

1/ Hey [#NephTwitter](#)! Welcome to a [#tweetorial](#) [#xtorial](#) brought to you by

[@KIReports](#)

2/ ★ Our author is Agavriiloaei Bogdan [@AgavriiloaeiB](#) nephrologist from Romania. Our topic: Stopping ADPKD progression

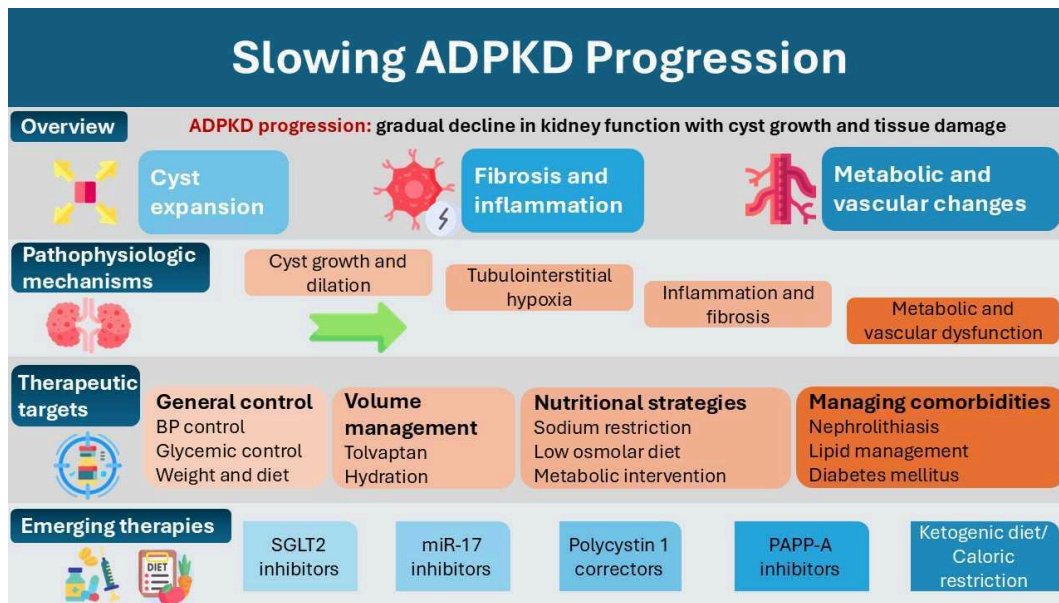


[#MedTwitter](#) [#nephtwitter](#) [@ISNkidneycare](#) [#XTwitter](#)

3/ 👍 There are no conflicts of interest. Please also check out [#KIReportsCommunity](#) educational [#blogposts](#) at <https://kireportscommunity.org>. FOLLOW US at [@KIReports](#)

for more expert [#MedEd](#) in [#kidneydisease](#). [#FOAMed](#) [@MedTweeterials](#)

4/ 📍 Our [#Tweeterial](#) is about Stopping progression in ADPKD and VA by [@KajareeG](#)



5/Intro

▶ ADPKD is the most common genetic renal disorder with an estimated prevalence between 1:1000 and 1:2500.

