



Association of pegylated liposomal doxorubicin and ifosfamide in early recurrent ovarian cancer patients: A Multicenter Phase II Trial

Florence Joly^{a,*}, Emmanuel Sevin^a, Alain Lortholary^b, Frank Priou^c, J.F. Paitel^d, Michel Fabbro^e, Michel Henry-Amar^a, Karim Hamond^a, Hugues Bourgeois^f

^a Centre François Baclesse, 3 avenue du Général Harris, 14076 CAEN cedex 05, France

^b Centre Catherine de Siemie, 2 rue Eric Tabarly, BP 20215, 44202 NANTES cedex 2, France

^c CHD, Service d'onco-hématologie, 85025 LA ROCHE SUR YON, France

^d Hôpital St Louis, Rue du Dr Schweitzer, 17000 LA ROCHELLE, France

^e Centre Val D'Aurelle Paul Lamarque, 31 rue de la croix verte, Parc Euromédecine, 34298 MONTPELLIER Cedex 5, France

^f Centre Jean Bernard, 18 rue Victor Hugo, 72015 LE MANS cedex 2, France

ARTICLE INFO

Article history:

Received 19 June 2009

Available online 3 November 2009

Keywords:

Pegylated doxorubicin

Ifosfamide

Ovarian carcinoma

Platinum-free interval

ABSTRACT

Objective. To evaluate the efficacy of pegylated liposomal doxorubicin (PLD) and continuous infusion ifosfamide (IFO) in ovarian cancer patients who relapse within 1 year after first-line paclitaxel-platinum-based chemotherapy.

Methods. Patients were stratified according to treatment-free interval (TFI) (< or ≥ 6 months). PLD (40 mg/m², day 1), IFO (1700 mg/m², infusion days 1–3), and mesna were given every 28 days for 6–9 cycles. Primary endpoint was objective response rate (ORR). Secondary endpoints were response duration, progression free survival (PFS), overall survival (OS), and toxicity.

Results. There were 98 evaluable patients (58%, TFI < 6 months). Median number of cycles was 5 (range: 1–9). The frequency of grade 3/4 anemia, thrombocytopenia, and neutropenia was 7%, 3%, and 48%, respectively; febrile neutropenia was 3%. A low rate of grade 3/4 non-hematologic toxicities was reported, including nausea/vomiting (3/4%), hand-foot syndrome (2%), and mucositis (2%). The ORR was 28% (41% and 19% in patients with TFI ≥ 6, or < 6 months, respectively); rate of disease stabilization was 26%; response duration and median OS were 6 (2.4–26) and 14 (1–46) months, respectively.

Conclusion. The combination of PLD and continuous IFO is a feasible and efficient treatment in patients with relapsed ovarian cancer, especially with TFI between 6 and 12 months. This regimen may represent an alternative to platinum reintroduction and should be evaluated in a randomized trial.

© 2009 Elsevier Inc. All rights reserved.

Introduction

Despite advances in surgery and chemotherapy during the past 20 years, most patients with advanced ovarian cancer relapse and die from the disease, and the overall 5-year survival rate is below 45% [1,2]. The standard first-line regimen is nowadays carboplatin–paclitaxel combination therapy [3]. Prior to the introduction of taxanes, alkylating agents and anthracyclines have been a longstanding part of first-line regimens [4,5]. When patients relapse 12 months after first-line chemotherapy, there is a consensus to retreat with a platinum-based regimen, with an expected response rate between 40% and 70% [6,7]. Treatment options are not as clear when relapse

occurs before one year. For partially platinum-sensitive patients (relapse between 6 and 12 months) with response rates between 25% and 30%, the benefit of reintroducing a platinum compound is more controversial [8,9], and alternative non-platinum combinations are needed [10]. When disease is platinum resistant (patients relapsing before 6 months), single-agent chemotherapy induces modest response rates (<20%) and combination regimens may be a way to increase efficacy [11]. However, the main objective of chemotherapy is to improve length and quality of survival without increased toxicity. For these two groups of patients, there is no clinical trial that could answer whether a non-platinum combination is an option for partially platinum-sensitive disease and whether a chemotherapy doublet is better than monotherapy in platinum-resistant relapse [11].

Single-agent pegylated liposomal doxorubicin (PLD) is currently the standard of treatment for patients with early recurrent ovarian cancer [12–14]. Response rates and median progression-free survival with PLD are 12% and 2 months and 28% and 7 months among

* Corresponding author. Service d'oncologie médicale, Centre François Baclesse, Boulevard du Général Harris, BP 5026, Cedex 05, France. Fax: +33 02 31 45 50 97.

E-mail address: f.joly@baclesse.fr (F. Joly).

¹ CHU Côte de Nacre, 14076 Caen, 14035 Caen, France.