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Drug assessment in the Ebola virus disease epidemic in west Africa

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In their Personal View, Simone Lanini and colleagues1 argued that an adaptive randomised controlled trial (RCT) is the optimum solution to assess experimental therapeutics for Ebola virus disease and that non-RCTs are "profoundly unethical".

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Lanini and colleagues distinguished study designs of experimental agents as randomised versus non-randomised studies, including within the latter anecdotal experiences and compassionate use. It is irrational to make no distinction between phase 2 clinical trials and compassionate treatment. Studies by our groups, which were also cited by Lanini and colleagues, are fully regulated phase 2 clinical trials with explicit study frameworks.

Moreover, we studied interventions that have been approved by regulatory authorities for use in man and implemented them only following full ethical review and approval. Clinical drug trials can be legitimately done only with the consent of individuals and communities. We worked with communities to facilitate open dialogue and partnership, which shows that RCTs would not have been accepted at the time the trials were initiated.

In 1990, recognising that traditional approaches to clinical trial processes were unnecessarily rigid and unsuitable for study of HIV treatments, Byar and colleagues2 concluded, in their paper design considerations for AIDS trials, that non-RCTs could be considered in the following situations. First, “there must be sufficient experience to ensure that the patients not receiving therapy will have a uniformly poor prognosis”. Second, “there must be no other treatment appropriate to use as a control”. Third, “the therapy must not be expected to have substantial side effects”. Fourth, “there must be a justifiable expectation that the potential benefit to the patient will be sufficiently large to make interpretation of a non-RCT unambiguous”. Fifth, “the scientific rationale for the treatment must be sufficiently strong that a positive result would be widely accepted”.

The Ebola epidemic clearly fulfils the first and second criteria, since the fatality is high.3,4 The third criterion was met for most of the strategies studied. Regarding criterion four, our approach was to triage treatments into those with no effect that should be discarded quickly, from those with clear benefits that should be rolled out immediately, and those with promise that needs to be assessed in a RCT, in which combination antivirals could be also studied.5 This strategy is also more acceptable to patients, physicians, and local communities.

A debate on clinical trial design during humanitarian crises is needed, but it has to be based on an accurate characterisation of the events and issues.

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