Cardamon

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

CASE REPORT FORMS

Patient Initials ☐☐☐

Site ☐

Trial Number C A R – ☐☐☐

Please send forms to:

Cardamon Trial Coordinator
CR UK & UCL Cancer Trials Centre
90 Tottenham Court Road
London W1T 4TJ

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 and UCL Cancer Trials Centre

General instructions for completing Case Report Forms (CRFs)

Schedule of Forms

The schedule of forms below is designed to help you track patient visits. (This form does not need to be sent to the CTC).

- When a patient is registered fill in the Anticipated Date of visits according to the protocol
- When a CRF has been completed fill in the Completed Date
- When a CRF has been checked and sent fill in the Date Sent to UCL CTC date

CRF Name	Schedule	Anticipated Date *(DD/MM/YYYY)*	Completed Date *(DD/MM/YYYY)*	Date Sent to UCL CTC *(DD/MM/YYYY)*
Preliminary Registration Form		/ /	/ /	/ /
Full Registration Form + QoL		/ /	/ /	/ /
Demographics Form		/ /	/ /	/ /
Induction Form Cycle 1		/ /	/ /	/ /
Induction Form Cycle 2		/ /	/ /	/ /
Induction Form Cycle 3		/ /	/ /	/ /
Induction Form Cycle 4		/ /	/ /	/ /
End of Induction Form		/ /	/ /	/ /
PBSCH, Post-PBSCH and Randomisation Forms + QoL		/ /	/ /	/ /
Consolidation Form Cycle 1		/ /	/ /	/ /
Consolidation Form Cycle 2		/ /	/ /	/ /
Consolidation Form Cycle 3		/ /	/ /	/ /
Consolidation Form Cycle 4		/ /	/ /	/ /
Post-Consolidation Form + QoL		/ /	/ /	/ /
Transplant Form		/ /	/ /	/ /
Day 100 Post-ASCT Form + QoL		/ /	/ /	/ /
Treatment Summary Form		/ /	/ /	/ /
Maintenance Form *(repeating up to 18 cycles)*		/ /	/ /	/ /
6 Month Post-start of Maintenance Form + QoL		/ /	/ /	/ /
End of Maintenance Form		/ /	/ /	/ /
Maintenance Summary Form		/ /	/ /	/ /
Follow-up/Long Term Follow up Form		/ /	/ /	/ /
Withdrawal/Lost to Follow Up Form	As required	N/A	/ /	/ /
Serious Adverse Event (SAE) Report	As required	N/A	/ /	/ /
Urgent Event (TMA) Form	As required	N/A	/ /	/ /
Pregnancy Report	As required	N/A	/ /	/ /
Lactational Exposure Report	As required	N/A	/ /	/ /
1st Progression/Relapse Form	As required	N/A	/ /	/ /
2nd Progression/Relapse Form	As required	N/A	/ /	/ /
Death Form	As required	N/A	/ /	/ /

General instructions for completing Case Report Forms (CRFs)

Registration Procedure

- To register a patient
  - All inclusion/exclusion criteria must be met
  - All required tests/scans must be completed as per the protocol
  - The registration form should be completed
- Once the above are completed you should fax the completed form to the CTC on **020 7679 9861**
- A member of the CTC trials team will check the eligibility criteria and register the patient if all criteria are met
- Upon successful registration a trial number will be allocated to the patient and the Case Report Forms will be sent by email

Completing Forms

- Ensure all entries are clear, legible and written in black ink
- Avoid the use of abbreviations and acronyms
- The CRF should be completed as soon as possible after the scheduled visit
- The Principal Investigator (PI) is responsible for the accuracy of the data reported on the CRF
- Please ensure that all adverse events are recorded on the adverse event form and the form is attached
- CRFs may only be completed by an appropriately qualified individual delegated as responsible by the PI on the site delegation log
- CRF Footer section
  - The "completed by" Name should be clearly legible
  - Each CRF should be signed and dated by the person completing the form
  - Do not complete the *UCL CTC Use only* section
- **The CRF should be sent/faxed to the UCL Cancer Trials Centre (CTC) with a copy retained at the Site** (ensure when photocopying the page that the copy is added to the CRF booklet in the same place where the original was stored)
- Serious Adverse Events (SAEs) must be faxed within 24 hours of the site being aware of the event to **020 7679 9861**
- If you have any queries or require clarification about completing a CRF please contact a member of the CARDAMON Trial Team on **020 7679 9860**
- Completed CRFs should be sent to the CTC within **30** days of the scheduled visit at the address below:

Cardamon Trial
CR UK & UCL Cancer Trials Centre
90 Tottenham Court Road
London W1T 4TJ

Corrections to entries

- If an error is made draw a single line through the item, then write the correct entry on an appropriate blank space near the original data point on the CRF and initial and date the change

- **Do NOT**
  - Obscure the original entry by scribbling it out
  - Try to correct/modify the original entry
  - Use Tippex or other correction fluid

General instructions for completing Case Report Forms (CRFs)

Review of CRF

Before sending the CRF to the CTC please review it by:

- Checking the legibility of the form entries
- Checking all corrections have been appropriately made
- Checking that all appropriate fields have been updated
    - If a test has not been performed or a measure not taken enter ND (Not Done), if applicable state the reason.
    - If a measure is not applicable enter NA (Not Applicable)
    - If data is unknown enter NK (Not Known). This should only be used once every effort to obtain the data has been exhausted

CRF Queries

- When the form is received at the CTC it will undergo various checks and the information added onto a trial database by CTC data management staff
- Query sheets may be generated which will detail a description of the data being queried, there will be a section to comment on the query
- A query may require an update to a CRF or just a clarification on the query sheet
- The query sheet must be signed and dated and the original sent to the CTC with a copy retained with the patient's CRF
- Data that is likely to be queried includes missing values, ambiguous entries, illogical data and out of range values

Patients stopping treatment

- In the event a patient stops trial treatment during Induction/ASCT/Transplant/ Consolidation please complete the Treatment Summary Form and continue to follow up the patient
- In the event a patient stops trial treatment during Maintenance please complete the Maintenance Summary Form and continue to follow up the patient
- If the patient withdraws consent or is lost to follow-up please complete the Withdrawal/Lost to Follow Up Form
- If the patient dies at any point after registration please complete the Death Form

Cardamon

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

Preliminary Registration Form

Patient Initials	☐☐☐
Site	
Date sent	D D M M Y Y Y Y
Sent by	
Phone number	
Research contact email address	

(This form has 2 pages including cover sheet)

Please fax form to

Cardamon Trial Coordinator
0207 679 9861

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**

To be completed by the UCL CTC

Trial Number	C A R – ☐☐☐
Date of Preliminary Registration	D D M M Y Y Y Y
Registered by	

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]

Preliminary Registration form

Preliminary Registration

Patient Information

Sex: ☐ Male ☐ Female

Consultant

NHS Number

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:

Treatment plan

Anticipated start of treatment [D][D][M][M][Y][Y][Y][Y]

Has the patient's bone marrow biopsy been scheduled? (1= Yes; 2= No) ☐ Date scheduled [D][D][M][M][Y][Y][Y][Y]

Section to be completed by the PI or a co-investigator delegated the responsibility on the site delegation log

Based on peripheral blood and radiology results performed to date, does the patient provisionally meet the eligibility criteria for the Cardamon study? **1= Yes 2= No** ☐

Investigator name (print):

Investigator signature:

Date signed: [D][D][M][M][Y][Y][Y][Y]

Preliminary registration does not guarantee study entry, and trial treatment must not start until full registration is complete

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

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 ≥ 0.8×10^9/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			

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) ☐☐☐.☐

Weight (kg) ☐☐☐.☐

Temperature (^{0}C) ☐☐☐.☐

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

Date ECOG performed D D M M Y Y Y Y

Blood Pressure (mmHg) [1] ☐☐☐ / ☐☐☐

Pulse rate (bpm) ☐☐☐

Respiratory Rate (breaths per minute) ☐☐☐

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

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*

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

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 ☐

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

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:

Cardamon

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

Demographics Form

Patient Initials	☐☐☐
Trial Number	C A R – ☐☐☐

(This form has 3 pages including cover sheet)

Please send forms to:

Cardamon Trial Coordinator
CR UK & UCL Cancer Trials Centre
90 Tottenham Court Road
London W1T 4TJ

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

Additional instructions for completing forms

Demographics Form

The Demographics Form is used to capture demographic information about the patient.

Completing the form

- For new patients, this form should be completed and submitted at baseline with the registration form and after the patient has provided informed consent.
- For existing patients, this form should only be completed after re-consent to v7.0 of the PIS and consent form, or later.

Specific Fields

- *Ethnicity*
  - Only one ethnicity box should be ticked
  - *Other, please* specify- If ethnicity is not detailed please enter it in the box provided

If you have any questions about how to complete this form please contact the Cardamon Trial Coordinator on:
020 7679 9860

Cardamon Trial Number C A R – ☐☐☐ Patient Initials ☐☐☐

Demographics Form

Informed Consent

Main trial consent form signed? **1= Yes 2= No** ☐

Version number of consent form signed ☐.☐

Version number of patient information sheet ☐.☐

NOTE: Ethnicity should only be provided if patient has signed consent v7.0 or later.

Date consent form signed D D M M Y Y Y Y

Ethnicity

Please tick one of the following options

White:	White - British	1	White - European	2	White - Other*	3		
Mixed Race:	White and Black Caribbean	4	White and Black African	5	White and Asian	6		
Asian or Asian British:	Indian	7	Pakistani	8	Bangladeshi	9	Asian - Other*	10
Black or Black British:	Caribbean	11	African	12	Black - Other*:	13		
Chinese	14	Arab	15	Any other ethnic group*	16	Any other mixed / multiple ethnic background*	17	

*Other, please specify ☐

Name of person completing form: ☐ Signature of person completing form: ☐ Date completed: D D M M Y Y Y Y

Please return to: **Cardamon** Trial Coordinator, CR UK & UCL Cancer Trials Centre, 90 Tottenham Court Road, London, W1T 4TJ

Date form received: _____ Date form entered: _____ Initials: _____

For UCL CTC use only: Date Checked: _____ Initials: _____ Date entered: _____ Initials: _____

Cardamon

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

Induction form

Patient Initials	☐☐☐
Trial Number	C A R – ☐☐☐
Cycle number	☐

(This form has 7 pages including cover sheet)

Please send forms to:

Cardamon Trial Coordinator
CR UK & UCL Cancer Trials Centre
90 Tottenham Court Road
London W1T 4TJ

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**

Additional instructions for completing forms

The Induction Form is used to record the first 4 cycles of CarCyDex treatment for the Patient.

