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The characteristics of unsolicited clinical oncology literature provided by pharmaceutical industry

The pharmaceutical industry plays an important role in the development of new cancer treatments. Data from clinical phase I to III trials will, if convincing, eventually lead to the licensing of the drug. At that stage, and even before, companies embark on marketing and promotion of their new products [1, 2], by advertising in professional journals, through visits by drug company representatives, the organization of promotional meetings or sponsoring of continuous medical education. Finally, many drug companies maintain promotional mailing services to physicians to provide them with regular information, particularly on new drugs. Concern has been voiced that advertising may lead to uncritical and inappropriate prescribing of new drugs in clinical practice [3]. Articles prepared with drug company support have been shown to be more likely to report favourably on a drug of interest than articles published without such support [4]. In advertisements for antihypertensive and lipid-lowering drugs in Spanish medical journals, the promotional statement was not supported by the studies cited in ~40%, most frequently because the advert recommended the drug in a patient group other than that assessed in the respective trial [5]. Drug companies may exert a considerable influence over which drugs doctors prescribe [6], and also influence continuous medical education. A recent letter to the *Annals of Oncology* pointed out that visits of pharma representatives in clinical departments are increasing apparently with the aim of pushing clinicians towards using their specific drugs [7–9]. Whereas the relationship and interactions between doctors and drug company representatives and the advertising practices of industry have been examined in several studies [5, 10, 11], promotional mailings have not been analysed in depth. We studied the characteristics of literature and other material mailed by the pharmaceutical industry to a medical oncologist in Switzerland.

One of us (MFF) prospectively and comprehensively collected all unsolicited mail posted to his hospital address from pharmaceutical companies from 1st January to 30th September 2002. We classified the material as follows: (i) peer-reviewed journal articles (reprints of original research or reviews), (ii) abstracts from peer-reviewed articles, (iii) customized abstracts, (iv) lists of references and (v) publications prepared by industry or communication

companies working for industry. The latter consisted of newsletters or conference reports, for example editorials written by opinion leaders, reviews prepared by industry and interviews with keynote speakers. Abstracts published in journals or conference proceedings that had been rewritten or edited by industry were classified as customized abstracts. We assessed whether in material reporting on clinical trials of anticancer drugs, results were interpreted as showing superiority or inferiority of the new drug, or no difference between comparison groups. Statements such as ''new treatment offers significant improvement over …'', ''new drug significantly better …'', etc. were interpreted as indicating superiority.

Forty-nine mailings including a total of 961 items from 13 different pharmaceutical companies were received during the study period (1.25 mailings and 24.6 items per week). The vast majority of items received were customized abstracts (768, 80%; Table 1). Thirty items were original abstracts (3%) and seven (0.7%) were reprints of articles published in peer-reviewed journals. A total of 156 items (16.3%) were from industry newsletters or conference reports. Among the 805 items selected from the literature and conference proceedings, reports on clinical trials (276 items, 28.7%) and narrative review articles (271 items, 28.2%) were most common. Among clinical trials, phase II studies (125, 46%) were more frequently included than phase III (95, 34%) and phase I studies (56, 20%). Only 12 (1.2%) items reported on systematic reviews. The drugs most frequently examined in the 220 phase II and phase III studies were tamoxifen, anastrozole and docetaxel. Head-to-head comparisons of different drugs were reported in 120 (55%) items (86 phase III and in 34 phase II clinical trials). The remaining articles compared different dosages of the same drug in dose-finding studies or the effect of different numbers of treatment cycles.

Table 1. Types of studies and articles selected by industry for mailing from the literature and conference proceedings

Design	Type of article			
	Peer-reviewed journal article	Original abstract	Customized abstract	Total
Clinical trial	2	27	247	276 (28.7%)
Phase I	0	6	50	56
Phase II	1	16	108	125
Phase III	1	5	89	95
Narrative review	2	2	267	271 (28.2%)
Systematic review	0	0	12	12 (1.2%)
Cohort study	2	0	67	69 (7.2%)
Case–control study	0	0	28	28 (2.9%)
Case series	1	1	85	87 (9.1%)
Case report	0	0	28	28 (2.9%)
Laboratory study	0	0	22	22 (2.3%)
Economic study	0	0	12	12 (1.2%)
Subtotal including scientific articles	7 (0.7%)	30 (3%)	768 (80%)	805 (83.7%)
Total				961 (100%)

A total of 173 reports of phase II and III trials (79%) reported results that favoured the drug produced by the company responsible for mailing the item (Table 2). Most of them reported unpublished data from meeting abstracts.

