light of wider clinical use. Since the perceived difference between these states is principally one of frequency and severity of specific symptoms, a frequency and severity response to all items is included. The categories "all or most of the time" and "severely present" are scored 2; "from time to time" and "mildly present" are scored 1; and "not at all" and "not present" are scored 0. The maximum anxiety and depression frequency and severity score is 24 in both cases. Measures of internal consistency/inconsistency and reliability/unreliability are also incorporated. The ESI scale uses one side of an A4 sheet and is completed and scored in minutes. Full details are available from S.B.

Eur J Cancer, Vol. 27, No. 2, pp. 174–178, 1991.
Printed in Great Britain

0277–5379/91 $3.00 + 0.00

Pefloxacin and Vancomycin vs. Gentamicin, Colistin Sulphate and Vancomycin for Prevention of Infections in Granulocytopenic Patients: a Randomised Double-blind Study

Eric Archimbaud, Denis Guyotat, Jean Maupas, Christine Ploton, Alain Nageotte, Yves Devaux, Xavier Thomas, Jean Fleurette and Denis Fiere

To test the value of pefloxacin for the prevention of infections in patients with chemotherapy-induced neutropenia, oral pefloxacin plus vancomycin (PV) (n=76) or gentamicin, colistin sulphate and vancomycin (GCV) (n=74) were administered in a randomised double-blind study. Infections were significantly less severe in the PV than in the GCV group. Patients receiving PV had significantly fewer episodes of bacteraemia and central venous line infections than patients treated with GCV. Gram-positive and gram-negative infections were significantly less frequent in patients receiving PV, because of fewer infections with *Staphylococcus* species and enterobacteriaceae. Stool culture detected significantly more gram-positive organisms in the PV group and more gram-negative organisms in the GCV group. Thus, PV was more efficacious than GCV for the prevention of gram-positive and gram-negative infections in the neutropenic patients, despite lower efficacy in eradicating gram-positive organisms from the lower intestinal tract.
Eur J Cancer, Vol. 27, No. 2, pp. 174–178, 1991.

INTRODUCTION

DESPITE EMPIRICAL broad-spectrum parenteral antibiotics, systemic bacterial infections remain a major cause of death during chemotherapy-induced neutropenia [1]. These infections predominantly originate from the gastrointestinal tract and are favoured by chemotherapy-induced damage of the mucosal barrier [1, 2].

New fluorinated quinolones have shown promise for gastrointestinal decontamination and infection prevention in the neutropenic patient because of their broad spectrum of activity on aerobic bacterial species (mainly gram-negative), their reduced tendency to induce rapid appearance of bacterial resistance, lower toxicity than the widely used cotrimoxazole and moderate toxicity for colonisation-protective anaerobic gastrointestinal flora [3–6]. Norfloxacin, which is poorly diffusible was first tested and was superior to placebo [7], non-absorbable antibiotics including polymyxin and vancomycin [8], and the well-absorbed cotrimoxazole [9, 10] for prevention of both colonisation and systemic infections, with excellent tolerance. The highly diffusable ciprofloxacin [11] and ofloxacin [12, 13] gave similar results to those of norfloxacin. However, none of these quinolones adequately prevented colonisation and systemic infections due to gram-positive organisms [7–13].

Pefloxacin has potential advantages over ciprofloxacin: an approximately two times longer half-life and five times higher trough steady-state level [14, 15], and the drug is more diffusible than ciprofloxacin in sputum, oropharyngeal mucosa, and skin [15, 16], which are potential ports of entry for gram-positive organisms. Furthermore, compared with ciprofloxacin, pefloxacin has equivalent minimal inhibitory concentrations (MIC) against gram-positive organisms and slightly higher MIC against gram-negative organisms [18].