Specific Fields

- Please ensure that you are using the correct units (i.e. haemoglobin in g/dL). If your local report uses different units please convert these before entering them on the form
- Omission/Reduction/Delay: Please do not leave these blank, if there were no omissions, reductions or delays please ensure that you have entered "0" in each box. A discrepancy will be raised for all fields left blank
- If the patient has non-secretory or light chain only myeloma, there is no need to answer the paraprotein and immunofixation questions in the efficacy section (page 1). Please simply enter N/A in these fields
- Disease responses must be confirmed by the local investigator and done on day 1 of each cycle. The response assessment section for cycle 1 should be left blank, however, paraprotein, serum free light chain and urinary Bence Jones protein levels must be recorded if available
- Disease response assessment should be based on blood and/or urine tests performed at the start of each cycle (day 1, ± 7 days), this must be assessed by the PI or delegated investigator (see appendix 3 of protocol).
- Disease response for each cycle must be assessed according to the paraprotein/BJP/SFLC results of tests performed at the beginning of the subsequent cycle, for example, response to cycle 1 would be assessed on cycle 2, day 1, and documented on the cycle 2 CRF.
- At the end of induction, disease assessment must be performed within 14 days of the last treatment and prior to PBSCH. This should be reported on the end of induction CRF
- Please ensure that the patient diary card has been completed and returned
- Pregnancy tests should be performed in each cycle prior to the first dose being given
- Please ensure a progression/relapse form is submitted for patients with progressive disease
- If the response is not yet confirmed, please send the CRF regardless and re-send the amended page when the response is confirmed

Completing forms

- Ensure all entries are clear, legible and written in black ink
- Avoid the use of abbreviations and acronyms
- **Do not leave any fields blank. In case of missing data**
  - ND (not done) if a test has not been performed or a measure not taken. If applicable state the reason
  - NA (not applicable) if a measure is not applicable
  - NK (not known) if data is unknown. This should only be used once every effort to obtain the data has been exhausted.
- The Principal Investigator (PI) is responsible for the accuracy of the data reported on the CRF
- Please ensure that all adverse events are recorded on the adverse event form and the form is attached
- CRFs may only be completed by an appropriately qualified individual delegated as responsible by the PI on the site delegation log
- CRF Footer section
  - The "completed by" Name should be clearly legible
  - Each CRF should be signed and dated by the person completing the form
  - Do not complete the *UCL CTC Use only* section
- **The CRF should be sent/faxed to the Cancer Trials Centre (CTC) with a copy retained at the Site** (ensure when photocopying the page that the copy is added to the CRF booklet in the same place where the original was stored)

If you have any questions about how to complete this form please contact the Cardamon Trial Coordinator on: 020 7679 9860

Induction Form

Cycle No:

Haematology

Test	Day 1 result	Day 2 result	Day 8 result	Day 9 result	Day 15 result	Day 16 result
Date (dd/mm/yyyy)						
Haemoglobin (g/dL)						
WBC (x10^9/L)						
Platelets (x 10^9/L)						
Neutrophils (x10^9/L)						
Lymphocytes (x 10^9/L)						
Blood pressure (mmHg)						

- Patients must have FBC and biochemistry tests prior to days 1, 8, & 15 of each cycle
- These are to be repeated on days 2, 9 & 16 **if clinically indicated**
- The validity period for FBC is 48 hours, and for biochemistry it is 72 hours

Induction Form

Cycle No: ☐

Biochemistry

Test	Day 1 result	Day 8 result	Day 15 result
Date (dd/mm/yyyy)			
Calcium (corrected) (mmol/L)			
Potassium (mmol/L)			
Phosphate (mmol/L)			
Urea (mmol/L)			
Sodium (mmol/L)			
Serum Urate (µmol/L)			
Creatinine (µmol/L)			
Creatinine clearance (ml/min) *if clinically indicated, otherwise enter ND*			
Albumin (g/L)			
Bilirubin (µmol/L)			
Alkaline Phosphatase (IU/L)			
Aspartate Transaminase (IU/L)			
Alanine Transaminase (IU/L)			

Adverse events

Has patient returned their diary card? ☐ 1 = Yes 2 = No

Did the patient experience any adverse events? ☐ 1 = Yes *(please ensure adverse event form is submitted)* 2 = No

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

Induction Form

Cycle No:

Efficacy assessments

Date of test D D M M Y Y Y Y

If patient has secretory myeloma, please complete this section:

Paraprotein expression *(choose one option only)*

1= Single paraprotein expressed
2= Light chain only
3 = Biclonal

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 paraprotein type: (*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) • **OR** Tick if not done

Serum free light chain: Lambda (mg/L) • **OR** Tick if not done

Serum free light chain Kappa/Lambda ratio: •

Normal range of Kappa/Lambda FLC ratio: –

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 (only to confirm CR)

Immunofixation Serum

1= Positive
2= Negative
3= Not done

Date of test D D M M Y Y Y Y

Immunofixation Urine

1= Positive
2= Negative
3= Not done

Date of test D D M M Y Y Y Y

Induction Form

Cycle No: ☐ ***Please note: this page should not be completed in cycle 1***

Response assessment

This section must be completed and signed by the local principal investigator / delegated investigator and done on day 1 of each cycle (from cycle 2 onwards)

Date of response assessment: D D M M Y Y Y Y

Patient's response to induction treatment cycle : ☐
(choose <u>one</u> option only)
(e.g. this is the response to last cycle received, i.e. cycle 1 would be assessed on cycle 2, day 1 and documented on the cycle 2 CRF)

1= sCR
2= CR
3= VGPR
4= PR
5= MR
6= SD
7= PD — *Patient off protocol treatment—to be followed up as per protocol (Complete first progression and treatment summary form)*
8= Unable to assess—
Specify reason:

Investigator name (print):

Investigator signature:

Date signed: D D M M Y Y Y Y

- Disease response assessment should be based on blood and/or urine tests performed at the start of each cycle (day 1, ± 7 days), this must be assessed by the PI or delegated investigator (see appendix 3 of protocol)
- Disease response for each cycle must be assessed according to the paraprotein/BJP/SFLC results of tests performed at the beginning of the subsequent cycle, for example, response to cycle 1 would be assessed on cycle 2, day 1, and documented on the cycle 2 CRF.
- At the end of induction, disease assessment must be performed within 14 days of the last treatment and prior to PBSCH. This should be reported o the end of induction CRF

Induction Form

Cycle No:

Date cycle started: D D M M Y Y Y Y

Patient BSA . m^2 *Patients with a BSA >2.2m^2 should receive dose based on BSA of 2.2m^2*

Did the patient receive pre-dose IV hydration in line with protocol? 1 = Yes 2 = No

Any delays reductions or omissions during this cycle of induction? 1 = Yes 2 = No

Please complete all boxes in table below (if no delay / reduction / omission, please enter = 0)

Drug	Day	Dose given	Route (PO or IV)	Omission (see codes below)	Reduction (see codes below)	Delay (see codes below)
Dexamethasone (40mg PO or IV)	1	mg				
	8	mg				
	15	mg				
	22	mg				
Carfilzomib (56mg/m^2* IV) *except cycle 1 days 1 & 2 (20mg/m^2)*	1	mg				
	2	mg				
	8	mg				
	9	mg				
	15	mg				
	16	mg				
Cyclophosphamide (500mg PO Or 375mg IV)	1	mg				
	8	mg				
	15	mg				

0=No delay/reduction/omission, 1=Haematological Toxicity, 2=Hepatotoxicity, 3=Cardiotoxicity 4= Neurotoxicity, 5=Infusion-related toxicity 6=Allergic reaction/hypersensitivity 7=Infection, 8=Patient Choice, 9=Clinician Choice, 10=Administrative, 11=Tumour Lysis syndrome, 12=Other (specify below), 13=Protocol approved reduction/omission

12 = OTHER Reduction/Delay/Omission Reason

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

Cardamon

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

End of Induction Form

Patient Initials	☐☐☐
Trial Number	C A R – ☐☐☐

(This form has 6 pages including cover sheet)

Please send forms to:

Cardamon Trial Coordinator
CR UK & UCL Cancer Trials Centre
90 Tottenham Court Road
London W1T 4TJ

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**

Additional instructions for completing forms

The End of Induction Form should be used to collect patient data once they have completed their first 4 cycles of CarCyDex treatment. The End of Induction Form should be completed within 14 days of the completion of the 4th cycle of CarCyDex Induction and prior to PBSCH.

Specific Fields

- Please ensure that you are using the correct units (i.e. haemoglobin in g/dL). If your local report uses different units please convert these before entering them on the form.
- Please ensure that you have answered the regarding adverse events
  - ◊ If no adverse events occurred, then simply answer "no" and there is no need to attach an adverse event form
  - ◊ If an adverse event is still ongoing from the previous cycle **you must provide an adverse event** form and enter these AEs, using the original start date of the AE
- For tests which are only required if clinically indicated (e.g. 24hr BJP) please indicate if they were not done by completing the boxes with ND
- Disease responses must be confirmed by the local investigator
- Please ensure a progression/relapse form is submitted for patients with progressive disease

Completing forms

- Ensure all entries are clear, legible and written in black ink
- Avoid the use of abbreviations and acronyms
- **Do not leave any fields blank. In case of missing data**
  - ND (not done) if a test has not been performed or a measure not taken. If applicable state the reason
  - NA (not applicable) if a measure is not applicable
  - NK (not known) if data is unknown. This should only be used once every effort to obtain the data has been exhausted.
- The Principal Investigator (PI) is responsible for the accuracy of the data reported on the CRF
- Please ensure that all adverse events are recorded on the adverse event form and the form is attached
- CRFs may only be completed by an appropriately qualified individual delegated as responsible by the PI on the site delegation log
- CRF Footer section
  - The "completed by" Name should be clearly legible
  - Each CRF should be signed and dated by the person completing the form
  - Do not complete the *UCL CTC Use only* section
- **The CRF should be sent/faxed to the Cancer Trials Centre (CTC) with a copy retained at the Site** (ensure when photocopying the page that the copy is added to the CRF booklet in the same place where the original was stored)

If you have any questions about how to complete this form please contact the Cardamon Trial Coordinator on: 020 7679 9860

End of Induction Form

Haematology

Date of Haematology: D D M M Y Y Y Y

Haemoglobin g/dL

Platelets x 10^9/L

Neutrophils x10^9/L

WBC Count x10^9/L

Lymphocytes x 10^9/L

Biochemistry

Date of Biochemistry D D M M Y Y Y Y

Calcium (corrected) mmol/L

Potassium mmol/L

Sodium mmol/L

Creatinine µmol/L

Creatinine Clearance ml/min

Serum urate µmol/L

Urea (mmol/L)

Bilirubin µmol/L

Albumin g/L

Alkaline Phosphatase IU/L

Alanine Transaminase (ALT) IU/L

Or

Aspartate Transaminase (AST) IU/L

Phosphate mmol/L

Adverse events

Has patient returned their diary card?

1 = Yes
2 = No

Did the patient experience any adverse events between their last cycle of induction and their post-induction assessment?

1 = Yes *(please ensure adverse event form is submitted)*
2 = No

Soft tissue plasmacytoma/Extramedullary lesions *(if present at registration)*

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

End of Induction Form

Efficacy assessments

Date of test D D M M Y Y Y Y

If patient has secretory myeloma, please complete this section:

Paraprotein expression *(choose one option only)*

1= Single paraprotein expressed
2= Light chain only
3 = Biclonal

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 paraprotein type: *(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) • **OR** Tick if not done

Serum free light chain: Lambda (mg/L) • **OR** Tick if not done

Serum free light chain Kappa/Lambda ratio: •

Normal range of Kappa/Lambda FLC ratio: –

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 (only to confirm CR)

Immunofixation Serum

1= Positive
2= Negative
3= Not done

Date of test D D M M Y Y Y Y

Immunofixation Urine

1= Positive
2= Negative
3= Not done

Date of test D D M M Y Y Y Y

End of Induction Form

Imaging *(Only if clinically indicated, or if soft tissue plasmacytomas present at registration)*

		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= Evidence of myeloma 2= No evidence of myeloma 3= Not done	D D M M Y Y Y Y	
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

Has an increase in number or size of lytic bone lesions been seen on any radiograph? 1 = Yes 2 = No

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

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

End of Induction Form

Response post-induction

This section must be completed and signed by the local principal investigator or delegated investigator

Date of response assessment D D M M Y Y Y Y

Patient's response to induction treatment: *(choose one option only)* ☐

1= sCR
2= CR
3= VGPR
4= PR
Patient should now proceed to peripheral blood stem cell harvest

5= MR
6= SD
Patient off protocol treatment—to be followed up as per protocol (Please submit treatment summary form)

7= PD — *Patient off protocol treatment—to be followed up as per protocol (Please complete first progression and treatment summary form)*

Is this response confirmed? (1=yes, 2=no) *(refer to IMWG criteria/protocol appendix 3)* ☐ Date confirmed: D D M M Y Y Y Y

Investigator name (print): Investigator signature: Date signed: D D M M Y Y Y Y

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

Cardamon

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

PBSCH, Post-PBSCH and Randomisation forms

Site	
Name of sender	
Contact email address	
Contact phone number	
Contact fax number	
Pharmacy contact	
Pharmacy email address	
Pharmacy fax number	
Date	D D M M Y Y Y Y

Please fax forms (9 pages in total) to
Cardamon Trial Coordinator
0207 679 9861

The forms will be checked for accuracy and eligibility and the trial arm allocation faxed/emailed back to the site & pharmacy contacts

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

Additional instructions for completing forms

The 'Peripheral Blood Stem Cell Harvest (PBSCH) Form' should be used to collect patient data on the patient's stem cell harvest and randomisation, if applicable.

