

Topoisomerase I inhibitors for the treatment of Lupus erythematosus

It is shown that administration of irinotecan (Campto®, Pfizer), an inhibitor of topoisomerase I, which is used as chemotherapeutic agent for the treatment of metastatic colorectal cancer, is able to reverse established murine *Lupus erythematosus*. The results strongly indicate that these findings are transferable to other topoisomerase I inhibitors.

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Keywords Second medical use, Topoisomerase I inhibitor, *Lupus erythematosus*, autoimmune disease, Irinotecan, Campto, camptothecin

Reference Frese-Schaper, M. et al. *J. Immunol.* Jan 18, 2010.

Methods A *Lupus erythematosus* mouse model (NZB/W F1, generated as the F1 hybrid of New Zealand Black and New Zealand White mice) was used to study the influence of the topoisomerase I inhibitor irinotecan (Campto®, Pfizer) on the course of established *Lupus erythematosus*. The beginning of the disease was defined as two times proteinuria grade 3+ (≥ 300 mg/dl) or proteinuria grade 4+ (≥ 2000 mg/dl). The two groups (12 animals each) were treated thrice weekly with 50 mg/kg irinotecan for two weeks and compared with a group treated with saline 0.9% (12 animals). The same treatment was performed for relapsing disease.

Invention Treatment with irinotecan reversed existing levels of proteinuria and prolonged the median survival of NZB/W F1 mice to 73 weeks (grade 3+ and grade 4+ combined) vs 40 weeks for saline-treated animals. Remarkably, 5 out of 12 animals treated from grade 3+ proteinuria were still alive at week 90 whereas all animals treated with saline had died.

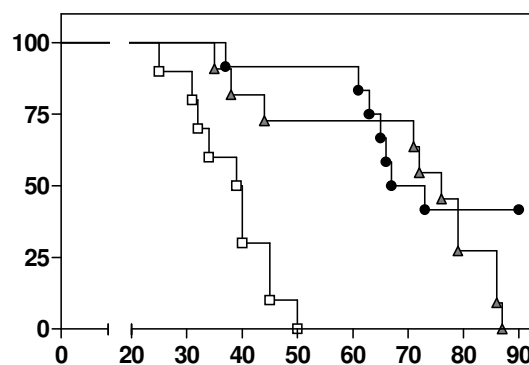


Figure: Survival of NZB/W F1 mice with established *lupus erythematosus* treated with irinotecan vs. saline (12 animals in each).

Axis of ordinates: survival in percent. Axis of abscissae: age of mice in weeks.

□ open squares: treatment with saline started from proteinuria grade $\geq 3+$,

● filled circles: treatment with 50 mg/kg irinotecan initiated from proteinuria grade $\geq 3+$,

▲ filled triangles: treatment with 50 mg/kg irinotecan initiated from proteinuria grade $\geq 4+$.

Fields of Use Treatment of Lupus erythematosus

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