Cardamon

Carfilzomib/Cyclophosphamide/Dexamethasone with maintenance carfilzomib in untreated transplant-eligible patients with symptomatic MM to evaluate the benefit of upfront ASCT

Full Registration form

Patient Initials	☐☐☐
Site	
Date sent	D D M M Y Y Y Y
Trial Number (if known)	C A R – ☐☐☐
Sent by	
Phone number	
Research contact email address	
Pharmacy contact email address	

(This form has 12 pages including cover sheet)

Please fax form to:

Cardamon Trial Coordinator
0207 679 9861

Or email form to:
CTC.Cardamon@ucl.ac.uk*
**if sending by email please ensure DOB and NHS number are redacted*

General enquires: **020 7679 9860**
Randomisations: **020 7679 9860** between 9.00am and 5.00pm
Fax: **020 7679 9861**
E-mail: **ctc.cardamon@ucl.ac.uk**

CANCER RESEARCH UK

Cancer Research UK and UCL Cancer Trials Centre

UCL

Cardamon | **Patient Initials** [ ][ ][ ] | **Patient Date of Birth** D D M M Y Y Y Y

Full Registration form

Eligibility Checklist

Answers to the following questions must be Yes (or N/A for Q11, if appropriate)

	Inclusion Criteria	Yes	No	N/A
1	Age ≥ 18 years			
2	Life expectancy ≥ 3 months			
3	Eastern Cooperative Oncology Group (ECOG) performance status 0–2			
4	Previously untreated patient with symptomatic MM, with the exception of the following treatments: • local radiotherapy to relieve bone pain and/or spinal cord compression • bisphosphonates • corticosteroids within the last 3 months. Within 14 days prior to study entry the maximum permitted dose is 160mg (i.e. 4 days at 40mg, or equivalent) unless otherwise agreed by the TMG)			
5	Measurable disease as defined by one of the following: • Secretory myeloma: Monoclonal protein in the serum (≥10g/L) or monoclonal light chain in the urine (Bence Jones protein ≥200mg/24hours), or serum free light chain (SFLC, involved light chain ≥100mg/L provided the FLC ratio is abnormal) • Non-secretory myeloma: ◊ Either ≥30% clonal plasma cells in bone marrow (aspirate or trephine) ◊ Or 10-30% clonal plasma cells in the marrow and >1 soft tissue or extra-osseous plasmacytoma ≥ 2 cm that is measurable for response assessment by CT or MRI			
6	Suitable for high dose therapy and ASCT			
7	Adequate hepatic function, with serum ALT ≤ 3.5 times the upper limit of normal and serum direct bilirubin ≤ 2 mg/dL (34 µmol/L) within 14 days prior to registration			
8	Adequate blood counts within 14 days prior to registration with: • Absolute Neutrophil Count (ANC) ≥ 1.0 × 10^9/L and patient has not received any growth factor support within 7 days of testing or ≥ 0.8 x 10^9/L for patients with racial neutropenia • Haemoglobin ≥ 8 g/dL (80 g/L) • Platelet count ≥ 75 × 10^9/L (≥ 50 × 10^9/L if myeloma involvement in the bone marrow is > 50%) and patient has not received any platelet transfusions within 7 days prior to testing			
9	Creatinine clearance (CrCl) ≥ 30 mL/minute within 14 days prior to registration, either measured or calculated using a standard formula (e.g. Cockcroft and Gault)			
10	Written informed consent			
11	If female of childbearing potential (FCBP): has agreed to ongoing pregnancy testing and to practice contraception (if female is not of childbearing potential, tick N/A) If male, patient has agreed to practice contraception			

Cardamon | **Patient Initials** [ ][ ][ ] | **Patient Date of Birth** [D][D][M][M][Y][Y][Y][Y]

