the Cumulative Illness Rating Scale Geriatrics (CIRS-G). The median number of comorbidities was 2 (range 0–5) with a median CIRS-G score 1 (range 1–2); the median index of complex comorbility was 1 (range 0–4). The pts were treated with carboplatin AUC 5 combined with cyclophosphamide (23 pts) or with paclitaxel (13 pts); 13 pts were treated with single agent carboplatin and one patient with cisplatin, epirubicin and cyclophosphamide.
Results: a) *Tolerability*: grade 3 or 4 neutropenia was observed in 21 cases (42%; grade 4 in 10 pts); grade 4 thrombocytopenia and grade 3 anemia were seen in one (2%) and in 2 pts (4%) respectively. Excluding alopecia, grade 3–4 extra-haematological toxicity was observed only in one case (grade 3 diarrhoea). A 10 to 30% dose-reduction because of side effects was required in 15 pts (30%) and the dose was reduced by 50% in one patient because of haematological toxicity. Furthermore 3 pts treated with combination carboplatin and paclitaxel were shifted to single agent carboplatin because of hypersensitivity reactions.
b) *Efficacy*: 16 pts (32%) are not evaluable for response because there was no evidence of disease after surgery; in seven more pts (14%) the response was not evaluated because of withdrawal from treatment after the first cycle (2 cases) or because the treatment is still ongoing (5 cases). In 27 evaluable pts we observed 5 (19%) cCRs and 11 PRs (41%), 9 (33%) stable diseases and 2 (7%) progressions. The cCRs were observed in 3 pts treated with first-line chemotherapy for stage IIIC and IV EOC and in 2 pts treated for relapsed EOC. The age of complete responders ranged from 70 to 78 years, their KPS was 70–100% and their median CIRS-G score was 1.
Conclusions: in our experience with carboplatin-based chemotherapy in patients aged 70 or over in good general conditions the remission rate was 60%, including 5 clinical complete remissions and the toxicity was moderate; a dose reduction because of toxicity was required in 38% of the patients.

1346 PUBLICATION

Clinical overview of electroporation with bleomycin sulfate: the potential role of this novel therapy in the management of solid tumors with different histologies

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This abstract describes the experience with the MedPulser® Electroporation Therapy System for the treatment of solid tumors using the drug bleomycin sulfate injected locally into tumors. The MedPulser® has been used for over 9 years and 178 patients with 390 lesions have been treated. These included various cutaneous malignancies, squamous cell head and neck carcinoma, recurrent breast cancer. In cutaneous tumors there was an objective response in 86% of 256 lesions treated. These include squamous and basal cell cancers of the skin as well as Merkel cell tumors, Kaposi's sarcomas, and metastatic melanomas. Four clinical studies using electroporation have been completed thus far for the treatment of advanced head and neck cancer, with 59% objective response rate in 64 patients evaluated.
In a separate study of primary and limited recurrent squamous cancer of the head and neck, there was an 80% histologically confirmed complete response in 20 patients who received electroporation, followed 4 weeks later by excision of the treated tumor. Currently, there is an ongoing global Phase III study in limited recurrent and second primary head and neck cancer for US registration and a Phase IV pharmacoeconomic study for recurrent and primary head and neck cancer being conducted in selected countries in Europe. Preliminary studies are underway to evaluate EPT with bleomycin in the management of cutaneous recurrences of breast cancer. Two patients with pancreatic cancer have been treated and in one, the disease appeared to stabilize for several months. This will be further evaluated in additional clinical studies. In previous clinical studies conducted in France 15 patients with 31 hepatic lesions were treated with EPT-bleomycin with stabilization in 65% of the lesions for 3 to 6 months. The incidence and severity of complications in these studies appears to be no worse than that reported in a series of patients treated surgically for similar disease. This abstract summarizes the largest series of patients treated with electroporation using bleomycin to date.

