Kadmon®

AMCP Clinical Presentation: REZUROCK™ for cGVHD

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About Kadmon

Kadmon®

In-house Research

Clinical Pipeline

Commercial Operation

- **Clinical stage biopharmaceutical company headquartered in New York, NY (NYSE: KDMN)**
- **FDA approved product: REZUROCK™ (belumosudil) 200 mg once daily (QD) for the treatment of adult and pediatric patients 12 years and older with chronic GVHD after failure of at least two prior lines of systemic therapy**
- Therapeutic areas of interest beyond cGVHD:
  - Fibrotic diseases
  - Immuno-oncology

cGVHD, chronic graft-versus-host disease; NDA, New Drug Application; NYSE, New York Stock Exchange; ROCK2, Rho-associated coiled-coil kinase 2.

Kadmon Pipeline

CANDIDATE	INDICATION	STATUS
KD025 (Selective ROCK2 inhibitor)	**Systemic Sclerosis**	• Phase 2 clinical trials ongoing
KD033 (anti-PD-L1/IL-15 fusion protein)	**Immuno-oncology**	• Phase 1 dose escalation/expansion trial ongoing
KD045 (pan-ROCK inhibitor)	**Fibrotic Diseases**	• IND-enabling activities ongoing

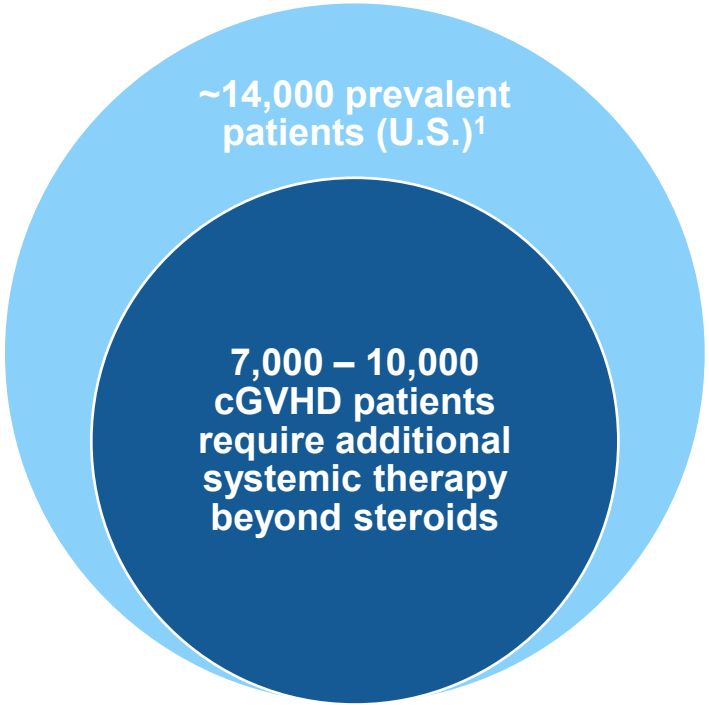
FDA, Food and Drug Administration; IL-15, interleukin-15; IND, Investigational New Drug; PD-L1, programmed-death ligand 1; ROCK, Rho-associated coiled-coil kinase; RTOR, Real-Time Oncology Review; SSc, systemic sclerosis.

Chronic Graft-Versus Host Disease

Pathophysiology

- cGVHD occurs following allogeneic HSCT when donor immune cells contained in the allograft mount an attack against the recipient antigens
- Cells in the graft see recipient tissue as foreign
- The process involves inflammation, cell-mediated immunity, humoral immunity and fibrosis
- cGVHD may impact one or many organs such as the mouth, eyes, skin, joints/fascia, GI tract, liver and lungs
- Clinical manifestations nearly always present within the first years following transplant

Significant cGVHD Market with Unmet Medical Needs



- **Significant cGVHD market**
  - 5,000 new cGVHD patients/year[1]
  - 5-year OS of 55%[2]
- **Unmet therapeutic needs**
  - Steroids are SoC in frontline treatment[1]
    - **80%** of cGVHD patients require additional treatment beyond initial therapy[3]
    - Patients cycle through lines of therapy every 2-4 months[1]

OS, overall survival; SoC, standard of care.

1. Bachier CR et al. 2019 epidemiology and real-world treatment of chronic graft-versus-host disease post allogeneic hematopoietic cell transplantation: a US claims analysis. Proceedings from the 61st American Society of Hematology Annual Meeting & Exposition; December 7-10, 2019; Orlando, FL. Abstract 2109. **2.** Arora M et al. Chronic GVHD risk score: a Center for International Blood and Marrow Transplant Research analysis. *Blood*. 2011; 117(24): 6714-6720. **3.** Lee SJ et al. Success of Immunosuppressive Treatments in Patients with Chronic Graft-versus-Host Disease. *Biol Blood Marrow Transplant*. 2018; 24(3): 555-562.

cGVHD Patients Cycle Through Multiple Lines of Therapy with Roughly 50% Reaching 3L of Treatment[1]

Patient Population by Progression

cGVHD Diagnosis: 14,017 Patients in the US

75% of cGVHD Patients Present with ≥3 Organ Involvement at Time of Diagnosis

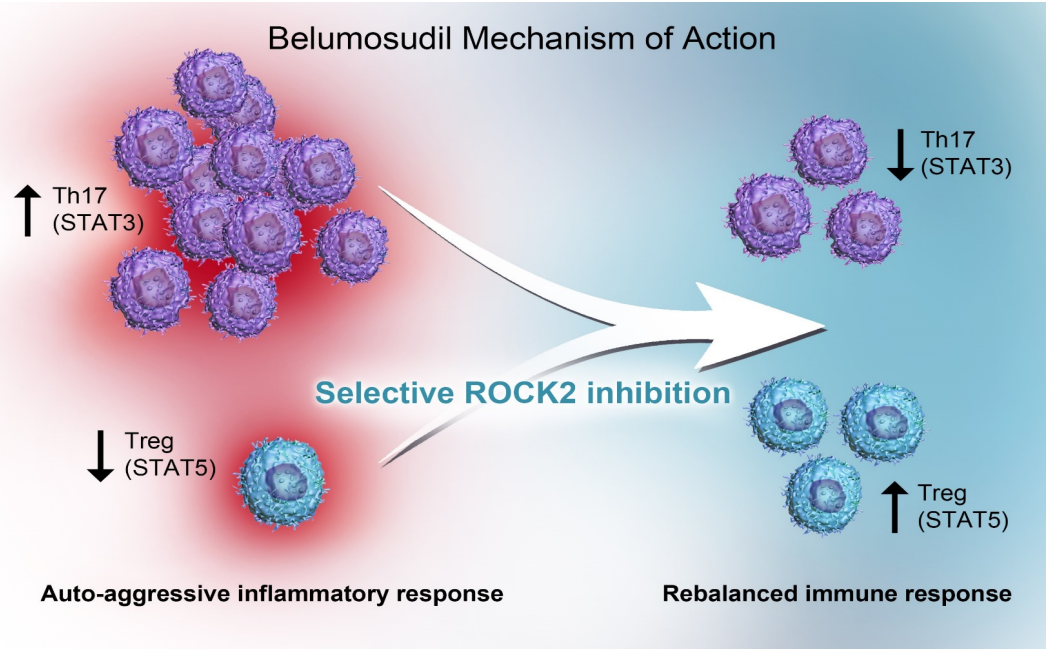
	Time	Treatments by Line of Therapy
1L cGVHD Patients: ~96%	~2-3[2] Months	Steroids are SoC in 1L. There is no SoC after the use of steroids in 1L
2L cGVHD Patients: ~70%	~2-3[2] Months	CNIs are most commonly used with the goal of stabilizing disease
3L+ cGVHD Patients: ~50%	4+ Months	Treatment options include REZUROCK™ /ibrutinib / sirolimus /CNIs / ruxolitinib

CNI, calcineurin inhibitor; L, line of therapy; QoL, quality of life.

