Planned withdrawal of dexamethasone after pomalidomide low-dose dexamethasone induction for lenalidomide-refractory multiple myeloma (ALLG MM14)

Anna Kalff,[1,2,3] Tiffany Khong,[1,2] Malarmathy Ramachandran,[1,2] P Joy Ho,[4] Peter Mollee,[5] James D'Rozario,[6] Kerry Taylor,[7] Jane Estell,[8] Sam Norton,[9,10] Roslyn Kemp,[10] Andrew J. Mitchell,[11] John Reynolds,[12] Nola Kennedy,[1] Hang Quach[13] and Andrew Spencer[1,2,3]

[1]Malignant Hematology and Stem Cell Transplantation, Alfred Hospital, Melbourne, Victoria, Australia; [2]Myeloma Research Group, Australian Center for Blood Diseases, Alfred Hospital Monash University, Melbourne, Victoria, Australia; [3]Department of Clinical Hematology, Monash University, Clayton, Victoria, Australia; [4]Royal Prince Alfred Hospital, Sydney, New South Wales, Australia; [5]Princess Alexandra Hospital and University of Queensland, Brisbane, Queensland, Australia; [6]The Canberra Hospital, Canberra, New South Wales, Australia; [7]Icon Cancer Center, Brisbane, Queensland, Australia; [8]Concord Repatriation General Hospital, University of Sydney, Sydney, New South Wales, Australia; [9]Nanix Ltd., Dunedin, New Zealand; [10]Department of Microbiology and Immunology, University of Otago, Dunedin, New Zealand; [11]Materials Characterization and Fabrication Platform, Department of Chemical Engineering, University of Melbourne, Melbourne, Victoria, Australia; [12]Department of Epidemiology and Preventive Medicine, Alfred Health – Monash University, Melbourne, Victoria, Australia and [13]Faculty of Medicine, University of Melbourne, St Vincent's Hospital Melbourne, Melbourne, Vitoria, Australia (on behalf of The Australasian Leukemia and Lymphoma Group [ALLG])

Correspondence: ANDREW SPENCER - Andrew.spencer@monash.edu

doi:10.3324/haematol.2021.278655

Planned withdrawal of dexamethasone after pomalidomide low dose dexamethasone induction for lenalidomide refractory multiple myeloma (ALLG MM14)

Supplementary files

- Supplementary Table 1. Mass cytometry antibodies (Clone and Tag)
- Supplementary Table 2. All grade adverse events >20% incidence (CTCAE version 4.0) plus AEs of interest (infections and haematologic) regardless of causality
- Supplementary Figure 1. Post progression therapy

Supplementary Table 1. Mass cytometry antibodies (Clone and Tag) Cells were barcoded using the Cell-ID 20-Plex Pd barcoding kit (Fluidigm) followed by staining with sub-set defining antibodies (targeting myeloid, B, T and NK cells). Samples were acquired on a Helios mass cytometer (Fluidigm) instrument.

NO	Antibody	Clone	Tag
1	Anti-Human CD8	RPA-T8	115In
2	Anti-Human CD24	ML5	161Dy
3	Anti-Human CD335 NKp46	9E2 FG	141Pr
4	Anti-Human CD194 (CCR4)	L291H4	150Nd
5	Anti-Human CD158b (KIRDL2/L3, NKAT2)	DX27	DX27 173Yb
6	Anti-Human CD197 (CCR7)	G043H7	175Lu
7	Anti-Human CD158a(KIR2DL1)	LS-C16155	156Gd
8	Anti-Human CD336	p44-8	168Er
9	Anti-Human CD159a	Z199	165HO
10	Anti-Human IgD	IA6-2	146Nd
11	Anti-Human CD19	HIB19	142Nd
12	Anti-Human CD4	RPA-T4	145Nd
13	Anti-Human CD20	2H7	171Yb
14	Anti-Human CD16	3G8	209Bi
15	Anti-Human CD127	A019D5	176Yb
16	Anti-Human CD38	HIT2	167Er
17	Anti-Human CD25	2A3	149Sm
18	Anti-Human CD3	UCHT1	154Sm
19	Anti-Human CD56	B159	155Gd
20	Anti-Human CD57	HCD57	163Dy

