Interim Analysis of KD025-213: A Phase 2, Randomized, Multicenter Study to Evaluate the Efficacy and Safety of KD025 in Subjects with Chronic Graft Versus Host Disease (cGVHD) after at Least 2 Prior Lines of Systemic Therapy (The ROCKstar Study)

Corey Cutler, MD, MPH[1], Stephanie Lee, MD, MPH[2], Sally Arai, MD[3], Marcello Rotta, MD[4], Behyar Zoghi, MD[5], Aravind Ramakrishnan, MD[6], Aleksandr Lazaryan, MD, MPH, PhD[7], David A Eiznhamer, PhD[8], Olivier Schueller, PhD[8], Zhongming Yang, PhD[8], Laurie S. Green, MEd[8], Sanjay K. Aggarwal, MD[8], The ROCKstar Study Group[9], Bruce R. Blazar, MD[10], Steven Z. Pavletic, MD[11] and Madan Jagasia, MD[12]

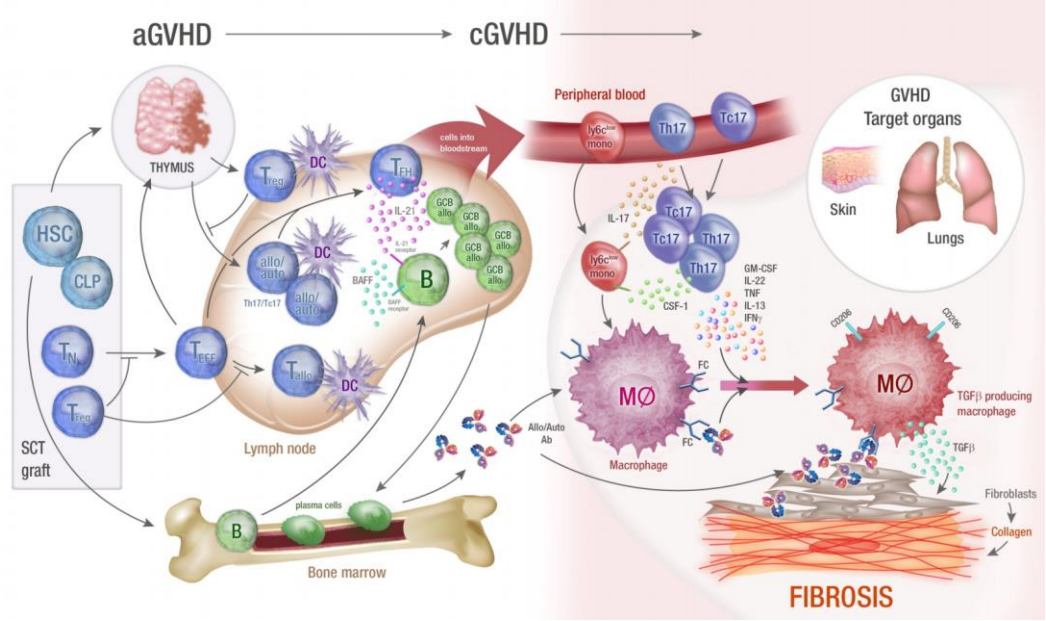
[1] Department of Hematologic Malignancies, Dana-Farber Cancer Institute and Harvard Medical School, Boston, MA, [2] Clinical Research Division, Fred Hutchinson Cancer Research Center, Seattle, WA, [3] Stanford University, Stanford, CA, [4] James Cancer Center, Ohio State University, Columbus, OH, [5] Texas Transplant Institute, Methodist Hospital, San Antonio, TX, [6] Blood and Marrow Transplant, Texas Transplant Institute at St. David's South Austin Medical Center, Austin, TX, [7] Blood and Marrow Transplantation and Cellular Immunotherapy, H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL, [8] Kadmon Corporation, LLC, New York, NY, [9] The ROCKstar Study Group, New York, NY, [10] Division of Pediatric Blood and Marrow Transplantation, University of Minnesota, Minneapolis, MN, [11] Experimental Transplantation and Immunology Branch, Center for Cancer Research (CCR), National Cancer Institute (NCI), National Institutes of Health (NIH), Bethesda, MD, [12] Hematology/Oncology, Vanderbilt University Medical Center, Nashville, TN

