Ethical Responsibility of Phase 0 Trials

To the Editor: We read with great interest the article by Abdoler et al. (1) on the ethics-based interpretation of phase 0 trials in cancer patients. In our opinion, drugs that consistently show favorable toxicity profile and beneficial therapeutic activity in preclinical models should be tested in *anima nobile*. This is particularly important for molecular targeted therapies, in which impressive responses are sometimes seen in particular subpopulations.

As pointed out by the authors, the reconceptualization of the investigator-subject relationship and a deep evaluation of the subjects’ understanding of phase 0 trials are essential for subject enrollment. Paying modest quantities was also recommended. This must be seriously considered especially in the developing countries where most participants are in a vulnerable condition due to lower per capita incomes (2, 3).

Whereas recruitment of terminally ill cancer patients in phase 0 trials is controversial, the issues of indirect and/or direct benefits such as access to therapy once successful are also equally disputed. Paragraph 30 of Declaration of Helsinki and its clarification note emphasize the needed assurance of post-trial access by study participants to the best therapeutic method identified as beneficial during the drug development. This is particularly important for subjects enrolled in phase III trials. However, because cancer patients that are eligible to phase 0 trials are end-staged, their chances of direct clinical benefits from proven therapy are highly limited. In this context, the nontherapeutic nature of such trials will always raise ethical and/or moral-based discussions (4). Therefore, access to identified beneficial therapy should be expanded to subjects enrolled in earlier trials on which phase III were based.

Paragraph 19 of the Declaration of Helsinki states that medical research is ethically justified only if there is a reasonable chance that the population on which it is conducted will benefit from the results. It is expected that subsequent trials using information derived from phase 0 would lead to fewer toxicities and higher probability of clinical benefits. Therefore, the community or population from which the subjects are derived may benefit from data originated in phase 0 trials, if the emphasis of subsequent trials is placed to the same tested population. Importantly, by extending the access of subsequent trials where phase 0 was conducted, the population, and not only the tested individuals per se, may benefit from the proven therapy.

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Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

References

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