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Prolonging resuscitation and postponing the death of activated protein C or is it?

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The November issue of *Intensive Care Medicine* features three separate editorials [1–3] and one special article [4] about the design of a new trial investigating activated protein C (APC). This trial is done at the behest of EMEA (the European drug agency) as a requirement for further licensing of APC in Europe.

This PROWESS SHOCK trial is funded by Lilly which chose its investigators and pays for their services. It was also agreed that statisticians appointed by Lilly would independently conduct a separate analyses of the data and any discrepancies will be resolved to the satisfaction of both the investigators and Eli Lilly. It goes onto say that all documents required for regulatory purposes will be prepared by Lilly. Some people involved in the conduct of the trial previously endorsed APC as an effective drug and promoted prescription of APC in subsequent guidelines. This presents a clear conflict of interest.

When there is collaboration between parties with a conflict of interest it raises suspicion in the mind of many in the wider Intensive Care Community.

Coming to the point of research related to activated protein C from Eli Lilly, the Intensive care Community is watching in dismay at the way research has been manipulated and prescribing strategies influenced. It has not only created a polarised intensive care community but also has casts doubts over the validity of future trials sponsored by the pharmaceutical companies. The PROWESS trial was seriously flawed: the protocol was changed during the trial, the drug manufacturing was changed half way through the study and selective 28-day mortality reporting ignored lack of statistical difference in overall mortality.

Those who believe APC decreases mortality will still not openly admit that overall mortality in prowess trial was not statistically significant. That same group were also recommending its inclusion in the surviving sepsis campaign, to the point where non believers in APC could be held to be negligent if it was not prescribed.

It would be negligent, however, if we dismiss APC and it is then found to have significant benefits. In my opinion any further trial should be conducted independently without involvement of the manufacturer or anyone involved in previous trails of APC who has received or is receiving a honorarium from Lilly. This would go a long way towards dispelling any doubts concerning the results. Similar arguments can be put forward preventing authors of the surviving sepsis campaign joining this study as their opinion may be biased in favour of APC use. It will be more credible if the people who are critical of APC use are involved in the PROWESS SHOCK trial.

If the French study and the PROWESS SHOCK trial return conflicting results, will we continue to siphon money out of the budgets allocated to critically ill septic shock patients for another 10 years?

The Lilly collaboration of the study is a greatest disservice to patients, intensivists, regulating bodies and taxpayers all for the benefit of Lilly.

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