2020 TCT | Transplantation and Cellular Therapy Meetings

Pathophysiology of Chronic GVHD (cGVHD)

cGVHD is Driven by Immune Cells and Pro-inflammatory Cytokines

- **cGVHD involves both T cells and B cells**
  - Overproduction of pro-inflammatory IL-21 and IL-17 cytokines
  - Over-activation of T follicular helper (Tfh) cells and B cells, leading to over-production of antibodies
  - Deficiency of regulatory T (Treg) cells, leading to a lack of appropriate regulation of immune response

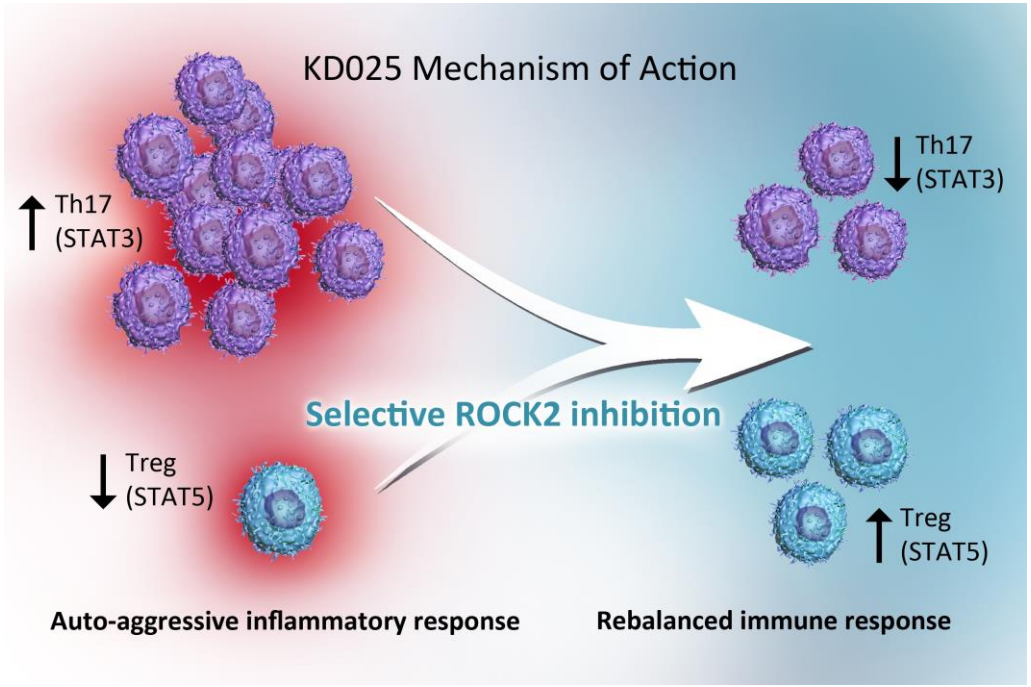


Blood. 2017 Jan 5;129(1):13-21

ROCK2 Plays Key Role in Immune Diseases

ROCK2 Inhibition Rebalances Immune Response to Treat Immune Dysfunction[1,2]

- **Rho-associated coiled-coil kinase (ROCK) is a serine/threonine kinase**
  - Two isoforms: ROCK1 and ROCK2[1]
- **ROCK2 inhibition rebalances the immune system**
  - Downregulates pro-inflammatory Th17 cells
  - Increases regulatory T cells