Full Registration form

Eligibility Checklist

Answers to the following questions must be No

	Exclusion Criteria	Yes	No
1	Pregnant or breast-feeding female (lactating women may participate if breastfeeding ceases for the duration of trial treatment and until 12 months after last treatment)		
2	Previous systemic chemotherapy for myeloma, with the exception of steroids, as defined in the inclusion criteria		
3	Any major surgery within 21 days prior to registration which in the investigator's opinion would compromise trial treatment and/or the patient's ability to comply with trial visits. Surgery to relieve spinal cord compression or for treatment of bone fractures is permitted		
4	Acute active infection requiring treatment (systemic antibiotics, antivirals, or antifungals) 7 days prior to planned start of treatment, unless otherwise agreed by the TMG		
5	Known HIV infection or active Hepatitis B or C infection		
6	Unstable angina or myocardial infarction within 4 months prior to registration, NYHA Class III or IV heart failure, uncontrolled angina, history of severe coronary artery disease, severe uncontrolled ventricular arrhythmias, sick sinus syndrome, or electrocardiographic evidence of acute ischemia or Grade 3 conduction system abnormalities unless patient has a pacemaker		
7	Uncontrolled hypertension or uncontrolled diabetes within 14 days prior to registration		
8	Non-haematologic malignancy within the past 3 years with the exception of: a) adequately treated basal cell carcinoma, squamous cell skin cancer, or thyroid cancer b) carcinoma in situ of the cervix or breast c) prostate cancer of Gleason Grade 6 or less with stable prostate-specific antigen levels d) cancer considered cured by surgical resection or unlikely to impact survival during the duration of the study, such as localized transitional cell carcinoma of the bladder or benign tumours of the adrenal or pancreas		
9	Significant neuropathy (Grades 3–4, or Grade 2 with pain) within 14 days prior to registration		
10	Known history of allergy to Captisol® (a cyclodextrin derivative used to solubilize carfilzomib)		
11	Contraindication to any of the required concomitant drugs or supportive treatments, including hypersensitivity to all anticoagulation and antiplatelet options, antiviral drugs, or intolerance to hydration due to pre-existing pulmonary, renal or cardiac impairment		
12	Patient with pleural effusion(s) requiring thoracentesis or ascites requiring paracentesis within 14 days prior to registration		
13	Any other clinically significant medical disease or condition that, in the Investigator's opinion, may interfere with protocol adherence or a subject's ability to give informed consent		

Pregnancy test (for females of child bearing potential only)

Result [ ]
1 = Negative
2 = Positive
3 = Not applicable

Date of pregnancy test [D][D][M][M][Y][Y][Y][Y] *To be performed within 14 days prior to registration*

If N/A please specify reason [ ]
1 = Male
2 = Total abdominal hysterectomy and/or bilateral oophorectomy/salpingectomy
3 = Post menopausal for 24 consecutive months
4 = Other: [ ]

Full Registration form

Registration

Has the patient been allocated a trial number? ☐ **Yes**—please enter trial number and skip to pre-treatment assessments on page 4 **C A R** – ☐☐☐

☐ **No**—please complete section below:

Informed Consent

Main trial consent form signed? **1= Yes 2= No** ☐ ***Optional* consent for future research** signed? **1= Yes 2= No** ☐

Version number of consent form signed ☐.☐ Date consent form signed D D M M Y Y Y Y

Version number of patient information sheet ☐.☐ Has patient initialled all boxes? **1= Yes 2= No** ☐

Has patient signed and personally dated? **1= Yes 2= No** ☐ Has person taking consent signed and dated (on same day as patient)? **1= Yes 2= No** ☐

Name of person taking consent: ☐

***Optional* PET-CT sub-study** consent form signed? ☐ **1= Yes** —*please complete details below:*
2= No or not applicable —*please skip to* ***Patient Information*** *section below*

Version number of consent form signed ☐.☐ Date consent form signed D D M M Y Y Y Y

Version number of patient information sheet ☐.☐ Has patient initialled all boxes? **1= Yes 2= No** ☐

Has patient signed and personally dated? **1= Yes 2= No** ☐ Has person taking consent signed and dated (on same day as patient)? **1= Yes 2= No** ☐

Name of person taking consent: ☐

Patient Information

Consultant name ☐

Sex Male ☐ Female ☐

NHS Number ☐☐☐☐☐☐☐☐☐☐

Anticipated start of treatment D D M M Y Y Y Y

Full Registration form

Pre-treatment assessments

Date of Assessment D D M M Y Y Y Y

Height (cm) . Blood Pressure (mmHg) [1] /

Weight (kg) . Pulse rate (bpm)

Temperature (^{0}C) . Respiratory Rate (breaths per minute)

ECOG Performance Status *Must be ≤2 unless due complications related to myeloma*

[1]If patient has controlled hypertension/single episode of raised BP (delete as applicable), the investigator may confirm eligibility below:

Date ECOG performed D D M M Y Y Y Y

Investigator name (print):

Investigator signature:

Date signed: D D M M Y Y Y Y

Quality of Life Questionnaire

Has the Quality of Life (QoL) been completed?

