# Improving chemotherapy capacity by switching from IV to oral vinorelbine

Oral vinorelbine reduced the time spent by patients and pharmacists in chemotherapy delivery but care pathways differed across the EU facilities studied. Possible reasons include differing organisation and competency frameworks.

## Introduction

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Chemotherapy facilities deliver treatments using a complex interaction between nurses, pharmacists and doctors. There is a wide consensus that one should define optimal delivery by qualitative criteria (safety, patient-centred care) as well as quantitative criteria (efficiency and financial balance). However, no international guidelines define the optimal service model for achieving safety and efficiency. Over the last ten years across the EU, there have been rapid increases in demand for chemotherapy for advanced non-small cell lung cancer (NSCLC) and metastatic breast cancer (MBC) and this trend is likely to continue [1]. Increased utilisation of chemotherapy is associated with pressures on the resources needed for service delivery [2-6].

The number of orally active agents available, particularly the targeted therapies, is also likely to increase substantially for the foreseeable future [4]. The global market of biological therapies for cancer, many of which are oral, is projected to rise from US$37.9 billion in 2009 to US$53.7 billion in 2014, a five-year compound annual growth rate of 7.2% [7]. Oral products have been shown to improve patient-centred care by allowing treatment at home, avoiding long waits and journeys and the need for central lines. Oral chemotherapy can also improve productivity and profitability in chemotherapy facilities [8-10].

Vinorelbine (Navelbine, Pierre Fabre Limited) is a standard treatment for advanced NSCLC and MBC. Its oral formulation (Navelbine Oral, Pierre Fabre Médicament) is bioequivalent, clinically equivalent and similarly well tolerated. It was recently introduced as a line extension of IV vinorelbine. Vinorelbine is one of four modern agents recommended by NICE for the treatment of advanced NSCLC, either in combination with cisplatin or carboplatin, or as single agent. Vinorelbine is the only NICE-approved chemotherapy agent available in both an oral and IV formulation. Oral vinorelbine is bioequivalent with the IV formulation so any IV dose can be substituted with oral vinorelbine [11].

Taylor et al. showed that patients treated with oral vinorelbine spent 1 h 30 min less in hospital and required 33% less pharmacy time than patients treated with IV vinorelbine [12]. Le Lay et al. have shown improvements in productivity and health resource utilisation due to oral vinorelbine compared with IV products [13]. The *care pathway* for chemotherapy service delivery is complex, requiring expertise from differing professional groups, including doctors, pharmacists and nurses.

## Objectives

The objective of Tamino (time and motion international study with Navelbine oral) was to explore across the EU whether switching from IV to oral vinorelbine as a single agent for patients treated at the hospital for advanced NSCLC or MBC would result in a similar reduction of time for patients, doctors and pharmacists.

## Study design

A time and motion audit was carried out on chemotherapy pathways for patients receiving vinorelbine as part of their chemotherapy treatment, either in IV or oral form. The audit was carried out in eight chemotherapy facilities with diverse patient care pathways situated in four EU countries: Denmark (2 centres), Germany (2 centres), Italy (3 centres) and Spain (1 centre), see Table 1.

**Table 1: Study design**

| Variable | Materials |
|---|---|
| Countries (Facilities) | Italy (3)<br>Germany (2)<br>Denmark (2)<br>Spain (1) |
| Measurements | Process times:<br>• blood test<br>• consultation/prescription<br>• pharmacy preparation/dispensing<br>• post-treatment observation<br>Waiting times:<br>• between processes |
| Patients | Number:<br>121 (average of 15 patients [range 8-20] at each centre)<br>Diagnosis:<br>• Non Small Cell Lung Cancer (NSCLC): 81 (67%)<br>• Advanced Breast Cancer (ABC): 40 (33%)<br>Measurements performed:<br>• Oral vinorelbine: 72 (60%)<br>• IV vinorelbine: 49 (40%) |
| Calculations | Average and standard deviation for each process-time |

**Inclusion and exclusion criteria**

To be included, patients had to be eligible for vinorelbine-based chemotherapy in NSCLC or MBC, with Karnofsky performance status 80% or above. Patients for oral vinorelbine were required to have adequate gastrointestinal absorption. Patients were excluded if they were taking part in another investigation protocol or receiving treatment at home.

**Regimens**

Patients were either receiving single agent vinorelbine (monochemotherapy) or vinorelbine in combination with other agents (combination chemotherapy). However, for consistency, in those receiving combination chemotherapy, measurements were restricted to those cycles when only vinorelbine (IV or oral) was administered. For example, in a patient receiving oral vinorelbine on days 1 and 8 in combination with cisplatin or trastuzumab, only the day 8 event (when vinorelbine was administered as a single agent) was measured.

