pattern and duration of antidepressant use. Multiple regression analysis of data from a large prescription and medical claims database (MarketScan®) for the years 1993 and 1994 were used to estimate the determinants of antidepressant drug use patterns for 1,034 patients with a "new" episode of antidepressant therapy who were prescribed one of three most often prescribed selective serotonin reuptake inhibitors (SSRIs) paroxetine, sertraline, or fluoxetine.

The results indicated that patients initiating therapy on sertraline or paroxetine were less likely than patients initiating therapy on fluoxetine to have at least four prescriptions of their initial antidepressant within the first six months. The findings suggest that antidepressant selection is an important determinant of antidepressant use patterns consistent with current recommended depression treatment guidelines.

Tues-P22

THE COST-EFFECTIVENESS OF IXEL®, A NEW SNRI, IN COMPARISON WITH A PANEL OF TCAs AND SSRIs, IN THE TREATMENT OF DEPRESSION

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A model based on the theory of clinical decision analysis was constructed in order to estimate costs and outcomes when treating patients with a major depressive episode. Ixel® (milnacipran - Pierre Fabre Médicament), a new serotonin and norepinephrine reuptake inhibitor (SNRI), was compared with a French representative panel of tricyclic antidepressant (TCA) and selective serotonin reuptake inhibitor (SSRI).

The effectiveness of the alternatives, based on the safety/efficacy ratios, was evaluated from a meta-analysis of the studies included in the NDA dossier, taken into account the compliance as observed in usual practice. The other data used in the model came mainly from the literature and from a panel of psychiatrists.

Direct medical costs included antidepressant drugs, visits, lab tests and hospitalisations. Economic appraisal was performed according to the viewpoint of the French National Sickness Fund.

The model concluded in favour of a better cost-effectiveness of Ixel®: its expected cost of treatment per depressive episode was lower than either the one of the panel of TCAs (savings: 228 FF., 1 EURO = 6.62 FF.) or SSRIs (savings: 961 FF.). Moreover, its expected length of clinical remission was slightly higher. The robustness of these findings were supported by several threshold sensitivity analyses conducted on the main parameters.

Tues-P23

CITALOPRAM TREATS MAJOR DEPRESSION IN THE ELDERLY, WITH FEWER SIDE EFFECTS THAN AMITRIPTYLINE

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Depression is more common in the elderly than in the general population. Elderly patients, however, are more sensitive to the anticholinergic side effects of tricyclic antidepressants (TCAs), making their treatment especially problematic. Citalopram is the most selective of the serotonin re-uptake inhibitors, a class that is as efficacious as the TCAs, but causes fewer side effects. This double-bind, multicentre general practice study in the UK and Ireland compared citalopram and amitriptyline with respect to safety and efficacy in 365 elderly patients (65–90 years) with major depression. Patients with a diagnosis of major depression (including a score of ≥ 22 on the Montgomery-Asberg Depression Rating Scale [MADRS]) were randomised to receive either citalopram (20 or 40 mg once daily; n = 179) or amitriptyline (50 or 100 mg/day; n = 186) for 8 weeks. Efficacy was measured at weeks 1, 2, 4, 6 and 8 using the MADRS, the Hamilton Depression (HAMD) Scale and the Clinical Global Impression (CGI) Scale. The incidence of withdrawal due to adverse events (the main reason for discontinuation) was higher in amitriptyline- than in citalopram-treated patients (25% *vs* 17%; NS). A further 5% and 7% of patients, respectively, withdrew for other reasons. Adverse events considered to be treatment-related were experienced by significantly ($p < 0.001$) fewer patients in the citalopram group (45%) than in the amitriptyline group (63%). Confusion, hallucination, anxiety and suicide attempt occurred only in patients receiving amitriptyline. Nausea was the only adverse event to be observed more frequently with citalopram than with amitriptyline. The response (MADRS $\leq$ 12) rate was 54.5% and 53.5% in the citalopram and amiptriptyline groups, respectively (intent-to-treat). Improvements in HAMD and CGI were also comparable for the two groups. Thus, citalopram is as efficacious as amitriptyline in treating major depression, but causes fewer side effects; importantly, it does not cause the anticholinergic effects observed with amitriptyline. Citalopram is therefore an excellent candidate for treating depression in the elderly.

