Mini- Round Presentation-JOURNAL

HALT- Early and Late PKD Trials

Wednesday, March 11, 2015

Presenter: Dr. Joseph Edwin Kanu
Facilitators: Prof. J Kayima
Dr.AJ Were
OUTLINE OF PRESENTATION

❑ INTRODUCTION
❑ BACKGROUND OF HALT TRIALS
❑ HALT EARLY PKD TRIAL (methodology, statistical analysis, results & discussion)
❑ HALT LATE PKD TRIAL (methodology, statistical analysis results & discussion)
❑ CRITICAL APPRAISAL OF BOTH STUDIES
❑ TAKE HOME
INTRODUCTION

ADPKD is a multisystem disorder characterized by multiple, **bilateral renal cysts** associated with **cysts in other organs**, such as liver, pancreas, and arachnoid membranes.

It is a genetic disorder mediated primarily by mutations in **two different genes** and is expressed in an **autosomal dominant** pattern, with variable expression.

<table>
<thead>
<tr>
<th>Gene</th>
<th>Protein</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADPKD1</td>
<td>Polycystin 1</td>
</tr>
<tr>
<td>ADPKD2</td>
<td>Polycystin 2</td>
</tr>
<tr>
<td>ARPKD</td>
<td>Fibrocytisin/polyductin</td>
</tr>
</tbody>
</table>
INTRODUCTION

ADPKD

4th leading cause of ESRD
Cyst growth results in increase kidney volume
- Activation of RASS
- High blood pressure and
- Renal failure

No clear evidence that BP control or RASS blockade slows the progression of renal disease.

What is the ideal level of BP control in ADPKD?
Pathogenesis of Cyst Formation

Abnormal extracellular matrix metabolism
Thickened tubular basement membrane, mitral valve prolapse, intracerebral aneurysms

- Increased apoptosis
- Increased proliferation
- Abnormal fluid secretion
- Cilia
Pathogenetic role of RAAS in ADPKD

Schrier JASN 20:1888-1893, 2009
Loss of Kidney Function in ADPKD
THE HALT PROGRESSION OF POLYCYSTIC KIDNEY DISEASE TRIALS (HALT- EARLY AND LATE PKD TRIALS- PUBLISHED IN DEC 14 - NEJM)  
STUDY A & STUDY B
BACKGROUND – HALT TRIALS

- HTN is common in ADPKD and is associated with increase in TKV & activation of RASS.
- HTN occurs early and is associated with progression to ESRD and death from CVS causes in patients with ADPKD.
- It is unclear whether more aggressive anti-HTN therapy or an ↑ use of RAAS inhibitors delays progression to ESRD in patients with ADPKD.
ACE-I slow the progression of renal dysfunction in KDz. On this basis, the use of ACE inhibitors as 1\textsuperscript{st} line agents to treat HTN in ADPKD has become standard clinical practice.

However no large RCT have shown their superiority over other anti-HTN agents in ADPKD.

The HALT- PKD trials were designed to have to ascertain the effect of intensive blockade of the RAAS and BP control on the progression of KDz in patients with an early or advanced stage of ADPKD.
HALT- Early PKD- STUDY A

AIM: To study the efficacy of ACE-I+ARB as compared to ACE-I alone on ΔTKV as well as standard vs low BP control on Δ TKV.

HYPOTHESIS:
- Low (95-110/60-75mmhg) vs std (120-130/70-80mmhg) BP will reduce the rate of Dz progression measured by annual Δ in TKV.
- Dual blockade of RASS with ACE-I (Lisinopril) ARB (Telmisartan) will reduce the rate of dz progression compared to ACE-I therapy alone.
METHODOLOGY

❑ STUDY DESIGN: Multi-center, double blinded, randomized placebo control trial.

❑ STUDY SITES: 7 centers in USA, including Mayo clinic, Cleveland clinic, KUMC etc.

❑ STUDY PATIENTS: ADPKD patients 15 to 49 yrs ADPKD with eGFR) of > 60ml/min.

