Possible Impact of the NHK Special Questioning Cancer Treatment in Japan on Clinicians’ Prescriptions of Oxaliplatin

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Medical information through media may influence physicians’ prescriptions of medication. The Japan Broadcasting Corporation (NHK) aired on April and May 2005, a special program called ‘Questioning Cancer Treatment in Japan’, covering oxaliplatin. We investigated potential impact of this program on prescriptions, utilizing a post-marketing clinical trial monitoring of all patients receiving oxaliplatin. The post-marketing clinical trial reached the target sample size of 1200 by the 4th week of May, 44 weeks sooner than anticipated. The newly registered numbers of facilities and patients exhibited a bimodal peak in April and June. The viewer rating of NHK special was 8.3%, whereas three national newspapers and one weekly magazine took up the minor articles of oxaliplatin. In July 2007, 405 clinicians sent a written opinion to NHK, stating ‘NHK special invites misperceptions and confusions to public.’ NHK special might have had an impact on clinicians’ prescriptions of oxaliplatin.

Key words: oxaliplatin – television program – post-marketing clinical trial – colon cancer

INTRODUCTION

The increasing incidence of malignant tumors associated with the aging population has become an object of public concern in Japan (1). In 2004, deaths from malignant tumors accounted for 31.1% of the total number of deaths, and was the leading cause of death (2). Although the age-adjusted mortality from malignant tumors has declined after 1996 due to early diagnosis and the progress in treatment (2), many patients remain uncured (2).

Oxaliplatin is a promising anticancer drug for advanced colorectal cancer. Oxaliplatin was approved in France in 1996 (3) and in the United States in 2002 as a combination therapy with 5-FU/leucovorin for colorectal cancer resistant to irinotecan combination therapy (4). In Japan, combination therapy (FOLFOX4 treatment) with continuous intravenous administration of oxaliplatin and 5-FU/leucovorin for inoperable advanced and recurrent colorectal carcinoma was approved in March 2005 (5), following petition to the Minister of Health, Labor and Welfare for early approval by cancer patient societies (6). As the experience in FOLFOX4 treatment had been little in Japan, the package leaflet attached to Elplat (the brand name of oxaliplatin) contains a warning stating that ‘only physicians who are sufficiently knowledgeable and experienced can use this product. Administer only to selected patients. Provide patients with a thorough explanation of the risk involved with the use of this product’. Monitoring all patients that use oxaliplatin was...
mandated as part of a post-marketing clinical trial once oxaliplatin went on the market in Japan on 6 April 2005 (7). Registered patients were followed for a minimum of 3 months, and the decision whether to continue monitoring after the 3 month of administration was left to each medical facility. The distributor (Yakult Pharmaceutical Inc. Co. Ltd, Tokyo, Japan) estimated the number of patients eligible to administration of oxaliplatin to be 1400 people for a year. The target sample size of the post-marketing clinical trial was 1200 patients (8).

In 2005, the Japan Broadcasting Corporation (NHK) began a ‘Cancer Support Campaign’ (9). As a part of this, NHK aired on April 30 and May 1, 2005 a three-part, audience-participation program called ‘Questioning Cancer Treatment in Japan’. Viewer ratings were estimated to be 8.3%, 6.3% and 8.4% (10), comprising a total of approximately three million people. The first program of the series dealt with oxaliplatin. After introducing patients who had privately imported oxaliplatin for personal use, the in-studio audience then debated the issue. Approximately 24 min were spent on introducing and debating oxaliplatin. After the program was aired, clinicians issued to NHK a letter claiming that some parts of the story were medically inappropriate (11).

The possibility has been suggested that providing medical information to the public through advertisements and media may influence physicians’ prescriptions of medication (12), although it is unclear. Meanwhile, physicians involved in cancer treatment may not easily be influenced as they have a high level of specialty. A detailed analysis of the NHK special and changes in the number of prescriptions of oxaliplatin may provide information on the media impact on cancer specialists’ prescriptions.

MATERIALS AND METHODS

We investigated the weekly numbers of contracted facilities, registered facilities, registered patients and collected questionnaires which were listed on Yakult Honsha’s homepage (monitoring all patients using Elplat) (13). We also collected data on fatal patients from ‘the Line List of adverse effects and fatal patients from monitoring of all patients using Elplat’ (14) on the same homepage. We followed the judgments of attending physicians listed on the homepage with regard to the causal relationship between deaths and oxaliplatin.