The 'Post-Peripheral Blood Stem Cell Harvest (PBSCH) and Randomisation Form' should be used to collect patient data once they have completed their first 4 cycles of CarCyDex treatment and PBSCH. Assessments should be performed within 14 days after PBSCH.

Specific Fields

- Please ensure that you are using the correct units (i.e. haemoglobin in g/dL). If your local report uses different units please convert these before entering them on the form
- Please ensure you complete the drug details for both the original mobilisation and subsequent remobilisations if applicable
- Patients achieving a response of <PR will not proceed to randomisation and should be followed up in line with the protocol
- Disease responses must be confirmed by the local investigator
- Please ensure a progression/relapse form is submitted for patients with progressive disease

Completing forms

- Ensure all entries are clear, legible and written in black ink
- Avoid the use of abbreviations and acronyms
- **Do not leave any fields blank. In case of missing data**
  - ND (not done) if a test has not been performed or a measure not taken. If applicable state the reason
  - NA (not applicable) if a measure is not applicable
  - NK (not known) if data is unknown. This should only be used once every effort to obtain the data has been exhausted.
- The Principal Investigator (PI) is responsible for the accuracy of the data reported on the CRF
- Please ensure that all adverse events are recorded on the adverse event form and the form is attached
- CRFs may only be completed by an appropriately qualified individual delegated as responsible by the PI on the site delegation log
- CRF Footer section
  - The "completed by" Name should be clearly legible
  - Each CRF should be signed and dated by the person completing the form
  - Do not complete the *UCL CTC Use only* section
- **The CRF should be sent/faxed to the Cancer Trials Centre (CTC) with a copy retained at the Site** (ensure when photocopying the page that the copy is added to the CRF booklet in the same place where the original was stored)

If you have any questions about how to complete this form please contact the Cardamon Trial Coordinator on: 020 7679 9860

PBSCH Form

Stem cell mobilisation and harvest

Did the patient undergo stem cell mobilisation and harvest post-CarCyDex therapy? ☐

1= Yes, please go to the next section
2= No, please complete below:

If **No**, please specify reason: *(choose <u>one</u> option only)* ☐

1 = Disease progression—Patient off protocol treatment—to be followed up as per protocol *(please complete first progression and treatment summary forms)*
2 = Patient withdrawal—Patient off protocol treatment—to be followed up as per protocol *(please complete treatment summary form)*
3 = Patient died *(please complete treatment summary and death forms)*
4 = Patient unfit, please specify below:
5 = Other, please specify below:

☐

Patient off protocol treatment—to be followed up as per protocol (please complete a treatment summary form)

Mobilisation

Drug	Total dose given (mg)	Start date (DD/MM/YYYY)	End date (DD/MM/YYYY)
		/ /	/ /
		/ /	/ /
		/ /	/ /
		/ /	/ /

Date of first stem cell collection D D M M Y Y Y Y

Number of harvest days: ☐

Number of stem cells collected ☐☐ • ☐☐ x10^6 CD34+ cells/kg

Did the patient undergo remobilisation? ☐

1= Yes, please go to the next section (Remobilisation) on page 4
2= No, please go to Harvest outcome section of page 4

PBSCH Form

Re-Mobilisation

Drug	Dose given (mg)	Start date (DD/MM/YYYY)	End date (DD/MM/YYYY)
		/ /	/ /
		/ /	/ /
		/ /	/ /

Date of stem cell collection D D M M Y Y Y Y Number of harvest days:

Number of stem cells collected • x10^6 CD34+ cells/kg

Harvest Outcome

Was the peripheral blood stem cell harvest successful?

1= Yes, please complete below
2= No—*Patient off protocol treatment—to be followed up as per protocol (please complete a treatment summary form)*

End of successful harvest D D M M Y Y Y Y Number of harvest days:

Total number of stem cells collected • x10^6 CD34+ cells/kg

Post-PBSCH and Randomisation form

Haematology

Date of Haematology: D D M M Y Y Y Y

Haemoglobin g/dL ☐☐.☐☐

Platelets x 10^9/L ☐☐☐☐

Neutrophils x10^9/L ☐☐.☐☐

WBC Count x10^9/L ☐☐.☐☐

Lymphocytes x 10^9/L ☐☐.☐☐

Biochemistry

Date of Biochemistry D D M M Y Y Y Y

Calcium (corrected) mmol/L ☐☐.☐☐

Potassium mmol/L ☐☐.☐☐

Sodium mmol/L ☐☐☐

Creatinine µmol/L ☐☐☐.☐

Creatinine Clearance ml/min ☐☐☐☐

Serum urate µmol/L ☐☐☐.☐

Urea (mmol/L) ☐☐.☐☐

Bilirubin µmol/L ☐☐☐

Albumin g/L ☐☐☐

Alkaline Phosphatase IU/L ☐☐☐☐

Alanine Transaminase (ALT) IU/L ☐☐☐

OR

Aspartate Transaminase (AST) IU/L ☐☐☐

Note: Please confirm ND if only AST or ALT assessed.

Phosphate mmol/L ☐☐☐.☐

Adverse events

Did the patient experience any adverse events between their post-induction assessment until post-PBSCH? ☐

1 = Yes *(please ensure adverse event form is submitted)*
2 = No

Quality of Life Questionnaire

Has the Quality of Life (QoL) been completed? ☐

1 = Yes; *please send to the CTC as soon as possible*
3 = Not done; please provide reason in box below:

☐

Post-PBSCH and Randomisation 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

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

Bone marrow aspirate sample must be sent to HMDS, Leeds following the PBSCH

	Sent? 1=Yes 2= No	**Date sample sent to lab:**
BM aspirate for MRD (2ml) sent to HMDS, Leeds?	☐	D D M M Y Y Y Y

If No, please specify a reason: ☐

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	☐

Post-PBSCH and Randomisation form

Efficacy assessments

Date of test D D M M Y Y Y Y

If patient has secretory myeloma, please complete this section:

Paraprotein expression *(choose one option only)*
1= Single paraprotein expressed
2= Light chain only
3 = Biclonal

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 paraprotein type: *(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) • **OR** Tick if not done

Serum free light chain: Lambda (mg/L) • **OR** Tick if not done

Serum free light chain Kappa/Lambda ratio: •

Normal range of Kappa/Lambda FLC ratio: –

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 (only to confirm CR)

Immunofixation Serum
1= Positive
2= Negative
3= Not done

Date of test D D M M Y Y Y Y

Immunofixation Urine
1= Positive
2= Negative
3= Not done

Date of test D D M M Y Y Y Y

Post-PBSCH and Randomisation form

Imaging ***(If clinically indicated or for response assessment if persistent soft tissue plasmacytomas present)***

		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= Evidence of myeloma 2= No evidence of myeloma 3= Not done	D D M M Y Y Y Y	
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

Has an increase in number or size of lytic bone lesions been seen on any radiograph? 1 = Yes 2 = No

Post-PBSCH and Randomisation form

Response post-PBSCH

This section must be completed and signed by the local principal investigator or delegated investigator

Date of response assessment: D D M M Y Y Y Y

Disease response post PBSCH
Choose one option only

- 1= sCR
- 2= CR
- 3= VGPR
- 4= PR

Patient should proceed to Randomisation

- 5= MR
- 6= SD

Patient off protocol treatment—to be followed up as per protocol (Please submit treatment summary form)

7= PD — *Patient off protocol treatment—to be followed up as per protocol (Please complete first progression and treatment summary form)*

Is this response confirmed? (1=yes, 2=no)
(refer to IMWG criteria/protocol appendix 3)

Date confirmed: D D M M Y Y Y Y

Investigator name (print):

Investigator signature:

Date signed: D D M M Y Y Y Y

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

Randomisation Details (CTC USE ONLY)

Patient eligible for randomisation? **Yes** **No**

Trial arm allocated? **Consolidation** **ASCT**

Randomised by

Date of randomisation: D D M M Y Y Y Y

Cardamon

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

Consolidation Form

Patient Initials	☐☐☐
Trial Number	C A R – ☐☐☐
Cycle number	☐

(This form has 7 pages including cover sheet)

Please send forms to:

Cardamon Trial Coordinator
CR UK & UCL Cancer Trials Centre
90 Tottenham Court Road
London W1T 4TJ

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**

Additional instructions for completing forms

The Consolidation Form is used to record the 4 cycles of CarCyDex treatment for the patients randomised to the consolidation arm.

Specific Fields

- Cycle number—please take cycle number from the start of consolidation not all treatment i.e. the first cycle after randomisation will be cycle 1 not cycle 5
- Omission/Reduction/Delay: Please do not leave these blank, if there were no omissions, reductions or delays please ensure that you have entered "0" in each box. A discrepancy will be raised for all fields left blank
- If any efficacy tests have not been done because they are not clinically indicated, please ensure that you complete the boxes with ND to confirm that the tests were not done. A discrepancy will be raised for those fields left completely blank
- Please ensure that you are using the correct units (i.e. haemoglobin in g/dL). If your local report uses different units please convert these before entering them on the form
- Disease response assessment should be based on blood and/or urine tests performed at the start of each cycle (day 1, ± 7 days), this must be assessed by the PI or delegated investigator (see appendix 3 of protocol)
- Disease response for each cycle must be assessed according to the paraprotein/BJP/SFLC results of tests performed at the beginning of the subsequent cycle, for example, response to cycle 1 would be assessed on cycle 2, day 1, and documented on the cycle 2 CRF
- At the end of consolidation, disease assessment must be performed within 14 days of the last treatment and prior to starting maintenance. This should be reported on the end of consolidation CRF
- Please ensure that the patient diary card has been completed and returned
- Pregnancy tests should be performed in each cycle prior to the first dose being given
- Please ensure a progression/relapse form is submitted for patients with progressive disease

