

Supplement Table 1. Pomalidomide dose modification protocol rules

Common Terminology Criteria (CTCAE) Version 4.0	Adverse Event	Dose Change for Pomalidomide
Allergy/Immunology	Allergic reaction/hypersensitivity (including drug fever) - Grade 2	Hold study drug until resolved to < Grade 1; Decrease dose by 1 dose level
	Allergic reaction/ hypersensitivity (including drug fever) - Grade 3 or 4	Discontinue Study Drug
Blood/Bone Marrow	Neutropenia (ANC) - Grade 3 with fever or Grade 4	Hold study drug until < Grade 2; Decrease dose by 1 dose level
	Thrombocytopenia - Grade 3 or 4	Hold study drug until < Grade 2; Decrease dose by 1 dose level
	Anemia – Grade 3 or 4	Hold study drug and treat anemia as needed until Hgb within 0.5 g/dl of lower limit of normal; Decrease dose by one dose level
Cardiac Arrhythmia	Grade 2	Hold study drug until resolved to < Grade 1; Decrease dose by 1 dose level
	Grade 3 or 4	Discontinue study drug
Prolonged QTc Interval	Grade 3 (<0.50 second)	Hold study drug; decrease dose by 1 dose level and restart when resolved to < Grade 2
	Grade 4 (>0.5 second, life threatening symptoms)	Discontinue study drug
Vascular	Thrombosis/embolism - Grade 2, 3 or 4	Discontinue study drug
Dermatology/Skin	Rash non-desquamation - Grade 3	Hold study drug until resolved to < Grade 1. Decrease dose by 1 dose level
	Rash non-desquamation - Grade 4	Discontinue study drug
	Rash/desquamation - Grade 3, 4	Discontinue study drug
	Rash/desquamation - Grade 2	The dose may be modified or discontinued at the investigator's discretion.
	Rash Erythema multiforme	Discontinue study drug
Endocrine	Elevated or Reduced Thyroid Function Test results without symptoms of hyper- or hypothyroidism	Confirm test results and if significant, refer for therapy; Do not alter study drug regimen
	Elevated or Reduced Thyroid Function Test results with symptoms of hyper- or hypothyroidism	Hold study drug; Evaluate etiology and refer for appropriate therapy; Restart at the prior dose once symptoms have resolved and thyroid function has been stabilized with medical and/or surgical intervention
Neurology	Neuropathy cranial/motor/sensory - Grade 2	Hold study drug; Restart at same or 1 dose level lower once event has resolved to < Grade 1
	Neuropathy cranial/motor/sensory Grade 3 or recurrence of Grade 2	Hold study drug until resolved to < Grade 1; Decrease dose by 1 dose level
	Neuropathy cranial/motor/sensory - Grade 4	Discontinue study drug
Other pomalidomide related toxicity	Grade 3 or Grade 4	Hold pomalidomide therapy; Decrease dose by 1 dose level and restart when resolved to < Grade 2

Supplement Table 2. List of antibodies with manufactures used in analysis by flow cytometry

Antibody	Manufacturer	Clone
CD45	Biolegend 304006	CD45 FITC (clone HI30)
CD56	BD 555516	CD56 PE (clone B159)
CD16	Biolegend 302028	CD16 PerCP-Cy5.5 (clone 3G8)
CD14	FisherSci 25-0149-42	CD14 PE-Cy7 (clone 61D3)
CD19	Biolegend 302212	CD19 APC (clone HIB19)
CD3	BD 557943	CD3 Alexa700 (clone UCHT-1)
CD4	Biolegend 300518	CD4 APC-Cy7 (clone RPA-T4)
CD8	Ebio 48-0088-42	CD8 e450 (clone RPA-T8)
CD31	Ebio 11-0319-42	CD31 FITC (clone WM-59)
CCR7	BD 560765	CCR7 PE (clone 150503)
CD45RA	Beckman Coulter IM2711U	CD45RA ECD (clone 2H4)
CD39	Ebio 46-0399-42	CD39 PerCP-e710 (clone eBioA1)
CD25	Ebio 25-0259-42	CD25 PE-Cy7 ((clone BC96)
CD127	Ebio 17-1278-41	CD127 APC (clone eBioRDR5)
CD3	BD 557943	CD3 Alexa700 (clone UCHT-1)
CD27	Ebioscience 47-0279-42	CD27 APC-e780 (clone O323)
CD8	Ebio 48-0088-42	CD8 e450 (clone RPA-T8)
CD4	Biolegend 317444	CD4 bv510 (clone OKT4)
IgD	BD 555778	IgD FITC (clone IA6-2)
CD21	Biolegend 354904	CD21 PE (clone Bu32)
CD20	Beckman Coulter IM3607U	CD20 ECD (clone B9E9)
CD10	Biolegend 312216	CD10 PerCP-Cy5.5 (clone HI10a)
CD24	BD 561646	CD24 PE-Cy7 (clone ML5)
CD38	Biolegend 303510	CD38 APC (clone HIT2)
CD3	BD 557943	CD3 Alexa700 (clone UCHT-1)
CD27	Ebioscience 47-0279-42	CD27 APC-e780 (clone O323)
CD11c	Biolegend 301628	CD11c bv421 (clone 3.9)
CD19	Biolegend 302242	CD19 bv510 (clone HIB19)
CCR7	BD 561271	CCR7 FITC (clone 150503)
ICOS	BD 557802	ICOS PE (clone DX29)
CD4	Biolegend 317448	CD4 PE-DAZZLE (clone OKT4)
CD39	Ebio 46-0399-42	CD39 PerCP-e710 (clone eBioA1)
CD25	Ebio 25-0259-42	CD25 PE-Cy7 (clone BC96)
FoxP3	Ebio 13-4777-82	FoxP3 biotin (clone 236A/E7)
CD3	BD 557943	CD3 Alexa700 (clone UCHT-1)
CD45RA	FisherSci 50-245-971	CD45RA APC-e780 (clone HI100)
Ki-67	Ebio 48-5699-42	Ki-67 e450 (clone 20Raj1)

