

PharmaMar to Present New Studies for YONDELIS® and PM1183 in Ovarian Cancer during ESGO 2015

Madrid, October 26th, 2015: For the next few days, thousands of oncology experts in gynecologic cancers are gathering during the 19th Biennial Meeting of the European Society of Gynecological Oncology (ESGO 2015), which is taken place from October 24-27, 2015 in Nice, France. ESGO is the European leading organization that aims to advance gynecologic cancer care and is strongly committed to help women in Europe with this disease. This forum is an excellent opportunity for clinicians, researchers, patient associations and drug developers to learn about the most exciting developments in the field of gynecologic cancers, which include ovarian, cervical, uterine, vaginal and vulvar cancers.

The initial standard treatment for ovarian cancer implies a platinum-based combination therapy. However, after recurrence, leading oncologists in the field recommend evaluating patients on a case-by-case basis to identify the best therapeutic option for each patient. In this scenario, platinum-free therapies keep gaining traction among clinicians.

"Making the most of every option in the treatment of ovarian cancer. Choosing the optimal sequency" is the title of the satellite symposium organized by PharmaMar, which gathered more than 600 oncologists, during ESGO 2015 to bring together national and international oncologists and discuss the different aspects that need to be considered from a clinical standpoint to treat women with recurrent ovarian cancer. Among the most crucial topics to be discussed are the best approaches to manage and overcome platinum hypersensitivity and the clinical benefit of platinum-free therapies after recurrence.

One of the participants, Nicoletta Colombo, MD, European Oncology Institute, University of Milan-Bicocca, Milan, has pointed how certain platinum sensitive tumors can also respond to other therapies and said "among the benefits of switching from a platinum-based therapy to a non-platinum treatment you can find two important aspects of the management of these patients; the probable recovery from neurotoxicity that is associated to platinum, and the potential to reduce and

even prevent the hypersensitivity often found during treatment of these women with platinum”.

When a patient is partially sensitive to platinum, that is the patient relapses within 6 to 12 months after treatment with platinum, among the recommended therapeutic options, oncologists and the most recent ESMO Clinical Practice Guidelines suggest a treatment combining YONDELIS® (trabectedin) with pegylated liposomal doxorubicin followed by a platinum-based therapy. Dr. Colombo explained that with this sequential treatment, an overall survival of 6 months and a 41 percent reduction in the risk of death can be obtained. Also, the treated patient can recover from the toxicity caused by platinum-based therapies¹”. The hypothesis to explain the benefit of this sequential treatment is that such approach could enhance the sensitivity of the tumor to a next platinum therapy, thus increasing the survival of the patient.

Studies highlighted at ESGO 2015

PharmaMar introduces several posters to show clinical data about the treatment combining YONDELIS® with PLD in different patient profiles.

YONDELIS® (trabectedin)

- ***Complete response to trabectedin in combination with pegylated liposomal doxorubicin (PLD) in heavily pre-treated BRCA-2 mutated platinum-sensitive intermediate epithelial ovarian cancer (EOC)***
Poster: Saturday 24th, October, e-poster station
Lead author: P. Biondani, Hôpital Tenon 4 Rue de la chine 75020 Paris
- ***BRCA mutated ovarian cancer complete remission following second line treatment with trabectedin and liposomal Adriamycin***
Poster: Saturday 24th, October, e-poster station
Lead author: Dr. Raffaella Bracci, Clinica di Oncologia Medica
Centro Regionale Genetica Oncologica, Azienda Ospedaliero-Universitaria
Ospedali Riuniti, Italy
- ***Extending the platinum-free interval (PFI) with trabectedin plus pegylated liposomal doxorubicin (PLD) in a patient with partially platinum-sensitive (PPS) recurrent ovarian cancer (ROC)***

Poster: Saturday 24th, October, e-poster station

Lead autor: Dr.ssa Sara Giovannoni, U.O.C.Oncologia B, Policlinico Umberto I Roma

- ***Long-lasting complete response with trabectedin plus pegylated liposomal doxorubicin (PLD) in a young BRCA-mutated woman with platinum-sensitive relapsed ovarian cancer (ROC): a case report***

Poster: Saturday 24th, October, e-poster station

Lead autor: Dr.ssa Sara Giovannoni, U.O.C.Oncologia B, Policlinico Umberto I Roma

- ***Prolonged treatment with trabectin plus pegylated liposomal doxorubicin (PLD) combination in a heavily pretreated patient with metastatic relapsed ovarian cancer (ROC)***

Poster: Saturday 24th, October, e-poster station

Lead author: Dr Pierre Guillet, Centre Hospitalier Sainte Musse, Toulon

- ***Trabectedin in combination with pegylated liposomal doxorubicin to treat heavily-treated patient with relapsed ovarian cancer***

