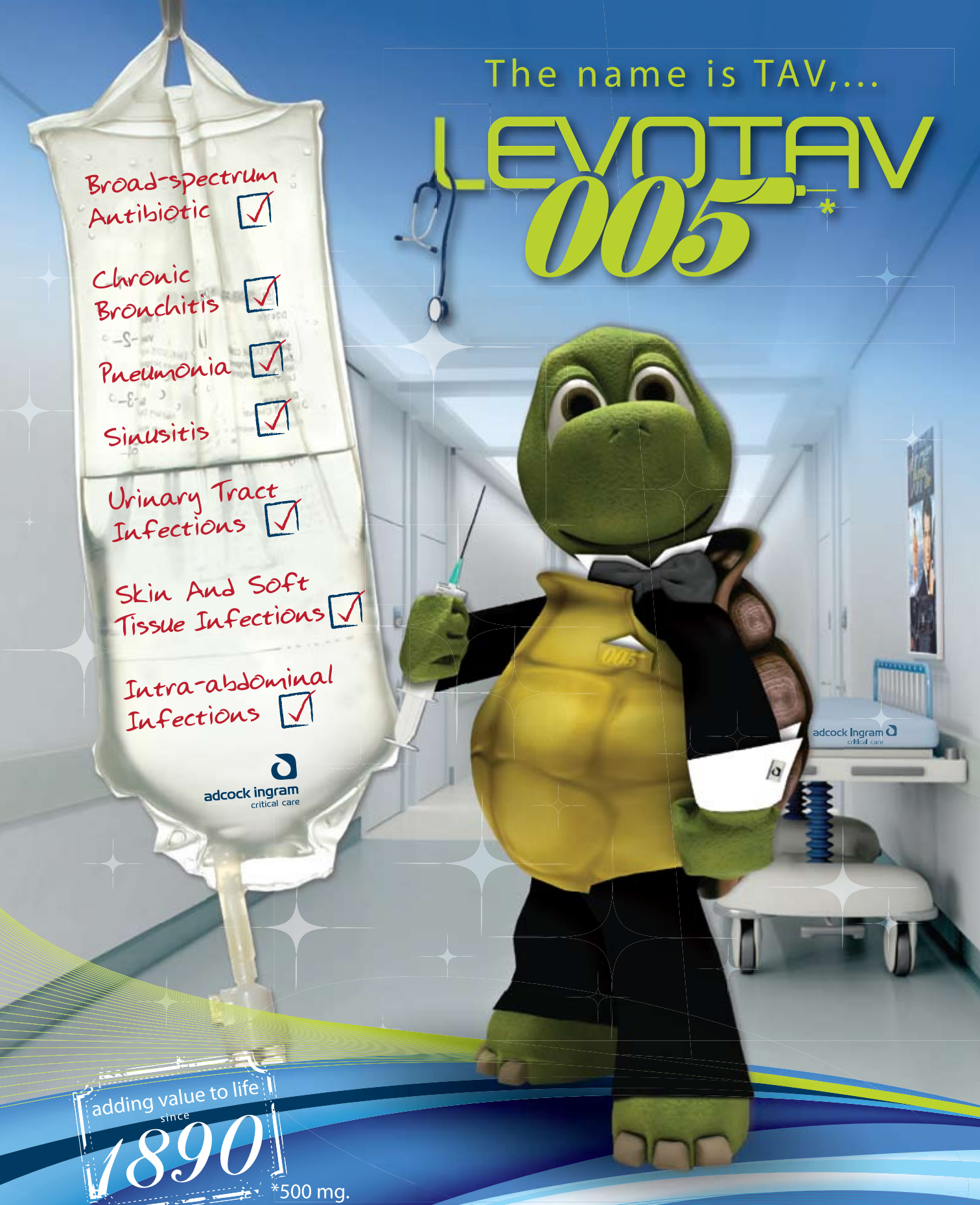

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Lifelong Learning

Levofloxacin in the Treatment of Community-Acquired Pneumonia

Fluoroquinolones are an increasingly important class of drugs for treating a wide range of infections, with ofloxacin being one of the most commonly used of these compounds.

Levofloxacin, the *l*-isomer of ofloxacin, is twice as potent as its parent compound, and therefore possesses all of the advantages offered by ofloxacin, as well as providing additional benefits. Improved effectiveness without any increase in side effects makes levofloxacin a very useful and advantageous antibiotic.

Levofloxacin is a fluoroquinolone that has a broad spectrum of activity against several causative bacterial pathogens of community-acquired pneumonia (CAP). Levofloxacin can be used as a monotherapy in patients with CAP, however, levofloxacin combination therapy with anti-pseudomonal beta-lactam (or aminoglycoside) should be considered if *Pseudomonas aeruginosa* is the causative pathogen of the respiratory infection.

