Great News! DSMB Recommends Study Continuation & Database Best Practices

Dear DO-IT investigators and study coordinators,

DSMB recommendation: Trial continues as planned

We are pleased to share that the independent **Data and Safety Monitoring Board** has completed its safety review (10% interim analysis). The DSMB **recommended that the trial should continue as planned, without any modifications**, and **did not identify any safety concerns**.

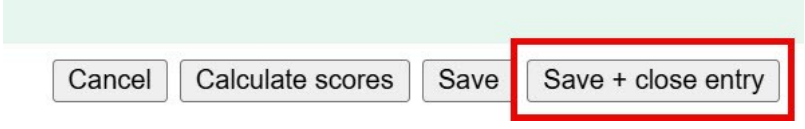
We would like to thank all investigators and study teams for your careful work and timely safety reporting, which made this review possible.

Central Data Monitoring - a few helpful reminders

The latest Central Data Monitoring review identified several recurring issues across multiple sites. Most of these are easy to avoid and a few small adjustments can further improve data quality while reducing the number of queries.

1. Always fully save the eCRF

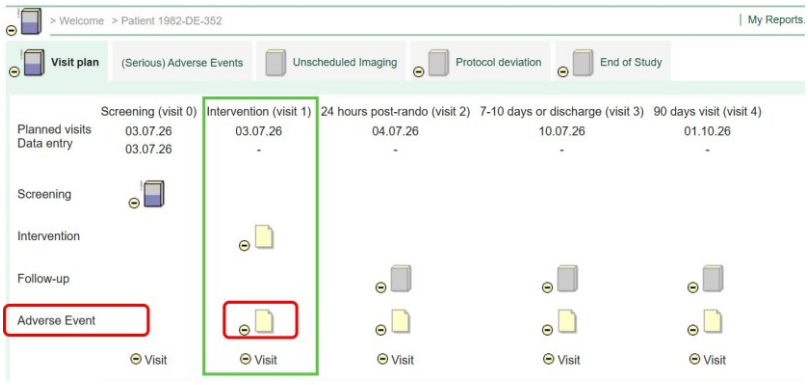
After completing an eCRF, please use **"Save + Close Entry"**. If a soft check appears, a second click on **"Save + Close Entry"** is required. Otherwise, the form remains incomplete and cannot be reviewed, monitored or locked.



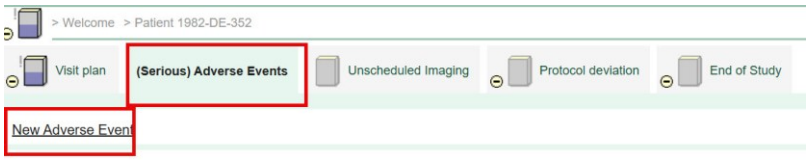
2. AESI documentation

Please remember:

- Enter each AESI in the **visit-specific AESI form** where it occurred.



- Use the separate **(S)AE case node** only if an additional AESI occurred during the same time period.

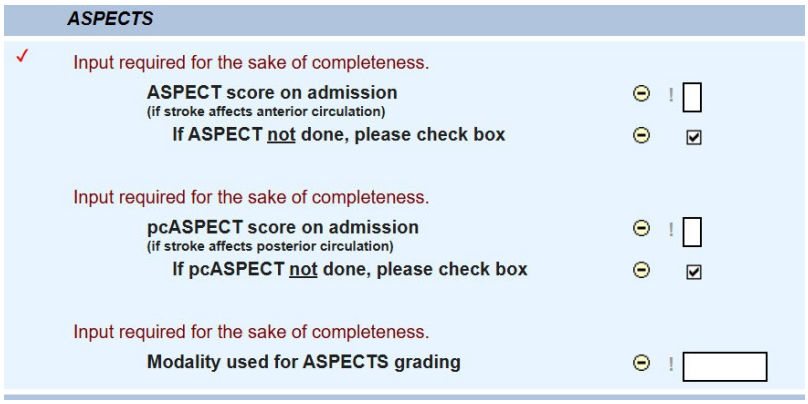


- Update ongoing AESIs in the **original AESI form** rather than creating a new entry at each visit.
- The AESI assessment date should correspond to the visit date.
- If a participant died before a scheduled visit, complete the AESI form according to the study instructions and indicate that the participant had died.