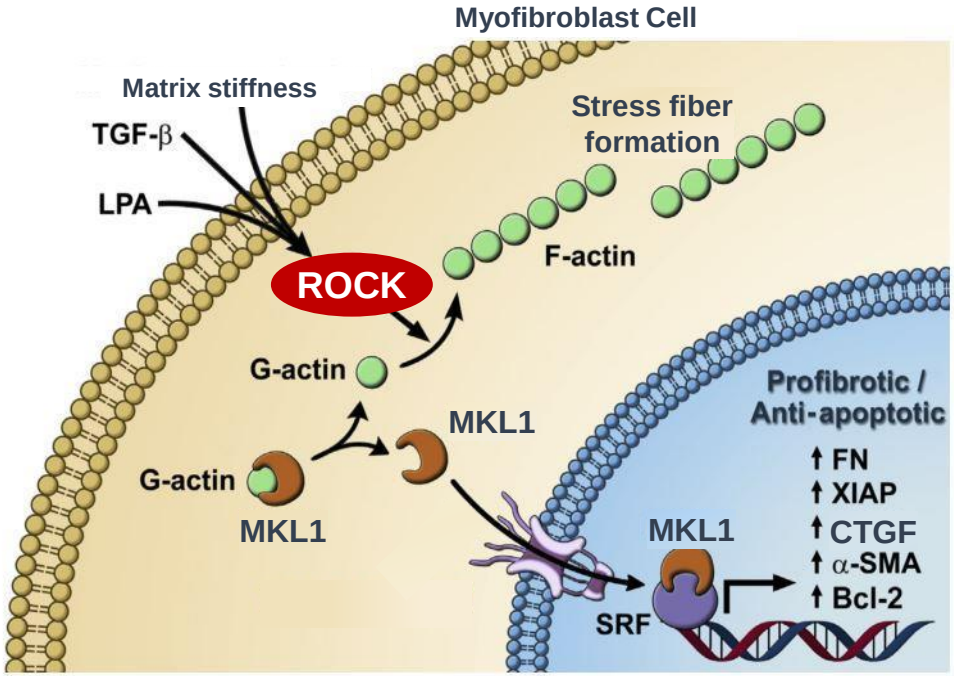


[1]*Proc Natl Acad Sci U S A. 2014 Nov 25;111(47):16814-9*; [2]*Blood*. 2016 Apr 28;127(17):2144-54

ROCK is an Intracellular Integrator of Pro-Fibrotic Signals

ROCK Regulates Multiple Profibrotic Processes, Including Myofibroblast Activation

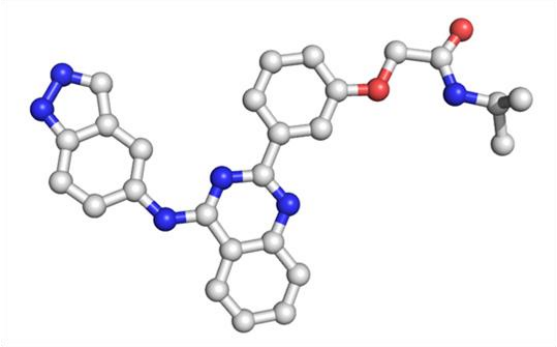
- **ROCK is downstream of major pro-fibrotic mediators**
- **ROCK mediates stress fiber formation**
- **ROCK regulates transcription of pro-fibrotic genes**



Am J Pathol. 2015 Apr;185(4):909-12.

