

Initial results from a phase 1a/b study of Etigilimab (OMP-313M32), an anti-T cell immunoreceptor with Ig and ITIM domains (TIGIT) antibody, in advanced solid tumors

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313M32-001 Study Design

Phase 1a

Dose Escalation

Tumor types for inclusion in dose escalation cohort:

- Histologically confirmed advanced relapsed or refractory solid tumors
- Preference to enroll subjects with the tumor types specified for the dose expansion cohort.
- Optional pre and post-tumor biopsies

(n~18)

20mg/kg Q2W
N=3+3

10mg/kg Q2W
N=3+3

3mg/kg Q2W
N=3+3

1mg/kg Q2W
N=3+3

0.3mg/kg* Q2W
N=3+3

MTD

Expansion Cohort

Tumor types for inclusion in expansion cohort:

- Head and neck cancer
- Esophageal cancer
- Gastric cancer
- Cervical cancer
- Triple-negative breast cancer
- Anal cancer
- Hepatocellular cancer
- Known MSI high solid tumors (including MSI CRC and others)
- NSCLC

(n~12)

Mandatory pre- and post-treatment biopsies

N=30 Total to be enrolled

Phase 1b

Dose Escalation

Tumor types for inclusion in dose escalation cohort:

- Histologically confirmed advanced relapsed or refractory solid tumors
- Refractory to or progressed after anti-PD1/L1
- Pre and post-tumor biopsies for cohorts 2/3

20mg/kg Q2W + nivolumab
N=3+3

10mg/kg Q2W + nivolumab
N=3+3

3mg/kg Q2W + nivolumab
N=3+3

P1a cleared 10 mg/kg

P1b triggered at -1 dose

N=12 Total to be enrolled

Primary objective:

- Safety, tolerability

Secondary objectives:

- Establish MTD
- Establish RP2D
- PK/immunogenicity
- Preliminary efficacy

Exploratory objectives:

- PD and predictive biomarkers

Baseline Characteristics

	Dose Escalation					Phase 1a Overall (N=18)
	0.3 mg/kg Q2W (N=3)	1.0 mg/kg Q2W (N=3)	3.0 mg/kg Q2W (N=3)	10.0 mg/kg Q2W (N=3)	20.0 mg/kg Q2W (N=6)	
Age (years)^[1]						
<65	2 (66.7%)	1 (33.3%)	1 (33.3%)	1 (33.3%)	5 (83.3%)	10 (55.6%)
>=65 - <75	1 (33.3%)	2 (66.7%)	2 (66.7%)	2 (66.7%)	1 (16.7%)	8 (44.4%)
>=75						
Missing						
Sex						
Male	1 (33.3%)	2 (66.7%)	1 (33.3%)	1 (33.3%)	2 (33.3%)	7 (38.9%)
Female	2 (66.7%)	1 (33.3%)	2 (66.7%)	2 (66.7%)	4 (66.7%)	11 (61.1%)
Initial Diagnosis (Cancer Type)						
Colorectal cancer	2 (11.1%)	1 (5.6%)	1 (5.6%)	1 (5.6%)	1 (5.6%)	6 (33.3%)
Endometrial cancer				1 (5.6%)	1 (5.6%)	2 (11.1%)
Pancreatic cancer				1 (5.6%)	1 (5.6%)	2 (11.1%)
Uterine cancer		1 (5.6%)			1 (5.6%)	2 (11.1%)
Adenoid cystic carcinoma					1 (5.6%)	1 (5.6%)
Anal Cancer						1 (5.6%)
Ewing sarcoma			1 (5.6%)			1 (5.6%)
Fallopian tube cancer			1 (5.6%)			1 (5.6%)
Gallbladder cancer	1 (5.6%)					1 (5.6%)
Head and neck cancer		1 (5.6%)				1 (5.6%)
Triple-negative breast cancer					1 (5.6%)	1 (5.6%)
Microsatellite Status						
MSI (Microsatellite Instability)					1 (16.7%)	1 (5.6%)
MSS (Microsatellite Stable)	2 (66.7%)	1 (33.3%)		1 (33.3%)	1 (16.7%)	5 (33.3%)
Unknown	1 (33.3%)	2 (66.7%)	3 (100.0%)	2 (66.7%)	4 (66.6%)	12 (66.7%)

Safety

Adverse Events (all Grades ≥15%)

