Breast Cancer
DOI 10.1007/s12282-009-0156-2

CASE REPORT

High safety profile and activity of oral vinorelbine in an elderly patient with metastatic breast cancer

David Rossi · Anna Maria Baldelli · Vincenzo Catalano · Virginia Casadei · Paolo Alessandroni · Paolo Giordani · Francesco Graziano · Stefano Luzi Fedeli

Received: 23 June 2008 / Accepted: 17 June 2009

Abstract Visceral metastases of breast cancer have been commonly treated with "aggressive" anthracyclines/taxanes-based chemotherapy. In contrast, this case report concerns an elderly patient with advanced breast cancer (pleural effusion, peritoneal carcinosis, and bone metastases) who firmly declined intravenous chemotherapy and was treated for a long time (28 months) with oral vinorelbine. The oral formulation of this drug had activity and a high safety profile, enabling the patient's wishes to be respected.

Keywords Breast cancer · Elderly · Oral therapy · Vinorelbine · Safety

Introduction

For many years, the management of breast cancer has been a major challenge for oncologists. As a result, the treatment of advanced disease has undergone continuous evolution not only with the aim of improving the duration of remissions and, possibly, of survival, but also of paying particular attention to the role of patients' quality of life, which cannot be underestimated. Intravenous vinorelbine, in particular, turned out to be very suitable in this setting on account of its efficacy in both previously treated and untreated patients and on account of its favorable toxicity profile. In this regard, it is worth mentioning the experiences of Romero et al. [1] who reported 60% response rate with median survival of 17 months using vinorelbine combined with paclitaxel, and of Vici et al. [2] who achieved 70% response rate by combining vinorelbine with epirubicin. However, whereas most of the new agents developed in recent years have mainly achieved improvements in terms of efficacy, toxicity still remains a problem not completely solved. The introduction of the oral formulation of vinorelbine has disclosed new and very interesting perspectives: in fact, not only has it offered further opportunities to the general population for more flexible and suitable treatments which could result in an even higher enhancement of the therapeutic index, but it has also widened the possibility of tailoring appropriate treatments to selected patient populations, for example elderly patients or those who, for many reasons, are no longer amenable to intravenous treatment. Pharmacokinetic data in humans using gel-filled capsules have shown that peak plasma levels of vinorelbine are achieved within 1–2 h after oral administration, with a 43% availability of the parent compound, moderate interindividual variability, and a negligible effect of food on drug absorption. Clinical studies comparing weekly administration of 60 mg/m^2 oral vinorelbine and 25 mg/m^2 i.v. vinorelbine have demonstrated very similar levels of activity of the two forms with a toxicity profile slightly in favor of the oral formulation [3, 4]. A study by Freyer et al. [5] with oral vinorelbine 60 mg/m^2 weekly as first-line treatment of patients with locally advanced and metastatic breast cancer yielded response rates of 31% and progression-free survival of 17.4 months. Another study by Baweja et al. [6] carried out on elderly patients who had received at most one prior chemotherapy regimen for metastatic disease has shown that oral vinorelbine 60 mg/m^2, along with a good safety

D. Rossi · A. M. Baldelli · V. Catalano · V. Casadei · P. Alessandroni · P. Giordani · F. Graziano · S. L. Fedeli
Operative Oncology Unit, S. Salvatore Hospital, Pesaro, Italy

D. Rossi (✉)
Hematology-Oncology Department, S. Salvatore Hospital, via Lombroso 61100 Pesaro, Italy
e-mail: d.rossi63@libero.it

Published online: 10 September 2009

profile, is still able to induce control of the disease with a benefit rate of 12% and a median time to progression of 4.7 months.

Case report

In November 1991, a 57-year-old woman underwent left Madden mastectomy for infiltrating ductal carcinoma. Post-operative staging was: pT2 N+ (six out of 22 positive axillary lymph nodes) M0, ER+PgR+. Thus, we decided to start adjuvant chemotherapy with tamoxifen 30 mg/daily continuous dosing. In September 1996, the chest-CT-scan revealed a mediastinal adenopathy (diameter 3 cm), suspected of being disease progression. A bronchoscopy was performed without histological findings. In October the patient underwent minimal toracothomy with mediastinal adenopathy biopsy which led to the histological diagnosis of "lung sarcoidosis". From 1996 to 2002, periodical clinical and instrumental evaluations consisting of chest X-ray and liver ultrasonography did not show any evidence of disease. In August 2002, after 11 years of treatment, it was decided to stop tamoxifen. In November 2005 the patient presented dyspnea, and a chest-X-ray revealed right pleural effusion; cytological exam confirmed "neoplastic cells of breast cancer". Chest-abdomen CT scan showed right pleural effusion, peritoneal carcinosis, bilateral idroureteronephrosis, and enlargement of abdominal lymph nodes; bone-scan showed bone metastasis. Because of progressive creatinine increase, a nephrostomy was performed. Because the patient refused any intravenous treatment mainly for fear of alopecia as possible side effect (the patient accepted only i.v. infusion of zoledronic acid), in December 2005 chemotherapy with capecitabine 1000 mg/m^2 twice daily for 14 days followed by seven days rest was started. In April 2006, total-body CT-scan revealed partial remission of pleural effusion and stable disease of peritoneal carcinosis with a volume reduction of abdominal lymph nodes.