To investigate the potential impact of mass media on oxaliplatin prescriptions, we reviewed media reports on oxaliplatin between April and June 2005 among four newspapers (Asahi Shimbun, Yomiuri Shimbun, Mainichi Shimbun and Nikkei Shimbun), seven magazines (Weekly Shincho, Weekly Bunshun, Weekly Post, Weekly Gendai, Weekly Mainichi, Weekly Asahi and Weekly Yomiuri), and five nationally broadcasted television programs (NHK, Asahi Television, Fuji Television, Tokyo Broadcasting System and Nippon Television).

To investigate reactions of medical practitioners and patients to the NHK special, we reviewed media reports and commentaries on the NHK special between July 2005 and February 2006 among four forementioned newspapers, seven forementioned and some more magazines, and blogs. We used an internet database (15–19) to search newspapers and blogs and the Oya Soichi Library to search magazines (20). We contacted television stations for broadcasts pertaining to television programs on oxaliplatin.

RESULTS

CHANGES IN THE NUMBER OF CONTRACTED FACILITIES

Figure 1 shows changes in the number of newly contracted facilities per day during the post-marketing clinical trial. The graph exhibited a bimodal peak on April 6–19 and June 1–7.

NUMBER OF PATIENTS USING OXALIPLATIN

Figure 1 shows changes in the number of patients registered in the oxaliplatin post-marketing clinical trial. The target sample size of 1200 patients was reached in the 4th week of May. This was 44 weeks sooner than anticipated by the pharmaceutical distribution company.

As of 7 February 2006, reports on 4019 patients had been submitted. Of these, 381 patients (9.5%) had died. Within 30 days of administration, 138 patients (3.4%) died. Deaths related to adverse events of oxaliplatin were diagnosed in 22 patients (0.5%).

Figure 1. Changes in the number of contracted facilities and the number of patients registered in the post-marketing clinical trial for 3 months after oxaliplatin release. The bars show the average number of newly contracted facilities per day during the post-marketing clinical trial; the line indicates the average number of newly registered patients per day.
**Media Reports on Oxaliplatin**

Table 1 shows media reports on oxaliplatin from April to June 2005 and Table 2 shows media reports on the NHK special from April 2005 to February 2006.

**DISCUSSION**

As the government mandates monitoring all patients for a minimum of 3 months when hospitals first introduced oxaliplatin, the number of patients registered in the post-marketing clinical trial from April to June 2005 accurately reflects the number of patients who received oxaliplatin. The present study demonstrates the possibility that physicians’ prescriptions may have been influenced by media. The number of patients registered in the post-marketing clinical trial increased sharply after mid-May, peaking in June 1–7. The number of contracted facilities in the post-marketing clinical trial also peaked during the same period (Fig. 1). The increase in the number of patients who received oxaliplatin resulted from an increase in the number of facilities that introduced oxaliplatin, not because patients were concentrated at any particular facility.

Interestingly, the increase in the number of contracted facilities exhibited a bimodal peak during the short period of 2 months. There are four possible explanations. First, the change in the number of contracted facilities may exhibit an intrinsic bimodal peak since there are two groups of facilities; some sign the contract before the drug was released and initiate prescribing at the time of drug release, whereas others begin contractual procedures after the drug release. To further investigate this possibility, it would be useful to compare drugs for which post-marketing clinical trials were carried out during the same period. We found the status of Arava contrasts with that of oxaliplatin. The number of monitoring facilities peaked in the second year after the drug release and fell off flatly after the peak. Therefore, this hypothesis alone would be difficult to explain the change in the number of contracted facilities for oxaliplatin.

Second, the number of patients treated in the first month of approval was relatively small compared with that of contracted hospitals at the first peak, because the physicians selected patients and used oxaliplatin carefully for the safety at the beginning of inexperienced treatment. The second peak of the contracted hospitals coincided with the increase of patients as the physicians got used to the treatments. This scenario seems also reasonable and understandable, whereas it was not the case with Arava.

Third, some information released after oxaliplatin went on the market may have influenced prescriptions. In addition to the NHK special, three national newspapers and one weekly magazine covered the topic of oxaliplatin between April 6 and July 6 (Table 1). Although Yomiuri Shimbun, Asahi Shimbun and Weekly Gendai published minor articles or a column on cancer treatment, they did not emphasize oxaliplatin. These media reports probably had little influence on oxaliplatin prescriptions. Meanwhile, the NHK special and Nikkei Shimbun mentioned oxaliplatin as the main topic of the program or an article. Yet, Nikkei Shimbun mentioned oxaliplatin in a minor article similarly to Yomiuri Shimbun and Asahi Shimbun, which had less impact than did the NHK program with special emphasis on oxaliplatin. On the basis of these search results, there is little possibility that media reports on oxaliplatin between April and July 2005 other than the NHK special had an impact on oxaliplatin prescriptions.