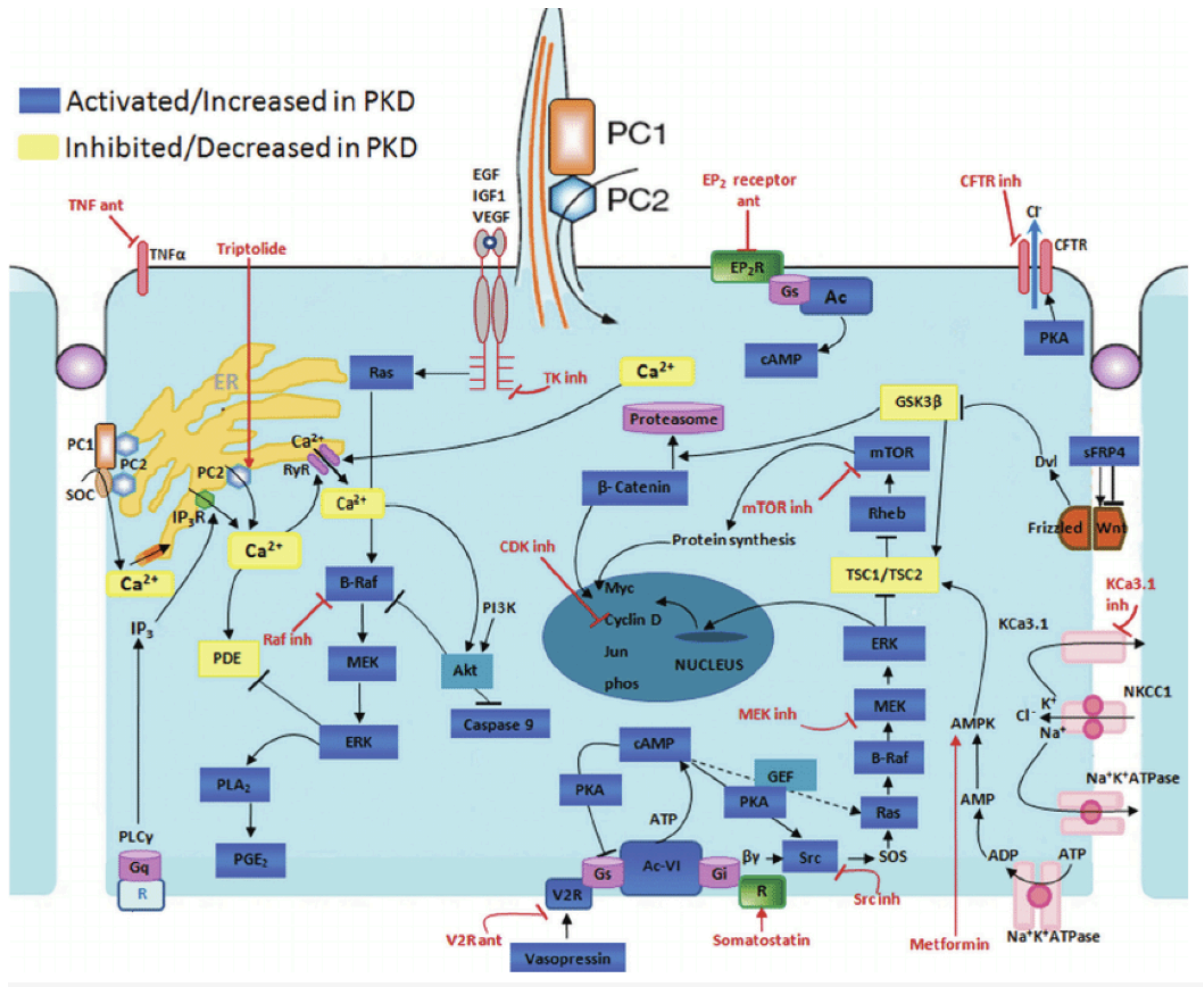
▶ The condition is primarily caused by mutations in two genes: PKD1 and PKD2

<https://pubmed.ncbi.nlm.nih.gov/26530876/>

6/ADPKD progression

✓ The hallmark manifestation of ADPKD is the progressive development of renal cysts.

✓ Cyst formation involves dysregulation of multiple intracellular signaling pathways.



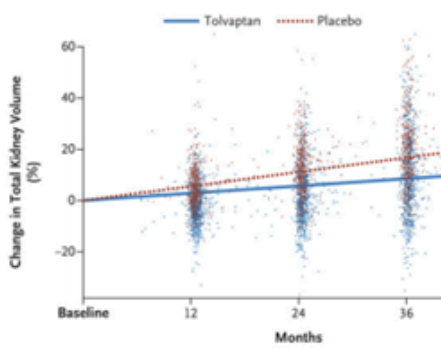
https://www.mdpi.com/ijms/ijms-23-03317/article_deploy/html/images/ijms-23-03317-g001.png

7/Interventions to slow ADPKD progression

Tolvaptan – V2 receptor antagonist – is the only treatment approved by KDIGO guidelines to slow progression in ADPKD

