Hypersensitivity (e.g., anaphylaxis, rash) to JYNARQUE

Unable to sense or respond to thirst

With uncorrected abnormal blood sodium concentrations

Taking strong CYP3A inhibitors

Because of the risks of serious liver injury, JYNARQUE is

IMPORTANT SAFETY INFORMATION:

or any component of the product

uncomplicated polycystic liver disease

serious hepatotoxicity

hepatic injury can mitigate, but not eliminate, the risk of

transplantation has been reported

change the course of their disease

For your patients at risk for rapidly progressing ADPKD

to see how JYNARQUE may help

Concomitant use of JYNARQUE

Inhibitors of CYP3A:

within the normal range.

hypotension because they may signal dehydration. Ensure

and night if awake. Monitor for weight loss, tachycardia and

4 weeks after initiation, then monthly for 18 months and every

and bilirubin prior to initiating JYNARQUE, at 2 weeks and

abnormalities or signs or symptoms of liver injury (such as

ADPKD experience. Discontinuation in response to laboratory

Serious Liver Injury:

• Uncorrected urinary outflow obstruction

•   V2-Receptor Agonist:

•  Strong CYP3A Inducers:

Data only included those patients who remained in the study for 3 years; effect in those who discontinued is unknown.

In years 4 and 5 during the TEMPO 3:4 extension trial, both groups received JYNARQUE and the difference between the groups in TKV was not maintained.

Ravine criteria defined as at least 2 unilateral or bilateral kidney cysts in at-risk individuals between 15 and 30 years of age; 2 cysts in each kidney in individuals between 30 and 59 years of age, and at least 4 cysts in each kidney in individuals older than 60 years of age.3

(e.g., ketoconazole, itraconazole, lipovinavir/ritonavir, indinavir/ritonavir, and conivaptan) increases tolvaptan exposure. Use with strong CYP3A inhibitors is contraindicated; dose reduction of JYNARQUE is recommended for patients taking moderate CYP3A inhibitors. Patients should avoid grapefruit juice beverages while taking JYNARQUE

Adverse Reactions: Most common observed adverse reactions with JYNARQUE (incidence >10% and at least twice that for placebo) were thirst, polyuria, nocturia, pollakiuria, and polydipsia.


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CONTINUED ON PAGE 26

Temperatures:

Converting:

Scale:

1” = 1”

CMYK: Cyan, Magenta, Yellow, Black

Colors:

Sizing:

PDFx1A

10US22EBP0201

OTSUKA JYNARQUE HCP

Hypertension

JYNARQUE® (tolvaptan)

has been proven effective in the 2 largest clinical trials of over 2800 patients with ADPKD across CKD stages 1-4

The difference in TKV between treatment groups was most prominent within the first year, at the earliest assessment; the difference was minimal in years 2 and 3. JYNARQUE had little effect on kidney size beyond what accrued during the first year of treatment.6

Study design: TEMPO 3:4 was a double-blind, placebo–controlled randomized trial of 1445 patients with ADPKD. The inclusion criteria were: 18 to 50 years of age, early rapidly progressing ADPKD (meeting modified Ravine criteria);7 TKV ≥750 mL; creatinine clearance ≥60 mL/min. Patients were treated for up to 3 years. The primary endpoint was annual rate of change in the total kidney volume.4

Study design: REPRISE was a double-blind, placebo–controlled randomized withdrawal trial of 1370 patients with ADPKD. The inclusion criteria were: CKD with an eGFR between 25 and 65 mL/min/1.73 m² if younger than age 56; or eGFR between 25 and 44 mL/min/1.73 m² if age 56-65. Subjects were to be treated for 12 months; after completion of treatment, patients entered a 3-week follow-up period to assess renal function. The primary endpoint was the treatment difference in the change of eGFR from pre-treatment baseline to post-treatment follow-up, annualized by dividing each subject’s treatment duration.

49% reduction

total kidney volume vs placebo at the end of 3 years

(P=0.001; month 36 treatment effect:

-9.2%)

35% reduction

drop in decline of kidney function vs placebo

(treatment effect: 1.3 mL/min/1.73 m²/year; 95% CI: 0.86 to 1.68; P=0.0001)

REPRISE Trial — A double-blind, placebo–controlled randomized withdrawal trial of 1370 patients with ADPKD. The inclusion criteria were: CKD with an eGFR between 25 and 65 mL/min/1.73 m² if younger than age 56; or eGFR between 25 and 44 mL/min/1.73 m² if age 56-65. Subjects were to be treated for 12 months; after completion of treatment, patients entered a 3-week follow-up period to assess renal function. The primary endpoint was the treatment difference in the change of eGFR from pre-treatment baseline to post-treatment follow-up, annualized by dividing each subject’s treatment duration.

Most common observed adverse reactions with JYNARQUE (incidence >10% and at least twice that for placebo) were thirst, polyuria, nocturia, pollakiuria and polydipsia.
**Findings**

Anti-CD38 Shows Safety in Antibody-Mediated Rejection

Continued from page 25

experienced mild to moderate infusion reactions. Serious adverse events, primarily infection-related, occurred in one patient with falcetam versus four patients with placebo. Crallos loss occurred in one patient in the placebo group; there were no deaths in either group.

Renal biopsy performed at 24 weeks showed resolution of morphologic antibody-mediated rejection in 82% of patients (9 of 11) assigned to falcetam versus 20% (2 of 10) in the placebo group. Other efficacy outcomes also favored falcetam, including a lower rate of serious infection-related, median score of 0 versus 25; a molecular score indicating probability of antibody-mediated rejection, 0.17 versus 0.77; and donor-derived cell-free DNA level, 0.31% versus 0.82%.

As for antibody-mediated rejection occurred in three of the nine patients who responded to falcetam. Recurrence was associated with rising rejection-related molecular scores and natural killer cell burden.

CD38 is a promising target for depletion of plasma cells producing donospecific anti-

<table>
<thead>
<tr>
<th>Table 1: TEMPO 2, Treatment-Directed Advances in 23% of JYNARQUE Treated Subjects with Risk Difference 1.5% (Temple Bron 2018)</th>
</tr>
</thead>
</table>
| **JYNARQUE** (tolvaptan) for uncontrolled polyuria and nocturia. **See full prescribing information for JYNARQUE.**

**MILD STRESSING KNOWNHEHE**

<table>
<thead>
<tr>
<th><strong>JYNARQUE</strong></th>
<th><strong>Placebo</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Number of Subjects</strong></td>
<td>250</td>
</tr>
<tr>
<td><strong>Proportion (</strong>)**</td>
<td>0.515</td>
</tr>
<tr>
<td><strong>Normalized Rate (</strong>)**</td>
<td>0.317</td>
</tr>
<tr>
<td><strong>3-Weeks</strong></td>
<td>0.20</td>
</tr>
<tr>
<td><strong>4-Weeks</strong></td>
<td>0.19</td>
</tr>
<tr>
<td><strong>5-Weeks</strong></td>
<td>0.18</td>
</tr>
<tr>
<td><strong>6-Weeks</strong></td>
<td>0.17</td>
</tr>
<tr>
<td><strong>7-Weeks</strong></td>
<td>0.16</td>
</tr>
<tr>
<td><strong>8-Weeks</strong></td>
<td>0.15</td>
</tr>
<tr>
<td><strong>9-Weeks</strong></td>
<td>0.14</td>
</tr>
<tr>
<td><strong>10-Weeks</strong></td>
<td>0.13</td>
</tr>
</tbody>
</table>

**ABORTIVE REACTIONS**

Clinical Trials Experience Clinical trials of a drug are conducted in controlled clinical trials under well-defined conditions. The results observed in clinical studies may not predict the behavior of the drug under different conditions. Patients and their caregivers should be advised to report any adverse reactions to the prescribing healthcare professional.

Adverse events that were not considered serious and resulted in treatment discontinuation were observed in 0.5% of patients (5 of 1048) assigned to JYNARQUE compared to 0.3% (3 of 1048) assigned to placebo. These events included headache, dizziness, and fatigue.

**CLOSING REMARKS**

**No Decrease in CKD Admissions With “ICD-Pieces”**

A primary care intervention to promote guideline-based care for patients with the "kidney dysfunction triplet" does not lead to reduced rates of hospitalization due to chronic kidney disease (CKD), reports a pragmatic trial in *The New England Journal of Medicine.*

The cluster-randomized Improving Chronic Disease Management with Pieces (ICD-Pieces) trial evaluated a multidisciplinary intervention to promote guideline-directed care for CKD.

The intervention included a personalized algorithm, based on electronic health record data, to identify patients with the trial of CKD, type 2 diabetes, and hypertension, as well as practice facilitators who assisted primary care physicians in implementing evidence-based interventions.

A total of 11,182 patients at 141 clinics in four large health systems were assigned to intervention or usual-care groups. All cause hospitalization at 1 year was compared between groups, along with secondary outcomes. Patient characteristics were similar between intervention and usual-care groups.

Rates of hospitalization for any cause were not significantly different between groups: 20.7% for patients assigned to the ICD-Pieces intervention and 21.1% in the usual-care group. Secondary outcomes were similar as well, including emergency department visits, hospital readmissions, cardiovascular events, dialysis, and death from any cause.

The ICD-Pieces intervention was associated with a higher rate of acute kidney injury: 12.7% versus 11.3%. Other adverse events were comparable between groups.

Patients with the kidney dysfunction triplet are at high risk for cardiovascular events and kidney failure. Although several guideline-directed therapies targeting these patients have been developed, few studies have evaluated the effects on morbidity and mortality.


**Notes**


2. Benjamin Lee/Sarah Potter.

3. Tolvaptan (N=961) Placebo (N=483)

4. *Hyperuricemia 37 3.9 1.6 9 1.9 0.7

5. *Thirst includes polydipsia and thirst

6. *All members of a subject’s family included in another subject’s family

7. *Randomized study included patients with eGFRCKD-Epi 25 to 65 mL/min/1.73m2.

8. *Patients assigned to the intervention were more likely to receive treatment than those in the usual-care group.

9. *The investigators conclude. The study

10. *Recurrence was associated with rising rejection-related molecular scores and natural killer cell burden.

11. *Telehealth has the potential to improve access to care for patients with diabetes, chronic kidney disease, and other chronic conditions. A pragmatic trial of telehealth for patients with diabetes and CKD showed that telehealth was associated with improved diabetes control, reduced hospitalizations, and reduced healthcare costs. (Mayer KA, et al. *N Engl J Med* 2024; 390:1196–1206, doi: 10.1056/NEJMoas2400763)."