**Introduction:** Hepatocellular carcinoma HCC is resistant to many combination chemotherapy without any survival benefits. This mandates the search for biomarker that may predict the response and or prognosis in this dull disease. We conduct this study to evaluate the relation between Topoisomerase II alpha level in the liver tissue and response to therapy.

**Methods:** The study included 50 unresectable HCC patients, who were diagnosed and treated in the NCI, Cairo University. The mean age was 54.5 years; 47 of them were males and 3 females. Doxorubicin 50 mg/ m2 every 3 weeks was given for 3 cycles and the response was evaluated according to Response Evaluation Criteria in Solid Tumors (RECIST).

**Results:** Over expression of TopoIIα was found in 19/50 (38%) and was negative in 31/50 (62%). No CR was seen after treatment with doxorubicin, while PR was 8/50 (16%), SD 21/50 (42%) and PD 21/50 (42%). There was a significant correlation between TopoIIα and the response to the chemotherapy (P = 0.001) (Table1). The study showed significant correlation between TopoIIα and OS; 8 months for over expression compared to 14 months in negative expression (figs1).

**Conclusion:** Detection of Topoisomerase II alpha level in liver tissue showed a significant correlation to both response to therapy and survival in 50 HCC patients. TopoIIα is a promising prognostic and predictive factor that may reflect an aggressive behavior as seen with less survival in positive group but it represents a good response to therapy. With further studies in the near future Topoisomerase II alpha together with others factors as tumor size, pathological grade may help for more personalized therapy in HCC.