



Polymeric drug loaded film to implant for local release of anticancer drugs after tumor resection.

WHO WE ARE

PlumeStars, Italian innovative start-up company, laid its foundation from Biopharmanet-TEC, the Interdipartimental Center of the University of Parma, in September 2013. PlumeStars leverages on its strong technological know-how to design and develop dry powders for inhalation and orphan medicines designation. PlumeStars holds a patented technology claiming the molecular deposition of fatty acids on drug microparticles applicable to several drugs.

The founders of PlumeStars, Paolo Colombo (CEO), Anna Giulia Balducci, Francesca Buttini and Ruggero Bettini, are four scientists that share the same passion for science and technology. In the Advisory board Fabio Borella, is the mentor of PlumeStars.

WHAT WE DO

Nowadays, treatment of tumors, in particular lung mesothelioma, combines surgery, radiotherapy and chemotherapy using two or more anticancer drugs. The malignant pleural mesothelioma is surgically treated by the pleurectomy/decortication (P/D) or the extra pleural pneumonectomy (EPP). The main chemotherapy administration before or after surgery is intravenous route that exposes the organism to high drug levels, also in body districts where the medication is not required. The local pleural administration of the chemotherapeutic agent, where the primary tumor has been surgically resected, offers the opportunity to achieve high local concentrations on the affected area, sparing healthy tissues.

Preclinical studies in rat malignant pleural mesothelioma model have been performed using polymeric films loaded with cisplatin. The intrapleural implant demonstrated a clear superiority in the prevention of local recurrences compared to the IV administration. Further preclinical studies in sheep evidenced the safety of this approach, demonstrating a reduced renal and hepatic toxicity of cisplatin. In summary, after primary tumor ablation, the application of the cisplatin polymeric film in the pleural cavity prevented the tumor local metastases.

This novel technology could be applied to other chemotherapeutic drugs. The films could be implanted in other body districts for different tumors such as ovarian, peritoneal or other solid accessible tumors, alone or in combination by using different loaded films.

The release rate of drug from the film depends on the film area in contact with body tissue. A number of films can be used in order to cumulate the dose of chemotherapeutic agent. Finally, the film could be also implanted with a minimal surgery procedure in situation in which the subject cannot bear a radical and invasive surgery. This alternative implies that the application can be easily repeated.



DESCRIPTION OF THE PRODUCT

The medicinal product obtained the EMA orphan medicine designation in 2017. EMA gave also the protocol assistance for the preparation of the registration dossier. The application for orphan drug has been sent to FDA.

The product under development is a thin and flexible polymeric film, sufficiently resistant to be applied intrapleural or in other districts, adhering to the mesothelial or epithelial surfaces. For example, the in vitro release of cisplatin from the film resulted prolonged for at least three days, in release conditions where the entire film was immersed in the dissolution medium. In vivo, a continuous release for more than 10 days could be extracted from the plasma level curve obtained in PK study on a sheep model.

This prolongation provided high local concentrations of drug, where the residual tumour could be present. Therefore, hyaluronate-cisplatin film (HA-CisPt) is a novel cisplatin delivery system. Hyaluronic acid (HA), a physiological component of the extracellular matrix, is a biocompatible polymer.

MAIN ADVANTAGES

Preclinical studies on rats showed that hyaluronate films loaded with cisplatin were significantly more effective in reducing tumour recurrence and assuring higher and prolonged plasmatic drug concentrations than cisplatin solution, without increasing systemic toxicity. Subsequent preclinical studies conducted on Sardinian sheep showed that polymeric films application in the pleural cavity was easy and homogenous to place in thoracic cavity of the sheep. Plasmatic drug concentration was much higher after polymeric films treatment than drug solution after 7-9 days.

TECHNOLOGY KEY WORDS

Polymeric Film, Drug delivery, Loco-regional Administration, Hyaluronic Acid, Malignant Pleural Mesothelioma.

CURRENT STAGE OF DEVELOPMENT

Preclinical studies already be done - *Tested in laboratory.*

TECHNICAL AND SCIENTIFIC PUBLICATIONS

Intrapleural polymeric films containing cisplatin for malignant pleural mesothelioma in a rat tumour model: a preliminary study, European Journal of Cardio-thoracic Surgery 37 (2010) 557—565.