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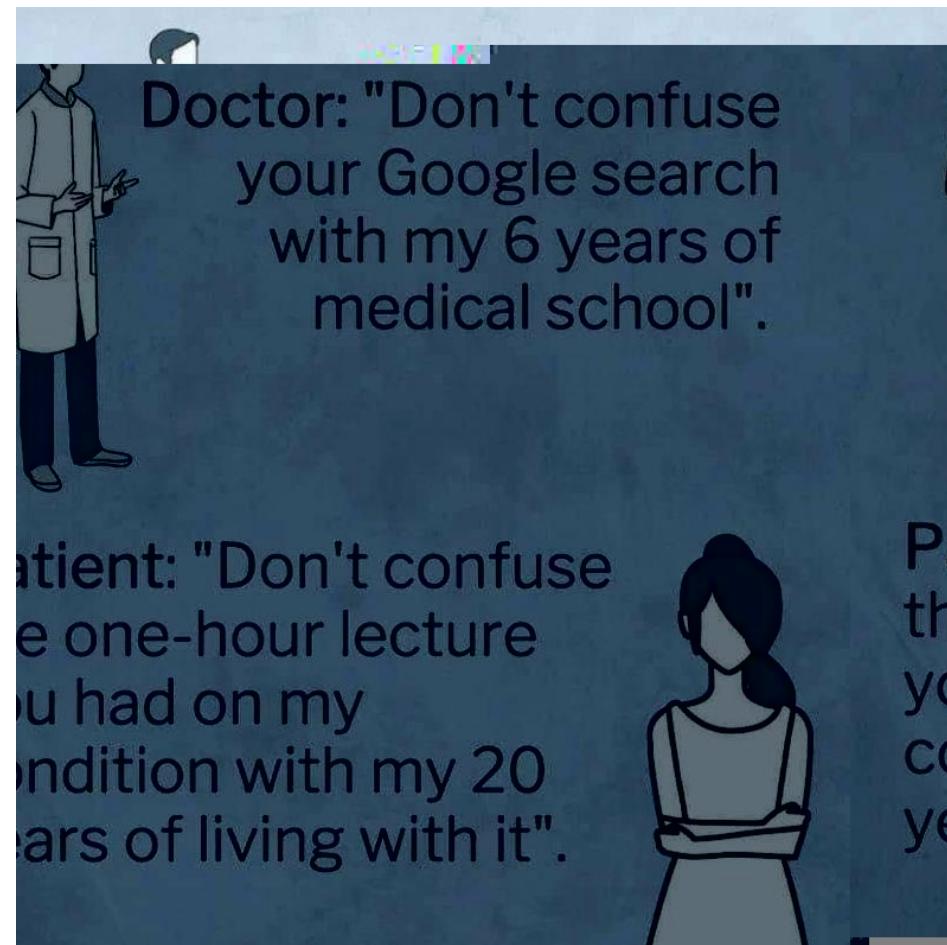
SwissPKD
Schweizer Gesellschaft
polyzystischer Nierenerkrankung

Unsere Erfahrungen und systematische Beurteilung der Tolvaptan (Jinarc®) Therapie bei ADPKD





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Doctor: "Don't confuse
your Google search
with my 6 years of
medical school".

Patient: "Don't confuse
the one-hour lecture
you had on my
condition with my 20
years of living with it".

...next: impressions from observing >400 times on average >40 patient-years (total >3600 years) of life with ADPKD



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GFR0	GFR0_fut_w	GFRdate0	stage_GFR1	GFR1	GFR1_fut	GFRdate1	stage_GFR2	GFR2	GFR2_fut	GFRdate2	stage_GFR3	GFR3	GFR3_fut	GFRdate3	stage_GFR4	GFR4	GFR4_fut	GFRdate4	stage_GFR5
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67.4	-16.71428	1/12/2017	3	56.1	4.428571	6/9/2017	3.5	39.8	18.42857	9/15/2017	3	58.7	31.42857	12/15/2017	3	54.2	58.42857	6/22/2018	3
69.7	0	5/5/2020	2	69.7	0	5/5/2020	2	71.2	4	6/2/2020	2	67	14	8/11/2020	2	67	26.28572	11/5/2020	.
54.2	-8.571428	12/3/2016	3	57.1	4.142857	3/2/2017	3	54.5	20	6/21/2017	3	46.1	33	9/20/2017	3	56.7	59.28571	3/23/2018	3
65.4	-6.571429	12/10/2016	3	55.4	2.857143	2/24/2017	3	55.4	15.85714	5/27/2017	3	46.4	27.28572	8/24/2017	3	56.8	56.85714	2/27/2018	3

