

## STUDY REPORT SYNOPSIS

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### Non-Interventional Study (NIS)/ D1843R00249

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#### An epidemiological to evaluate standard daily practice in managing patients with arterial hypertension in Egypt

<b>Milestones:</b>	<b>Milestone</b>	<b>Date</b>
	First subject in	3-Apr-2016
	Last Subject in	30-Oct-2017
	Last subject last visit	14-Feb-2018
	Study Report	12-Feb-2018
<b>Phase of development:</b>	Non Interventional Study	
<b>Sponsor:</b>	AstraZeneca	

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This study was performed in compliance with Good Clinical Practice (GCP) and Good Pharmacoepidemiology Practice (GPP), including the archiving of essential documents.

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## **Background/rationale:**

Hypertension is an increasingly important medical and public health issue. Data from different national and regional surveys show that HTN is prevalent in developing countries, particularly in urban areas, and that rates of awareness, treatment, and control are low. The recent data from epidemiological studies and clinical trials have demonstrated that elevations in resting heart rate and reduced heart-rate variability are associated with higher cardiovascular risk. In the Framingham Heart Study, an average resting heart rate of 83 beats per minute was associated with a substantially higher risk of death from a cardiovascular event than the risk associated with lower heart rate levels. In the present study, we aimed to evaluate response rate to different classes of the antihypertensive treatment in real life practice including patients' characteristics, and patients' management/treatment. Furthermore, we aimed to evaluate the response rate of the different class of antihypertensive treatment in real life practice

## **Objectives:**

### **Primary objective:**

- To Evaluate the Proportion of hypertensive patients who were newly diagnosed and/or patients with essential hypertension on current antihypertensive pharmacological treatment reaching SBP treatment goals according the ESC 2013 criteria (<140 mmHg\*) after being treated for at least 3 months.

### **Secondary objectives:**

- To evaluate proportion of patients on antihypertensive pharmacological treatment reaching DBP goals according to the ESC 2013 guidelines (<90 mmHg\*).
- To evaluate proportion of patients on antihypertensive pharmacological treatment reaching combined SBP and DBP treatment goals according to the ESC 2013 guidelines (SBP <140 mmHg and DBP <90 mmHg\*).
- To collect local epidemiological data on patients with hypertension; Demographic data; Age, Weight and Gender. Hypertension management data; Number of Patients on Each Anti-Hypertensive Class. Hypertension Associated co morbid diseases; Number of Patients with creatinine clearance (CrCl) < 90 ml/min using Cockcroft-Gault Equation, Number of patients with Diabetes (on Current Anti-Diabetic therapy or Fasting plasma glucose (FPG)  $\geq 126$  mg/dl and/or Postprandial Glucose (PPG)  $\geq 200$  mg/dl and/or Glycosylated haemoglobin (HbA1c)  $\geq 6.5\%$ . and the Mean LDL, HDL and Triglycerides Levels in study population.

## **Study design:**

This study was an epidemiological non-interventional trial that records real-life clinical practice with no additional diagnostic or monitoring procedures.



## Data source:

Data were collected from the following the internal medicine and hypertension clinics in Cairo, Giza, Delta, Upper Egypt and Alexandria.

The data were collected on CRFs. For each patient that has signed the Informed Consent, a CRF was completed. The monitor of the trial collected the original CRF and the physician kept a copy. At the Data Management agency, the data were entered in a database.

## Study population:

The present observational study included 1436 patients and all of them fulfilled the inclusion and exclusion criteria.

## Inclusion criteria:

Male or female patients who were willing to give written informed consent and aged >21 years with newly diagnosed essential arterial hypertension. Also, Females of childbearing potential using a reliable method of contraception and patients with uncontrolled essential arterial hypertension currently receiving treatment with any of the following antihypertensive classes: a Thiazide Diuretics, calcium antagonist, Angiotensin Converting enzyme Inhibitor, Angiotensin II receptor blocker and Beta Blocker for at least 3 months.