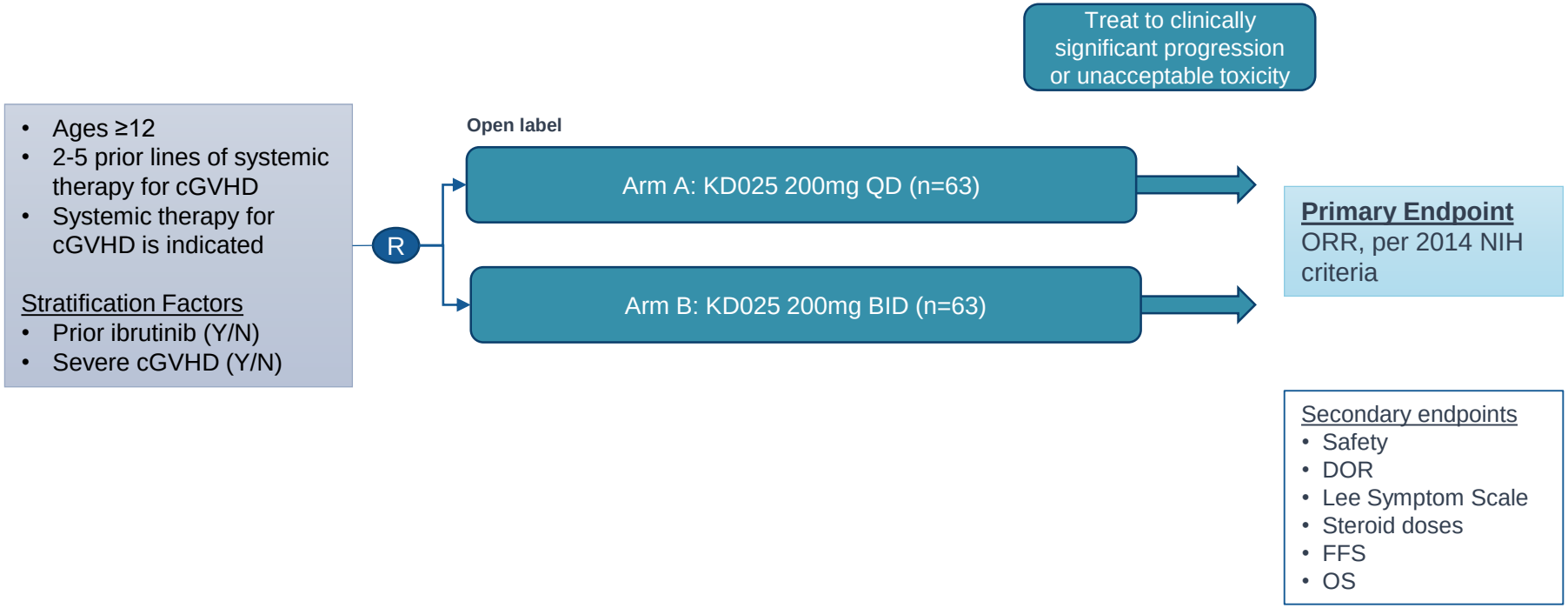
Rationale for KD025 in cGVHD

- **KD025 is an orally available, selective inhibitor of ROCK2**
  - Over 550 individuals have received KD025 in ongoing and completed studies
- **Targets both immune and fibrotic pathophysiology of cGVHD**
- **Preclinical data in sclerodermatous mouse model**[1]
- **Study KD025-208**[2]
  - Phase 2a study of KD025 showed an Overall Response Rate (ORR) of 65% with KD025 in cGVHD patients after 1-3 prior lines of systemic therapy *(see Poster #275, TCT 2020)*
  - Data from this study led to:
    - FDA Breakthrough Therapy Designation for KD025 for the treatment of adult patients with cGVHD after failure of two or more lines of systemic therapy
    - KD025-213 (The ROCKstar Study)[3]