We therefore decided to test pefloxacin for infection prevention in profoundly neutropenic patients. Because of the lack of efficacy of quinolones to prevent intestinal gram-positive colonisation [7–13] and the efficacy of vancomycin in achieving this goal [8, 19], vancomycin was added (PV). This regimen was compared with the best conventional decontamination regimen used in our department, namely gentamicin, colistin sulphate and vancomycin (GCV) [19], which gives equivalent results to cotrimoxazole [20]. To detect potentially small differences

Correspondence to E. Archimbaud.
E. Archimbaud, D. Guyotat, Y. Devaux, X. Thomas and D. Fiere are at the Service d'Hématologie; J. Mapaus is at the Service de Pharmacologie Clinique; C. Ploton and J. Fleurette are at the Laboratoire de Bactériologie; and A. Nageotte is at the Pharmacie Centrale, Hôpital Edouard Herriot, UFR Alexis Carrel, Lyon, France.
Revised 16 Nov. 1990; accepted 23 Nov. 1990.

between these two regimens, we decided to enter a larger number of patients than is usual. No placebo arm was included because of the demonstrated superiority of quinolones over placebo [7] and that of GCV over gentamicin and colistin sulphate alone [19].

PATIENTS AND METHODS

Patients

Over 15 months, 150 adult patients presenting aplasia (granulocyte count under 0.1×10^9/l) expected to last more than 2 weeks after intensive chemotherapy for acute leukaemia or bone marrow transplantation for various haematological malignancies, were randomly assigned to receive GCV (74 patients) or PV (76). All patients gave informed consent according to our institutional policy.

Prophylactic antibiotherapy

Only initially afebrile patients who had received no antibiotics in the previous 48 h were randomised. Prophylactic oral antibiotherapy was started on the day before initiation of haematotoxic therapy and was administered double-blind. The daily doses were divided in 4 takes. GCV included gentamicin 100 mg, colistin sulphate, 3×10^6 U day and vancomycin 800 mg; PV included pefloxacin 800 mg and vancomycin 800 mg. Only the pharmacy staff responsible for the preparation of the drugs were aware of the allocation of a patient. Oral prevention was continued until the granulocyte count went above 0.5×10^9/l, or death. Compliance and possible side-effects were recorded daily.

Adjuvant therapies

Patients received antifungal gastrointestinal decontamination with nystatin tablets (400 000 U per day). Empirical parenteral antibiotherapy was started, as soon as the patient became febrile (oral temperature over 38.5°C once or over 38°C for 4 h) in the absence of an obvious non-infectious cause of fever, with piperillin or ticarcillin and moxalactam. Vancomycin and/or amphotericin B were added empirically to the initial sequence when the patient remained febrile without bacteriological documentation. All patients had a central venous line. Patients were nursed in conventional reverse isolation rooms with low bacterial content cooked food (65 cases) or in sterile laminar airflow rooms with sterile food (85 cases).

Bacteriological methods

Surveillance cultures of urine and semi-quantitative cultures of throat and stools with identification of abnormally present or predominant microorganisms were done before the start of antibioprophylaxis and twice a week thereafter. Febrile episodes were classified as: microbiologically documented infections, when a microorganism was isolated from the site of infection or blood; clinically documented infections, when there was clinical or radiological evidence of infection in the absence of isolated microorganism; and fevers of unknown origin (FUO), when both clinical and microbiological evidence of infection were lacking. Severity of infections was graded 1–5 [21]: 0 = no infection, 1 = FUO, 2 = benign, 3 = severe, 4 = life-threatening and 5 = lethal infection. Acquired organisms were defined as organisms that were not present in initial surveillance cultures but were isolated thereafter while the patient was on prophylaxis. Sensitivity of isolated organisms against antibiotics used in the study was assayed with the agar dilution method [22] and those with MICs less than or equal to 4, 2, 4 and 1 were considered sensitive to gentamicin, colistin sulphate, vancomycin and pefloxacin, respectively.

Table 1. Characteristics of patients

	GCV ($n = 74$)	PV ($n = 76$)
Age (yr)	43 (18)*	41 (16)
M/F	38/36	44/32
Diagnosis		
AML	46	43
ALL	9	10
CML	4	6
Lymphoma	14	16
Solid tumour	1	1
Therapy		
Chemotherapy	47	41
Autologous BMT	11	15
Allogeneic BMT	16	20
Isolation		
Reverse	37	28
Laminar airflow room	37	48
Duration of aplasia (days)		
Granulocytes $< 0.5 \times 10^9$/l	21 (11)	22 (8)
Granulocytes $< 0.1 \times 10^9$/l	15 (10)	15 (8)
Compliance with therapy (%)	87 (22)	81 (25)

*Mean (S.D.).
AML = acute myeloblastic, ALL = acute lymphoblastic and CML = chronic myelocytic leukaemia. BMT = bone marrow transplantation.