## Exclusion criteria:

If participating in any clinical trial, the subject couldn't take part in this study. As well as Pregnant and lactating women.

## Statistical methods:

A comprehensive Statistical Analysis Plan (SAP) was prepared before database lock. Continuous data were described by their mean, standard deviation, quartile, median, minimum and maximum. Categorical data were described by frequency and percentage. Comparative analysis and inferential statistics were performed using paired-t-test/ Wilcoxon signed-rank/ McNamara test for continuous variables, and Chi-square tests was used in case of categorical variables. 95% two-sided confidence intervals and two-sided on a 5% level was provided as appropriate. No adjustment for multiple testing was done. SPSS, version 21 was used for analysis of this study, missing data were described for each variable as a percentage.

## Results:

The present study included 1436 patients. Of them, 721 (50.2%) were male. The mean age of the patients was  $54.0 \pm 11.2$  years, mean of BMI was  $32.0 \pm 5.9$ . The majority of the patients were Egyptian 1427 (99.4%) and the rest were other nationalities 9 (0.6%). Most of included patients were married (82.7%) and live in urban areas (79%). Regarding education level, 615 (43.1%) in the university, 306 (21.5%) primary education, 259 (18.2%) post-secondary education, 245 (17.2%) secondary education. Unemployed participated patients constituted 577 (40.5%) of the total participations, employed 494 (34.7%), self-employed 187 (13.1%), and retired 167 (11.7%).



Regarding the medical history of the patients, only 470 (32.7%) patients were early diagnosed and 971(67.6%) were known with hypertension. Most of the hypertensive patients were receiving beta-blockers 545 (38%) followed by Angiotensin II Receptor Blockers 332 (23.1%), ACE inhibitors 265 (18.5%), Calcium antagonists 232 (16.2%), and diuretics 201 (14%).

The most common reason for patients' visit was Headache 793 (55.2%) followed by dizziness 400 (27.9%). About 320 (22.3%) of the patients were performing a regular check-up.

Regarding the hypertensive complications (organ damage), about 202 (14.1%) patients presented with coronary artery disease, 77 (5.4%) with kidney disease, 73 (5.1%) with retinopathy, and 31 (2.2%) with congestive heart failure. The rest of patients 1059 (73.7%) were free from any organ damage.

The mean of heart rate was  $83.0 \pm 10.4$  beat per minute, systolic BP right arm  $162.2 \pm 15.6$  mmHg, diastolic BP right arm  $97.6 \pm 9.7$  mmHg, systolic BP left arm  $160.9 \pm 15.4$  mmHg, and the mean of diastolic BP left arm  $96.8 \pm 9.2$ . A total of 831 (57.9%) patients reported with a high BP  $<140/90$  without compelling indication. While, 478 (33.3%) patients had BP  $<140/85$  with diabetes, 104 (7.2%) with BP  $<130/90$  with kidney disease with proteinuria, and 23 (1.6%) with BP  $<140/90$  with kidney disease without proteinuria.

**In the second visit**, the main reason for the visit of was regular scheduled check-up in 1259 (88.2%) patients, and uncontrolled BP in 145 (10.2%) patients. The change in medication was reported in 159 (11.1%) patients. Out of 324 smokers, 148 patients stopped smoking. In terms of anti-hypertension treatment, 75 (5.2%) patients were added to ACEI and 50 (3.5%) were removed, 123 (8.6%) were added to ARBs and 15 (1%) were removed, 102 (7.1%) added to Calcium antagonist and 18 (1.3%) were removed, and 95 (6.6%) were added to beta-blockers and 26 (1.8%) were removed.

**In the third visit**, the main reason for the visit of 1345 (93.7%) patients was regular scheduled check-up, and uncontrolled BP in 39 (6.6%) patients. There was a minimal change in medication reported in 60 (4.2%) patients. Out of 324 smokers, 139 patients stopped smoking. In terms of anti-hypertension treatment, 10 (0.7%) patients were added to ACEI and 6 (0.4%) were removed, 10 (0.7%) were added to ARBs and 5 (0.3%) were removed, 18 (1.3%) added to Calcium antagonist and 6 (0.4%) were removed, and 24 (1.7%) were added to diuretic and 8 (0.6%) were removed.