Supplement Figure 1. Example of patient with improvement in cGvHD-related sclerosis after one year of pomalidomide.



Supplement Figure 1. Picture on the left side shows sclerotic chronic graft-*versus*-host (cGvHD) skin involvement at baseline. Picture on the right side shows improvement in cGvHD of involved skin after 12 months on pomalidomide therapy.

Supplement Table 7. Number (proportion) of patients experiencing adverse event recorded according to CTCAE criteria version 4 (excluding serious).

Adverse Event*	High-dose group	Low-dose group
	Number (Percent)	Number (Percent)
Total	17/17 (100%)	17/17 (100%)
Blood and lymphatic system disorders		
Anemia	2/17 (12%)	3/17 (18%)
Hemolysis	1/17 (6%)	0/17 (0%)
Cardiac disorders		
ST depression	0/17 (0%)	1/17 (6%)
Sinus bradycardia	1/17 (6%)	0/17 (0%)
Sinus tachycardia	1/17 (6%)	0/17 (0%)
Ear and labyrinth disorders		
Hearing impaired	0/17 (0%)	2/17 (12%)
Eye disorders		
Blurred vision**	2/17 (12%)	2/17 (12%)
Dry eye**	2/17 (12%)	2/17 (12%)
Glaucoma	0/17 (0%)	1/17 (6%)
Photophobia	0/17 (0%)	1/17 (6%)
Retinal vascular disorder	0/17 (0%)	1/17 (6%)
Gastrointestinal disorders		
Constipation	2/17 (12%)	0/17 (0%)
Diarrhea**	4/17 (24%)	2/17 (12%)
Dry mouth**	2/17 (12%)	0/17 (0%)
Esophageal ulcer**	0/17 (0%)	1/17 (6%)
Gastroesophageal reflux disease**	1/17 (6%)	2/17 (12%)
Reflux + fullness**	0/17 (0%)	1/17 (6%)
Mucositis oral**	1/17 (6%)	0/17 (0%)
Nausea**	3/17 (18%)	2/17 (12%)
Oral pain**	1/17 (6%)	0/17 (0%)
Toothache	1/17 (6%)	0/17 (0%)
Vomiting**	1/17 (6%)	1/17 (6%)
General disorders		
Edema limbs	3/17 (18%)	4/17 (24%)
Fatigue**	10/17 (59%)	3/17 (18%)
Flu like symptoms	0/17 (0%)	2/17 (12%)
Pain**	0/17 (0%)	1/17 (6%)

Adverse Event*	High-dose group	Low-dose group
	Number (Percent)	Number (Percent)
Immune system disorders		
Throat tightness, dry mouth, pruritus**	1/17 (6%)	0/17 (0%)
Infections and infestations		
Bronchial infection	1/17 (6%)	0/17 (0%)
CMV reactivation	1/17 (6%)	0/17 (0%)
Lung infection	4/17 (24%)	3/17 (18%)
Sinusitis	3/17 (18%)	0/17 (0%)
Skin infection	1/17 (6%)	2/17 (12%)
Urinary tract infection	1/17 (6%)	0/17 (0%)
Injury, poisoning and procedural complications		
Spinal fracture	0/17 (0%)	1/17 (6%)
Investigations		
Alanine aminotransferase increased**	2/17 (12%)	1/17 (6%)
Aspartate aminotransferase increased**	0/17 (0%)	1/17 (6%)
Creatinine increased	0/17 (0%)	3/17 (18%)
Lymphocyte count decreased	10/17 (59%)	8/17 (47%)
Lymphocyte count increased	0/17 (0%)	1/17 (6%)
Neutrophil count decreased	6/17 (53%)	2/17 (12%)
Weight loss**	1/17 (6%)	0/17 (0%)
White blood cell decreased	2/17 (12%)	2/17 (12%)
Metabolism and nutrition disorders		
Hyperglycemia	2/17 (12%)	0/17 (0%)
Hyperkalemia	2/17 (12%)	1/17 (6%)
Hypermagnesemia	0/17 (0%)	1/17 (6%)
Hyperuricemia	0/17 (0%)	1/17 (6%)
Hypoalbuminemia	2/17 (12%)	3/17 (18%)
Hypocalcemia	0/17 (0%)	1/17 (6%)
Hypokalemia	1/17 (6%)	0/17 (0%)
Hypophosphatemia	9/17 (53%)	4/17 (24%)
Musculoskeletal and connective tissue disorders		
Arthralgia**	2/17 (12%)	1/17 (6%)
Back pain	0/17 (0%)	1/17 (6%)
Generalized muscle weakness**	1/17 (6%)	0/17 (0%)
Joint range of motion decreased**	1/17 (6%)	1/17 (6%)
Joint range of motion decreased cervical spine**	1/17 (6%)	0/17 (0%)
L. plantar fasciitis**	0/17 (0%)	1/17 (6%)

