

Translational Studies of Protandim(RTM) as a Candidate Nutraceutical Approach to Treating Ovarian Cancer

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Abstract:

Background: Nutraceutical approaches are increasing in cancer patients. We encountered a recurrent ovarian cancer patient who incurred durable tumor regression and decreasing CA-125 with initiation of the nutraceutical Protandim, a combination of five phytochemical extracts (ashwagandha, bacopa, green tea, milk thistle, turmeric). Preclinical studies were undertaken to investigate Protandim and its constituent anticancer effects and underlying mechanism(s). Methods: In vitro ovarian cancer models were used to assess Protandim effects. Colony forming assays, Hoechst nuclear/Trypan exclusion staining, immunoblotting, and flow cytometric methods were used to assess cytotoxic and to identify mechanism (s) of action. Combined effects of Protandim components were assessed by the methods of Chou and Talalay; ex vivo myeloma patient model was used to assess cancer selectivity. In vivo studies assessed tolerability and toxicity effect of Protandim. Results: Anticancer effects of Protandim demonstrated induction of necrotic-morphological cell death. Ex vivo assays showed Protandim to selectively kill freshly collected patient myeloma cells, relatively sparing paired patient normal bone marrow cells. Immunoblotting and flow cytometric experiments indicated that Protandim induced cellular reactive oxygen species (ROS) level. Similar cytotoxic effects in wild-type- and Rho-MOLT4 cells indicated non-mitochondrial mediated ROS induction. Assessment of the combined effects of Protandim constituents showed antagonism or additivity. In vivo studies showed no Protandim toxicities in mice. Conclusions: Protandim has promising activity in ovarian cancer models, associated with induction of non-mitochondrial mediated-ROS and necrosis. Protandim is well-tolerated in mice, and has anti-cancer selectivity. Further investigations to more specifically assess molecular mechanism and in vivo efficacy are presently underway.



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3



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