1. 2016 IQVIA Pharmetrics commercial medical claims; 2016 CMS Medicare Fee-for-Service medical claims (5% Non-Institutional Sample). **2.** Gonzalez RM, Pidala J. Evolving therapeutic options for chronic graft vs. host disease [published online ahead of print May 22 2020]. *Pharmacotherapy*. doi: 10.1002/phar.2427.

ROCK-2 Inhibition

ROCK2 Plays a Key Role in Immune Diseases



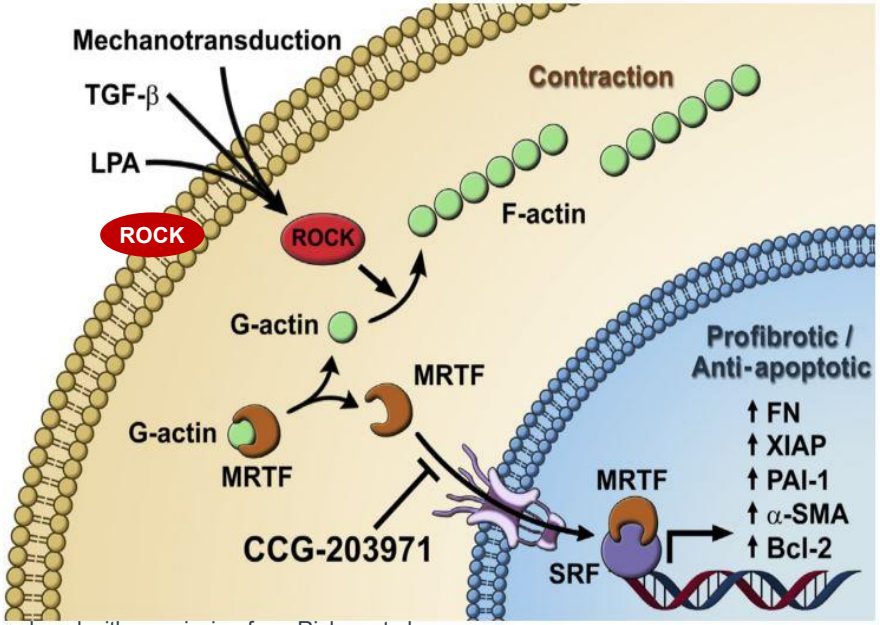
ROCK2 inhibition rebalances immune response to treat immune dysfunction

- ROCK2 inhibition rebalances the immune system
  - Downregulates pro-inflammatory Th17 cells
  - Increases Treg cells

Th17 cell, T helper 17 cell; Treg cell, regulatory T cell; STAT3, signal transducer and activator of transcription 3; STAT5, signal transducer and activator of transcription 5.

1. Zanin-Zhorov A et al. Selective oral ROCK2 inhibitor down-regulates IL-21 and IL-17 secretion in human T cells via STAT3-dependent mechanism. *Proc Natl Acad Sci.* 2014; 111(47): 16814-16819. **2.** Flynn R et al. Targeted Rho-associated kinase 2 inhibition suppresses murine and human chronic GVHD through a Stat3-dependent mechanism. *Blood.* 2016; 127(17): 2144-2154.

ROCK Is an Intracellular Integrator of Profibrotic Signals



Reproduced with permission from Riches et al.

ROCK regulates multiple profibrotic processes, including myofibroblast activation

- ROCK is downstream of major profibrotic mediators
- ROCK mediates stress fiber formation
- ROCK regulates transcription of profibrotic genes

α-SMA, α-smooth muscle actin; Bcl-2, B-cell lymphoma 2; CTGF, connective tissue growth factor; FN, fibronectin; LPA, lysophosphatidic acid; MRTF, myocardin-related transcription factor; SRF, serum response factor; XIAP, X-linked inhibitor of apoptosis.Riches DWH et al. *Am J Pathol.* 2015;185(4):909-912. doi:10.1016/j.ajpath.2015.01.005

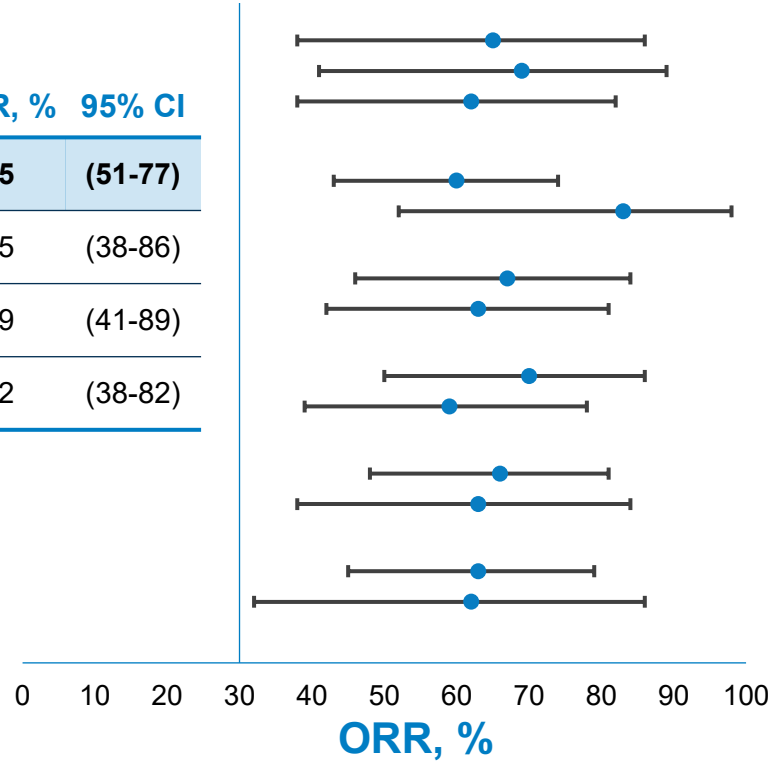
Clinical Studies

KD025-208 and KD025-213 ROCKstar Trials

KD025-208: High ORRs in Advanced cGVHD Patients[1,2]

REZUROCK	n	ORR, %	95% CI
mITT	**54**	**65**	**(51-77)**
200 mg QD	17	65	(38-86)
200 mg BID	16	69	(41-89)
400 mg QD	21	62	(38-82)

mITT, modified intention-to-treat.



mITT
200 mg QD (n=17, 65%)
200 mg BID (n=16, 69%)
400 mg QD (n=21, 62%)

NIH severity
Severe (n=42, 60%)
Nonsevere (n=12, 83%)

Time from diagnosis to study enrollment
>50th percentile (n=27, 67%)
≤50th percentile (n=27, 63%)

Organs involved
≥4 (n=27, 70%)
<4 (n=27, 59%)

Prior lines of systemic therapy
≥2 (n=35, 66%)
<2 (n=19, 63%)

Best response to line of therapy
Refractory (n=35, 63%)
Responsive (n=13, 62%)

Pooled responses across arms, unless stated

1. Data on file. **2.** Jagasia M et al. ROCK2 inhibition with belumosudil (KD025) for the treatment of chronic Graft-Versus Host Disease. *Journal of Clinical Oncology*. 2021; 39(17): 1888-1898.

