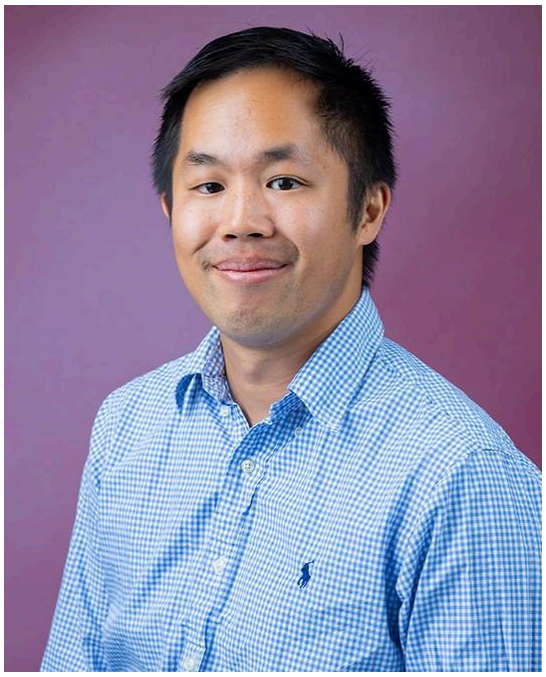
Articles
https://www.kireports.org/article/S2468-0249(25)00163-9/fulltext

🧵 Tweetorial Alert 🧵

1/
Hey #NephTwitter!
Welcome to a 🆕 #tweetorial #xtorial brought to you by @KIReports.

2/
Our author is Melvin @MChanMD (pediatric nephrologist)
Our topic: Kidney Function Trajectories with Tolvaptan in ADPKD Patients

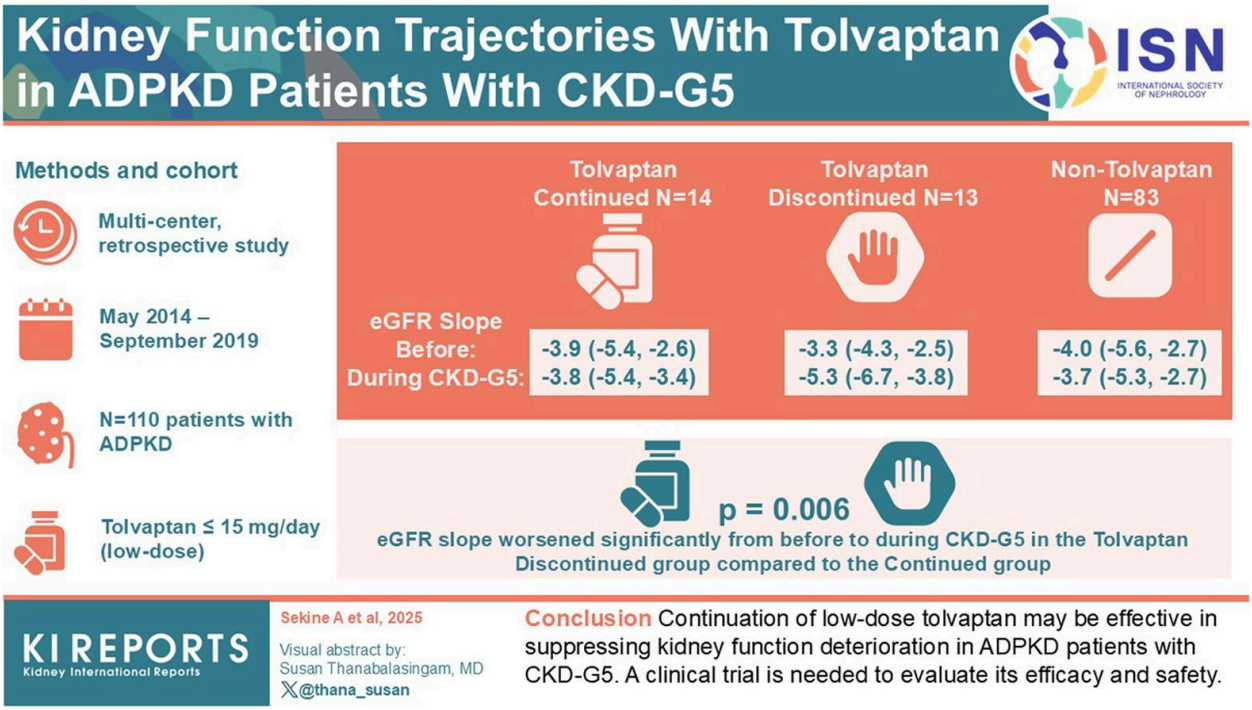
#MedTwitter #nephtwitter @ISNkidneycare #XTwitter



