Identify appropriate patients with ADPKD for JYNARQUE® (tolvaptan) in your practice, similar to Patrick

Patrick, 44—Stage 3 CKD

When Patrick passed a large kidney stone, his PCP, knowing his family history of ADPKD and treated hypertension, referred him to a nephrologist

Patrick manages a grocery store and enjoys spending time outdoors with his wife and their 2 teenagers.

Patient image and patient case are fictional.

Physical Findings and Labs:

- **Age:** 44
- **Height:** 6'0"
- **Weight:** 190 lbs
- **BMI:** 25.8
- **BP:** 135/82 mm/Hg before treatment, now controlled on an ARB therapy
- **Creatinine:** 2.6 mg/dL
- **Current eGFR:** 30 mL/min/1.73 m^2
- **htTKV:** 3090 mL/m
- **Mayo Imaging Classification:** 1E (high risk) **Click here for TKV calculation.**

Medical History:

- Diagnosis of ADPKD
- Hypertension
- Kidney stones

Family History:

- Family history of ADPKD (mother and brother)
- Mother reached early ESKD at age 51

ADPKD=autosomal dominant polycystic kidney disease; ARB=angiotensin II receptor blockers; BMI=body mass index; BP=blood pressure; CKD=chronic kidney disease; eGFR=estimated glomerular filtration rate; ESKD=end-stage kidney disease; htTKV=height-adjusted total kidney volume; PCP=primary care physician; TKV=total kidney volume.

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INDICATION:

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WARNING: RISK OF SERIOUS LIVER INJURY

- **JYNARQUE® (tolvaptan) can cause serious and potentially fatal liver injury. Acute liver failure requiring liver transplantation has been reported**
- **Measure transaminases (ALT, AST) and bilirubin before initiating treatment, at 2 weeks and 4 weeks after initiation, then monthly for the first 18 months and every 3 months thereafter. Prompt action in response to laboratory abnormalities, signs, or symptoms indicative of hepatic injury can mitigate, but not eliminate, the risk of serious hepatotoxicity**
- **Because of the risks of serious liver injury, JYNARQUE is available only through a Risk Evaluation and Mitigation Strategy program called the JYNARQUE REMS Program**

Please see **IMPORTANT SAFETY INFORMATION** on pages 5 and 6.

Calculating Patrick's TKV

Patrick's TKV can be calculated using measurements of kidney length, width, and depth with the ellipsoid equation.[2,3]

Left kidney **Right kidney**

π/6 • (L x W x D) + π/6 • (L x W x D) = TKV (mL)

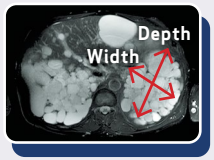
Height-adjusted (ht) TKV

Patrick's htTKV can be used to estimate his future kidney function decline.

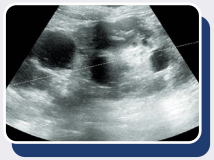
TKV/height (m) = htTKV (mL/m)

TKV: 5562 mL
Height: 1.8 m
Patrick's htTKV: 3090 mL/m

Units for kidney dimensions are in mm. To get kidney volume in mL, multiply by 0.001.



