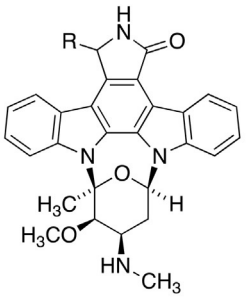
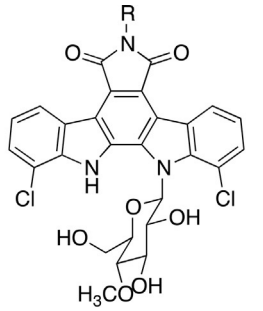
water-soluble rebeccamycin analogs that have been developed, compound NSC-655649 (BMY-27557-14) entered phase II clinical trials for renal cancer.[109] Interestingly, the presence of the aminoethyl side chain in this compound led to specific Top2 inhibitory activity.

The analog NB-506 has been characterized as a Top1 inhibitor that enhances DNA cleavage mediated by this enzyme. Because it shows cross-resistance with CPT, it has been suggested that they share a common binding site in the Top1–DNA complex, although NB-506 probably targets other additional cellular processes.[110] Intercalation is apparently not required to stabilize its complex with Top1–DNA, and in fact, a regioisomer of NB-506 without capacity to intercalate into DNA is an extremely potent Top1 poison.[111] Clinical studies on NB-506 started in 1994, and it has shown particular good activity in ovarian and breast cancer.

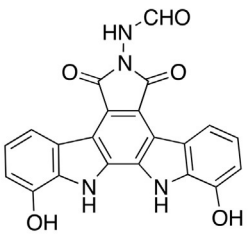
The related hydroxy derivative edotecarin (J-107088) is more active *in vitro* than NB-506 or CPT in the induction of Top1 cleavage complexes.[112] This glycoside has been studied clinically and has shown potent activity against lung and prostate cancers with a wider therapeutic window than many established drugs.[113] It has also shown activity in clinical trials for colon, breast, and other cancers.[114] The larger size of the imide nitrogen substituent in this compound hampers imide ring opening and glucuronidation, and it leads to an increased half-life.



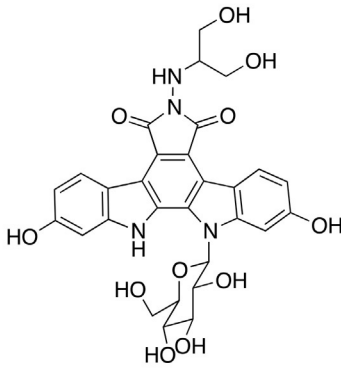
Compound	R
Staurosporine	H
UCN-01	OH



Compound	R
Rebeccamycin	H
NSC 655649 (BMY-27557-14)	$(CH_2)_2NEt_2$



NB-506



Edotecarin
(PHA-782615, J-107088)