Adverse Event*	High-dose group	Low-dose group
	Number (Percent)	Number (Percent)
Myalgia/Muscle cramps**	4/17 (24%)	1/17 (6%)
Myositis	0/17 (0%)	1/17 (6%)
Neck pain**	1/17 (6%)	0/17 (0%)
Non-cardiac chest pain	0/17 (0%)	1/17 (6%)
Pain in extremity**	2/17 (12%)	1/17 (6%)
Nervous system disorders		
Amnesia	1/17 (6%)	0/17 (0%)
Dizziness	2/17 (12%)	2/17 (12%)
Dysesthesia	1/17 (6%)	0/17 (0%)
Dysphasia	1/17 (6%)	0/17 (0%)
Headache	0/17 (0%)	2/17 (12%)
Memory impairment	1/17 (6%)	1/17 (6%)
Peripheral sensory neuropathy**	1/17 (6%)	1/17 (6%)
Syncope	0/17 (0%)	1/17 (6%)
Tremor	5/17 (29%)	1/17 (6%)
Psychiatric disorders		
Depression	1/17 (6%)	0/17 (0%)
Insomnia	1/17 (6%)	1/17 (6%)
Renal and urinary disorders		
Urinary frequency	2/17 (12%)	0/17 (0%)
Reproductive system and breast disorders		
Testicular pain	1/17 (6%)	0/17 (0%)
Vaginal inflammation	1/17 (6%)	0/17 (0%)
Respiratory, thoracic and mediastinal disorders		
Dyspnea**	2/17 (12%)	1/17 (6%)
Epistaxis	0/17 (0%)	1/17 (6%)
Forced expiratory volume decreased**	1/17 (6%)	2/17 (12%)
Nasal congestion	1/17 (6%)	1/17 (6%)
Upper respiratory infection	7/17 (41%)	9/17 (53%)
Skin and subcutaneous tissue disorders		
Bullous dermatitis**	1/17 (6%)	2/17 (12%)
Dry skin**	1/17 (6%)	0/17 (0%)
Hyperhidrosis	1/17 (6%)	0/17 (0%)
Pain of skin**	0/17 (0%)	3/17 (18%)
Pruritus**	0/17 (0%)	1/17 (6%)
Rash maculo-papular**	5/17 (29%)	5/17 (29%)

