Girodazole : "from the lagoon of Noumea to cancer patients"

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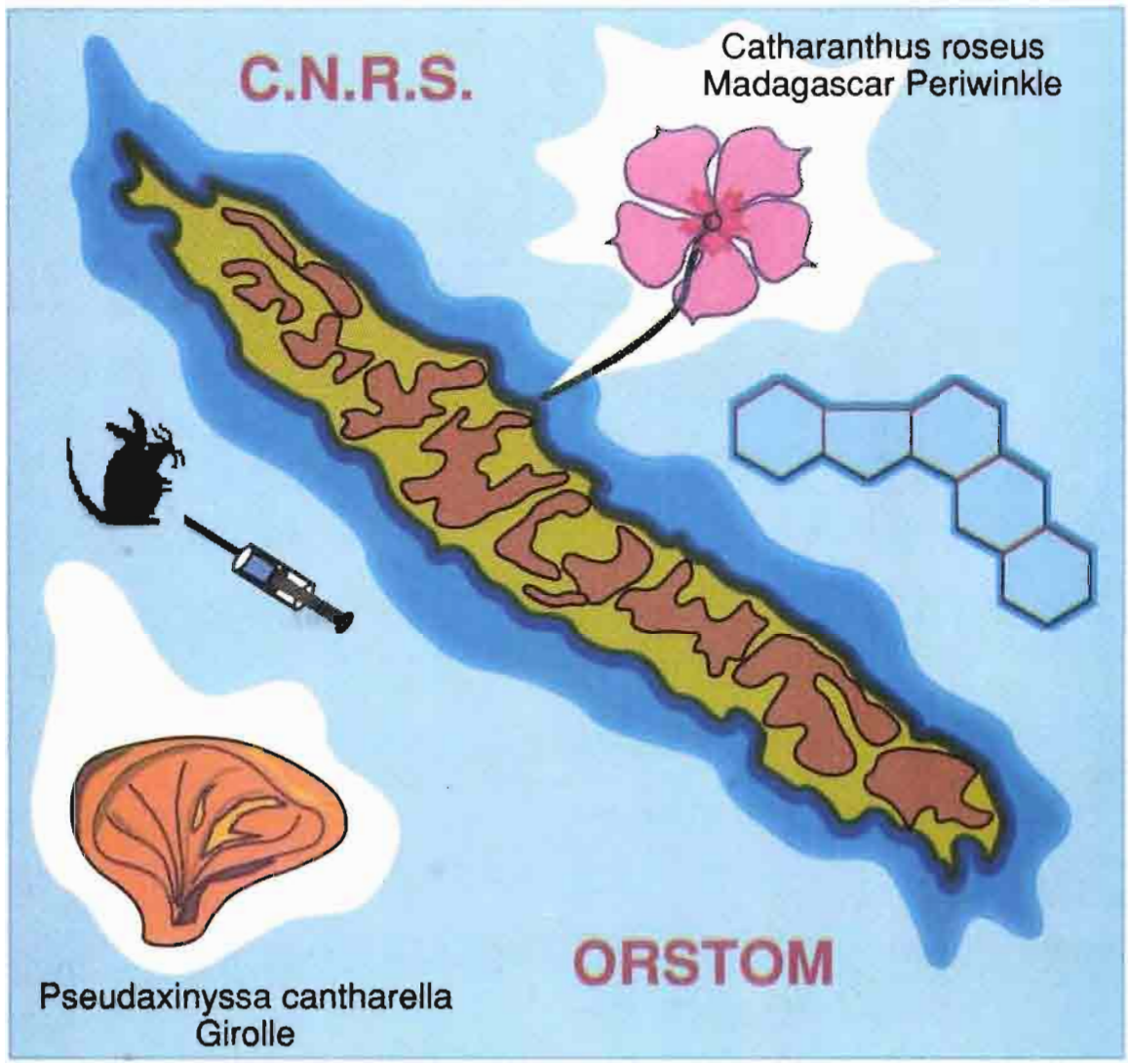
Girodazole ("girolline", RP 49532A, NSC 627434) is an antitumor agent isolated from the sponge *Pseudaxynissa cantharella* collected in New Caledonia (C.R. Acad. Sci. Paris 307 (II) 145-148, 1988). Girodazole (3-amino-1-[4-(2 amino-1 H-imidazolyl)]-2 chloro-1-propanol, 2HCl) has a unique chemical structure different from those of all the other anticancer drugs and of new compounds in clinical trials.

Girodazole is active *in vivo* on several grafted murine tumors used for preclinical evaluation (P388 leukemia, L1210 leukemia, M5076 histiocytosarcoma, MA/16C mammary adenocarcinoma). In addition, Girodazole retains activity on P388/DOX, a subline of P388 leukemia resistant to anthracyclines and vinca alkaloids.

Antitumor properties of Girodazole are due to protein synthesis inhibition (elongation / termination).

All these innovative properties prompted us to purify large quantities of Girodazole for preclinical, toxicological studies and clinical trials. Several toxic effects were detected in dogs and rodents. However none of them precluded administration in cancer patients.

Phase I clinical studies were done in three european Institutions. different schedules of i.v. administration were used during these tolerance studies. The starting dose was equal to $2mg/m^2$. The dose escalation was interrupted at $15mg/m^2$ by a severe and delayed hypotension uncontroled by antidotes. The plasmatic concentrations of Girodazole obtained in patients at the maximal tolerated dose of $15mg/m^2$ are far below those which preclinical activities were observed in animals. The maximal tolerated dose of $15mg/m^2$ is considered to be too low for expecting clinical responses during phase II clinical trials. Consequently, clinical development has due to be stopped.



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