Two main studies that show the impact of Tolvaptan: TEMPO 3:4 and REPRIS

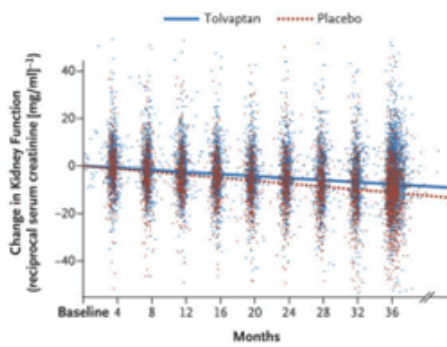
A Total Kidney Volume



B Treatment Effect for Total Kidney Volume

Subgroup	Absolute Treatment Effect	Relative Treatment Effect		Annual Slope	P Value
	Difference in annual slope (%/yr)	%	Tolvaptan %/yr		
Sex					
Male		37.3	4.15	6.62	<0.001
Female		71.1	1.24	4.29	<0.001
Age					
<35 yr		28.0	4.37	6.06	0.02
≥35 yr		58.2	2.23	5.34	<0.001
Hypertension					
Yes		50.5	3.01	6.09	<0.001
No		51.2	1.62	3.32	0.008
Estimated creatinine clearance					
<80 ml/min		57.2	2.27	5.32	<0.001
≥80 ml/min		47.5	2.92	5.56	<0.001
Total kidney volume					
<1500 ml		48.8	2.24	4.37	<0.001
≥1500 ml		51.1	3.29	6.74	<0.001
All patients		49.2	2.80	5.51	<0.001

C Kidney Function



D Treatment Effect for Kidney Function

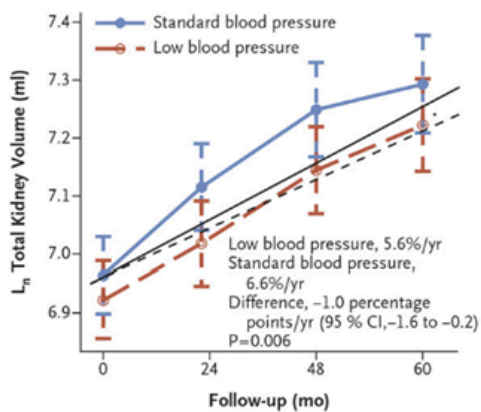
Subgroup	Absolute Treatment Effect	Relative Treatment Effect		Annual Slope	P Value
	Difference in annual slope ([mg/ml] ⁻¹)	%	Tolvaptan (mg/ml) ⁻¹		
Sex					
Male		32.1	-2.37	-3.49	<0.001
Female		30.7	-2.85	-4.11	0.02
Age					
<35 yr		26.5	-1.93	-2.62	0.19
≥35 yr		30.6	-2.84	-4.09	<0.001
Hypertension					
Yes		35.0	-2.72	-4.19	<0.001
No		9.6	-2.09	-2.31	0.69
Estimated creatinine clearance					
<80 ml/min		32.0	-3.69	-5.43	0.01
≥80 ml/min		29.7	-2.21	-3.14	0.001
Total kidney volume					
<1500 ml		21.7	-1.97	-2.52	0.10
≥1500 ml		36.6	-3.24	-5.11	<0.001
All patients		31.6	-2.61	-3.81	<0.001

<https://www.nejm.org/doi/full/10.1056/NEJMoa1205511>

8/Interventions to slow ADPKD progression

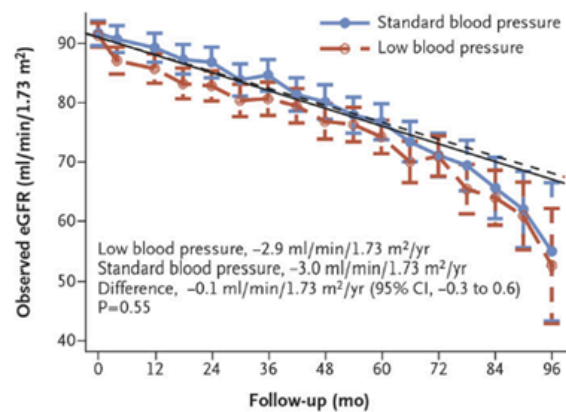
- Blood pressure control is the cornerstone of ADPKD progression
- HALT-PKD study A and HALT-PKD study B are the most important studies in blood pressure control

A Changes in Total Kidney Volume over Time



No. of Patients	0	24	48	60
Standard blood pressure	280	247	228	224
Low blood pressure	271	236	216	213

B Changes in eGFR over Time



No. of Patients	0	12	24	36	48	60	72	84	96
Standard blood pressure	283	251	251	239	232	226	159	90	15
Low blood pressure	274	243	239	224	217	202	137	81	9

<https://www.nejm.org/doi/full/10.1056/NEJMoa1402685>

9/Interventions to slow ADPKD progression

💧 Evidence on increased water intake in ADPKD remains controversial, as randomized trials have not shown meaningful effects on TKV growth or eGFR decline.

