Justification for CARiAD close-out arrangements

CARiAD recruitment ended 15/3/2019. As of 15/5/2019, three patients of dyads recruited to the trial are still alive. This document details the close-out arrangements for these dyads.

Only data available more than one calendar week (i.e. five working days) before the MACRO data lock date will be included in the primary analysis. This allows time for the trial team to input the data in readiness for MACRO data lock.

The MACRO data lock is set for Friday 12/7/2019 at 17:00, hence only data available up to Monday 8/7/2019 at 09:00 will be included in the primary analysis. Data collected after this time may be used in subsequent analyses.

The study end date is 30/9/2019.

Intervention arm

If the **patient dies before 27/5/2019**, research nurse (RN) follow-up as per the protocol is possible. Normal trial procedures will continue.

If the **patient dies after 27/5/2019** (i.e. within 6 weeks of 8/7/2019), RN follow-up will be offered 6-8 weeks after bereavement. The follow-up data will not be included in the primary analysis, but may be used in subsequent analyses. The carer will be made aware that this is the case.

Reason to continue RN follow-up: Data available for subsequent analyses.
Supporting documents:
Information sheet for bereaved carers (CARiAD Close out PIS Carer Continuation PB v1 150519)

If, on 8/7/2019, **the patient is not deemed to be in the last days of life AND the carer has not been trained to give injections**, the dyad will be withdrawn from the trial. There will be a discussion between the research team and the patient's clinical team on who is best placed to relay that information to the patient and carer (supported by an information sheet). The research team will assist the clinical team in informing all clinicians who should know of the withdrawal.

Reason for withdrawal: The patient is not deemed to be in the last days of life AND the carer has not been trained to give injections, this is a safe point for withdrawal from the trial.
Supporting documents:
Information sheet for dyads (CARiAD Close out PIS Dyad Intervention Withdrawal A v1 150519)
Information sheet for HCPs (CARiAD Close out PIS HCP Intervention Withdrawal A v1 150519)

If, on 8/7/2019, **the patient is not deemed to be in the last days of life BUT the carer has been trained to give injections**, the dyad will be withdrawn from the trial. There will be a discussion between the research team and the patient's clinical team on who is best placed in the clinical team to relay that information to the patient and carer (supported by an information sheet). The research team will assist the clinical team in informing all clinicians who should know of the withdrawal. The clinical team will support the carer in giving injectable medication in due course (i.e. when the patient reaches the last days of life), but CARiAD trial materials cannot be used.

Reason for withdrawal: trial mechanisms will not be available past the study end date when the patient reaches the last days of life.

Supporting documents:

Information sheet for dyads (CARiAD Close out PIS Dyad Intervention Withdrawal B v1 150519)

Information sheet for HCPs (CARiAD Close out PIS HCP Intervention Withdrawal B v1 150519)

If, on 8/7/2019, **the patient is deemed to be in the last days of life AND the carer has been trained to give injections BUT the carer has not administered any injections**, the dyad will continue in the trial (including RN follow-up 6-8 weeks after bereavement). It will be made clear that data will not be included in the primary analysis, but may be used in subsequent analyses. All trial safety mechanisms will continue until the study end date. The clinical team will have the discussion with the dyad.

Reason to continue in the trial: At this point, the carer would already have been informed of what to expect in the last days of life, and will have prepared themselves mentally that they may need to start giving injections soon. This position aims to strike a balance between following through on a course of action (noting that the safety mechanisms of the trial will still be active for the duration of the patient's life) and the fact that the data will not be used in the primary analysis.

Supporting documents:

Information sheet for dyads (CARiAD Close out PIS Dyad Continuation A v1 150519)

If, on 16/9/2019 (i.e. two weeks before the study end date), **the patient is deemed to be in the last days of life AND the carer has been trained to give injections BUT the carer has not administered any injections**, the dyad will be withdrawn from the trial. There will be a discussion between the research team and the patient's clinical team on who is best placed in the clinical team to relay that information to the patient and carer (supported by an information sheet). The research team will assist the clinical team in informing all clinicians who should know of the withdrawal from the trial. The clinical team will support the carer in giving injectable medication in due course (i.e. when the patient reaches the last days of life), but CARiAD trial materials cannot be used.