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17.0
MP-Parallel Edition

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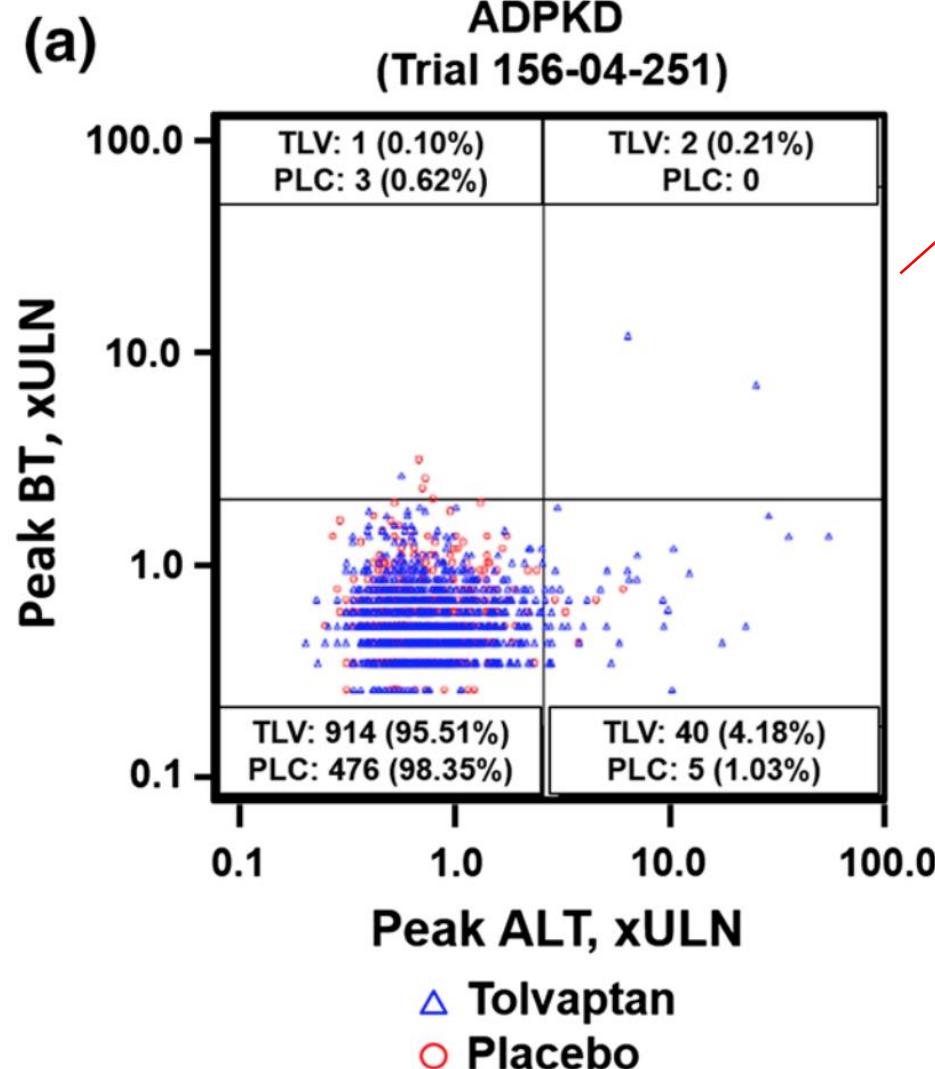


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Tolvaptan bei ADPKD



Hepatotoxicity surveillance of tolvaptan in phase III clinical trial (ADPKD patients)