3/
There are no conflicts of interest. Please also check out #KIReportsCommunity educational #blogposts at https://www.kireportscommunity.org/. FOLLOW US at @KIReports for more expert #MedEd in #kidneydisease. #FOAMed @MedTweetorials

4/ Our #Tweetorial is based on a recent publication by Dr. Akinari Sekine and VA by Dr. Susan Thanabalasingam (X @thana_susan):
Kidney Function Trajectories with Tolvaptan in ADPKD Patients with CKD-G5

🗞️https://www.kireports.org/article/S2468-0249(25)00163-9/fulltext



5/ Intro

💡ADPKD is the most prevalent hereditary kidney disease in adults

💡Common genetic mutations are PKD1 and PKD2, affecting proteins in cilia and proper cell signaling

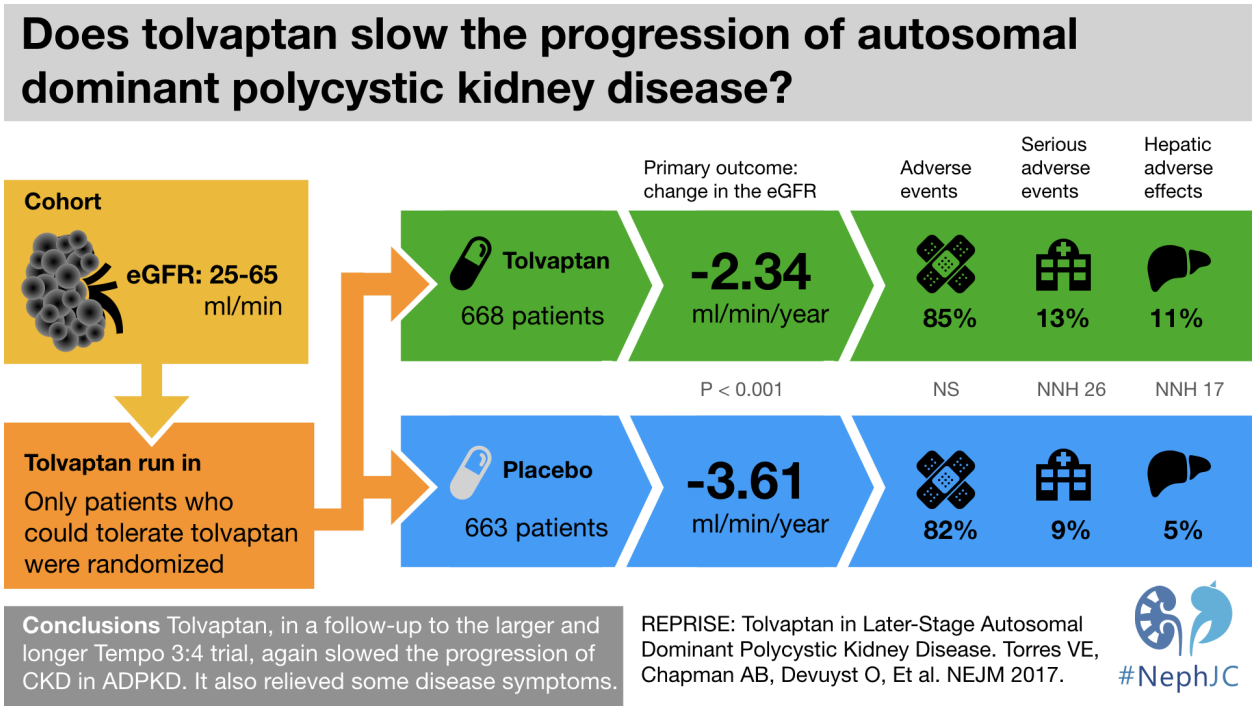
💡Abnormal signaling lead to cyst formation and impaired urine concentration