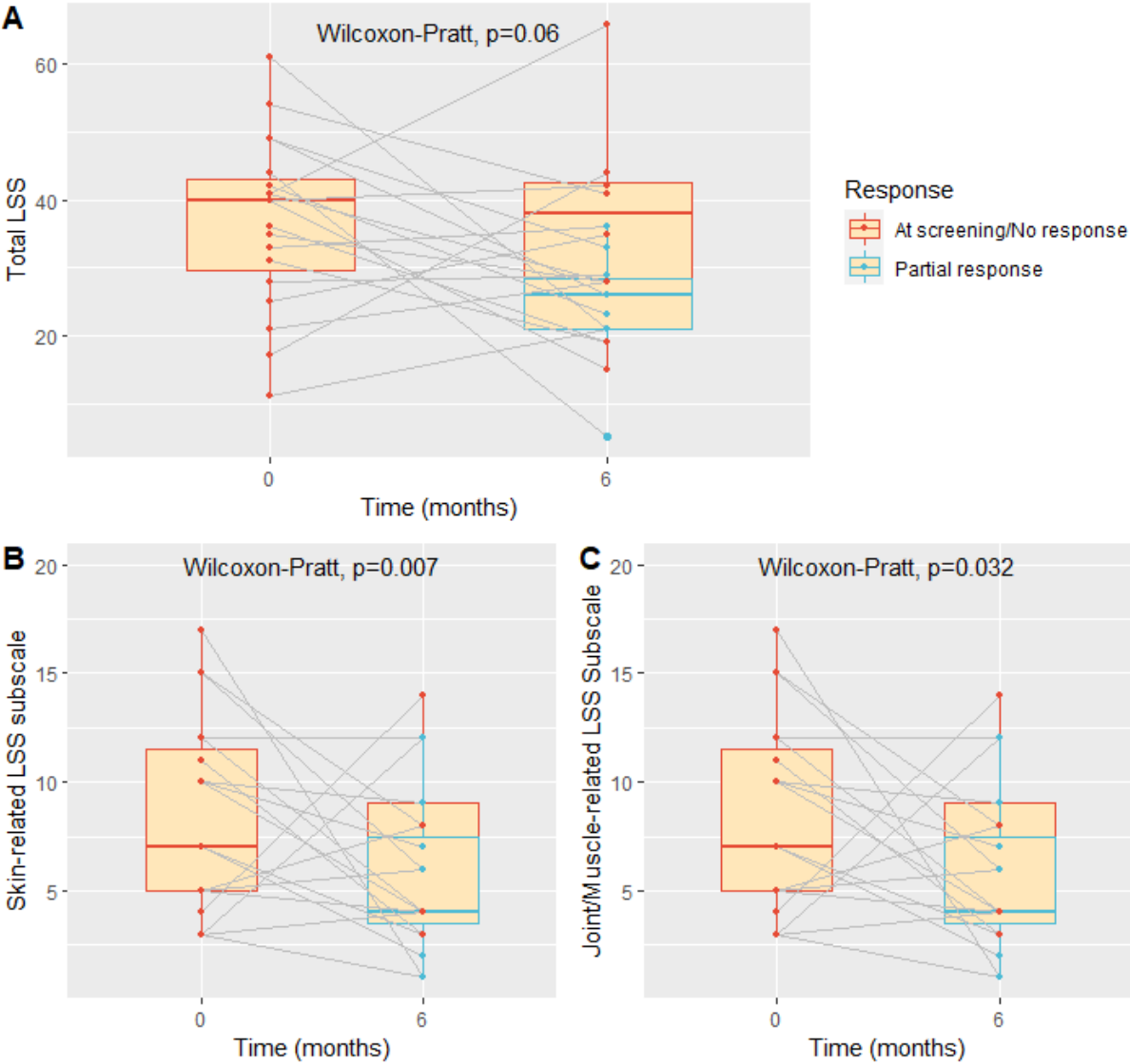
Adverse Event*	High-dose group	Low-dose group
	Number (Percent)	Number (Percent)
Increased plaques**	1/17 (6%)	0/17 (0%)
Leg wounds**	0/17 (0%)	1/17 (6%)
Upper extremity and leg tightness**	0/17 (0%)	1/17 (6%)
Skin ulceration**	1/17 (6%)	3/17 (18%)
Vascular disorders		
Hypertension	2/17 (12%)	3/17 (18%)
Hypotension	1/17 (6%)	1/17 (6%)
*Multiple occurrences of the same adverse event in 1 patient were counted only once per preferred term. Only grade ≥ 2 adverse events were recorded. ** Possibly related to cGVHD.		

Supplement Table 8. Number of patients experiencing serious adverse events recorded according to CTCAE criteria version 4

Serious Adverse Event ^{*,**}	High-dose group	Low-dose group
	Number (Percent)	Number (Percent)
Total	11/17 (65%)	8/17 (47%)
Blood and lymphatic system disorders		
Anemia	1/17 (6%)	0/17 (0%)
Cardiac disorders		
Chest pain - cardiac	0/17 (0%)	1/17 (6%)
Sinus bradycardia	1/17 (6%)	0/17 (0%)
Eye disorders		
Retinopathy	0/17 (0%)	1/17 (6%)
Gastrointestinal disorders		
Duodenal ulcer ^{***}	1/17 (6%)	0/17 (0%)
Gastroenteritis ^{***}	0/17 (0%)	1/17 (6%)
General disorders		
Fever	0/17 (0%)	1/17 (6%)
Infections and infestations		
Bronchial infection	1/17 (6%)	1/17 (6%)
CMV reactivation	0/17 (0%)	1/17 (6%)
Lung infection	2/17 (12%)	5/17 (29%)
Salivary gland infection	1/17 (6%)	0/17 (0%)
Sepsis	1/17 (6%)	0/17 (0%)
Skin infection	1/17 (6%)	2/17 (12%)
Wound infection	0/17 (0%)	2/17 (12%)
Injury, poisoning and procedural complications		
Fall	0/17 (0%)	1/17 (6%)
Investigations		
Alanine aminotransferase increased	1/17 (6%)	0/17 (0%)
Alkaline phosphatase increased	1/17 (6%)	0/17 (0%)
Aspartate aminotransferase increased	1/17 (6%)	0/17 (0%)
Carbon monoxide diffusing capacity decreased ^{***}	2/17 (12%)	0/17 (0%)
Neutrophil count decreased	1/17 (6%)	0/17 (0%)
Metabolism and nutrition disorders		
Dehydration	0/17 (0%)	2/17 (12%)
Hyperkalemia	1/17 (6%)	0/17 (0%)
Musculoskeletal and connective tissue disorders		
Generalized muscle weakness ^{***}	1/17 (6%)	0/17 (0%)
Muscle weakness lower limb ^{***}	0/17 (0%)	1/17 (6%)
Nervous system disorders		
Syncope	1/17 (6%)	0/17 (0%)
Renal and urinary disorders		
Acute kidney injury	0/17 (0%)	1/17 (6%)
Respiratory, thoracic and mediastinal disorders		
Hypoxia ^{***}	1/17 (6%)	1/17 (6%)
Skin and subcutaneous tissue disorders		