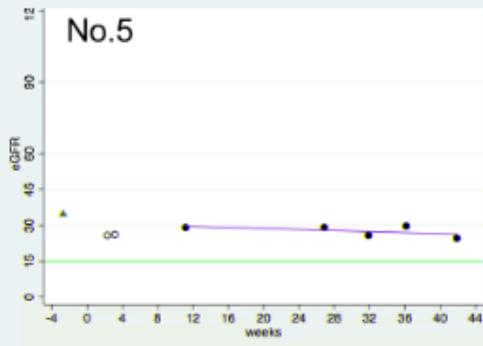


Data from SUISSe ADPKD cohort

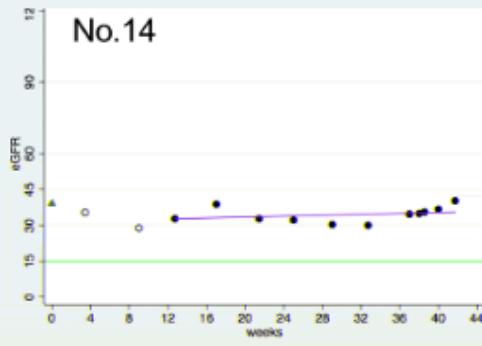
2018 analysis, 76 patients

Representative Samples of 4 Patients

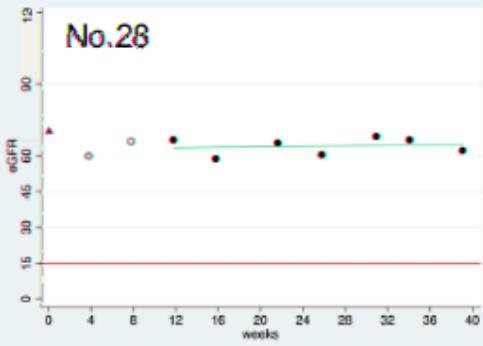
Course of eGFR



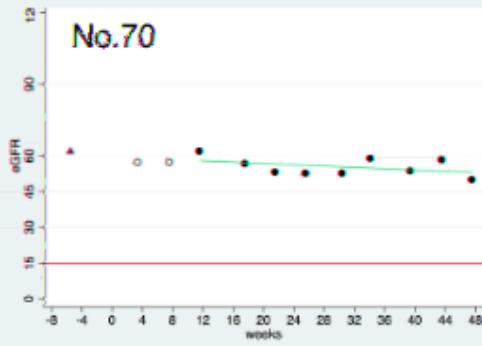
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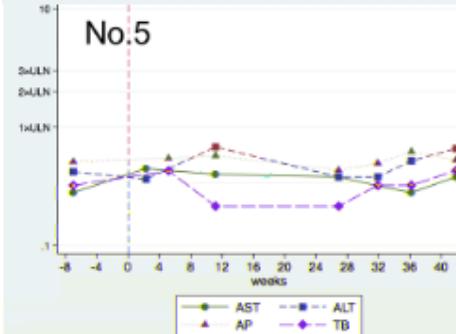
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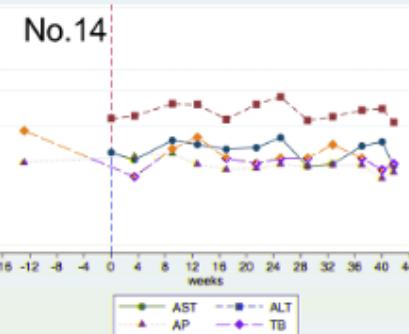
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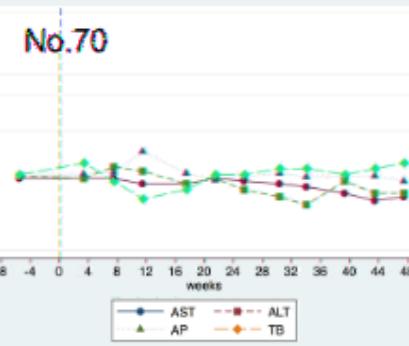
Course of liver values



No.28



No.70



The x-axis represents time in weeks from start of tolvaptan. The y-axis represents eGFR (mL/min/1.73 m²). These samples were selected because there were more than 2 visits within 11 weeks and 5 visits from 11 weeks after start of tolvaptan.

Triangle: baseline value; Hollow circle: values until 11 weeks after start of tolvaptan; Circle: values from 11 weeks after start of tolvaptan; Line: simple linear regression from 11 weeks after start of tolvaptan. eGFR: estimated glomerular filtration rate.

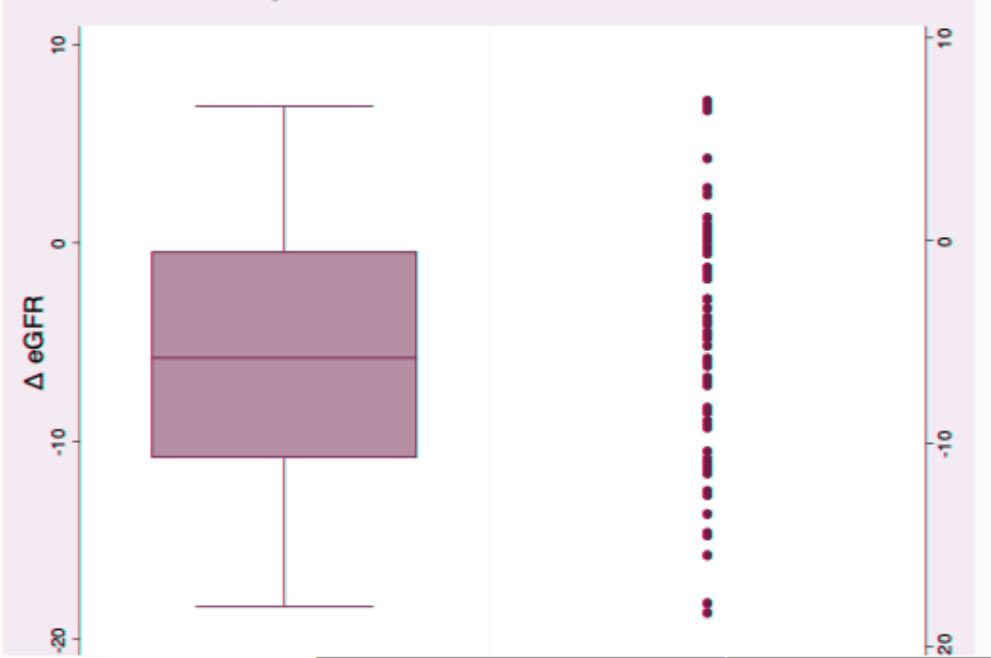
ULN: upper limits of normal, ALT: alanine aminotransferase, AST: aspartate aminotransferase, AP: alkaline phosphatase, TB: total bilirubin.