In August 2006, after nine capecitabine cycles, evaluation with CT-scan revealed progression of pleural effusion (Fig. 1). The patient continued to refuse intravenous treatment; therefore, we decided to start oral vinorelbine 60 mg/m^2 on day 1, 8, 15, 22 every 28 days. In December 2006, after 12 weekly administrations, disappearance of pleural effusion and stable disease of peritoneal carcinosis were reported (Fig. 2). Subsequent evaluations with CT-scans carried out in April 2007, September 2007, and May 2008 confirmed a stable disease; also the bone-scan confirmed a stable disease even on bone metastasis. In December 2008, total body CT-scan revealed progression of peritoneal carcinosis and vinorelbine was stopped. To date (March 2009), the patient has ECOG PS 0 and does not report noteworthy symptoms; moreover, during

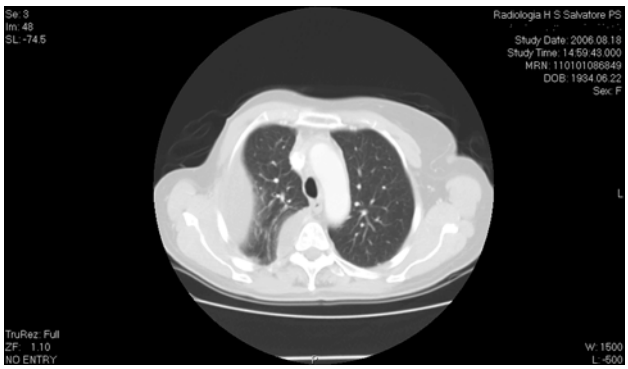

Fig. 1 CT-scan image of right pleural effusion before starting vinorelbine

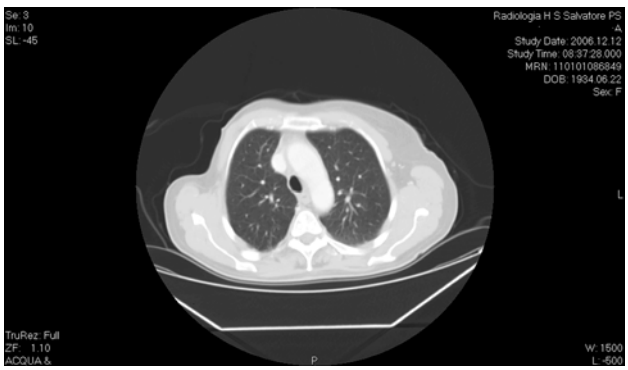

Fig. 2 CT-scan image of lung without pleural effusion after four months of vinorelbine

28 months of treatment the patient did not report any serious side effect except mild hematological toxicity (grade 2 leukopenia and grade 2 anemia).

Discussion

This experience raises some very important considerations. When planning a long-lasting therapeutic approach in an old woman with advanced breast cancer, a series of factors such as characteristics of the tumor, performance status, previous treatment in adjuvant setting, co-morbidities, patients' considerations about convenience, compliance, type, incidence, and severity of toxicity strongly influencing the quality of life of patients, esthetic aspects (alopecia, i.v. port) extremely crucial for a lady, and, last but not least, organizational and medical-economic concerns should be carefully evaluated and taken into serious consideration. There are in fact situations where a soft treatment could turn out extremely advantageous for the patients. Typical are cases of women who, after having taken advantage of hormone manipulations, no longer respond and show slow-progressive, non-immediately life-threatening disease; in such situations the availability of a drug able to achieve

disease control and, simultaneously, strongly reduce all the inconveniences of an heavy chemotherapy negatively affecting quality of life seems very useful. It is unlikely, in fact, that this could be achieved with most of the drugs currently available for treatment of breast cancer; toxicity risks linked with the prolonged use of taxanes (risk of cumulative fluid retention with docetaxel, risk of cumulative neurotoxicity with paclitaxel) and cardiac toxicity risks linked to cumulative doses of anthracyclines are facts which cannot be disregarded and which strongly limit any alternative therapeutic approach; at the present time, on the contrary, oral vinorelbine seems to be the only drug meeting all these aspects and needs.

Our case report confirms the possibility of delivering oral vinorelbine for a long time and of controlling disease progression with a high safety profile. This is essential for patients who decline intravenous chemotherapy or with a number of concurrent co-morbidities that increase the risk of severe side effects.

References

1. Romero A, Rabinovich MG, Vallejo CT, Perez JE, Rodriguez R, Cuevas MA, et al. Vinorelbine as first line chemotherapy for metastatic breast carcinoma. J Clin Oncol. 1994;12:336–41.
2. Vici P, Colucci G, Gebbia V, Amodio A, Giotta F, Belli F, et al. First-line treatment with epirubicin and vinorelbine in metastatic breast cancer. J Clin Oncol. 2002;20:2689–94.
3. Jassem J, Ramlau R, Karnicka-Mlodkowska H, Krawczyk K, Krzakowski M, Zatloukal P, et al. A multicenter randomized phase II study of oral vs intravenous vinorelbine in advanced non-small-cell lung cancer patients. Ann Oncol. 2001;12:1375–81.
4. Terenziani M, Demicheli R, Brambilla C, Ferrari L, Moliterni A, Zambetti M, et al. Vinorelbine: an active, non cross-resistant drug in advanced breast cancer. Results from a phase II study. Breast Cancer Res Treat. 1996;39:285–91.
5. Freyer G, Delozier T, Lichinister M, Gedouin D, Bougnoux P, His P, et al. Phase II study of oral vinorelbine in first-line advanced breast cancer chemotherapy. J Clin Oncol. 2003;21:35–40.
6. Baweja M, Surman VJ, Fitch TR, Mailliard JA, Bernath A, Rawland KM, et al. Phase II trial of oral vinorelbine for the treatment of metastatic breast cancer in patients $\geq$65 years of age: an NCCTG study. Ann Oncol. 2006;17:623–9.