#### **Comparison among studied groups through the three visits as regards different measures of blood pressure.**

Regarding the mean difference (MD) in the systolic BP between the first and third visit, our findings show highly significant ( $p < 0.001$ ) reduction in the SBP in the right arm (MD= -30.6 mmHg), in the left arm (MD= -30 mmHg), and at the higher value arm (MD= -31 mmHg). **In patients with Hypertension with chronic kidney disease with Proteinuria**, we reported a significant reduction in the SBP in the right arm (MD= -20.5 mmHg,  $p = 0.009$ ), the left arm (MD= -19.7 mmHg,  $p = 0.005$ ), and at the higher value arm (MD= -20.8 mmHg,  $p = 0.012$ ). The total number of patients who reached the targeting right arm SBP ( $<130$  mmHg) was 17 (16.3%) and 31 (29.8%) in the second and third visit, respectively. The total number of patients who reached the targeting left arm SBP ( $<130$  mmHg) was 22 (25%) and 44 (42.3%) in the second and third visit, respectively. The total number of patients who reached the targeting higher value arm SBP ( $<130$  mmHg) was 15 (14.4%) and 32 (30.8%) in the second and third visit, respectively. The total number of patients who reached the targeting left arm DBP ( $<90$  mmHg) was 62 (59.6%) and 83 (79.8%) in the second and third visit, respectively. The total number of patients who reached the targeting higher value arm DBP ( $<90$  mmHg) was 51 (49%) and 79 (76%) in the second and third visit, respectively. Our results demonstrated that there was no significant difference between the patients who reached the target and patients who did not reach wither SPB or DBP at the first visit ( $p=0.493$ ). However, in the third visit, we found a highly significant deference between the two groups regarding SBP ( $p<0.001$ ) and DBP ( $p=0.001$ ).



