



Protocol Violations and Deviations for the TARDIS Trial

The study should be conducted in accordance with the approved protocol and that changes to that protocol will only be made to protect the safety, rights, or welfare of the subject.

Protocol Violation

A protocol violation is a major deviation from the trial protocol where a participant is enrolled in spite of not fulfilling all the inclusion and exclusion criteria, or where deviations from the protocol could affect the trial delivery or interpretation significantly.

The following baseline characteristics constitute a protocol violation

1. Randomisation > 48 hours from onset of symptoms
2. Participant less than 50 years of age
3. For ischaemic stroke:
 - a. No cranial imaging results available prior to randomisation
 - b. Isolated sensory symptoms, vertigo or dizziness or facial weakness as presenting symptoms of the index event
4. For TIAs:
 - a. Limb weakness and/or dysphasia lasting less than 10 minutes
 - b. ABCD2 score <4 and not a crescendo TIA and not on dual antiplatelet therapy or monotherapy antiplatelets.
5. Failure to obtain appropriate consent prior to randomisation
6. Pre-morbid dependency (mRS) >2
7. Participant unable to swallow and does not have enteral access
8. Baseline cranial imaging shows parenchymal haemorrhagic transformation (PH I/II)
9. Subarachnoid haemorrhage
10. Intracerebral haemorrhage
11. On anticoagulation therapy except low dose low molecular weight heparin
12. Participant has taken dipyridamole between the index event and prior to stroke randomisation, where clopidogrel is the control treatment.
13. Participant has taken clopidogrel between the index event and prior to stroke randomisation, where AD is the control treatment.
14. Thrombolysis less than 24 hours prior to randomisation
15. Presumed cardioembolic stroke or history of atrial fibrillation
16. Concomitant STEMI or NSTEMI
17. Baseline SBP reading >185 mm Hg or DBP > 110 mm Hg
18. Major bleeding within one year prior to randomisation
19. Planned surgery within the 3-month follow-up period
20. Randomising event was secondary to a surgical procedure
21. Glasgow Coma Score < 8
22. Known history of dementia
23. Known probable life expectancy of less than 6 months
24. Unavailable for follow-ups
25. Female patient of childbearing potential, pregnant or breastfeeding at randomisation
26. Patient receiving treatment that they are not randomised to.
27. Patients who do not have a post thrombolysis scan.

28. Patient does not receive the correct loading dose.

The following practice during the trial constitutes a 'protocol violation'

1. Subsequent randomisation into another drug or devices trial
2. Patient does not receive 5 days of randomised treatment in the first seven days and 16 days in the next 3 weeks
3. Failure to complete SAEs where appropriate
4. Failure to complete outcomes where appropriate
5. Follow-up assessments are performed (as opposed to submitted) outside the specified time as shown below:
 - a. 7-day follow-up: >7 days past the due date
 - b. 35-day follow-up: >7 days past the due date
 - c. Hospital event form: >30 days past the due date
 - d. 90-day follow up: >30 days past the due date

Protocol Deviation

A Protocol Deviation is a minor deviation from the protocol that affects the conduct of the trial in a minor way. This includes any deviation from the trial protocol that is not listed as a Protocol Violation. Examples of Deviations are given below but this is not exhaustive.

The following practice during the trial constitutes a 'protocol deviation'

1. Failure to switch to standard treatment following completion of treatment period
2. Patient receives more than 450 mg dipyridamole daily
3. Patient receives >75mg of aspirin or clopidogrel after Day 0
4. Non-receipt of Day 7 or Day 35 Full Blood Count
5. No blood pressure measurements at baseline, D7 or D35 follow-ups
6. Follow-up assessments are performed (as opposed to submitted) outside the specified time as shown below:
 - a. 7-day follow-up: >1day past the due date
 - b. 35-day follow-up: >3days past the due date
 - c. Hospital event form: >7days past the due date
 - d. 90-day follow-up: >7 days past the due date

Review of Protocol Violations and Deviations

Protocol Violations will be reviewed annually by both the Data Monitoring Committee (using unblinded data) and the Trial Steering Committee (with blinding to treatment assignment).

The list of protocol violations and deviations will be updated, as necessary, in a working practice document which will be uploaded and available on the trial website.