A Practical guide for treatment of rapidly progressive ADPKD with tolvaptan

Fouad T Chebib, Ronald D Perrone, Arlene B Chapman, Neera K Dahl, Peter C Harris, Michal Mrug, Reem A Mustafa, Anjay Rastogi, Terry Watnick, Alan SL Yu , Vicente E Torres.

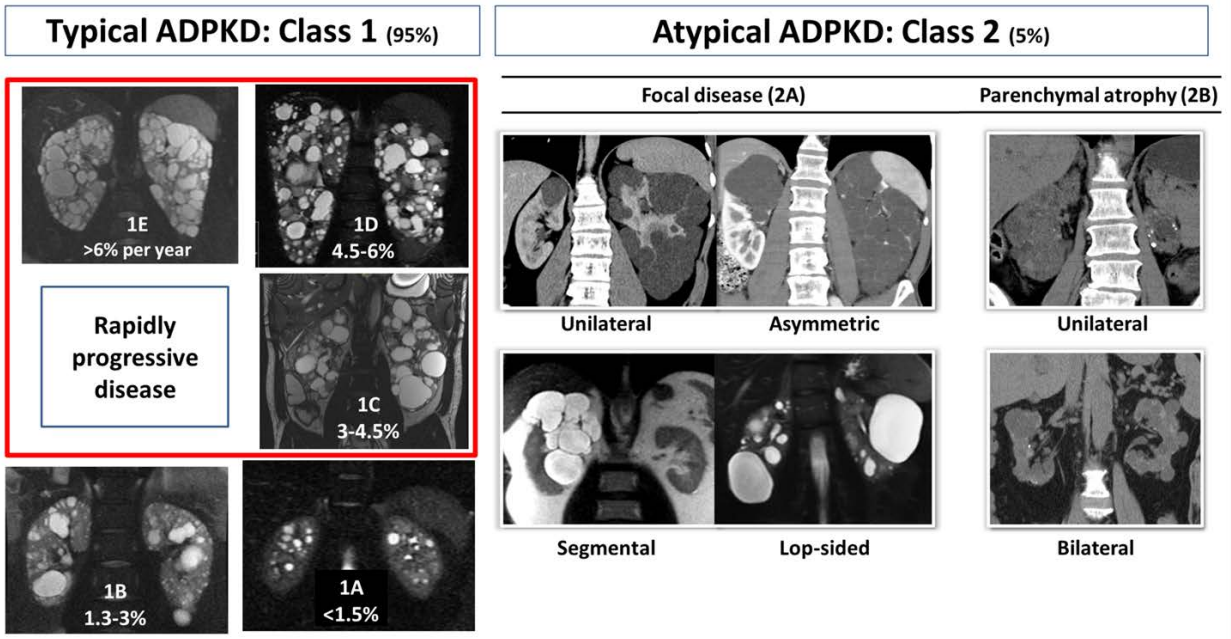
Mayo Clinic College of Medicine, Rochester MN (FTC, VET, PCH); Tufts Medical Center, Boston, Massachusetts (RDP); University of Chicago School of Medicine, Chicago IL (ABC); Yale University School of Medicine, New Haven CT (NKD); Department of Veterans Affairs Medical Center and University of Alabama, Birmingham AL (MM); University of Kansas Medical Center, Kansas City KS (RAM, ASY); University of California, Los Angeles, CA (AR); University of Maryland School of Medicine Baltimore, MD (TW).