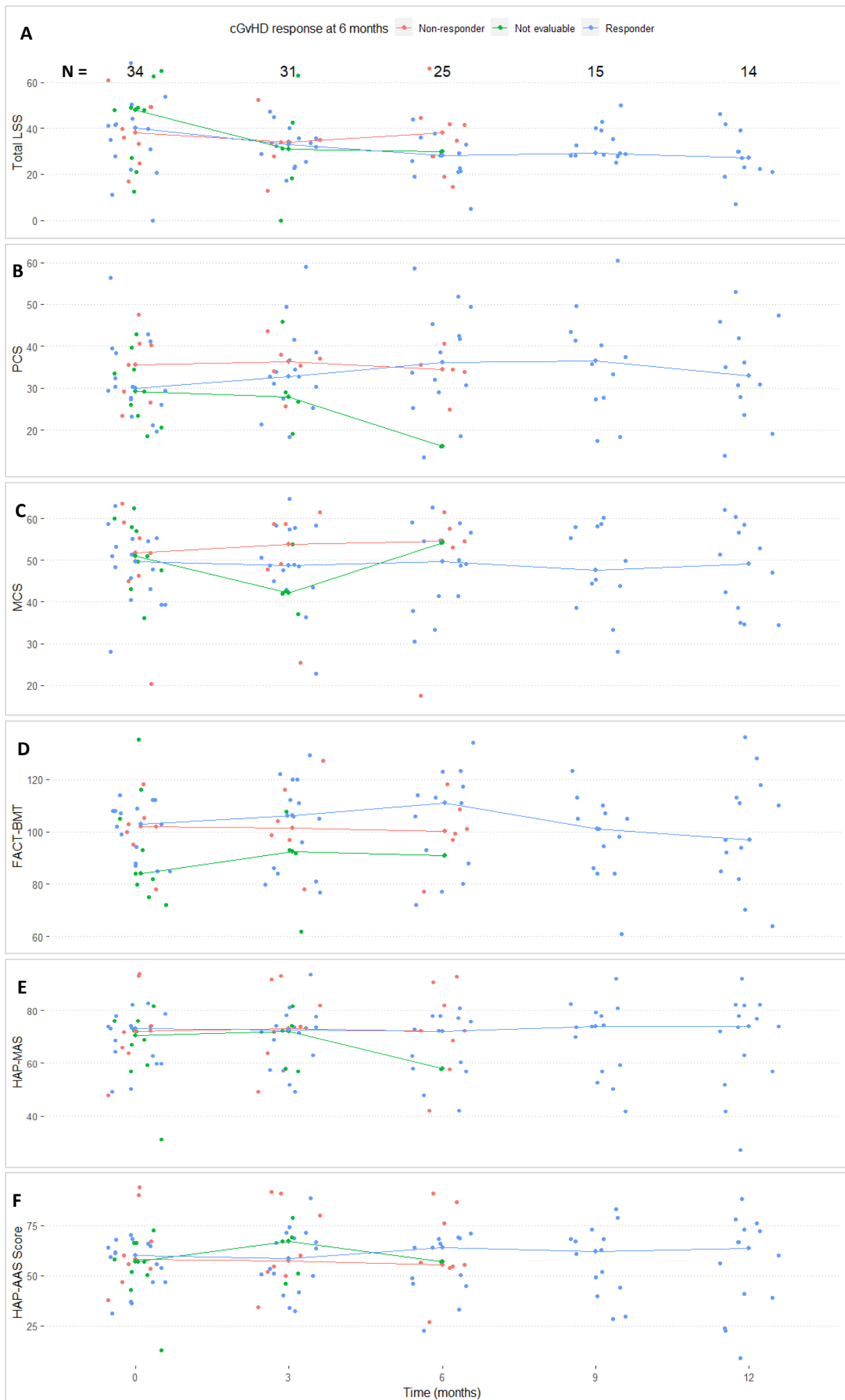
Serious Adverse Event ^{*,**}	High-dose group	Low-dose group
	Number (Percent)	Number (Percent)
Rash maculo-papular ^{***}	0/17 (0%)	1/17 (6%)
Vascular disorders		
Hypotension	1/17 (6%)	2/17 (12%)
Thromboembolic event	1/17 (6%)	0/17 (0%)
<p>* Multiple occurrences of the same serious adverse event in 1 patient were counted only once per preferred term.</p> <p>** An adverse event or suspected adverse reaction was considered serious if in the view of the investigator or the sponsor, it results in any of the following:</p> <ul style="list-style-type: none"> • Death, • A life-threatening adverse drug experience • Inpatient hospitalization or prolongation of existing hospitalization • Persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions • A congenital anomaly/birth defect. • Important medical events that may not result in death, be life-threatening, or require hospitalization may be considered a serious adverse drug experience when, based upon appropriate medical judgment, they may jeopardize the patient or subject and may require medical or surgical intervention to prevent one of the outcomes listed in this definition. <p>*** Possibly related to cGVHD.</p>		