[1]*Blood*. 2016 Apr 28;127(17):2144-54; [2]NCT02841995; [3]NCT03640481

KD025-213: Study Design and Endpoints



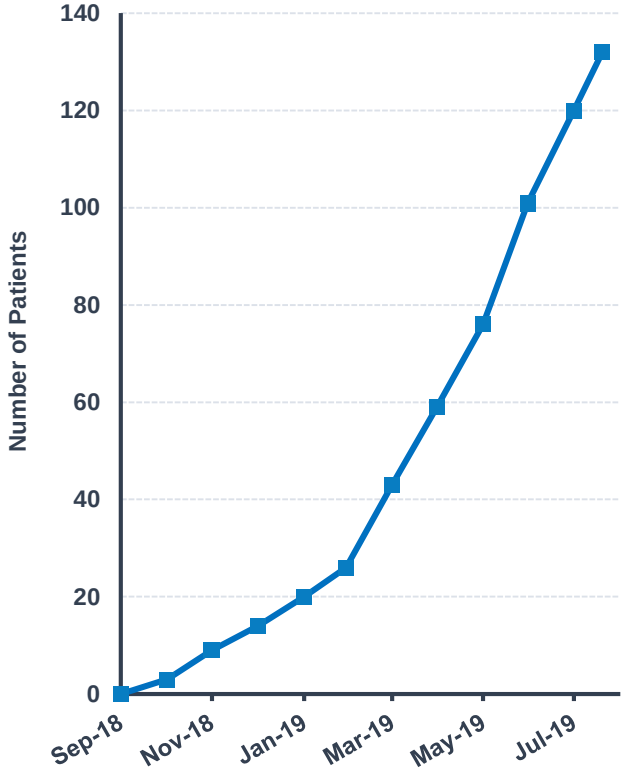
KD025-213: Statistical Analysis Plan

Primary Endpoint: ORR

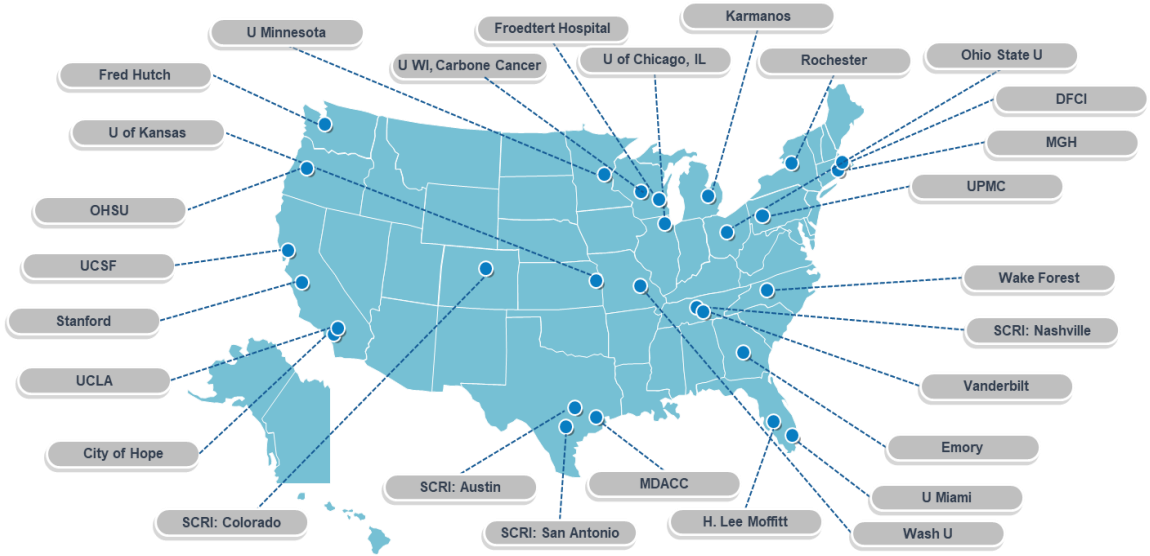
Statistical significance is achieved if the lower bound of the 95% CI of ORR exceeds 30%

	Timepoint	Status
Interim Analysis	2 months after completion of enrollment 1-sided alpha = 0.0025	Data cutoff date: 17 October, 2019 Data presented at TCT, 23 February, 2020
Primary Analysis	6 months after completion of enrollment	Expected 2Q 2020
Follow-up Analysis	12 months after completion of enrollment	Expected 4Q 2020

KD025-213: Fully Enrolled in Less Than 10 Months



- Enrolled at 28 U.S. sites
- First Patient In: Oct 2018; Last Patient In: Aug 2019