Tues-P24

CITALOPRAM IS EFFECTIVE AND WELL TOLERATED IN PATIENTS WITH MAJOR DEPRESSIVE DISORDER

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Citalopram is the most selective of the selective serotonin re-uptake inhibitors currently available and has a chemical structure unrelated to that of other SSRIs or other available antidepressants. This double-blind, randomised, placebo-controlled trial was designed to confirm the safety, efficacy and minimum effective dose of citalopram in patients with moderate to severe depression. In total, 650 patients were randomised to receive citalopram 10 mg (n = 131), 20 mg (n = 130), 40 mg (n = 131) or 60 mg (n = 129), or placebo (n = 129), given once daily for 6, weeks. The percentage of responders (defined as $\geq$ 50% decrease from baseline on the Montgomery-Asberg Depression Rating Scale) was significantly ($p < 0.05$) greater in each of the citalopram groups (49 to 61%) than in the placebo group (35%). The reduction in Hamilton Depression Scale total score was significantly ($p < 0.05$) greater in patients receiving citalopram 40 mg than in those receiving placebo. Increasing the dose to 60 mg appeared to offer little additional benefit. A similar number of patients withdrew from each treatment group. There were more withdrawals because of lack of efficacy, and fewer withdrawals because of adverse events in the placebo and citalopram 10 mg groups than in the higher-dose citalopram groups. The incidence of withdrawal because of adverse events was similar in the citalopram 20, 40 and 60 mg groups. The most frequent treatment-emergent events were nausea, insomnia, dry mouth, somnolence and increased sweating. The incidence of accepted SSRI-related side effects, including nausea and dry mouth, did not appear to be dose-dependent, although there was a trend towards a higher frequency of insomia, somnolence and fatigue in the citalopram 40 and 60 mg groups. In conclusion, this trial confirmed that citalopram is efficacious in moderate to severe

depression, and that dosage can be increased within the range 20 to 60 mg without risk of increasing SSRI-type side effects.

Tues-P25

CITALOPRAM INFUSION IS A USEFUL ALTERNATIVE TO TABLETS IN HOSPITALISED PATIENTS WITH DEPRESSION

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It has been suggested that it can be advantageous to use intravenous (IV), rather than oral antidepressants in severely depressed patients. The IV route avoids first-pass metabolism of the drug, and may result in a faster onset of action; infusion may also have a psychotherapeutic effect. Few of the second-generation antidepressants are available for IV therapy, and citalopram is the only selective serotonin re-uptake inhibitor that has been formulated for infusion. Citalopram is highly efficacious and has a good safety profile. Its bioavailability is high, and its metabolites are of little clinical significance; therefore, oral and IV doses are equivalent. This randomised, parallel-group study compared citalopram tablets with citalopram two-hour infusion, each given once daily in a double-blind, double-dummy design, followed by open-label oral citalopram. Sixty patients (mean age 43 years), hospitalised for moderately - severe depression, received either citalopram tablet plus placebo infusion (n = 30), or placebo tablet plus citalopram infusion (n = 30) for 10 days. All patients then received open treatment with oral citalopram (Days 11–42). The daily dosage in both groups was 20 mg on Days 1–2, 40 mg on Days 3–14, and 60 mg on Days 15–21, reducing thereafter to 40 mg if clinically indicated. On Day 7, the reduction from baseline on the Hamilton Depression (HAMD) Scale was numerically greater in the infusion group than in the tablet group (6.3 *vs* 4.3; NS) suggesting a more rapid onset of effect with infusion. This trend was also apparent on Day 11, when 50% and 37% of patients in the infusion and tablet groups, respectively, were classed as responders on the Clinical Global Impression (CGI) scale. On Day 42, the proportion of responders in the two groups was identical (73%), and the decrease from baseline in HAMD and CGI was significant in both groups ($p < 0.001$). There were no clinically relevant differences in adverse events or safety variables between the groups. These results suggest that slow-drop infusion of citalopram has a similar risk/benefit ratio, and may have a more rapid onset of antidepressant effect, than oral citalopram.