Completing forms

- Ensure all entries are clear, legible and written in black ink
- Avoid the use of abbreviations and acronyms
- **Do not leave any fields blank. In case of missing data**
  - ND (not done) if a test has not been performed or a measure not taken. If applicable state the reason
  - NA (not applicable) if a measure is not applicable
  - NK (not known) if data is unknown. This should only be used once every effort to obtain the data has been exhausted.
- The Principal Investigator (PI) is responsible for the accuracy of the data reported on the CRF
- Please ensure that all adverse events are recorded on the adverse event form and the form is attached
- CRFs may only be completed by an appropriately qualified individual delegated as responsible by the PI on the site delegation log
- CRF Footer section
  - The "completed by" Name should be legible
  - Each CRF should be signed and dated by the person completing the form
  - Do not complete the *UCL CTC Use only* section
- **The CRF should be sent/faxed to the Cancer Trials Centre (CTC) with a copy retained at the Site** (ensure when photocopying the page that the copy is added to the CRF booklet in the same place where the original was stored)

If you have any questions about how to complete this form please contact the Cardamon Trial Coordinator on: 020 7679 9860

Consolidation Form

Cycle No:

Haematology

Test	Day 1 result	Day 2 result	Day 8 result	Day 9 result	Day 15 result	Day 16 result
Date (dd/mm/yyyy)						
Haemoglobin (g/dL)						
WBC (x10^9/L)						
Platelets (x 10^9/L)						
Neutrophils (x10^9/L)						
Lymphocytes (x 10^9/L)						
Blood pressure (mmHg)						

- Patients must have FBC and biochemistry tests prior to days 1, 8, & 15 of each cycle
- These are to be repeated on days 2, 9 & 16 **if clinically indicated**
- The validity period for FBC is 48 hours, and for biochemistry it is 72 hours

Consolidation Form

Cycle No:

Biochemistry

Test	Day 1 result	Day 8 result	Day 15 result
Date (dd/mm/yyyy)			
Calcium (corrected) (mmol/L)			
Potassium (mmol/L)			
Phosphate (mmol/L)			
Urea (mmol/L)			
Sodium (mmol/L)			
Serum Urate (µmol/L)			
Creatinine (µmol/L)			
Creatinine clearance (ml/min) *if clinically indicated, otherwise enter ND*			
Albumin (g/L)			
Bilirubin (µmol/L)			
Alkaline Phosphatase (IU/L)			
Aspartate Transaminase (IU/L)			
Alanine Transaminase (IU/L)			

Adverse events

Has patient returned their diary card? 1 = Yes 2 = No

Did the patient experience any adverse events? 1 = Yes *(please ensure adverse event form is submitted)* 2 = No

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

Consolidation Form

Cycle No:

Efficacy assessments

Date of test D D M M Y Y Y Y

If patient has secretory myeloma, please complete this section:

Paraprotein expression *(choose one option only)*
1= Single paraprotein expressed
2= Light chain only
3 = Biclonal

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 paraprotein type: (*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) • **OR** Tick if not done

Serum free light chain: Lambda (mg/L) • **OR** Tick if not done

Serum free light chain Kappa/Lambda ratio: •

Normal range of Kappa/Lambda FLC ratio: –

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 (only to confirm CR)

Immunofixation Serum
1= Positive
2= Negative
3= Not done

Date of test D D M M Y Y Y Y

Immunofixation Urine
1= Positive
2= Negative
3= Not done

Date of test D D M M Y Y Y Y

Consolidation Form

Cycle No: ☐ ***Please note: this page should not be completed in cycle 1***

Response assessment

This section must be completed and signed by the local principal investigator / delegated investigator and done on day 1 of each cycle (from cycle 2 onwards)

Date of response assessment: D D M M Y Y Y Y

Patient's response to consolidation treatment: ☐
(choose <u>one</u> option only)
(e.g. this is the response to last cycle received, i.e. cycle 1 would be assessed on cycle 2, day 1 and documented on the cycle 2 CRF)

1= sCR
2= CR
3= VGPR
4= PR
5= MR
6= SD
7= PD — *Patient off protocol treatment—to be followed up as per protocol*
(Complete first progression and treatment summary form)
8= Unable to assess—
Specify reason:

Investigator name (print):

Investigator signature:

Date signed: D D M M Y Y Y Y

- Disease response assessment should be based on blood and/or urine tests performed at the start of each cycle (day 1, ± 7 days), this must be assessed by the PI or delegated investigator (see appendix 3 of protocol)
- Disease response for each cycle must be assessed according to the paraprotein/BJP/SFLC results of tests performed at the beginning of the subsequent cycle, for example, response to cycle 1 would be assessed on cycle 2, day 1, and documented on the cycle 2 CRF
- At the end of consolidation, disease assessment must be performed within 14 days of the last treatment and prior to starting maintenance. This should be reported on the end of consolidation CRF

Consolidation Form

Cycle No:

Date cycle started: D D M M Y Y Y Y

Patient BSA . m^2 *Patients with a BSA >2.2m^2 should receive dose based on BSA of 2.2m^2*

Any delays reductions or omissions during this cycle of consolidation? 1 = Yes 2 = No ***Please complete all boxes in table below (if no delay / reduction / omission, please enter = 0)***

Drug	Day	Dose given	Route (IV or PO)	Omission (see codes below)	Reduction (see codes below)	Delay (see codes below)
Dexamethasone (20mg PO or IV)	1	mg				
	8	mg				
	15	mg				
	22	mg				
Carfilzomib (56mg/m^2)	1	mg				
	2	mg				
	8	mg				
	9	mg				
	15	mg				
	16	mg				
Cyclophosphamide (500mg PO or 375mg IV)	1	mg				
	8	mg				
	15	mg				

0=No delay/reduction/omission, 1=Neurotoxicity, 2=Hepatotoxicity, 3=Cardiotoxicity 4=Haematological Toxicity, 5=Infusion-related toxicity 6=Pancreatitis 7=Patient Choice, 8=Clinician Choice, 9=Administrative, 10=Tumour Flare reaction, 11=Tumour Lysis syndrome, 12=Other (specify below), 13=Protocol approved reduction/omission

12 = OTHER Reduction/Delay/Omission Reason

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

Cardamon

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

Post-Consolidation Form

Patient Initials	☐☐☐
Trial Number	C A R – ☐☐☐

(This form has 7 pages including cover sheet)

Please send forms to:

Cardamon Trial Coordinator
CR UK & UCL Cancer Trials Centre
90 Tottenham Court Road
London W1T 4TJ

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**

Additional instructions for completing forms

The Post-Consolidation form collects details of the patient's response to consolidation treatment. Assessments are to be performed within 14 days of completing the last cycle of consolidation

Specific Fields

- Please ensure that you are using the correct units (i.e. haemoglobin in g/dL). If your local report uses different units please convert these before entering them on the form.
- If any efficacy tests have not been done because they are not clinically indication, please ensure that you complete the boxes with ND to confirm that the tests were not done. A discrepancy will be raised for those fields left completely blank.
- Disease response should be confirmed by a local investigator
- Please ensure a progression/relapse form is submitted for patients with progressive disease

Completing forms

- Ensure all entries are clear, legible and written in black ink
- Avoid the use of abbreviations and acronyms
- **Do not leave any fields blank. In case of missing data**
  - ND (not done) if a test has not been performed or a measure not taken. If applicable state the reason
  - NA (not applicable) if a measure is not applicable
  - NK (not known) if data is unknown. This should only be used once every effort to obtain the data has been exhausted.
- The Principal Investigator (PI) is responsible for the accuracy of the data reported on the CRF
- Please ensure that all adverse events are recorded on the adverse event form and the form is attached
- CRFs may only be completed by an appropriately qualified individual delegated as responsible by the PI on the site delegation log
- CRF Footer section
  - The "completed by" Name should be legible
  - Each CRF should be signed and dated by the person completing the form
  - Do not complete the *UCL CTC Use only* section
- **The CRF should be sent/faxed to the Cancer Trials Centre (CTC) with a copy retained at the Site** (ensure when photocopying the page that the copy is added to the CRF booklet in the same place where the original was stored)

If you have any questions about how to complete this form please contact the Cardamon Trial Coordinator on: 020 7679 9860

Post-Consolidation Form

Haematology

Date of Haematology: D D M M Y Y Y Y

Haemoglobin g/dL

Platelets x 10^9/L

Neutrophils x10^9/L

WBC Count x10^9/L

Lymphocytes x 10^9/L

Biochemistry

Date of Biochemistry D D M M Y Y Y Y

Calcium (corrected) mmol/L

Potassium mmol/L

Sodium mmol/L

Creatinine µmol/L

Creatinine Clearance ml/min

Serum urate µmol/L

Urea (mmol/L)

Bilirubin µmol/L

Albumin g/L

Alkaline Phosphatase IU/L

Alanine Transaminase (ALT) IU/L

OR

Aspartate Transaminase (AST) IU/L

Phosphate mmol/L

Adverse events

Has patient returned their diary card?

1 = Yes
2 = No

Did the patient experience any adverse events between their last cycle of consolidation and their post-consolidation assessment?

1 = Yes *(please ensure adverse event form is submitted)*
2 = No

Has the Quality of Life (QoL) been completed?

1=Yes; please ensure the form is attached
3=No, please provide reason if not done:

Date of QoL completion: D D M M Y Y Y Y

Post-Consolidation 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

Bone marrow aspirate sample must be sent to HMDS, Leeds after 4 cycles of consolidation treatment
Bone marrow aspirate and peripheral blood samples must also be sent to the UCL Cancer Institute Myeloma Lab at this time point

	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

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

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 ☐	

Post-Consolidation Form

PET-CT sub study: Post-Consolidation scan details

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

Date of PET-CT: D D M M Y Y Y Y

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

Efficacy assessments

Date of test D D M M Y Y Y Y

If patient has secretory myeloma, please complete this section:

Paraprotein expression *(choose <u>one</u> option only)* ☐
1= Single paraprotein expressed
2= Light chain only
3 = Biclonal

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 paraprotein type: ☐ *(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) ☐☐☐•☐☐ **OR** ☐ Tick if not done

Serum free light chain: Lambda (mg/L) ☐☐☐•☐☐ **OR** ☐ Tick if not done

Serum free light chain Kappa/Lambda ratio: ☐☐☐•☐☐ Normal range of Kappa/ Lambda FLC ratio: ☐ – ☐

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 <u>one</u> only):* ☐ 1= Kappa 2= Lambda 3 = N/A

Immunofixation (only to confirm CR)

Immunofixation Serum ☐ 1= Positive 2= Negative 3= Not done Date of test D D M M Y Y Y Y

Immunofixation Urine ☐ 1= Positive 2= Negative 3= Not done Date of test D D M M Y Y Y Y

Post-Consolidation Form

Imaging *(If clinically indicated or for response assessment if persistent soft tissue plasmacytomas present)*

NB: If patient is participating in PET-CT sub study please complete section at the end of this page

		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= Evidence of myeloma 2= No evidence of myeloma 3= Not done	D D M M Y Y Y Y	
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

Has an increase in number or size of lytic bone lesions been seen on any radiograph? 1 = Yes 2 = No

Post-Consolidation Form

Response post-consolidation

This section must be completed and signed by the local principal investigator or delegated investigator

Date of response assessment: D D M M Y Y Y Y

Patient's response to consolidation treatment: *(choose one option only)* ☐

1= sCR
2= CR
3= VGPR
4= PR
5= MR
6= SD

Patient may proceed to maintenance treatment *(please ensure a treatment summary form is submitted)*

7= PD — *Patient off protocol treatment—to be followed up as per protocol (Complete first progression and treatment summary form)*

8= Unable to assess—
Specify reason:

Is this response confirmed? (1=yes, 2=no) *(refer to IMWG criteria/protocol appendix 3)* ☐

Date confirmed: D D M M Y Y Y Y

Investigator name (print):

Investigator signature:

Date signed: D D M M Y Y Y Y

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

Cardamon

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

Transplant Form

Patient Initials	☐☐☐
Trial Number	C A R – ☐☐☐

(This form has 3 pages including cover sheet)

Please send forms to:

Cardamon Trial Coordinator
CR UK & UCL Cancer Trials Centre
90 Tottenham Court Road
London W1T 4TJ

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**

Additional instructions for completing forms

The transplant form collects details of the patient's transplant for those patients randomised to the ASCT arm of the trial. Patients should proceed to transplant as soon as possible after randomisation and high dose Melphalan should be given no more than 4 weeks after randomisation.