1347 PUBLICATION

Breast cancer-Anaemia and the Value of Erythropoietin (BRAVE): preliminary results from a study of the efficacy of epoetin beta 30,000 IU once weekly in patients with metastatic breast cancer receiving chemotherapy

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Background: Anthracycline and/or taxane-based chemotherapy (CT) regimens are commonly used to treat metastatic breast cancer and there is a high incidence of anaemia in patients receiving this treatment. The BRAVE study is being conducted to assess the impact of once-weekly epoetin beta (NeoRecormon®) 30,000 IU on haemoglobin (Hb), survival, disease progression, safety and quality of life in patients with metastatic breast cancer receiving anthracycline and/or taxane-based CT.
Methods: Adult patients with metastatic breast cancer, Hb levels <12.9 g/dl and scheduled to receive anthracycline and/or taxane-based CT were entered into this open-label, randomised, multicentre, two-arm study. Patients received epoetin beta 30,000 IU once weekly or control therapy (standard care) over 24 weeks (treatment phase). The primary endpoint is overall survival, available 18 months after the last patient's last treatment visit.
Results: Recruitment was completed with 463 patients enrolled. The treatment groups were well balanced with regard to baseline characteristics (Table). There was a significant mean increase in Hb from week 5 to end of treatment of 1.4 g/dl (SD 1.3 g/dl) in the epoetin beta group versus a mean decrease of −0.2 g/dl (SD 1.3 g/dl) in the control group ($p < 0.0001$). The number of blood transfusions was reduced by around 50% in the epoetin beta treatment group, with 33 patients (14%) receiving at least one blood transfusion versus 62 patients (27%) in the control.

	Epoetin beta (n = 231)*	Control (n = 231)*
Mean age (± SD), years	55.8±10.8	56.7±11.4
Mean weight (± SD), kg	67.3±12.9	67.0±13.6
Race, % Caucasian	90%	90%
Breast cancer subtype, % ductal	79%	79%
Mean time (± SD) between diagnosis of metastatic disease and study entry, months	21.2±30.3	21.0±32.6
Hormonal status, % positive	72%	71%
Mean baseline Hb (± SD), g/dl	11.5±1.2	11.2±1.3

*Safety Population (n = 462)

Conclusion: These data show that treatment with epoetin beta 30 000 IU once weekly results in a highly significant increase in Hb levels in patients with metastatic breast cancer receiving anthracycline and/or taxane-based CT. Mature data on the primary survival endpoints will be available after the last patient has finished the 18-month follow-up period in 2006.

1348 PUBLICATION

Safety management in outpatient cancer chemotherapy

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Introduction: The advances and greater specialization of medical technologies and the increasing number of elderly people are all factors in the occurrence of medical adverse events. However, a simple mistake can lead to a fatal accident as time. In our hospital, if an accident was occurred, the risk-manager concerned in these events has to present the detailed analysis of them by the method of pm-SHEL model in immediate meeting of safety management. Prompt measures should be taken in the meeting to prevent similar events and the meeting report is notified in the whole hospital within few days. As for the cancer patients in particular, there is a marked decline in the personal immunity, compared with general patients. In addition to that, they are in the high risk situation because of strong side effects of cancer drugs, large invasions with wide lymphnodes dissection or dangerous examinations. Therefore, greater efforts are now demanded in the medical safety management for cancer patients than ever before. Thus now improved safety management for outpatient cancer chemotherapy is introduced.
This procedure of outpatient cancer chemotherapy is recently revised, and chemotherapies are performed with the following 8 rules in order to prevent

medical adverse events by the side effects, overdoses and extravasation of anticancer drugs.

Aims and Methods: Our method of outpatient cancer chemotherapy is presented as follows.

1. We must entry every kind of cancer chemotherapy regimen. Every regimen is under dept. of pharmacy control.
2. We make an application to dept. of pharmacy about patient's name and regimens with another doctor's reconfirmation of species, dosages and processes.
3. Then special doctors, pharmacists, nurses have a proper understanding of detailed treatment for cancer patients.
4. Every regimen is performed according to clinical pathway.
5. Further information of side effects of cancer drugs for the patients is provided by special pharmacists.
6. Patients are carefully observed during the administration of cancer drugs by the well trained full-time nurses and pharmacists.
7. Outpatient's private room for chemotherapies is in full-time nurse's attendance. The room is furnished with TV, CD-player and refrigerator. They have a good quality of life.
8. Cancer drugs were injected only by special doctors.

Results: To my great relief, since our safety management committee adopted this method of outpatient cancer chemotherapy, medical adverse events decreased remarkably (Table 1) and then patients have been comfortable and safe without even trifling incidents. This outpatient chemotherapy fee with full-time pharmacists and nurses is 30 dollars a day.

Table 1: Adverse events in outpatient cancer chemotherapy

	2001	2002	2003	2004
Total Patients	782	845	921	949
Grade 1	44	52	31	22
Grade 2–3	18	13	7	4
Grade 4	2	1	0	0
Grade 5	0	0	0	0

Grade of adverse events: 1. need observation; 2. need minor treatment; 3. need major treatment; 4. serious aftereffects; 5. death

Conclusion: Consequently this method brought a great profit to our cancer patients and hospital.