3. ASPECT score

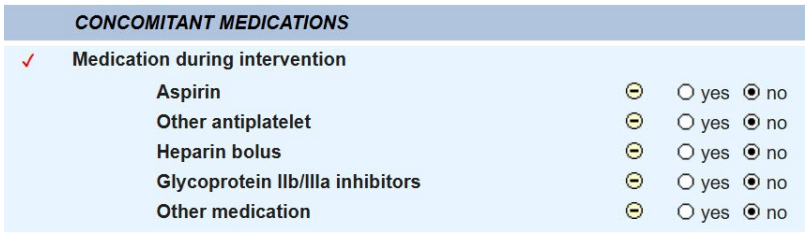
If no ASPECT (or pcASPECT) score was performed:

- tick **"ASPECT score not done"**
- do **not** enter a value of "0".



4. Medication during intervention

Please enter **only medication administered during the intervention** in this section. Regular medication at admission should not be documented here.



5. Visit 2 imaging

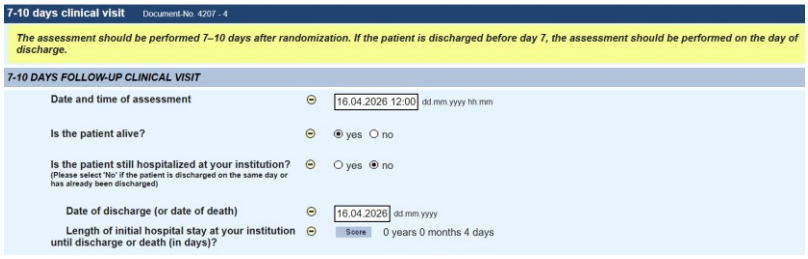
Please schedule the 24-hour imaging to be performed 24 hours (±12 hours) after randomization, regardless of the patient's randomization group or clinical course. These images are essential for assessing our safety outcomes by the blinded core-lab. A plain CT is sufficient in the timeframe from 12-36h after randomization.

6. Visit 3 timing

Visit 3 should be performed:

- 7 - 10 days after randomization, or
- on the day of discharge/death if the participant leaves hospital before Day 7 or dies before that

If the assessment is performed before Day 7 on the day of discharge, click on "no" for "Is the patient still hospitalized at your institution."

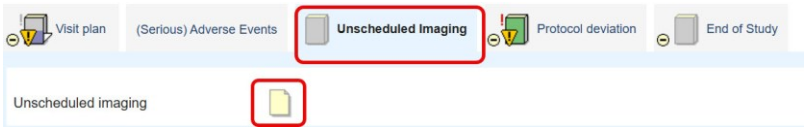


7. Visit 4 after death

If a participant dies before Visit 3, **Visit 4 should not be completed**. In this situation, only the SAE documentation and the End of Study form are required.

8. Unscheduled imaging

Please remember to document all unscheduled imaging examinations in the **"Unscheduled Imaging"** tab.



9. Serious adverse events

SAEs must be reported to the sponsor **within 24 hours of awareness**, in accordance with the protocol. Timely reporting is essential for participant safety and regulatory compliance.

10. Protocol deviations

Please do everything possible to avoid any protocol deviations including cross-overs and missed visits / 24h imaging. However, if something does not go according to plan, please report transparently. If more than one protocol deviation occurs, please create **a separate entry for each deviation** using the **"More"** button at the bottom.

11. Please avoid "Unknown" and complete “unknown” data during follow-up

We have noted that for several baseline variables, approximately 5% (and up to 10% in some cases/sites) of entries are currently marked as "Unknown." While we understand that certain information may not be immediately available upon admission, data completeness is essential to ensure the scientific rigor and validity of our study.Therefore, we kindly ask that you make every effort to resolve these data gaps at later time points. Please review entries marked "Unknown" during follow-up visits and update them with valid responses (e.g., Yes/No) wherever possible. Please note that data monitoring queries for "Unknown" entries will be increased moving forward.

The success of DO-IT depends on the dedication of every participating site. We greatly

appreciate your continued commitment to recruiting participants, ensuring patient safety, and maintaining high-quality study data.
Together, we are generating the evidence needed to answer an important clinical question.
Thank you for your excellent collaboration.

Thank you!

Reach out to us with any questions, concerns of hurdles - we are happy to help you!

DO-IT Principal Investigators	Trial Coordination / Management	Contact details
Thomas Meinel Luciana Catanese Urs Fischer Aristeidis Katsanos David Seiffge Ashkan Shoamanesh	Freschta Zipser-Mohammadzada Nerea Fernandez Trigo Stefanie Abend	Email: do-it@insel.ch Phone: +41 31 632 60 83 +41 31 632 98 84 +41 31 632 67 80

Thank you for your continued commitment and collaboration.

Recruit. Care. Cure. DO-IT!

https://www.linkedin.com/in/do-it-trial-a5b76537a/

https://x.com/DOIT_trial

https://www.doit-trial.ch