

Preserved antitumor activity and reduced cardio-toxicity of first-line pegylated liposomal doxorubicin compared with conventional doxorubicin in patients with metastatic breast cancer



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Introduction

Anthracyclines are an important class of agents used for the treatment of early and advanced stage breast cancer. Doxorubicin is an anthracycline used in the treatment of breast cancer, but its use is limited by cumulative dose-dependent cardio-toxicity which can manifest as acute or sub acute injury immediately after treatment or also as late-onset cardiomyopathy years later. Pegylated liposomal doxorubicin is a novel drug delivery system that reduces plasma levels of free drug as well as drug delivery to normal tissues, potentially decreasing cardio-toxicity^{1, 2}. Our aim is to compare the efficacy and cardio-toxicity of pegylated liposomal doxorubicin and conventional doxorubicin in first-line treatment of metastatic breast cancer (MBC).

Methods

A literature search of Cochrane library, EMBASE and PUBMED was conducted in May 2010 for English language randomised controlled trials (RCTs) assessing the efficacy and cardio-toxicity of pegylated liposomal doxorubicin compared to conventional doxorubicin in first-line treatment of metastatic breast cancer (MBC). Study selection for inclusion in the review was based on a pre-specified protocol with the following inclusion criteria (Table 1):

Table 1: Inclusion criteria

Criteria	Inclusion
Study design	Randomised controlled trials
Disease	Metastatic breast cancer
Intervention	Pegylated liposomal doxorubicin
Comparator	Conventional doxorubicin
Line of therapy	First line therapy
Language	English

Two reviewers independently selected trials, assessed quality, and extracted data; a third reviewer resolved any discrepancies. The fixed effects meta-analysis was performed in STATA 9.0 using a standard meta-analysis approach.

Results

- Forty-five citations met the first pass inclusion criteria, out of 1595 retrieved from the database searches. Only two studies met the inclusion criteria after second passing for extraction of outcomes (Figure 1).

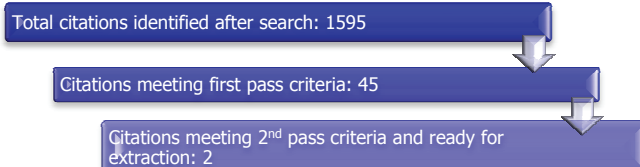


Figure 1. Study flow diagram

- Data for outcomes used in the meta-analysis is shown in Table 2 and Table 3

Table 2: Overall survival data for meta-analysis^{1, 3}

Study	HR (pegylated vs. conventional doxorubicin)	CI min	CI max
O'Brien 2004	0.94	0.74	1.19
Harris 2002	0.76	0.56	1.04

Table 3: Overall response rate and cardio-toxicity data for meta-analysis^{1, 3}

Study	Pegylated Doxorubicin		Conventional Doxorubicin	
	N	n	N	n
Overall Response rate				
O'Brien 2004	254	69	255	76
	108	28	108	30
Cardio-toxicity				
Harris 2002	254	10	255	48
	108	12	108	25

- Meta-analysis of two studies indicated overall survival (HR = 0.869 [95% CI: 0.720, 1.049]) was comparable between the two arms
- Results were similar for overall response rate (RR = 0.908 [95% CI: 0.725, 1.139]) showing comparable efficacy of treatments
- Treatment with pegylated liposomal doxorubicin resulted in a significant reduction in cardio-toxicity as compared to conventional doxorubicin (RR = 0.312 [95% CI: 0.198, 0.490])

Conclusions

Pegylated liposomal doxorubicin provides comparable antitumor activity in terms of efficacy and is better tolerated as compared to conventional doxorubicin in the treatment of metastatic breast cancer. Thus, the liposomal drug delivery system can play a significant role in the use of doxorubicin in MBC treatment which is otherwise limited by its cardio-toxicity. Hence, there is a need to look at conventional drug delivery systems in a novel way for all other classes of drugs which are otherwise limited by the toxicity.

References

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