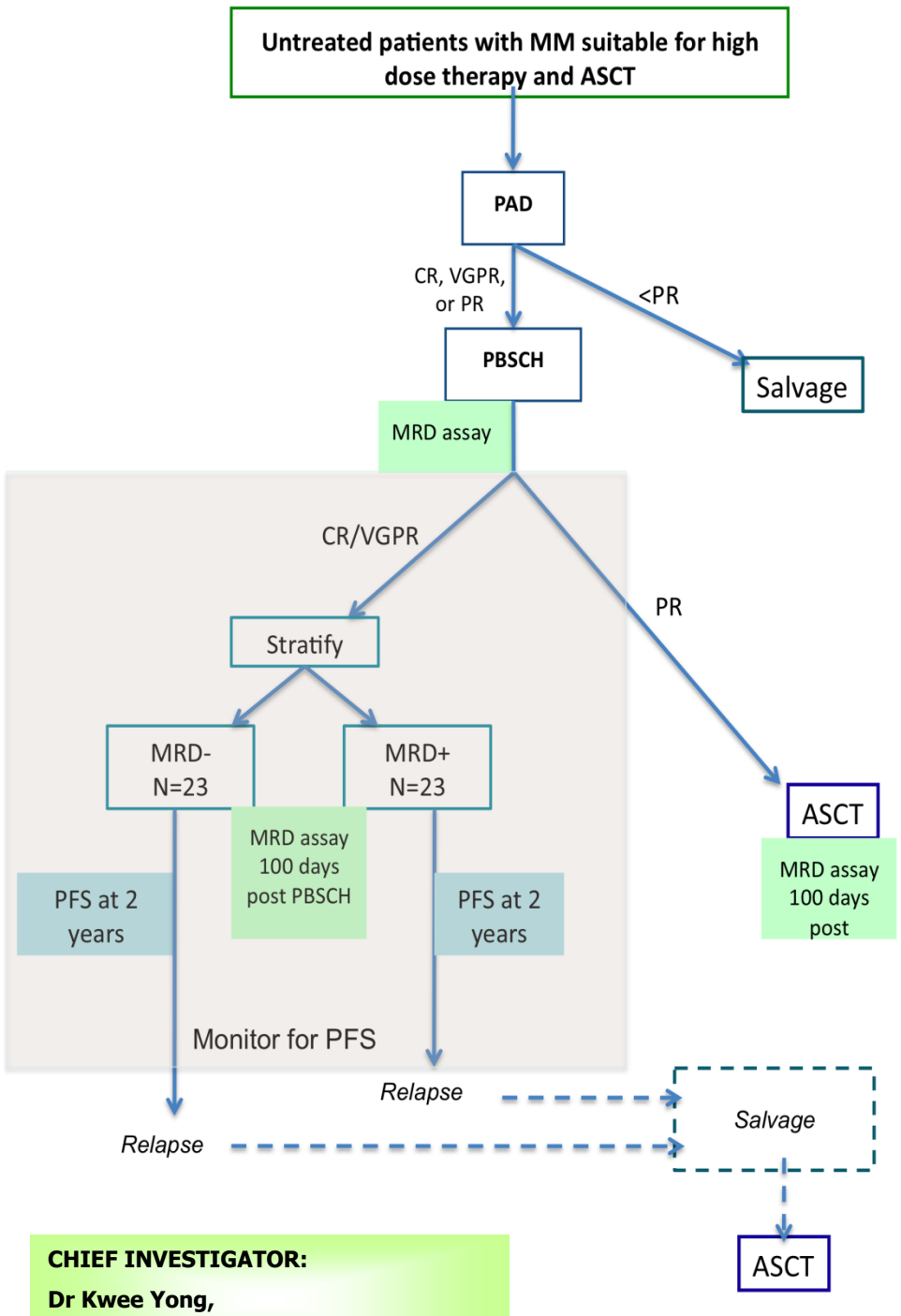
Padimac

Phase II study of Bortezomib, Adriamycin and Dexamethasone (**PAD**) therapy for previously untreated patients with multiple myeloma: **I**mpact of minimal residual disease (**M**RD) in patients with deferred **ASC**T