***In patients with Hypertension with chronic kidney disease with no Proteinuria***, the MD in the SBP between the first and second visit shows a significant reduction in the right arm (MD= -20.4 mmHg, p=0.0213), the left arm (MD= -21.3 mmHg, p=0.0213), and at the higher value arm (MD= -22.4 mmHg, p=0.041). The MD in the SBP between the second and third visit shows insignificant reduction in the right arm (MD= -5.9 mmHg, p=0.31), the left arm (MD= -3.6 mmHg, p=0.31), and at the higher value arm (MD= -8.8 mmHg, p=0.361). The total number of patients who reached the targeting right arm SBP (<140 mmHg) was 9 (39.1%) and 13 (56.5%) in the second and third visit, respectively. The total number of patients who reached the targeting left arm SBP (<140 mmHg) was 9 (39.1%) and 13 (56.5%) in the second and third visit, respectively. The total number of patients who reached the targeting higher value arm SBP (<140 mmHg) was 7 (30.4%) and 10 (43.4%) in the second and third visit, respectively. The total number of patients who reached the targeting right arm DBP (<90 mmHg) was 9 (39.1%) and 13 (56.5%) in the second and third visit, respectively. The total number of patients who reached the targeting left arm DBP (<90 mmHg) was 12 (52.2%) and 17 (73.9%) in the second and third visit, respectively. The total number of patients who reached the targeting higher value arm DBP (<90 mmHg) was 8 (34.8%) and 14 (60.9%) in the second and third visit, respectively. Our findings demonstrated a significant difference between the patients who reached the target and patients who did not reach the targeted DBP (p=0.011) at the first visit. Moreover, in the third visit, we found a highly significant difference between the two groups regarding SBP (p<0.001), while in DBP, we found insignificant difference (p=0.056). ***In patients with Hypertension with diabetes***, the MD in the SBP between the first and second visit shows a significant reduction in the right arm (MD= -21.6 mmHg, p<0.001), the left arm (MD= -22.6 mmHg, p<0.001), and at the higher value arm (MD= -23.3 mmHg, p<0.001). The total number of patients who reached the targeting right arm SBP (<140 mmHg) was 204 (42.7%) and 336 (70.3%) in the second and third visit, respectively. The total number of patients who reached the targeting left arm SBP (<140 mmHg) was 230 (48.1%) and 358 (74.9%) in the second and third visit, respectively. The total number of patients who reached the targeting higher value arm SBP (<140 mmHg) was 194 (40.6%) and 328 (68.6%) in the second and third visit, respectively. The total number of patients who reached the targeting right arm DBP (<85 mmHg) was 216 (45.2%) and 324 (67.8%) in the second and third visit, respectively. The total number of patients who reached the targeting left arm DBP (<85 mmHg) was 224 (46.9%) and 342 (71.5%) in the second and third visit, respectively. The total number of patients who reached the targeting higher value arm DBP (<85 mmHg) was 196 (41.0%) and 304 (63.6%) in the second and third visit, respectively. Our findings demonstrate a significant difference between the patients who reached the target and patients who did not reach regarding SPB (p=0.046) and DBP (p=0.006) at the first visit. Moreover, in the third visit, we found a highly significant difference between the two groups regarding SBP (p<0.001) and DBP (p<0.001). ***In patients with hypertension without compelling indication***, The total number of patients who reached the targeting right arm SBP (<140 mmHg) was 383 (46.1%) and 619 (74.5%) in the second and third visit, respectively. The total number of patients who reached the targeting left arm SBP (<140 mmHg) was 403 (48.5%) and 621 (74.7%) in the second and third visit, respectively. The total number of patients who reached the targeting higher value arm SBP (<140 mmHg) was 366 (44.0%) and 589 (70.9%) in the second and third visit, respectively. The total number of patients who reached the targeting right arm DBP (<90 mmHg) was 463 (55.7%) and 664 (79.9%) in the second and third visit, respectively. The total number of patients who reached the targeting left arm DBP (<90 mmHg) was 477 (57.4%) and 665 (80.0%) in the second and third visit, respectively. The total number of patients who reached the targeting higher value arm DBP (<90 mmHg) was 433 (52.1%) and 635 (76.4%) in the second and third visit, respectively. Our findings demonstrated a significant difference between the patients who reached the target and patients who did not reach regarding SPB (p=0.021) and DBP (p<0.001) at the first visit. Moreover, in the third visit, we found a highly significant difference between the two groups regarding SBP (p<0.001) and DBP (p<0.001).

***In terms of newly diagnosed patients***, we found that there was a highly significant (p<0.001) difference between the newly diagnosed patients and previous known on one side and the patients who reached the BP target and who not reached on the other side in both second and third visits. (Table 17)

**The comparison between studied cases that reached and did not reach target blood pressure after the third visit** demonstrated an insignificant difference between cases that reached and did not reach target blood pressure after the third visit in terms of; sex (p=0.393), nationality (p=0.213), marital status (p=0.549), residence (p=0.593), work experience (p=0.232), healthcare insurance (p=0.414), weight (p=0.089), and height (p=0.999). On the other hand, we found a slightly significant difference between two groups in terms of; living alone/with family (p=0.039), education level (p=0.042), and BMI (p=0.041). Besides we found a highly significant difference in the following parameters, age (p=0.002), waist circumference (p=0.003), SBP higher value arm (p<0.001) and, DBP higher value arm (p<0.001). **Regression analysis** shows that the following factors was significantly associated with not reaching the BP target among studied group; D2HVA (OR 0.958, p<0.001), waist circumference (OR 0.993, p=0.019), newly diagnosed patient (OR 0.472, p<0.001), diabetes (OR 1.707, p<0.001), smoking (OR 1.503, p=0.004), CHF (OR 4.277, p= 0.011), and pre-existing condition (OR 0.322, p<0.001).

**Conclusion:**

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**Publications:** NA

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