Completing forms

- Ensure all entries are clear, legible and written in black ink
- Avoid the use of abbreviations and acronyms
- **Do not leave any fields blank. In case of missing data**
  - ND (not done) if a test has not been performed or a measure not taken. If applicable state the reason
  - NA (not applicable) if a measure if not required
  - NK (not known) if data is unknown. This should only be used once every effort to obtain the data has been exhausted.
- CRFs may only be completed by an appropriately qualified individual delegated as responsible by the PI on the site delegation log
- CRF Footer section
  - The "completed by" Name should be legible
  - Each CRF should be signed and dated by the person completing the form
  - Do not complete the *UCL CTC Use only* section
- **The CRF should be sent/faxed to the UCL Cancer Trials Centre (CTC) with a copy retained at the Site** (ensure when photocopying the page that the copy is added to the CRF booklet)

If you have any questions about how to complete this form please contact the Cardamon Trial Coordinator on: 020 7679 9860

Transplant Form

Did the patient receive an autologous stem cell transplant? ☐ 1= Yes 2 = No

If no, please give the reason: ☐ 1 = Disease progression, 2 = Patient unfit to proceed 3 = Other (specify)

Specify: ☐

Admission date: D D M M Y Y Y Y

Date of transplant: D D M M Y Y Y Y

Melphalan dose: ☐☐☐ mg

Have neutrophils recovered? ☐ 1 = Yes 2 = No

Date of 1st of three consecutive days Neutrophils ≥ $0.5x10^9$/L after first post-transplant nadir: D D M M Y Y Y Y

Have platelets recovered? ☐ 1 = Yes 2 = No

Date of 1st of three consecutive days platelets ≥$20x10^9$/L (unsupported): D D M M Y Y Y Y

Was the patient admitted to ITU or HDU during their transplant? ☐ 1 = Yes 2 = No

If yes, how many days? ☐☐☐ days

Date of discharge from hospital: D D M M Y Y Y Y

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

Cardamon

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

Day 100 Post-ASCT Form

Patient Initials	☐☐☐
Trial Number	C A R – ☐☐☐

(This form has 7 pages including cover sheet)

Please send forms to:

Cardamon Trial Coordinator
CR UK & UCL Cancer Trials Centre
90 Tottenham Court Road
London W1T 4TJ

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**

Additional instructions for completing forms

The Day 100 post-ASCT form collects details of the patient's response to transplant for those patients randomised to the ASCT arm of the trial.

Specific Fields

- If any efficacy tests have not been done because they are not clinically indicated, please ensure that you complete the boxes with ND to confirm that the tests were not done. A discrepancy will be raised for those fields left completely blank.
- Please ensure that you are using the correct units (i.e. haemoglobin in g/dL). If your local report uses different units please convert these before entering them on the form.
- Disease response should be confirmed by a local investigator
- Please ensure a progression/relapse form is submitted for patients with progressive disease

Completing forms

- Ensure all entries are clear, legible and written in black ink
- Avoid the use of abbreviations and acronyms
- **Do not leave any fields blank. In case of missing data**
  - ND (not done) if a test has not been performed or a measure not taken. If applicable state the reason
  - NA (not applicable) if a measure is not applicable
  - NK (not known) if data is unknown. This should only be used once every effort to obtain the data has been exhausted.
- CRFs may only be completed by an appropriately qualified individual delegated as responsible by the PI on the site delegation log
- CRF Footer section
  - The "completed by" Name should be legible
  - Each CRF should be signed and dated by the person completing the form
  - Do not complete the *UCL CTC Use only* section
- **The CRF should be sent/faxed to the Cancer Trials Centre (CTC) with a copy retained at the Site** (ensure when photocopying the page that the copy is added to the CRF booklet in the same place where the original was stored)

If you have any questions about how to complete this form please contact the Cardamon Trial Coordinator on: 020 7679 9860

Day 100 post-ASCT Form

Haematology

Date of Haematology: D D M M Y Y Y Y

Haemoglobin g/dL ☐☐•☐☐

Platelets x 10^9/L ☐☐☐☐

Neutrophils x10^9/L ☐☐•☐☐

WBC Count x10^9/L ☐☐•☐☐

Lymphocytes x 10^9/L ☐☐•☐☐

Biochemistry

Date of Biochemistry D D M M Y Y Y Y

Calcium (corrected) mmol/L ☐☐•☐☐

Potassium mmol/L ☐☐•☐☐

Sodium mmol/L ☐☐☐

Creatinine µmol/L ☐☐☐•☐

Creatinine Clearance ml/min ☐☐☐☐

Serum urate µmol/L ☐☐☐•☐

Urea (mmol/L) ☐☐•☐☐

Bilirubin µmol/L ☐☐☐

Albumin g/L ☐☐☐

Alkaline Phosphatase IU/L ☐☐☐☐

Alanine Transaminase (ALT) IU/L *Or* Aspartate Transaminase (AST) IU/L ☐☐☐

Phosphate mmol/L ☐☐☐•☐

Adverse events

Did the patient experience any adverse events between PBSCH and their day 100 post-ASCT assessment? ☐

1 = Yes *(please ensure adverse event form is submitted)*
2 = No

Has the Quality of Life (QoL) been completed? ☐

1 = Yes; please ensure the form is attached
3 = No, please provide reason if not done:

Date of QoL completion: D D M M Y Y Y Y

Day 100 post-ASCT 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
[ ] [ ] [ ] %

Bone marrow aspirate sample must be sent to HMDS, Leeds after 4 cycles of consolidation treatment
Bone marrow aspirate and peripheral blood samples must also be sent to the UCL Cancer Institute Myeloma Lab at this time point

	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

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

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	[ ]

Day 100 post-ASCT Form

PET-CT sub study: Post-Consolidation scan details

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

Date of PET-CT: D D M M Y Y Y Y

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

Efficacy assessments

Date of test D D M M Y Y Y Y

If patient has secretory myeloma, please complete this section:

Paraprotein expression *(choose <u>one</u> option only)* ☐
1= Single paraprotein expressed
2= Light chain only
3 = Biclonal

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 paraprotein type: (*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) ☐☐☐•☐☐ **OR** ☐ Tick if not done

Serum free light chain: Lambda (mg/L) ☐☐☐•☐☐ **OR** ☐ Tick if not done

Serum free light chain Kappa/Lambda ratio: ☐☐☐•☐☐ Normal range of Kappa/Lambda FLC ratio: ☐ – ☐

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 <u>one</u> only):* ☐ 1= Kappa 2= Lambda 3 = N/A

Immunofixation (only to confirm CR)

Immunofixation Serum ☐ 1= Positive 2= Negative 3= Not done Date of test D D M M Y Y Y Y

Immunofixation Urine ☐ 1= Positive 2= Negative 3= Not done Date of test D D M M Y Y Y Y

Day 100 post-ASCT Form

Imaging *(If clinically indicated or for response assessment if persistent soft tissue plasmacytomas present)*

NB: If patient is participating in PET-CT sub study please complete section at the end of this page

		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= Evidence of myeloma 2= No evidence of myeloma 3= Not done	D D M M Y Y Y Y	
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

Has an increase in number or size of lytic bone lesions been seen on any radiograph? 1 = Yes 2 = No

Day 100 post-ASCT Form

Response day 100 post-ACST

Date of response assessment: D D M M Y Y Y Y

Patient's response to ASCT and high-dose Melphalan treatment: *(choose one option only)* ☐

1= sCR
2= CR
3= VGPR
4= PR
5= MR
6= SD

Patient may proceed to maintenance treatment *(please ensure a treatment summary form is submitted)*

7= PD — *Patient off protocol treatment—to be followed up as per protocol (Complete first progression and treatment summary form)*

8= Unable to assess—
Specify reason:

Is this response confirmed? (1=yes, 2=no) *(refer to IMWG criteria/protocol appendix 3)* ☐

Date confirmed: D D M M Y Y Y Y

Investigator name (print):

Investigator signature:

Date signed: D D M M Y Y Y Y

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

Cardamon

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

Treatment Summary Form

Patient Initials	☐☐☐
Trial Number	C A R – ☐☐☐

(This form has 3 pages including cover sheet)

Please send forms to:

Cardamon Trial Coordinator
CR UK & UCL Cancer Trials Centre
90 Tottenham Court Road
London W1T 4TJ

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

Additional instructions for completing forms

The treatment summary form collects details of the patient's treatment up until the start of maintenance.

Specific fields:

- Total number of cycles should include all treatment cycles regardless of whether the cycle was completed —even if a patient completed only 1 day of a cycle, it is considered a cycle.

Completing forms

- Ensure all entries are clear, legible and written in black ink
- Avoid the use of abbreviations and acronyms
- **Do not leave any fields blank. In case of missing data**
  - ND (not done) if a test has not been performed or a measure not taken. If applicable state the reason
  - NA (not applicable) if a measure if not required
  - NK (not known) if data is unknown. This should only be used once every effort to obtain the data has been exhausted.
- CRFs may only be completed by an appropriately qualified individual delegated as responsible by the PI on the site delegation log
- CRF Footer section
  - The "completed by" Name should be legible
  - Each CRF should be signed and dated by the person completing the form
  - Do not complete the *UCL CTC Use only* section
- **The CRF should be sent/faxed to the Cancer Trials Centre (CTC) with a copy retained at the Site** (ensure when photocopying the page that the copy is added to the CRF booklet in the same place where the original was stored)

If you have any questions about how to complete this form please contact the Cardamon Trial Coordinator on: 020 7679 9860

Treatment Summary Form

To be completed for all patients

Did patient receive full protocol treatment? ☐ 1= Yes, please complete this section only 2= No, please complete both sections

Date treatment stopped/completed: D D M M Y Y Y Y

Total number of CarCyDex treatment received: (Induction + Consolidation) ☐

Did patient have a Melphalan conditioned ASCT? ☐ 1= Yes 2= No

Will the patient start maintenance Carfilzomib? ☐ 1= Yes 2= No

---

Specify a reason for discontinuation or not completing protocol treatment: ☐ *(choose one option only from below)*
(This includes Induction, Consolidation, PBSCH and ASCT where applicable)

1 = Disease Progression / Relapse *(Please complete a Progression/Relapse form)*

2 = Death *(Please complete a Death form)*

3 = Toxicity , please specify: ☐
(Please complete an AE/SAE form as appropriate)

4 = Lost to follow up *(Please complete a Withdrawal/Lost to Follow up form*

5 =Intercurrent illness preventing further treatment, please specify: ☐

6 = Inadequate harvest

7 =Other, please specify: ☐

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

Cardamon

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

Maintenance Form

Patient Initials	☐☐☐
Trial Number	C A R – ☐☐☐
Cycle number	☐☐

(This form has 7 pages including cover sheet)

Please send forms to:

Cardamon Trial Coordinator
CR UK & UCL Cancer Trials Centre
90 Tottenham Court Road
London W1T 4TJ

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**

Additional instructions for completing forms

The Maintenance Form collects details of the patient's maintenance treatment; in the absence of PD, a patient may receive up to 18 cycles of maintenance.