Supplement Figure 2. Lee Symptom Score (LSS) at baseline and 6-month endpoint



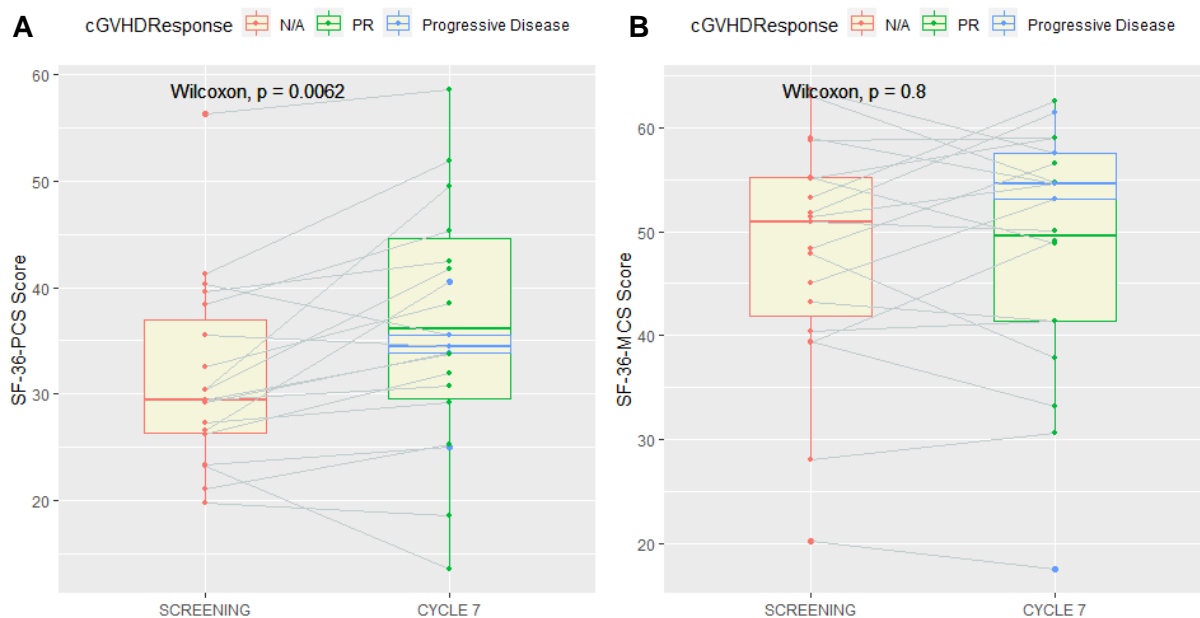
Supplement Figure 2. (A) Total Lee Symptom Scale (LSS) at baseline and 6-month endpoint represented by box-plot mean and dots stratified with color representing values at screening and non-responders at 6-months (red) and responder at 6-months (green). (B) Skin-related LSS subscale for same subjects on same time-points. (C) Muscle/Joints-related LSS subscale for same subjects on same time points. Comparison was done with Wilcoxon test Pratt modification for tied values.

Supplement Figure 3. Patient reported outcomes – trajectories during the study treatment