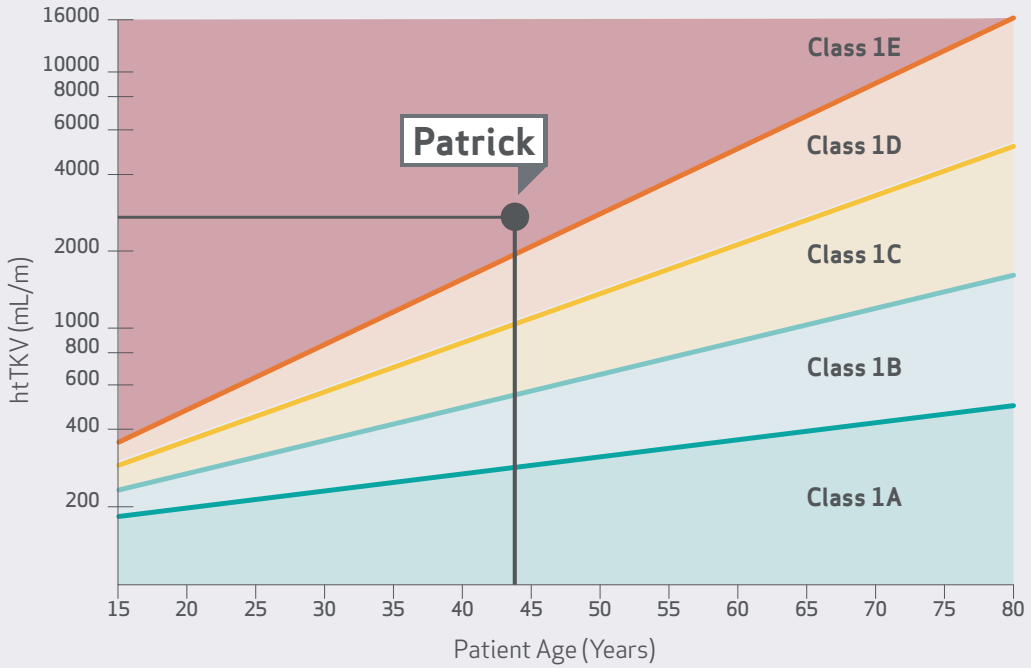
MRI/CT



Ultrasound

CT=computed tomography; D=depth; L=length; MRI=magnetic resonance imaging; W=width.

Plotting htTKV and age predicts the change in eGFR over time in patients with typical ADPKD[1*]



A patient's ADPKD imaging classification can help estimate their disease progression

Class	Estimated kidney growth rate: yearly percentage increase	Estimated slope of change in eGFR
1E	>6.0%	-4.78

Patrick is Mayo Classification 1E

*Bilateral and diffuse distribution, with mild, moderate, or severe replacement of kidney tissue by cysts, where all cysts contribute similarly to TKV.[1]

Republished with permission of the American Society of Nephrology, from Imaging classification of autosomal polycystic kidney disease: a simple model for selecting patients for clinical trials. *J Am Soc Nephrol*. 2015;26(1):160-172.

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Assessing ADPKD progression and treatment consideration

- Due to Patrick's kidney stones and family history of ADPKD, his PCP promptly took a multidisciplinary approach and referred Patrick to a nephrologist, who ordered an ultrasound
  - — Though more extensive research is needed, based on the available data, it's also important to consider that other conditions more common in Black patients, such as hypertension or diabetes, have the potential to mask an ADPKD diagnosis[4]
- After the nephrologist ordered the ultrasound, Patrick's ADPKD diagnosis was confirmed
- Knowing the rate of ADPKD progression can vary within the same family, as well as Patrick's family history of early ESKD, the nephrologist then measured his TKV because **CRISP data** show that a **one-time measurement of TKV** can help assess the rate of progression and **predict the rate of future kidney function decline**[5*]
- Even though ADPKD impacts all races, research shows that patient outcomes such as early diagnosis and treatment of ADPKD, may vary by race and ethnicity attributed to social determinants of health (SDOH)
  - — In a nearly 10-year (2004-2013) retrospective cohort study that included 23,647 patients with ADPKD, Black patients with ADPKD reached ESKD approximately 1.5 years faster (54.4 ± 13 years of age) than White patients with ADPKD (55.9 ± 12.8 years of age)[4]
- Given the Mayo Imaging Classification of 1E, Patrick's nephrologist determined he was at **high risk for rapidly progressing ADPKD**[1] and recommended he start treatment with JYNARQUE® (tolvaptan)

*CRISP is an NIH-funded, 14-year observational study (N=241) of adult ADPKD patients. The primary goal was to determine the extent to which TKV forecasts the development of renal insufficiency in ADPKD.[5,6]
CRISP=Consortium for Radiologic Imaging Studies of Polycystic Kidney Disease; NIH=National Institutes of Health.