KD025-208 Conclusions [1,2]

ORR was 65% in the mITT population

- Responses were observed in all affected organ systems, including in organs with fibrotic disease

AEs were overall consistent with those expected in patients with cGVHD who were receiving corticosteroids and other immunosuppressants

Sustained and clinically meaningful outcomes

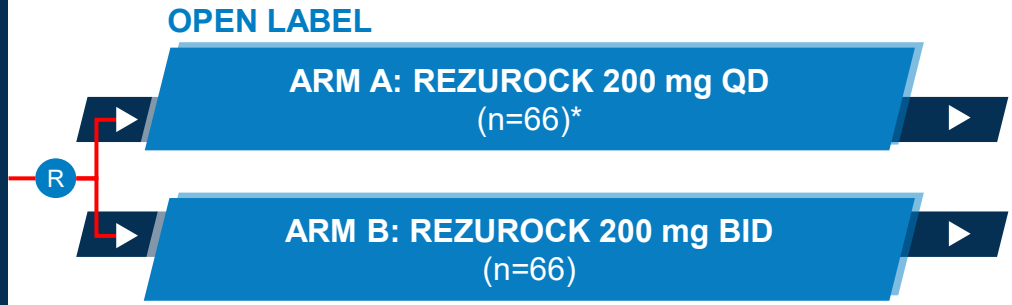
- The median DOR was 35 weeks in responders
- **28% of patients** remained on REZUROCK for >18 months
- **67% of patients** reduced their CS dose
- **19% of patients** discontinued CS therapy
- **50% of patients** experienced clinically meaningful improvement in LSS scores from baseline
- **FFS rate at 1 year:** 47%
- **OS rate at 2 years:** 82%

CMV, cytomegalovirus; DOR, duration of response; FFS, failure-free survival.

1. Data on file. **2.** Jagasia M et al. ROCK2 inhibition with belumosudil (KD025) for the treatment of chronic Graft-Versus Host Disease. *Journal of Clinical Oncology*. 2021; 39(17): 1888-1898.

The ROCKstar Study: Design and End Points

- **ELIGIBILITY CRITERIA**
- Aged ≥12 years
- Underwent an HCT
- Had active cGVHD
- 2 to 5 prior lines of systemic therapy for cGVHD
- Systemic therapy for cGVHD is indicated
- **STRATIFICATION FACTORS**
- Prior ibrutinib (Y/N)
- Severe cGVHD (Y/N)



Treat until clinically significant progression or unacceptable toxicity

PRIMARY END POINT

ORR, according to the 2014 NIH cGVHD Consensus Criteria

SECONDARY END POINTS

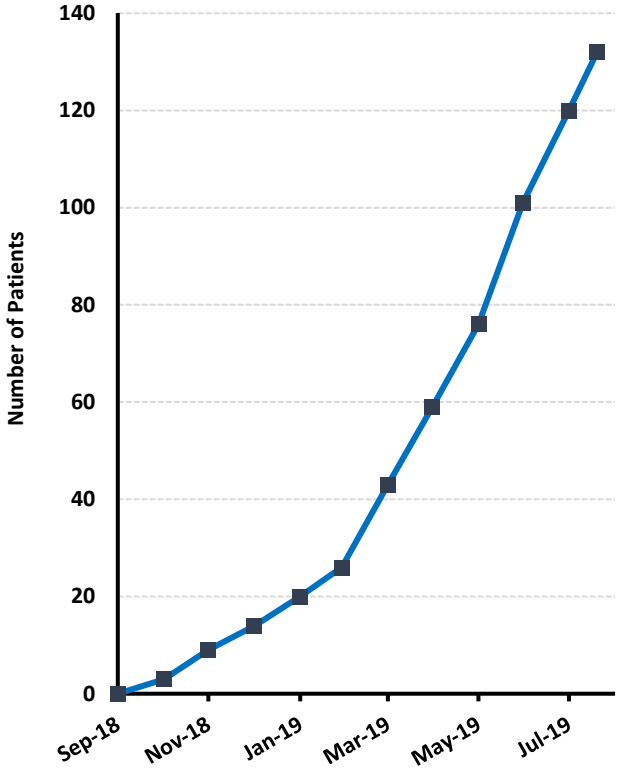
- Safety
- DOR
- TTR
- LSS score
- CS and CNI doses
- FFS
- OS

*In the PI, one non-GVHD patient in the 200mg QD arm was omitted from the primary analysis (N=65).

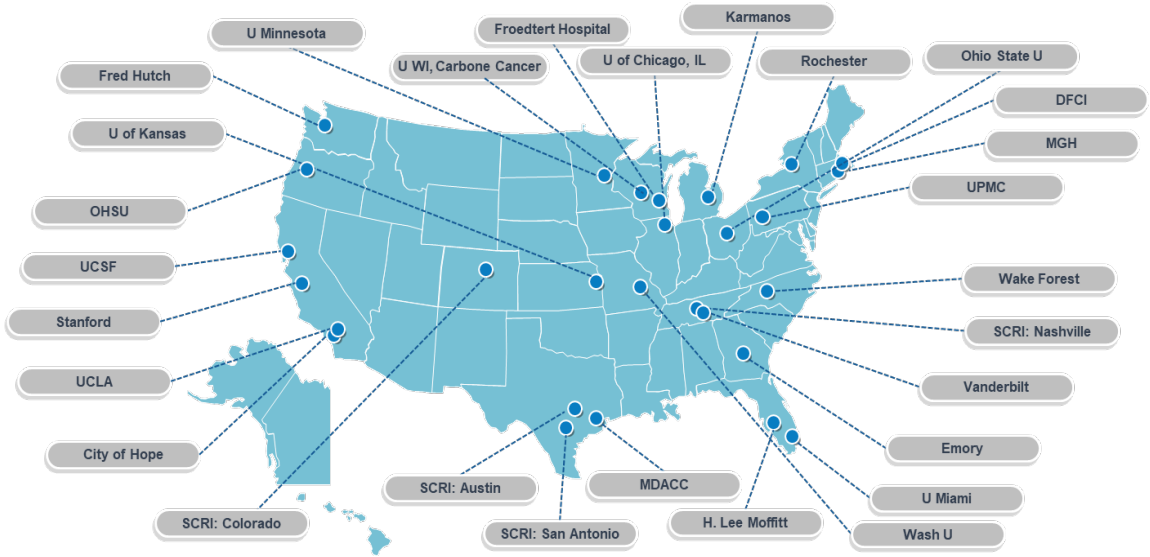
BID, twice a day; DOR, duration of response; FFS, failure-free survival; HCT, hematopoietic cell transplant; LSS, Lee Symptom Scale; NIH, National Institutes of Health; OS, overall survival; QD, every day.

Cutler C et al. Belumosudil for chronic Graft-Versus Host Disease (cGVHD) after 2 or more lines of therapy: The ROCKstar Study. *Blood*. 2021. blood.2021012021. doi: https://doi.org/10.1182/blood.2021012021.

The ROCKstar Study: Fully Enrolled in Less Than 10 Months



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



DFCI, Dana-Farber Cancer Institute; MDACC, MD Anderson Cancer Center; MGH, Massachusetts General Hospital; OHSU, Oregon Heath & Science University; SCRI, Sarah Cannon Research Institute; UCLA, University of California, Los Angeles; UCSF, University of California, San Francisco; UPMC, University of Pittsburgh Medical Center.