TRIAL SCHEMA



TRIAL OBJECTIVES

Primary objective:

2-year PFS for patients in CR/VGPR following PAD therapy who receive no further treatment (i.e. no ASCT)

Secondary objectives:

- Overall response rate to PAD therapy
- Proportion of patients who are MRD negative following PAD therapy
- Proportion of patients proceeding to ASCT who have become MRD negative at 100 days post-ASCT
- PFS following ASCT
- PFS from start of PAD to 2nd relapse or death
- 2nd PFS from start of salvage
- OS for all patients

INCLUSION CRITERIA

- Previously untreated patients with symptomatic myeloma
- Patients suitable for high dose therapy and ASCT
- ≥ 18 years of age
- Performance score (PS) of 0-3 (ECOG)
- Measurable disease
- Adequate full blood count, renal, pulmonary, cardiac and hepatobiliary function
- If female of CBP, must have a negative pregnancy test
- Able to give informed consent

EXCLUSION CRITERIA

- Grade 2 peripheral neuropathy or neuropathic pain
- Pregnant or breast-feeding
- Unwilling to use adequate contraception during the study and for 6 months after the end of the study
- Known history of allergy contributable to compounds containing boron or mannitol
- Any medical or psychiatric condition which contraindicates the patient's participation in this study

CHIEF INVESTIGATOR:
Dr Kwee Yong,
University College Hospital

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PAD treatment schedule:

SAMPLE SIZE: 153 patients over 3 years

Day: (1 cycle=21days)	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
Bortezomib* (P) subcutaneous or IV** injection, 1.3mg/m^2	1			4				8			11										
Doxorubicin (A), continuous IV infusion or by IV bolus injection, 9mg/m^2	1	2	3	4																	
Dexamethasone (D), PO, 40mg/day	1	2	3	4				8	9	10	11				15	16	17	18			
								First cycle only							First cycle only						

**Bortezomib will be supplied for the trial by Janssen-Cilag free of charge*

*** IV injection is only allowed for patients who experience grade 2 or worse local reactions to SC injection*

TRIAL VISITS

Screening visit	On Day 1, 4, 8 and 11 of each cycle	At end of PAD therapy	Post PBSCH	ASCT visit (if applicable)	POST ASCT or PBSCH		
					Day 100	6, 12,18 & 24 months	Follow Up after 24 months (6 monthly)

TRIAL SITES

- University College London Hospital
- St Bartholomew's Hospital
- Guy's Hospital & St Thomas's Hospital
- St George's Hospital
- St James's University Hospital, Leeds
- King's College Hospital
- Birmingham Heartlands Hospital & Good Hope Hospital
- Hammersmith Hospital
- Addenbrooke's Hospital
- Barnet Hospital
- Belfast Hospital
- Mount Vernon CC
- Queen Elizabeth Hospital, Birmingham
- Royal United, Bath

BIOLOGICAL SAMPLES

Nf-kappaB pathway assay:

Bone marrow aspirate to be sent to UCL, Cancer Institute for central analysis prior to starting PAD therapy and at relapse, prior to start of salvage therapy.

MRD assay:

Bone marrow aspirate to be sent to HMDS, Leeds at two timepoints:

- Post PBSCH
- At 100 days post ASCT/PBSCH

Chief Investigator: Dr Kwee Yong, University College London Hospital, email: kwee.yong@ucl.ac.uk

Trial Coordinator: Toyin Adedayo, Tel 0207 679 9867, email: ctc.padimac@ucl.ac.uk
Haematology & Brain Trials Group, CR UK & UCL Cancer Trials Centre,
90 Tottenham Court Road, London
W1T 4TJ
Tel: 0207 679 9860, Fax: 0207 679 9861