News & Notes

New compound enters myeloma research pipeline

CEP-18770, a boronic-acid based compound, is a new research drug being developed by Cephalon as a possible new treatment for multiple myeloma. One compound from this drug class that has already been approved for use in myeloma is bortezomib (Velcade®). In pre-clinical (animal) studies, CEP-18770 showed superior activity in myeloma models versus Velcade. Most importantly, it was able to overcome Velcade resistance. In addition, CEP 18770 showed a safety profile with significantly less toxicity to the nervous system compared to Velcade.

The first in human (Phase I) study with CEP-18770 is being conducted in Italy and Switzerland. The research study is enrolling patients with multiple types of cancers. The trial's goals are to:

- determine the safety of the drug (side effects)
- determine if patients are able to take the drug without too many side effects (the tolerability of the drug)
- measure the amount of drug in the patient's blood [pharmacokinetics (PK) and pharmacodynamics (PD)]

Data from the Phase I study set the highest dose at which the study drug should be given (maximum tolerated dose). It also looked at the PK, PD and safety profile. This study will also test if CEP-18770 is effective and safe for patients with multiple myeloma.

Cephalon is planning to conduct an open-label, Phase I/Phase II research study with CEP-18770 in patients with relapsed and refractory multiple myeloma. The Phase I portion of the trial will set the dose needed for this patient population (maximum tolerated dose). Once the Phase I of the trial is completed, the Phase II portion will start. This portion will look to see if CEP-18770 in patients with relapsed and refractory multiple myeloma is effective and safe.

The Phase II portion of this trial will have two stages. Stage 1 will enroll 23 patients and if enough patients have a response to CEP-18770 the trial will begin stage 2. Thirty-two patients will be enrolled during stage 2. All patients will receive CEP 18770 intravenously in a 21 day cycle, for up to 8 cycles (24 weeks). During this Phase II portion of the trial, patients with poor response to CEP-18770 will have low dose dexamethasone (a manmade adrenocortical steroid) added into the regimen.

After 8 cycles of initial therapy, patients with responding or stable disease may continue CEP-18770 maintenance treatment for another eight 21-day cycles. Seventy to ninety patients in total will be enrolled in this Phase I/ Phase II study. Thirty clinical centers in the USA, Canada and Europe will be used. Spain, Belgium, and France may participate in the trial. The study will likely start by December 2009.

Medicare to cover PET scans

The decision by the Centers for Medicare and Medicaid Services (CMS) to cover the use of positron emission tomography (PET scans) in multiple myeloma can significantly change the course of treatment for many patients. The case for using PET scans in myeloma was published in the Journal of Nuclear Medicine and presented to CMS by IMF chairman and medical director Dr. Brian G.M. Durie with the support of Dr. Barry Siegel, co-chair of the National Oncologic PET Registry, a comprehensive national study of PET scans in cancer.

"With PET scans doctors can visualize the whole body to see the full extent of disease on initial diagnosis, follow the response to treatment more accurately, and better determine when further treatment is needed and when it is not," said Dr. Durie. "In the national demonstration project, the course of treatment for myeloma was changed almost half the time with the use of PET scans. That's the highest impact for any cancers in the project."

Dr. Siegel added, "There are times when standard testing indicates patients are in complete remission, but with PET scans we can see that lesions, areas of cancer, are present, indicating that more or more aggressive treatment is required. Likewise, when we can be certain there is no detectable cancer, we can help patients avoid needless and expensive treatments. We are pleased to have contributed to this change in Medicare coverage."

PET scans utilize a sugar analogue that concentrates in cancer cells and emits a radioactive tracer that can be detected and located by the scan. Whole body PET scans can be used to detect unsuspected or new outbreaks of multiple myeloma both to aid in initial diagnosis and to assess ongoing treatment. PET scans have been approved for several cancers including breast, colon cancer and lymphoma. The new decision adds myeloma and ovarian cancer to the list.

"This is not only great news for patients, it is cost effective," said Michael Katz, board member of the IMF. "PET scans can cover the entire body and in our experience with myeloma patients, depending on their insurance coverage, PET scans can cost significantly less than other imaging techniques such as CT or MRI and provide better information when used as whole

body scans. We believe many private insurers will now follow this lead and with more widespread use, we believe the full potential of this important medical technology can be realized. The IMF is pleased to have played a leading role in encouraging this decision."

Pesticide exposure and MGUS

As reported in Blood (18 June 2009, Vol. 113, No. 25, pp. 6386-6391), pesticides are associated with excess risk of multiple myeloma, albeit inconclusively. The study looked at 678 men (ages 30 to 94) to assess the risk of monoclonal gammopathy of undetermined significance (MGUS). Age-adjusted prevalence estimates of MGUS were compared with MGUS prevalence in 9,469 men from Minnesota, and associations between pesticide exposures and MGUS prevalence were assessed by logistic regression models adjusted for age and education level. Among 555 study participants older than 50 years, 38 were found to have MGUS, yielding a prevalence of 6.8%. Compared with men from Minnesota, the age-adjusted prevalence of MGUS was higher among male pesticide applicators. Increased risk of MGUS prevalence was observed among users of the chlorinated insecticide dieldrin, the fumigant mixture carbon-tetrachloride/carbon disulfide, and the fungicide chlorothalonil. The prevalence of MGUS among pesticide applicators was twice that in a population-based sample of men from Minnesota, adding support to the hypothesis that specific pesticides are causatively linked to the origins of myeloma.

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