The ROCKstar Study: Diverse Patient Population

Select Demographics and Baseline Characteristics

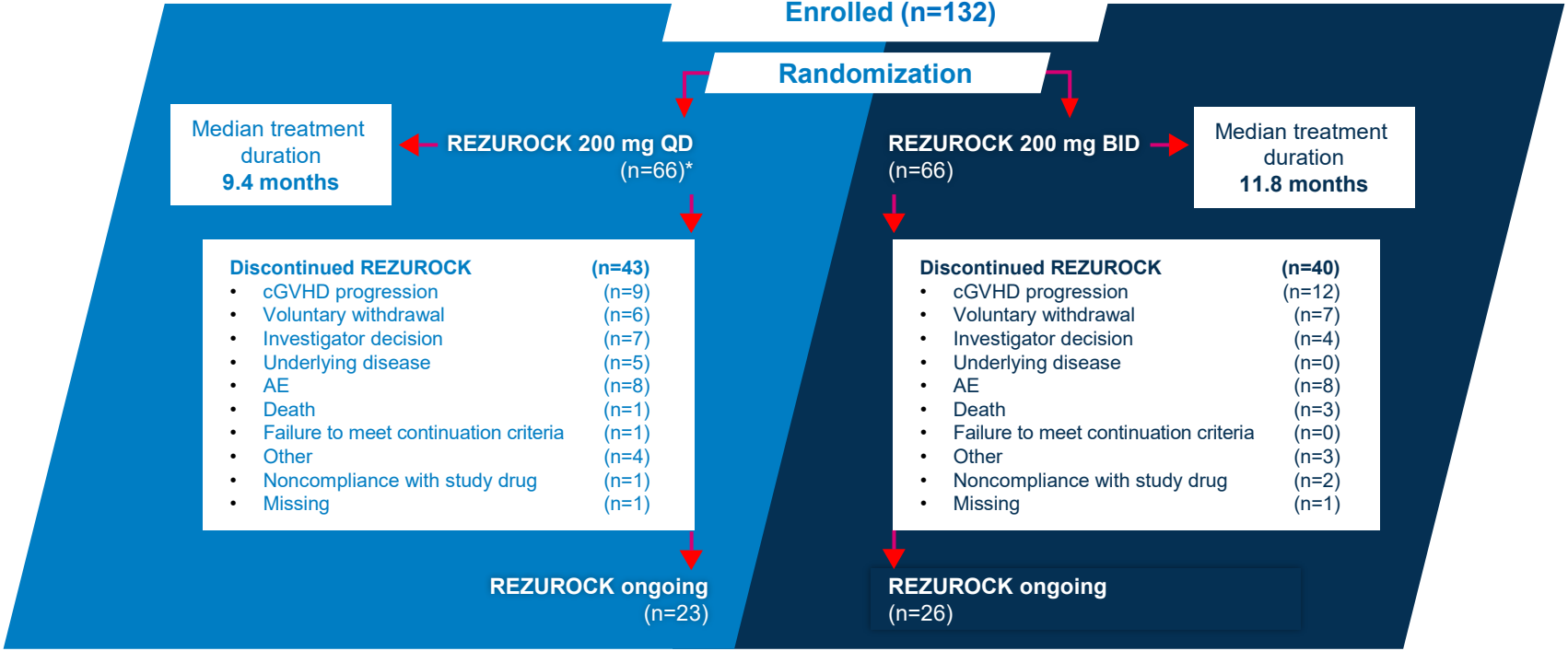
Demographics	REZUROCK 200 mg QD (n=66) *	REZUROCK 200 mg BID (n=66)	Overall (N=132)
Median age, y (range)	53 (21-77)	57 (21-77)	56 (21-77)
Male, %	64	50	57
Median prior lines of systemic therapy, n	3	4	3
Median time from cGVHD diagnosis to enrollment, mo	25	30	28
NIH moderate cGVHD, n (%)	18 (27)	23 (35)	41 (31)
NIH severe cGVHD,[a] n (%)	46 (70)	43 (65)	89 (67)
Median prednisone dose, mg/kg/d	0.19	0.20	0.19
≥4 organs involved, n (%)	33 (50)	35 (53)	68 (52)
Prior ibrutinib treatment,[a] n (%)	22 (33)	23 (35)	45 (34)
Prior ruxolitinib treatment, n (%)	20 (30)	18 (27)	38 (29)
Refractory to last prior lines of systemic therapy, n (%)	44 (79)	35 (65)	79 (72)

[a]Stratification factor.

*In the PI, one non-GVHD patient in the 200mg QD arm was omitted from the primary analysis (N=65).

Cutler C et al. Belumosudil for chronic Graft-Versus Host Disease (cGVHD) after 2 or more lines of therapy: The ROCKstar Study. *Blood*. 2021. blood.2021012021.
doi: https://doi.org/10.1182/blood.2021012021.

The ROCKstar Study: Patient Disposition



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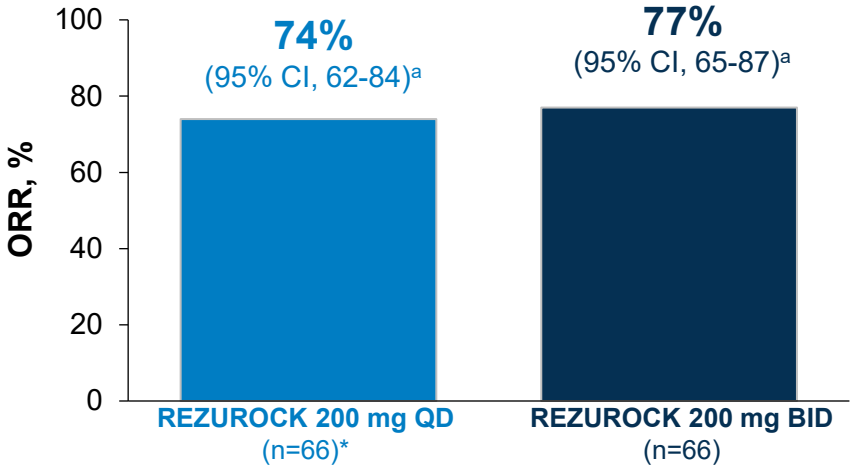
The ROCKstar Study: Primary Endpoint Met

REZUROCK achieved clinically meaningful and statistically significant ORRs in both arms



- Follow-up analysis occurred 12 months after the last patient was enrolled
- Seven patients achieved CR in all affected organs
- Statistical significance is achieved if the lower bound of the 95% CI of ORR exceeds 30%

CR, complete response.

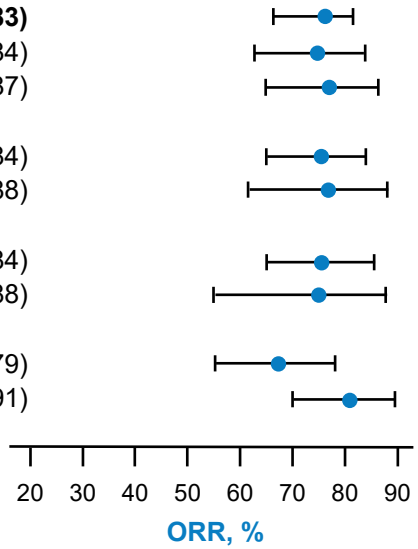
[a]*P*<.0001.

*In the PI, one non-GVHD patient in the 200mg QD arm was omitted from the primary analysis (N=65).

Cutler C et al. Belumosudil for chronic Graft-Versus Host Disease (cGVHD) after 2 or more lines of therapy: The ROCKstar Study. *Blood*. 2021. blood.2021012021. doi: https://doi.org/10.1182/blood.2021012021.

The ROCKstar Study: Responses Observed Across All Key Subgroups

Group name	ORR, % (95% CI[a])
All patients (N=132)	**76 (68-83)**
REZUROCK 200 mg QD (n=66)*	74 (62-84)
REZUROCK 200 mg BID (n=66)	77 (65-87)
Severe cGVHD at screening[b]	
Yes (n=89)	75 (65-84)
No (n=43)	77 (61-88)
Best response to last prior line of systemic therapy	
Refractory (n=79)	75 (64-84)
Nonrefractory (n=31)	74 (55-88)
Duration of cGVHD before enrollment	
>50th percentile (n=66)	68 (56-79)
≤50th percentile (n=66)	83 (72-91)



[a]CI is calculated using the Clopper-Pearson interval (exact) method.
[b]Stratification factor.