Fourth, information provided to physicians from the academic community or pharmaceutical companies may have influenced oxaliplatin prescriptions; however, no major meetings pertaining to clinical oncology (Japanese Cancer Association, Japanese Society of Medical Oncology, Japan Society of Clinical Oncology) were held in Japan between

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<tr>
<td>Television</td>
<td>NHK</td>
<td>30 April 2006</td>
<td>NHK supesharu ‘nihon no gyou iryou wo tou’ (NHK Special: ‘Questioning Cancer Treatment in Japan’)</td>
<td><a href="http://www.nhk.or.jp/special/">http://www.nhk.or.jp/special/</a></td>
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<td>Newspapers</td>
<td>Nikkei Shimbun</td>
<td>6 April 2006</td>
<td>Yakuruto, daichougan chiryouyaku, kokunai de hanbai kaiishi (Yakult to Begin Selling Drug Treatment for Colon Cancer in Japan)</td>
<td><a href="http://www.yomiuri.co.jp/iryou/medi/gantotomoni/20050411sq01.htm">http://www.yomiuri.co.jp/iryou/medi/gantotomoni/20050411sq01.htm</a></td>
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<td>Yomiuri Shimbun</td>
<td>11 April 2006</td>
<td>Touyaku ha ‘kumiawase’ to ‘sajikagen’ (Medication ‘Combinations’ and ‘Prescriptions’)</td>
<td><a href="http://www.yomiuri.co.jp/iryou/medi/gantotomoni/20050411sq01.htm">http://www.yomiuri.co.jp/iryou/medi/gantotomoni/20050411sq01.htm</a></td>
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<td>Magazines</td>
<td>Weekly Gendai</td>
<td>30 April 2006</td>
<td>Kouganzai ‘okisaripurachin’ (The Anticancer Drug ‘Oxaliplatin’)</td>
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NHK, Nihon Hoso Kyokai (Japan Broadcasting Corporation).
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<td>Asahi Shimbun</td>
<td>8 July 2005 Morning edition; page 2 of Nation section</td>
<td>Ishi 400 nin, NHK ni ikensho; gan tokuban, kyokkansei wo kaku (Written opinion from 400 physicians claims NHK cancer special lacks objectivity)</td>
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<td>9 July 2005 Morning edition; page 2 of Nation section</td>
<td>Gan tokuban ‘gokai maneku’; ishira ikensho, NHK ha ‘de-ta seikaku’ (In response to a written opinion from physicians claiming cancer special ‘invites misperceptions’, NHK says ‘data is correct’)</td>
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<td>Yomiuri Shimbun</td>
<td>10 July 2005 Morning edition</td>
<td>NHK gan tokuban ni rinshouirga ga ikensho (Physicians issue written opinion on NHK cancer special)</td>
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<td>Mainichi Shimbun</td>
<td>13 July 2005 Morning edition</td>
<td>NHK gan iryou bangumi ni ikensho; ishira 405 nin okaru (405 physicians issue written opinion on NHK cancer treatment program)</td>
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<td></td>
<td>AERA</td>
<td>8 August 2005 edition; released 1 August 2005</td>
<td>Kougonzai ha kiku no ka? (Do Anticancer Drugs Work?)</td>
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<td>Blogs</td>
<td>Demonono haremono tokoro kirawuzu (Rashes and Tumors Everywhere)</td>
<td>8 January 2006</td>
<td>‘NHK no gan tokushuu, sono ichi’ (NHK cancer special: part 1)</td>
<td><a href="http://black.ap.teacup.com/applet/saikyou/200601/archive?b=7">http://black.ap.teacup.com/applet/saikyou/200601/archive?b=7</a></td>
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<td>‘Hirogaru NHK gan supesharu no hankyou’ (Widespread reactions to NHK cancer special)</td>
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<td>Yusa nako no okiraku na iryou nikki (Nako Yusa’s Personal Medical Diary)</td>
<td>11 January 2006</td>
<td>NHK supesharu ‘nihon no gan iryou wo tou’ wo susumenai wake (Why I do not recommend the NHK Special ‘Questioning Cancer Treatment in Japan’)</td>
<td><a href="http://nakoysusa.blog42.fc2.com/blog-entry-40.html">http://nakoysusa.blog42.fc2.com/blog-entry-40.html</a></td>
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<td>Kougonzai herupudesuku (Helpdesk for Anticancer Drugs)</td>
<td>11 January 2006</td>
<td>‘NHK supesharu: nihon no gan iryou wo tou’ ni kunrenshii jouhou kaiji wo kangaeru (Taking a look at information disclosure in connection with the ‘NHK Special: Questioning Cancer Treatment in Japan’)</td>
<td><a href="http://ac-drugs-blog.try-2-live-4-a.com/?eid=394873">http://ac-drugs-blog.try-2-live-4-a.com/?eid=394873</a></td>
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April and July 2005. The meeting of the American Society of Clinical Oncology was held on 14–17 May 2005, without any presentation on the results of large-scale clinical trials of oxaliplatin for advanced cancer. Although the distributor Yakult held a symposium commemorating the release of oxaliplatin on 1 July 2005 (22), it does not explain the increase in the number of oxaliplatin prescriptions in the first week of June. The above circumstances suggest that media or other information sources other than the NHK special could have hardly influenced oxaliplatin prescriptions.