❑ INCLUSION CRITERIA: i. Informed consent
ii. FMHx+dx of ADPKD based on Ravine's Criteria
iii. -ve FMHx, the dx based on ≥ 5 cysts bilaterally in the absence of findings suggestive of other cystic renal diseases
iv. Pts 15-49yrs with eGFR of > 60ml/min.
METHODOLOGY CON’TD

- **EXCLUSION CRITERIA:**
  1. Pregnancy
  2. Renal vasculaar Dz
  3. Diabetes
  4. Spot urine ALB-Cr ratio ≥ 0.5 +/or findings supportive of other Kidney Dz
  5. Hypersensitivity to ACE-I or ARBs
  6. Pts on immuno-suppressants
  7. Serous comorbid Dz with life expectancy < 2yrs
  8. Drug/alcohol dependence +/or any Psych Dz

- Pts were assigned in a 1:1 ratio to lisinopril + telmisartan or lisinopril + placebo. Randomization was performed with the use of permuted blocks. Also pts were assigned in a 1:1 ratio to a std BP (120/70 to 130/80 mm Hg) or a low BP (95/60 to 110/75 mm Hg).

- MRI was used determine TKV, LVM index, and RBF at baseline and at 24, 48, and 60 mnths.

- Drug dosages were adjusted to targets BP with home BP measures while plasma Cr and K+ monitored
Methodology - Randomization

1301 Patients were prescreened for eligibility

- 145 Were excluded owing to absence from prescreening

1156 Patients were assessed for eligibility

- 598 Were excluded
  - 523 Were eligible for a companion study
  - 43 Were excluded from both studies
  - 26 Did not meet inclusion criteria
  - 6 Declined to participate

558 Underwent randomization

- 284 Were assigned to standard-blood-pressure group
- 274 Were assigned to low-blood-pressure group
**Std BP**

- 140 Were assigned to receive lisinopril–telmisartan
- 140 Received intervention
  - 142 Did not receive intervention
    - 1 Had normal blood pressure
    - 1 Withdrawed from study at baseline

- 22 Were lost to follow-up
  - 1 Died
  - 7 Had modified consent to less than full participation at last visit
  - 95 Were receiving medication

- 139 Were included in the analysis
  - 1 Was excluded owing to lack of TKV measures

**Low BP**

- 141 Were assigned to receive lisinopril–placebo
- 140 Received intervention
  - 1 Did not receive intervention
    - 12 Had modified consent to less than full participation at last visit
    - 103 Were receiving medication

- 20 Were lost to follow-up
  - 109 Had full participation at last visit
  - 139 Were included in the analysis
    - 2 Were excluded owing to lack of TKV measures
STUDY OUTCOMES

❑ 1º OUTCOME : The percentage Δ in TKV over time
❑ 2º OUTCOMES:

✓ Slope of eGFR
✓ Urine albumin and aldosterone excretion
✓ L V mass index, Renal blood flow and renal vascular resistance, frequency of all cause and CVS hospitalization
✓ Quality of life, pain and PKD related symptoms
✓ Adverse effects of related study medications.
STATISTICAL ANALYSIS AND RESULTS

- All the analyses were based on the intention-to-treat principle.
- The 1\textsuperscript{st} outcome was analyzed using natural logarithms with linear mixed effects model.
- The eGFR was calculated using CKD Epid Collaboration equation with the serum Cr.
- Remaining 2\textsuperscript{nd} outcomes were analyzed with the use of generalized linear mixed models.
Table 1. Demographic, Clinical, and Laboratory Characteristics at Baseline, According to Study Group of the 2-by-2 Factorial Design Trial.*