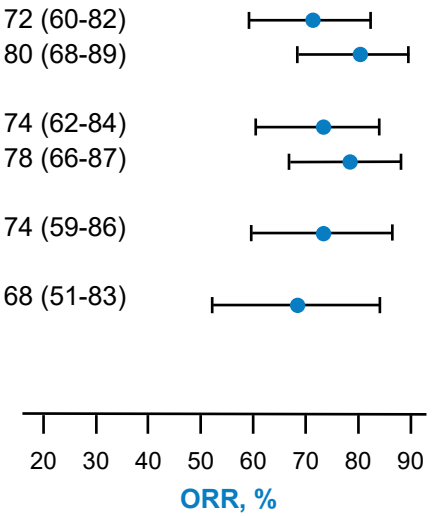
*In the PI, one non-GVHD patient in the 200mg QD arm was omitted from the primary analysis (N=65).

Response assessments performed on or after the initiation of a new systemic therapy for cGVHD were excluded from the analysis. Pooled responses across arms, unless stated.

Cutler C et al. Belumosudil for chronic Graft-Versus Host Disease (cGVHD) after 2 or more lines of therapy: The ROCKstar Study. *Blood*. 2021. blood.2021012021. doi: https://doi.org/10.1182/blood.2021012021.

The ROCKstar Study: Responses Observed Across All Key Subgroups

Group name	ORR, % (95% CI[a])
Number of organs involved at baseline	
≥4 (n=68)	72 (60-82)
<4 (n=64)	80 (68-89)
Number of prior lines of systemic therapy	
≥4 (n=65)	74 (62-84)
<4 (n=67)	78 (66-87)
Prior ibrutinib[b]	
Yes (n=46)	74 (59-86)
Prior ruxolitinib	
Yes (n=38)	68 (51-83)



[a]CI is calculated using the Clopper-Pearson interval (exact) method.
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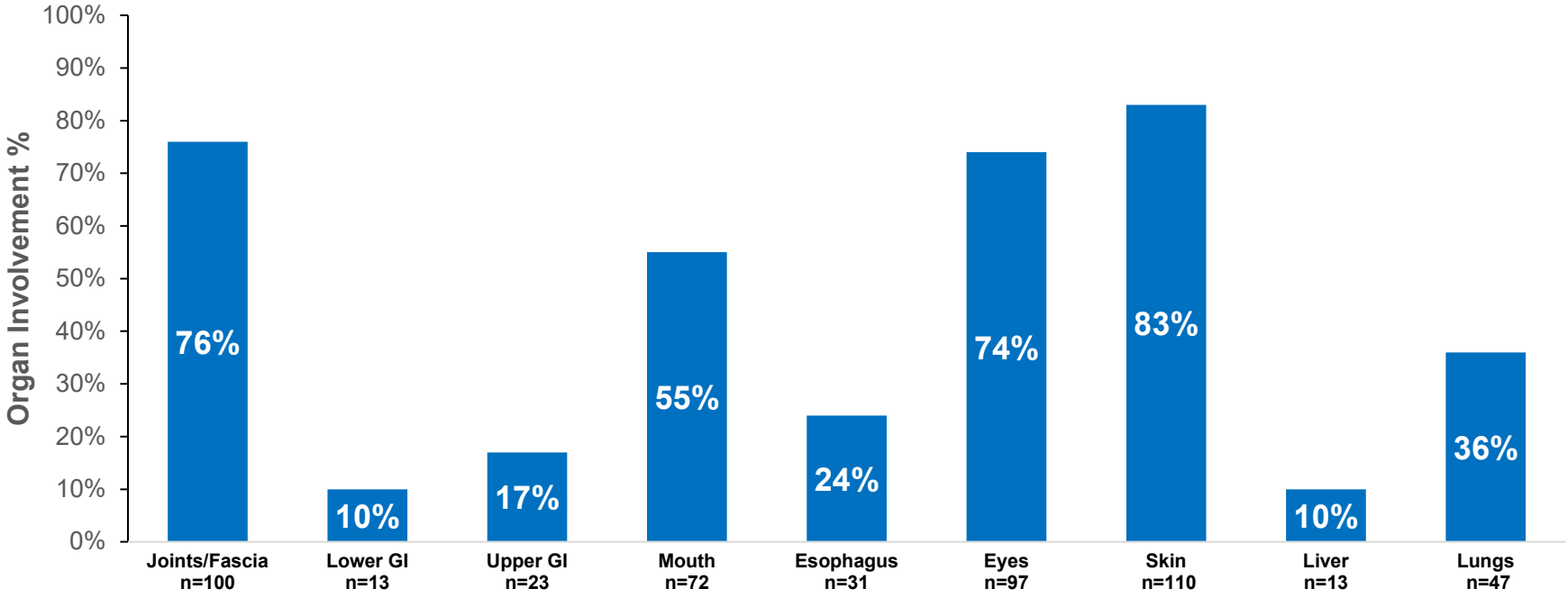
ROCKstar: Organ Involvement at Baseline

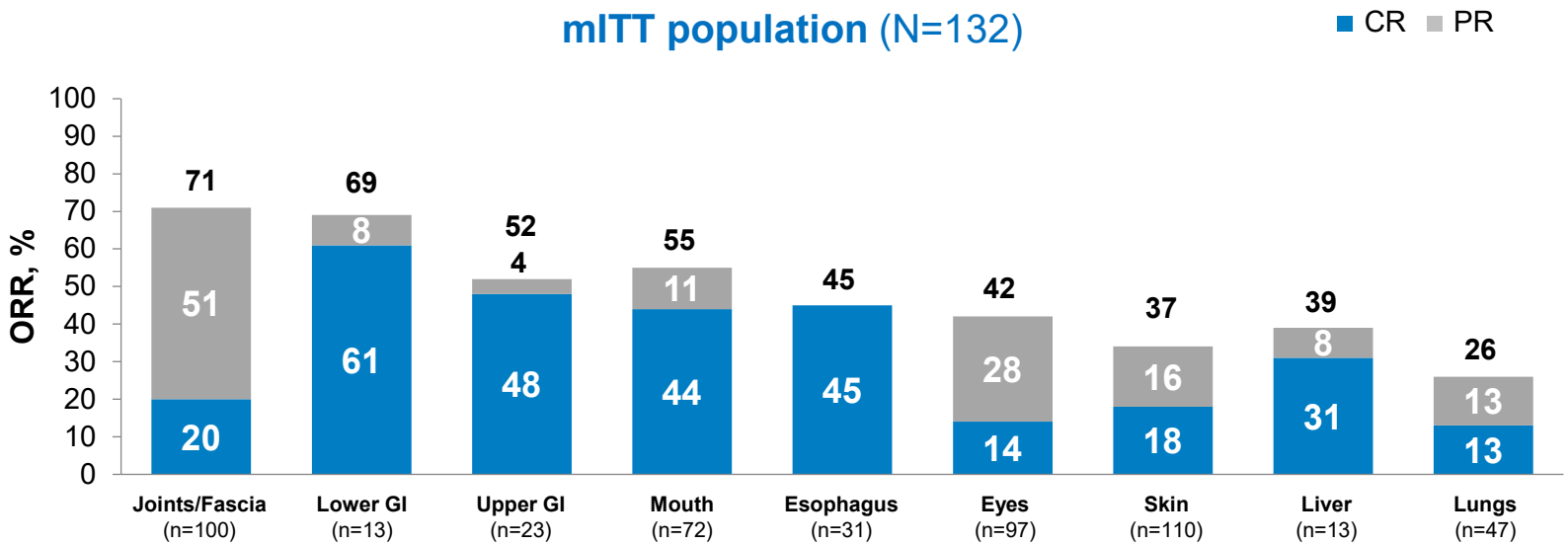


Pooled involvement across arms

Cutler C et al. Belumosudil for chronic Graft-Versus Host Disease (cGVHD) after 2 or more lines of therapy: The ROCKstar Study. *Blood*. 2021. blood.2021012021. doi: https://doi.org/10.1182/blood.2021012021.