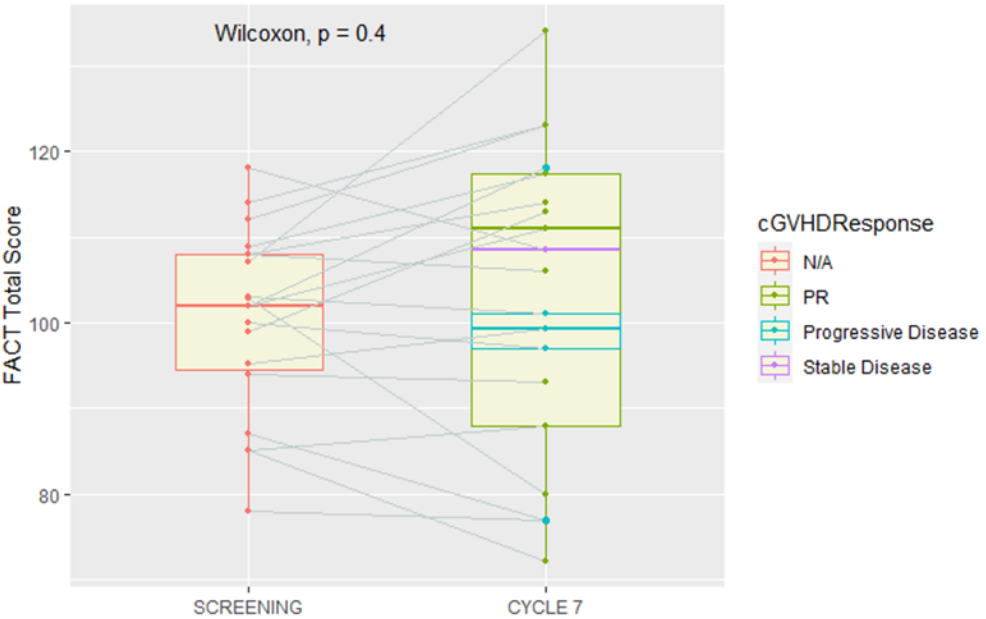
Supplement Figure 3. Combined line/dot plot represents trajectories of patient reported outcomes (PRO) stratified by chronic graft-versus-host disease (cGVHD) response at 6-month endpoint. Lines represent trajectories of PROs median values with dots representing values of every patient with available data at specified time point. Blue color represents patients who achieved partial response, red, patients who did not achieve response and green, patients who were not evaluable for cGVHD response at 6-month endpoint. Numbers at the top of figure represent numbers of patients with available data at corresponding time point. (A) Total Lee Symptom Score. (B) Short Form – 36 (SF-36) Physical Component Summary (PCS) represents subscale for physical functioning. (C) SF-36 Mental Component Summary (MCS) represents mental functioning subscale. (D) Functional Assessment of Cancer Therapy - Bone Marrow Transplant represents measurement of quality of life in bone marrow transplant patients. (E) Human Activity Profile (HAP) – Maximum Activity Score (MAS) and (F) HAP – Adjusted Activity Score (AAS) are self-report measures of energy expenditure or physical fitness.

Supplement Figure 4. Patient reported outcomes – Short Form-36



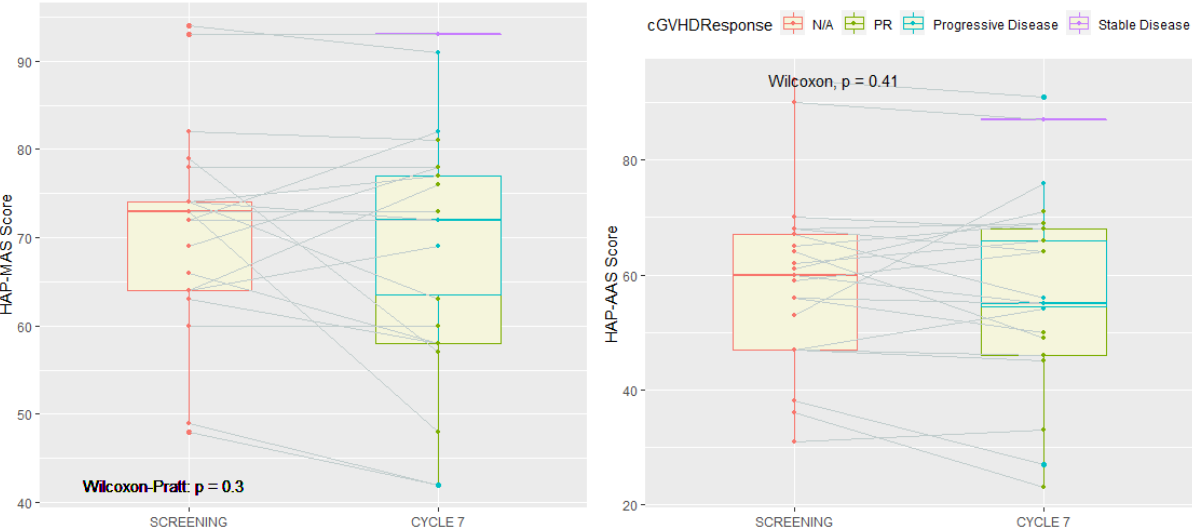
Supplement Figure 4. Health-related quality of life measured by Short Form-36 (SF-36) physical (PCS) and mental (MCS) component scores. Of 24 evaluable patients for ORR at 6-month endpoint, 19 patients (14 responders and 5 non-responders) were evaluable for SF-36 physical component score (PCS) and mental component score (MCS). (A) Median SF-36-PCS of 29.48 (19.79-56.29) at screening was increased on 6-month endpoint to a median of 34.44 (13.53-58.60, $p = 0.062$). Fourteen responders had median SF-36-PCS 29.92 (19.79-56.29) at enrollment and 36.17 (13.53-58.60) at 6-month endpoint. Five non-responders had median SF-36-PCS at corresponding time points 29.15 (23.36-40.32) and 34.44 (24.99-40.58), respectively. (B) Median change in SF-36-MCS was almost unchanged.