SELECT IMPORTANT SAFETY INFORMATION:

CONTRAINDICATIONS:

- History, signs or symptoms of significant liver impairment or injury. This contraindication does not apply to uncomplicated polycystic liver disease
- Taking strong CYP3A inhibitors
- With uncorrected abnormal blood sodium concentrations
- Unable to sense or respond to thirst
- Hypovolemia
- Hypersensitivity (e.g., anaphylaxis, rash) to JYNARQUE or any component of the product
- Uncorrected urinary outflow obstruction
- Anuria

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Starting JYNARQUE® (tolvaptan) in patients similar to Patrick who have several risk factors associated with risk of rapid progression

- Patrick's nephrologist **explained the benefits and risks** associated with treatment, including the risk of serious liver injury and the requirements of the REMS program, and he also reviewed the medication guide prior to starting treatment
- Patrick's nephrologist also urged him to talk to his family about ADPKD, since he has a 50% chance of passing the disease on to each of his children[7,8]
- Concerned with his family history and risk of rapidly progressing ADPKD, Patrick chose to go on JYNARQUE after his nephrologist explained that JYNARQUE has the ability to **slow the progression of ADPKD**[9]
  - The REPRISE trial included 48 patients who are Black, like Patrick
  - 75% of the patients in the REPRISE trial had CKD stage 3, like Patrick
- Patrick's nephrologist advised him to take JYNARQUE **twice daily**, the first dose upon waking and the second dose 8 hours later
  - He explained that JYNARQUE may cause aquaretic side effects and advised him to **drink more water to avoid thirst and dehydration**
- Patrick contacted an Otsuka Patient Experience Liaison (PEL), who provided access education and support over the phone to help him receive his JYNARQUE prescription*
- Based on Patrick's commercial insurance coverage, his specialty pharmacy determined he was eligible for **$10/month copay support**†

*PELs cannot provide product counseling, give medical advice, or complete any paperwork on behalf of the physician's office or the patient.
†Assumes one 28-day supply prescription per month. If more than one prescription is filled in a calendar month, patients may pay more than $10 in that month. Other terms and conditions may apply.

PEL=patient experience liaison; REMS=Risk Evaluation and Mitigation Strategy; REPRISE=Replicating Evidence of Preserved Renal Function: an Investigation of Tolvaptan Safety and Efficacy.

SELECT IMPORTANT SAFETY INFORMATION:

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.

References: 1. Irazabal MV, Rangel LJ, Bergstralh EJ, et al. Imaging classification of autosomal dominant polycystic kidney disease: a simple model for selecting patients for clinical trials. *J Am Soc Nephrol*. 2015;26(1):160-172. **2.** Magistroni R, Corsi C, Martí T, Torra R. A review of the imaging techniques for measuring kidney and cyst volume in establishing autosomal dominant polycystic kidney disease progression. *Am J Nephrol*. 2018;48:67-78. **3.** Chapman AB, Bost JE, Torres VE, et al. Kidney volume and functional outcomes in autosomal dominant polycystic kidney disease. *Clin J Am Soc Nephrol*. 2012;7(3):479-486. **4.** Murphy EL, Dai F, Blount KL, et al. Revisiting racial differences in ESRD due to ADPKD in the United States. *BMC Nephrol*. 2019;20(1):55. **5.** Yu ASL, Shen C, Landsittel DP, et al; for the Consortium for Radiologic Imaging Studies of Polycystic Kidney Disease (CRISP). Long-term trajectory of kidney function in autosomal-dominant polycystic kidney disease. *Kidney Int*. 2019;95(5):1253-1261. **6.** Chapman AB, Guay-Woodford LM, Grantham JJ, et al. Renal structure in early autosomal-dominant polycystic kidney disease (ADPKD): The Consortium for Radiologic Imaging Studies of Polycystic Kidney Disease (CRISP) cohort. *Kidney Int*. 2003;64(3):1035-1045. **7.** Ness B, Stovall K. Current recommendations for treating autosomal dominant polycystic kidney disease. *JAAPA*. 2016;29(12):24-28. **8.** Chapman AB. Autosomal dominant polycystic kidney disease: time for a change? *J Am Soc Nephrol*. 2007;18:1399–1407. **9.** Torres VE, Chapman AB, Devuyst O, et al; for the REPRISE Trial Investigators. Tolvaptan in later-stage autosomal dominant polycystic kidney disease. *N Engl J Med*. 2017;377(20):1930-1942. **10.** Gansevoort RT, Arici M, Benzing T, et al. Recommendations for the use of tolvaptan in autosomal dominant polycystic kidney disease: a position statement on behalf of the ERA-EDTA Working Groups on Inherited Kidney Disorders and European Renal Best Practice. *Nephrol Dial Transplant*. 2016;31(3):337-348. **11**. Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. *Kidney Intern Suppl*. 2013;3(1):1-150.

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INDICATION and IMPORTANT SAFETY INFORMATION for JYNARQUE® (tolvaptan)

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- **JYNARQUE® (tolvaptan) can cause serious and potentially fatal liver injury. Acute liver failure requiring liver transplantation has been reported**
- **Measure transaminases (ALT, AST) and bilirubin before initiating treatment, at 2 weeks and 4 weeks after initiation, then monthly for the first 18 months and every 3 months thereafter. Prompt action in response to laboratory abnormalities, signs, or symptoms indicative of hepatic injury can mitigate, but not eliminate, the risk of serious hepatotoxicity**
- **Because of the risks of serious liver injury, JYNARQUE is available only through a Risk Evaluation and Mitigation Strategy program called the JYNARQUE REMS Program**

CONTRAINDICATIONS:

- History, signs or symptoms of significant liver impairment or injury. This contraindication does not apply to uncomplicated polycystic liver disease
- Taking strong CYP3A inhibitors
- With uncorrected abnormal blood sodium concentrations
- Unable to sense or respond to thirst
- Hypovolemia
- Hypersensitivity (e.g., anaphylaxis, rash) to JYNARQUE or any component of the product
- Uncorrected urinary outflow obstruction
- Anuria

Serious Liver Injury: JYNARQUE can cause serious and potentially fatal liver injury. Acute liver failure requiring liver transplantation has been reported in the post-marketing ADPKD experience. Discontinuation in response to laboratory abnormalities or signs or symptoms of liver injury (such as fatigue, anorexia, nausea, right upper abdominal discomfort, vomiting, fever, rash, pruritus, icterus, dark urine or jaundice) can reduce the risk of severe hepatotoxicity. To reduce the risk of significant or irreversible liver injury, assess ALT, AST and bilirubin prior to initiating JYNARQUE, at 2 weeks and 4 weeks after initiation, then monthly for 18 months and every 3 months thereafter.

Please see **FULL PRESCRIBING INFORMATION**, including **BOXED WARNING**.

(continued on next page)

IMPORTANT SAFETY INFORMATION for JYNARQUE® (tolvaptan) (cont'd)

Hypernatremia, Dehydration and Hypovolemia: JYNARQUE therapy increases free water clearance which can lead to dehydration, hypovolemia and hypernatremia. Instruct patients to drink water when thirsty, and throughout the day and night if awake. Monitor for weight loss, tachycardia and hypotension because they may signal dehydration. Ensure abnormalities in sodium concentrations are corrected before initiating therapy. If serum sodium increases above normal or the patient becomes hypovolemic or dehydrated and fluid intake cannot be increased, suspend JYNARQUE until serum sodium, hydration status and volume status parameters are within the normal range.

Inhibitors of CYP3A: Concomitant use of JYNARQUE with drugs that are moderate or strong CYP3A inhibitors (e.g., ketoconazole, itraconazole, lopinavir/ritonavir, indinavir/ritonavir, 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.

Other Drug Interactions:

- **Strong CYP3A Inducers:** Co-administration with strong CYP3A inducers reduces exposure to JYNARQUE. Avoid concomitant use of JYNARQUE with strong CYP3A inducers
- **V_2-Receptor Agonist:** Tolvaptan interferes with the V_2-agonist activity of desmopressin (dDAVP). Avoid concomitant use of JYNARQUE with a V_2-agonist

Pregnancy and Lactation: Based on animal data, JYNARQUE may cause fetal harm. In general, JYNARQUE should be discontinued during pregnancy. Advise women not to breastfeed during treatment with JYNARQUE.

To report SUSPECTED ADVERSE REACTIONS, contact Otsuka America Pharmaceutical, Inc. at 1-800-438-9927 or FDA at 1-800-FDA-1088 (www.fda.gov/medwatch).

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Talk to your sales representative or visit JYNARQUEhcp.com to learn more about other appropriate patient types for JYNARQUE® (tolvaptan)

Bob, 53—Stage 3A CKD

His rapidly declining eGFR is evidence of rapidly progressing ADPKD[10,11]

Tim, 31—Stage 2 CKD

Mayo Classification of 1C (high risk) and TKV greater than expected for his age point to risk of rapidly progressing ADPKD[1]

Julia, 40—Stage 2 CKD

Multiple risk factors as well as her concerning kidney length are signs of risk of rapidly progressing ADPKD[2,10]

Patient images and patient cases are fictional.

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