6/ Intro

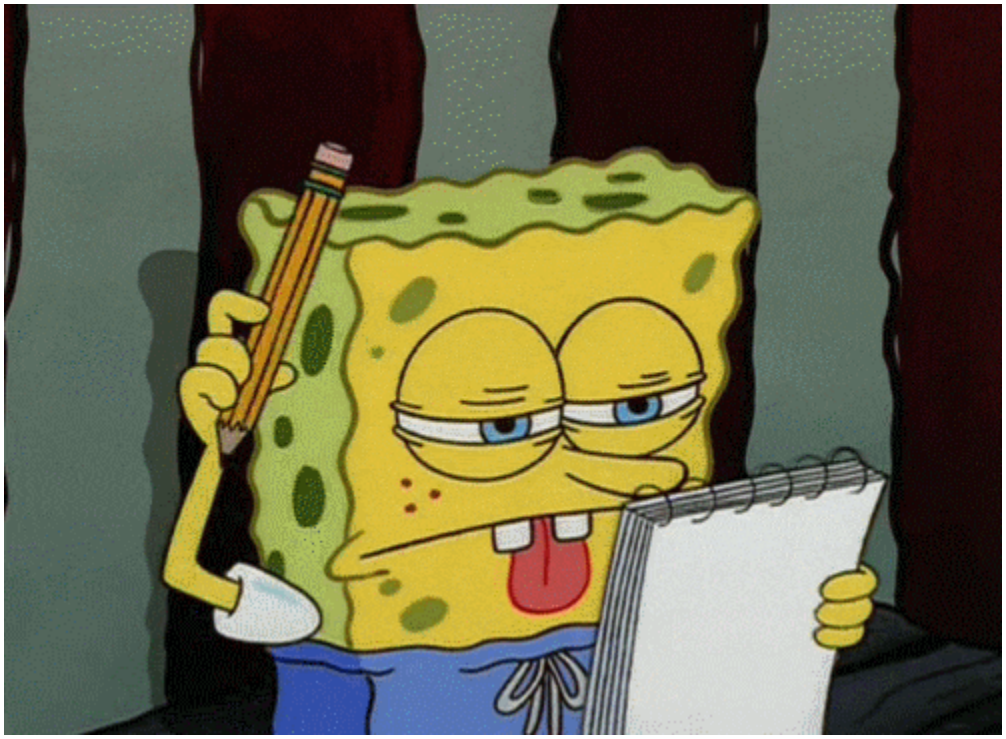
💡 Vasopressin has been implicated in cyst enlargement and kidney deterioration

💡 Multiple RCTs (TEMPO 3:4 and REPRISE) have found tolvaptan, a vasopressin receptor antagonist, to be effective in blunting kidney decline in CKD stage 4 and lower.

