PEGylated human IL-10 (AM0010, Pegilodecakin) in Combination with an anti-PD-1 in Advanced NSCLC

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Background

At therapeutic concentrations, AM0010 stimulates the cytotoxicity, survival and proliferation of intratumoral antigen activated CD8+ T cells in pre-clinical cancer models and in patients. AM0010 activates antigen stimulated CD8 T cells while PD-1 inhibits them, providing a rationale for combining AM0010 with PD-1 inhibitors.

AM0010 monotherapy induced durable objective responses in ocular melanoma and renal cell cancer. AM0010 alone or in combination with chemotherapy and anti-PD-1 has been well tolerated in this Phase 1 basket trial.

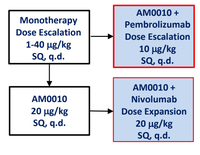
Study Design and Eligibility

AM0010
- 9 pts. with metastatic NSCLC were treated with AM0010 (20µg/kg SQ, q.d.) (7 pts. were evaluable for tumor response)

AM0010 + Pembrolizumab
- 5 pts. with advanced NSCLC treated with AM0010 (10µg/kg SQ, q.d.) and pembrolizumab (2mg/kg, IV q3wk).

AM0010 + Nivolumab
- 29 pts. with advanced NSCLC treated with AM0010 (20µg/kg daily SQ, q.d.) and nivolumab (3mg/kg, IV q2wk).

Tumor responses were measured according to irRC criteria.

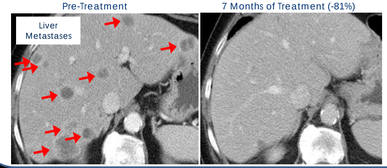


Key Eligibility in AM0010 + Nivolumab Expansion Cohort
- Advanced NSCLC with progression on prior platinum based regimen, no prior anti-PD-1/PD-L1 containing therapy.
- Excluded prior Guillain-Barré syndrome and neuro-inflammatory diseases
- Allowed all other autoimmune diseases (example RA, Crohn's disease, psoriasis)

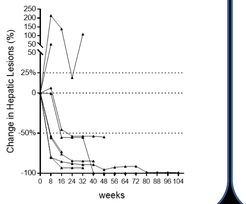
NSCLC Liver Metastases Respond Well to AM0010 + Anti-PD-1

- NSCLC patients with liver metastasis have a lower overall response rate to immune checkpoint inhibition. Tumeh et al. Cancer Imm. Res. 2017; Pillai et al ASCO 2017
- On AM0010 + anti-PD-1, six of eight patients with NSCLC metastases to the liver had a reduction of the liver metastases of more than 50%.

AM0010 + Pembrolizumab in PD-L1 neg. NSCLC

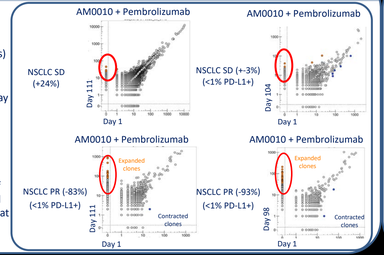


Average change in target lesions in the liver of each NSCLC patient (n=8)



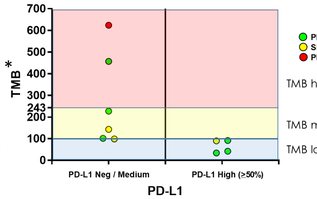
Clonal T cell Expansion correlates with Tumor Response

- T cell clonality analysis from peripheral blood by TCRb deep sequencing (Adaptive Biotechnologies)
- Comparison of on-treatment samples with pretreatment baseline (Day 1); NSCLC (PD-L1<1%+)
  - Expansion of novel T cells continues throughout the treatment
  - Sustained expansion of "newly expanded T cell clones (not detectable at Day 1) correlates with objective responses



Responses in Patients with low TMB / low or high PD-L1

- NSCLC patients with low or intermediate tumor mutational burden had a reduced response rate to nivolumab alone (n=23 of 111, 21%). Carbone et al. NEJM 2017
- Five of eight patients (62.5%) with low or intermediate TMB had a partial response on AM0010 + anti-PD-1, including 2 patients which were <1% PD-L1+. Additional three patients had SD for more than six months
- Archival tumor tissues (FFPE slides) were analyzed for tumor mutational burden (TMB) by whole exome sequencing and by immuno-histochemistry for PD-L1 expression (22C3, evaluated by an independent pathologist)



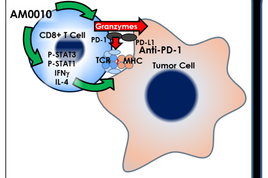
* Missense mutation per exome

AM0010 - Mechanism of Action (Background cont.)

