#2568: Phase I Dose Escalation of KD033, a PDL1-IL15 Bispecific Molecule, in Advanced Solid Tumors

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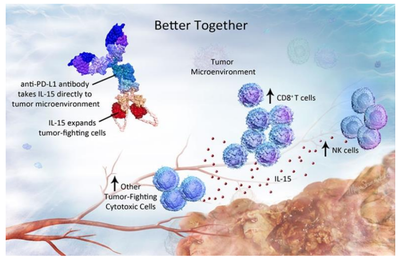
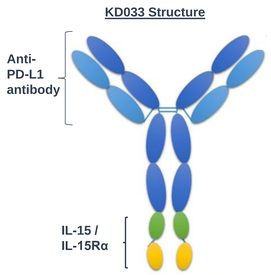
Mechanism of Action

KD033 is an anti-PD-L1/IL-15 fusion protein and is the lead molecule from Kadmon's IL-15 fusion protein platform.





Background

KD033 is a fusion antibody molecule generated by combining a fully human, high affinity anti-human Programmed Death Ligand 1 (PD-L1) IgG1 antibody with the human IL-15 receptor alpha (IL15Rα) sushi domain and human IL-15 (IL-15).

The fusion of anti-PD-L1 antibody to IL-15 significantly increases the maximal-tolerated dose (MTD) and increased efficacy in mice compared to free-IL-15.

Objectives

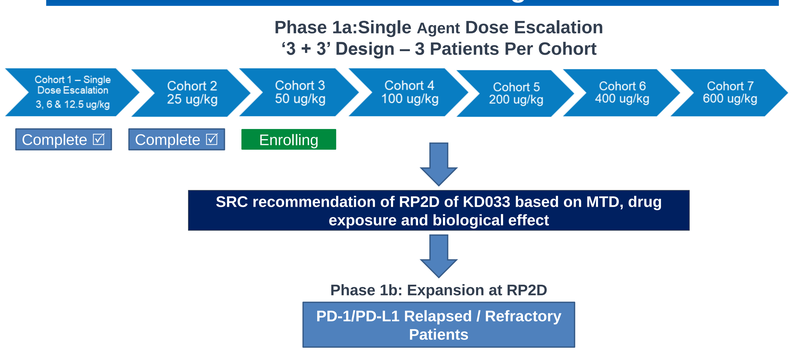
The primary objective is to determine the safety and tolerability and the MTD/RP2D of KD033. KD033 is administered as an IV infusion over 30 minutes every 14 days (i.e., a cycle equals 2 weeks).

Secondary objectives include characterization of PK and immunogenicity, evaluation of immune correlates that will potentially differentiate the impact of KD033 as well as investigate IL-15 biology and determine best overall response and duration of response.

Methodology

- **The starting dose of KD033 is 3 µg/kg, with step-up dosing to 12.5 µg/kg in the first cohort of 3 patients.**
- **After the first cohort, the dose escalation will use a standard 3+3 design with planned doses from 25 µg/kg to 600 µg/kg.**
- **The dose escalation phase will be followed by expansion cohorts, which will enroll patients with solid tumors who received PD-1/PD-L1 inhibitors but have either progressed or are refractory to therapy.**