1= Yes; *please send to the CTC as soon as possible*
2= No; *to be completed and sent prior to day 1 of cycle 1*
3= Not done; please provide reason in box below:

Haematology

Date of sample D D M M Y Y Y Y *To be performed within 14 days prior to registration*

Test Result

Haemoglobin g/dL . *≥8 g/dL (80 g/L)*

Platelets x 10^9/L *≥75 x10^9/L (≥50 x10^9/L if myeloma in marrow is >50%*

Neutrophils x10^9/L [2] . *≥1.0 x 10^9/L (≥0.8 x10^9 if due to racial neutropenia)*

White Blood Cell (WBC) Count x10^9/L .

[2]If patient has racial neutropenia, the investigator may confirm eligibility below:

Investigator name (print):

Investigator signature:

Date signed: D D M M Y Y Y Y

Full Registration form

Biochemistry

Date of sample	D D M M Y Y Y Y	*To be performed within 14 days prior to registration**
Calcium (corrected) mmol/L	☐☐•☐☐	
Potassium mmol/L	☐☐•☐☐	
Sodium mmol/L	☐☐☐	
Creatinine µmol/L	☐☐☐•☐	
Creatinine Clearance ml/min	☐☐☐☐	*≥30 mL/minute*
Serum urate µmol/L	☐☐☐•☐	
Urea (mmol/L)	☐☐•☐☐	
Bilirubin µmol/L	☐☐☐	*Bilirubin must be ≤2 mg/dL (34 µmol/L)*
Albumin g/L	☐☐☐	
Alkaline Phosphatase IU/L	☐☐☐☐	
Alanine Transaminase (ALT) IU/L	☐☐☐	*ALT must be ≤3.5 x ULN* ALT upper limit of normal (IU/L) ☐☐☐
Aspartate Transaminase (AST) IU/L	☐☐☐	
Phosphate mmol/L	☐☐☐•☐	
Total Protein g/L	☐☐☐	
Lactate dehydrogenase (LDH) IU/L	☐☐☐☐	**Within 6 weeks prior to registration*
B2 microglobulin mg/L	☐☐•☐☐	**Within 6 weeks prior to registration*

Cardamon Patient Initials [ ][ ][ ] Patient Date of Birth [D][D][M][M][Y][Y][Y][Y]

Full Registration form

Bone marrow biopsies

Bone marrow aspirate Date of sample: [D][D][M][M][Y][Y][Y][Y]

[ ] 1= Present, complete % of plasma cells: [ ][ ][ ] %
2= Present, not measured
3= Absent
4= Not done

Bone marrow trephine Date of sample: [D][D][M][M][Y][Y][Y][Y]

[ ] 1= Present, complete % of plasma cells: [ ][ ][ ] %
2= Present, not measured
3= Absent
4= Not done

3 bone marrow samples must be taken and sent to the central labs prior to starting trial treatment (see details below)
1 peripheral blood sample must also be taken and sent to the central lab (see details below)
N.B. Sites unable to perform cytogenetics/FISH must send an additional 4-8ml of BM aspirate to the UCL Cancer Institute Myeloma Lab

	Sent? 1=Yes 2= No	Date sample sent to lab
BM aspirate for MRD (2ml) to HMDS, Leeds	[ ]	[D][D][M][M][Y][Y][Y][Y]
BM aspirate for genomic analyses (8ml) to the UCL Cancer Institute Myeloma Lab	[ ]	[D][D][M][M][Y][Y][Y][Y]
Peripheral blood sample for genomic analyses (8ml) to the UCL Cancer Institute Myeloma Lab	[ ]	[D][D][M][M][Y][Y][Y][Y]
BM trephine block (or slides) for immunohistochemistry to UCL Department of Research Pathology	[ ]	[D][D][M][M][Y][Y][Y][Y]

If No to any of the above, specify a reason: [ ]

Molecular tests

Baseline molecular tests are being reviewed centrally on the Cardamon trial, please attach a copy of the anonymised report sheet to the registration form when it is faxed.