🔊https://www.nephjc.com/news/reprise

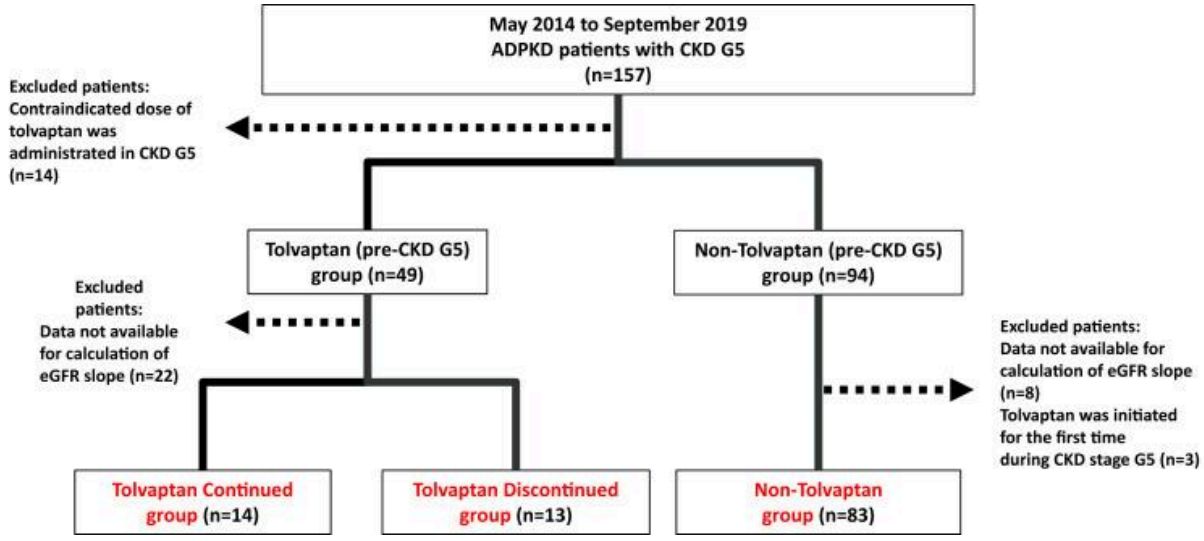


7/ Little data exists for those with CKD stage 5. How do you think tolvaptan will fare in such a population? We hope this article provides some 🔆!



8/ Methods

🎨16-site 🇯🇵Retrospective Observational Study



9/ Intervention

👉A dose of 60-120mg of tolvaptan was used in patients with eGFR > 15mL/min/1.73m2

👉A dose of < 15mg of tolvaptan was used in patients with eGFR < 15mL/min/1.73m2

10/ Statistical Considerations

🫘Primary Outcome: eGFR slope based on least least squares method

🫘Comparisons of slopes was done via Wilcoxon test

11a/ Clinical Characteristics

📌No difference in sex, family history, or height-adjusted Total Kidney Volume at CKD stage 5.

📌Similar comorbidities

📌Patients in the non-tolvaptan group were older than the tolvaptan groups at the start of CKD stage 5

Table 1. Clinical and laboratory characteristics: Tolvaptan Continued, tolvaptan discontinued, and non-tolvaptan groups

	Tolvaptan continued group ($n = 14$)	Tolvaptan discontinued group ($n = 13$)	Non tolvaptan group ($n = 83$)	*P*-value
Male/Female	5/9	9/4	50/33	0.16
Family history of ADPKD	12 (86%)	9 (69%)	60 (72%)	0.27
At start of observation				
eGFR (ml/min per 1.73 m^2)	42.3 [35.6, 47.5]	37.8 [34.5, 44.0]	28.0 [23.0, 37.4]	0.0003
At start of tolvaptan				
eGFR (ml/min per 1.73 m^2)	25.9 [23, 32.4]	23.5 [21.2, 32.0]		0.66
At start of CKD G5				
eGFR (ml/min per 1.73 m^2)	14.1 [13.6, 14.5]	14.2 [14.0, 14.3]	14.3 [13.9, 14.7]	0.54
Age (y)	55 [50, 60]	58 [54, 61]	64 [52, 70]	0.044
BMI (TKV corrected)	23 [20, 24]	22 [20, 25]	21 [20, 24]	0.82
Diabetes	1 (7%)	1 (8%)	4 (5%)	0.97
Hypertension	14 (100%)	13 (100%)	79 (95%)	0.51
Cerebral aneurysm	3 (21%)	3 (23%)	23 (28%)	0.70
Cardiac valvular disease	5 (36%)	3 (23%)	27 (33%)	0.53
Liver cysts > 20	10 (71%)	11 (85%)	62 (75%)	0.73
HtTKV (ml)	1593 [1458, 2052]	2129 [1615, 2319]	1410 [934, 2242]	0.080
Mayo HtTKV class 1 A/B/C	0/2/4 total 6 (43%)	0/1/5 total 6 (46%)	4/15/29 total 48 (73%)[a]	0.10
Mayo HtTKV class 1 D/E	5/3 total 8 (57%)	5/2 total 7 (54%)	11/7 total 18 (27%)[a]	0.10
At start of KRT				
Age (y) (at HD start)	56 [42, 62], $n = 7$	58 [57, 63], $n = 5$	68 [57, 71], $n = 44$	0.039
Age (yr) (at PD start)	-, $n = 0$	-, $n = 0$	56 [46, 71], $n = 4$	-
Age (yr) (at KT)	59, $n = 1$	47 [37, 59], $n = 3$	58 [40, 65], $n = 4$	0.66
Period				
Period from G5 to KRT (d)	672 [490, 981], $n = 8$	566 [483, 698], $n = 8$	787 [596, 1152], $n = 52$	0.091
G5 period (yr)	2 [1, 2]	1 [1, 2]	2 [1, 3]	0.64
All period (yr)	7 [7, 9]	7 (5, 8)	6 [4, 8]	0.042