<table>
<thead>
<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td>Age — yr</td>
<td>37.0±8.3</td>
<td>36.3±8.3</td>
<td>36.3±8.4</td>
<td>36.9±8.2</td>
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<tr>
<td>Male sex — no. (%)</td>
<td>141 (51.6)</td>
<td>142 (49.8)</td>
<td>143 (50.4)</td>
<td>140 (51.1)</td>
</tr>
<tr>
<td>Race — no. (%)†</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>255 (93.4)</td>
<td>262 (91.9)</td>
<td>258 (90.8)</td>
<td>259 (94.5)</td>
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<td>Black</td>
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<td>8 (2.8)</td>
<td>7 (2.5)</td>
<td>7 (2.6)</td>
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<tr>
<td>Other</td>
<td>10 (3.7)</td>
<td>17 (6.0)</td>
<td>18 (6.3)</td>
<td>9 (3.3)</td>
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<td>2 (0.7)</td>
<td>0</td>
<td>2 (0.7)</td>
<td>0</td>
</tr>
<tr>
<td>PKD genotype — no./total no. (%)‡</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PKD1</td>
<td>190/252 (75.4)</td>
<td>192/260 (73.8)</td>
<td>204/260 (78.5)</td>
<td>178/252 (70.6)</td>
</tr>
<tr>
<td>PKD2</td>
<td>42/252 (16.7)</td>
<td>42/260 (16.2)</td>
<td>34/260 (13.1)</td>
<td>50/252 (19.8)</td>
</tr>
<tr>
<td>No mutation detected</td>
<td>20/252 (7.9)</td>
<td>26/260 (10.0)</td>
<td>22/260 (8.5)</td>
<td>24/252 (9.5)</td>
</tr>
<tr>
<td>Body-mass index§</td>
<td>27.4±5.2</td>
<td>27.1±5.1</td>
<td>27.3±5.4</td>
<td>27.1±4.9</td>
</tr>
<tr>
<td>Estimated GFR — ml/min/1.73 m²¶</td>
<td>90.4±17.5</td>
<td>92.6±17.4</td>
<td>91.7±17.8</td>
<td>91.4±17.2</td>
</tr>
<tr>
<td>Urinary aldosterone — μg/24 hr</td>
<td>12.2±10.0</td>
<td>12.2±9.1</td>
<td>13.0±10.6</td>
<td>11.4±8.2</td>
</tr>
<tr>
<td>Urinary albumin — mg/24 hr</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>19.3</td>
<td>17.6</td>
<td>19.1</td>
<td>17.7</td>
</tr>
<tr>
<td>Interquartile range</td>
<td>12.7–35.2</td>
<td>11.7–30.6</td>
<td>12.8–31.8</td>
<td>11.7–33.3</td>
</tr>
<tr>
<td>Total kidney volume — ml</td>
<td>1264.6±786.2</td>
<td>1164.0±661.0</td>
<td>1240.6±747.1</td>
<td>1185.2±704.0</td>
</tr>
<tr>
<td>Renal blood flow — ml/min/1.73 m²</td>
<td>607.7±195.3</td>
<td>609.2±216.2</td>
<td>592.4±206.1</td>
<td>624.7±205.3</td>
</tr>
<tr>
<td>Left-ventricular-mass index — g/m²</td>
<td>64.1±13.2</td>
<td>63.7±12.9</td>
<td>63.8±13.8</td>
<td>63.9±12.2</td>
</tr>
</tbody>
</table>
- Pts the low-BP gp had a slower annual increase in TKV as compared with those in the std BP gp (5.6% vs 6.6%, P = 0.006)
- The TKV was ↑ed by 38.0% from baseline in the low-BP gp and by 44.2% from baseline in the std BP gp
The overall change in the eGFR was similar in the low-BP gp and the std BP gp (−2.9 and −3.0 ml/min per 1.73 m² per year, respectively; P = 0.55).
SECONDARY OUTCOMES CONT’D

Urinary Alb in the ↓ low-BP gp, as compared with an ↑ in the std BP gp (-3.7% vs 2.4% P<0.001). PANEL A

The low- BP gp had a greater reduction in the LV-mass index than the std BP gp (-1.17 vs -0.57 g /m² per year, P<0.001). PANEL B
Renal vascular resistance ↑ more in the std gp than in the low BP gp (P<0.001) PANEL D

Renal blood flow declined similarly in the two groups and there was no statistical significance
The frequencies of death, serious cardiovascular or renal events, hyperkalemia, acute kidney injury, and cancer did not differ significantly between the two groups.
# Adverse Events Rates in Std vs Low BP

<table>
<thead>
<tr>
<th>Event</th>
<th>STANDARD BP N= 284</th>
<th>Low BP N= 274</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean follow – up ( duration in yrs)</td>
<td>5.7</td>
<td>5.6</td>
</tr>
<tr>
<td>Acute Kidney Injury events, Participants (%)</td>
<td>4.6%</td>
<td>5.8%</td>
</tr>
<tr>
<td>Hyperkalaemia - any events, Participants (%)</td>
<td><strong>3.2%</strong></td>
<td>2.6%</td>
</tr>
<tr>
<td>Hospitalization</td>
<td>7.43</td>
<td>6.07</td>
</tr>
<tr>
<td>CVS related Hospitalization</td>
<td>0.80</td>
<td>0.59</td>
</tr>
<tr>
<td>Death – total events, participants (%)</td>
<td>0.7%</td>
<td>0.0%</td>
</tr>
</tbody>
</table>
DISCUSSION – HALT Early

- Rigorous BP control attenuated the annual rate of increase in TKV by 14.2% and was associated with reduced urinary Alb excretion.

