



PIC QUESTION OF THE WEEK: 09/25/06

Q: Is there an indication for thalidomide other than its use in types of cutaneous leprosy?

A: The historical association between thalidomide and a unique birth defect known as phocomelia (attachment of the hands and feet close to the body, thus resembling the flippers of a seal) will always characterize this compound. In 1998, the FDA approved the marketing of thalidomide (with appropriate precautions) for the acute treatment and maintenance therapy of cutaneous manifestations of moderate to severe erythema nodosum leprosum (ENL). The drug subsequently received FDA approval in May 2006 for use in combination with dexamethasone for the treatment of patients with newly diagnosed multiple myeloma. It has also been investigated in the treatment of a number of other conditions including lupus erythematosus, malignant melanoma, sarcoidosis, etc. An analog, lenaldomide (Revlamid®), was approved in late 2005 and possesses a similar indication. Lenaldomide is also labeled for specific variants of transfusion dependent myelodysplastic syndrome. It is estimated that approximately 17,000 new cases of multiple myeloma will be diagnosed in the U.S. in 2006. Thalidomide affects multiple factors in the immune system and reduces the survival of myeloma cells. Three proposed mechanisms for the activity of thalidomide in multiple myeloma include inhibition of angiogenesis, alteration of production and activity of cytokines (TNF- α and IL-6), and stimulation of T-cells that directly destroy tumor cells. In a recent clinical trial, the addition of thalidomide to a high-dose melphalan regimen and autologous stem-cell transplantation increased the number of complete responses and event-free survival. Unfortunately, the overall five-year survival rate was similar in both groups (65%). In addition, peripheral neuropathy and deep vein thrombosis (DVT) were more common in the thalidomide-treated group. This result was similar to that observed in comparable studies of thalidomide in multiple myeloma. Thalidomide has been used as maintenance therapy after stem-cell transplantation; however, this is not currently a labeled indication for the drug. As mentioned above, DVT and peripheral neuropathy are frequent serious and potentially life-threatening consequences of thalidomide therapy. Other severe adverse effects include toxic epidermal necrolysis (TEN) and leukopenia. Thalidomide has been used to treat multiple myeloma for several years. The most effective regimen remains to be determined.

References:

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