

Neoadjuvant Chemotherapy - A New Therapeutic Challenge in Treatment of Ovarian Cancer- A Review

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Abstract

As per literature survey reveals that ovarian cancer is the most lethal gynecologic malignancy in females all over the world. In majority of patients who suffering from ovarian cancer clinical complete remissions are obtained through combinations of cytoreductive surgery and chemotherapy. This review represents an overview of the origin of ovarian cancer, history of chemotherapeutic regimens and also focused on chemotherapeutic agents which are useful in the treatment of ovarian cancer. Taxanes are most promising drug used in neoadjuvant chemotherapy. This review adds better advances in medical field may be based on the better understanding of drugs regimens and better control of cost in routine practice which opens the new doors for neoadjuvant chemotherapy which proves a better option in ovarian cancer treatment.

Keywords: Neoadjuvant chemotherapy, ovarian cancer, drugs regimens, anti-tumor agents.

1. Introduction

Cancer is a major public health problem in the United States and many other parts of the world. Currently, one in four deaths in the United States is due to cancer. (Table 1) has been shows the expected number of deaths from ovarian cancer projected for 2011 in the US[1].

Table1: Estimated New Cancer Cases and Deaths by Sex, United States, 2011

ESTIMATED NEW CASES			ESTIMATED DEATHS	
Sites	Total deaths	FEMALE	Total deaths	FEMALE
Ovarian Cancer	21990	21990	15460	15460

An ovarian cancer is the most lethal gynecologic malignancy in the women. The origin and pathogenesis of epithelial ovarian cancer have long been investigated but still poorly understood. Studies have shown that epithelial ovarian cancer is not a single disease but is composed of diverse group of tumors that can be classified based on distinctive morphologic and molecular genetic features. Treatment of ovarian cancer is based on the combination of cytoreductive surgery and combination chemotherapy using taxane and platinum [2][3]. Still primary cytoreductive surgery followed by platinum and paclitaxel based chemotherapy is currently standard regimen for advanced ovarian cancer[4][5].

Table 2: Origin of Ovarian Cancer

Origin of ovarian carcinoma[6]			
Theories	Serous	Endometrioid/Clear	Mucinous/Brenner
Traditional theory	Ovarian surface epithelium (mesothelium)	Ovarian surface epithelium (mesothelium)	Ovarian surface epithelium (mesothelium)
Recent theory	Fimbria	Endometrial tissue	Tubal-mesothelial junction

Ovarian cancer is one of the most sensitive of all solid tumors to antineoplastic chemotherapy, and responses are expected in over 80% of women who receive standard platinum and paclitaxel based treatment [7]. Despite this fact; the majority of women with advanced ovarian cancer will ultimately relapse and develop drug-resistant disease. Treatment of epithelial ovarian cancer is based on the combination of surgery and chemotherapy

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[8][9]. Over the last few decades; surgical tumor debulking followed by platinum-based chemotherapy is the well recognized treatment for ovarian cancer. Although response rates and complete in disease are greater than 80% and 40-60% respectively. After treatment with paclitaxel and carboplatin most patients free survival up to 18 months [10].

While the focus of this manuscript is systemic or regional chemotherapy, selected patients may benefit from secondary cytoreductive surgery, in any discussion of second-line ovarian cancer therapy. Clinicians and patients can benefit from a shared understanding of basic treatment goals [11].

Now-a-days; patients who progress stable disease during first-line treatment within one month are considered to be 'platinum-refractory'. Patients who respond to primary treatment and relapse within six months are considered to be 'platinum-resistant'; and patients who relapse more than six months after completion of therapy are considered to be 'platinum-sensitive' [12].

Literature survey reveals that the longer platinum free interval (PFI) increases the chances for a benefit by platinum re-challenge. This has been reported for PFI longer than 12 months and who are relapsing 6-12 months classified as 'partially sensitive'[13] (Table 3).

Table 3: Association of Platinum Sensitivity and PFI

Association of platinum sensitivity and PFI [6]				
Platinum sensitivity	Resistant		Sensitive	
	Refractory	Resistant	Partially sensitive	Sensitive
PFI	During chemotherapy	< 06 months	06-12 months	>12 months

2. History of chemotherapy regimens

Over the years; experts and research groups have explored different combinations of drugs in order to improve the prognosis of ovarian cancer. In 1976, the report by Witshaw and Kroner on the efficacy of cisplatin in treatment produced the modern era of combination chemotherapy. In early 1990 a new turning point in the treatment of ovarian cancer was related to discovery of paclitaxel. By comparing cisplatin/paclitaxel with cisplatin/cyclophosphamide, shown extra benefit when cyclophosphamide was replaced by paclitaxel. The carboplatin-paclitaxel combination is now considered universal regimen in treatment of ovarian cancer [14-16].

3. Overview of anti-tumor agents for ovarian cancer therapy

3.1 Paclitaxel

Paclitaxel has been established as an important initial component of ovarian cancer chemotherapy[8], and should be considered in the management of patients with recurrence. As a component of initial platinum-based chemotherapy, paclitaxel is currently administered as either a 3-h (175 mg/m²) or 24-h (135 mg/m²) intravenous infusion. Phase III randomized trials in patients with recurrent disease have evaluated dose intensity (135 versus 175 and 175 versus 250 mg/m²) and infusion duration (3 versus 24 h) without a clear advantage to either higher doses or prolonged infusion[17][18].

3.2 Docetaxel

Docetaxel has been examined in several clinical trials for management of platinum-resistant ovarian cancer, with an objective response rate of approximately 20% to 35% being documented in this clinical setting [19-21]. This level of activity is comparable to that of paclitaxel observed in a similar patient population. The dose of single agent docetaxel in these studies has been 100 mg/m², delivered on an every-three-week schedule. It is not known if a lower dose regimen (e.g., 60 or 80 mg/m²) might result in a similar response rate with reduced toxicity. Preliminary data suggest that some patients with paclitaxel resistance may respond to subsequent therapy with Docetaxel [22].

3.3 Tamoxifen

Several clinical trials have been documented that tamoxifen is an active antineoplastic agent in platinum-resistant ovarian cancer, with an objective response rate of approximately 15% [23-26]. The major advantage of tamoxifen in this clinical setting is the highly favorable toxicity profile for the agent, certainly compared to cytotoxic chemotherapy. As a result, tamoxifen may be considered the "treatment of choice" in several specific circumstances in the second-line setting for patients with ovarian cancer.

3.4 Gemcitabine

Gemcitabine, recently approved by the FDA for treatment of pancreatic cancer, has been demonstrated to be an active second-line agent in ovarian cancer. Several phase II trials have revealed a 15% to 20% response rate in this clinical setting [27][28] although minimal activity was apparent when evaluated as front-line therapy in poor prognosis patients with advanced disease[29]. Because of the ability of gemcitabine to inhibit DNA repair, combinations with cisplatin and carboplatin are under development [30-32].

3.5 Ifosfamide

Several clinical trials have demonstrated ifosfamide to be an active agent in ovarian cancer patients after initial platinum-based therapy (10%-20% objective response rate) [33-35].

4. Conclusion

Neoadjuvant chemotherapy of ovarian cancer continues to evolve as new agents with diverse mechanism of action. In view of the chronic nature of recurrent ovarian cancer, the achievement of stable disease with maintenance of performance status is an acceptable goal for many patients. This review covers better advances in medical field may be based on the better understanding of drugs regimen and better control of cost in routine practice which opens the new doors for neoadjuvant chemotherapy which proves a better option in ovarian cancer treatment.

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Declaration of interest

The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript.

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