- However Lisinopril+telmisartan Rxn did not show a benefit, as compared with Lisinopril alone, with regard to the change in TKV or eGFR.

- Patients < 30 yrs with the largest kidneys were more likely to benefit from rigorous BP control than were patients of similar age with smaller kidneys. Men, but not women, also had evidence of a benefit from low BP control.
DICUSSION CONT’D

- The overall rate of change in the eGFR was similar in the two BP gp in the long term (P = 0.05). A beneficial effect on cyst burden (rate of TKV growth) was not associated with an improvement in the slope of the eGFR.

- Whether a time lag between the therapeutic effect on TKV and stabilization of the eGFR occurs in patients with ADPKD is not yet known.

- In conclusion, the rate of TKV growth and the slope of the eGFR were not affected by dual blockade of the RAAS.
Aggressive BP control was safe in young, HTN patients with ADPKD and preserved kidney fxn.

This level of BP control, as compared with std BP control, was associated with a modest ↓ in TKV over time, without differences in the eGFR.

Improvement in markers of the 2º outcomes, including the LV-mass index and urinary Alb excretion, also suggests a benefit of aggressive BP control.
HALT- Late  PKD- STUDY B

AIM: To study the effects of ACE-I+ARB compared to ACE-I alone in the setting of std BP control (110-130/70-80 mm Hg) on the time to doubling of serum Cr, ESRD, or death in ADPKD pts with eGFR 25-60 ml/min.

HYPOTHESIS: Dual blockade of RASS with ACE + ARB will reduce the rate of dz progression compared to ACE-I therapy alone independent of std BP control a
METHODOLOGY

- **STUDY DESIGN:** Multi-center, double blinded, randomized placebo control trial

- **STUDY PATIENTS:** ADPKD patients 18 to 64 yrs with eGFR) of 25-60ml/min.

- **INCLUSION CRITERIA:**
  i. A diagnosis of ADPKD as described in Study A.
  ii. ADPKD pts 18-64 yr with eGFR 25-60ml/min.
  iv. Informed consent.

- **EXCLUSION CRITERIA:** Same as in STUDY A
METHODOLOGY - Randomization

1301 Patients were prescreened for eligibility

- 145 Were excluded owing to absence from prescreening

1156 Patients were assessed for eligibility

- 670 Were excluded
  - 590 Were eligible for a companion study
  - 43 Were not eligible for either study
  - 23 Did not meet inclusion criteria
  - 14 Declined to participate

486 Underwent randomization
244 Were assigned to receive lisinopril–telmisartan
243 Received lisinopril–telmisartan
 1 Did not receive lisinopril–telmisartan owing to randomization error

16 Were lost to follow-up
19 Had modified consent to less than full participation at last visit
208 Had full participation at last visit
187 Were receiving medication

243 Were included in analysis
 1 Was excluded from analysis owing to randomization error

242 Were assigned to receive lisinopril–placebo
242 Received lisinopril–placebo

15 Were lost to follow-up
 9 Had modified consent to less than full participation at last visit
218 Had full participation at last visit
204 Were receiving medication

242 Were included in analysis
STUDY OUTCOMES

❑ **1⁰ Composite outcome** - The time to death, ESRD (defined as the initiation of dialysis or preemptive transplantation), or a 50% ↓ from the baseline eGFR.

❑ **2⁰ Outcomes:**
  ✓ Slope of eGFR
  ✓ Urine albumin and aldosterone excretion
  ✓ Frequency of all cause and CVS hospitalization
  ✓ Quality of life, pain and PKD related symptoms
  ✓ Adverse effects of related study medications.

NB- LV mass index, RBF and renal vascular resistance not included in STUDY B
A Cox proportional-hazards model was fitted to model the hazard ratio during the analysis.

The eGFR was calculated using CKD Epid Collaboration equation with the serum Cr.

Safety outcomes were compared with the use of logistic regression.
### Table 1. Demographic, Clinical, and Laboratory Characteristics of the Participants at Baseline.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Lisinopril–Telmisartan (N = 244)</th>
<th>Lisinopril–Placebo (N = 242)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age — yr</td>
<td>48.6±8.5</td>
<td>48.9±8.1</td>
</tr>
<tr>
<td>Male sex — no. (%)</td>
<td>115 (47.1)</td>
<td>120 (49.6)</td>
</tr>
<tr>
<td>Race — no. (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>230 (94.3)</td>
<td>224 (92.6)</td>
</tr>
<tr>
<td>Black</td>
<td>5 (2.0)</td>
<td>7 (2.9)</td>
</tr>
<tr>
<td>Other</td>
<td>9 (3.7)</td>
<td>11 (4.5)</td>
</tr>
<tr>
<td>PKD genotype — no./total no. (%)♀</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>PKD1</strong></td>
<td>179/223 (80.3)</td>
<td>183/224 (81.7)</td>
</tr>
<tr>
<td><strong>PKD2</strong></td>
<td>30/223 (13.5)</td>
<td>30/224 (13.4)</td>
</tr>
<tr>
<td>No mutation detected</td>
<td>14/223 (6.3)</td>
<td>11/224 (4.9)</td>
</tr>
<tr>
<td>Body-mass index§</td>
<td>28.0±4.9</td>
<td>28.0±5.5</td>
</tr>
<tr>
<td>Serum creatinine — mg/dl¶</td>
<td>1.5±0.4</td>
<td>1.6±0.4</td>
</tr>
<tr>
<td>Estimated GFR — ml/min/1.73 m²∥</td>
<td>48.5±11.5</td>
<td>47.9±12.2</td>
</tr>
<tr>
<td>Urinary sodium — mmol/24 hr</td>
<td>177.4±78.2</td>
<td>178.2±84.0</td>
</tr>
<tr>
<td>Urinary aldosterone — μg/24 hr</td>
<td>10.2±8.4</td>
<td>9.1±5.8</td>
</tr>
<tr>
<td>Urinary albumin — mg/24 hr</td>
<td>29.7</td>
<td>28.1</td>
</tr>
<tr>
<td>Median</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Interquartile range</td>
<td>16.6–71.8</td>
<td>17.3–78.0</td>
</tr>
</tbody>
</table>
In most pts, adequate BP control was achieved with lisinopril+ placebo or Lisinopril+ telmisartan.

As compared with patients Rxn with lisinopril + telmisartan, those in the Lisinopril+placebo gp had a ↑SBP (Δ of 1.23mmhg P = 0.02) and MAP ( P = 0.02)
No significant $\Delta$ in the composite $1^\circ$ outcome of time to death, ESRD, or 50% ↓ from the baseline eGFR was detected between the 2 Rxn gps
SECONDARY OUTCOMES

- There were no significant Δs btw Lisinopril+ placebo gp and Lisinopril+ telmisartan gp in the rate of hospitz for any reason (13.75 vs 10.90 events /100 person-years) or hospitz for CVD (2.30 Vs 1.28 events / 100 person-year)

- No significant Δ btw Rxn grps were detected in the remaining 2° outcomes ,including frequency of symptoms related to ADPKD & QoL
<table>
<thead>
<tr>
<th>Outcome</th>
<th>Label</th>
<th>Estimate/OR</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CKD EPI eGFR (ml/min/1.73m2)</td>
<td>Lisinopril+ telmisartan vs Lisinopril+ placebo</td>
<td>0.0339</td>
<td>0.8585</td>
</tr>
<tr>
<td>Log Urine Albumin (mg/24 hrs)</td>
<td>Lisinopril+ telmisartan vs Lisinopril+ placebo</td>
<td>-0.0002</td>
<td>0.8808</td>
</tr>
<tr>
<td>Kidney Pain (Back or Flank Pain)</td>
<td>Lisinopril+ telmisartan vs Lisinopril+ placebo</td>
<td>1.00</td>
<td>0.6423</td>
</tr>
<tr>
<td>Urinary Tract Infection</td>
<td>Lisinopril+ telmisartan vs Lisinopril+ placebo</td>
<td>1.00</td>
<td>0.4375</td>
</tr>
<tr>
<td>Kidney stone(s)</td>
<td>Lisinopril+ telmisartan vs Lisinopril+ placebo</td>
<td>0.99</td>
<td>0.0647</td>
</tr>
</tbody>
</table>
This study showed that, as compared lisinopril + placebo grp, telmisartan + lisinopril resulted in slightly ↓ BP but did not reduce the incidence of 1⁰-outcome events, the rate of decline in the eGFR, or the incidence of other 2⁰outcomes.