➡ The KDIGO 2025 guideline does not recommend specific dietary measures, instead supporting a balanced diet similar to that advised for CKD patients.

10/managing comorbidities

✅ Metabolic comorbidities may influence CKD progression in ADPKD, making their management clinically important.

✅ Diabetes is a key factor associated with faster renal decline, highlighting the need for strict glycemc control. <https://pmc.ncbi.nlm.nih.gov/articles/PMC3398061/>

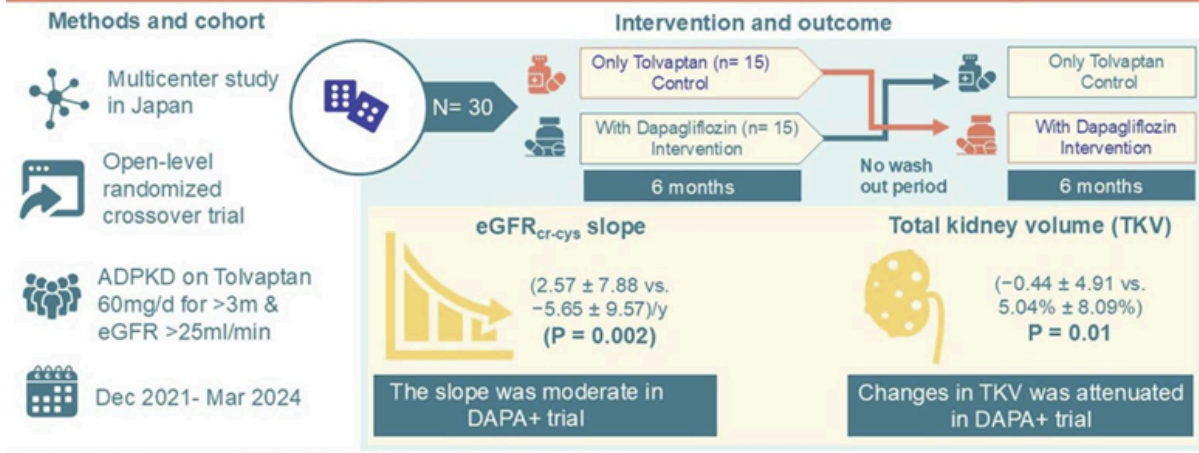
11/Emerging therapies – SGLT2 inhibitors

💊 SGLT2 inhibitors show strong renoprotective effects in CKD, but patients with ADPKD were excluded from major trials; in experimental ADPKD models in mice, SGLT2 inhibition has been associated with increased cyst growth and kidney cystic volume.

<https://pubmed.ncbi.nlm.nih.gov/25927597/>

👍 Preliminary data suggest potential benefits, and dedicated randomized trials in ADPKD are currently underway.

Open-label, Randomized, Controlled, Crossover Trial on the Effect of Dapagliflozin in Patients With Autosomal Dominant Polycystic Kidney Disease Receiving Tolvaptan



KI REPORTS Uchiyama K et al, 2025
Kidney International Reports
Visual abstract by: Abdul Qader, MD
@md_abdulqader83

Conclusion In patients with ADPKD treated with tolvaptan, dapagliflozin may have an additive effect to tolvaptan in slowing ADPKD progression.

12/Summary

Stopping ADPKD progression – key points

- ADPKD = most common genetic kidney disease (PKD1/PKD2)
- Progression → cyst growth drives decline
- 📄 Tolvaptan = only approved disease-modifying therapy
- 📍 BP control = cornerstone (HALT-PKD)
- 💧 Diet/water → unclear benefit
- ⚠️ Comorbidities (e.g. diabetes) accelerate decline
- 📄 SGLT2i:
 - strong in CKD
 - excluded in ADPKD trials
 - ongoing clinical trials

👉 **Take-home: integrated approach + future therapies needed**

? What matters most in slowing ADPKD?

Conclusion

☀️ Slowing ADPKD progression requires an integrated approach combining disease-modifying therapy with management of modifiable risk factors.

☀️ Future advances in imaging and biomarkers may enable more personalized, risk-guided treatment strategies.

