Event Adjudication Changes Key Results in Open-Label Trials: The AFFIRM Experience

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Abstract

Event occurrence assessed at follow-up visits, submitted by unblinded local investigator (cardiologist) based on event definitions (manual of operations).

Methods – Stroke

First stroke was defined as earliest ischemic event for each patient, reported by local investigators.

First adjudicated stroke was defined as earliest ischemic event for each patient as classified by adjudication process.

Goal was to compare the stroke event that would have been counted in a time-to-failure analysis, with and without central adjudication.

Results – Stroke (first event per patient)

The first reported stroke event was confirmed by the adjudication committee 77% (147/189) of the time overall, 83% (73/88) of the time for rate control and 73% (74/101) of the time for rhythm control (p=0.11).

Using reported events, the risk of stroke was 15% higher using rhythm compared to rate. Based on adjudicated events, the risk was 4% higher (p=0.05).

Confusion Rates in Aggregate Data

The rate of confirmation of cardiovascular events by central adjudication varied significantly according to the type of event, from a high of 98% for myocardial infarctions to a low of 36% for non-CNS emboli.

Based on first reported ischemic stroke, 15/24 (63%) patients in Canada had event confirmed versus 132/165 (80%) in the US (p=0.054).

Based on first reported cardiac arrest, 4/10 (21%) women had event confirmed versus 22/36 (61%) men (p=0.047).

Conclusions

• There is suggestive evidence of biased reporting of ischemic stroke events by unblinded local investigators.
• While not statistically significantly different, clinically relevant differences in the effect of treatments on stroke were seen using unadjudicated vs. centrally adjudicated events.
• Stroke events rates were 26% lower using centrally adjudicated events.
• The likelihood of confirmation of locally reported events varied with the type of event.
• Even the large number of sites and different investigators in this unblinded trial, central event adjudication added importantly to understanding the relative effects of the interventions on cardiovascular outcomes and absolute event rates in AFFIRM.

Limitations

Results and conclusions reflect the effect of event adjudication in AFFIRM. The results may be influenced by the following characteristics:

1. AFFIRM was open label. Reporting bias may be different in a double-blind setting.
2. The protocol did not give as much detail to investigators about event classification as would be expected in a setting without central adjudication.
3. Except for death, adjudicated events are secondary endpoints.
4. AFFIRM was not powered to see differences in stroke rates.

References