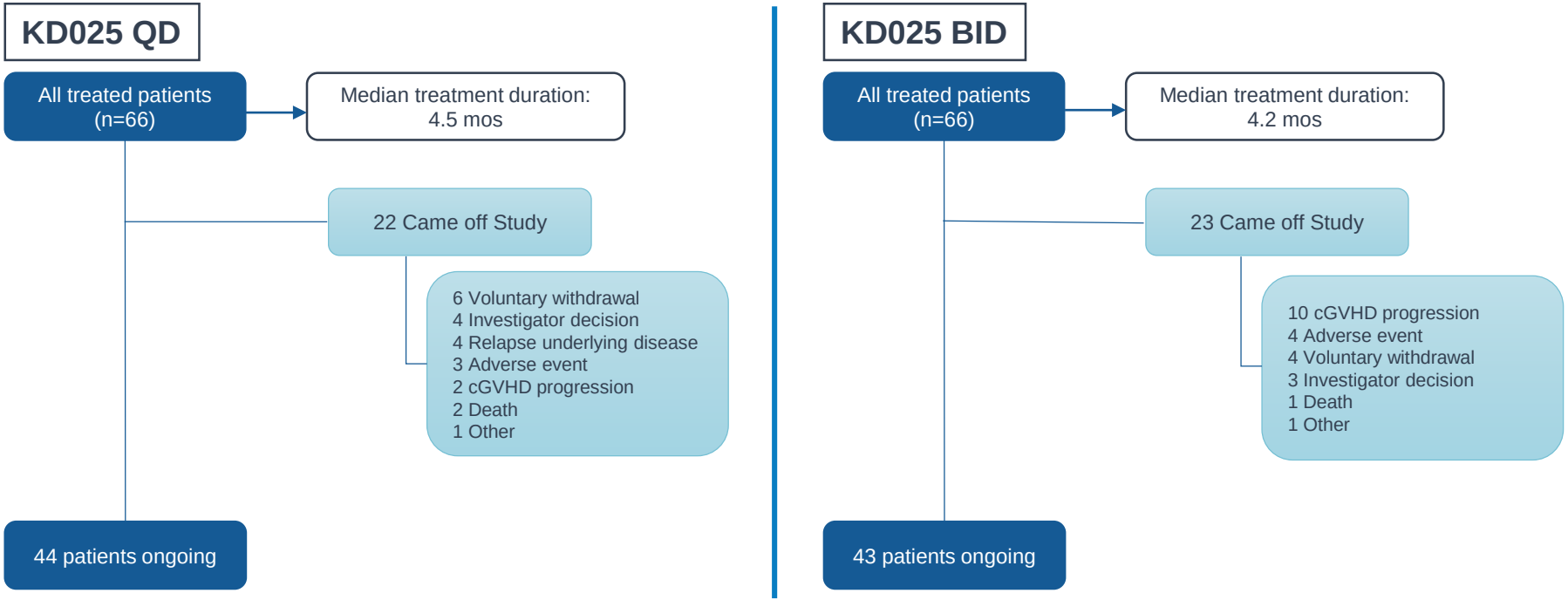
KD025-213: Advanced Patient Population

Demographics and Baseline Characteristics			
Demographics	**KD025 QD (n=66)**	**KD025 BID (n=66)**	**Overall (n=132)**
Median age [years (range)]	53 (21-77)	57 (21-77)	56 (21-77)
Male (%)	64	50	57
Median prior lines of therapy	3	4	4
Median time from cGVHD diagnosis to enrollment (months)	25	30	28
* NIH Severe cGVHD [n (%)]	45 (68%)	42 (64%)	87 (66%)
Median prednisone dose (mg/kg/day)	0.2	0.2	0.2
≥4 Organs involved [n (%)]	34 (52%)	35 (53%)	69 (52%)
* Prior ibrutinib treatment	22 (33%)	23 (35%)	45 (34%)
Refractory to line prior to enrollment, excluding unknown / missing	81% (42/52)	65% (32/49)	73% (74/101)

* Stratification factor

KD025-213: Patient Disposition

Median Duration of Follow-Up: 5 months



KD025-213: Safety and Tolerability

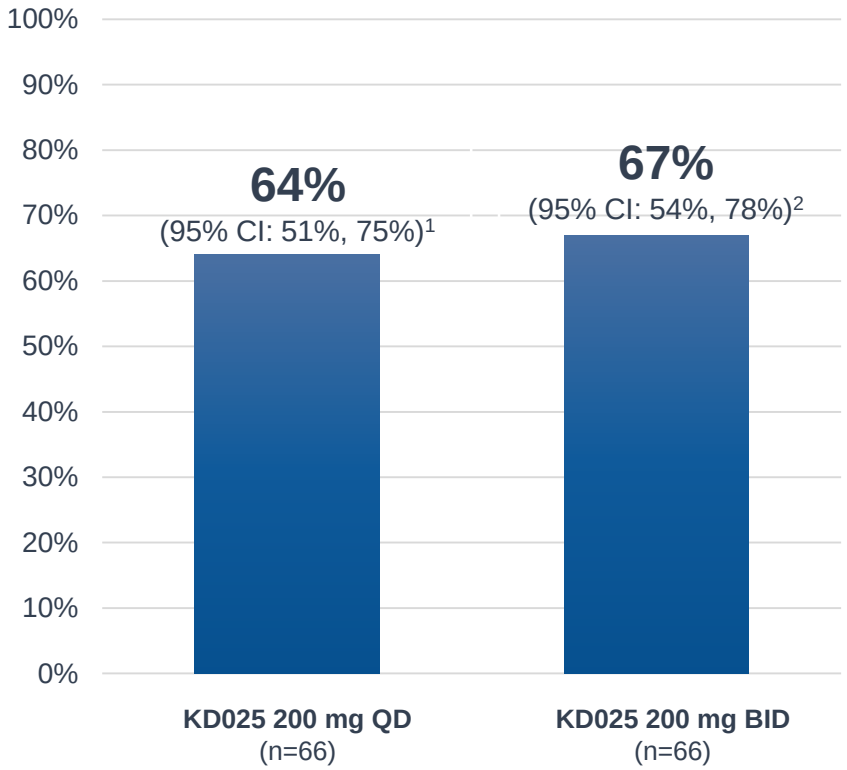
- **AEs were overall consistent with those expected in cGVHD patients receiving corticosteroids and other immunosuppressants**
- **No apparent increased risk of infection**
  - No CMV reactivation

