Why Should Phase 1 Cancer Trial Participation and Optimal End-of-Life Care Be Incompatible?

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The revolutionary changes in our understanding of the molecular basis of cancer have led to the development of an unprecedented number of objectively transformative new “targeted” antineoplastic agents. As a result, it is increasingly the situation that patients treated in even the earliest stages of cancer drug trials (“phase 1”) have a meaningful opportunity to experience benefit if the hypothesized target of the drug being administered is documented to be present in an individual patient’s cancer [1, 2].

Therefore, considering therapeutic intent as an objectively realistic goal in both the design and conduct of such early phase studies is highly appropriate. Further, in the not-so-distant future such intent may even be considered essential. As a result, it should come as no surprise that “phase 1 trial participants” elect to become research subjects specifically because they have rational hope that they may achieve clinical benefit.

Unfortunately, even for patients in whom an objectively favorable outcome is observed (e.g., prolongation of the time to subsequent measurable disease progression; improvement in distressing cancer-related symptoms), the current and likely future reality is that at some point the cancer will grow and in some cases possibly quite rapidly.

Active palliation of symptoms (e.g., pain) is absolutely essential in all aspects of cancer care, but the need is par-

ticularly acute and crucial when patients are receiving what has been labeled end-of-life care. Moreover, in a setting where the transition to end-of-life care is anticipated to possibly be relatively sudden, such as can occur in a previously stable advanced cancer patient being managed on an early phase clinical trial, it is critical that there be a highly efficient process to permit an existing focus on active management of investigative treatment and its side effects to quickly move to a sole focus on supportive and comfort measures.

Unfortunately, as important as this transition may be for the welfare of an individual patient, the process itself may be unnecessarily complex. In this issue of *Oncology*, investigators in a large phase 1 cancer program (MD Anderson Cancer Center) describe a rather extensive experience with patients who required inpatient hospital care while participating in their program and were discharged to hospice [3]. They note an unsurprisingly limited overall survival (median 46 days after the last treatment; 17% at 3 months) in this population, with an even shorter survival after entry into hospice (median 16 days).

However, what is perhaps most poignant in this entire description is the discussion highlighting certain existing governmental regulations (United States) or insurance policies which appear to interfere with optimal management by denying the recognized beneficial end-of-life resources (“hospice benefits”) until any “active anti-cancer

therapy” has ceased. While the fiscal intent of such decisions is not difficult to understand, the complexities of cancer management in this patient population and the speed at which progressive disease may necessitate that these services be implemented to optimize patient comfort at the end of the cancer journey has the most unfortunate potential to make this bureaucratic arrangement very problematic.

Based on the number of truly exciting anticancer agents certain to enter phase 1 trials in the near future, it can realistically be anticipated that the number of patients entering such studies will only increase. As a result, insuring that patients are provided essential end-of-life care if, or more realistically “when,” that transition occurs should be considered an indispensable component of planning when a patient initially agrees to be a research subject in a phase 1 cancer study.

Moreover, to the extent possible, it will be critical that governmental and third party insurer policies and regulations be examined and modified (if necessary) to insure that unintended bureaucratic barriers do not hinder this essential component of optimal cancer care.

References

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