Hepatotoxicity monitoring in SUISSE ADPKD cohort

2018 analysis, 76 patients

Initial delta eGFR and analysis of Drug-Induced Serious Hepatotoxicity

Box and scatter plot of delta eGFR from baseline to 4 week visit after start of tolvaptan

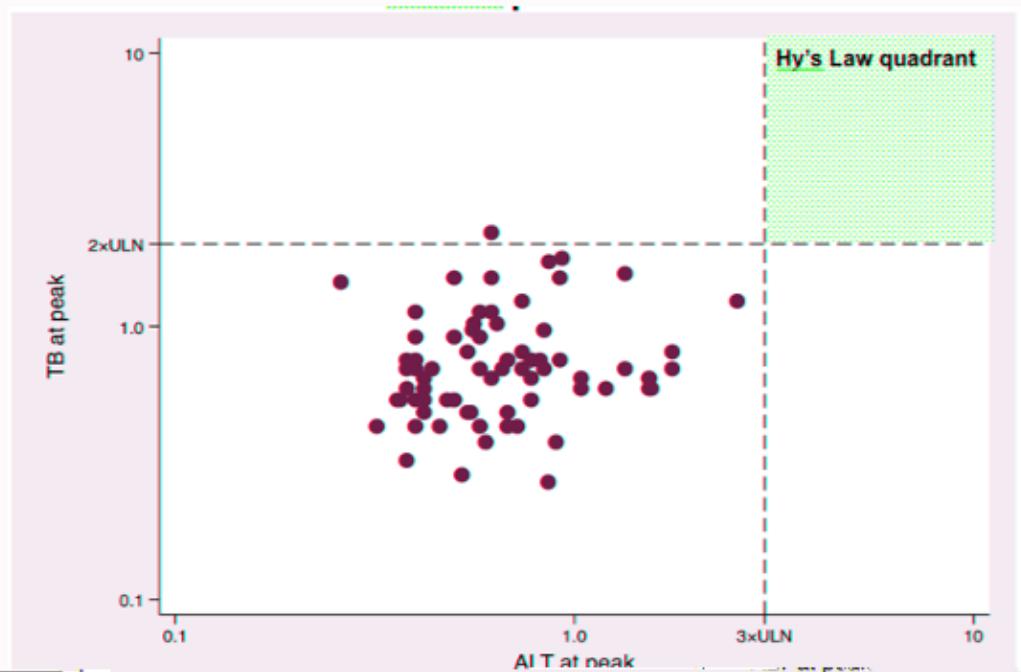


peak serum ALT time. Peak
is shown along

The y-axis represents the delta of eGFR between baseline and the first visit after start of tolvaptan (mL/min/1.73 m²). Number of observations was 67, since 9 patients did not have a documented value of eGFR.

the box represents the median. The line with
the upper adjacent value and the lower a

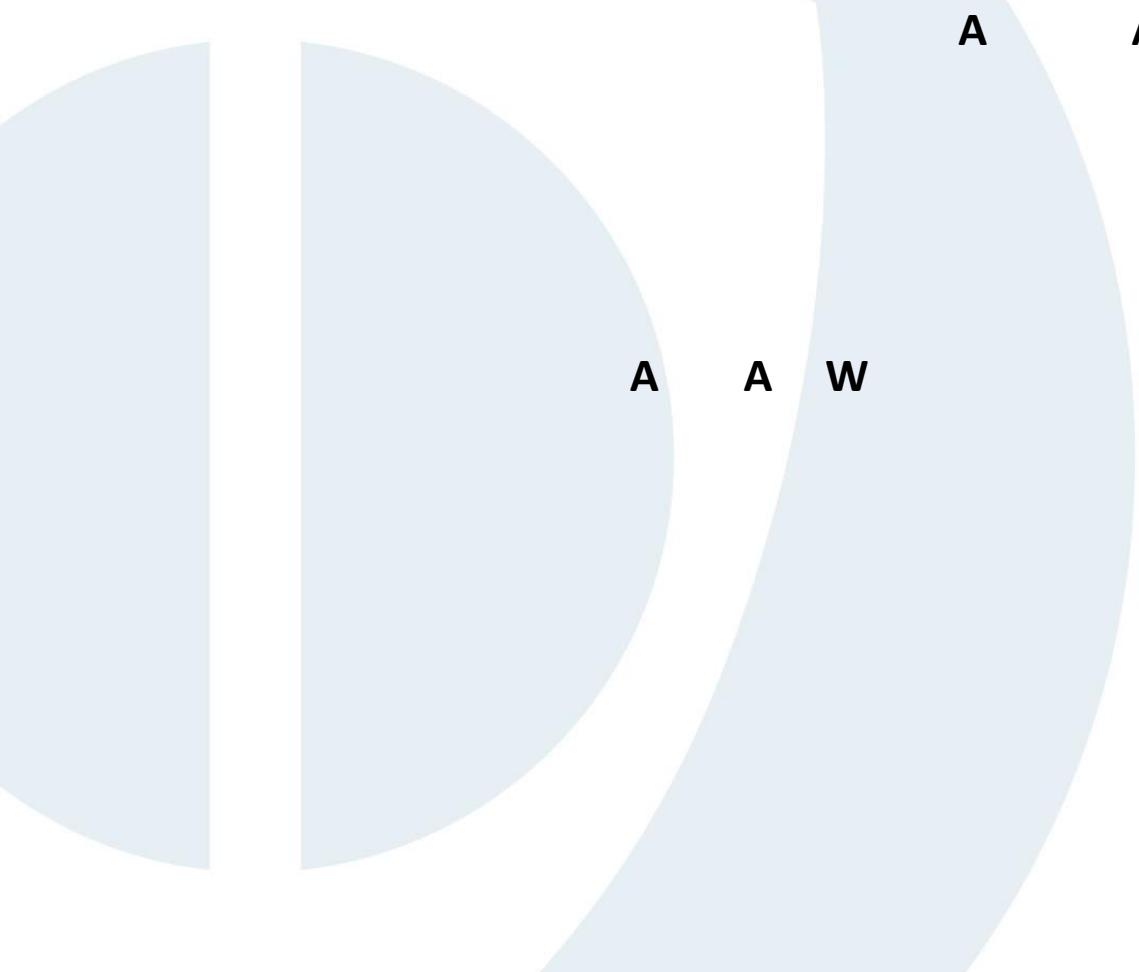
eDISH - Evaluation of Drug-Induced Serious Hepatotoxicity