Data are expressed as the number (percentage) or median [25th, 75th percentiles].
ADPKD, Autosomal Dominant Polycystic Kidney Disease; BMI, body mass index; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; HD, hemodialysis; KRT, kidney-replacement therapy; KT, kidney transplantation; PD, peritoneal dialysis; NS, not significant; TKV, total kidney volume; HtTKV, height-adjusted TKV; y, year.
[a]In non-tolvaptan group, 66 out of 83 patients were able to confirm the results of the TKV.

11b/ Clinical Characteristics

📌No differences in clinical or laboratory characteristics amongst those who continued and discontinued tolvaptan.

Table 3. Clinical and laboratory characteristics: tolvaptan continued and tolvaptan discontinued groups

	Tolvaptan continued group ($n = 14$)	Tolvaptan discontinued group ($n = 13$)	*P*-value
Male/Female	5/9	9/4	0.087
Family history of ADPKD	12 (86%)	9 (69%)	0.081
At start of observation			
eGFR (ml/min/1.73 m^2)	42.3 [35.6, 47.5]	37.8 [34.5, 44.0]	0.31
At start of Tolvaptan			
eGFR (ml/min/1.73 m^2)	25.9 [23, 32.4]	23.5 [21.2, 32.0]	0.66
At start of CKD G5			
eGFR (ml/min/1.73 m^2)	14.1 [13.6, 14.5]	14.2 [14.0, 14.3]	0.54
Age (yrs)	55 [50, 60]	58 [54, 61]	0.45
BMI (TKV corrected)	23 [20, 24]	22 [20, 25]	0.88
Diabetes	1 (7%)	1 (8%)	0.98
Hypertension	14 (100%)	13 (100%)	1.00
Cerebral aneurysm	3 (21%)	3 (23%)	0.94
Cardiac valvular disease	5 (36%)	3 (23%)	0.38
Liver cysts >20	10 (71%)	11 (85%)	0.56
HtTKV (ml)	1593 [1458, 2052]	2129 [1615, 2319]	0.26
Mayo HtTKV class 1A/1B/1C	0/2/4 total 6 (43%)	0/1/5 total 6 (46%)	0.88
Mayo HtTKV class 1D/1E	5/3 total 8 (57%)	5/2 total 7 (54%)	0.88
At start of KRT			
Age (yrs) (at HD start)	56 [42, 62], $n = 7$	58 [57, 63], $n = 5$	0.33
Age (yrs) (at PD start)	-, $n = 0$	-, $n = 0$	-
Age (yrs) (at KT)	59, $n = 1$	47 [37, 59], $n = 3$	0.37
Period			
Period from G5 to KRT (d)	672 [490, 981], $n = 8$	566 [483, 698], $n = 8$	0.37
G5 period (yr)	2 [1, 2]	1 [1, 2]	0.47
All period (yr)	7 [7, 9]	7 (5, 8)	0.37

Data are expressed as the number (percentage) or median [25th, 75th percentiles].
ADPKD, Autosomal Dominant Polycystic Kidney Disease; BMI, body mass index; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; HD, hemodialysis; KRT, kidney-replacement therapy; KT, kidney transplantation; PD, peritoneal dialysis; NS, not significant; TKV, total kidney volume; HtTKV, height-adjusted TKV.

12a/ eGFR Slope

☝ Stable slope in the tolvaptan continued group between before and during CKD stage 5