Safety Overview, n (%)	KD025 QD (n=66)	KD025 BID (n=66)	Overall (n=132)
Median duration of treatment (months)	4.5	4.2	4.3
Any Adverse Event (AE)	64 (97)	61 (92)	125 (95)
Grade 3/4 AE	23 (35)	27 (41)	50 (38)
SAE	22 (33)	15 (23)	37 (28)
Drug related AE			
Any related AE	38 (58)	28 (42)	66 (50)
Related SAE	3 (5)	1 (2)	4 (3)
On study deaths[1]	4 (6)	1 (2)	5 (4)

[1] KD025 QD: Aspiration pneumonia; Hemoptysis; MODS/Septic shock; Relapse AML. KD025 BID: Cardiac arrest.

Commonly Reported AEs, n (%)	KD025 QD (n=66)	KD025 BID (n=66)	Overall (n=132)
All Grade, in ≥10%			
Fatigue	20 (30)	12 (18)	32 (24)
Diarrhea	16 (24)	12 (18)	28 (21)
Nausea	15 (23)	13 (20)	28 (21)
Liver related investigations (SMQB)	13 (20)	14 (21)	27 (20)
Peripheral edema	16 (24)	10 (15)	26 (20)
Cough	12 (18)	9 (14)	21 (16)
Dyspnea	13 (20)	8 (12)	21 (16)
Headache	10 (15)	9 (14)	19 (14)
Vomiting	11 (17)	7 (11)	18 (14)
Hypertension	8 (12)	9 (14)	17 (13)
Muscle spasm	9 (14)	7 (11)	16 (12)
URTI	6 (9)	10 (15)	16 (12)
Pyrexia	11 (17)	4 (6)	15 (11)
Hyperglycemia	7 (11)	7 (11)	14 (11)
Grade ≥3, in ≥3%			
Hypertension	3 (5)	4 (6)	7 (5)
Hyperglycemia	2 (3)	3 (5)	5 (4)
Pneumonia	2 (3)	3 (5)	5 (4)
GGT increased	3 (5)	1 (2)	4 (3)
Nausea	3 (5)	1 (2)	4 (3)
Vomiting	3 (5)	1 (2)	4 (3)

