IRINOTECAN: A NEW TREATMENT FOR SLE?

Lupus nephritis is a major cause of mortality in patients with systemic lupus erythematosus (SLE), and the drugs currently used to treat this disease, such as cyclophosphamide, prednisolone, azathioprine and mycophenolate mofetil, have not been shown to reverse established lupus nephritis and associated proteinuria in mice.

While researching receptor-mediated apoptosis in lung cancer, a research group at the University of Bern, Switzerland, discovered that the topoisomerase I inhibitor irinotecan (an approved treatment for colorectal cancer) prevented death in mice injected with foreign cytokines, which suggests that this agent in some way inhibits immune hyper-reactivity. In light of this finding, the group investigated the effects of irinotecan in the NZB × NZW F1 mouse model of SLE.

All mice that received high-dose irinotecan (50 mg/kg administered by intraperitoneal injection three times per week every 4 weeks) from the age of 13 weeks survived to the end of the study (90 weeks) without developing lupus nephritis or high-grade proteinuria. By contrast, all control mice developed at least grade 2 proteinuria (≥100 mg/dl) by week 42 (median survival 36 weeks).

In mice with established lupus nephritis, as indicated by grade 3 or grade 4 proteinuria (≥300 mg/dl and ≥2,000 mg/dl, respectively), irinotecan injections (50 mg/kg three times per week for 2 weeks) resulted in decreased levels of proteinuria within 2 weeks, and disease remission in up to 75% of animals after the first treatment cycle. Median survival was also markedly increased compared with control mice (73 weeks versus 40 weeks).

The researchers conclude that these findings compare favorably with similar mouse studies of other agents, and indicate that irinotecan might be an effective new option for SLE therapy.

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Original article Frese-Schaper, M. *et al.* Reversal of established lupus nephritis and prolonged survival of New Zealand black × New Zealand white mice treated with the topoisomerase I inhibitor irinotecan. *J. Immunol.* **184**, 2175–2182 (2010)