N.B: Sites unable to perform cytogenetics/FISH must send an additional 4-8ml of BM aspirate to the UCL Myeloma Lab

	Attached? 1=Yes 2= No	Date of test
Cytogenetic analysis	[ ]	[D][D][M][M][Y][Y][Y][Y]
FISH	[ ]	[D][D][M][M][Y][Y][Y][Y]

OR [ ] Tick if sample sent to Myeloma lab

Cardamon Patient Initials [ ][ ][ ] Patient Date of Birth [D][D][M][M][Y][Y][Y][Y]

Full Registration form

Soft tissue plasmacytoma/Extramedullary lesions

Does the patient have any soft tissue plasmacytomas/ Extramedullary lesions? [ ] 1= Yes, complete date of test and a separate line for each site involved 2= No

If yes, date of test [D][D][M][M][Y][Y][Y][Y]

		Long axis		Short axis
Site involved:		Bidimensional measurements (cm):	X	
Site involved:		Bidimensional measurements (cm):	X	
Site involved:		Bidimensional measurements (cm):	X	

PET-CT sub-study: Baseline scan details

(please complete for patients participating in the PET-CT sub-study only)

Date of baseline PET-CT scan: [D][D][M][M][Y][Y][Y][Y]

Date images transferred to PET core lab: [D][D][M][M][Y][Y][Y][Y]

Myeloma diagnosis

Date of diagnosis: [D][D][M][M][Y][Y][Y][Y]

Stage of disease (ISS stage): [ ] 1= I 2= II 3= III

Type of myeloma: [ ] 1= Secretory 2= Non-secretory

Paraprotein expression: *(choose <u>one</u> option only)* [ ] 1= Single paraprotein expressed 2= Light chain only 3 = Biclonal 4 = N/A, non-secretory patient

Date of test [D][D][M][M][Y][Y][Y][Y]

Paraprotein type key: 1 = IgG, 2 = IgA, 3 = IgM, 4 = IgD

Specify paraprotein type: [ ]

Serum paraprotein: [ ] 4= Present, please complete result 5= Too faint to quantify 6= Absent 7= Not Done [ ][ ][ ] (g/L)

Specify 2nd paraprotein : (*If biclonal)* [ ]

Serum paraprotein: [ ] 4= Present, please complete result 5= Too faint to quantify 6= Absent 7= Not Done [ ][ ][ ] (g/L)

Serum free light chain: Kappa (mg/L) [ ][ ][ ] • [ ][ ]

Serum free light chain: Lambda (mg/L) [ ][ ][ ] • [ ][ ]

Serum free light chain Kappa/Lambda ratio: [ ][ ][ ] • [ ][ ]

Normal range of Kappa/Lambda FLC ratio: [ ] – [ ]

Full Registration form

Urinary light chain measurement

☐ 1= Present, quantifiable
Please complete 24h BJP result (in g/24h): ☐☐☐.☐
2= Too faint to quantify (24h BJP only)
3= Absent
5= Present, not formally quantified
(if unable to perform 24h BJP)

Light chain type *(please choose one only):* ☐ 1= Kappa 2= Lambda 3 = N/A

Immunofixation

Immunofixation Serum ☐ 1= Positive 2= Negative — Date of test D D M M Y Y Y Y

Immunofixation Urine ☐ 1= Positive 2= Negative — Date of test D D M M Y Y Y Y

Imaging *(as per local policy)*

NB: If patient is participating in PET-CT sub study please also complete section on page 8

		Date of test	Lytic or focal lesions? 1= Yes 2= No
MRI	☐ 1= Evidence of myeloma 2= No evidence of myeloma 3= Not done	D D M M Y Y Y Y	☐
CT	☐ 1= Evidence of myeloma 2= No evidence of myeloma 3= Not done	D D M M Y Y Y Y	☐
PET	☐ 1= Evidence of myeloma 2= No evidence of myeloma 3= Not done	D D M M Y Y Y Y	☐
Skeletal survey[1]	☐ 1= Evidence of myeloma 2= No evidence of myeloma 3= Not done	D D M M Y Y Y Y	☐

[1]Osteoporosis reported? ☐ 1= Yes 2= No

Other imaging ☐ 1= Evidence of myeloma 2= No evidence of myeloma 3= Not done — D D M M Y Y Y Y — ☐