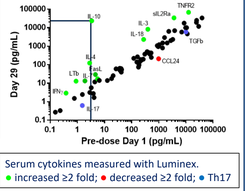
- IL-10 is anti-inflammatory and at higher concentrations and continuous exposure leads to the activation and expansion of antigen activated CD8+ T cells
- Tumor antigen recognition by CD8+ T cells (TCR) induces the IL-10 receptor on CD8+ T cells
- IL-10 activates CD8+ T cells ("Cytotoxic License")
- PEG-IL-10 induces phosphorylation of the STAT1 and STAT3 in CD8+ T cells. This leads to increased cytotoxicity, proliferation and survival of CD8+ T cells and the persistence of antigen activated intratumoral CD8+ T cells

PEG-IL-10 treatment in preclinical tumor models with large tumors induced tumor rejection and the establishment of anti-tumor immune memory. (Mumm Cancer Cell 2011; Emmerich Cancer Res 2012).

In a large Phase 1 study, 144 patients with advanced solid tumors have been treated with **AM0010 monotherapy**.
AM0010 Monotherapy increased Th1 cytokine and the products of cytotoxic T cells in the serum of patients.

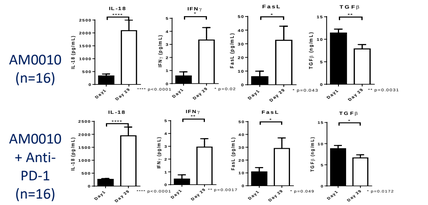


AM0010 Induced Serum Cytokines



Serum cytokines measured with Luminex.
● increased ≥2 fold; ● decreased ≥2 fold; ● Th17

Th1 Cytokines Changes with AM0010 or AM0010+ Pembrolizumab (RCC patients)



Results

AM0010 / AM0010 + anti-PD-1 in NSCLC Patients

- A cohort of 34 NSCLC pts. was fully enrolled on AM0010 (10-20µg/kg SC, q.d.) and pembrolizumab (2mg/kg, q3wk IV; n=5) or nivolumab (3mg/kg, q2wk IV; n=29).
- Pts had a median of 2 prior therapies (range 1-3).
- The median follow-up is 18.75 months (range 8.3 to 33). Tumor responses were assessed by irRC.
- 24 patients were analyzed for PD-L1 expression (22C3), 66.7% had <1%, 12.5% had 1-49% and 20.8% had >50% PD-L1+ tumor cells.
- Immune responses were measured by analysis of serum cytokines (Luminex), activation of blood derived T cells (FACS) and peripheral T cell clonality (TCR sequencing by Adaptive Biotechnology).

	AM0010 Monotherapy 2mg (20 µg/kg) N=9	AM0010 1mg (10 µg/kg) + Pembrolizumab N=5	AM0010 2mg (20 µg/kg) + Nivolumab N=29
Median Age, years (range)	58 (44, 68)	74 (56, 80)	62 (40, 84)
Sex, n (%)			
Male	2 (22%)	4 (80%)	14 (48%)
Female	7 (78%)	1 (20%)	15 (52%)
ECOG Performance Status, n (%)			
0	3 (33%)	0 (0%)	8 (25%)
1	6 (66%)	5 (100%)	21 (75%)
Histology type, n (%)			
Squamous	0	2 (40%)	4 (14%)
Non-squamous	9 (100%)	3 (60%)	24 (83%)
Unknown	0	0	1 (3%)
Prior Therapy, median (range)	3 (1-7)	2 (0-5)	2 (1-3)
PD-L1+ Status n(%) <1% PD-L1+: 1-49% PD-L1+: >50% PD-L1+:	5 tested n=5 (100%)	4 tested n=4 (100%)	20 tested n=12 (60%) n=3 (15%) n=5 (25%)

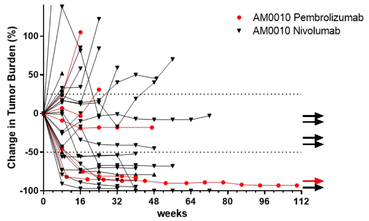
* Includes 16 patients evaluable for tumor response

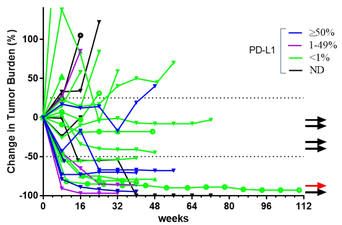
AM0010 / AM0010 + anti-PD-1 in NSCLC Safety Profile