Poster: Saturday 24th, October, e-poster station

Lead author: Professor Dr Saad Tahir. Broomfield Hospital. Chelmsford

- ***Trabectedin in monotherapy, a therapeutic option***

Poster: Saturday 24th, October, e-poster station

Lead autor: Dr S. Rego, Hospital da Arrábida, Portugal

- ***METASTATIC OVARIAN CANCER – CHRONIC DISEASE?***

Poster: Saturday 24th, October, e-poster station

Lead autor: Dr S. Rego, Hospital da Arrábida, Portugal

- ***Multicenter retrospective study to analyze the effectiveness and safety of trabectedin (T) + PLD in recurrent ovarian cancer (ROC) patients according to SMPC. GEICO-1402r study***

Poster: Saturday 24th, October, e-poster station

Lead author: Dr L. Vidal, Hospital Universitari Clinic de Barcelona

- ***Trabectedin in advanced gynaecological carcinosarcomas - a single institution series (abstract #57)***

Poster: Sunday 25th, October, poster area (endometrial cancer)

Lead author: Dr. J. Gounaris, Department of Oncology, Addenbrooke's Hospital, Cambridge, UK

PM1183 (lurbinectedin)

The Company also shows another poster about PM1183, a novel transcription inhibitor and DNA repair, to treat relapsed platinum-sensitive ovarian cancer

- ***LURBINECTEDIN (PM01183) EFFICACY IN PLATINUM-RESISTANT/REFRACTORY OVARIAN CANCER (PRROC) PATIENTS CORRELATES WITH DRUG EXPOSURE USING PHARMACOKINETIC/PHARMACODYNAMIC (PK/PD) MODELLING (abstract #157)***

Poster: Monday 26th, October, poster area

Lead author: C. Fernandez-Teruel

About YONDELIS® (trabectedin)

YONDELIS® (trabectedin) is a novel, multimodal, synthetically produced antitumor agent, originally derived from the sea squirt, *Ecteinascidia turbinata*. The drug exerts its activity by targeting the transcriptional machinery and impairing DNA repair. It is approved in 80 countries in North America, Europe, South America and Asia for the treatment of advanced soft tissue sarcomas as a single-agent and for relapsed ovarian cancer in combination with DOXIL®/CAELYX® (doxorubicin HCl liposome injection). Under a licensing agreement with PharmaMar, Janssen Products, L.P. has the rights to develop and sell YONDELIS® globally except in Europe, where PharmaMar holds the rights, and in Japan, where PharmaMar has granted a license to Taiho Pharmaceuticals.

About PM1183 (lurbinectedin)

PM1183 is an investigational drug from the class of inhibitors of the enzyme RNA polymerase II, which is crucially involved in transcription. By targeting transcription, the drug inhibits the expression of factors important for tumor progression, and impairs the DNA repair system called NER, thereby enhancing tumor cell killing. PM1183 (lurbinectedin) is currently being investigated in different tumor types, including a Phase 3 study for platinum-resistant ovarian cancer, a Phase 2 study for BRCA1/2-associated metastatic breast cancer and a Phase 1b study for small cell lung cancer.

About ovarian cancer

It is estimated that about 240,000 cases will be diagnosed worldwide and about 150,000 women will die of ovarian cancer. Among gynaecological malignancies, it is the second most common cancer and the

one causing more deathsⁱⁱ. Most patients with ovarian cancer have late-stage disease, in which the cancer has spread, at the moment of diagnosisⁱⁱⁱ. Debulking surgery to remove most of the tumor is usually followed by chemotherapy; however, about 80% of women will relapse after treatment with platinum or a taxane and they may benefit from other therapeutic alternatives^{iv}.

About PharmaMar

Headquartered in Madrid, PharmaMar is a world-leading biopharmaceutical company in advancing cancer care through the discovery and development of innovative marine-derived anticancer drugs. The company has a strong pipeline of drug candidates and a robust R&D oncology program. YONDELIS[®] is commercially available in 80 countries for the treatment of advanced soft tissue sarcomas and for relapsed platinum-sensitive ovarian cancer. PharmaMar develops and commercializes YONDELIS[®] in Europe and has three clinical-stage programs under development for several types of solid and hematological cancers, PM1183, plitidepsin, and PM60184. PharmaMar is a global biopharmaceutical company with subsidiaries in Germany, Italy, France, Switzerland, United Kingdom and the United States. To learn more about PharmaMar, please visit us at www.pharmamar.com.

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ⁱ Poveda A et al. *Annals of Oncology* 2011;22 (1): 39-48

ⁱⁱⁱ Ferlay J, Soerjomataram I, Ervik M, Dikshit R, Eser S, Mathers C, Rebelo M, Parkin DM, Forman D, Bray, F. GLOBOCAN 2012 v1.0, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 11 [Internet]. Lyon, France: International Agency for Research on Cancer; 2013. Available from: <http://globocan.iarc.fr>, accessed on 15 April 2015.

^{iv} <http://www.cancer.org/cancer/ovariancancer/>

^v *Ann Oncol* (2013) 24 (suppl 10):x69-x76.doi: 10.1093/annonc/mdt475