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Newsletter March 2018

Safety: Causality

According to ICH GCP Guidelines, an adverse event (AE) is any untoward medical occurrence in a clinical investigation participant. An AE is classified as serious (SAE) when it results in death, is life-threatening, requires in-patient hospitalization or prolongation of an existing hospitalization, or is a congenital anomaly or birth defect.

(Serious) AEs do not necessarily have a causal relationship with the trial procedure. Therefore, the causal relationship between a given AE and the intervention (decompressive craniectomy or best medical treatment) needs to be carefully assessed based on the following criteria:

Relationship	Description
Definitely	A clinical event occurring in a plausible time relationship to intervention arm (or drug administration), and which cannot be explained by concurrent disease or other drugs or chemicals.
Probably	A clinical event with a reasonable time sequence to intervention arm (or drug administration), unlikely to be attributed to concurrent disease or other drugs or chemicals.
Possibly	A clinical event with a reasonable time sequence to intervention arm (or drug administration), but which could also be explained by concurrent disease, other drugs or chemicals.
Unlikely	A clinical event with a temporal relationship to intervention arm (or drug administration) which makes a causal relationship improbable, and in which other drugs, chemicals or underlying disease provide plausible explanations.
Not related	Causal relationship can be ruled out.

Source: adapted from WHO

The assessment of causality always refers to the intervention, which is in SWITCH either DC or BMT. The causality should not refer to underlying diseases (e.g. ICH).

Examples:

- Subgaleal hematoma following bone-flap reimplantation, requiring a new surgery: AE related to procedure → **causality = definite**
- Rebleeding i.e. enlargement of a deep basal ganglia ICH: AE not related to procedure but natural history of ICH → **causality = not related**

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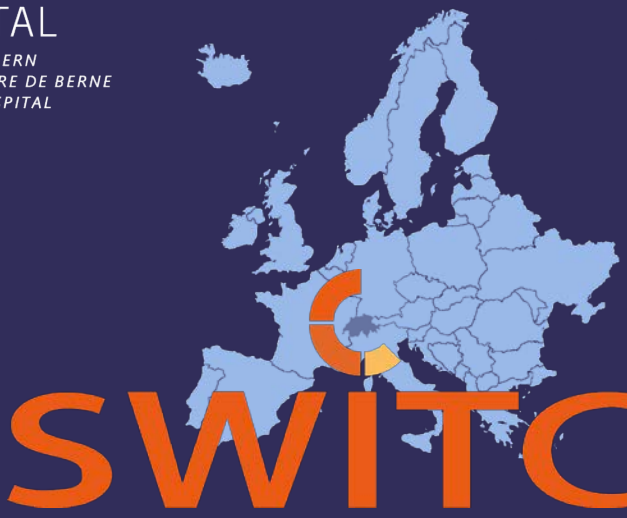

SWITCH

Current patient accrual (28.02.2018)

Randomized trial: 68
Observational arm: 11

Top recruiting sites

1. Bern (12 patients randomized)
2. Berlin (9 patients randomized, 1 patient in observational arm)
2 Helsinki (9 patients randomized, 1 patient in observational arm)
3. Aachen (6 patients randomized)
4. Giessen (4 patients randomized, 3 patients in observational arm)
5. Mainz (4 patients randomized)

SWITCH sites

We currently have 31 sites open for the recruitment of patients.

Recruiting	Aachen, Amsterdam, Barcelona – Bellvitge Hospital, Barcelona – Santa Creu i Sant Pau Hospital, Bern, Berlin, Bonn, Düsseldorf, Erlangen, Erfurt, Essen, Frankfurt, Freiburg, Geneva, Giessen, Göttingen, Helsinki, Innsbruck, Kassel, Linz, Madrid, Mainz, Mannheim, München, Münster, Lübeck, Lucerne, Lugano, Sevilla, Utrecht, Würzburg
Coming soon	Paris, Créteil, Caen, Edinburgh
Planned	Siegen, Tübingen

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