System Organ Class / Preferred Term	Grade 1/2 mono N=9	Grade 1/2 anti-pd1 combo N=34	Grade 3/4 mono N=9	Grade 3/4 anti-pd1 combo N=34
Blood and lymphatic system disorders				
Anaemia	3 (33.3%)	6 (17.6%)	2 (22.2%)	8 (23.5%)
Thrombocytopenia	2 (22.2%)	6 (17.6%)	3 (33.3%)	8 (23.5%)
Gastrointestinal disorders				
Diarrhoea		2 (5.9%)		
General disorders and administration site conditions				
Chills	1 (11.1%)	3 (8.8%)		
Fatigue	1 (11.1%)	6 (17.6%)	2 (22.2%)	6 (17.6%)
Injection site reaction		3 (8.8%)		
Pyrexia	3 (33.3%)	7 (20.6%)		2 (5.9%)
Investigations				
International normalised ratio increased	1 (11.1%)	4 (11.8%)		
Metabolism and nutrition disorders				
Decreased appetite		6 (17.6%)		
Hypertriglyceridaemia	1 (11.1%)	4 (11.8%)		3 (8.8%)
Hypoalbuminaemia	3 (33.3%)			
Musculoskeletal and connective tissue disorders				
Arthralgia		3 (8.8%)		
Myalgia	3 (33.3%)	3 (8.8%)		
Nervous system disorders				
Headache	2 (22.2%)	3 (8.8%)		
Peripheral sensory neuropathy		2 (5.9%)		
Respiratory, thoracic and mediastinal disorders				
Dyspnoea		3 (8.8%)	1 (11.1%)	
Pneumonitis		2 (5.9%)		1 (2.9%)
Skin and subcutaneous tissue disorders				
Dry skin	1 (11.1%)	2 (5.9%)		
Pruritus	2 (22.2%)	4 (11.8%)		
Rash	3 (33.3%)	7 (20.6%)		1 (2.9%)
Rash maculo-papular	1 (11.1%)	5 (14.7%)		3 (8.8%)
Vascular disorders				
Hypotension	1 (11.1%)	2 (5.9%)		

Table includes all patients with a G1-4 TrAEs according to NCI-CTCAE v4.02, (>1 AE & > 5% in at least one cohort)

Combination of AM0010 and anti-PD-1



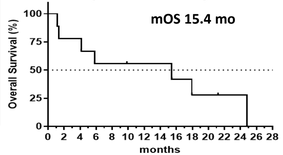


Disease	Treatment Combo	ORR by PD-L1 status (%) All	<1% PD-L1+ (n=12)	1-49% PD-L1+ (n=3)	➢ 50% PD-L1+ (n=5)
NSCLC	**AM0010 + anti-PD-1 mAbs**	41% (n=27)	33 %	67%	80.0%
	Pembrolizumab (Garon, NEJM; 2015)	19.4%	9.1%	15.6%	43.9%

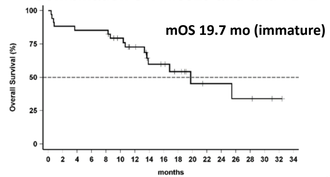
A cohort of 9 NSCLC pts. were enrolled on AM0010 (20µg/kg SQ, q.d.).

A cohort of 34 NSCLC pts. was enrolled on AM0010 (10-20µg/kg SQ, q.d.) + pembrolizumab (2mg/kg, q3wk IV; n=5) or nivolumab (3mg/kg. q2wk, IV; n=29).

AM0010 Monotherapy (Median 4th LOT)



Combination of AM0010 and anti-PD-1



Summary of Results

- **AM0010 + anti–PD-1 is well tolerated in NSCLC**
  - No increase or exacerbation of autoimmune toxicities
  - Recommended Phase2/3 dose is 10 µg/kg, SQ, q.d. in combination with an anti-PD-1.
- **CD8+ T cell invigoration and clonal expansion of novel T cells confirms the activation of an essential MOA for immune therapy of cancer**
- **The ORR and durability of responses regardless of PD-L1 expression suggests an efficacious combination for phase 2/3 studies.**
- **Preliminary PFS and OS findings are encouraging.**

Disease	Treatment Combo (n=Evaluable Patients/ Enrolled Patients)	Prior Therapies Median (Range)	DCR (%)	ORR (%)	mPFS (Months)	mOS (Months)
NSCLC	**AM0010** (n=7/9)[1]	3 (1-7)	57%	–	1.7	15.4
	AM0010 + anti-PD-1 [3] (n=27/34)	2 (0-5)	85%	11 (41%)[2]	7.4[3]	19.7[3]
	Anti-PD-1 (Pembrolizumab) (Garon NEJM 2015)	1	41%	19.4%	3.0[4]	9.3[4]

(1) 5 of 5 patients tested are <1% PD-L1+; 4 of 4 patients tested are <1% PD-L1+; (2) of all evaluable patients, n=27, numbers of 10/29/2017; (3) intend to treat population, (n=34) Study in progress. Numbers as of 10/29/2017. 60% alive, median follow-up 18.75 months (range 8.3 to 33) ; (4) Garon et al NEJM 2015, previously treated patients

Information

SPONSOR

AM0010 is being developed by ARMO BioSciences.

REFERENCES

1. Garon et al., NEJM 2015; 2. Naing et al., JCO 2016; 3. Carbone et al., NEJM 2017; 4. Mumm et al., Cancer Cell; 2011; 5. Emmerich et al., Cancer Research; 2012; 6. Oft, CIR; 2014 (Review)

CONTACT INFORMATION

The pdf of this poster is available at http://www.armobio.com/news-presentations.php. For more information on this trial, go to clinicaltrials.gov (NCT02009449) or contact martin.oft@armobio.com