Specify type of other imaging ☐

Creatinine Clearance (EDTA) ml/min ☐☐☐☐ **OR** tick if not done ☐

Cardamon | **Patient Initials** [ ][ ][ ] | **Patient Date of Birth** D D M M Y Y Y Y

Full Registration form

Serology

Date of Serology: D D M M Y Y Y Y *To be performed within 3 months prior to registration*

Result Codes (please enter below): 1 = Positive 2 = Negative

Test	Result	Test	Result
HCV		Hepatitis B surface antibody	
HIV		Hepatitis B core antibody [1]	
Hepatitis B surface antigen		HBV DNA (if indicated, otherwise enter ND)	

Note: Active hepatitis B / C infection and / or known HIV infection are exclusion criteria.

[1] If patient has previous Hep B infection, the investigator may confirm eligibility below *(see Appendix 4 of protocol for full details):*

Investigator name (print):

Investigator signature:

Date signed: D D M M Y Y Y Y

Cardiac function

Type of scan performed:

[ ] 1= Echocardiogram
2= MUGA scan

ECHO / MUGA [ ] 1= Normal 2= Abnormal, specify: Date of test : D D M M Y Y Y Y

To be performed within 6 weeks prior to registration

ECG [ ] 1= Normal 2= Abnormal, specify: Date of test : D D M M Y Y Y Y

To be performed within 14 days prior registration

Cardamon | **Patient Initials** [ ][ ][ ] | **Patient Date of Birth** [D][D][M][M][Y][Y][Y][Y]

Full Registration form

Medical History

Enter details of all significant conditions past or present, e.g. hypertension, allergies, malignancies, details of any recent surgery, etc.
Where a condition is continuing and symptomatic (e.g. uncontrolled hypertension), please insert the CTCAE grade
If condition is ongoing enter C (Continuing) as End Date.

Does the patient have a significant medical history or baseline symptoms? [ ] 1= Yes 2= No

No	**Condition or Procedure** please record all significant conditions or procedures. Use the **CTCAE adverse event name** where applicable	**Status** Resolved/ Asymptomatic = 0 Continuing = 1	**Onset Date** (DD/MM/YYYY)	**End Date** (DD/MM/YYYY)	**Specify grade of Adverse Event**	**Treatment Ongoing** 1=Yes 2=No
1			/ /	/ /		
2			/ /	/ /		
3			/ /	/ /		
4			/ /	/ /		
5			/ /	/ /		
6			/ /	/ /		
7			/ /	/ /		
8			/ /	/ /		
9			/ /	/ /		
10			/ /	/ /		
11			/ /	/ /		
12			/ /	/ /		

NOTE: please refer to the exclusion criteria for a full list of excluded conditions / procedures

Full Registration form

Concomitant Treatment of Interest

Has the patient received any local radiotherapy treatment? [ ] 1= Yes—please specify below 2= No

Treatment Site	Treatment Start Date (DD/MM/YYYY)	Treatment End Date (DD/MM/YYYY)	Total Dose (Gy)	Number of Fractions
	/ /	/ /		
	/ /	/ /		
	/ /	/ /		

Has the patient received any bisphosphonate treatment? [ ] 1= Yes—please specify below 2= No

	Generic Drug Name	Start Date (DD/MM/YYYY)	End Date (DD/MM/YYYY)	Treatment Ongoing (1 = Yes; 2 = No)
1		/ /	/ /	
2		/ /	/ /	

Has the patient received any corticosteroid treatment? [ ] 1= Yes—please specify below 2= No

	Generic Drug Name	Start Date (DD/MM/YYYY)	End Date (DD/MM/YYYY)	Dose	Unit	Total days given	Treatment Ongoing (1 = Yes; 2 = No)
1		/ /	/ /				
2		/ /	/ /				

Name of person completing form: | Signature of person completing form: | Date completed: [D][D][M][M][Y][Y][Y][Y]

The site PI or delegated investigator must sign to confirm that information within the CRF is accurate

Investigator name: | Investigator signature: | Date completed: [D][D][M][M][Y][Y][Y][Y]

To be completed by the UCL CTC

Trial Number **C A R** – [ ][ ][ ] [ ] New patient [ ] Pre-registered

Date of Registration [D][D][M][M][Y][Y][Y][Y] Registered by: