**Evaluation of the Angiotensin II Receptor-Blocker Azilsartan Medoxomil in African-American Patients with Hypertension**

BACKGROUND:

- This study was conducted because there is a lack of hypertension studies that evaluate the efficacy of hypertension medications, specifically ACEI and ARB medications, in the African-American population.

OBJECTIVE:

- The purpose of this study was to evaluate the safety and efficacy of the angiotensin II receptor blocker azilsartan medoxomil in African American patients with stage 1 or 2 hypertension.

METHODS

- **Design**: Multicenter, controlled experimental, parallel, randomized, double-blind
- **Duration**: 6 weeks
- **Inclusion criteria**: At least 18 years old; clinic SBP ≥150 and ≤180 mmHg and a 24 hour mean SBP ≥130 and ≤170 mmHg
- **Exclusion criteria**: Known or suspected secondary hypertension or severe diastolic hypertension (seated diastolic [DBP] >114 mmHg); severe renal impairment (estimated GFR <30 mL/min/1.73m$^2$); history of a major cardiovascular event in the previous 6 months; type 1 or poorly controlled type 2 diabetes mellitus (glycated hemoglobin >8%); poor compliance with study medication during the placebo run-in period; hyperkalemia (serum K+ concentration > upper limit of normal for the reference laboratory). In addition, night shift workers, pregnant or nursing women, and women of childbearing potential not using approved means of contraception were excluded from participation; concomitant medications known to affect BP, listed in the protocol and available to all study personnel, were not permitted
- **# patients enrolled**: 413 total; 138 patients placebo; 138 patients AZL-M 40 mg; 137 patients AZL-M 80 mg
- **Drug regimens/dosages**: Placebo, AZL-M 40 mg, or AZL-M 80mg all given once daily by mouth
- **Outcome measures:**
  **Primary outcome measure**: Change from baseline to week 6 in 24-hour mean systolic blood pressure (SBP) by ABPM
  **Secondary outcome measures**: Change in trough sitting clinic SBP; changes in 24-hour mean diastolic blood pressure (DBP) by ABPM and clinic DBP
- **Power:** At least 90% to detect a 6mmHg difference between AZL-M and placebo
- **Data handling method**: Intent-to-treat

RESULTS

- 365 patients completed the study. There were 15 dropouts in placebo (123 completed), 14 dropouts in AZL-M 40mg (126 completed), and 21 dropouts in AZL-M 80mg (116 completed).
- **Primary outcome measure**: Treatment differences in 24-hour SBP between AZL-M 40 mg and placebo (−5.0 mm Hg; 95% confidence interval, −8.0 to −2.0) and AZL-M 80 mg and placebo (−7.8 mm Hg; 95% confidence interval, −10.7 to −4.9) were significant ($P \leq .001$ vs. placebo for both comparisons).

- **Secondary outcome measures**: All secondary outcome measures were statistically significant. Decreases in clinic SBP were –6.5 mm Hg for both AZL-M 40 mg (95% CI, −10.2 to −2.8) and AZL-M 80 mg (95% CI, −10.3 to −2.8) ($P \leq .001$ vs. placebo for both). Decreases in 24-hour DBP were −3.4 mm Hg (95% CI, −5.5 to −1.4) for AZL-M 40 mg and −5.8 mm Hg (95% CI, −7.8 to −3.8) for AZL-M 80 mg ($P \leq .001$ vs. placebo for both comparisons). Decreases in clinic DBP were −3.1 mm Hg (95% CI, −5.2 to −1.0) for AZL 40 mg and −3.0 mm Hg (95% CI, −5.1 to −0.8) for AZL-M 80 mg ($P = .004$ and $P = .006$ vs. placebo, respectively).
- **Author's conclusion:** AZL-M significantly reduced ambulatory and clinic BPs in a dose-dependent manner and was well tolerated in African-Americans.

STRENGTHS
- "Gold standard" study design was used – controlled experimental, parallel, randomized, double-blind
- Addressed a needed research question

LIMITATIONS
- Study was only conducted for a short period of time (6 weeks)
- Study was conducted almost exclusively by individuals who have ties to and have been paid by the company that sponsored the study and manufacturers the study drug
- Adherence was only addressed prior to the study beginning, not throughout the study or at the end of the study
- Possibility of unbinding was not discussed
- Patients with stage 2 hypertension, who are likely already on more than one antihypertensive, were included in this single treatment study

CONCLUSION
- This study was designed well and provided some useful information on the safety and efficacy of azilsartan in African Americans. The results that were presented were statistically significant, however, the results did not appear to be clinically significant.
- This treatment could potentially be a useful addition to current therapy in African-American patients, but further research is still needed. It is much more expensive than drugs currently in use and only showed very small reductions in BP compared to placebo in this study.
- Further studies should be designed in a way to make the study period longer and to compare other hypertensive medications with azilsartan. In addition, individuals not affiliated with the manufacturer should perform future studies.

**Reference:** Johnson W, White WB, Sica D, et al. Evaluation of the angiotensin II receptor blocker azilsartan medoxomil in African-American patients with hypertension. *J Clin Hypertens.* 2017;00:1-7. doi: 10.1111/jch.12993

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