Each point in the figure represents the unique subject's peak serum ALT and peak serum TB values during the available follow-up time. Peak serum ALT is shown along the x-axis and peak serum TB is

within 11 weeks after start of tolvaptan. The observed data points between the 1st and the 3rd quartiles. The line with the upper adjacent value and the lower a

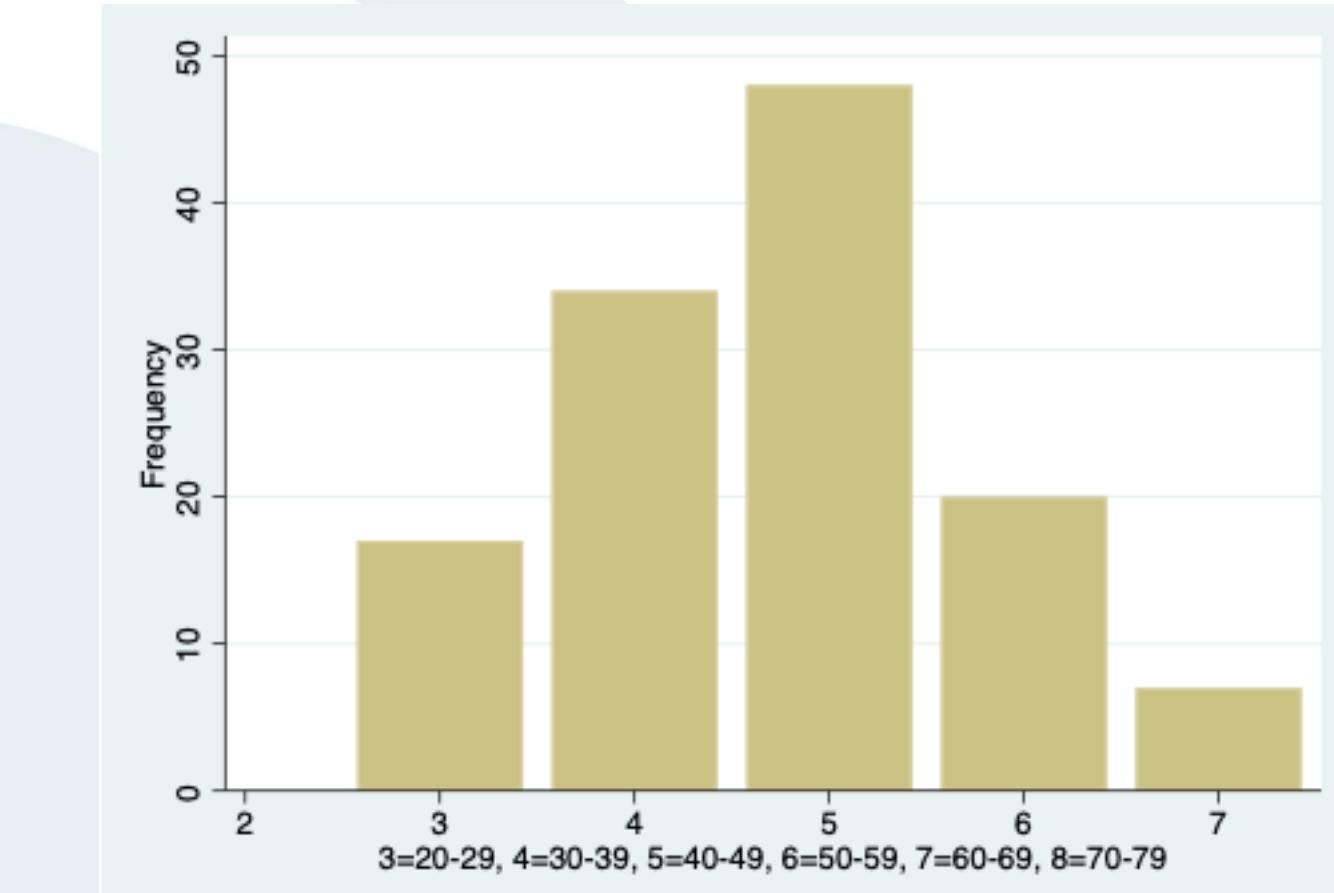
Hepatotoxicity monitoring after 2018



Characteristics of our tolvaptan patients - age

2021 analysis, 126 patients

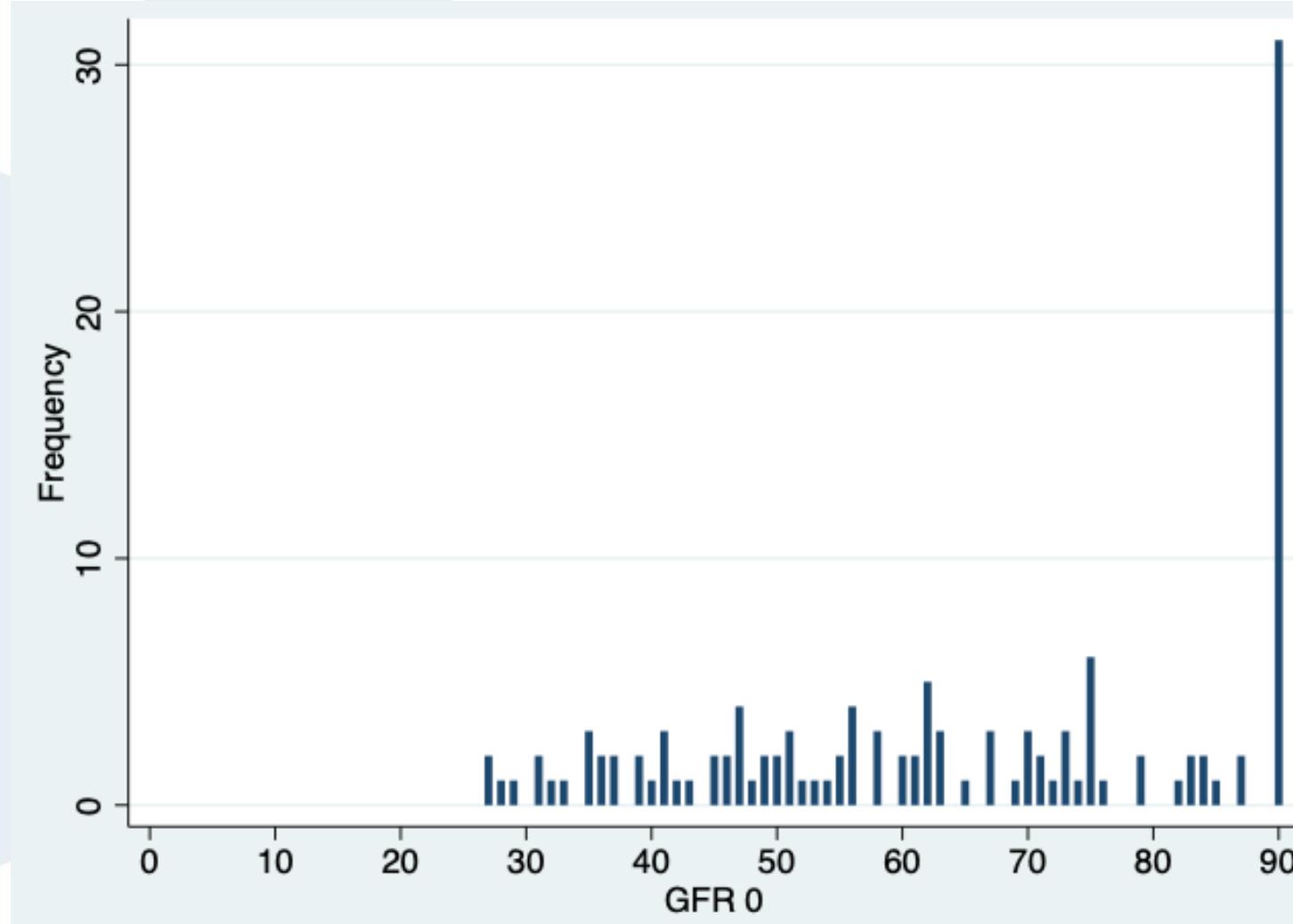
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Characteristics of our tolvaptan patients - renal function

