Does the expert panel at the St Gallen meeting provide an unbiased opinion about the management of women with early breast cancer?

The 11th International Conference on primary therapy for early breast cancer took place in St Gallen from 11 to 14 March 2009. About 4500 delegates from 96 nations attended the meeting, which was designed to review recent results of clinical trials for early breast cancer. The final day of the meeting was reserved to update the International Consensus on treatment recommendations for the primary therapy for early breast cancer, which traditionally ends the biannual conference. An international panel of 41 experts under the leadership of two cochairs tried to reach consensus by voting on several aspects of treatment of women with early breast cancer. These recommendations will be published, and publications from previous meetings [1, 2] have been influential in guiding the treatment of women with breast cancer worldwide.

The expert panel is multidisciplinary but a majority of its members are medical oncologists. The panel discussed a variety of strategies for the management of early breast cancer, and the discussion was of great interest for the large audience. However, the presence of potential conflicts of interest among the panelists raises concern as to whether their opinions were free of bias. Some of the panel members are known to have long-standing associations with pharmaceutical companies that market various types of chemotherapy, aromatase inhibitors or targeted agents. Some of them have given lectures in company-sponsored symposia and/or are involved in ongoing Internet ‘education’ programs for one or more companies.

Unfortunately, neither the program at the St Gallen meeting nor its Internet site provided disclosure of potential conflicts of interest of the expert panel or its chairs, and they were not declared during the meeting.

Aromatase inhibitors provide a recent example of aggressively marketed products, which have a similar clinical efficacy and safety profile. Three companies are trying to increase their share of the market by convincing doctors and patients of the superiority of their own product compared with another, and with the much cheaper tamoxifen, which is the older adjuvant treatment of breast cancer with a well-known safety profile.

Aromatase inhibitors have been shown to lead to a small increase in disease-free survival compared with tamoxifen when evaluated as adjuvant therapy for postmenopausal women with hormone-responsive breast cancer in large clinical trials [3–5]. They are useful as alternatives for women who have contraindications to the use of tamoxifen and might lead to a small improvement in survival when used after initial tamoxifen. However, there is no evidence for superiority of overall survival or quality of life compared with tamoxifen when they are used as initial adjuvant treatment of postmenopausal women with hormone-responsive breast cancer, which should be the key end point for a clinician when considering replacement of a well-established agent with a newer and more expensive alternative [6].

Some members of the expert panel with open long-standing relationships with companies that market aromatase inhibitors encouraged the panel to vote on the question “should aromatase inhibitors or tamoxifen be used first?” Other members of the panel stated: “we do not have enough data to address this”, but the decision to vote was made by the chair, after some hesitation. The result was 69% in favor of the initial use of aromatase inhibitors—some were against, some were undecided.

The above events stimulated my interest in criteria for appointment of the panel members and their associations with pharmaceutical companies. I therefore undertook a search to identify possible conflicts of interest of each of the panel
members and chairs. My search strategy included identification in PubMed (http://www.ncbi.nlm.nih.gov/pubmed/) of all articles related to medical treatment of breast cancer published during 2006–2009 for which panel members were authors and review of these articles to identify declared relationships with companies (provided routinely in Journal of Clinical Oncology, New England Journal of Medicine, Lancet and some other journals). The Faculty/Program Committee Disclosure Index of American Society of Clinical Oncology (ASCO) Breast Cancer Symposium 2007 was added to the search. The reporting of the authors of European Society for Medical Oncology clinical guidelines in breast cancer was also checked.

The search results are summarized in Table 1. Eleven of the 41 panel members did not have possible conflicts of interest or relevant publications. Twenty-four of the panel, including both chairs, had reported financial relationships with companies that market aromatase inhibitors, and as many had relationships with other companies that market other therapeutic agents used in the treatment of breast cancer. The search results may provide an underestimate of potential conflicts of interest because many journals do not demand disclosure, the reporting was sometimes inconsistent and some articles may have been missed.

There have been constructive and legitimate relationships between the pharmaceutical industry and academia, and a disclosed financial relationship with industry does not necessarily entail bias. Yet, it is equally true that full disclosure does not prevent one from having substantial bias. Doctors have a tendency to believe that their education as scientists protects them from influences that might generate bias in their opinions. Interestingly, the same doctors will recognize the potential for bias in clinical research by requiring clinical trials to be conducted ‘double blind’ whenever this is feasible. Bias is not necessarily intentional and is a natural human phenomenon [7–10].