Furthermore, levofloxacin is generally well tolerated, has good tissue penetration and adequate concentrations can be maintained at the site of infections.

Levofloxacin IV safe, effective in hospitalised patients - A study

In 2006, Polish authors Karwat KJ and others published a study to determine the efficacy and safety of levofloxacin in the treatment of CAP in outpatients with ineffective antibiotic management, requiring hospitalisation.

The examined group included 25 patients (11 male, 14 female) of mean age 70+/-17.5 years with abnormalities in x-ray on admission to hospital. Risk factors for pneumonia and previous antibacterial therapy were analysed.

In the hospital they were treated for seven days with levofloxacin 500mg twice a day administred intravenously. Body temperature, blood cell count, ESR, CRP, AST, ALT, LDH, CPK, creatine, urea, potassium, sodium, ABG, and ECG were measured on admission and in the third and seventh day of therapy. Chest x-rays were performed and analysed on hospital discharge.

Eighteen patients were aged >65yrs, cardiovascular diseases co-existed in 14, COPD in nine, smoking habit in twelve, renal failure in three, diabetes in three and alcohol addiction in one cases. On admission four patients had respiratory failure, and ten hypoxaemia.

During therapy a decrease of body temperature ($p<0,001$), concentration of CRP ($p<0,004$) and LDH ($p<0,03$), CPK ($p<0,04$) and increase of PaO_2 ($p<0,012$) were observed. The changes of other parameters were not statistically significant. Researchers did not observe any changes in ECG.

On discharge from the hospital in 16 patients complete regression and in six patients partial regression of lesions in chest x-ray examination were observed.

Levofloxacin effective and safe in patients where previous therapy failed

In three patients levofloxacin therapy was non-effective: in two because of persistent high body temperature after three days of treatment and in one patients because of recurrent of fever.

Adverse events were mild. Transient exacerbation of renal failure was observed in three patients.

The authors concluded that 2x500mg levofloxacine given intravenously for seven days is effective and safe in treatment of CAP in patients with previously ineffective antibacterial therapy.

High penetration, 100% bioavailable

In an interview with a US online journal, Dr Charles Fogarty, Medical Director; Respiratory Therapy, Spartanburg Regional Medical Center, South Carolina, said: Levofloxacin, which is the active *l*-isomer of ofloxacin, is twice as potent as its parent compound. Levofloxacin is 100% bioavailable and rapidly penetrates into tissues, where it achieves high levels. In fact the plasma levels themselves are bactericidal for the vast majority of community-acquired pathogens, specifically *Streptococcus pneumoniae*.

Other very favourable pharmacokinetic effects include an 80%-85% renal excretion with virtually no metabolites, a plasma half-life of six to seven hours and a two to three hour post antibiotic effect (Table 1).

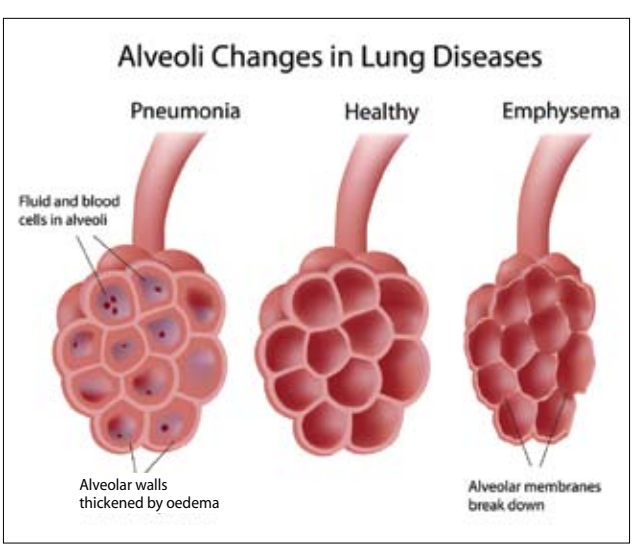


Figure 1

Table 1

Characteristics of levofloxacine

Metabolism	Minimal (<5%)
Excretion	Renal
Distribution	Widely distributed High tissue penetration Low plasma binding
Dose proportionality	Linear
Bioavailability	Rapid absorption Food effects rate not extent 100% bioavailable

Dr Fogarty continued: *S. pneumoniae* accounts for 20% of the CAP pathogens in most studies. There is another 30% which is unspecified and probably half of that is *S. pneumoniae*. *Haemophilus* and *Moraxella* are also important pathogens. Levofloxacin has minimum inhibitory concentration values of 1.9 for *S. pneumoniae*, 0.2 for *Haemophilus influenzae*, and 0.09 for *Moraxella catarrhalis*.

