

Phase II studies of anticancer chemotherapy: indirect evidence of poor quality

We carried out a literature search on the Web for clinical studies dealing with chemotherapy drugs or associations with biotherapies (i.e. antibodies, small molecules, cytokines) published in 2005 on peer-reviewed international journals in order to describe their content. We used both PubMed and Science Citation Index to search the terms 'chemotherapy' + either 'phase II (or 2)' or 'phase III (or 3)' in all text including title, keywords, and abstract, and selected only articles published in English. After the preliminary selection, we went through each of the abstracts and eliminated (i) studies reporting only 'interim' results, (ii) clinical cases, and (iii) meta-analyses or reviews. The impact factors (IF) of the journals were divided in two classes: low IF (<3) and high IF (≥ 3). The information was collected with a methodological approach described elsewhere [1]. We selected 80 trials: 48

studies were published in journals with low IF and 32 with high IF. We did not identify any publication bias as we did in biotherapy studies [2]. In fact, no significant correlation between study results according to study phase and IF of journals ($P = 0.8660$ for phase II trials; $P = 0.7212$ for phase III trials) was found (Table 1). We, however, found that phase II studies were more likely to be published in low IF journals than phase III studies ($P < 0.0001$) (Table 1). Evidence in literature indicates that this is more likely related to the quality of these studies than to editorial policy. Several authors have already raised concerns about the quality of phase II studies which is generally poor [3–5]. In fact, the percentage of phase II trials with adequate and identifiable statistical design (a good quality-related factor) is reported to be 12%–35% [3–5]. This concern is more important if we consider that phase II studies are the basis for the selection of drugs and/or new combinations for phase III studies. The poor quality of phase II studies could lead to well-designed but inappropriate and unuseful phase III studies. Thus, continuing effort and monitoring (*ad hoc* questionnaires for quality assessment, standardisation of reviewing procedures, presence of biostatistics in clinical trials, tighter control of the approval process, biological, and preclinical studies, etc.) is still much needed to enhance the quality of phase II studies of anticancer chemotherapy and biochemotherapy.

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Table 1. Correlations between journal's impact factor, results and study phase

Journal's impact factor	Phase II study results			Phase III study results			Study phase		
	Negative	Positive	P^a	Negative	Positive	P	II	III	P
Low (<3)	4	29	0.8660	8	7	0.7212	33	15	<0.0001
High (>3)	–	6		11	15		6	26	

^a P values were obtained with chi-square test as explained in Ottaiano et al. [1].