Specific Fields

- Cycle number—please take cycle number from the start of maintenance not all treatment i.e. for patients on the consolidation arm the first cycle will be cycle 1 not cycle 9
- Omission/Reduction/Delay: Please do not leave these blank, if there were no omissions, reductions or delays please ensure that you have entered "0" in each box. A discrepancy will be raised for all fields left blank
- Please ensure that you are using the correct units (i.e. haemoglobin in g/dL). If your local report uses different units please convert these before entering them on the form.
- Response assessments should be only be carried out by the principal investigator or co-investigator
- The response assessment section for cycle 1 should be left blank, however, paraprotein, serum free light chain and urinary Bence Jones protein levels must be recorded if available
- Disease response assessment should be based on blood and/or urine tests performed at the start of each cycle (day 1, ± 7 days), this must be assessed by the PI or delegated investigator (see appendix 3 of protocol)
- Disease response for each cycle must be assessed according to the paraprotein/BJP/SFLC results of tests performed at the beginning of the subsequent cycle, for example, response to cycle 1 would be assessed on cycle 2, day 1, and documented on the cycle 2 CRF
- At the end of maintenance, disease assessment must be performed within 14 days of the last treatment. This should be reported on the maintenance summary CRF
- Please ensure a progression/relapse form is submitted for patients with progressive disease

Completing forms

- Ensure all entries are clear, legible and written in black ink
- Avoid the use of abbreviations and acronyms
- **Do not leave any fields blank. In case of missing data**
    - ND (not done) if a test has not been performed or a measure not taken. If applicable state the reason
    - NA (not applicable) if a measure is not applicable
    - NK (not known) if data is unknown. This should only be used once every effort to obtain the data has been exhausted.
- CRFs may only be completed by an appropriately qualified individual delegated as responsible by the PI on the site delegation log
- CRF Footer section
    - The "completed by" Name should be legible
    - Each CRF should be signed and dated by the person completing the form
    - Do not complete the *UCL CTC Use only* section
- **The CRF should be sent/faxed to the Cancer Trials Centre (CTC) with a copy retained at the Site** (ensure when photocopying the page that the copy is added to the CRF booklet in the same place where the original was stored)

If you have any questions about how to complete this form please contact the Cardamon Trial Coordinator on: 020 7679 9860

Maintenance Form

Cycle No: ☐☐

Haematology

Test	Day 1 result	Day 8 result	Day 15 result
Date (dd/mm/yyyy)			
Haemoglobin (g/dL)			
WBC (x10^9/L)			
Platelets (x 10^9/L)			
Neutrophils (x10^9/L)			
Lymphocytes (x 10^9/L)			
Blood pressure (mmHg)			

- Patients must have FBC and biochemistry tests prior to days 1, 8, & 15 of each cycle
- The validity period for FBC is 48 hours, and for biochemistry it is 72 hours

Maintenance Form

Cycle No:

Biochemistry

Test	Day 1 result	Day 8 result	Day 15 result
Date (dd/mm/yyyy)			
Calcium (corrected) (mmol/L)			
Potassium (mmol/L)			
Phosphate (mmol/L)			
Urea (mmol/L)			
Sodium (mmol/L)			
Serum Urate (µmol/L)			
Creatinine (µmol/L)			
Creatinine clearance (ml/min) *if clinically indicated, otherwise enter ND*			
Albumin (g/L)			
Bilirubin (µmol/L)			
Alkaline Phosphatase (IU/L)			
Aspartate Transaminase (IU/L)			
Alanine Transaminase (IU/L)			

Adverse events

Did the patient experience any adverse events? ☐ 1 = Yes *(please ensure adverse event form is submitted)* 2 = No

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

Maintenance Form

Cycle No:

Efficacy assessments

Date of test D D M M Y Y Y Y

If patient has secretory myeloma, please complete this section:

Paraprotein expression *(choose one option only)*
1= Single paraprotein expressed
2= Light chain only
3 = Biclonal

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 paraprotein type: (*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) • **OR** Tick if not done

Serum free light chain: Lambda (mg/L) • **OR** Tick if not done

Serum free light chain Kappa/Lambda ratio: •

Normal range of Kappa/Lambda FLC ratio: –

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 (only to confirm CR)

Immunofixation Serum
1= Positive
2= Negative
3= Not done

Date of test D D M M Y Y Y Y

Immunofixation Urine
1= Positive
2= Negative
3= Not done

Date of test D D M M Y Y Y Y

UCL CTC Use only: Form received: _____ Date form entered: _____ Initials: _____

Maintenance Form

Cycle No: ☐☐ ***Please note: this page should not be completed in cycle 1***

Response assessment

This section must be completed and signed by the local principal investigator / delegated investigator and done on day 1 of each cycle (from cycle 2 onwards)

Date of response assessment: D D M M Y Y Y Y

Patient's response to maintenance treatment: ☐
(choose <u>one</u> option only)
(e.g. this is the response to last cycle received, i.e. cycle 1 would be assessed on cycle 2, day 1 and documented on the cycle 2 CRF)

1= sCR
2= CR
3= VGPR
4= PR
5= MR
6= SD
7= PD — *Patient off protocol treatment—to be followed up as per protocol*
(Complete first progression and treatment summary form)
8= Unable to assess—
Specify reason:

Investigator name (print):

Investigator signature:

Date signed: D D M M Y Y Y Y

- Disease response assessment should be based on blood and/or urine tests performed at the start of each cycle (day 1, ± 7 days), this must be assessed by the PI or delegated investigator (see appendix 3 of protocol)
- Disease response for each cycle must be assessed according to the paraprotein/BJP/SFLC results of tests performed at the beginning of the subsequent cycle, for example, response to cycle 1 would be assessed on cycle 2, day 1, and documented on the cycle 2 CRF.
- At the end of maintenance, disease assessment must be performed within 14 days of the last treatment. This should be reported on the maintenance summary CRF

Maintenance Form

Cycle No:

Date cycle started: D D M M Y Y Y Y

Patient BSA . m^2 *Patients with a BSA >2.2m^2 should receive dose based on BSA of 2.2m^2*

Did the patient receive dexamethasone (10mg) on the day of administration and day after each dosing in line with the protocol? 1 = Yes
2 = No—please specify reason below:

Any delays reductions or omissions during this cycle of maintenance? 1 = Yes
2 = No

Please complete all boxes in table below (if no delay / reduction / omission, please enter = 0)

Drug	Day	Dose given	Omission (see codes below)	Reduction (see codes below)	Delay (see codes below)
Carfilzomib (56mg/m^2, except cycle 1 day 1 when patients should receive 20mg/m^2)	1	mg			
	8	mg			
	15	mg			

0=No delay/reduction/omission, 1=Neurotoxicity, 2=Hepatotoxicity, 3=Cardiotoxicity 4=Haematological Toxicity, 5=Infusion-related toxicity 6=Pancreatitis 7=Patient Choice, 8=Clinician Choice, 9=Administrative, 10=Tumour Flare reaction, 11=Tumour Lysis syndrome, 12=Other (specify below), 13=Protocol approved reduction/omission

12 = OTHER Reduction/Delay/Omission Reason

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

UCL CTC Use only: Form received: _____ Date form entered: _____ Initials: _____

Cardamon

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

6 Month Post-Start of Maintenance Form

Patient Initials	☐☐☐
Trial Number	C A R – ☐☐☐

(This form has 6 pages including cover sheet)

Please send forms to:

Cardamon Trial Coordinator
CR UK & UCL Cancer Trials Centre
90 Tottenham Court Road
London W1T 4TJ

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**

Additional instructions for completing forms

The 6 Month Post-Start of Maintenance Form should be completed after the patient has completed 6 months of maintenance, and sent along with Maintenance cycle 6

Completing forms

- Ensure all entries are clear, legible and written in black ink
- Avoid the use of abbreviations and acronyms
- **Do not leave any fields blank. In case of missing data**
  - ND (not done) if a test has not been performed or a measure not taken. If applicable state the reason
  - NA (not applicable) if a measure is not applicable
  - NK (not known) if data is unknown. This should only be used once every effort to obtain the data has been exhausted.
- CRFs may only be completed by an appropriately qualified individual delegated as responsible by the PI on the site delegation log
- CRF Footer section
  - The "completed by" Name should be legible
  - Each CRF should be signed and dated by the person completing the form
  - Do not complete the *UCL CTC Use only* section
- **The CRF should be sent/faxed to the Cancer Trials Centre (CTC) with a copy retained at the Site** (ensure when photocopying the page that the copy is added to the CRF booklet in the same place where the original was stored)

If you have any questions about how to complete this form please contact the Cardamon Trial Coordinator on: 020 7679 9860

6 Month Post-Start of Maintenance Form

Visit date D D M M Y Y Y Y

Has the Quality of Life (QoL) been completed? [ ] 1=Yes; please ensure the form is attached 3=No, please provide reason if not done: [ ]

Date of QoL completion: D D M M Y Y Y Y

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

Bone marrow aspirate sample must be sent to HMDS, Leeds 6 months post-start of maintenance

	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

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

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	[ ]

6 Month Post-Start of Maintenance Form

PET sub study: 6 month post-start of Maintenance scan details

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

Date of PET-CT: D D M M Y Y Y Y

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

Efficacy assessments

Date of test D D M M Y Y Y Y

If patient has secretory myeloma, please complete this section:

Paraprotein expression *(choose <u>one</u> option only)* ☐
1= Single paraprotein expressed
2= Light chain only
3 = Biclonal

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 paraprotein type: ☐ *(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) ☐☐☐•☐☐ **OR** ☐ Tick if not done

Serum free light chain: Lambda (mg/L) ☐☐☐•☐☐ **OR** ☐ Tick if not done

Serum free light chain Kappa/Lambda ratio: ☐☐☐•☐☐ Normal range of Kappa/ Lambda FLC ratio: ☐☐☐ – ☐☐☐

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 <u>one</u> only):* ☐
1= Kappa
2= Lambda
3 = N/A

Immunofixation (only to confirm CR)

Immunofixation Serum ☐
1= Positive
2= Negative
3= Not done
Date of test D D M M Y Y Y Y

Immunofixation Urine ☐
1= Positive
2= Negative
3= Not done
Date of test D D M M Y Y Y Y

6 Month Post-Start of Maintenance Form

Imaging *(If clinically indicated or for response assessment if persistent soft tissue plasmacytomas present)*

NB: If patient is participating in PET-CT sub study please complete section at the end of this page

		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= Evidence of myeloma 2= No evidence of myeloma 3= Not done	D D M M Y Y Y Y	
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

Has an increase in number or size of lytic bone lesions been seen on any radiograph? 1 = Yes 2 = No

6 Month Post-Start of Maintenance Form

Response 6 months post-start of maintenance

Date of response assessment: D D M M Y Y Y Y

Patient's response to maintenance treatment: *(choose one option only)*

1= sCR
2= CR
3= VGPR
4= PR
5= MR
6= SD

7= PD — *Patient off protocol treatment—to be followed up as per protocol (Complete first progression and treatment summary form)*

8= Unable to assess—
Specify reason:

Investigator name (print):

Investigator signature:

Date signed: D D M M Y Y Y Y

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

Cardamon

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

End of Maintenance Form

Patient Initials	☐☐☐
Trial Number	C A R – ☐☐☐

(This form has 5 pages including cover sheet)

Please send forms to:

Cardamon Trial Coordinator
CR UK & UCL Cancer Trials Centre
90 Tottenham Court Road
London W1T 4TJ

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**

Additional instructions for completing forms

The End of Maintenance form collects details of the patient's response to maintenance treatment. Assessments are to be performed within 14 days of completing the last cycle of maintenance.

