

Teaching an old drug new tricks

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Anti-cancer therapies derived from the notorious drug thalidomide are entering clinical trials worldwide. These new generation compounds, so-called immunomodulatory drugs (ImiD™s), show powerful anti-cancer activity and low side-effects and could soon become the drug of choice in the treatment of multiple myeloma (MM).



Thalidomide analogue

Researchers at the Celgene Corporation (<http://www.celgene.com>) in New Jersey, USA, are confident that a new analogue of thalidomide is going to become the drug of choice for the treatment of multiple myeloma and possibly other types of blood cancer.

Thalidomide reached an undesirable peak of fame in the early 1960s after it showed unexpected teratogenic side effects when used to treat morning sickness in pregnant women. Developmental deformities in children born to women taking the drug quickly halted its use. Subsequently, thalidomide was found to have anti-angiogenic, anti-inflammatory and immunomodulatory activity, and in the 1990s its ability to selectively inhibit TNF- α led to renewed interest in the

potential use of the drug as a therapeutic agent.

George Muller of Celgene presented the latest clinical data on his company's new class of thalidomide analogs, ImiD™s, at a meeting of the Society for Medicines Research in London, 4 December 2003 (<http://www.socmr.org>).

At present, the next generation compounds are undergoing clinical trials in Phases I, II and III and are showing positive results in around 85% of patients at Phase II, says Muller. Data from the Phase III trials are not yet available.

Anti-inflammatory and anti-cancer activity

The new drugs are structurally related to thalidomide and have potent

anti-inflammatory activity and anti-cancer activity. The results of the clinical trials indicate low side-effect profiles, making the use of these agents an attractive addition to the anti-cancer armamentarium, says Muller.

The findings are cautiously welcomed by Blake Marriott of the Division of Oncology at St George's Hospital Medical School in London (<http://www.sghms.ac.uk>). 'The main advantage with these compounds in the treatment of cancer is the fact that they appear to work very well in patients with advanced cancers who have had multiple rounds of previous chemotherapeutic treatment,' said Blake. The side-effect profiles are also promising, he says, and better than thalidomide itself.

However, he warned, 'Close monitoring for signs of neuropathy and vigilance in prescribing to women of childbearing potential are still major issues. As these compounds get moved to earlier stage disease these issues will become even more important. However, these patients are extremely ill. The signs so far are good, in particular with patients with MM and myelodysplastic syndromes.'

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