Illuminating Hope for Ovarian Cancer Treatment: Pyropheophorbide *a* coupled to Folic Acid Derivatives as Promising Photosensitizers

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Pyropheophorbide *a* is a photosensitizer that offers many advantages as therapeutic agent for cancer treatment. It has a strong absorption in the red region of visible light, allowing deeper penetration into tumor tissues. Furthermore, activation of this photosensitizer by light of an appropriate wavelength, through the mechanism of photodynamic therapy (PDT), generates reactive oxygen species, such as singlet oxygen, which damages cancer cells and leads to their destruction. Therefore, the use of this photosensitizer for the development of new photosensitizing agents for cancer treatment is a significant choice, especially for application of PDT (*Figure 1*).

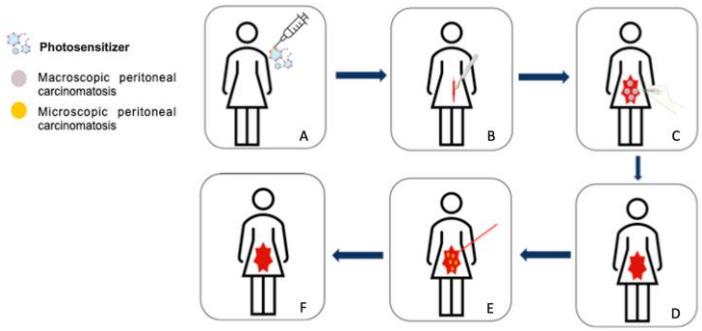

Figure 1: *Intraperitoneal photodynamic therapy protocol for peritoneal metastases of advanced ovarian cancer. (A) Administration of the photosensitizer, (B) open approach (laparotomy) to perform macroscopic complete cytoreductive surgery, (C) cytoreductive surgery (hysterectomy, bilateral adnexectomy, omentectomy, appendectomy +/- pelvic and para-aortic lymphadenectomies, removal of all visible peritoneal metastases), (D) end of the cytoreductive surgery, (E) illumination of the peritoneal cavity to treat by photodynamic therapy microscopic peritoneal metastases, (F) end of the procedure.*[1]

To summarize, our team has developed photosensitizers based on the coupling of pyropheophorbide *a* with folic acid (FA) derivatives. Indeed, FA is used as a targeting agent to target the α isoform of the FA receptor (FRα) that is overexpressed by several tumoral tissues, including metastases of ovarian cancer[2] (also called peritoneal carcinomatosis). To circumvent the stability issues related to the folic acid molecule[3], analogues of this latter were synthesized and then coupled to pyropheophorbide *a*.

The first photosensitizer obtained shows a very promising photodynamic activity with a cell viability of 0%, either after 5 min (0.3J/cm²), 15 minutes (0.9 J/cm²) or 30 minutes of illumination (1.8 J/cm²) with concentrations ranging from 2.25 to 4.5 uM of PS.

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