Specific Fields

- Please ensure that you are using the correct units (i.e. haemoglobin in g/dL). If your local report uses different units please convert these before entering them on the form
- If any efficacy tests have not been done because they are not clinically indication, please ensure that you complete the boxes with ND to confirm that the tests were not done. A discrepancy will be raised for those fields left completely blank
- Disease response should be confirmed by a local investigator
- Please ensure a progression/relapse form is submitted for patients with progressive disease

Completing forms

- Ensure all entries are clear, legible and written in black ink
- Avoid the use of abbreviations and acronyms
- **Do not leave any fields blank. In case of missing data**
  - ND (not done) if a test has not been performed or a measure not taken. If applicable state the reason
  - NA (not applicable) if a measure is not applicable
  - NK (not known) if data is unknown. This should only be used once every effort to obtain the data has been exhausted
- The Principal Investigator (PI) is responsible for the accuracy of the data reported on the CRF
- Please ensure that all adverse events are recorded on the adverse event form and the form is attached
- CRFs may only be completed by an appropriately qualified individual delegated as responsible by the PI on the site delegation log
- CRF Footer section
  - The "completed by" Name should be legible
  - Each CRF should be signed and dated by the person completing the form
  - Do not complete the *UCL CTC Use only* section
- **The CRF should be sent/faxed to the Cancer Trials Centre (CTC) with a copy retained at the Site** (ensure when photocopying the page that the copy is added to the CRF booklet in the same place where the original was stored)

If you have any questions about how to complete this form please contact the Cardamon Trial Coordinator on: 020 7679 9860

End of Maintenance Form

Adverse events

Did the patient experience any adverse events between their last cycle of maintenance and their end of maintenance assessment? ☐

1 = Yes *(please ensure adverse event form is submitted)*
2 = No

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

Bone marrow biopsies (to confirm CR only)

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

If No to the above, specify a reason: ☐

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	☐

End of Maintenance Form

Efficacy assessments

Date of test D D M M Y Y Y Y

If patient has secretory myeloma, please complete this section:

Paraprotein expression *(choose one option only)*
1= Single paraprotein expressed
2= Light chain only
3 = Biclonal

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 paraprotein type: *(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) • **OR** Tick if not done

Serum free light chain: Lambda (mg/L) • **OR** Tick if not done

Serum free light chain Kappa/Lambda ratio: •

Normal range of Kappa/Lambda FLC ratio: –

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 (only to confirm CR)

Immunofixation Serum
1= Positive
2= Negative
3= Not done

Date of test D D M M Y Y Y Y

Immunofixation Urine
1= Positive
2= Negative
3= Not done

Date of test D D M M Y Y Y Y

End of Maintenance Form

Imaging *(If clinically indicated or for response assessment if persistent soft tissue plasmacytomas present)*

		Date of test (D D M M Y Y Y Y)	Lytic or focal lesions? 1= Yes 2= No
MRI	1= Evidence of myeloma 2= No evidence of myeloma 3= Not done		
CT	1= Evidence of myeloma 2= No evidence of myeloma 3= Not done		
PET	1= Evidence of myeloma 2= No evidence of myeloma 3= Not done		
Skeletal survey	1= Evidence of myeloma 2= No evidence of myeloma 3= Not done		
Other imaging	1= Evidence of myeloma 2= No evidence of myeloma 3= Not done		

Specify type of other imaging

Has an increase in number or size of lytic bone lesions been seen on any radiograph? 1 = Yes 2 = No

Response at the end of maintenance

Date of response assessment (D D M M Y Y Y Y)

Patient's response to maintenance treatment: *(choose <u>one</u> option only)*

1= sCR
2= CR
3= VGPR
4= PR
5= MR
6= SD
7= PD
8= Unable to assess—Specify reason:

Investigator name (print):

Investigator signature:

Date signed: (D D M M Y Y Y Y)

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)

Cardamon

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

Maintenance Summary Form

Patient Initials	☐☐☐
Trial Number	C A R – ☐☐☐

(This form has 3 pages including cover sheet)

Please send forms to:

Cardamon Trial Coordinator
CR UK & UCL Cancer Trials Centre
90 Tottenham Court Road
London W1T 4TJ

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

Additional instructions for completing forms

The maintenance summary form collects details of the patient's maintenance treatment.

Specific Fields

- Total number of Maintenance cycles should be entered—even if a patient completed only 1 day of a cycle, it is considered a cycle
- Maintenance summary form should be completed at the end of the Maintenance treatment phase. If a patient withdraws at any time during maintenance, the maintenance form detailing the last cycle the patient received should be submitted to the UCL CTC concurrently with this form

Completing forms

- Ensure all entries are clear, legible and written in black ink
- Avoid the use of abbreviations and acronyms
- **Do not leave any fields blank. In case of missing data**
  - ND (not done) if a test has not been performed or a measure not taken. If applicable state the reason
  - NA (not applicable) if a measure if not required
  - NK (not known) if data is unknown. This should only be used once every effort to obtain the data has been exhausted.
- CRFs may only be completed by an appropriately qualified individual delegated as responsible by the PI on the site delegation log
- CRF Footer section
  - The "completed by" Name should be legible
  - Each CRF should be signed and dated by the person completing the form
  - Do not complete the *UCL CTC Use only* section
- **The CRF should be sent/faxed to the Cancer Trials Centre (CTC) with a copy retained at the Site** (ensure when photocopying the page that the copy is added to the CRF booklet in the same place where the original was stored)

If you have any questions about how to complete this form please contact the Cardamon Trial Coordinator on: 020 7679 9860

Maintenance Summary Form

To be completed for all patients

Did patient receive full maintenance treatment? ☐ 1= Yes, please complete this section only 2= No, please complete both sections

Total number of Carfilzomib maintenance treatment cycles received: ☐☐

Date treatment stopped/completed: D D M M Y Y Y Y

Specify a reason for discontinuation or not completing maintenance treatment: ☐
(choose one option only from below)

1 = Disease Progression / Relapse *(Please complete a Progression/Relapse form)*

2 = Death *(Please complete a Death form)*

3 = Toxicity , please specify:
(Please complete an AE/SAE form as appropriate)

4 = Lost to follow up *(Please complete a Lost to Follow up/ Withdrawal form)*

5 =Intercurrent illness preventing further treatment, please specify:

6 =Other, please specify:

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

Cardamon

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

1st Progression/Relapse Form

Patient Initials	☐☐☐
Trial Number	C A R – ☐☐☐

(This form has 7 pages including cover sheet)

Please send forms to:

Cardamon Trial Coordinator
CR UK & UCL Cancer Trials Centre
90 Tottenham Court Road
London W1T 4TJ

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**

Additional instructions for completing forms

The 1st progression/Relapse Form should be completed at the time of first relapse.

Completing forms

- Ensure all entries are clear, legible and written in black ink
- Avoid the use of abbreviations and acronyms
- **Do not leave any fields blank. In case of missing data**
  - ND (not done) if a test has not been performed or a measure not taken. If applicable state the reason
  - NA (not applicable) if a measure is not applicable
  - NK (not known) if data is unknown. This should only be used once every effort to obtain the data has been exhausted.
- CRFs may only be completed by an appropriately qualified individual delegated as responsible by the PI on the site delegation log
- CRF Footer section
  - The "completed by" Name should be legible
  - Each CRF should be signed and dated by the person completing the form
  - Do not complete the *UCL CTC Use only* section
- **The CRF should be sent/faxed to the Cancer Trials Centre (CTC) with a copy retained at the Site** (ensure when photocopying the page that the copy is added to the CRF booklet in the same place where the original was stored)

If you have any questions about how to complete this form please contact the Cardamon Trial Coordinator on: 020 7679 9860

1st Progression/Relapse Form

Haematology

Date of Haematology: D D M M Y Y Y Y

Haemoglobin g/dL [ ][ ] • [ ][ ]

Platelets x 10^9/L [ ][ ][ ][ ]

Neutrophils x10^9/L [ ][ ] • [ ][ ]

WBC Count x10^9/L [ ][ ] • [ ][ ]

Lymphocytes x 10^9/L [ ][ ] • [ ][ ]

Biochemistry

Date of Biochemistry D D M M Y Y Y Y

Calcium (corrected) mmol/L [ ][ ] • [ ][ ]

Potassium mmol/L [ ][ ] • [ ][ ]

Sodium mmol/L [ ][ ][ ]

Creatinine µmol/L [ ][ ][ ] • [ ]

Creatinine Clearance ml/min [ ][ ][ ][ ]

Serum urate µmol/L [ ][ ][ ] • [ ]

Urea (mmol/L) [ ][ ] • [ ][ ]

Bilirubin µmol/L [ ][ ][ ]

Albumin g/L [ ][ ][ ]

Alkaline Phosphatase IU/L [ ][ ][ ][ ]

Alanine Transaminase (ALT) IU/L [ ][ ][ ]

Or

Aspartate Transaminase (AST) IU/L [ ][ ][ ]

Phosphate mmol/L [ ][ ][ ] • [ ]

1st Progression/Relapse 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

Bone marrow aspirate and peripheral blood samples must also be sent to the UCL Cancer Institute Myeloma Lab at relapse
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 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

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

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	☐

1st Progression/Relapse Form

To be completed upon first disease progression/relapse.

Efficacy assessments

Date of test D D M M Y Y Y Y

If patient has secretory myeloma, please complete this section:

Paraprotein expression *(choose one option only)*
1= Single paraprotein expressed
2= Light chain only
3 = Biclonal

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 paraprotein type: *(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) • **OR** Tick if not done

Serum free light chain: Lambda (mg/L) • **OR** Tick if not done

Serum free light chain Kappa/Lambda ratio: •

Normal range of Kappa/Lambda FLC ratio: –

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

1st Progression/Relapse Form

Imaging ***(If clinically indicated or for response assessment if persistent soft tissue plasmacytomas present)***

		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= Evidence of myeloma 2= No evidence of myeloma 3= Not done	D D M M Y Y Y Y	
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

Has an increase in number or size of lytic bone lesions been seen on any radiograph? 1 = Yes 2 = No

1st Progression/Relapse Form

Date of **first** Progression/Relapse D D M M Y Y Y Y

Has progression been confirmed by cytogenetics/FISH? ☐ 1=Yes 2= No; *please provide reason cytogenetics/FISH not performed:*

Please specify the nature of disease progression in the table below: 1=Yes *(See Appendix 3 for further details)* 2=No

≥25% increase in serum paraprotein (absolute increase ≥5g/l)	
≥25% increase in urine light chain excretion (absolute increase ≥200mg/24h)	
≥25% increase in the difference between involved and uninvolved light chains (absolute increase ≥100mg/l)	
≥25% increase in bone marrow plasma cell percentage (absolute increase ≥10%)	
Development of new lytic bone lesions or soft tissue plasmacytomas	
Definite increase in the size of existing bone lesions or soft tissue plasmacytomas	
Development of hypercalcaemia (>2.8mmol/l) attributed solely to myeloma	
Other, please specify below: _____	

Further Treatment Plan:

Is further myeloma treatment planned? *(choose one option only)* ☐ 1= Yes *(please complete treatment details and start date below)* 2= Palliation/no further treatment 3= Watch and wait or not known at present

If **Yes**, please specify the treatment:

and provide the start date : D D M M Y Y Y Y

Is Salvage ASCT planned for this patient in second remission? ☐ 1= Yes 2= No, please complete below 3= Not known at this time, please amend this form once this information is available

If **No**, please specify a reason for not planning to proceed to salvage ASCT:

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

Cardamon

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

2nd Progression/Relapse Form

Patient Initials	☐☐☐
Trial Number	C A R – ☐☐☐

(This form has 4 pages including cover sheet)

Please send forms to:

Cardamon Trial Coordinator
CR UK & UCL Cancer Trials Centre
90 Tottenham Court Road
London W1T 4TJ

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**

Additional instructions for completing forms

The 2nd Progression/Relapse Form should be completed at the time and in the event of a second relapse.

