# POPULATION IMPACT OF LOSARTAN USE IN FRANCE

## Riou França L.[1], Souchet T.[2], Ragot S.[3], Herpin D.[4], Launois R.[1]

1. REES France, Paris, France ; 2. Merck Sharp & Dohme-Chibret, Paris, France ;
3. Clinical Reseach Center, University Hospital, Poitiers, France ; 4. Department of Cardiology, University Hospital, Poitiers, France

## INTRODUCTION

The crude annual incidence of first stroke in France is of 138 per 100,000 population. The number of first strokes in France is then of 85,000 per year, the total number of incident or recurrent strokes is of 120,000 per year [1].

### The LIFE Study

In this randomized, multicenter, clinical trial, [2] including 9193 patients, atenolol, a beta-blocker, was compared to losartan, an angiotensin-II type 1-receptor antagonist, among hypertensive patients aged 55-80 years with electrocardiogram diagnosed (ECG) left ventricular hypertrophy (LVH). Patients were randomly assigned to losartan or atenolol-based regimens in order to reach a target blood pressure of less than 140/90 mmHg and were followed for a mean duration of 4.8 years. The primary endpoint was a composite endpoint of cardiovascular death, myocardial infarction, and stroke. The relative risk (RR) was of 0,87 (p = 0.021) in favor of losartan, despite comparable degree of blood pressure control. Regarding specifically fatal and non-fatal stroke, there was a 24.9% relative risk reduction in favor of losartan (p = 0.001).

## OBJECTIVES

To estimate the number of patients in France meeting the LIFE inclusion criteria.

To estimate the impact of a losartan-based therapy on the cumulative incidence of first stroke.

## METHODS

### Patients

The selection criteria used in the model are not in exact match with those of the LIFE trial, since no epidemiological information was available for some of these, but they remain consistent of the ones available for a physician in daily practice. Table 1 summarizes the inclusion criteria used in this model and in the LIFE clinical trial.

**Table 1: Model Patient selection criteria used in the LIFE clinical trial and in the model**

| LIFE trial | Model |
|---|---|
| **Inclusion criteria** ||
| 55-80 years old ||
| Treated or untreated hypertension ||
| Systolic blood pressure 160-200 mm Hg or diastolic blood pressure 95-115 mmHg after 1-2 of placebo | All treated patients and untreated patients with blood pressure ≥ 160/95 mm Hg |
| ECG-diagnosed LVH ||
| **Exclusion criteria** ||
| Heart failure or left ventricular ejection fraction ≤ 40 % | Heart failure followed by a cardiologist |
| Angina pectoris requiring treatment by ß-blockers or calcium antagonists | Angina pectoris treated by ß-blockers or calcium antagonists |
| Secondary hypertension ||
| Myocardial infarction or stroke within the previous 6 months ||

### Data sources

The National Institute of Statistics and Economic Studies (INSEE) provides population tables based on the 1999 census and projected to the year of 2004. The French subset of the MONICA project [3] reports blood pressure measured in the period of 1994/1997 in three reporting units in Lille, Strasbourg and Toulouse for the population aged 35-64 years. The Thalès permanent epidemiological observatory allows the estimation of the broad patterns of prescriptions in France. The prevalence of left ventricular hypertrophy in a pilot study conducted in Scandinavia [4] and the incidence of stroke in the LIFE study [5] were applied to the model.

**Table 2: Model key parameters and sources for numerical values**

| Parameter | Source |
|---|---|
| • French Population 55-80 years | INSEE January 2004 |
| • Blood pressure 160/95 mm Hg | MONICA+ Projection |
| • No heart failure | Thalès |
| • No angina pectoris treated by ß-blockers or calcium antagonists | Thalès |
| • Left Ventricular Hypertrophy, ECG-diagnosed | LIFE pilot study |
| • Treated hypertension | MONICA+ Projection |
| • Drugs prescribed | Thalès |
| • Stroke incidence | LIFE study |

The prevalence of hypertension for the population aged 65-80 years was extrapolated from the MONICA study presuming a linear trend between hypertension and age class and a logarithmic trend between the proportion of treated hypertensive patients and age class.