Statistical analysis

Clinical endpoints of the study included the number and severity of infectious episodes, the delay until use of parenteral antibiotics, the number of febrile days and number of days under parenteral antibiotics during hospital stay and the final outcome of aplasia. Bacteriological endpoints included the documentation of infectious episodes, the prevalence of bacterial colonisation of the monitored sites and the sensitivity of bacterial isolates to antibiotics administered in the study.

Differences between the two therapeutic groups were evaluated with Yates' corrected χ^2 and Student's t tests. $P \leq 0.1$ was considered significant.

RESULTS

Initial characteristics and compliance

Age, sex, diagnosis, haematotoxic therapy, duration of aplasia and type of isolation were similar in both arms, although there tended to be more patients isolated in laminar airflow rooms and receiving bone marrow transplantation in the PV arm (Table 1). Average compliance to therapy was over 80% and did not differ significantly between the two groups.

Clinical results

The average number of febrile days, time to first use of parenteral antibiotics and duration of parenteral antibiotherapy did not significantly differ between the two arms (Table 2). Overall 6 patients in each arm had no fever or infection and did not receive parenteral antibiotics.

The average severity of infections was significantly lower in the PV than in the GCV group (Table 2). 13 patients died in the GCV arm, including 10 infectious deaths (8 from pneumopathy) 1 case of cerebral haemorrhage and 2 cases of metabolic coma.

Table 2. Clinical results

	GCV	PV
No. of febrile days	8 (7)	8 (7)
WHO grade of infections (0/1/2/3/4/5)	2.7 (1.4) (6/10/6/40/2/10)	2.1 (1.3)* (6/27/5/34/0/4)
Time to first use of parenteral antibiotics (days)	8 (6)	9 (5)
Duration of parenteral antibiotherapy (days)	20 (8)	19 (8)

Mean (S.D.).
*Significant difference between GCV and PV groups, $P = 0.005$.

10 patients died in the PV arm (not significantly different from the GCV arm), 4 from infection (2 cases of pneumopathy), 2 from cardiac failure, 2 from hepatic veno-occlusive disease after allogeneic bone marrow transplantation, 1 from cerebral haemorrhage and 1 from unknown cause. No toxicity could definitely be attributed to antibioprophylaxis in either of the groups, although more episodes of rash were observed in patients receiving PV (13 vs. 5, $P = 0.05$).

Site and documentation of infections

Overall, in comparison with patients receiving GCV, patients receiving PV had significantly fewer episodes of bacteraemia, especially those due to gram-negative organisms, and less central venous line infections (Table 3). There was no significant difference between the groups with regard to other sites of infection. In addition to microbiologically documented infections, there were 11 cases of clinically documented infections in the GCV arm, (7 cases of central venous line infection, 3 cases of pneumopathy and 1 case of oral cellulitis) and 6 cases in the PV arm (cutaneous cellulitis in 3 cases, and oral cellulitis, central venous line infection and pneumopathy in one case each).

Organisms responsible for bacteriologically documented infections

Gram-positive infections were less frequent in the PV than in the GCV group (64 vs. 100 episodes, $P = 0.007$). This difference was explained by a lower frequency of infections due to both *Staphylococcus aureus* (0 vs. 12, $P = 0.002$) and coagulase-negative staphylococci (29 vs. 59, $P = 0.005$) in patients receiving PV. Overall, coagulase-negative staphylococci were isolated from blood or other sites of infection in 27 patients receiving PV and 46 patients receiving GCV. The frequency of infections due to other gram-positive bacteria did not significantly differ between the two groups.