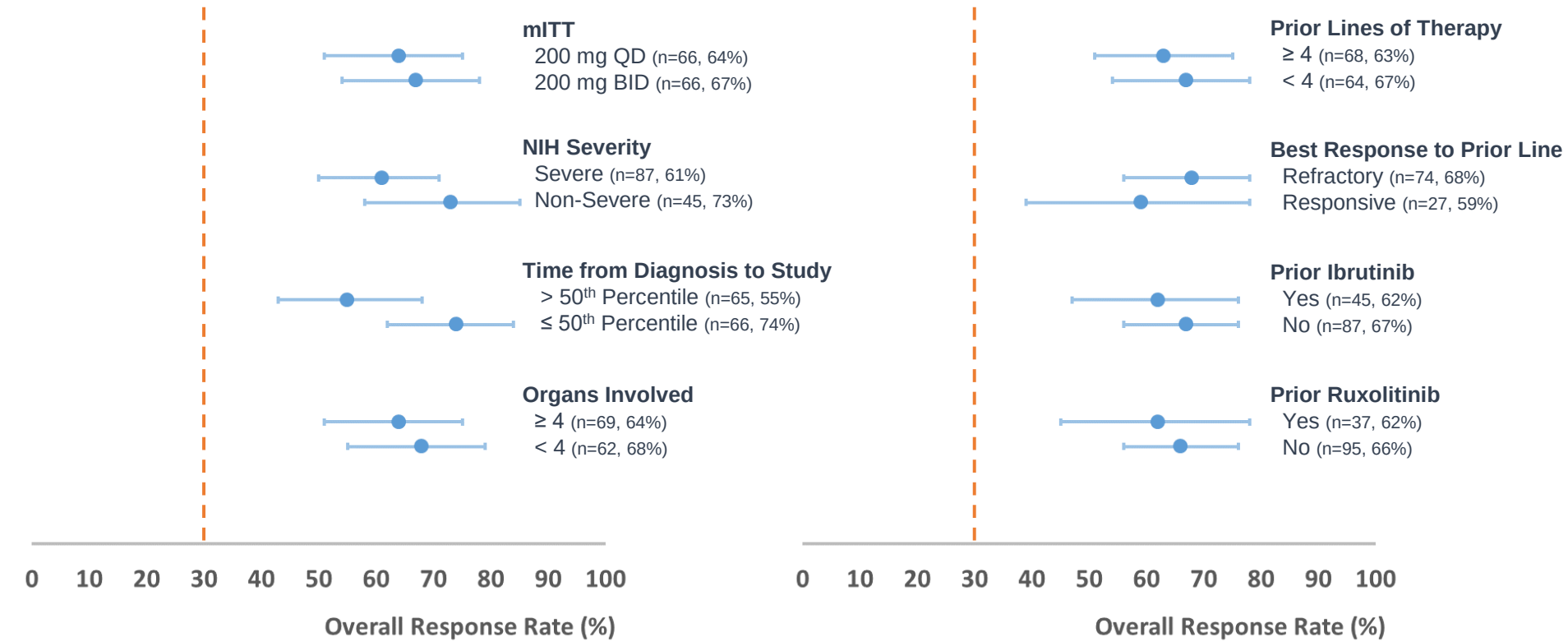
KD025-213: Primary Endpoint Met at Interim Analysis



- **Interim analysis occurred 2 months after last patient was enrolled**
- **KD025 achieved clinically meaningful and statistically significant ORRs in both arms**
  - Statistical significance is achieved if the lower bound of the 95% CI of ORR exceeds 30%
- **Three patients achieved a complete response (CR)**

[1]p<0.0001; [2]p<0.0001

KD025-213:Responses Observed Across All Key Subgroups



Pooled responses across arms, unless stated

KD025-213: Conclusions

KD025 was Well Tolerated and Achieved Clinically Meaningful Outcomes

- **KD025 was well tolerated**
  - No apparent increased risk of infection; no CMV reactivation
- **ORR of 65% across QD and BID arms**
  - Responses observed across all key subgroups
  - Responses observed in all affected organ systems, including in organs with fibrotic disease
- **Additional endpoint data will be available later in 2020 including:**
  - Duration of response
  - FFS, OS
  - Lee Symptom Scale (LSS) reductions
  - Corticosteroid dose reductions
  - PK and PD

Acknowledgements

- **Trial patients and their caregivers**
- **All ROCKstar study investigators and all site staff, nurses, study coordinators**
- **The KD025-213 Steering Committee:**
  - Madan Jagasia, MD (Chair), Vanderbilt University Medical Center, Nashville, TN
  - Steven Z. Pavletic, MD (Co-chair), National Cancer Institute, Bethesda, MD
  - Bruce R. Blazar, MD, Department of Pediatrics, University of Minnesota, Minneapolis, MN
  - Corey Cutler, MD, Dana Farber Cancer Institute, Boston, MA
  - Stephanie Lee, MD, Fred Hutchinson Cancer Research Institute, Seattle, WA
  - Sanjay K. Aggarwal, MD, SVP Clinical Development, Kadmon, Cambridge, MA
- **Kadmon Holdings, Inc.**
- **Partner CROs**