Preferred Term (group)	Grade (Maximum per subject)			Total
	1	2	3	
Rash	4 (22.2%)		3 (16.7%)	7 (38.9%)
Nausea	6 (33.3%)			6 (33.3%)
Pruritus	4 (22.2%)			4 (22.2%)
Constipation	4 (22.2%)			4 (22.2%)
Abdominal pain	2 (11.1%)		2 (11.1%)	4 (22.2%)
Vomiting	3 (16.7%)			3 (16.7%)
Fatigue		3 (16.7%)		3 (16.7%)
Dyspnoea		3 (16.7%)		3 (16.7%)
Cough	3 (16.7%)			3 (16.7%)
Chills	3 (16.7%)			3 (16.7%)
Abdominal distension	3 (16.7%)			3 (16.7%)

Adverse Events (Grade ≥3, ≥10%)

Preferred Term (group)	Grade (Maximum per subject)		Total
	3	5	
Rash	3 (16.7%)		3 (16.7%)
Pulmonary embolism	2 (11.1%)		2 (11.1%)
Hypertension	2 (11.1%)		2 (11.1%)
Embolism	2 (11.1%)		2 (11.1%)
Abdominal pain	2 (11.1%)		2 (11.1%)

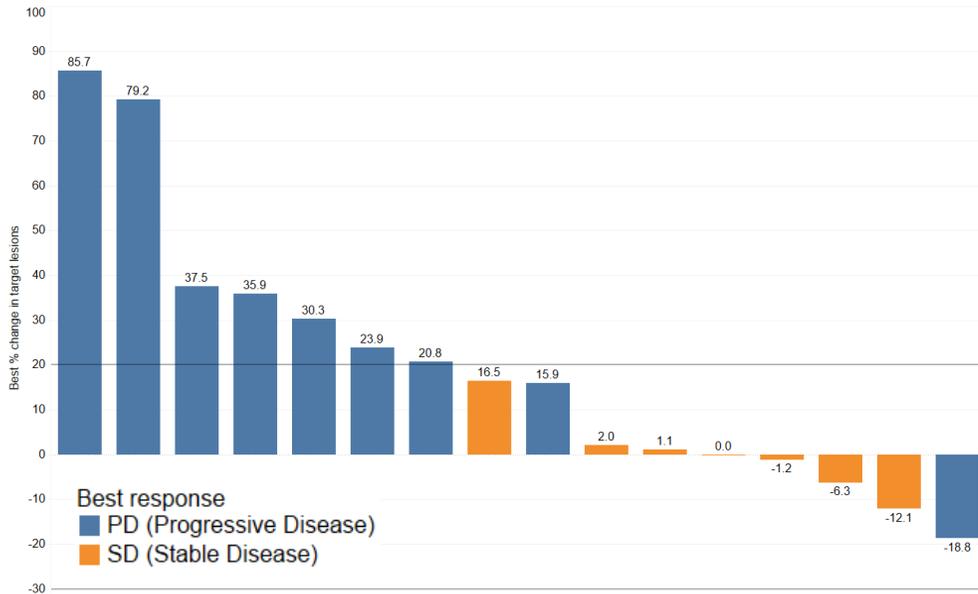
Immune-Related Adverse Events

Preferred Term (group)	Dose Cohort / Max. Grade (Maximum per subject)			
	1.0 mg/kg	3.0 mg/kg	10.0 mg/kg	20.0 mg/kg
	3	1 3	1 3	1 3
Rash	1	1	3	
Pruritus		1	1	1
Autoimmune hepatitis				1
Stomatitis				1

Efficacy

Dose Escalation

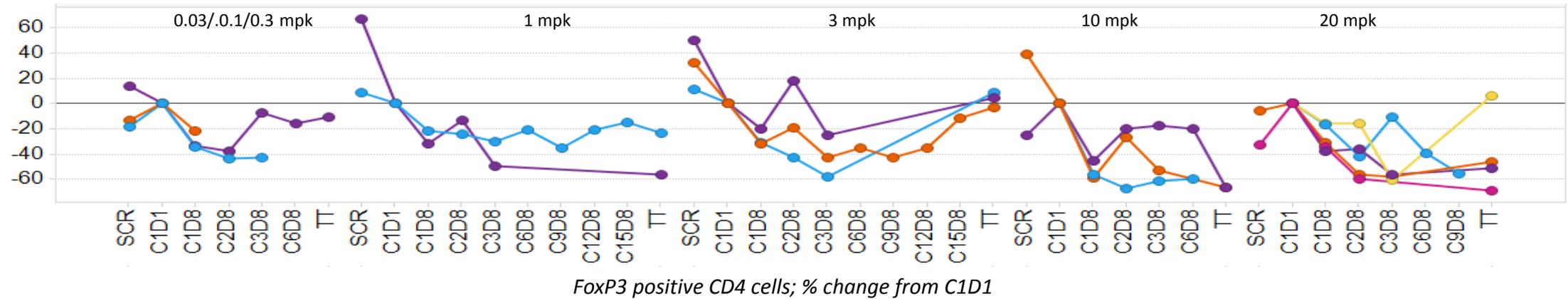
	0.3 mg/kg Q2W (N=3)	1.0 mg/kg Q2W (N=3)	3.0 mg/kg Q2W (N=3)	10.0 mg/kg Q2W (N=3)	20.0 mg/kg Q2W (N=6)	Total
Best Overall Tumor Response						
Complete Response (CR)	0	0	0	0	0	0
Partial Response (PR)	0	0	0	0	0	0
Stable Disease (SD)	1 (5.6%)	2 (11.1%)	1 (5.6%)	1 (5.6%)	2 (11.1%)	7 (38.9%)
Progressive Disease (PD)	1 (5.6%)	1 (5.6%)	2 (11.1%)	2 (11.1%)	4 (22.2%)	10 (55.6%)
Not Evaluable (NE)	1 (5.6%)	0	0	0	0	1 (5.6%)
Overall Response Rate (CR/PR)	0	0	0	0	0	0