ROCKstar: Complete Responses Observed in All Organ Systems

CR Observed in All Organs



Pooled responses across arms

Cutler C et al. Belumosudil for chronic Graft-Versus Host Disease (cGVHD) after 2 or more lines of therapy: The ROCKstar Study. *Blood*. 2021. blood.2021012021. doi: https://doi.org/10.1182/blood.2021012021.

The ROCKstar Study: Safety and Tolerability

Commonly reported AEs, n (%)	REZUROCK 200 mg QD (n=66)	REZUROCK 200 mg BID (n=66)	Overall (N=132)
All grades in ≥20% of patients			
Fatigue	30 (46)	20 (30)	50 (38)
Diarrhea	23 (35)	21 (32)	44 (33)
Nausea	23 (35)	18 (27)	41 (31)
Cough	20 (30)	17 (26)	37 (28)
Upper respiratory tract infection	17 (26)	18 (27)	35 (27)
Dyspnea	21 (32)	12 (18)	33 (25)
Headache	13 (20)	18 (27)	31 (24)
Liver-related AEs	12 (18)	19 (29)	31 (24)
Peripheral edema	17 (26)	13 (20)	30 (23)
Vomiting	18 (27)	10 (15)	28 (21)
Muscle spasms	13 (20)	13 (20)	26 (20)
Grade ≥3 in ≥5% of patients			
Pneumonia	6 (9)	4 (6)	10 (8)
Hypertension	4 (6)	4 (6)	8 (6)
Hyperglycemia	3 (5)	3 (5)	6 (5)

- AEs were overall consistent with those expected in patients with cGVHD receiving corticosteroids and other immunosuppressants
  - There was 1 reported case of Epstein-Barr virus and 1 reported case of CMV reactivation

Safety overview	REZUROCK 200 mg QD (n=66)	REZUROCK 200 mg BID (n=66)	Overall (N=132)
Median duration of treatment, mo	9.4	11.8	10.4
Any AE, n (%)	65 (99)	66 (100)	131 (99)
Grade ≥3 AEs, n (%)	37 (56)	34 (52)	71 (54)
SAEs, n (%)	27 (41)	23 (35)	50 (38)
Drug-related AEs, n (%)			
Any related AE	49 (74)	40 (61)	89 (67)
Related SAEs	5 (8)	2 (3)	7 (5)
On study deaths,[a] n (%)	4 (6)	4 (6)	8 (6)

[a]**REZUROCK QD:** aspiration pneumonia; hemoptysis; MODS/septic shock; relapse AML.
[a]**REZUROCK BID:** cardiac arrest (2); infection; respiratory failure.

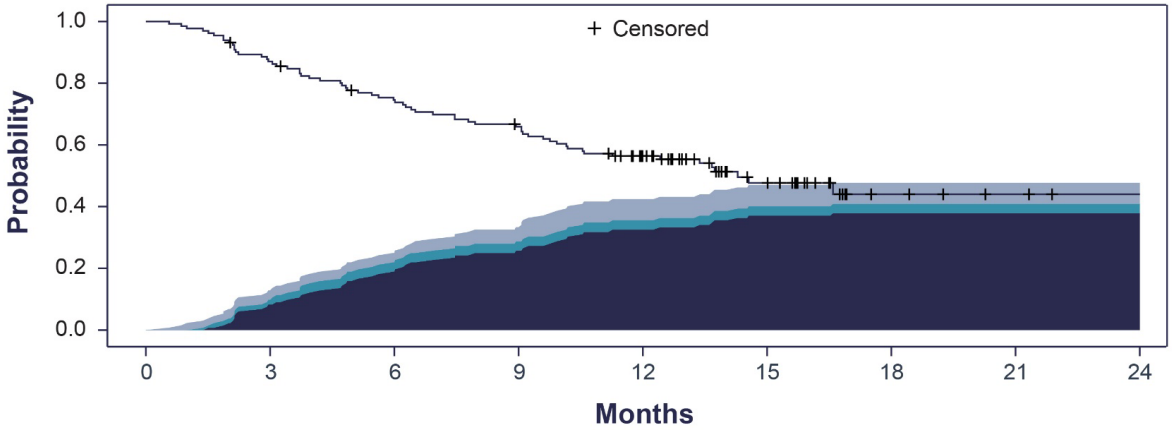
AE, adverse event; AML, acute myeloid leukemia; MODS, multiple organ dysfunction syndrome; SAE, serious adverse event.

Cutler C et al. Belumosudil for chronic Graft-Versus Host Disease (cGVHD) after 2 or more lines of therapy: The ROCKstar Study. *Blood*. 2021. blood.2021012021. doi: https://doi.org/10.1182/blood.2021012021.

The ROCKstar Study: Failure Free Survival

Kaplan-Meier Plot of FFS

Treatment: Overall



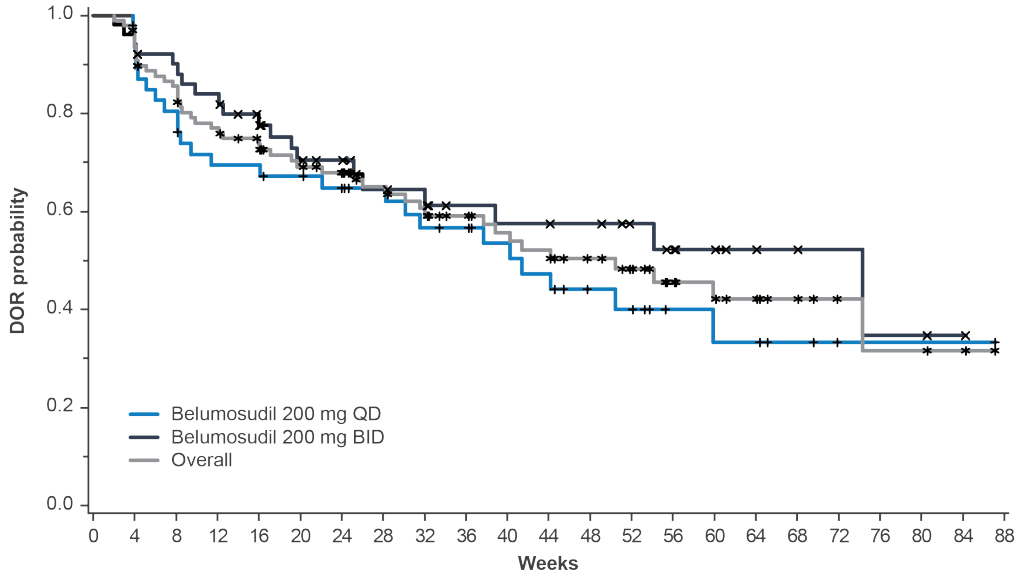
Number at risk	132	114	96	84	62	26	7	3	1
FFS	100	87	74.6	65.9	56.4	47.7	44	44	44
New treatment for cGVHD	0	8.3	18.9	25.8	32.6	37.1	37.9	37.9	37.9
Relapse	0	1.5	3	3	3	3	3	3	3
Death	0	3	3	4.5	6.8	6.8	6.8	6.8	6.8

An FFS rate of **56%** was maintained at 12 months.

