Targeting the EWS-FLI1 transcription factor in Ewing sarcoma.

Abstract:
Preclinical data indicate there is strong synergism of action against Ewing sarcoma in sequential treatment with trabectedin followed by irinotecan and it appears to be related to a selective blockade of the transcription factor EWS-FLI1. This combination was evaluated in Ewing sarcoma patient who was progressing with standard therapies. Trabectedin was given as a 24-h iv infusion on day 1 at the dose of 1 mg/sqm, and irinotecan 75 mg/sqm on day 2 and then on days 2 and 4, every 3 weeks from the seventh course. The therapy was well tolerated with transient hematological toxicity and transaminitis and induced stabilization of the disease lasting for 11 courses, with clinical improvement and marked reduction of the need for opioids. However, shortly before the 12th course, sudden death occurred, possibly due to cerebral stroke, presumably not related to the drug treatment. The encouraging clinical benefit observed with the combination and its good tolerability deserves further investigation in Ewing sarcoma.