Table 3. Site of infections and bacteriological documentation

Site of infection and documentation	GCV	PV
Blood	104	70*
Gram-positive bacteria	83	62†
Gram-negative bacteria	12	3‡
Fungi	9	5
Skin/soft tissues	7	5
Clinically documented	1	4
Gram-positive bacteria	5	1
Fungi	1	0
Central venous line	16	1§
Clinically documented	7	1‡
Gram-positive bacteria	9	0‖
Lung	13	8
Clinically documented	3	1
Gram-positive bacteria	2	1
Gram-negative bacteria	3	3
Fungi	5	3
Central nervous system	1	0
Gram-positive bacteria	1	0

Significant difference between GCV and PV groups: *$P = 0.02$, †$P = 0.07$, ‡$P = 0.03$, §$P < 0.001$, ‖$P = 0.002$.

15 patients in the GCV arm and 6 in the PV arm had infections due to gram-negative organisms ($P = 0.05$). Infections due to *Pseudomonas aeruginosa* and other *Pseudomonas* species were observed with a similar frequency in both groups (3 episodes with GCV vs. 4 with PV), while *Enterobacteriaceae* and *Acinetobacter* species were more frequent in the GCV arm (9 vs. 1 episodes). 2 cases of *Legionella pneumophila* infection were observed in the GCV group.

Yeast infections tended to be more frequent in patients receiving GCV, although at a borderline significance level (13 vs. 6 episodes, $P = 0.07$), while invasive pulmonary aspergillosis was detected in 2 patients in each group. Organisms rendered responsible, alone or in association, for infectious death, were in the GCV arm, coagulase-negative staphylococci (4 cases), *Streptococcus viridans* (1), *Ps. aeruginosa* (1), *L. pneumophila* (2), *Candida* species (3), *Torulopsis* and *Aspergillus* species (1 each); and in the PV, group corynebacterium, *Ps. aeruginosa* and *Acinetobacter calcoaceticus* (1 each), *Candida* species (2) and *Aspergillus* species (1).

Organisms acquired in surveillance cultures

The oral cavity of patients in the PV group was significantly less frequently colonised than that of patients in the GCV group by gram-negative ($P < 0.001$) and, at a borderline significance level, ($P = 0.08$) gram-positive organisms. In the lower intestinal tract, gram-positive bacteria were more frequently isolated in the PV arm ($P = 0.001$), mainly due to more frequent colonisation by *Strep. faecalis* ($P = 0.005$) and lactobacillus ($P = 0.007$). In contrast, gram-negative species were more frequently isolated from the stools in patients receiving GCV ($P = 0.007$). In the urine, gram-positive strains were equally prevalent in both arms while gram-negative organisms were isolated in 25 opportunities in patients receiving GCV and never in patients receiving PV ($P < 0.001$). *Candida* and *Torulopsis* species tended to colonise less frequently the lower intestinal tract and urine of patients in the PV arm when compared to patients in the GCV arm. Overall only 5 bacterial isolates acquired in surveillance cultures were eventually responsible for bacteremia in each arm.

Bacterial sensitivity

37 out of 42 gram-positive isolates and 6 out of 8 gram-negative isolates in the PV group were resistant to pefloxacin (Table 4). The proportion of bacterial isolates resistant to pefloxacin according to MIC measurement was significantly higher in the PV arm than in the GCV arm among gram-positive and gram-negative isolates, indicating a selection of resistant strains in this arm. However, the frequency of resistant organisms did not differ between the groups. Sensitivity to other antibiotics was similar in both groups.

There was a high percentage of resistance among *Streptococcus* and *Pseudomonas* species (Table 4). All 4 isolates of *Ps. aeruginosa* tested were resistant to pefloxacin. No difference was found in the sensitivity to pefloxacin of organisms isolated during the first half of the study in comparison with those isolated during the second half.

Table 4. Sensitivity of bacterial isolates to pefloxacin

Bacterial strains	GCV	PV
Gram-positive strains	35/60*	37/42*
Staphylococcus	18/42	18/22
Streptococcus	15/16	15/16
Other	2/2	4/4
	5/47	6/8‡
Gram-negative strains		
Pseudomonas	2/3	4/5
Other	3/45	2/3

*Number of organisms with MIC over 1 mg/l/number tested.
Significant difference between GCV and PV groups: †$P \leq 0.002$ and ‡$P < 0.001$.