Cutler C et al. Belumosudil for chronic Graft-Versus Host Disease (cGVHD) after 2 or more lines of therapy: The ROCKstar Study. *Blood*. 2021. blood.2021012021. doi: https://doi.org/10.1182/blood.2021012021.

The ROCKstar Study: DOR

Kaplan-Meier Plot of DOR



Number at risk																						
Belumosudil 200 mg QD	48	43	37	31	31	29	26	24	21	20	17	15	11	10	6	5	5	3	1	1	1	1	0
Belumosudil 200 mg BID	51	48	44	41	35	30	28	21	19	16	15	15	14	11	9	7	5	4	3	2	2	1	0
Overall	99	91	81	72	66	59	54	45	40	36	32	30	25	21	15	12	10	7	4	3	3	2	0

Overall, 44% of patients have remained on REZUROCK therapy for >1 year.

The median DOR was **54 weeks**, and 60% of responders maintained responses for ≥20 weeks.

Note: The median DOR in the REZUROCK PI is different from what was reported in the ROCKstar study due to a difference in the final FDA analysis.

Cutler C et al. Belumosudil for chronic Graft-Versus Host Disease (cGVHD) after 2 or more lines of therapy: The ROCKstar Study. *Blood*. 2021. blood.2021012021. doi: https://doi.org/10.1182/blood.2021012021.

REZUROCK Prescribing Information: ORR and DOR

The efficacy of REZUROCK was based on overall response rate (ORR) through Cycle 7 Day 1 where overall response included complete response or partial response according to the 2014 NIH Response Criteria. The ORR results are presented in **Table 5**. The ORR was 75% (95% CI: 63, 85). The median duration of response, calculated from first response to progression, death, or new systemic therapies for chronic GVHD, was 1.9 months (95% CI: 1.2, 2.9). The median time to first response was 1.8 months (95% CI: 1.0, 1.9). In patients who achieved response, no death or new systemic therapy initiation occurred in 62% (95% CI: 46, 74) of patients for at least 12 months since response.

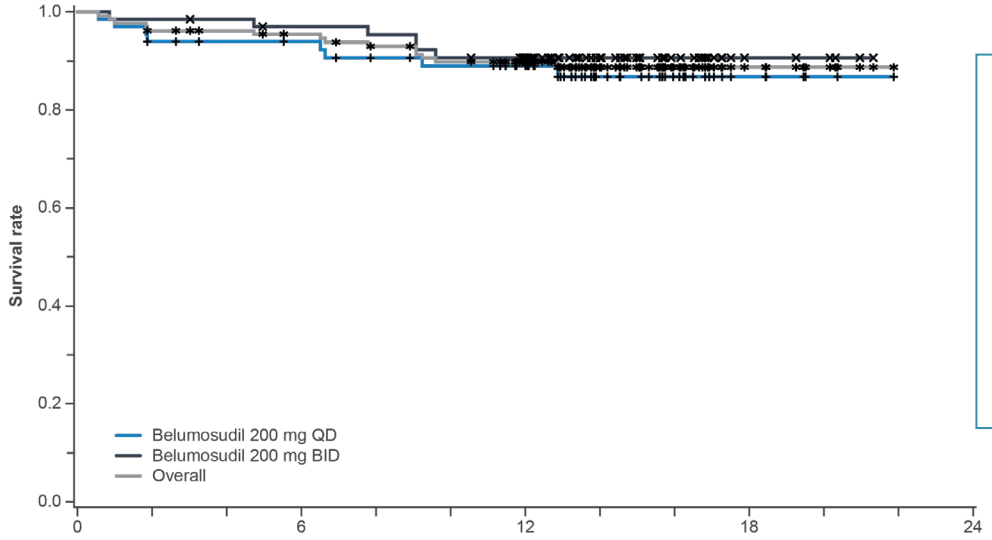
Table 5: Overall Response Rate through Cycle 7 Day 1 for Patients with Chronic GVHD in Study KD025-213

	REZUROCK 200 mg once daily (N=65)
Overall Response Rate (ORR)	49 (75%)
95% Confidence Interval[a]	(63%, 85%)
Complete Response	4 (6%)
Partial Response	45 (69%)

[a] Estimated using Clopper-Pearson method

The ROCKstar Study: Overall Survival

Kaplan-Meier plot of OS



Number at risk					
Belumosudil 200 mg QD	66	58	44	6	0
Belumosudil 200 mg BID	66	62	50	5	0
Overall	132	120	94	11	0

The OS rate
at **24 months**
was 89%
(95% CI, 82%-93%).

The ROCKstar Study: Additional Efficacy End Points

- Overall, 64% of patients were able to reduce their **CS dose**, and 21% discontinued **CS therapy**
  - The mean CS dose was reduced by 44%; 52% in responders and 17% in non-responders
- Overall, 45% of patients were able to reduce their **CNI dose**, and 22% discontinued **CNI therapy**
- Overall, clinically meaningful improvement in **LSS score** from baseline was observed in 60% of patients
  - Both responders and non-responders achieved clinically meaningful improvements in LSS

CNI, calcineurin inhibitor; CS, corticosteroid

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REZUROCK PI:

Indication, Dosage, Dose Modifications, Adverse Events, Drug Interactions

REZUROCK Prescribing Information: Indication and Dosage

1 INDICATIONS AND USAGE

REZUROCK is indicated for the treatment of adult and pediatric patients 12 years and older with chronic graft-versus-host disease (chronic GVHD) after failure of at least two prior lines of systemic therapy.

2 DOSAGE AND ADMINISTRATION

2.1 Recommended Dosage

The recommended dose of REZUROCK is 200 mg given orally once daily until progression of chronic GVHD that requires new systemic therapy.

Instruct the patient on the following:

- Swallow REZUROCK tablets whole. Do not cut, crush, or chew tablets.
- Take REZUROCK with a meal at approximately the same time each day *[see Clinical Pharmacology (12.3)]*.
- If a dose of REZUROCK is missed, instruct the patient to not take extra doses to make up the missed dose.

Treatment with REZUROCK has not been studied in patients with pre-existing severe renal or hepatic impairment. For patients with pre-existing severe renal or hepatic impairment, consider the risks and potential benefits before initiating treatment with REZUROCK *[see Clinical Pharmacology (12.3)]*.

REZUROCK Prescribing Information: Dose Modifications

2.2 Dose Modifications for Adverse Reactions

Monitor total bilirubin, aspartate aminotransferase (AST), and alanine aminotransferase (ALT) at least monthly.

Modify the REZUROCK dosage for adverse reactions as per **Table 1**.

Table 1: Recommended Dosage Modifications for REZUROCK for Adverse Reactions

Adverse Reaction	Severity*	REZUROCK Dosage Modifications
Hepatotoxicity *[see Adverse Reactions (6.1)]*	Grade 3 AST or ALT (5x to 20x ULN) or Grade 2 bilirubin (1.5x to 3x ULN)	Hold REZUROCK until recovery of bilirubin, AST and ALT to Grade 0-1, then resume REZUROCK at the recommended dose.
	Grade 4 AST or ALT (more than 20x ULN) or Grade ≥ 3 bilirubin (more than 3x ULN)	Discontinue REZUROCK permanently.
Other adverse reactions *[see Adverse Reactions (6.1)]*	Grade 3	Hold REZUROCK until recovery to Grade 0-1, then resume REZUROCK at the recommended dose level.
	Grade 4	Discontinue REZUROCK permanently.

