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References

Response
Radiologic and nuclear events
We thank Fliedner et al for their comments on our review and look forward to collaborative efforts between the Radiation Injury Treatment Network (RITN) and the European Group for Blood and Marrow Transplantation (EBMT) to enhance event response, communication, and data collection. We agree that logistically cumbersome approaches to biodosimetry will not be useful for classifying the vast majority of victims after a mass casualty incident. Protocols that rely on clinical findings and/or peripheral blood cell counts, such as METREPOL (Medical Treatment Protocols for Radiation Accident Victims), are currently the most practical means for large-scale dosimetry. In fact, the RITN Acute Radiation Syndrome Treatment Guidelines incorporate the METREPOL assessment, but include additional dosimetry estimators that rely solely on time-to-vomiting or lymphocyte depletion kinetics.

Although METREPOL can accurately identify victims of radiation accidents with irreversible marrow damage, it does not clearly distinguish those who may benefit from hematopoietic stem cell transplantation from those who received invariably lethal doses. The latter group may best be served with only comfort measures. Also, METREPOL is based on collective experience from victims of radiation accidents. Important differences between accidental and intentional exposures may exist. For example, partial body shielding from buildings and other structures may...
differ between radiation accidents and intentional events like an improvised nuclear device.

There are significant research efforts under way in the United States to develop more efficient and accurate technologies to estimate radiation dose. With the impending availability of personalized genomic sequencing, future methods for biodosimetry could even include genetic polymorphisms that affect radiation response. Obviously, practical aspects such as cost, turnaround time, ease of use, and availability within a disaster zone remain of paramount importance.

Manuscript space limitations prevented us from outlining RITN efforts at training and emergency communications. Since August 2006, more than 700 staff members at RITN centers have completed the RITN Basic Radiation Training Course. RITN is also coordinating an advanced Radiation Emergency Medicine course through the Radiation Emergency Assistance Center/Training Site (REAC/TS).

To enhance communication after an event, RITN established a comprehensive program designed for various scenarios. After events that cause minimal disruption to the communication infrastructure, RITN centers will utilize WebEOC, an Internet-based crisis information management system, to interact with other centers, review incident updates, and submit incident-related documents. All RITN centers are equipped with National Communication System Government Emergency Telecommunications Service (NCS GETS) calling cards, which allow users to bypass congested telephone lines and place calls during even the most disruptive events. Finally, all RITN centers are issued a portable satellite telephone.

To the editor:

Eliminating the complete response penalty from myeloma response criteria

Lonial and Gertz raise important concerns about the definition of disease progression used in patients who are in complete response following therapy for myeloma. They also correctly highlight the limitation of using immunofixation to categorize complete response (CR), and call for reporting combined CR plus very good partial response (VGPR) rates instead. We agree. The new International Myeloma Working Group (IMWG) uniform response criteria has now rectified these important concerns. In the new criteria, patients achieving CR will be considered to have progressive disease for purposes of estimating time to progression (TTP) or progression-free survival (PFS) only if there is an increase in M protein level to that required for all other response categories. A positive immunofixation will not be adequate to classify patients as having progressive disease in estimating TTP or PFS. The criteria also specifically define VGPR, and we agree that trials should report combined CR plus VGPR rates as the primary metric of depth of response.

The IMWG criteria including the above changes have been endorsed by a recent American Society of Hematology (ASH)/Food and Drug Administration (FDA) panel on regulatory endpoints in myeloma. Both the Eastern Cooperative Oncology Group (ECOG) and the Southwest Oncology Group (SWOG) have incorporated the IMWG criteria in all new trials, including all currently accruing phase 3 trials. Other myeloma groups are doing the same. Thus in the future we will have trials reporting results as suggested by Lonial and Gertz. The trials presented at the recent ASH meeting used older response criteria. For such trials that have already been completed and analyzed, it is often difficult to accurately recalculate TTP or PFS using the new definitions because once patients were considered to have disease progression they were typically taken off-study and often treated with nonprotocol therapy. Thus one may not be able to determine the correct time point at which they would have met the revised definition of progressive disease had they stayed on the trial. But in some cases with careful review it may be possible to do this, and we agree that when possible authors should adopt the revised definition of progressive disease and report corrected TTP and PFS estimates.

Finally, we would like to also point out that it is important to distinguish TTP and PFS, and report both endpoints in clinical trials. They cannot be used interchangeably. Although both use the same definition of disease progression, in TTP (the favorite end point in many industry-sponsored myeloma trials), deaths not due to disease progression (such as toxic deaths) are censored and not counted as progression events.

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Conflicts of interest: The authors declare no competing financial interests.

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References

Response: Radiologic and nuclear events

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