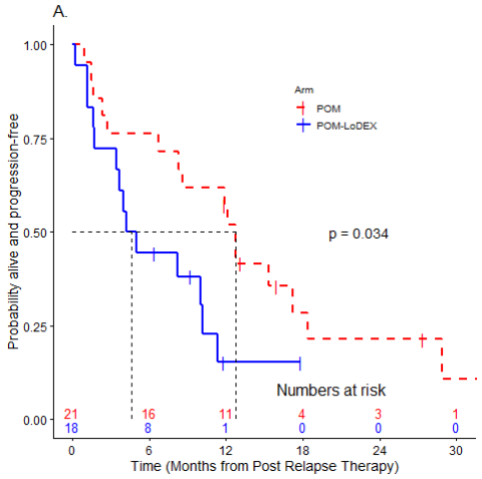
21	Anti-Human CD28	CD28.2	160Gd
22	Anti-Human CD11c	Bu15	162Dy
23	Anti-Human CD27	L128	158Gd
24	Anti-Human CD45RA	HI100	143Nd
25	Anti-Human CD304/Neuropilin-1	12C2	169Tm
26	Anti-Human CD14	M5E2	151Eu
27	Anti-Human CD274/PD-L1	29E.2A3	148Nd
28	Anti-Human CD45RO	UCHL1	164Dy
29	Anti-Hu HLA-DR	L243	170Er
30	Anti-Human CD66b	80H3	152Sm
31	Anti-Human CD314/NKG2D	ON72	166Er
32	Anti-Human CD337/NKp30	Z25	159Tb
33	Anti-Human CD279/PD-1	EH12.2H7	174Yb
34	Anti-Human CD45	HI30	89Y
35	Foxp3	PCH101	147SM
36	Anti-Human CD11b/Mac-1	ICRF44	144Nd

Supplementary Table 2. All grade adverse events >20% incidence (CTCAE version 4.0) plus AEs of interest (infections and haematologic) regardless of causality

	POM LoDEX (n = 38)		**POM (n = 40)**		**Excluded from mITT (n = 76)**	
	All grades n (%)	Grade 3+4	All grades n (%)	Grade 3+4	All grades n (%)	Grade 3+4
Adverse Event						
Fatigue	17 (44.7)	2	16 (40)	0	25 (32.9)	5
Musculoskeletal and connective tissue disorder - Other	14 (36.8)	1	7 (17.5)	0	4 (5.3)	0
Constipation	12 (31.6)	0	9 (22.5)	0	14 (18.4)	0
Dyspnoea	12 (31.6)	2	6 (15)	0	9 (11.8)	2
Peripheral sensory neuropathy	12 (31.6)	1	5 (12.5)	0	8 (10.5)	0
Diarrhea	11 (28.9)	2	6 (15)	0	9 (11.8)	1
Nausea	10 (26.3)	0	6 (15)	0	15 (19.7)	0
Pain	10 (26.3)	0	6 (15)	1	7 (9.2)	4
Back pain	9 (23.7)	1	4 (10)	1	5 (6.6)	2
Oedema (peripheral)	8 (21.1)	0	5 (12.5)	0	7 (9.2)	0
Infections						
Lung infection	21 (55.2)	9	9 (22.5)	4	13 (17.1)	8
Upper respiratory infection	18 (47.4)	4	12 (30)	0	7 (9.2)	0
Infections, Other	8 (21.1)	4	7 (17.5)	2	5 (6.6)	2
Skin infection	5 (13.2)	0	2 (5)	0	3 (3.9)	1
Urinary tract infection	3 (7.9)	1	4 (10)	4	3 (3.9)	0
Soft tissue infection	2 (5.3)	1	1 (2.5)	0		
Haematologic Toxicity						
Anaemia	14 (36.8)	4	9 (22.5)	3	32 (42.1)	17
Neutrophil count decreased	11 (28.9)	11	16 (40)	15	19 (25.0)	16
Febrile neutropenia	2 (5.3)	2	1 (2.5)	1	11 (14.5)	11
Thrombocytopenia	4 (10.5)	4	5 (12.5)	3	11 (14.5)	11

Supplementary Figure 1. Post progression therapy (Kaplan-Meier survivor functions): Of the mITT population (n=78), 39 patients had post progression therapy data available (POM n=21, POM-LoDEX n=18). Of the remainder, 18 were palliated and 21 did not have available data. (Noting that this is not a randomized comparison and should be interpreted in conjuction with results in Figure 1). (a) Median second PFS (defined from commencement of post progression therapy) significantly favoured patients previously treated in the POM arm: median 12.7m (IQR 6.7–17.2m) versus POM-LoDEX arm: median 4.6m (IQR 1.74–0.2m) (P=0.034) (Figure 2a). (b) Patients randomised to the POM arm also tended to have superior OS: median OS (from commencement of post progression therapy) for POM 19.4m (IQR 12.1m–NA) versus 12.5m (IQR 6.3–17.4m) for POM-LoDEX (P=0.092). There was no difference in response to salvage therapy between the two arms, and no difference in PFS/OS between individual treatment groups (bortezomib, carfilzomib, chemotherapy, thalidomide, LEN or other).

(a) Second PFS



(b) OS