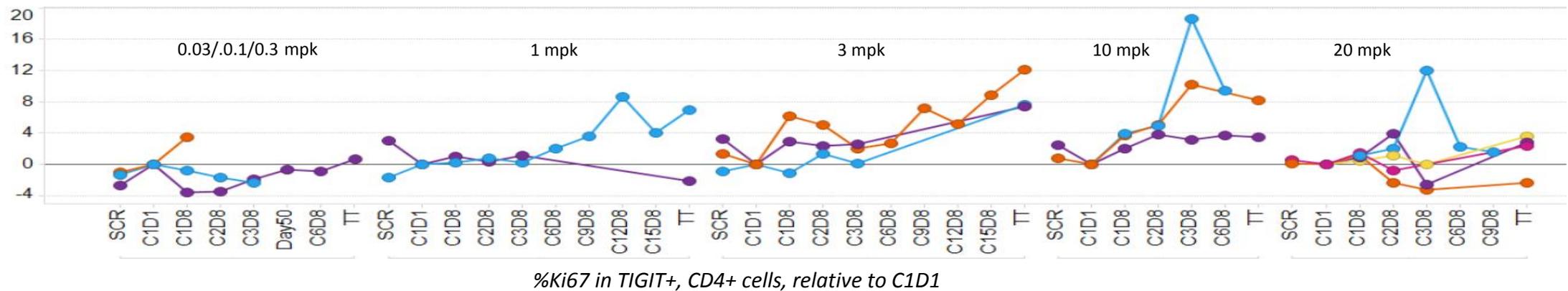
Dose Cohort	Diagnosis	MSI Status	Best Response	PFS (days)
0.3 mg/kg	Colorectal cancer	MSS	SD (Stable Disease)	113.0
	Colorectal cancer	MSS	PD (Progressive Disease)	58.0
1.0 mg/kg	Uterine cancer	Unknown	SD (Stable Disease)	85.0
	Head and neck cancer	Unknown	SD (Stable Disease)	225.0
3.0 mg/kg	Colorectal cancer	MSS	PD (Progressive Disease)	52.0
	Ewing sarcoma	Unknown	PD (Progressive Disease)	51.0
10.0 mg/kg	Colorectal cancer	Unknown	PD (Progressive Disease)	53.0
	Fallopian tube cancer	Unknown	SD (Stable Disease)	205.0
20.0 mg/kg	Endometrial cancer	Unknown	SD (Stable Disease)	112.0
	Colorectal cancer	MSS	PD (Progressive Disease)	51.0
20.0 mg/kg	Pancreatic cancer	Unknown	PD (Progressive Disease)	50.0
	Pancreatic cancer	MSS	PD (Progressive Disease)	50.0
20.0 mg/kg	Colorectal cancer	Unknown	SD (Stable Disease)	165.0
	Triple-negative breast cancer	Unknown	PD (Progressive Disease)	58.0
20.0 mg/kg	Adenoid cystic carcinoma	Unknown	SD (Stable Disease)	37.0
	Uterine cancer	Unknown	PD (Progressive Disease)	44.0
20.0 mg/kg	Endometrial cancer	MSI	PD (Progressive Disease)	53.0

Etigilimab decreases Tregs and enhances activation of T cells in blood

Anti-TIGIT decreases Treg frequency in peripheral blood



Anti-TIGIT enhances activation of TIGIT positive CD4+ T cells



Conclusions

- Etiligimab can be safely administered up to 20 mg/kg Q2W dose level
- Immune-related adverse events were observed in several subjects, consistent with activation of the immune system
- Blood-based biomarker analysis reveals significant reduction in Tregs and increases in proliferation and activation signals in CD4 T-cells
- 38.9% of subjects had stable disease as best response. 2 subjects had PFS of 205 and 225 days

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