*Based on CTCAE v 4.03

REZUROCK Prescribing Information: Dose Modifications for Drug Interactions

2.3 Dosage Modification Due to Drug Interactions

Strong CYP3A Inducers

Increase the dosage of REZUROCK to 200 mg twice daily when coadministered with strong CYP3A inducers *[see Drug Interactions (7.1)]*.

Proton Pump Inhibitors

Increase the dosage of REZUROCK to 200 mg twice daily when coadministered with proton pump inhibitors *[see Drug Interactions (7.1)]*.

REZUROCK Prescribing Information: Contraindications, Warnings, Precautions

4 CONTRAINDICATIONS

None.

5 WARNINGS AND PRECAUTIONS

5.1 Embryo-Fetal Toxicity

Based on findings in animals and its mechanism of action, REZUROCK can cause fetal harm when administered to a pregnant woman. In animal reproduction studies, administration of belumosudil to pregnant rats and rabbits during the period organogenesis caused adverse developmental outcomes including embryo-fetal mortality and malformations at maternal exposures (AUC) less than those in patients at the recommended dose. Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential and males with female partners of reproductive potential to use effective contraception during treatment with REZUROCK and for at least one week after the last dose *[see Use in Specific Populations (8.1, 8.3), Nonclinical Toxicology (13.1)]*.

REZUROCK Prescribing Information: Discontinuations

Permanent discontinuation of REZUROCK due to adverse reactions occurred in 18% of patients. The adverse reactions which resulted in permanent discontinuation of REZUROCK in > 3% of patients included nausea (4%). Adverse reactions leading to dose interruption occurred in 29% of patients. The adverse reactions leadin to dose interruption in ≥ 2% were infections (11%), diarrhea (4%), and asthenia, dyspnea, hemorrhage, hypotension, liver function test abnormal, nausea, pyrexia, edema, and renal failure with (2% each).

The most common (≥ 20%) adverse reactions, including laboratory abnormalities, were infections, asthenia, nausea, diarrhea, dyspnea, cough, edema, hemorrhage, abdominal pain, musculoskeletal pain, headache, phosphate decreased, gamma glutamyl transferase increased, lymphocytes decreased, and hypertension.

REZUROCK Prescribing Information: Adverse Reactions

Table 2: Nonlaboratory Adverse Reactions in ≥ 10% Patients with Chronic GVHD Treated with REZUROCK

Adverse Reaction	REZUROCK 200 mg once daily (N=83)	
	All Grades (%)	Grades 3-4 (%)
Infections and infestations		
Infection (pathogen not specified)[a]	53	16
Viral infection[b]	19	4
Bacterial infection[c]	16	4
General disorders and administration site conditions		
Asthenia[d]	46	4
Edema[e]	27	1
Pyrexia	18	1
Gastrointestinal		
Nausea[f]	42	4
Diarrhea	35	5
Abdominal pain[g]	22	1
Dysphagia	16	0
Respiratory, thoracic and mediastinal		
Dyspnea[h]	33	5
Cough[i]	30	0
Nasal congestion	12	0
Vascular		
Hemorrhage[j]	23	5
Hypertension	21	7
Musculoskeletal and connective tissue		
Musculoskeletal pain[k]	22	4
Muscle spasm	17	0
Arthralgia	15	2
Nervous system		
Headache[l]	21	0
Metabolism and nutrition		
Decreased appetite	17	1
Skin and subcutaneous		
Rash[m]	12	0
Pruritus[n]	11	0

[a] infection with an unspecified pathogen includes acute sinusitis, device related infection, ear infection, folliculitis, gastroenteritis, gastrointestinal infection, hordeolum, infectious colitis, lung infection, skin infection, tooth infection, urinary tract infection, wound infection, upper respiratory tract infection, pneumonia, conjunctivitis, sinusitis, respiratory tract infection, bronchitis, sepsis, septic shock.

[b] includes influenza, rhinovirus infection, gastroenteritis viral, viral upper respiratory tract infection, bronchitis viral, Epstein-Barr viremia, Epstein-Barr virus infection, parainfluenzae virus infection, Varicella zoster virus infection, viral infection.

[c] includes cellulitis, Helicobacter infection, Staphylococcal bacteremia, catheter site cellulitis, Clostridium difficile colitis, Escherichia urinary tract infection, gastroenteritis Escherichia coli, Pseudomonas infection, urinary tract infection bacterial.

[d] includes fatigue, asthenia, malaise.

[e] includes edema peripheral, generalized edema, face edema, localized edema, edema.

[f] includes nausea, vomiting.

[g] includes abdominal pain, abdominal pain upper, abdominal pain lower.

[h] includes dyspnea, dyspnea exertional, apnea, orthopnea, sleep apnea syndrome.

[i] includes cough, productive cough.

[j] includes contusion, hematoma, epistaxis, increased tendency to bruise, conjunctival hemorrhage, hematochezia, mouth hemorrhage, catheter site hemorrhage, hematuria, hemothorax, purpura.

[k] includes pain in extremity, back pain, flank pain, limb discomfort, musculoskeletal chest pain, neck pain, musculoskeletal pain.

[l] includes headache, migraine.

[m] includes rash, rash maculo-papular, rash erythematous, rash generalized, dermatitis exfoliative.

[n] includes pruritus, pruritus generalized.

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REZUROCK Prescribing Information: Lab Abnormalities

Table 3: Selected Laboratory Abnormalities in Patients with Chronic GVHD Treated with REZUROCK

	REZUROCK 200 mg once daily		
	Grade 0-1 Baseline	Grade 2-4 Max Post	Grade 3-4 Max Post
Parameter	**(N)**	**(%)**	**(%)**
Chemistry			
Phosphate Decreased	76	28	7
Gamma Glutamyl Transferase Increased	47	21	11
Calcium Decreased	82	12	1
Alkaline Phosphatase Increased	80	9	0
Potassium Increased	82	7	1
Alanine Aminotransferase Increased	83	7	2
Creatinine Increased	83	4	0
Hematology			
Lymphocytes Decreased	62	29	13
Hemoglobin Decreased	79	11	1
Platelets Decreased	82	10	5
Neutrophil Count Decreased	83	8	4

REZUROCK™ (belumosudil) Overall Clinical Summary

Despite Available Options, There Remains a Significant Unmet Need for New cGVHD Treatments

- cGVHD is a severe complication following allogeneic HCT that leads to inflammation and fibrosis in multiple tissues and organs and occurs in approximately 50% of transplant patients[1,2]
- Standard treatments result in roughly 50% of patients progressing to last line (3rd or 4th line) therapies[3]
- REZUROCK was well tolerated in two Phase 2 clinical trials and achieved meaningful outcomes
- ORR of 75% across QD and BID treatment arms in the ROCKstar Study[4]
- Responses were observed across all key subgroups and in all affected organ systems, including organs with fibrotic disease manifestations
- Additional end point data, including PK and PD data, are expected in 2021

1. Bachier CR et al. 2019 epidemiology and real-world treatment of chronic graft-versus-host disease post allogeneic hematopoietic cell transplantation: a US claims analysis. Proceedings from the 61st American Society of Hematology Annual Meeting & Exposition; December 7-10, 2019; Orlando, FL. Abstract 2109. **2.** Lee SJ et al. Success of Immunosuppressive Treatments in Patients with Chronic Graft-versus-Host Disease. *Biol Blood Marrow Transplant*. 2018; 24(3): 555-562. **3.** Gonzalez RM, Pidala J. Evolving. **4.** Cutler C et al. Belumosudil for chronic Graft-Versus Host Disease (cGVHD) after 2 or more lines of therapy: The ROCKstar Study. *Blood*. 2021. blood.2021012021. doi: https://doi.org/10.1182/blood.2021012021.

Q and A