


1: [Cytokine](#). 2002 Jan 7;17(1):43-52.  [Links](#)

Combination interleukin-2 and interleukin-12 induces severe gastrointestinal toxicity and epithelial cell apoptosis in mice.

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Interleukin 2 (IL-2) and interleukin 12 (IL-12) have potent anti-tumour activity as single agent therapy against several different murine and human tumours. Combining these cytokines may result in improved therapeutic effectiveness, however, the toxicity associated with simultaneous administration is prohibitive. This study was designed to determine the specific histopathologic changes associated with combination therapy. Mice were treated with 5 days of interleukin-2, interleukin-12, or both using standard doses and schedules. Histologic specimens were prepared from all internal organs on a daily basis to identify specific pathologic abnormalities. Treatment with interleukin-2, interleukin-12, or both resulted in pathologic insult to the liver and gastrointestinal tract. Mild lymphoplasmacytic infiltrates were seen in the liver. The most significant pathology was seen in the large bowel and consisted of apoptosis of colonic epithelial cells. While recovery of injured gastrointestinal mucosa occurred in mice treated with interleukin-2 or interleukin-12 alone, combination therapy resulted in death before recovery was possible. Combination interleukin-2 and interleukin-12 therapy results in irreversible injury of the colon as manifested by increased epithelial cell apoptosis and death in mice. Understanding the pathologic changes associated with combination cytokine therapy may lead to strategies that prevent toxicity while maintaining therapeutic effects. Copyright 2002 Elsevier Science Ltd.