T-cytotoxic specific immunotherapy in NSCLC with brain metastases.

WCLC 2015. Abstract 1202

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ABSTRACT

- **Background:** Cumulative incidence of brain metastasis (BM) in non-small cell lung cancer (NSCLC) is 16-35% and is associated with poor prognosis (1,2).. The overall survival (OS) of NSCLC patients with BM ranges from 3.0 to 14.8 months when stratified by lung specific graded prognostic assessment (GPA) score (3). The prevalence of BM in NSCLC is reported to be increasing, possibly due to improved brain imaging diagnosis tools and prolonged survival with new systemic therapies (4). Data from NSCLC patients with BM are lacking as patients are often excluded from clinical trials.
- **Methods:** We present the results of a subgroup of NSCLC patients with BM treated with OSE-2101 (T-cytotoxic specific immunotherapy combining 9 epitopes targeting 5 tumor associated antigens and 1 pan-DR epitope) during a phase IIb study of OSE-2101 (1 injection per 3 week for 6 injections followed by 1 injection every 2 to 3 months) in advanced stage IIIB and IV NSCLC (5). Patients were eligible whatever the number of prior chemotherapy (chemo) lines (65.5% entering 3rd line) and patients with stable BM for 2 months could be included. Six out of 64 treated patients had BM prior to inclusion and are reviewed.
- **Results:** Clinical characteristics of the patients are summarized in the table 1. Individual reports regarding overall survival (OS) and time without progression are reported in table 2. The 6 NSCLC patients with BM presented long survival (median 19 months, range 7-41) considering the advanced stage and the poor prognosis of these heavily pre-treated patients (all patients had received from 1 to 3 previous chemo lines). Evaluation of cytotoxic T lymphocytes (CTL) responses to 5 epitopes of OSE-2101 in 5 patients shows that each patient had a CTL response to at least one and up to 5 epitopes. Surprisingly patients with positive HTL response (patient 108, 150, 169) achieve the longest OS when compared with negative HTL patients (132 and 133).
- **Conclusions:** Long OS has been documented in NSCLC patients with BM treated with T-specific immunotherapy following RT and 1 to 3 previous chemo lines. Immunotherapy might be a new therapeutic strategy for BM patients.

BACKGROUND

- Cumulative incidence of brain metastasis (BM) in non-small cell lung cancer (NSCLC) is 16-35% and is associated with poor prognosis (1,2).
- The overall survival (OS) of NSCLC patients with BM ranges from 3.0 to 14.8 months when stratified by lung specific graded prognostic assessment (GPA) score (3).
- The prevalence of BM in NSCLC is reported to be increasing, possibly due to improved brain imaging diagnosis tools and prolonged survival with new systemic therapies (4)
- Data from NSCLC patients with BM are lacking as patients are often excluded from clinical trials.

MATERIAL and METHODS

- Six out of 64 stage IIIB and IV NSCLC patients included in the phase IIb study of OSE-2101 (T-cytotoxic specific immunotherapy combining 9 epitopes targeting 5 tumor associated antigens and 1 pan-DR epitope) (5) had BM. These patients were treated with OSE-2101 (1 injection per 3 week for 6 injections followed by 1 injection every 2 to 3 months). Patients were eligible whatever the number of prior chemotherapy lines (65.5% entering 3rd line) and patients with stable BM for 2 months could be included. These patients were reviewed to know their clinical outcome.

RESULTS

Patients Characteristics

Patient	108	150	169	132	133	135
Gender	F	M	M	M	M	M
Ethnic Origin	CAU	CAU	CAU	CAU	AA	CAU
Age	46	61	58	79	46	57
PS	1	1	1	1	1	1
Previous Treatment	RT 30 Gy, Chemo 2 lines	WBRT 30 Gy, Chemo 2 lines	RT 30Gy, Chemo 2 lines	WBRT 30 Gy, Chemo 3 lines	RT 30 Gy Chemo 1 line	WBRT 30Gy, Chemo 3liens

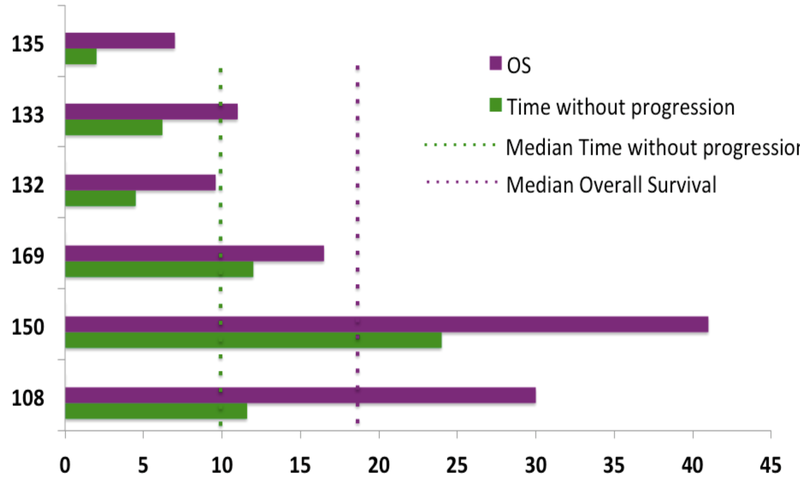
AA: African-American. CAU: Caucasian. Chemo: Chemotherapy. F: Female. M: Male. RT: Radiotherapy.
Gy: Gray. WBRT: Whole Brain RadioTherapy.

Survival and Time without Progression

- The 6 NSCLC patients with BM presented long survival (median 19 months, range 7-41) considering the advanced stage and the poor prognosis of these heavily pre-treated patients (all patients had received from 1 to 3 previous chemo lines).
- Individual reports regarding overall survival (OS), time without progression are reported in table 2

Patient	108	150	169	132	133	135
OS (mo)	30.2	41*	16,5	9.6	11	7**
Time without progression (mo)	11.6	24.4	12	4.5	5.2	2*
CTL response (positive epitopes out of 5 tested)	3	2	5	2	1	NT
HTL response	+	+	+	-	-	NT

* Patient still alive at the time of the last follow up, ** treatment stopped after 2 injections for progressive disease.
CTL: cytotoxic T lymphocytes, HTL: helper T lymphocytes, mo: months, OS: Overall survival,



- Evaluation of cytotoxic T lymphocytes (CTL) responses to 5 epitopes of OSE-2101 in 5 patients shows that each patient had a CTL response to at least one and up to 5 epitopes. Surprisingly patients with positive HTL response (patient 108, 150, 169) achieve the longest OS when compared with negative HTL patients (132 and 133), 29.2 months vs. 10.3 months.

CONCLUSIONS

- Long OS has been documented in NSCLC patients with BM treated with T-specific immunotherapy following RT and 1 to 3 previous chemo lines.
- Immunotherapy might be a new therapeutic strategy for BM patients.

References

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