Active Specific Immunotherapy with Racotumomab in the Treatment of Advanced Non Small Cell Lung Cancer (NSCLC)

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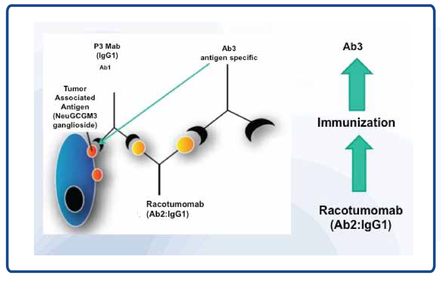
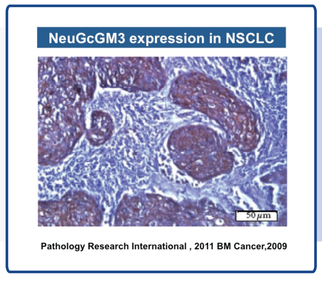
Background: Gangliosides, especially NeuGc-GM3, are an attractive target for cancer immunotherapy. They do not express in normal human cells but are overexpressed in several solid tumors including NSCLC and are involved in tumor development and growth. Racotumomab is therapeutic vaccine that induces an immune response against NeuGc-containing gangliosides, sulfatides and other antigens expressed in several human tumors but not in normal tissues. Previous phase I and II trials in melanoma, breast and lung cancer have shown the low toxicity and high immunogenicity of Racotumomab.





Methods: Multicenter, randomized, placebo controlled, double blind clinical trial in patients with advanced (IIIB and IV) NSCLC who had an ECOG status ≤ 2 and had achieved partial or complete response or disease stabilization after completion of onco-specific treatment. 176 patients were randomized 1:1 to Placebo or Racotumomab. Initially 1 dose was administered every 14 days (induction period, 5 doses in total), followed by 1 dose every 28 days (maintenance period) until patient refusal or worsening of ECOG status.

Results:

Baseline characteristics of the patients:

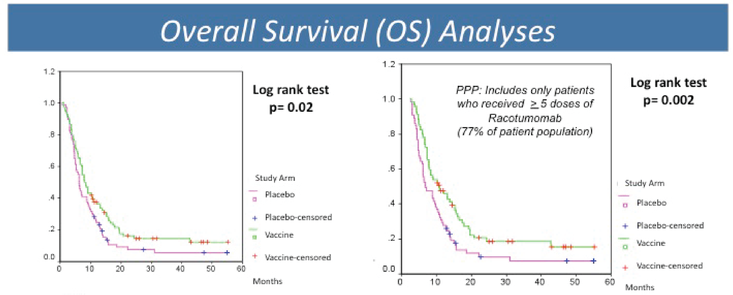
Characteristics	Vaccine N=88	Placebo N= 85
Age Mean (range)	62 (45-70)	61.9 (40-86)
Gender n (%)		
Female	21 (23.8%)	36 (42.3%)
Male	67(76.1%)	49(57.6%)
ECOG PS n (%)		
0	41 (46.6%)	38 (44.7%)
1	45 (51.1%)	43 (50.6%)
2	2 (2.3%)	4 (4.7%)
Race n (%)		
Caucasian	74 (84.1%)	65 (76.5%)
African-american	13 (14.8%)	11 (12.9%)
Other	1 (1.1%)	9(10.6 %)
Smoker n (%)	20 (22.7%)	14(16.4%)
Former smoker n (%)	64 (72.7%)	68 (80.0%)
non smoker	4(4.5%)	3 (3.5%)

Characteristics n (%)	Vaccine N=88	Placebo N= 85
Tumor Histology		
Squamous cell carcinoma	32 (36.3%)	34(40.0%)
Adenocarcinoma	27 (30.6%)	27 (31.7%)
Large Cell Carcinoma	17 (19.3%)	15(17.6%)
NSCLC (Other)	12 (13.6%)	9 (10.5%)
Disease Stage		
IIIB	54 (61.3%)	44 (51.7%)
IV	34(38.6%)	41(48.2%)
First-line Treatment		
CT	88(100%)	85(100%)
RT	55(62.5%)	40 (47.0%)
First line Chemotherapy drugs: Platinum compounds	88(100%)	85(100%)
Response to first-line treatment		
CR	3 (3.4%)	4(4.7%)
PR	42 (47.7%)	46 (54.1%)
SD	43 (48.9%)	35 (41.1%)

Safety: The most common adverse events were expected mild reactions at the injection site (pain and itching). No differences were observed between both groups.

AE	Racotumomab	%	Placebo	%	Total	%
Burning at injection site	225	21.1	199	21.2	424	21.1
Bone pain	108	10.1	94	10.0	202	10.1
Pain at injection site	95	8.9	67	7.1	162	8.2
Cough	88	8.2	65	6.9	153	7.6
Dyspnea	56	5.3	42	4.5	98	4.8
Asthenia	48	4.5	45	4.8	93	4.6
Local erythema	39	3.7	39	4.2	78	3.9
Anorexia	27	2.5	37	3.9	64	3.2
Vomiting-nausea	28	2.6	16	1.7	44	2.2
Induration	17	1.6	25	2.7	42	2.1
Headache	25	2.3	16	1.7	41	2.0
Hypersensitivity in the limb injected	21	2.0	15	1.6	36	1.8
Fever	16	1.5	18	1.9	34	1.7

Overall Survival:



OS (ITT)		
Arm	Mean	Median
Racotumomab (n= 88) Events: 73	15.7	8.3
Placebo (n= 85) Events: 77	10.6	6.3

OS (PPP)		
Arm	Mean	Median
Racotumomab (n= 69) Events: 54	18.9	10.9
Placebo (n= 65) Events: 58	11.4	6.9

OS Rate	6 m	12 m	18 m	24 m
Racotumomab	68	38	23	17
Placebo	55	24	11	7

OS Rate	6 m	12 m	18 m	24 m
Racotumomab	83	48	29	22
Placebo	63	28	13	8

Conclusions:

Immunization with Racotumomab is safe. There is an OS benefit for Racotumomab, both in the ITT and PPP analyses. Survival benefit appears to be increased when the patient's clinical condition allows completion of the induction period of vaccination.

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