Reason for withdrawal: Study end

Supporting documents:

Information sheet for dyads [mainly carer]) (CARiAD Close out PIS Dyad Intervention Withdrawal C v1 150519) (the wording is identical to PIS Dyad Intervention Withdrawal B v1 150519, but label as 'C' and the HCP PISs of these scenarios are different)

Information sheet for HCPs (CARiAD Close out PIS HCP Intervention Withdrawal C v1 150519)

If, on 8/7/2019, **the patient is deemed to be in the last days of life AND the carer has been trained to give injections AND the carer has administered injections**, the dyad will continue in the trial (including RN follow-up 6-8 weeks after bereavement). It will be made clear that data will not be included in the primary analysis, but may be used in subsequent analyses. The trial team will arrange for partially completed diaries to be collected and a fresh copy given for carer-completion. All trial safety mechanisms will continue until the study end date. The clinical team will have the discussion with the dyad (most likely the carer).

Reason to continue in the trial: This follows through on a course of action (noting that the safety mechanisms of the trial will still be active for the duration of the patient's life).
Supporting documents:
Information sheet for dyads (CARiAD Close out PIS Dyad Continuation B v1 150519)

If, on 16/9/2019 (i.e. two weeks before the study end date), **the patient is deemed to be in the last days of life AND the carer has been trained to give injections AND the carer has administered injections**, the dyad will be withdrawn from the trial. There will be a discussion between the research team and the patient's clinical team on who is best placed in the clinical team to relay that information to the patient and carer (supported by an information sheet). The research team will assist the clinical team in informing all clinicians who should know of the withdrawal from the trial. The clinical team will support the carer in giving injectable medication in due course (i.e. when the patient reaches the last days of life), but CARiAD trial materials cannot be used.

Reason for withdrawal: Study end
Supporting documents:
Information sheet for dyads [mainly carer] (CARiAD Close out PIS Dyad Intervention Withdrawal D, v1 150519),
Information sheet for HCPs (CARiAD Close out PIS HCP Intervention Withdrawal D, v1 150519)

Usual care arm

If the **patient dies before 27/5/2019**, research nurse (RN) follow-up as per the protocol is possible. Normal trial procedures will continue.

If the **patient dies after 27/5/2019** (i.e. within 6 weeks of 8/7/2019), RN follow-up will be offered 6-8 weeks after bereavement. The follow-up data will not be included in the primary analysis, but may be used in subsequent analyses. The carer will be made aware that this is the case.

Reason to continue RN follow-up: Data available for subsequent analyses.
Supporting documents:
Information sheet for bereaved carers (CARiAD Close out PIS Carer Continuation PB, v1 150519)

If, on 8/7/2019, **the patient is alive**, the dyad continue in the trial (including RN follow-up 6-8 weeks after bereavement). It will be made clear that the data will not be included in the primary analysis, but may be used in subsequent analyses. The trial team will arrange for partially completed diaries to be collected and a fresh copy given for carer-completion. All trial safety mechanisms will continue until the study end date. The clinical team will have the discussion with the dyad (most likely the carer).

Reason to continue in the trial: This follows through on a course of action (noting that the carer will already be mentally prepared for the last days of life, and safety mechanisms of the trial will still be active for the duration of the patient's life).

Supporting documents:

Information sheet for dyads (CARiAD Close out PIS Dyad Continuation A, v1 150519)

If, on 16/9/2019 (i.e. two weeks before the study end date), **the patient is alive**, the dyad will be withdrawn from the trial. There will be a discussion between the research team and the patient's clinical team on who is best placed to relay that information to the patient and carer (supported by an information sheet). The research team will assist the clinical team in informing all clinicians who should know of the withdrawal from the trial.

Reason for withdrawal: Study end

Supporting documents:

Information sheet for dyads (CARiAD Close out PIS Dyad Usual Care Withdrawal A, v1 150519)

Information sheet for HCPs (CARiAD Close out PIS HCP Usual Care Withdrawal A, v1 150519)