Entanglements with industry can differ in size, number and duration, and investigators may receive funds either for research or personal purposes (or both). The argument has been made that balance can be achieved by accepting rewards from all the competitors in a field [11]. However, accepting financial reward from everyone is not the same as being beholden to no one [12]. Also, the monetary relationship is not the only or even necessarily the dominant influence on one’s thinking—close and long-standing contacts and sometimes friendships with corporate actors and agencies can be even more powerful. That is human.

The purpose of clinical guidelines is to help the practicing physician to make decisions and to facilitate application of the most convincing evidence available for the diagnosis and treatment of a disease. They have become important tools for many physicians and influence substantially those who make decisions about the funding of medical care. Guidelines are expected to be unbiased, valid and directed only to the interests of the patients [12]. Specific guideline committees have adopted requirements to reduce the potential for bias; for example, guideline committees for ASCO are required to have more than half of the members with no relevant financial relationships with the pharmaceutical industry, and one cochair must have no relevant relationship with industry, while the other may have received research funding but no personal remuneration [13].

Several recent articles have highlighted the profound influence of the pharmaceutical industry on the medical profession [14–16]. Medical schools and professional associations have developed policies in response to potential conflicts of interest [17, 18]. A recent publication [19] indicates very rigorous recommendations for generating guidelines and states: “professional medical associations must hold the individuals who write guidelines and outcome measures to the most stringent conflict-of-interest standards. Disclosure of industry relationships by committee members is not sufficient protection. Professional medical associations should be encouraged to appoint to these committees only individuals who have no ties to industry. At a minimum, professional medical associations must exclude from such committees persons with any conflict of interest ($0 threshold) involving direct salary support, research support, or additional income from a company whose product sales could be affected by the guidelines”. Others recommend that the largest part of the guideline committee membership, and in particular the leaders, should be changed from one edition to the next [12]. There has been very little change in membership of the expert panel at the St Gallen meeting: 39 of the 43 members of the 2009 panel were also members in 2007 and 26 of them were members in 2005.

Finding appropriate members of expert panels that establish guidelines might seem difficult in the present environment, in

<table>
<thead>
<tr>
<th>Number of expert panel members who reported</th>
<th>Stock ownership</th>
<th>Consultant or advisory role</th>
<th>Honoraria/lecture fees and/or other remuneration</th>
<th>Research funding</th>
<th>Any potential conflict</th>
<th>No potential conflict of interest/no relevant articles</th>
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<td>Companies that market aromatase inhibitors³</td>
<td>1</td>
<td>18</td>
<td>18</td>
<td>17</td>
<td>24</td>
<td>19</td>
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<tr>
<td>Other companies</td>
<td>18</td>
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<td>14</td>
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<tr>
<td>Any company</td>
<td>23</td>
<td>26</td>
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<td>20</td>
<td>32</td>
<td>11</td>
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³Six panel members did not have relevant presentations or publications in journals that require reporting of potential conflicts of interest.
³Astra-Zeneca, Novartis and Pfizer.

Table 1. Number of expert panel members (a total of 43, including the two cochairs) who reported potential conflicts of interest in a publication or presentation during 2006–2009
which clinical research has become so heavily dependent on support from the pharmaceutical industry. However, it is essential to ensure public and practitioner confidence that guidelines that are free of commercial bias are established. Those most qualified to be members of guideline panels are not necessarily the most visible [19]. A minimum requirement should be the exclusion of those ‘thought leaders’ on company speakers’ bureaus, who are openly connected to the companies in question, and those who hold stock in such companies. The requirement for total disclosure of potential conflicts of interest in the context of a panel meeting should be self-evident and at least 50% of the membership should rotate off the panel between successive meetings.

The St Gallen consensus meeting and the updated recommendations have a huge influence on the treatment of early breast cancer worldwide. Any threat to the integrity of the guideline process is a serious one, and if the collective trust of the doctors and public is lost, it may be thereafter difficult to re-establish.

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references


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