DISCUSSION

This randomised double-blind study of 150 patients confirmed the higher efficacy of pefloxacin compared with standard non-absorbable antibiotics in diminishing infectious morbidity during chemotherapy-induced neutropenia, although the decrease in overall mortality was not statistically significant. This was achieved by preventing gram-negative colonisation and infections and gram-positive infections. The possibility that former use of GCV as a standard regimen might have decreased its efficacy by inducing bacterial resistance exists. However, pefloxacin had also been used parenterally in our patients during the 2 years before this trial. Furthermore, this trial was started shortly after the move of our clinical facilities to a different building and our patients were therefore presumably exposed to a different nosocomial flora.

The efficacy of pefloxacin in preventing colonisation and infection by common gram-negative enteric pathogens, and infections due to *Legionella* species, was expected in view of data on norfloxacin and ciprofloxacin prophylaxis [7–11]. Nosocomial legionella infection is uncommon: the 2 episodes observed in the GCV group occurred over short time when work was being done on the water supply of the hospital. In our study pefloxacin was not superior to non-absorbable antibiotics in preventing infections and colonisation by *Pseudomonas* species. Non-aeruginosa *Pseudomonas* species are resistant to quinolones [18]. In contrast, *Ps. aeruginosa* is generally sensitive to quinolones, and a recent trial with ciprofloxacin showed good preventive effect on both colonisation and infection by this organism compared with cotrimoxazole and colistin sulphate [11]. In another trial, ofloxacin did not prevent colonisation by *Ps. aeruginosa* but no infections were seen in treated patients [13]. However, the number of patients included in these trials was small. The lack of efficacy of pefloxacin to eradicate *Ps. aeruginosa* from our patients could be linked to the resistance to pefloxacin of the particular strains involved in our series. These strains might have been sensitive to ciprofloxacin since ciprofloxacin is known to have lower MICs than other quinolones against *Ps. aeruginosa* [18].

Quinolones are inadequate in preventing colonisation of the lower gastrointestinal tract by gram-positive organisms [7–13]. In this study, vancomycin did not appear to correct this defect, although its use in association with non-absorbable antibiotics appeared beneficial in our earlier study [19]. The prevention of staphylococcus infections by pefloxacin contrasted with the reported lack of efficacy of norfloxacin [7–10] and ciprofloxacin [11] in this regard. This apparent discrepancy could be due to the more favourable pharmacokinetics of pefloxacin, with higher diffusibility than ciprofloxacin in the skin, nasopharyngeal secretions and bronchial secretions, which are potentially originating sites of gram-positive infections, and longer half-life allowing higher serum levels for comparable MICs [14–18]. However, the results of throat surveillance culture in our study did not confirm this hypothesis since throat isolates were followed by bacteraemia in only 3 cases in GCV patients and 2 cases in patients receiving pefloxacin.

Of particular interest was the good prevention of catheter-related infections achieved in the PV group, since neutropenic patients often require parenteral nutrition through a central venous line. Such a result was not achieved with ciprofloxacin [11]. Overall, the observation of only 5 bacterial isolates in surveillance cultures followed by bacteraemia could indicate either a primary lack of predictive value of these cultures or the fact that adequate measures were taken at the time of first positivity of surveillance cultures.

The lower frequency of fungal infection and colonisation found in patients receiving pefloxacin has already been noted by others in patients treated with norfloxacin [8, 9] and could be related to an increased activity of antifungal agents in the presence of quinolones, as suggested by *in vitro* experiments [23].

Overall toxicity of both PV and GCV regimens was moderate and no increase in the duration of aplasia was noted with the use of pefloxacin, similar to what was found with other quinolones [7–13].