☝ Slope accelerated in the tolvaptan discontinued group during CKD stage 5

☝ Stable slope in the non-tolvaptan group between before and during CKD stage 5

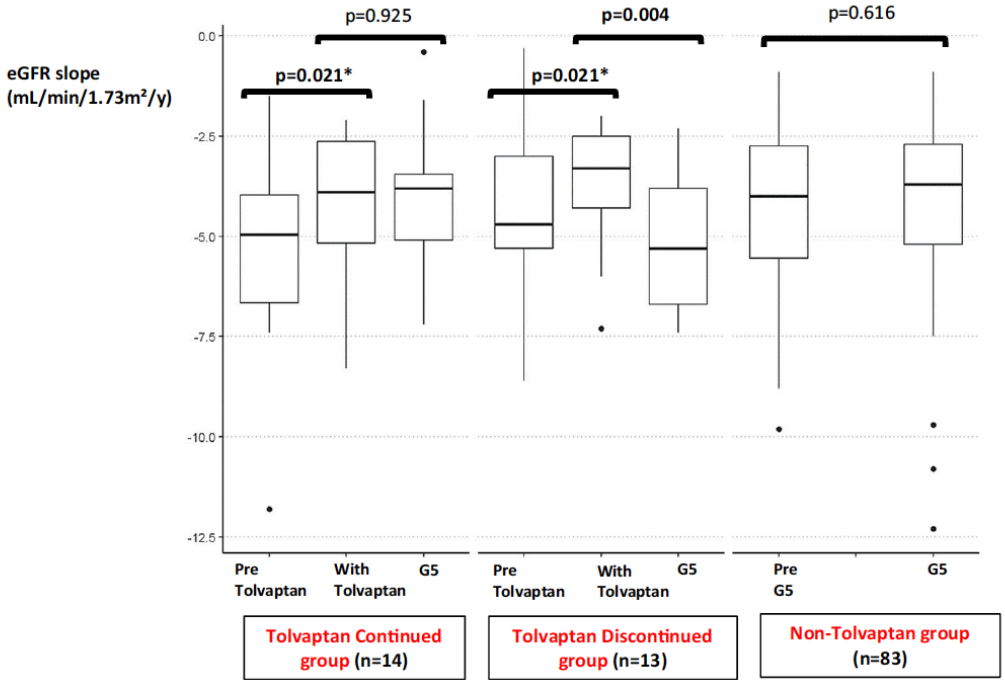


Figure 2. eGFR slope in tolvaptan continued, tolvaptan discontinued, and non- tolvaptan groups, at each phase (box-and-whisker diagram). CKD G5, Chronic kidney disease stage 5; eGFR, estimated glomerular filtration rate. *Tolvaptan continued and tolvaptan discontinued groups were mixed for analysis before and after tolvaptan treatment.

12b/ eGFR Slope

☝ Significant difference in slope between those who continued and discontinued tolvaptan during CKD stage 5

☝ Similar slope between those continued on tolvaptan and those on non-tolvaptan group during CKD stage 5, despite the latter having a lower Mayo class, suggesting slower disease progression