1349 PUBLICATION

APSI Project: research and development of a Robot Assistant for the Preparation of Injectable Solutions (APSI): application to chemotherapy in the clinical setting

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Injectable chemotherapeutic agents are often required in cancer treatment: an arsenal of high added value medications with intrinsic toxicity to which patients as well as operators handling these drugs are exposed. Conventional preparation systems (clean air hoods or isolators) are however fallible. At the end of serious thought which began in 1998, we considered that personnel and environmental exposures were no longer tolerable. Finally, the APSI Research and Development (R&D) programme: a Robot Assistant for the Preparation of Injectable Solutions, was born in February 2001. Our objectives were not only to respond to the needs of the Institut Gustave Roussy (IGR), one of the leading research and anticancer centres.

Applying robotics to the preparation process was a venture aimed at creating a solid and flexible machine able:

1. Eliminate risks of toxicity by preserving operators and the environment
2. Manage the toxic waste more efficiently
3. Eliminate human-related errors
4. Optimise production costs
5. Guaranteeing the tracability of TOs (Therapeutic Objects) e.g. bags, syringes
6. Enhance the quality of the process
7. Increase the production rate
8. Comply with regulatory requirements.

In 2004, prescription processing in the Department of Clinical Pharmacy (DCP) gave rise to ~35,000 TOs. In 2007, the DCP will generate ~65,000 TOs per year. The APSI program is funded by a co-development exclusivity contract between IGR via its DCP and BioTOM S.A., a High-Tech industrial partner. The Project Group (pharmacists, engineers, technicians) operates in a concurrent engineering context according to 12 items:

1. modelling
2. rapid prototyping, direct production, virtual validation
3. mechanical confinement, aeraulic
4. electronics
5. electromechanics, robotics
6. ergonomics, design
7. peri-robotics logistics
8. Man-Machine Interface development
9. development of a supervisor at the interface with APSI and computerised patient prescriptions
10. study of burden, simulation and management of drug preparation
11. process performance analysis, operation qualification
12. cost evaluation and business plan. After 30 months, the prototype is in the operational qualification phase.

We are launching the production of the first of 3 machines designed to equip the future DCP production unit (January 2006). We feel that we have overcome practically all the technical stumbling blocks: the milestone schedule has been followed. APSI is a "technological breakthrough" and the result of a model hospital-industry partnership with an R&D budget totalling 1.2 M.

1350 PUBLICATION

Indications for treatment by electrochemotherapy; results of the ESOPE European trials

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Background: Electrochemotherapy is a therapeutic approach providing delivery of nonpermeant cytotoxic drugs like bleomycin or cisplatin into the cells by electroporation of tumors.

Materials and methods: A European consortium (ESOPE: European Standard Operating Procedures of Electrochemotherapy) was set up to test a new clinical electroporator (Cliniporator, IGEA, Italy) and establish common European guidelines for treatment of cancer patients using electrochemotherapy. At the 5 centers, protocols for treatment were approved by the respective regional ethical committees. Cancer patients with tumors of all histologies were permitted, with cutaneous nodules in skin or subcutis. Patients had progressive and metastatic disease, and the patients were all offered standard care.

Results and Conclusions: Physico-chemical basis of this therapy allows prediction that electrochemotherapy has good antitumor effect on all tumor types, which was demonstrated in several clinical studies. Antitumor effectiveness of electrochemotherapy either with bleomycin or cisplatin in patients with recurrent cutaneous and subcutaneous tumors was shown to be in the range of 70–80% local tumor control rate. This enlists electrochemotherapy in line with other local treatments like radiation therapy and surgery with equally or even higher effectiveness.

The clinical experience gained so far in the ESOPE project provided evidence that electrochemotherapy is successful treatment in various clinical indications:

- Easy and effective treatment of single or multiple tumor nodules of any histology in the cutaneous and subcutaneous tissue.
- Treatment that increases quality of life in patients with progressive disease.
- Treatment of choice for tumors refractory to conventional treatments.
- Neoadjuvant treatment in form of cytoreductive therapy before conventional treatment.
- Organ sparing and function saving treatment.
- Treatment of hemorrhagic or painful nodules, since it reduces bleeding and in some cases pain level.

All these indications provide electrochemotherapy broad spectrum of use, predominantly because electrochemotherapy is effective local therapy and additionally quick and easy to perform.

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