In contrast, the NHK special was aired on April 30 and May 1, which preceded the second increase on June 1–7 in the numbers of contracted facilities and patients registered in the post-marketing clinical trial. Medical practitioners' reactions after the broadcast of the NHK special suggest that the NHK program significantly influenced prescriptions by physicians. The media reports and commentaries on the NHK special from April 2005 to February 2006 are listed in Table 2. Notably, 405 clinicians involved in cancer treatment sent a written opinion to NHK on 8 July 2005, stating that the NHK special invited misperceptions among its viewers as if life-prolonging anticancer drugs such as oxaliplatin were ‘curing’ drugs and caused confusions in patients (11), whereas changes in the degree of patient expectation on the efficacy of oxaliplatin were not directly surveyed. Major newspapers such as the Asahi Shimbun (23), Yomiuri Shimbun (24) and Mainichi Shimbun (25), a general-interest magazine (26,27) and numerous blogs mentioned this issue. They indicated that many clinicians felt the NHK special exerted an inappropriate impact on physicians' prescriptions of anticancer drugs. The above circumstances support the association between the NHK special and the increase in the number of oxaliplatin prescriptions.

The present study demonstrated the chronological association between the NHK special and the increase in the number of oxaliplatin prescriptions, suggesting the potential impact of television programs on prescriptions by medical specialists and provided valuable information for consideration on the relationship between media and cancer treatment, although our study left some issues to be mentioned. First, the exact causal association between the NHK special and the increase in the number of oxaliplatin prescriptions was not proven in our study. Second, we cannot ascertain whether the increase in oxaliplatin prescriptions after the NHK special was the result of its direct influence on physicians' judgment or its indirect influence on physicians' prescriptions to meet patients' expectations. Further studies need to focus on the reasons why physicians prescribed oxaliplatin.

In conclusion, we should recognize the possibility that media can be powerful tools for improving the national level of medical treatment, considering the impact of media on cancer treatment as demonstrated in the present study. Although it is essential to provide viewers with accurate information appropriately and to establish amicable relations between medical practitioners and media,

### Table 2. Continued

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<td>Radio</td>
<td>Rinshou de ndoru (Clinicians' written opinion)</td>
<td>Rinshou to iku (It's about raising our voices)</td>
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<td>Juku no kubu kushon (The physicians' report)</td>
<td>14 January 2006</td>
<td><a href="http://mayurinkimama.blog42.fc2.com/blog-entry-97.html">http://mayurinkimama.blog42.fc2.com/blog-entry-97.html</a></td>
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<td>NHK gosho noho no sanbashii (NHK Special)</td>
<td>NHK gosho noho no sanbashii (NHK Special)</td>
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<td>Yururito haigan ki (Lung Cancer at Your Own Pace)</td>
<td>Yururito haigan ki (Lung Cancer at Your Own Pace)</td>
<td>11 July 2005</td>
<td><a href="http://blog.saito-ortho.com/archives/2006082.html">http://blog.saito-ortho.com/archives/2006082.html</a></td>
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interdisciplinary studies/projects integrating media and medical practitioners have been conducted in Japan. Groundbreaking studies such as Media Doctor (28) in Australia, and Hollywood, Health and Society (29) could serve as useful references in Japan. Further interdisciplinary studies/projects integrating media and medical practitioners are awaited in Japan.

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Conflict of interest statement
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