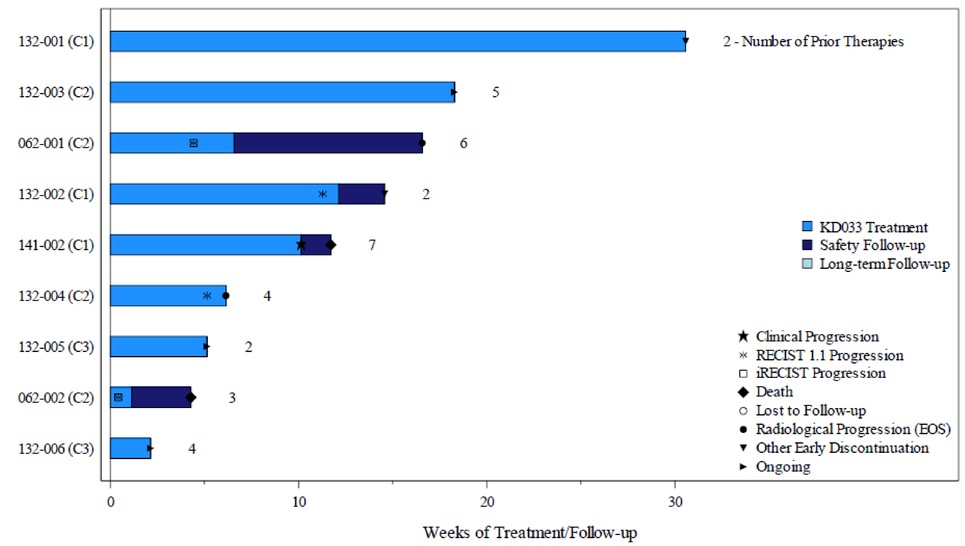
Phase 1 Trial Design



Patient Demographics & Results

Cohort	Patient	Age	Sex	Race	Tumor Type	Baseline ECOG	Prior Cancer Therapy (n)	Prior Treatment with PD-1/PD-L1
1	132-001	61	F	Black	Adenoid Cystic Carcinoma of the Hard Palate and Maxillary Sinus	0	2	No
1	132-002	68	M	White	Metastatic Peritoneal Mesothelioma	0	2	Yes
1	141-002	58	F	White	Triple Negative Breast Cancer	0	7	Yes
2	062-001	55	F	White	Cecal Adenocarcinoma	1	6	No
2	062-002	57	M	White	Pancreatic Body/Tail	0	3	No
2	132-003	65	F	White	Renal Cell Carcinoma	1	5	Yes
2	132-004	57	M	White	Metastatic Colon Adenocarcinoma	1	4	No
3	132-005	58	M	White	Metastatic Gastric Adenocarcinoma	1	2	No
3	132-006	58	M	White	Colorectal	1	4	No

Safety Population Study Duration & Tumor Type



Treatment Related Adverse Events

	All Treated Patients (N=9)	
	Grade 1-2	Grade ≥3
Chills	10	0
Fatigue	5	0
Pyrexia	5	0
Oedema Peripheral	3	1
Hypercalcaemia	3	0
AST Increased	2	0
Capillary Leak Syndrome	2	0
Nausea	2	0
Night Sweats	2	0
Vomiting	2	0
Lymphocyte Count Decreased	1	4
Activated Partial Thromboplastin Time Prolonged	1	0
ALT Increased	1	0
Blood Alkaline Phosphatase Increased	1	0
Blood Bilirubin Increased	1	0
Cytokine Release Syndrome	1	0
Dizziness	1	0
Hyperalbuminaemia	1	0
Infusion Related Reaction	1	0
Malaise	1	0
Neutrophil Count Decreased	1	0
Platelet Count Decreased	1	0
Pruritus	1	0
Swelling Face	1	0
Tachycardia	1	0
Weight Increased	1	0
White Blood Cell Count Decreased	1	0

Exposure & Safety

- **As of the April 21 2021, 9 patients have been treated with KD033 with the longest exposure being 30 weeks**
- **The majority of patients treated have not received prior PD-1/PD-L1 therapy**
- **To date, there have been no reported dose limiting toxicities (DLTs)**
- **All reported Lymphocyte Count Decreases were observed in Cohort 3 patients treated at a dose level of 50µg/kg**
- **Treatment Related Adverse Events (TRAEs) include causality reported as possibly, probably or related to KD033**

Conclusions

- **9 patients have been treated with KD033 with the longest exposure being 30 weeks**
- **KD033 has been well tolerated to date with expected and manageable adverse events**
- **On-target and expected pharmacodynamics for IL-15 agonism (lymphocyte modulation) has been observed**
- **Dose escalation continues**

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