Poster # 2634

Initial Findings of the First-in-human Phase I Study of AGEN2373, a Conditionally Active CD137 Agonist Antibody, in Patients (pts) With Advanced Solid Tumors

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Background

AGEN2373 is a CD137 agonist antibody designed to be conditionally active and selectively enhance innate and adaptive immunity only in presence of Fc-gamma receptors

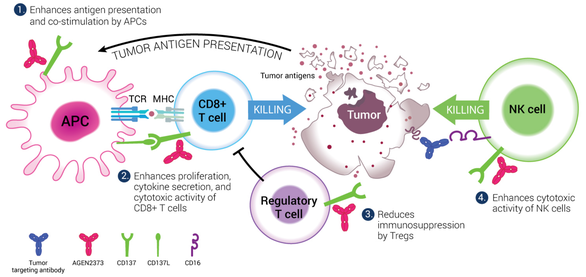

Figure 1. AGEN2373 (fully human, IgG1λ) is designed to enhance antitumor immunity through multiple mechanisms-of-action. Antibody-mediated CD137 agonist activity is anticipated to enhance antigen-presenting cell (APC), T cell, and natural killer (NK) cell function. [1, 2] AGEN2373 may also target intratumoral Tregs for antibody-dependent cell cytotoxicity or phagocytosis (ADCC/ADCP)-mediated destruction.[3]

Phase I Study Overview (NCT04121676)

Objective (Cohort 1: Q4W dose-escalation)

Evaluate the safety, tolerability, and dose-limiting toxicity (DLT) of AGEN2373 as monotherapy in patients with advanced solid tumors.

Treatment schedule

AGEN2373 was administered on Day 1 of a four-week week cycle (Q4W) using a standard 3+3 dose-escalation design. Treatment is permitted for up to 2 years or until progressive disease/unacceptable toxicity.

Summary of Dose Escalation

Cohort	AGEN2373 dose (mg/kg)	No. of patients	No. ongoing
1	0.03	3	-
2	0.06	6	-
3	0.3	3	-
4	1.0	4	-
5	2.0	3	1
6	3.0	3	3
Totals		**22**	**4**

Table 1. Cohort escalation summary. Twenty-two patients received AGEN2373 as monotherapy Q4W, with dosing escalated from 0.03 to 3.0 mg/kg across 6 cohorts. At data cut off, 4 patients remained on treatment. No DLTs have been observed at any dose level.

Safety and Tolerability

Adverse event summary

Event	All patients n (%)
Any TEAE	22 (100.0)
Grade ≥3 TEAE	12 (54.6)
Any TRAE	10 (45.5)
Grade ≥3 TRAE	0 (0)
TRAE leading to dose interruption	0 (0)
TRAE leading to discontinuation	0 (0)
TRAE leading to death	0 (0)
Any immune-related TEAE	0 (0)

Table 2. Overall adverse event summary in the safety population. TEAE, treatment-emergent adverse event; TRAE, treatment-related adverse event.

Treatment-related adverse events

Adverse Event	All patients n (%)
All grades	10 (45.5)
Fatigue	4 (18.2)
Nausea	2 (9.1)
Diarrhea	1 (4.5)
Vomiting	1 (4.5)
Colitis	1 (4.5)
Weight loss	1 (4.5)
Dysgeusia	1 (4.5)
Rash	1 (4.5)
Dry skin	1 (4.5)
Elevated TSH	1 (4.5)

Table 3. Individual treatment-related adverse events reported across all cohorts. All TRAEs were grade 1 or 2; no grade ≥3 events were observed. TSH, thyroid stimulating hormone.

Clinical Activity

Maximum change in target lesion size from baseline (%)

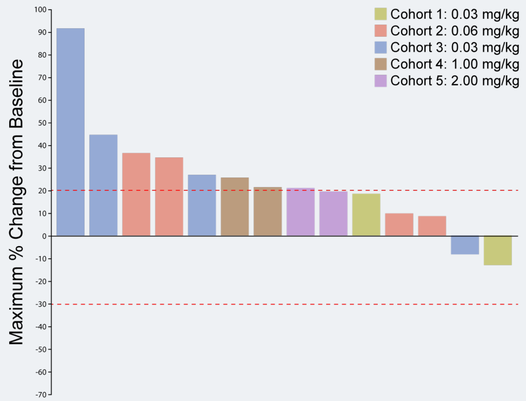

Figure 2. Waterfall plot showing best percentage change in target lesion size from baseline, with dose level indicated by color coding of bars. Data are presented for 14 evaluable patients who received at least one dose of AGEN2373 with available post-baseline measurements.

Percent changes in target lesions over time

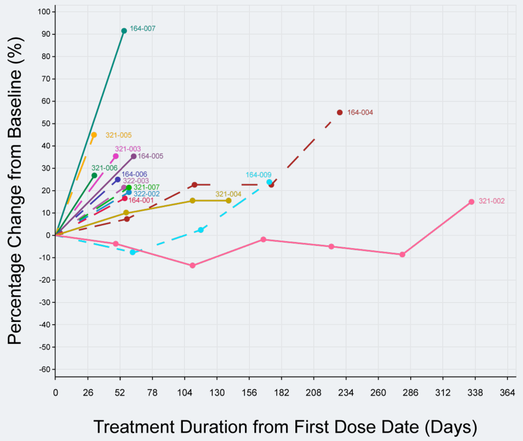

Figure 3. Spider plot showing changes in target lesions as a function of time. Data are presented as individual plots for the 14 evaluable patients. Five patients achieved stable disease (SD) as best overall response to therapy per RECIST v1.1; in 3 of these subjects prolonged SD (≥ 12 weeks) was seen.

Baseline Demographics

Characteristic	N = 22
Age	
Median (range)	63 (33-78)
Sex, *n (%)*	
Male	13 (59.1)
Female	9 (40.9)
ECOG PS, *n (%)*	
0	3 (13.6)
1	19 (86.4)
No. prior systemic therapies,* *n (%)*	
1-2	4 (18.2)
3-5	17 (77.3)
Prior anti-PD-1 immunotherapy, *n (%)*	
Yes	7 (31.8)
No	15 (68.2)

Table 4. Baseline demographics and patient characteristics. ECOG PS, Eastern Cooperative Oncology Group performance status. *Data missing for one individual.

Conclusions

- ✓ AGEN2373 is a CD137 agonist antibody designed to be conditionally active and selectively enhance tumor immunity while mitigating side effects associated with systemic activation of CD137
- ✓ Consistent with this, AGEN2373 demonstrated good tolerability in heavily pretreated patients with advanced solid tumors
- ✓ Dosing has been escalated to 3 mg/kg on a Q4W regimen – no DLTs or evidence of hepatotoxicity have been observed to date
- ✓ Prolonged disease stabilization (≥12 weeks) as best response was seen in 3 patients
- ✓ These initial findings underscore the suitability of AGEN2373 as a potential combination partner with other immunomodulatory agents
- ✓ Evaluation of Q2W monotherapy dosing is underway, with expansion into combination treatment with the anti-PD-1 antibody balstilimab planned

References:

1. Bartkowiak and Curran, *Front Oncol* 2015
2. Masu et al., *PLOS One* 2018
3. Freeman et al., *J Clin Invest* 2020

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