemotherapy could prolong progression-free survival (PFS) and overall survival (OS).

DCVAC/LuCa, manufacturing and treatment cycle:



1. Patient visits leukapheresis centre
2. Monocytes are separated
3. Lung cancer cell lines are prepared and killed by high hydrostatic pressure
4. Immature DCs are mixed with killed tumor cells and maturation of DCs is induced
5. Mature DCs are prepared
6. 15 doses of DCVAC/LuCa are produced and frozen
7. Patient receives DCVAC treatment

Primary objective:

- To compare efficacy of DCVAC/LuCa + chemotherapy (Arm A) vs. Chemotherapy alone (A rmC) in patients with stage IV NSCLC, as measured by OS.

Secondary objective:

- Comparison of PFS in patients treated with DCVAC/LuCa + chemotherapy (Arm A) vs. chemotherapy alone (Arm C).
- Comparison of safety in patients treated with DCVAC/LuCa + chemotherapy (Arm A) vs. chemotherapy alone (Arm C).
- Comparison of efficacy of DCVAC/LuCa + chemotherapy (Arm A) vs. chemotherapy (Arm C), measured by objective response rate (ORR) and duration of response (DoR) per RECIST 1.1.
- Comparison of safety in patients treated with DCVAC/LuCa + chemotherapy with immune enhancers (Arm B) vs. chemotherapy alone (Arm C), even if the Sponsor does not plan to further research the addition of immune enhancers to DCVAC/LuCa.

Exploratory objectives*:

- Changes in immune responses (blood) to lung cancer associated antigens in patients treated in Arms A and C.
- Exploratory search for prognostic biomarkers

Methods:

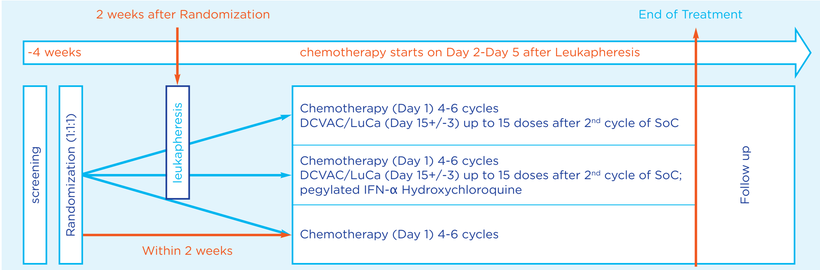
This study evaluated the efficacy and safety of DCVAC/LuCa in chemotherapy naive patients with stage IV NSCLC confirmed histologically or cytologically, ECOG status 0-1 pts were eligible. Stratification was done by histology subtype and smoking history. 112 pts at 12 sites were randomized (A/45 B/29 C/38). Patients were randomized 1:1:1 into one of the following groups:

Arm A: DCVAC/LuCa (active cellular immunotherapy based on dendritic cells) concomitantly added to chemotherapy (carboplatin/paclitaxel)
Arm B: DCVAC/LuCa plus immune modulators (IFN-α and hydroxychloroquine) concomitantly added to chemotherapy (carboplatin/paclitaxel)
Arm C: chemotherapy alone.

Patients in Arms A and B continued treatment with DCVAC up until 15 doses were used, or introduction of new anticancer treatment or intolerance, chemotherapy (carboplatin/paclitaxel) was given 4-6 cycles in all 3 arms. The chemotherapy recommended dose was paclitaxel 175 mg/m^2 over 3 hours followed by carboplatin AUC 6 mg/ml/min over 15-30 min. Patients with stable disease, partial response or complete response after 4 cycles of chemotherapy could continue with chemotherapy up to 6 cycles. The chemotherapy initiated at the 2nd to 5th day after leukapheresis, with the initial chemotherapy cycle without the addition of DCVAC/LuCa. From chemotherapy cycle 2 DCVAC/LuCa was administered on cycle day 15 (+/- 3 days). The length of cycles was the same for all treatment groups.