Short-term studies of dual RAAS blockade in pts with CKD have shown greater ↓ in BP and albuminuria but more frequent episodes of K+mia and AKI, as compared with ACE-I alone.
DISCUSSION

- In contrast to the safety findings in these studies, episodes of K+mia and AKI in the HALT-PKD trial were infrequent and mild, probably owing to the younger age of the pts, the exclusion of pts with a high risk of diabetic or CVS complications, and the use of a dose-adjustment protocol for anti-HTN agents that was aimed at achieving a specific BP target.

- In conclusion, The HALT- LATE PKD Trial showed no significant Δ btw the study grps in the incidence of the composite 1o outcome, decline in eGFr or other 2o end points.
CONCLUSIONS FROM THESE 2 STUDIES

❑ In conclusion, these were 2 large trials showed that combination therapy with ACEi+ ARB did not confer additional renoprotection over ACE-I alone.
❑ The trials included pts at both ends of the spectrum of PKD from preserved kidney fxn to stage 3 CKD.
❑ Looks like dual RAAS takes another hit in its utility to treat kidney Dz.
❑ The interesting finding was in the Early PKD study showed that intensive BP control to ≤ 110/75mmhg provide benefit.
CONCLUSIONS FROM THESE 2 STUDIES

- They showed that TKV, LV mass and urine Alb excretion all appeared better with targeting a lower BP. However, they did not detect a Δ in overall eGFR.
- Whether or not these changes in TKV will impact long term kidney fxn is a question open for debate
- The changes in LV mass could also confer additional long term CVS benefit.

- These studies provide important insights into the treatment of PKD.
- The debate about how to translate changes in TKV to long term renal function benefit will no doubt continue.
THE RACE FOR CURE

Many interventional studies in human looking at the effects of various drugs on ADPKD disease progression.
Tolvaptan in Patients with Autosomal Dominant Polycystic Kidney Disease

Vicente E. Torres, M.D., Ph.D., Arlene B. Chapman, M.D., Olivier Devuyst, M.D., Ph.D., Ron T. Gansevoort, M.D., Ph.D., Jared J. Grantham, M.D., Eiji Higashihara, M.D., Ph.D., Ronald D. Perrone, M.D., Holly B. Krasa, M.S., John Ouyang, Ph.D., and Frank S. Czerwiec, M.D., Ph.D., for the TEMPO 3:4 Trial Investigators*

RESULTS

Over a 3-year period, the increase in total kidney volume in the tolvaptan group was 2.8% per year (95% confidence interval [CI], 2.5 to 3.1), versus 5.5% per year in the placebo group (95% CI, 5.1 to 6.0; P<0.001). The composite end point favored tolvaptan over placebo (44 vs. 50 events per 100 follow-up-years, P=0.01), with lower rates of worsening kidney function (2 vs. 5 events per 100 person-years of follow-up, P<0.001) and kidney pain (5 vs. 7 events per 100 person-years of follow-up, P=0.007). Tolvaptan was associated with a slower decline in kidney function (reciprocal of the serum creatinine level, −2.61 [mg per milliliter]−1 per year vs. −3.81 [mg per milliliter]−1 per year; P<0.001). There were fewer ADPKD-related adverse events in the tolvaptan group but more events related to aquarexis (excretion of electrolyte-free water) and hepatic adverse events unrelated to ADPKD, contributing to a higher discontinuation rate (23%, vs. 14% in the placebo group).
Are Prevention of Decline in Renal Function and Cardiovascular Complications Interconnected in ADPKD?

Tevfik Ecder, M.D.
Istanbul School of Medicine
Division of Nephrology
High Blood Pressure is Significantly Associated with End Organ Damage in Patients with ADPKD


Controversies Conference on ADPKD | January 17-19, 2014 | Edinburgh, United Kingdom
Diuretics versus ACE Inhibitors in ADPKD

Annual Loss of Creatinine Clearance

Diuretic Group (n=14)

ACEI Group (n=19)

P < 0.0001

Proteinuria

ml/min/1.73m²

P < 0.05

mg/day

Baseline Year 5

Diuretic Group (n=14)

ACEI Group (n=19)


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A BP goal of less than 120/80 mm Hg and the use of an ACEI should be recommended for patients with ADPKD who have hypertension and LVH.
END OF PRESENTATION

QUESTIONS???

ASANTE SANA