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## 9° Giornata della Ricerca della Svizzera Italiana

Venerdì 15 marzo 2019

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### Modulo per la sottomissione abstract ricerca di LABORATORIO

**Titolo** (massimo **15 parole**)

Copanlisib plus venetoclax: from preclinical screening to a phase I study for lymphoma patients

**Autori** (cognome e iniziali, es: Grassi L.)

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**Testo** (massimo **250 parole**, preferibilmente in italiano (accettato anche in inglese), suddiviso in Introduzione, **Metodi, Risultati, Conclusioni e Finanziamento**)

**Introduction.** Copanlisib is a pan class I PI3K-i with predominant inhibitory activity against PI3K $\delta/\alpha$ , recently FDA approved for relapsed follicular lymphoma patients. After its first demonstration of clinical activity we had started a project to identify novel active combinations in 26 B and T cell lymphomas, combining the compound with additional 16 drugs.

**Methods.** Synergy was assessed by Chou-Talalay combination index (CI) on 72 h MTT proliferation data. In vivo experiments were done in SCID mice.

**Results.** Copanlisib as single agent showed an in vitro dose-dependent antitumor activity (median IC50 75nM, 95% C.I. 21-160nM) in a variety of models derived from mantle cell lymphoma (MCL), from marginal zone lymphoma (MZL) and T cell lymphomas. All B cell lymphomas had IC50 values well within the concentrations that are clinically achievable, while this occurred only for some of the T cell lymphomas that were, as whole, less sensitive.

The combination screening identified several compounds that synergized with copanlisib. The strongest combination was with the BCL2 inhibitor venetoclax. The benefit of the combination over the single agents was also validated in a MZL xenograft model and in two MCL primary cells, and was due to increased induction of apoptosis, likely sustained by the reduction of the anti-apoptotic proteins MCL1 and BCL-XL, observed in MCL and MZL cell lines, respectively.

**Conclusion.** These data provided the rationale for the design of the SAKK 66/18 phase I study exploring the combination of copanlisib and venetoclax in relapsed/refractory lymphomas.

**Visto superiore\*** (prego indicare **Nome e Cognome** del superiore) **\*campo obbligatorio**

Eugenio Gaudio

**Criteria per sottomissione Abstract:**  
NO Case report  
NO Abstract senza nessun risultato  
VISTO da un superiore

**Invio Abstract**