Tues-P26

BENEFITS OF CITALOPRAM *VS* VILOXAZINE, BOTH GIVEN AS AN INTRAVENOUS-TO-ORAL REGIMEN FOR SEVERE DEPRESSION

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There is anecdotal evidence that antidepressant effects are observed more quickly if the drug is administered intravenously (IV) rather than orally. In addition, compliance is assured by IV therapy. Therefore, commencing treatment with an infusion appears beneficial for severely depressed patients. Most available IV antidepressants are tricyclics (TCAs) or tetracyclics, and their use is limited by an unfavourable side effect profile, particularly cardiotoxicity. Selective serotonin re-uptake inhibitors (SSRIs) are as efficacious as TCAs but have a better safety profile. Citalopram is the most selective SSRI and the only one available as an infusion. This randomised, double-blind, parallel-group, multicentre study, conducted in France, compared the efficacy and safety of citalopram with viloxazine, each administered by slow-drop infusion for 2 weeks, then orally for 4 weeks, in 65 patients (aged 23–70 years) hospitalised for major depression. Patients received either citalopram (40 mg/day IV then orally; n = 32), or viloxazine (300 mg/day IV then 600 mg/day orally; n = 33). There were 11 withdrawals from each treatment group, the most common reasons for these being 'improvement' in the citalopram group, and 'lack of efficacy' in the viloxazine group. The mean Montgomery-Asberg Depression Rating Scale total score was 34 in both treatment groups at baseline. After treatment, this score was significantly ($p < 0.05$) lower in the citalopram group than in the viloxazine group, both on Day 14 (12.3 *vs* 16.9) and Day 42 (6.7 *vs* 13.1). Improvement in Clinical Global Impression scores was also significantly ($p < 0.015$) greater in the citalopram group (Day 42). Treatment-emergent nausea and constipation occurred most frequently in the viloxazine group, whereas weight gain and concentration difficulties were more frequent with citalopram. No clinically significant cardiac events occurred in either group, and injection site tolerability was good with both drugs. In conclusion, an IV/oral regimen of citalopram is more efficacious than a similar regimen of viloxazine in patients with severe depression.

Tues-P27

TOLERABILITY OF 15 VS 30 MG INITIAL DOSES OF MIRTAZAPINE: A RANDOMIZED, DOUBLE-BLIND STUDY

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Aim: To assess the tolerability of 2 different initial doses of mirtazapine, outpatients with a DSM IV diagnosis of a Major Depressive Episode were randomly assigned to an ascending dosage regimen (n = 71; mirtazapine 15 mg for 1 week, followed by 30 mg for 1 week) or a fixed dosage regimen (n = 69, 30 mg for 2 weeks).

Methods: Tolerability was assessed by recording of adverse events (AEs), and using the computer-assisted interactive telephone system for daily ratings on the VAMRS scale, with 'Alert/drowsy' factor as an index of a day-time sedation. Efficacy was assessed by the17-HAMD and CGI, and effects on sleep by self ratings on the LSEQ, using the same computer-assisted system.

Results: Tolerability of both treatments was good. A total of 3 patients in each treatment group dropped-out; respectively 1 and 2 patients because of adverse events. During the first treatment week, AEs were reported with a similar incidence in both groups: somnolence by 9.9% of patients in the 15 mg group, and by 10.1% in the 30 mg group; respective values for dizziness were 4.2% and 8.7%. On the 'Alert/drowsy' factor a similar level of a day-time sedation was registered in both groups after the first dose of study medication, with subsequent immediate increase in alertness to baseline values, and approx. at day 10, to the level of 'normal' state. In both groups 17-HAMD scores decreased similarely at endpoint (-9.5 ± 5.9 and -10.9 ± 6.5). On the LSEQ, 30 mg initial dose of mirtazapine was related to a statistically significantly longer duration of sleep at weeks 1 and 2, and to significantly faster initiation of sleep at week 2.

Conclusion: There are no differences in tolerability of mirtazapine administered in initial doses of 15 or 30 mg, and both dosage regimens are well tolerated. The results on LSEQ were in favor of 30 mg initial dose, with respect to onset and duration of sleep.

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