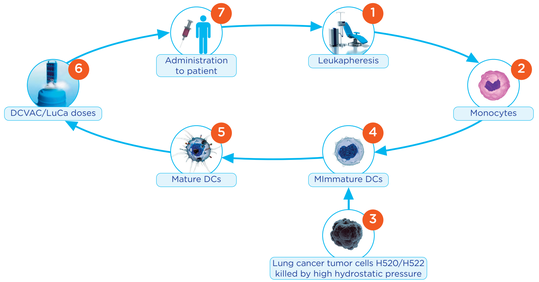
Dendritic-cell vaccine (DCVAC/LuCa) combined with the 1st line chemotherapy in patients with NSCLC Primary analysis of phase 2, open label, randomized, multicenter trial

Authors: Libor Havel[1], Milada Zemanova[2], Milos Pesek[3], Vitezslav Kolek[4], Radek Spisek[5], Jirina Bartunkova[6], Ladislav Pecen[7], Inna Krasnopolskaya[8], Markéta Cernovská[9], [1] Thomayer's Hospital, 1st Faculty of Medicine of Charles University in Prague, Prague, Czech Republic; [2] First Faculty of Medicine, Charles University in Prague, Prague, Czech Republic; [3] Department of Pneumooncology, University Hospital in Pilsen, Plzen, Czech Republic; [4] University Hospital Olomouc, Olomouc, CZ; [5,7,8] SOTIO a.s., Prague, Czech Republic; [6] University Hospital Motol, Prague, Czech Republic; [9] Thomayer hospital, Prague, Czech Republic

Background:

Immunotherapy for induction of tumor cell specific immune responses destroying tumor cells, has emerged as a promising treatment modality in lung cancer. Autologous 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 explore the efficacy of DCVAC/LuCa concurrent with chemotherapy compared to chemotherapy alone in patients with stage IV NSCLC, as measured by OS (one-year survival rate and two-year survival rate).

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:

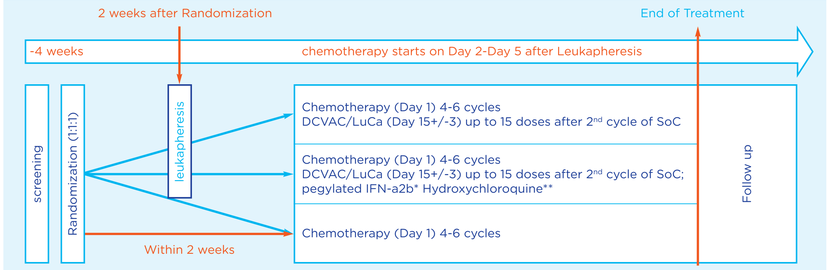
This study evaluated the efficacy and safety of DCVAC/LuCa in chemotherapy naive patients with stage IV NSCLCL confirmed histologically or cytologically, ECOG status 0-1 pts were eligible. Stratification was done by histology subtype and smoking history. 112 pts at 12 sites were randomized (A/45 B/29 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 intollerance, 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 2nd to 5th day after leukapheresis, with the initial chemotherapy cycle delivered 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.

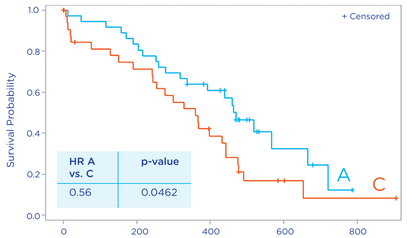
The first patient was enrolled into the trial in Dec 2014, recruitment was completed in Nov 2016. Primary efficacy analysis compared Arm A vs Arm C only as enrollment to Arm B was closed early based on Sponsor's assessment of further clinical development potential, there were no safety concerns or signals. 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:



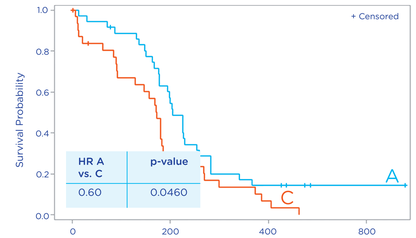
Product-Limit Survival Estimates

OS



Description of Planned Arm		A	B	C
DCVAC/LUCA PARALLEL TO STANDARD CARE	n	40	29	38
	deaths	22	24	26
STANDARD CARE				

PFS



Description of Planned Arm		A	B	C
DCVAC/LUCA PARALLEL TO STANDARD CARE	n	40	29	38
	PFS event	30	27	30
STANDARD CARE				

mITT population	primary analysis (mITT) A (40 pts)	B (29pts)	C (38 pts)
Median follow-up (months)		14.1 (0.03-29.77)	
Number of PFS events	30	27	30
Median PFS (months)	6.73	5.98	5.65
PFS HR A vs C (95% CI)		0.64	
PFS p-value		0.05	
PFS data maturity		81%	
Number of deaths	22	24	26
Median OS (months)	15.5	14.6	11.8
OS HR A vs C (95% CI)		0.56	
OS p-value		0.05	
OS data maturity		65%	
ORR A vs C	45%	NA	22.9%

Patients' baseline characteristics

mITT population		Arm An = 40	Arm Bn = 29	Arm Cn = 38
Age	Age (median) [years]	69	66	65
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%)

* Median OS in arm A: smokers 17 months, non-smokers 15 months. Arm C: smokers 11 months. 1 non-smoker patient in arm C, therefore prognostic/predictive influence of smoking status unclear and will be analyzed based on special sensitivity analysis

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, %: 50/50 (A) and 26/74 (C) and smoking history (75 % of smokers in A, 97 % in C). Most TEAEs were related to chemotherapy (anemia [37%-A, 32%-C], neutropenia [48% in A, 21%-C], thrombocytopenia [28% in A, 27% in C]). There were no grade ≥ 3 TEAEs solely related to DCVAC. Most common leukapheresis-related AEs were hematoma and hypotension.

Conclusions:

Addition of DCVAC-based immunotherapy to the standard of care chemotherapy significantly improved OS in stage IV NSCLC in this Phase 2 trial without adding significant toxicity. These results warrant further investigation in a definitive trial.

Download the poster:

EudraCT number 2014-003084-37

For further information contact Inna Krasnopolskaya, krasnopolskaya@sotio.com