Supplement Figure 5. Patient reported outcomes – Functional Assessment of Cancer Therapy – Bone Marrow Transplant (FACT-BMT)



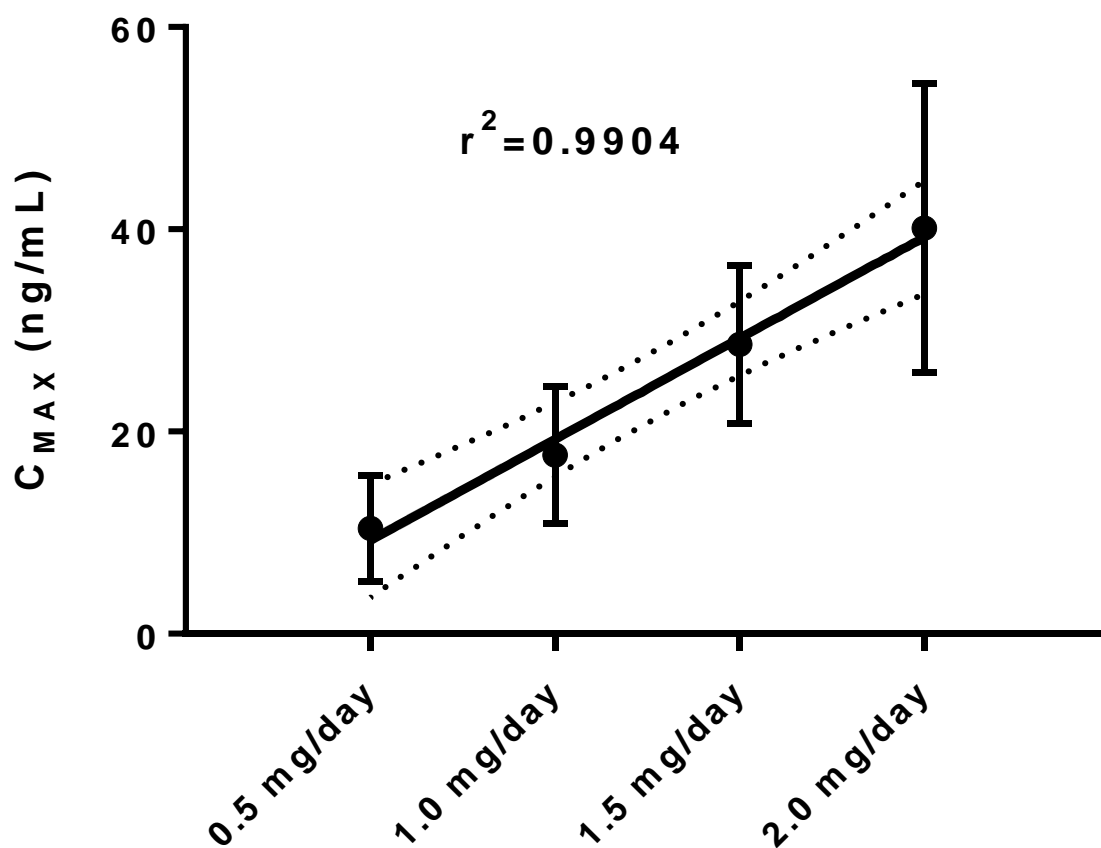
Supplement Figure 5. FACT-BMT scores were available for 13 responders and 6 non-responders at enrollment and 6-month endpoint. For all 19 patients, median total score at screening was 102 (78-118) and 106 (72-134) at 6-month endpoint. Responders had clinically meaningful increase in median total FACT-BMT score from baseline to 6-month time point (102.8 [85-114] versus 111 [72-134], respectively) compared to clinically unmeaningful change in non-responders (101 [78-118] versus 100.2 [77-118], respectively).

Supplement Figure 6. Patient reported outcomes – Human Activity Profile (HAP)



Supplement Figure 6. Twenty-one of 24 evaluable patients were evaluable by Human Activity Profile (HAP) measures. (A) Median value for HAP maximum activity (MAS) and (B) adjusted activity (AAS) scores at enrollment were 73 (48-94) and 60 (31-94), respectively. The same scores at 6-month endpoint were (A) 72 (42-93) and (B) 56 (23-91), respectively ($p > 0.3$). There were no significant changes in scores in group of responders or non-responders.

Supplement Figure 7. Pharmacokinetics of pomalidomide at different dose levels



Supplement Figure 7. Pomalidomide peak plasma concentrations in patients at different dose levels increasing in a dose-proportional manner. Depicted are linear regression model +/- 95% confidence interval.

Supplement Table 9. Pharmacokinetics

	0.5 mg	1.0 mg	1.5 mg	2.0 mg
Trough ² (ng/mL)	1.41 ± 1.76 (n=154)*	1.56 ± 2.27 (n=17)	2.11 ± 2.58 (n=18)	4.14 ± 3.19 (n=69)
Peak (ng/mL)	10.4 ± 5.28 (n=156)	17.7 ± 6.75 (n=17)	28.6 ± 7.84 (n=15)	40.1 ± 14.3 (n=66)

² Many Trough samples at each dose were D1 pre-dose samples on every cycle
Values expressed as arithmetic mean ± standard deviation with number of measurements made at that dose in parentheses