Workshop 3 – Discussion Guide

To Develop Recommendations for:

ACADEMIC AND INDUSTRY SPONSORED TRIALS: PATIENT- LEVEL POOLING EFFORTS

Clinical And Regulatory Issues

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GOAL: This workshop aims to achieve consensus on critical issues necessary to advance our understanding of acute stroke therapies based on completed trials. While discussion can often readily identify key areas of acute stroke that would benefit from pooled analysis, there are often real or perceived barriers to implementation of data pooling and associated analyses. This workshop will consider approaches to maximize collaboration, and to handle design considerations for pooled analyses. The result will be a roadmap for future data pooling efforts in acute stroke.

CONTENT OVERVIEW: The content of this session will be guided by topics arising out of presentations and discussion during the first day of STAIR, and by the enthusiasm and expertise of the group who participate. There will be insufficient time to cover every subject, and so it is desirable that we prioritize discussion towards reaching consensus on issues that are regarded as most important or urgent.
Among the potential topics, the following may be considered:

1. Outstanding Questions
Which therapies (endovascular, thrombolysis, other) currently need some form of pooled analysis and what are the key questions that such an analysis should aim to answer (time window, selection method, etc.)?

2. Existing Pooling Collaborations
Which groups are undertaking pooled analysis, to what extent may they overlap or duplicate each other, is there potential for confused messages or will duplication strengthen the message?

3. Competition

Industry is in a competitive situation, but clinical academics also compete for primacy. How do we achieve the greater good by combining data early, possibly before all trials have completed their data collection? An example from the endovascular field would be trials examining an extended time window (DAWN, DEFUSE, POSITIVE, WAKE-UP). How do we avoid 'queering the pitch' for ongoing trials by declaring a pooled result that parallels a question being asked by an ongoing trial?

4. Collaboration

How do we handle authorship? Combining trials adds a large team of authors from each. Scientific principles need to apply to authorship, yet fairness indicates that individuals should not be disadvantaged. Equally fairness based on financial investment may be a concern for commercial partners or even government funders.

5. Data Pooling

When should data be supplied? Who should hold the data and how many groups should work on the analyses? Once collated, who should have access to data? How do we balance commercial concerns, continued publication plans for publications from individual trials, allow time for thorough examination of research questions on pooled data against modern open access policies and requests from external groups to see data?

Should the data be kept in original formats or combined to a common format? What can be done to enhance uniformity of coding for baseline variables and timing of their collection without compromising desirable innovation and variation in trial design, and without overburdening patients and investigators? Can we even guarantee that we understand all questions in order to harmonize data collection? Will stroke trials networks assist in this or act as a barrier to desirable flexibility?

6. Analysis

Pooling of trial data is an ongoing process. When should analyses on subgroup or subsidiary questions be published, how often should an analysis be updated? Can we learn from Cochrane, rtPA or TREAT investigators' approaches? Should statistical approaches allow for the repeated analyses?