Completing forms

- Ensure all entries are clear, legible and written in black ink
- Avoid the use of abbreviations and acronyms
- **Do not leave any fields blank. In case of missing data**
  - ND (not done) if a test has not been performed or a measure not taken. If applicable state the reason
  - NA (not applicable) if a measure if not required
  - NK (not known) if data is unknown. This should only be used once every effort to obtain the data has been exhausted
- CRFs may only be completed by an appropriately qualified individual delegated as responsible by the PI on the site delegation log
- CRF Footer section
  - The "completed by" Name should be legible
  - Each CRF should be signed and dated by the person completing the form
  - Do not complete the *UCL CTC Use only* section
- **The CRF should be sent/faxed to the Cancer Trials Centre (CTC) with a copy retained at the Site** (ensure when photocopying the page that the copy is added to the CRF booklet in the same place where the original was stored)

If you have any questions about how to complete this form please contact the Cardamon Trial Coordinator on: 020 7679 9860

2nd Progression/Relapse 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

2nd Progression/Relapse Form

To be completed upon second disease progression/relapse.

Date of **second** Progression/ Relapse D D M M Y Y Y Y

Please specify the nature of disease progression in the table below: 1= Yes 2=No

≥25% increase in serum paraprotein (absolute increase ≥5g/l)*	
≥25% increase in urine light chain excretion (absolute increase ≥200mg/24h)*	
≥25% increase in the difference between involved and uninvolved light chains (absolute increase ≥100mg/l)*	
≥25% increase in bone marrow plasma cell percentage (absolute increase ≥10%)*	
Development of new lytic bone lesions or soft tissue plasmacytomas	
Definite increase in the size of existing bone lesions or soft tissue plasmacytomas	
Development of hypercalcaemia (>2.8mmol/l) attributed solely to myeloma	
Other, please specify below: _____	

*with respect to nadir values after first progression

Further Treatment Plan

Is further myeloma treatment planned? *(choose one option only)* ☐

1= Yes *(please complete treatment details and start date below)*
2= Palliation/no further treatment
3= Watch and wait/not known at present *(please provide update when known)*

If **Yes**, please specify the treatment:

If yes, please provide a start date : D D M M Y Y Y Y

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

Cardamon

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

Follow Up form / Long Term Follow Up Form

Patient Initials	☐☐☐
Trial Number	C A R – ☐☐☐

(This form has 3 pages including cover sheet)

Please send forms to:

Cardamon Trial Coordinator
CR UK & UCL Cancer Trials Centre
90 Tottenham Court Road
London W1T 4TJ

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**

Additional instructions for completing forms

The Follow up/Long Term Follow up Form is used to follow up all patients registered to the trial (provided they have not withdrawn consent) and to monitor overall and progression free survival. See section 9.7 of the protocol for further details.

Completing forms

- Ensure all entries are clear, legible and written in black ink
- Avoid the use of abbreviations and acronyms
- **Do not leave any fields blank. In case of missing data**
  - ND (not done) if a test has not been performed or a measure not taken. If applicable state the reason
  - NA (not applicable) if a measure is not applicable
  - NK (not known) if data is unknown. This should only be used once every effort to obtain the data has been exhausted.
- CRFs may only be completed by an appropriately qualified individual delegated as responsible by the PI on the site delegation log
- CRF Footer section
  - The "completed by" Name should be legible
  - Each CRF should be signed and dated by the person completing the form
  - Do not complete the *UCL CTC Use only* section
- **The CRF should be sent/faxed to the Cancer Trials Centre (CTC) with a copy retained at the Site** (ensure when photocopying the page that the copy is added to the CRF booklet in the same place where the original was stored)
-

Follow Up / Long Term Follow Up Schedule (see section 9.7 of the protocol)

- Patients who complete all trial treatment (induction, consolidation/ASCT and maintenance) or discontinue study treatment for any reason other than progression/inadequate response/ inadequate bone marrow harvest should be followed up 3 monthly for 12 months post last trial treatment. After 12 months, patients should enter long term follow-up—see section 9.9 of protocol for further details
- Patients who progress at any point during the study treatment, achieve <PR after induction treatment, or have an inadequate stem cell harvest should continue to be followed up for survival and subsequent treatment information **at 6 monthly intervals from the date of progression as per long-term follow-up**
- Patients on long term follow up should be seen according to routine clinical practice, though not less than every 6 months
- A progression/relapse form should be submitted as soon as possible in the case of a relapse, regardless of the time until the next follow up visit

If you have any questions about how to complete this form please contact the Cardamon Trial Coordinator on: 020 7679 9860

Follow Up / Long Term Follow Up Form

Date of Visit: D D M M Y Y Y Y

Follow up month: ___ Months post treatment / relapse (delete as applicable)

Since the patient's last follow up has the patient or patient's partner become pregnant? ___ 1 = Yes *(please complete the pregnancy report form)*

Has the patient developed a secondary malignancy since last visit? ___ 1 = Yes 2 = No

If yes please give details: _____

Patient status: ___
1 = Alive without progression
2 = Alive with progression/relapse (*Please complete disease progression form for 1st or 2nd relapse)*
3 = Deceased (*Please complete death form)*
4= Alive, in second remission
5= Alive, in third or later remission

If progressed, enter date of progression: D D M M Y Y Y Y

Has the patient had any further myeloma treatment since last visit? ___ 1 = Yes 2 = No

If yes, start date of further myeloma treatment? D D M M Y Y Y Y

Type of myeloma treatment: ___
1 = Chemotherapy
2 = Radiotherapy
4 = Biological therapy
5 = Combination therapy
6 = Other

Please specify the treatment regimen given: _____

Best response to further treatment given: *(choose one only)* ___
1= sCR 5= MR
2= CR 6= SD
3= VGPR 7= PD
4= PR 8= not yet known (*please complete at next follow-up visit)*

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

Cardamon

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

Withdrawal/Lost to Follow Up Form

Patient Initials	☐☐☐
Trial Number	C A R – ☐☐☐

(This form has 3 pages including cover sheet)

Please send forms to:

Cardamon Trial Coordinator
CR UK & UCL Cancer Trials Centre
90 Tottenham Court Road
London W1T 4TJ

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**

Additional instructions for completing forms

The Withdrawal/Loss to Follow Up Form is used to record details of a patient's withdrawing from the trial, or those lost to follow up

- In addition to this form, if the patient withdraws before they have started their first cycle of maintenance then sites should complete the **Treatment Summary Form** . For all withdrawals or losses to follow up after the patient has started maintenance treatment please complete the **Maintenance Summary Form**

Completing forms

- Ensure all entries are clear, legible and written in black ink
- Avoid the use of abbreviations and acronyms
- **Do not leave any fields blank. In case of missing data**
  - ND (not done) if a test has not been performed or a measure not taken. If applicable state the reason
  - NA (not applicable) if a measure is not applicable
  - NK (not known) if data is unknown. This should only be used once every effort to obtain the data has been exhausted
- CRFs may only be completed by an appropriately qualified individual delegated as responsible by the PI on the site delegation log
- CRF Footer section
  - The "completed by" Name should be legible Each CRF should be signed and dated by the person completing the form
  - Do not complete the *UCL CTC Use only* section
- **The CRF should be sent/faxed to the Cancer Trials Centre (CTC) with a copy retained at the Site** (ensure when photocopying the page that the copy is added to the CRF booklet in the same place where the original was stored)

If you have any questions about how to complete this form please contact the Cardamon Trial Coordinator on: 020 7679 9860

Withdrawal/Lost to Follow Up Form

Please specify patient's status:

☐ **Lost to Follow Up** *Please complete Sections A & C*

☐ **Withdrawn consent** *Please complete Sections B & C*

A: Lost to Follow Up

Date the patient was last known to be alive (DD/MM/YYYY) D D M M Y Y Y Y

Reason patient was lost to follow up

☐ Moved Away ☐ Emigrated ☐ Lost Contact ☐ Discharged to GP

☐ Other (specify reason) _____

B: Withdrawn

Date patient withdrew (DD/MM/YYYY) _ _ _ _ _ _ _ _

Please specify which aspects of the trial the patient has withdrawn from (*even though they cannot be personally identified in any results or publications i.e. anonymity will be preserved*):

1. Trial Follow Up
Patient has withdrawn from all future follow up visits and scans mandated by the trial protocol. Outcome data will continue to be collected unless indicated below.
☐ 1 = Yes 2 = No

2. Future Data Collection: Hospital Notes/GP
Patient has withdrawn consent for collection of any further data from hospital notes or their GP.
☐ 1 = Yes 2 = No

3. Future Data Collection: NHS Information Service
Patient has withdrawn consent for collection of information about their future health status from the NHS Information Service
☐ 1 = Yes 2 = No

4. Biological Samples
Patient withdraws consent for any previously collected tissue/blood samples to be used in future research
☐ 1 = Yes 2 = No

C: Contact Details

If available, please provide contact details of patient's GP or referral hospital to assist with collection of data regarding patient's future health status (*only if patient has consented, and has not withdrawn such consent*)

Contact Name: _____ Contact's Role (GP, Nurse etc): _____

Contact Address: _____

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

UCL CTC Use only: Form received: _____ Date form entered: _____ Initials: _____

Cardamon

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

Death Form

Patient Initials	☐☐☐
Trial Number	C A R – ☐☐☐

(This form has 3 pages including cover sheet)

Please send forms to:

Cardamon Trial Coordinator
CR UK & UCL Cancer Trials Centre
90 Tottenham Court Road
London W1T 4TJ

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

Additional instructions for completing forms

The Death Form is used to record the patient's cause of death

Completing forms

- Ensure all entries are clear, legible and written in black ink
- Avoid the use of abbreviations and acronyms
- **Do not leave any fields blank. In case of missing data**
    - ND (not done) if a test has not been performed or a measure not taken. If applicable state the reason
    - NA (not applicable) if a measure if not required
    - NK (not known) if data is unknown. This should only be used once every effort to obtain the data has been exhausted.
- CRFs may only be completed by an appropriately qualified individual delegated as responsible by the PI on the site delegation log
- CRF Footer section
    - The "completed by" Name should be legible
    - Each CRF should be signed and dated by the person completing the form
    - Do not complete the *UCL CTC Use only* section
- **The CRF should be sent/faxed to the Cancer Trials Centre (CTC) with a copy retained at the Site** (ensure when photocopying the page that the copy is added to the CRF booklet in the same place where the original was stored)

If you have any questions about how to complete this form please contact the Cardamon Trial Coordinator on: 020 7679 9860

Death Form

To be completed upon patient's death

Date of Death D D M M Y Y Y Y

Primary cause of Death*
(choose one option only from below)

1= Disease Progression

2= Treatment related toxicity, please specify:

3= Infection

4= Cardiac event

5= Renal failure

6= Other malignancy, please complete below:

Date confirmed D D M M Y Y Y Y

Type of cancer:

7= Other, please specify:

Please ensure that in case of a death due to treatment related toxicity & complications an SAE form is completed and faxed to UCL CTC within 1 business day of site becoming aware of death

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