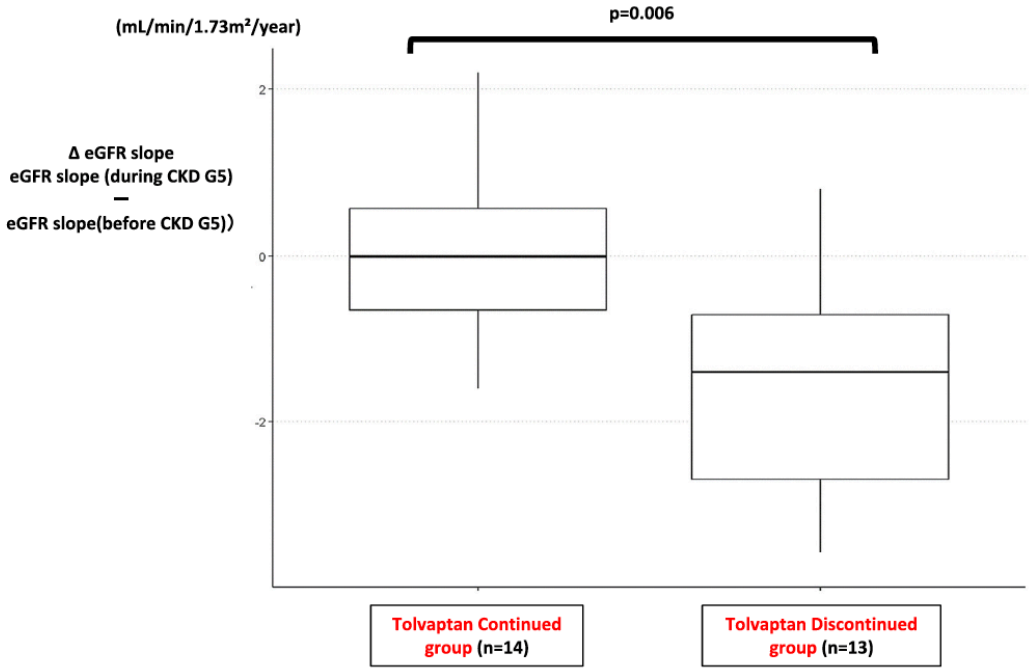


Figure 3. The difference in change in eGFR slope (Δ eGFR slope) from CKD G5 phase to pre-CKD G5 phase during tolvaptan treatment (eGFR slope [during CKD G5] minus eGFR slope [before CKD G5]) for the tolvaptan continued group vs. the tolvaptan discontinued group. CKD G5, Chronic kidney disease stage 5; eGFR, estimated glomerular filtration rate.

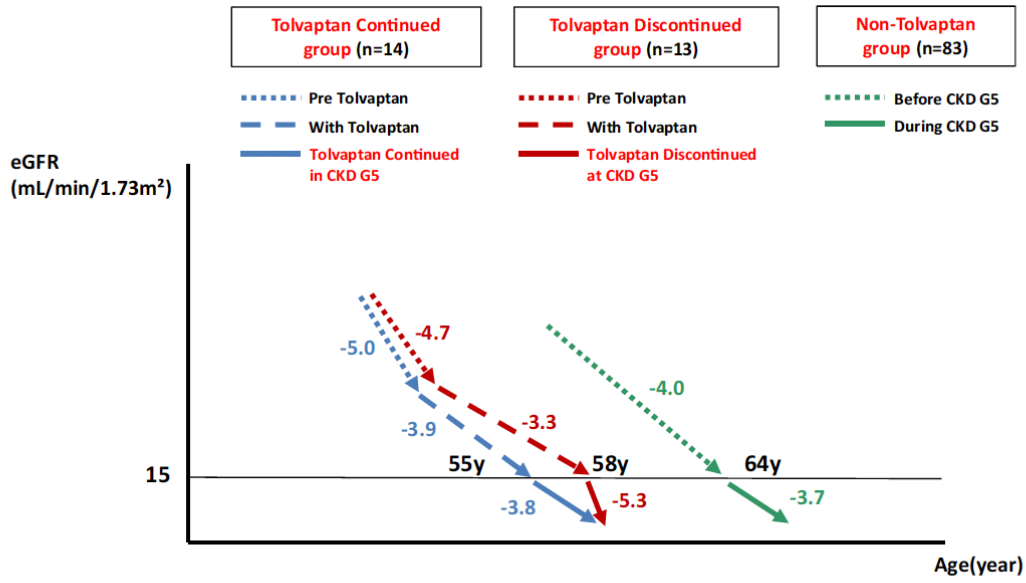


Figure 4. Imaged figure of eGFR slope from median of each phase. eGFR, estimated glomerular filtration rate. CKD G5, Chronic kidney disease stage 5; eGFR, estimated glomerular filtration rate.

13/ Adverse Events

☝No increase in side effects amongst the continued group, specifically liver dysfunction or hypernatremia.

14/ Summary
🔑eGFR slope decline was constant in the non-tolvaptan group
🔑Steeper eGFR slope decline in the tolvaptan discontinued group as compared to the continued group
🔑Low dose tolvaptan appears to still have renoprotective effects
🔑No patient discontinued tolvaptan due to increased adverse effect

15/ Limitations
👎Several missing data: total kidney volume changes, cardiac functional markers, copeptin levels, and urine osmolality
👎Retrospective study with small sample size
👎No genetic data

16/ Future Directions
🩺Randomized clinical trial on those with CKD stage 5
🩺Determining how patients respond to tolvaptan based on PKD1 or PKD2 mutations

17/ Now let's see if you have learned something!

Does tolvaptan seem to blunt renal decline in patients with CKD stage 5 with ADPKD?
1. Yes
2. No
3. More data please!

18/ The answer is 1 and 3. We hope this #tweetorial has improved your knowledge on the effects of tolvaptan and patients with CKD stage 5. Please share this #tweetorial with your followers and friends! Thanks to @MChanMD for authoring & *** for great feedback! @ISNkidneycare @KIReports