Although our study was based on the mail received by one Swiss medical oncologist, we assume that the material was representative of what was mailed to many, if not all, practising oncologists in Switzerland during the sampling period as a part of mass mailings. Mailings were frequent and mainly included abstracts of unpublished studies presented at conferences, which were often edited (customized) by industry. Clinical trials and narrative reviews dominated, whereas systematic reviews were virtually absent. Among phase II and phase III drug trials, a large majority of items reported results that were favourable to the drug produced by the company sending the material. An interesting finding of our study is the frequent use of customized, rewritten or edited, abstracts. Their content was often simplified, and data presented in more appealing ways, for example by using colour graphs rather than tables. Clearly, further research is needed to clarify whether and in what way content and conclusions may have changed in this process.

Many practising physicians value promotional efforts of pharmaceutical companies to communicate data on new drugs with possible relevance to their daily clinical work. Company-based promotion is highly organized and allegedly comprehensive, as evidenced, for example, by the inclusion of reference lists in the mailings examined in this study. The selection of the abstracts included in the mailings may well have favoured the company's drugs, similar to the well-documented selective publication of positive results [12]. Furthermore, the majority of the items related to conference presentations of unpublished studies. Meeting abstracts represent preliminary, immature and incomplete communications of clinical data. Their validity is therefore lower than that of peer-reviewed original articles published in scientific journals [13]. The conclusions published in meeting abstracts do not always match the conclusions from the corresponding original article that is typically published in peer-reviewed journals 1–2 years later. Finally, unsystematic narrative reviews of published evidence often reach erroneous conclusions, and systematic reviews and meta-analyses, which are based on comprehensive literature searches and careful assessment of the quality of component studies are more reliable [14]. The clear focus on narrative reviews in the material sent to oncologists

Table 2. Conclusions from phase II and III drug trials selected by industry

	Type of trial		
	Phase II	Phase III	Total
Experimental drug			
Less beneficial	8 (6.5%)	11 (11.5%)	19 (8.5%)
More beneficial	105 (84%)	68 (72%)	173 (79%)
Equivalent	8 (6.5%)	11 (11.5%)	19 (8.5%)
No clear statement	4 (3%)	5 (5%)	9 (4%)
Total	125 (100%)	95 (100%)	220 (100%)

must therefore be of concern, and represents another potential source of bias.

We found that ~80% of clinical trials were interpreted as showing superiority of the drug produced by the company mailing the item on the trial. In addition to the selective inclusion of positive studies, the inclusion of trials of low methodological quality, which tend to exaggerate effects, is another element of concern [15, 16]. Trials may be designed to produce positive results, for example by using comparison treatments that are known to be substandard. Such trials violate the uncertainty principle: patients should be enrolled in randomized clinical trials only, if there is substantial uncertainty about the efficacy of the treatments being compared. A recent survey of randomized clinical trials in patients with multiple myeloma [17] found that overall the uncertainty principle was upheld, with 56% of trials favouring experimental treatments and 44% standard treatments. However, this was not the case for studies funded by industry, which favoured the experimental drug in 74% of trials.

The material received during the study period mainly included literature about a restricted and selected number of newer drugs that were being heavily promoted during the study period. Articles addressing other important questions in oncology, including for example advances in the multidisciplinary treatment of cancer, and other important issues of interest were conspicuously under-represented in the collected material.

In summary, we conclude that mailed educational material provided by pharmaceutical companies appears to be biased to include selected positive data and trials on drugs of timely interest to the respective company. Although literature services of pharmaceutical companies offer much convenience, physicians should not rely on unsolicited literature when reviewing the evidence of the clinical efficacy and safety of new drugs. Doctors should be aware of the possible biases involved, review such material critically and consider its implications for their continuous medical education as well as their treatment decisions in clinical practice.

C. Wick[1,2], M. Egger[1], S. Trelle[1], P. Jüni[1] & M. F. Fey[2]*

[1]Department of Social and Preventive Medicine and [2]Department of Medical Oncology, University of Bern, Inselspital, Bern, Switzerland (*E-mail: martin.fey@insel.ch)

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