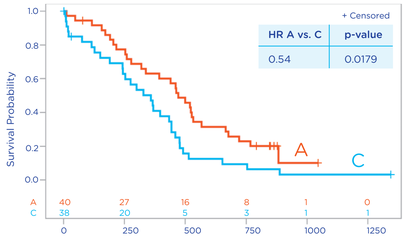
The first patient was enrolled into the trial in Dec 2014, recruitment was completed in Nov 2016. Final efficacy analysis compared Arm A vs. Arm C only as enrollment to Arm B was closed early based on Sponsor's assessment of further clinical development potential, there were no safety concerns or signals. Primary analysis performed in mITT population which consists of all randomized patients except patients randomized to Arm A or B who did not start the DCVAC/LuCa treatment due to leukapheresis or DCVAC/LuCa production failure.

Study design:



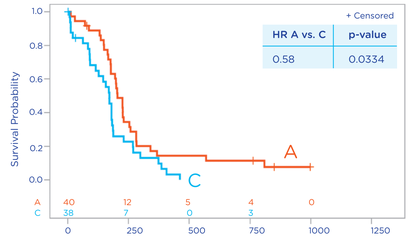
Comparison of Efficacy

OS



OS DATA MATURITY (A+C): 77%	A	B	C
n	40	29	38
deaths	29	24	31

PFS



PFS DATA MATURITY (A+C): 81%	A	B	C
n	40	29	38
PFS event	32	27	31

mITT population	A (40 pts)	B (29pts)	C (38 pts)
Median follow-up (months in all arms pooled: 25.8 (0.1-41.8)			
Overall survival (OS)			
Number of deaths	29	24	31
Median OS (months)	15.5	14.6	11.8
OS HR A vs. C: 0.54, 95% CI [0.32;0.91], p-value 0.0179 (unstratified log-rank test)			
OS HR A vs. C: 0.42, 95% CI [0.23;0.76], p-value 0.0041 (Cox model adjusted for smoking history, histological subtype and gender)			
Progression-free survival (PFS)			
Number of PFS events	32	27	31
Median PFS (months)	6.7	6.0	5.6
PFS HR A vs. C: 0.58, 95% CI [0.35; 0.97], p-value 0.0334 (unstratified log-rank test)			
Objective response rate (ORR)			
ORR (%)	45%	NA	34%

Patients' baseline characteristics

mITT population		A (40 pts)	B (29 pts)	C (38 pts)
Age	Age (median) [years]	69	65	64
Gender	Female (n, %)	14 (35%)	8 (28%)	10 (26%)
	Male (n, %)	26 (65%)	21 (72%)	28 (74%)
Histology	Non-squamous (n, %)	20 (50%)	16 (55%)	20 (53%)
	Squamous (n, %)	20 (50%)	13 (45%)	18 (47%)
Smoking history	Smoker	30 (75%)	29 (100%)	37 (97%)
	Non-smoker	10 (25%)	0 (0%)	1 (3%)

Results:

112 pts at 12 sites were randomized (A/45 B/29 C/38). Patients characteristics were comparable across the study groups with the exception of gender (m/f, %: 65/35 (A) and 74/26 (C) and smoking history 75 % of smokers in A, 97 % in C). Most TEAEs were related to chemotherapy (anemia [35% in A, 37% in B, 32% in C], neutropenia [48% in A, 30% in B, 21% in C], thrombocytopenia [25% in A, 41% in B, 27% in C]). Out of all 67 pts (A+B) who received DCVAC only 6 pts experienced AE related to DCVAC and there were no grade 3 TEAEs solely related to DCVAC. Out of 67 pts only 6 pts experienced leukapheresis- related AE (no grade 3 AEs occurred, two patients experienced vomiting, other AEs experienced in one patient).

Conclusions:

Addition of DCVAC-based immunotherapy to the standard of care chemotherapy significantly prolonged OS by about 3.7 months in stage IV NSCLC without adding-significant toxicity. These results warrant further confirmation in a definitive trial.

Download the poster:

*not presented in the poster

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