The use of diffusable quinolones might raise concerns about induction of microbial resistance to these molecules, although resistance is less likely to occur than with the widely used cotrimoxazole because of a different mechanism of action [4]. In this study, although there was a clear selection of resistant organisms in the PV arm, the similar frequency of resistant organisms in both groups rules out the short-term induction of resistance by pefloxacin, which corroborates previous results [3]. The resistance to pefloxacin of all 4 tested *Ps. aeruginosa* strains in our patients seems to reflect the initial resistance of the particular strains involved rather than induction of resistance during the study, since it was observed in both groups throughout the study.

Thus pefloxacin was superior both clinically and bacteriologically to standard non-absorbable antibiotics in the preventing gram-negative colonisation and infections and gram-positive infections in granulocytopenic patients. Gram-positive colonisation of the intestinal tract was not prevented despite co-administration of vancomycin. Since pefloxacin has better activity against gram-positive organisms than other quinolones, its place in preventive monotherapy should be considered.

1. Pizzo PA, Commers J, Cotton D, *et al.* Approaching the controversies in antibacterial management of cancer patients. *Am J Med* 1984, **76**, 436–449.
2. Slavin RE, Dias MA, Saral R. Cytosine arabinoside induced gastrointestinal toxic alterations in sequential chemotherapeutic protocols: a clinical-pathologic study of 33 patients. *Cancer* 1978, **42**, 1747–1759.
3. Tigaud S, Mercatello A, Gille Y, Robert D, Vincent P. Pefloxacin: evolution of *in vitro* activity during 18 months of use in an intensive care unit. *Drugs Exp Clin Res* 1985, **11**, 169–176.
4. Young LS. The new fluorinated quinolones for infection prevention in acute leukemia. *Ann Intern Med* 1987, **106**, 144–146.
5. Ball P. Long-term use of quinolones and their safety. *Rev Infect Dis* 1989, **11**(Suppl. 5), 1365–1370.

6. Murray B. Impact of fluoroquinolones on the gastrointestinal flora. *Rev Infect Dis* 1989, **11**(Suppl. 5), 1372–1378.
7. Karp JE, Merz, WG, Hendricksen C, *et al.* Oral norfloxacin for prevention of gram-negative bacterial infections in patients with acute leukemia and granulocytopenia. A randomized, double-blind, placebo-controlled trial. *Ann Intern Med* 1987, **106**, 1–7.
8. Winston DJ, Ho WG, Nakao SL, Gale RP, Champlin RE. Norfloxacin versus vancomycin/polymyxin for prevention of infections in granulocytopenic patients. *Am J Med* 1986, **80**, 884–889.
9. Winston DJ, Ho WG, Champlin RE, *et al.* Norfloxacin for prevention of bacterial infections in granulocytopenic patients. *Am J Med* 1987, **82**(Suppl. 6B), 40–46.
10. Bow EJ, Rayner E, Louie TJ. Comparison of norfloxacin with cotrimoxazole for infection prophylaxis in acute leukemia. The trade-off for reduced gram-negative sepsis. *Am J Med* 1988, **84**, 847–854.
11. Dekker AW, Rozenberg-Arska M, Verhoef J. Infection prophylaxis in acute leukemia: A comparison of ciprofloxacin with trimethoprim-sulfamethoxazole and colistin. *Ann Intern Med* 1987, **106**, 7–12.
12. Kern W, Kurrle E, Vanek E. Ofloxacin for prevention of bacterial infections in granulocytopenic patients. *Infection* 1987, **15**, 427–433.
13. Winston DJ, Ho WG, Bruckner DA, Gale RP, Champlin RE. Ofloxacin versus vancomycin/polymyxin for prevention of infections in granulocytopenic patients. *Am J Med* 1990, **88**, 36–42.
14. Wise R, Lister D, McNulty AM, Griggs D, Andrews JM. The comparative pharmacokinetics of five quinolones. *J Antimicrob Chemother* 1986, **18**(Suppl. D), 71–81.
15. Lode H. Pharmacokinetics and clinical results of parenterally administered new quinolones in humans. *Rev Infect Dis* 1989, **11**(Suppl. 5), 996–1004.
16. Fourtillan JB. Comportement pharmacocinétique de la péfloxacine chez l'homme. *Rev Méd Interne* 1986, **7**, 185–195.
17. Gerding DN, Hitt JA. Tissue penetration of the new quinolones in humans. *Rev Infect Dis* 1989, **11**(Suppl. 5), 1046–1057.
18. Shrire L, Saunders R, Traynor R, Koornhof HJ. A laboratory assessment of ciprofloxacin and comparable antimicrobial agents. *Eur J Clin Microbiol* 1984, **3**, 328–332.
19. Guyotat D, Ploton C, Fiere D. A randomized trial of oral vancomycin in neutropenic patients. In: Wostamn BS, ed. *Progress in Clinical and Biological Research, vol. 181.* Germfree Research: *Microflora Control and its Applications to the Biomedical Sciences.* New York, Alan R. Liss, 1985, 263–265.
20. Wade JC, Schimpff SC, Hargadon MT, Fortner CL, Young VM, Wiernik PH. A comparison of trimethoprim-sulfamethoxazole plus nystatin with gentamicin plus nystatin in the prevention of infections in acute leukemia. *New Engl J Med* 1981, **304**, 1057–1062.
21. World Health Organization Handbook for Reporting Results of Cancer Treatment. WHO Offset Publication 1979, **48**, Geneva, WHO.
22. Ericsson HM, Cheriss JC. Antibiotic sensitivity testing. Report of an international collaborative study. *Acta Pathol Microbiol* 1971, Scand Sect **B**(Suppl. 217), 1–90.
23. Walsh TJ, Wharton RC, Sprecher S, *et al.* Augmentation of in vitro antifungal activity by norfloxacin [abstr. 971]. Program and Abstracts of the 23rd Interscience Conference on Antimicrobial Agents and Chemotherapy, Las Vegas, 24–26 October 1983.

