PROJECT SUMMARY SHEET

TITLE: "Antitumor effects of growth hormone-releasing hormone (GHRH) in combination with chemotherapy for the treatment of malignant pleural mesothelioma."

"Antitumor role of GHRH antagonists, in association with chemotherapy agents, in malignant pleural mesothelioma."

RESEARCH ENTITY: Laboratorio di Endocrinologia Molecolare e Cellulare *(Molecular and Cellular Endocrinology Laboratory)*

Divisione di Endocrinologia, Diabete e Metabolismo *(Endocrinology, Diabetes and Metabolism Division)* - Dipartimento di Scienze Mediche *(Medical Sciences Department)* - Università di Torino *(University of Turin)*.

PROJECT LOCATION: Laboratorio di Endocrinologia Molecolare e Cellulare Divisione di Endocrinologia, Diabete e Metabolismo Dipartimento di Scienze Mediche - Università di Torino. Corso Dogliotti 14, 10126, Turin.

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ABSTRACT/SUMMARY

- INTRODUCTION: Malignant pleural mesothelioma (MPM) is associated with exposure to asbestos, and is often diagnosed at an advanced stage with a very poor prognosis. Although not curative, the current standard of care for MPM is chemotherapy with the anti-folate pemetrexed in combination with cisplatin. It is therefore essential to find new therapeutic approaches for treating MPM. Numerous studies have demonstrated the ability of growth hormone-releasing hormone (GHRH) antagonists to inhibit the growth of various tumors in *in vitro* and *in vivo* models, including in lung cancer. Our research group has also recently demonstrated how GHRH antagonists from the Miami series, MIA-602 and MIA-690, inhibited *in vitro* cell survival and proliferation in human MPM cell lines and primary cells, both alone and in combination with pemetrexed. MIA-602 and MIA-690 were also able to reduce *in vivo* tumor progression in a mouse xenograft

model of MPM. Nevertheless, the ability of GHRH antagonists to increase the effects of the combination with pemetrexed and cisplatin chemotherapy remains to be verified both *in vitro* and *in vivo.*

- METHOD

  In order to verify the antitumoral potential of MIA-690 in combination with pemetrexed and cisplatin in MPM, we will analyze the effect of this regimen both *in vitro* on cell survival and proliferation in human MPM cell lines and in primary cells isolated from MPM patients and identify the mechanisms involved, and *in vivo* in a mouse xenograft models with human MPM cells.

- OBJECTIVES

  The results of this research will not only provide new information on the pathogenesis of MPM, but will also improve current therapies by reducing the dosages and side effects of chemotherapy drugs.

PROJECT PRESENTATION DATE: 25 September 2020