**Pathway mapping and measurements**

For each patient included, only one administration of chemotherapy was recorded. An observer followed the care pathway of the patient and recorded on a time sheet the time of beginning and end of four distinct processes: the blood test, the consultation and prescription, the pharmacy preparation and dispensing, post-treatment observation. In addition the waiting times between processes were measured and interfering events (telephone calls, questions from other patients or from colleagues) were also recorded and taken into account when appropriate.

From the times measured, the four following durations were to be calculated: overall time spent by the patient at the hospital, consultation, preparation and dispensing, monitoring after administration.

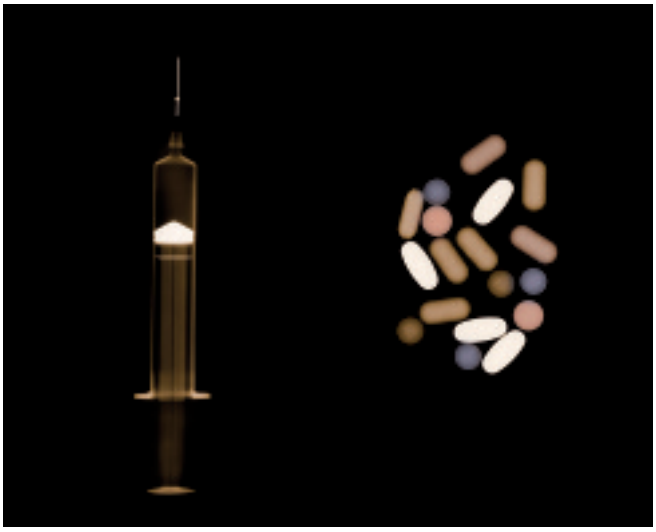
**Informed consent**

Local Research Ethics Committees have been approached for advice on the need for informed consent for a related study. It was felt that this was an audit of process times with no impact on the treatment prescribed and no patient interviews, and that no informed consent was required.

**Statistical Analysis**

The statistical analysis was performed by *Institut de Recherche Pierre Fabre*. Data were analysed using the SAS system software version 8.2 for Windows. Data collected in this study were mainly endpoints expressed in hours and minutes. Continuous data were summarised with the following items: frequency, median, range, mean and standard deviation if relevant. Categorical data were presented in contingency tables with frequencies and percentages of each modalities including missing data modality. Summary tables and listings were provided by drug (oral or IV vinorelbine) and overall.

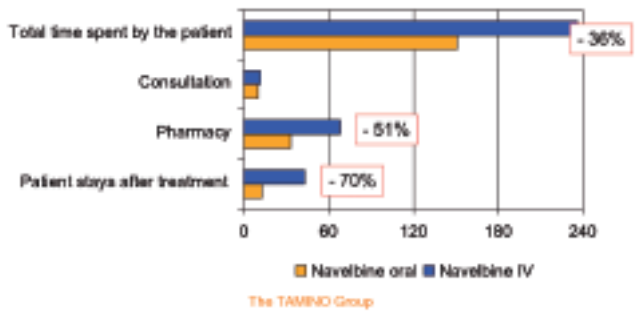
Overall time spent by the patient at the hospital was calculated from 'patient arrives at the hospital' to 'patient leaves the hospital'. Duration of consultation was the time from 'consultation starts' to 'consultation ends'. Duration of preparation and dispensing was the time from 'prescription arrives at the pharmacy' to 'treatment arrives at the clinic'. Duration of monitoring after administration was calculated from 'infusion ends' or 'capsules taken' to 'patient leaves the hospital'.



