Active immunotherapy in patients with progressive disease (PD) after first-line therapy: Racotumomab experience.

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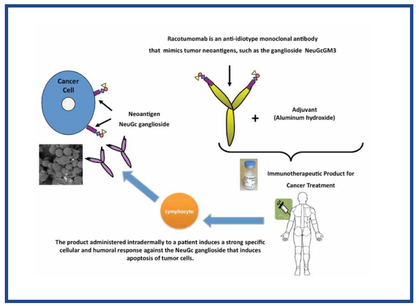
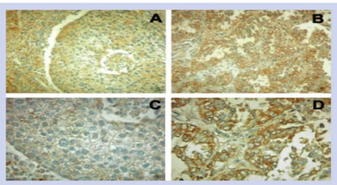
BACKGROUND

Racotumomab is a therapeutic vaccine that induces an immune response against NeuGc-containing gangliosides, sulfatides and other antigens expressed in several human tumors but not in normal tissues. Previous trials have demonstrated low toxicity, high immunogenicity and survival benefit in advanced lung cancer (NSCLC) when Racotumomab was administered in patients with objective response (partial or complete response or stable disease) to first line therapy.



NEUGCGM3 EXPRESSION IN NSCLC



Squamous cell lung carcinomas (A and C) and Lung Adenocarcinomas (B and D) were processed to stain NeuGc-GM3 ganglioside using the 14F7 mAb. Positive representative images are shown. Magnification are 20x (A and B) and 40x (C and D). Every assay were made with the correspondent negative control.

MATERIALS AND METHODS

An open, non- randomized study was performed to evaluate if Racotumomab could be beneficial in patients with progressive disease. Patients with recurrent and advanced stages of NSCLC, in progression after completion of first-line onco-specific treatment as per the NCCN Oncology Therapeutic Guidelines (surgery, chemotherapy and/or radiotherapy) were included in the study. Most of them had received 4 to 6 cycles of cisplatin/vinblastin. Racotumomab was administered intradermally; the first 5 doses every 14 days (induction period), followed by 1 dose every 28 days (maintenance period) until patient refusal or worsening of ECOG status. The patients did not receive second line therapy. At inclusion patients had progressive disease (PD) according to Recist. 89 patients were in stage IIIB, 71 were in stage IV (88.8%) and 20 patients (11.1%) had recurrent disease. 180 patients treated with Racotumomab and a control group of 85 consecutive patients treated at the same institution by the same investigators were included in an intent to treat (ITT) and per protocol (PPP = patients in the racotumomab group who received more than 5 doses, or patients with survival longer than 3 months in control group) survival analysis (Kaplan Meier estimate).

CLINICAL AND DEMOGRAPHIC CHARACTERISTICS

Variables N= 180	N (%)
Age	
Mean (Range)	63 (35-86)
Median	63.69
Race	
White	124(68.8 %)
Black	38 (21.1 %)
Other	18 (10 %)
Sex	
Male	107 (59.4%)
Female	73(40.5%)
ECOG Performance Status	
ECOG 0	56 (31.11 %)
ECOG 1	105 (58.3 %)
ECOG 2	18 (10%)
ECOG 3	1(0.55 %)

Variables	N (%)
Tumor stage	
IIIB	89 (49.4%)
IV	71 (39.4%)
Recurrent	20 (11.1%)
Tumor Histology	
NSCLC	23 (12,7%)
ADC	51 (28.3 %)
SCC	66 (36.6%)
LCC	40 (22.22%)

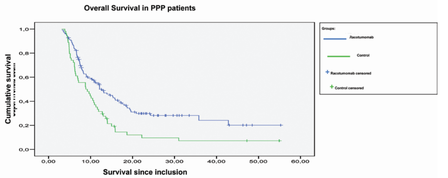
Previous Therapy	Yes	No
Radiotherapy	69 (38.3%)	111 (61.6 %)
Platinum-CT	176 (97.7 %))	4 (2.2 %)

RESULTS

SAFETY: MORE COMMON ADVERSE EVENTS RELATED WITH RACOTUMOMAB ADMINISTRATION. ALL OF THEM WHERE I-II GRADE (CTC-NCI VERSION (3.00)

AE		%
Burning at injection site	225	21.1
Bone pain	108	10.1
Pain at injection site	95	8.9
Cough	88	8.2
Dyspnea	56	5.3
Asthenia	48	4.5
Local erythema	39	3.7
Anorexia	27	2.5
Vomiting-nausea	28	2.6
Induration	17	1.6
Headache	25	2.3
Hypersensitivity in the limb injected	21	2.0
Fever	16	1.5

OVERALL SURVIVAL



ITT	Mean (months)	Median (months)	OS rate at 24 months (%)
Racotumomab N= 180 E= 132	16.6	8.06	21
Control N= 85 E= 77	10.6	6.26	7

PPP	Mean (months)	Median (months)	OS rate at 24 months (%)
Racotumomab N= 124 E=81	21.7	12.1	30
Control N= 54 E= 48	13.01	8.8	7.2

N = Number of patients E = Number of events ITT = Intent to treat
PPP = Racotumomab group patients who received more than 5 doses Control group patients with survival longer than 3 months.

CONCLUSIONS

In this study Racotumomab shows similar results to those previously reported in NSCLC clinical trials. Treatment with Racotumomab was safe and showed a promising survival improvement in advanced NSCLC patients in progression after first line onco-specific treatment.