## RESULTS

### Hypertension prevalence

Figure 1 gives the results of the linear estimation of hypertension prevalence for the age classes that were not measured in the MONICA study. The same was done to estimate the proportion of treated patients, using a logarithmic trend.
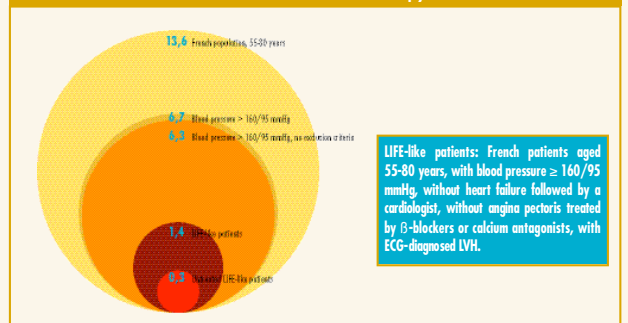


**Figure 1:** Projected sex-specific hypertension prevalence estimates for age classes 65-74 and 75-80 years
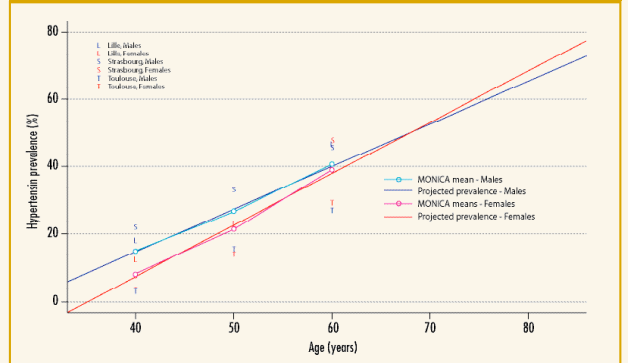
### French patients eligible for a losartan-based therapy

The French population aged 55-80 years is of 13.6 million. 6.7 million of them are hypertensive. 0.4 million of hypertensive patients are identified as having heart failure or angina pectoris. Among the remaining 6.3 million patients, 22% are considered to have an ECG-diagnosed LVH. 0.3 million of these 1.4 million patients are expected to be currently untreated. Figure 2 summarizes this repartition.



**Figure 2:** Estimated number of French patients eligible for a losartan-based therapy

13,6 French population, 55-80 years
6,7 Blood pressure > 160/95 mmHg
6,3 Blood pressure > 160/95 mmHg, no exclusion criteria
1,4 LIFE-like patients
0,3 Untreated LIFE-like patients

LIFE-like patients: French patients aged 55-80 years, with blood pressure ≥ 160/95 mmHg, without heart failure followed by a cardiologist, without angina pectoris treated by ß-blockers or calcium antagonists, with ECG-diagnosed LVH.

### Cumulative number of strokes avoided in the next 5.5 years

Applying the cumulative stroke incidence reported in the LIFE trial [5] to the estimated 1.4 million LIFE-like patients, the estimated number of strokes during the next 5.5 years using an atenolol-based treatment is of 90,147. Using a losartan-based strategy, this figure decreases to 67,957. In comparison with atenolol base therapy, 22,190 strokes would therefore be avoided.



**Figure 3:** Projected cumulative number of strokes in the next 5.5 years in France using losartan and atenolol-based treatment strategies to treat LIFE-like patients
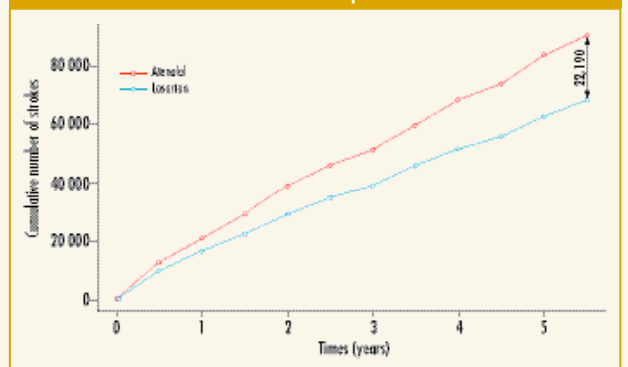
## CONCLUSIONS

The stroke incidence reduction using a losartan-based regimen instead of an atenolol-based therapy should be viewed as representing an incremental improvement relative to the benefit of conventional antihypertensive therapies: beta-blockers and diuretics. A nationwide prevention program using losartan in the treatment of hypertensive patients with left ventricular hypertrophy has the potential to have a major public health impact in France, as a consequence of the reduction in stroke incidence.

## ACKNOWLEDGEMENTS

## REFERENCES

[1] ARHIF. Rapport du groupe de travail AVC 2002.
[2] Dahlof B et al. Lancet. 2002;359(9311):995-1003.
[3] WHO MONICA Project principal investigators. J Clin Epidemiol. 1988;41(2):105-14.
[4] Dahlöf B et al. Am J Hypertens 1997 ; 10 : 705-713.
[5] Dahlöf B et al. J Human Hypertens 2004, 1-7.