## Results

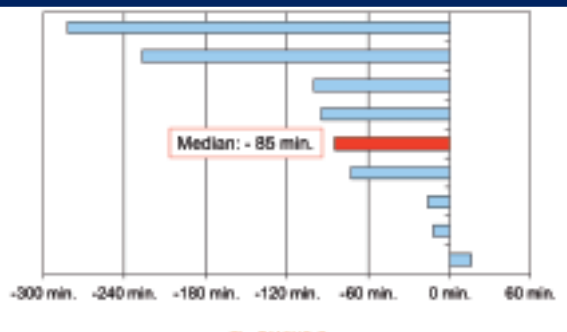
A total of 121 patients were included with an average of 15 patients at each centre (range 8–20). Diagnoses were: NSCLC 81 (67%), MBC 40 (33%). Vinorelbine was given by mouth in 72 measurements (60%) and by IV infusion in 49 measurements (40%). Global results showed that overall time spent by the patient, preparation and dispensing, and monitoring after administration were shorter when vinorelbine was given by mouth; only consultation showed no difference, see Table 1 and Figure 1. With regard to overall time in the facility, patients treated with oral vinorelbine spent on average 2 h 31 min relative to 3 h 56 min with IV vinorelbine, a 36% reduction, see Figure 2. The duration of consultation and prescribing by the oncologist was similar for oral vinorelbine and IV vinorelbine; 10 min relative to 12 min respectively, see Figure 3. The time for preparation and dispensing was 33 min for oral vinorelbine relative to 1 h 8 min for IV vinorelbine, a 51% reduction, see Figure 4. The time for observation after admin-

**Figure 1: Global result - Navelbine oral versus Navelbine IV**



istration was 13 min for oral vinorelbine relative to 43 min for IV vinorelbine, a 70% reduction, see Figure 5. Results were heterogeneous across the eight facilities regarding comparative process times between oral and IV vinorelbine. Comparing the overall time spent by the patients at the hospital resulted in a clear advantage for oral vinorelbine in five facilities, a modest advantage for oral vinorelbine in two, and a modest advantage for IV vinorelbine in one, see Figure 2. Comparing the time for preparing and dispensing resulted in a clear advantage for oral vinorelbine in six centres and a slight advantage for IV vinorelbine in two, see Figure 4.

**Figure 2: Overvall time spent in the hospital - in favour of oral**




Each blue bar represents aggregated results for one institution. The red bar is the median of all results.

**Figure 3: Consultation/prescription time - in favour of oral**

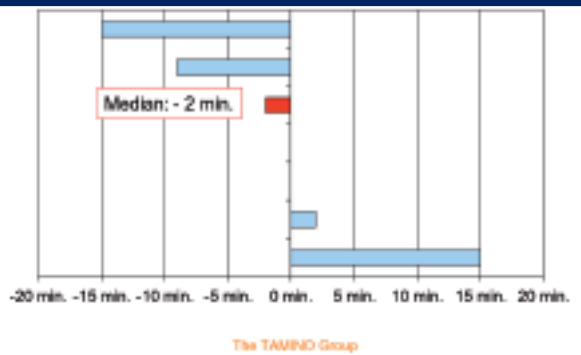



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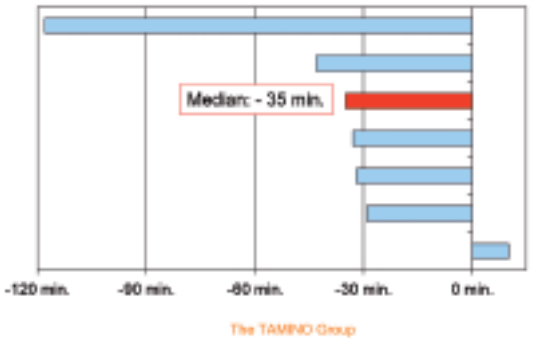
**Figure 4: Preparation and dispensing - in favour of oral**

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## Discussion

There are commonalities and differences across the EU in the way a single chemotherapy agent is delivered. This audit demonstrates that, summating data from the eight facilities studied, it takes less time to prepare and administer oral vinorelbine than equivalent IV chemotherapy and overall, patients spend less time in the facility. Patient-centred care is improved by reductions in waiting time. However, overall there was no difference in consultation/prescription times between oral vinorelbine and IV vinorelbine. The main savings were in the preparation and dispensing time and in the time taken in observation after treatment. This audit did not measure the administration time of IV vinorelbine, but published data shows a clear reduction in favour of administration (dispensing) of oral vinorelbine relative to IV vinorelbine [12].

However, the data from this study were heterogeneous; there were up to three-fold ranges between facilities in times for the same process and in one facility both preparation/dispensing time and observation time after treatment were shorter for IV vinorelbine than for oral vinorelbine. Further research is required to understand the reasons for differing care pathways in chemotherapy facilities across the EU. Possible variables include the type of facility (hospital bed, ambulatory centre or office), the way how pathways are designed for patients receiving oral or IV treatment, the skill mix of different professionals (nurses, pharmacists, oncologists) and the machinery for re-imbursement of the facility.