Eur J Cancer, Vol. 27, No. 2, pp. 178–181, 1991.
Printed in Great Britain

0277–5379/91 $3.00 + 0.00

Problems at Social Re-integration of Long-term Cancer Survivors

Johanna G.W. Greaves-Otte, Jaco Greaves, Philip M. Kruyt, Oscar van Leeuwen, Johannes C. van der Wouden and Emiel van der Does

To assess the long-term consequences of cancer for everyday life, a postal survey in the Netherlands was done among 849 ex-cancer patients. Almost all responders were self-supporting to a large extent. Compared with the period before diagnosis, the socioeconomic position had not changed in 62%. 28% of the responders who were employed at the time of diagnosis (10% of all responders), were now housekeepers (99% female). Absence from work at survey did not differ significantly from absence in the year before diagnosis. A history of cancer tended to have a negative impact on promotional prospects and income. Ex-cancer patients were often confronted with problems when they tried to take out insurance or to modify an existing policy. The psychological well-being of the responders was low, compared to the average Dutch population.
Eur J Cancer, Vol. 27, No. 2, pp. 178–181, 1991.

INTRODUCTION

IN PAST decades, the major emphasis in care of the cancer patient was directed at earlier diagnosis and refinement of treatment. The goal was to increase the quantity of life [1]. The number of cancer and ex-cancer patients is expected to increase in the future, in part because of the increased longevity of our population and the higher rates of cancer in the older population and in part because of advances made in diagnosis and treatment [2]. Cancer, primarily a chronic disease state, affects a person as a whole and restricts his or her somatic and psychosocial performance [3]. Most cancer patients are in their middle years, the period of greatest productivity and greatest family, social and community responsibility [4]. Work, leisure activities and social relationships are several of the many dimensions that determine a person's quality of life [5]. Increasing numbers of patients who have been treated for cancer are, given their medical state, able to return to society and to their duties [6, 7]. In many cases, "cured" cancer patients cannot easily re-adapt to

Correspondence to J.C. van der Wouden.
J.G.W. Greaves-Otte, J. Greaves, J.C. van der Wouden and E. van der Does are at Erasmus University Rotterdam, Department of General Practice, Mathenesserlaan 264a, 3021 HR Rotterdam; and P.M. Kruyt and O. van Leeuwen are at the Zuiderziekenhuis, Department of Surgery, Rotterdam, The Netherlands.
Revised 22 Oct. 1990; acepted 5 Nov. 1990.