2021 analysis, 126 patients

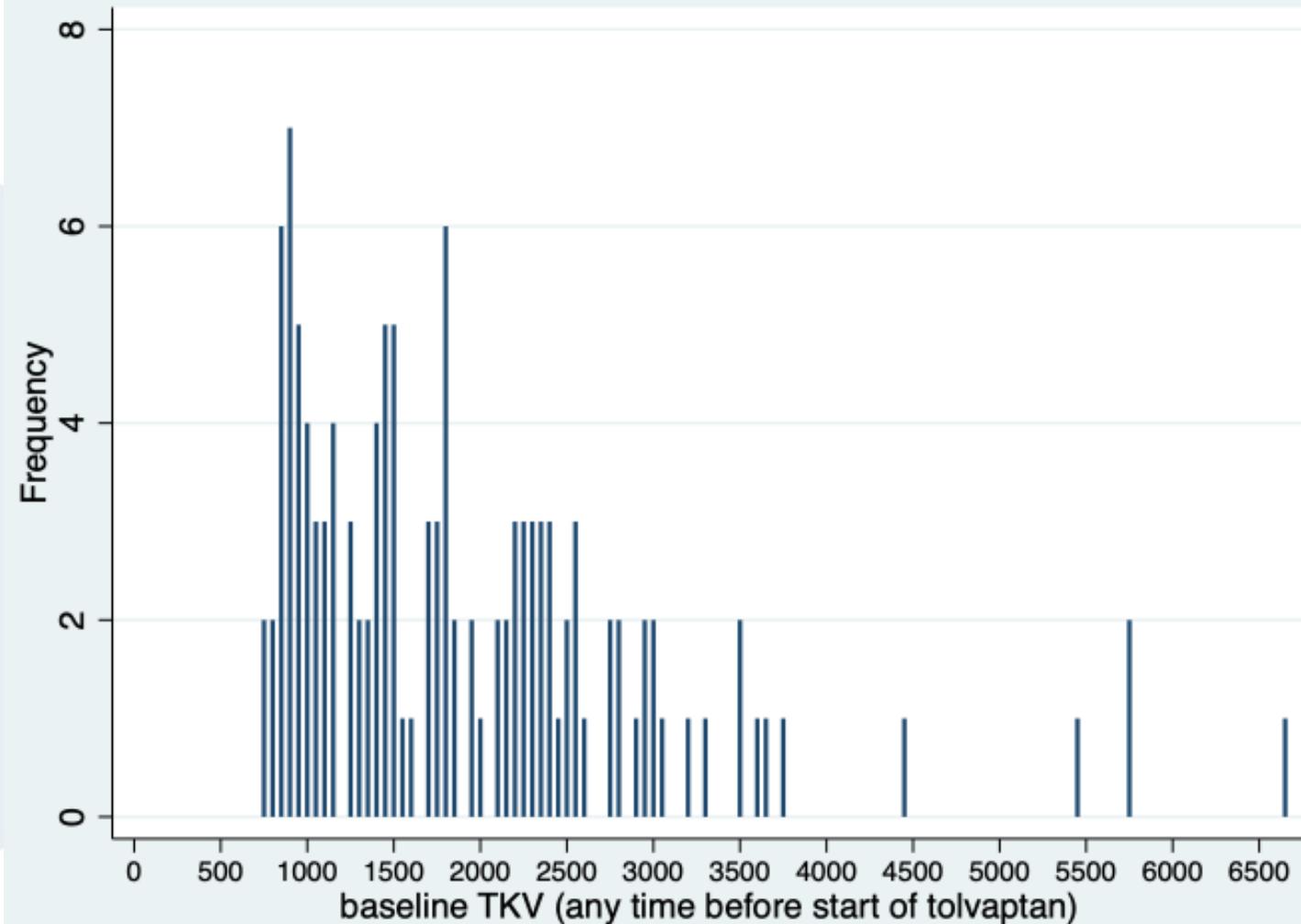
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Characteristics of our tolvaptan patients - kidney volume