Levofloxacin has a very broad spectrum of activity, excellent bioavailability, low toxicity, minimal risk of drug-drug interactions and very importantly, fewer problems with resistance. The frequency of one step mutations to resistant organisms appears to be lower with levofloxacin than for other fluoroquinolones. Like the quinolones in general, levofloxacin inhibits DNA gyrase but unlike many of the other quinolones, levofloxacin uses two separate mechanisms to avoid the development of resistance.

Another important levofloxacin advantage, is no interaction with drugs such as theophylline (in contrast to other fluoroquinolones, particularly ciprofloxacin). Levofloxacin has a very low side effect profile and although phototoxicity is a theoretical concern, it is definitely less of a problem than with other quinolones such as lomefloxacin and sparfloxacin.

Levofloxacin superior in hospitalised CAP patients: study

In 2002 Dr Pierre Veyssier of Compiègne Central Hospital; Compiègne, France, looked specifically at the treatment of severe infections in patients with risk factors for complications.

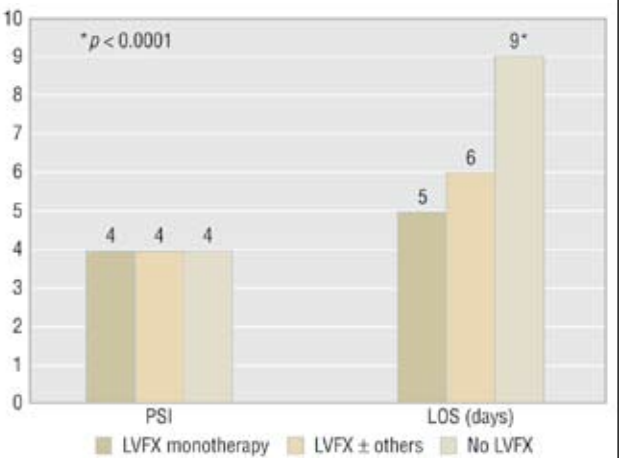
Dr Veyssier used guidelines from the Infectious Diseases Society of America (IDSA), to stratify patients into five risk groups based upon the Pneumonia Severity Scoring Index (PSSI) which was associated with changes in mortality, with classes III–V requiring hospitalisation.

Dr Veyssier reported results from an important study by Kahn et al. which investigated evofloxacin 500mg IV once daily versus ceftriaxone 1g-2g IV every 24 hours plus erythromycin 500mg-1000mg IV every 6 hours in CAP patients at high risk of mortality. Stringent criteria to identify the patients were used.

Levofloxacin was chosen due to earlier reports showing its efficacy in high risk patients. In addition, levofloxacin has maintained its efficacy despite being widely used for other infections, with the mean MICs of levofloxacin against both penicillin-susceptible and penicillin-resistant pneumonia not changing significantly and maintaining an excellent MIC ratio even against *S. pneumoniae* resistant to other fluoroquinolones.

Figure 2

Shorter hospital stay with levofloxacin empiric therapy



Abbreviations: PSI = Pneumonia severity-of-illness index class, LOS = length of hospital stay, LVFX monotherapy = levofloxacin monotherapy, LVFX ± others = levofloxacin plus or minus other antibiotics, such as a second-generation cephalosporin alone or a second-generation cephalosporin in combination with a macrolide, No LVXF = empiric antibiotic regimen not including levofloxacin, such as a second generation cephalosporin alone or a second-generation cephalosporin in combination with a macrolide.

In this trial 132 patients received levofloxacin and 137 were randomised to the comparator arm.

The clinical success rate for levofloxacin was 89.5% and only 83.1% for the comparator regimen. Levofloxacin was well tolerated with a 2.3% discontinuation compared to 8.8% for the comparators.

Chlamydia and *Legionella* too

In addition, the role of levofloxacin in managing atypical pathogens was emphasised by Dr Veyssier as regards agents needing to cover *Chlamydia* and *Legionella spp*.

A randomised trial of patients with severe CAP investigated a subgroup of patients with *Chlamydia pneumoniae* (9.4% of study population) - 83% of these patients were successfully treated with levofloxacin compared to only 67% in the comparator regimen (ceftriaxone plus erythromycin switching to clarithromycin plus amoxicillin/clavulanate).

This study also looked at a subgroup of *Legionella spp*. infected patients and demonstrated a greater than 90% clinical and microbiological success rate with levofloxacin. Results were also reported from assessing levofloxacin in immunocompromised patients with CAP.

Lower mortality; shorter hospital stay

A retrospective analysis showed that the patients with CAP treated with a fluoroquinolone demonstrated a lower mortality (7% vs 17%, p <0.05) and a shorter median length of stay in hospital (Figure 2).

In addition monotherapy with a fluoroquinolone was also associated with lower mortality rates and shortened hospital stay.

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