This audit included only single agent treatment and did not consider the platinum doublets that are commonly used in NSCLC. It could be argued that if a patient is attending for administration of IV platinum on day one, there is little advantage in switching the other drug from IV to oral. However, an independent study has identified time savings on day one as well as on day eight, particularly for nurses and patients [14].

Most patients prefer oral to IV chemotherapy administration [15-18]. In a questionnaire completed by 59 women with breast cancer, 58% answered that "oral chemotherapy would be advantageous", "would allow them to feel less sick", and about 40% that "oral chemotherapy would require less effort than IV treatment." [19]. In another study, 61 patients with NSCLC treated with vinorelbine plus carboplatin were randomised into two arms. For cycles 1 and 2, patients in one arm received vinorelbine by mouth and patients in the other arm received it by IV infusion. All underwent a cross-over for cycles 3 and 4. Finally, they were asked to choose oral or IV vinorelbine for the two subsequent administrations: 74% preferred oral vinorelbine, even combined to IV carboplatin, versus 24% for IV vinorelbine. The choice was independent of whether the patient experienced initially IV or oral vinorelbine and also independent of sex or age [20].

The preparation of IV chemotherapy requires intense labour, time-consuming aseptic preparation by trained pharmacy tech-

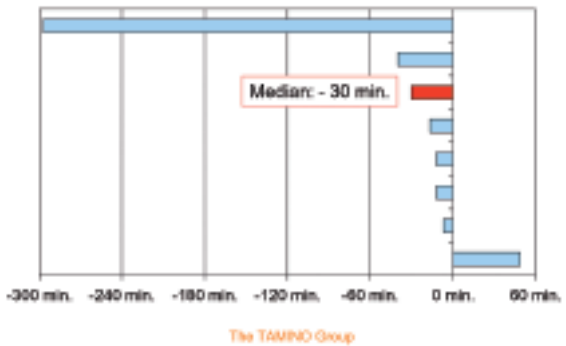
nicians in an isolator cabinet. Some facilities rely on off-site aseptic compounders to prepare chemotherapy and switching from IV to oral may reduce the need for off-site compounding, enabling local pharmacies to regain control of preparation and dispensing and encouraging more flexible working practices.

Some service providers have encountered financial incentives that discourage the switch from IV to bioequivalent oral preparations. Acquisition costs may be higher for oral than for the IV equivalent. Reimbursement and tariffs may vary from state to state within the EU [21]. In the EU, as in the US, the dispensing of oral agents from 'high street pharmacies' rather than within the chemotherapy facility may result in a loss of payment to the facility relative to the IV equivalent.

With adequate training and governance frameworks, some oral drugs such as vinorelbine may be dispensed from an outpatient pharmacy satellite or in outreach clinics at units, reducing patient waiting and journey times. However, the governance of oral chemotherapy and of nurse-led services is critically important in making service change safe [22]. A *UK National Patient Safety Agency Rapid Response Report* in January 2008 on the administration of oral chemotherapy concluded 'Doctors, nurses, pharmacists and their staff must be made aware that the prescribing, dispensing and administering of oral anticancer medicines should be carried out and monitored to the same standard as injected therapy.' [23]. The governance for oral chemotherapy, particularly for a nurse-led service, requires an agreed protocol base as well as a knowledge and skills framework. In UK the legislative background is set out by the Department of Health and professional health organisations [24-29]. The National Cancer Peer Review (NCPR) is the national quality assurance programme for NHS cancer services. NCPR publishes assessments of local services against chemotherapy specific measures [29].

A UK prospective audit confirmed that clinical outcomes following the switch from IV to oral were satisfactory [30]. Costly workforce and capital expansions should be predicated by improvements in productivity, including service re-design [31]. Oral chemotherapy facilitates patient-centred care closer to the patient's home [32-34]. Workforce developments include competency frameworks to enable trained nursing.

**Figure 5: Observation after administration - in favour of oral**

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## Conclusion

Care pathways differed across the EU chemotherapy facilities studied, but overall, oral vinorelbine reduced the time spent by patients and pharmacists in chemotherapy service delivery relative to IV vinorelbine. For patients there was a 36% reduction in attendance time, for pharmacists a 51% reduction for preparation and dispensing time, for nurses delivering chemotherapy a 70% reduction for post-treatment monitoring (a previous study showed a 60% reduction in nurse delivery time). However, in this study, for doctors there was no change in the duration of the oncology consultation and prescription. The methodology used in this study may be applicable to the introduction of other oral products. Pathway mapping and timing can be a significant driver for chemotherapy service reconfiguration. Further research is required to understand the reasons for differing care pathways in chemotherapy facilities across the EU.

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