2021 analysis, 126 patients

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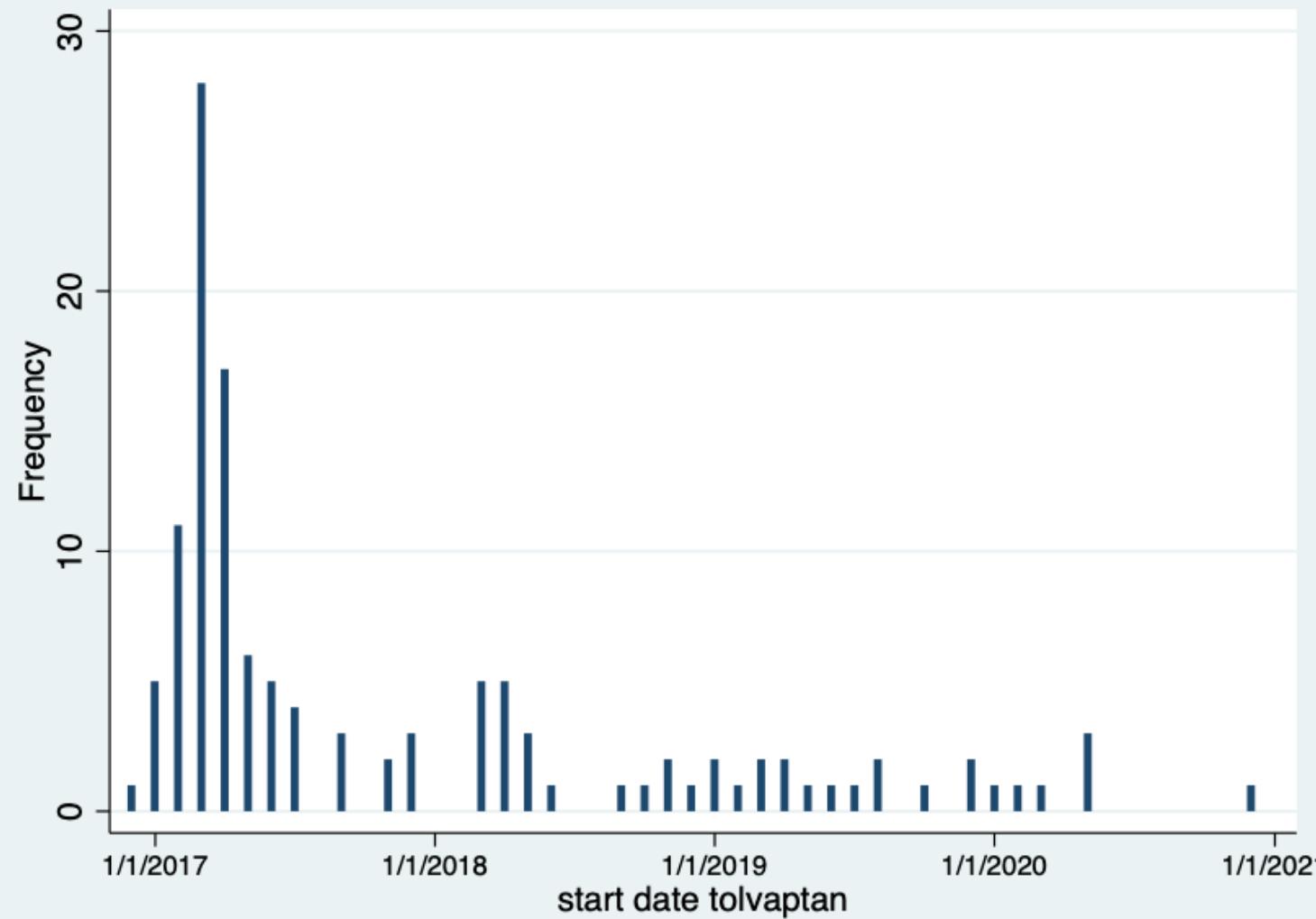
Tolvaptan start calendar date

2021 analysis, 126 patients



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Compliance with tolvaptan treatment

2021 analysis, 126 patients

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Therapy course	Freq.	Percent	Cum.
discontinued	7	5.56	5.56
continued	110	87.30	92.86
loss of follow-up	3	2.38	95.24
paused	2	1.59	96.83
renal failure	4	3.17	100.00
Total	126	100.00	

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Tolvaptan dose	Freq.	Percent	Cum.
45/15	8	6.35	6.35
60/30	8	6.35	12.70
90/30	109	86.51	99.21
90/0	1	0.79	100.00
Total	126	100.00	

Note: Among the 8 patients with a dose of 45/15 and the 8 patients with a dose of 60/30, this may not be the final maintenance dose yet if patients started tolvaptan therapy only recently.

Progression of eGFR under treatment with tolvaptan

2021 analysis, 126 patients

Delta eGFR vs. baseline after 1, 2 and 3 years

Follow-up time	Obs	Mean	Std. dev.	Min	Max
-----+-----					
1 year	61	-6.085246	6.646524	-20.1	9.900001
-----+-----					
2 years	54	-5.87963	6.762504	-22.2	10.9
-----+-----					
3 years	30	-8.456667	7.293866	-23.1	5.500001

Note: for calculation delta eGFR max = 90 ml/min/1.73m²

Progression of eGFR under treatment with tolvaptan

2021 analysis, 126 patients



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Mayo class D, course of eGFR



Delta eGFR vs. baseline after 1, 2 and 3 years

Follow-up time	Obs	Mean	Std. dev.	Min	Max
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Note: for calculation delta eGFR max = 90 ml/min/1.73m²



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Tolvaptan bei Hyponatriämie durch SIADH



ORIGINAL ARTICLE

Chlorthalidone for Hypertension in Advanced Chronic Kidney Disease

Rajiv Agarwal, M.D., Arjun D. Sinha, M.D., Andrew E. Cramer, B.S.,
Mary Balmes-Fenwick, M.S., Jazmyn H. Dickinson, B.S.,
Fangqian Ouyang, M.S., and Wanzhu Tu, Ph.D.

CONCLUSIONS

Among patients with advanced chronic kidney disease and poorly controlled hypertension, chlorthalidone therapy improved blood-pressure control at 12 weeks as compared with placebo. (Funded by the National Heart, Lung, and Blood Institute and the Indiana Institute of Medical Research; CLICK ClinicalTrials.gov number, NCT02841280.)

Prof. Dr. med. Stefan Russmann

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