## 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

[1]Santiago Viteri*, [2]Werner Hilgers, [3]Fabrice Denis, [4]Elisabeth Quoix, [5]Gilles Robinet, [6]Enriqueta Felip, [7]Rafal Dziadziuszko, [8]Nicolas Poirier, [8]Claudia Fromond, [8]Isabelle Girault, [8]Thomas Vandewalle, [8]Dominique Costantini, [8]Bérangère Vasseur, [9]Federico Cappuzzo, [10]Giuseppe Giaccone, [11]Benjamin Besse. *[1]Instituto Universitario Dexeus and UOMI cancer center, Clinica Mi NovAliança, Barcelona, Spain; [2]Institut Ste Catherine, Avignon, France; [3]Institut Inter-régional de Cancérologie Jean Bernard Elsan, Le Mans, France; [4]Hôpitaux Universitaires de Strasbourg, Nouvel Hôpital Civil, Strasbourg, France; [5]C.H.U. Brest – Hôpital Morvan, Brest, France; [6]Vall d'Hebron University Hospital, Barcelona, Spain; [7]Medical University of Gdansk, Gdansk, Poland; [8]OSE IMMUNOTHERAPEUTICS, Nantes, France; [9]Instituto Nazionale Tumori IRCCS, Rome, Italy; [10]Weill-Cornell Medicine, New York City, NY, USA; [11]Institut Gustave Roussy, Villejuif, France*

**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.

**Acknowledgements** We thank Julie Le Boulicaut, François Montestruc and Constant Josse (eXYSTAT, Malakoff, France) for the statistical analysis, and HalioDx for the IHC and NanoString analysis.

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

### REFERENCE

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.

http://dx.doi.org/10.1136/jitc-2021-SITC2021.366