366 COMBINED EXPLORATORY IMMUNOPHENOTYPING AND TRANSCRIPTOMIC TUMOR ANALYSIS IN PATIENTS TREATED WITH OSE2101 VACCINE IN HLA-A2+ ADVANCED NON-SMALL CELL LUNG CANCER (NSCLC) FROM THE ATALANTE-1 TRIAL

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Background OSE2101 (Tedopi®) is an anticancer vaccine with HLA-A2+ restricted modified epitopes targeting five tumor-associated antigens (TAAs) frequently expressed in lung cancer (CEA, HER2, MAGE2, MAGE3, P53). Step-1 results of the phase III, randomized, open-label ATALANTE-1 study comparing Tedopi® vs standard treatment (SoC) showed a favorable benefit/risk of Tedopi® over SoC (HR 0.71 for overall survival OS) in HLA-A2+ NSCLC patients in 2nd or 3rd line treatment after progression on immune checkpoint blockers (ICB).[1] We analyze available tumor biopsies at initial diagnosis from some patients treated with Tedopi® to determine the expression of the 5 TAAs and to identify other tumor factors associated with long-term survival.

Methods Tumor biopsies were available for 8 HLA-A2+ (blood test) stage IV NSCLC patients included in the trial. Primary (<12 weeks) and secondary (≥ 12 weeks) resistance to ICB were observed in 3 (38%) and 5 (62%) of patients. Best response to Tedopi® and OS were: 1 partial response (PR) (OS of 33 months), 3 stable disease (SD) (OS of 22, 26 and 41 mo.) and 4 disease progression (PD) (OS of 3, 4, 30 and 31 mo.). HLA-class I, PD-L1, CD8 T-cells, HER2, CEA and P53 tumor expression were evaluated by immunohistochemistry (IHC). NanoString gene expression profiling was performed using the Pan Cancer Immune gene set.

Results HLA-class I was expressed in all tumor samples. IHC analysis revealed that P53, CEA and HER2 were expressed in 6/7, 5/7 and 0/7 patients, respectively. P53, CEA, HER2, MAGE2, and MAGE3 were detected at RNA level in 5/5 tested patients (table 1). IMMUNOSCORE® IC CD8/PDL1 analysis showed High/High, High/Low and Low/Low scores for 1/7, 1/7 and 5/7 patients, respectively. The High/High IMMUNOSCORE® with a pronounced CD8+ T-cell tumor infiltration was observed in the patient with PR. High percentage of tumor cells expressing P53 (69%–97%) and overexpression of genes associated with activated macrophages (TREM2, MARCO, SLC11A1, CHIT1, SERPINB2) were observed in the PR and SD patients. High IFN-gamma and Expanded Immune Gene Signature scores were observed in long-term survivor patients with secondary resistance to ICB, even after progressive disease.

Abstract 366 Table 1 Summary of clinical and translational data

Patient ID	Secondary Resistance ICB	Best Response Tedopi	PFS Tedopi	OS Tedopi	Tumor HLA-class I	% CEA-positive cells	CEA mRNA	HER2 IHC Score	HER2 mRNA	% P53-positive cells	TP53 mRNA	Number of CD8+ T-cells/mm²	IMMUNOSCORE® IC CD8/PDL1	IFNγ signature (ssGSEA)	Expanded Immune Gene Signature
1708005	No	SD	16.8	41.0	Yes	ND	ND	ND	ND	ND	ND	285	High / Low	ND	ND
1208015	Yes	PR	4.3	33.2	Yes	10%	417	Negative	469	90%	864	425	High / High	171	102
1215018	Yes	SD	4.1	12.6	Yes	0%	ND	Negative	ND	69%	ND	ND	ND	ND	ND
1218013	Yes	SD	2.8	22.2	Yes	20%	395	Negative	1251	97%	873	46	Low / Low	74	37
1218008	Yes	PD	1.4	30.3	Yes	20%	281	Negative	1355	16%	739	107	Low / Low	136	55
1222021	No	PD	1.4	3.3	Yes	5%	ND	Negative	ND	5%	ND	142	Low / Low	ND	ND
1215019	No	PD	1.4	4.2	Yes	30%	135	Negative	2219	18%	1542	1	Low / Low	29	49
1708007	Yes	PD	1.2	30.5	Yes	0%	344	Negative	2248	0%	971	69	Low / Low	116	54

CEA Carcinoembryonic antigen; HER2: Human Epidermal Growth Factor Receptor-2; ICB: Immune checkpoint blocker; IHC: Immunohistochemistry; ND: Not determined; OS: Overall Survival; Patient ID: Patient identification; PDL1: Programmed death-ligand 1; PFS: Progression-free survival; ssGSEA: Single-sample Gene Set Enrichment Analysis. Blue bars = Length of overall survival; Green bars = Gene Signature upregulation; Red bars = Gene Signature downregulation

Conclusions This study shows that all HLA-A2+ patients (blood test), expressed HLA class I in the tumors at initial diagnosis. Transcriptomic data in the patients that benefited from Tedopi® showed activated macrophage pathway, high IFN-gamma and Expanded Immune Gene Signatures scores. These data will be validated on larger number of patients treated with Tedopi® after the step 2 analysis.

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Trial Registration EudraCT number: 2015-003183-36; NCT number: NCT02654587

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1.. Giaccone, et al. Activity of OSE-2101 in HLA-A2+ non-small cell lung cancer (NSCLC) patients after failure to immune checkpoint inhibitors (ICI): step 1 results of phase III ATALANTE-1 randomised trial. *ESMO meeting* 2020, abstract #1260MO.

Ethics Approval The study protocol and its related documents (including the patient information and informed consent form) received approval from the Institutional Review Board (IRB), and the Competent Authority prior to study initiation.

Consent Each patient gave his/her written informed consent prior to study enrolment.

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