

Metformin and ovarian cancer survival: is there a rational warrant for belief?

Raffaella Mormile¹ 

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Abstract

Metformin (MF) represents the first-line drug used to treat type 2 diabetes. Recently, MF has also been reported to be a potential and promising anti-cancer agent for some gynecological cancers' prevention. MF, as an anti-tumorigenic factor, may reduce the chance of developing ovarian cancer by targeting IL-6. By acting on IL-6 expression, metformin might have a positive impact on the main molecular pathways strictly connected with pathogenesis and biological features of ovarian cancer. Further investigation is warranted to better define the use of MF as a possible treatment option in the fight against ovarian cancer.

Metformin (MF) represents the first-line drug used to treat type 2 diabetes [1, 2]. Recently, MF has been observed to exert significant anti-neoplastic effects in a number of systemic malignancies [1]. Recently, MF has also been reported to be a potential and promising anti-cancer agent for some gynecological cancers' prevention [1]. However, it still remains unclear whether MF may be beneficial for people at any stage of ovarian cancer [1]. It has been recognized that blockade of interleukin-6 (IL-6)-induced epithelial–mesenchymal transition (EMT) is an antitumor mechanism of MF [2]. It has been detected that MF decreases IL-6 signaling and prevents EMT [2]. MF has been shown to reverse IL-6-induced EMT by preventing STAT3 phosphorylation [2]. IL-6 is a multifunctional cytokine that has attracted attention for its key role in mediating inflammation and immune responses [2]. IL-6 signaling has emerged to play a critical role in the pathogenesis of several diseases, including some cancers and a number of inflammatory conditions [3]. MF has also been detected to induce the repression of IL-6 signaling by specifically decreasing IL-6R expression [3]. Ovarian cancer is considered the most fatal gynecological malignancy in the USA and the fifth most common cancer-related cause of death in women [4]. Despite an initial promising response to therapeutic agents, most cancer patients become resistant to chemotherapy [4, 5]. Inflammation has

been demonstrated to have a major role in ovarian cancer tumor growth with IL-6 having been documented as the most potent inflammatory immunoregulatory cytokine [4]. IL-6 has been suggested to be a key player in ovarian cancer metastasis, which is based on ovarian tumor cell migration, proliferation, invasion, survival and chemoresistance, by activating some pathways including JAK/STAT and processes such as EMT [4]. IL-6 has been described to act as an important trigger of the EMT [4]. It has been found that IL-6-induced JAK/STAT activation results in constitutive activation of STAT3 which relates to enhanced tumor cell growth and resistance to chemotherapy [4]. Interestingly, expressions of IL-6 and IL-6 receptor (IL-6R) have been proved to be higher in therapy-resistant ovarian cancer cells in comparison to sensitive ones [5]. Higher expressions of IL-6 and its receptor have been associated with resistance to certain chemotherapeutic agents [5]. With respect to the above, I assume that there is a convincing rationale for the use of MF among women suffering from ovarian cancer with and without diabetes. I suppose that MF, as an anti-tumorigenic factor, may reduce the chance of developing ovarian cancer by targeting IL-6. By acting on IL-6 expression, MF might have a positive impact on the main molecular pathways strictly connected with pathogenesis and biological features of ovarian cancer. Further investigation is warranted to better define the use of MF as a possible treatment option in the fight against ovarian cancer.

✉ Raffaella Mormile
raffaellamormile@libero.it; raffaellamormile@alice.it

¹ Division of Pediatrics and Neonatology, Moscati Hospital,
Via A. Gramsci, 81031 Aversa, Italy

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Compliance with ethical standards

Conflict of interest The author declares no potential conflicts of interest.

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