Running title: Treating rapidly progressive ADPKD

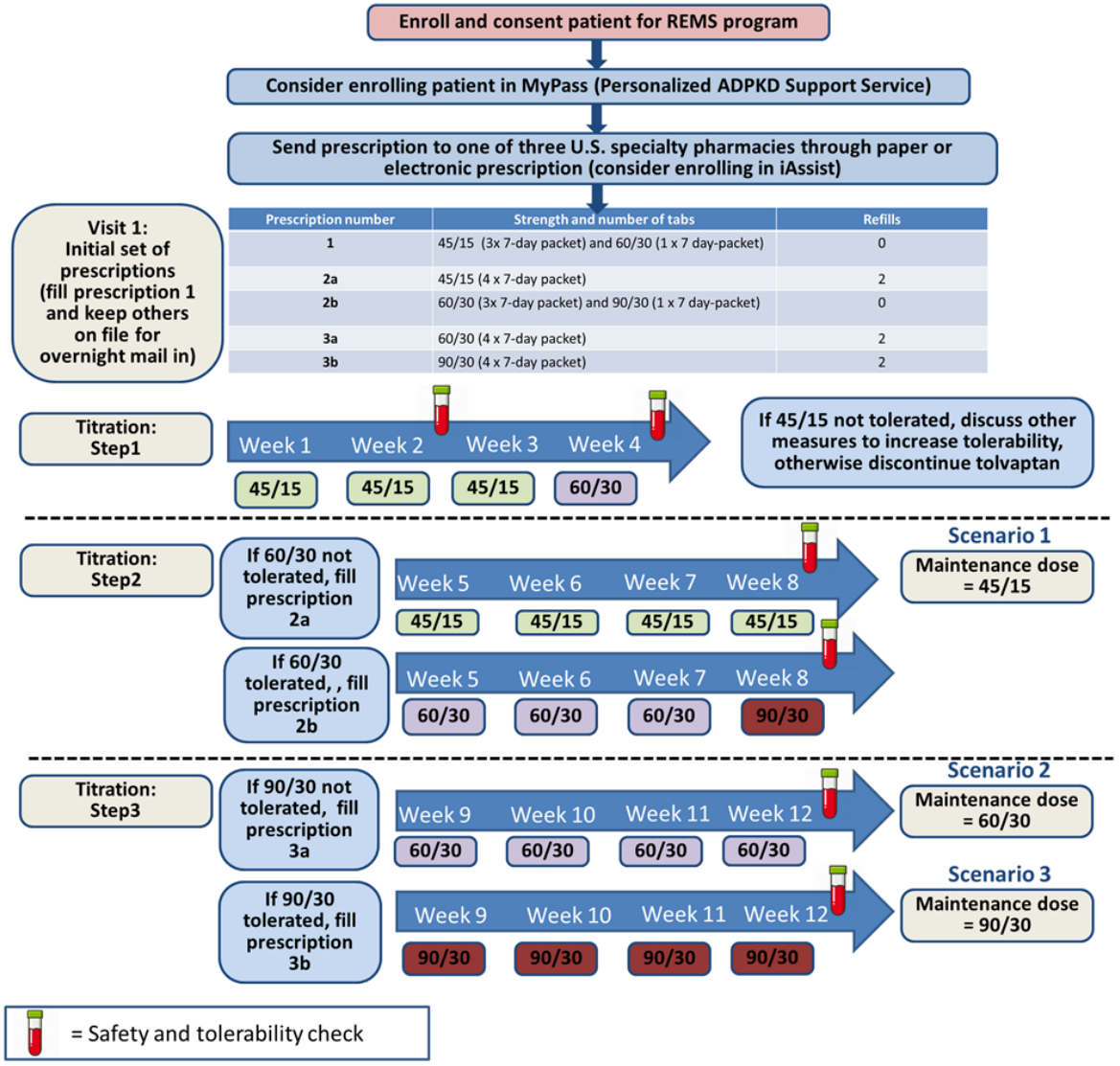
Word count: 4782
Abstract: 211

Corresponding Authors:
Fouad Chebib, M.D.
Vicente E. Torres, M.D., Ph.D.
Division of Nephrology and Hypertension, Mayo Clinic, Rochester, MN 55901
507-284-7527 - phone
507-266-9315 - fax
torres.vicente@mayo.edu
chebib.fouad@mayo.edu

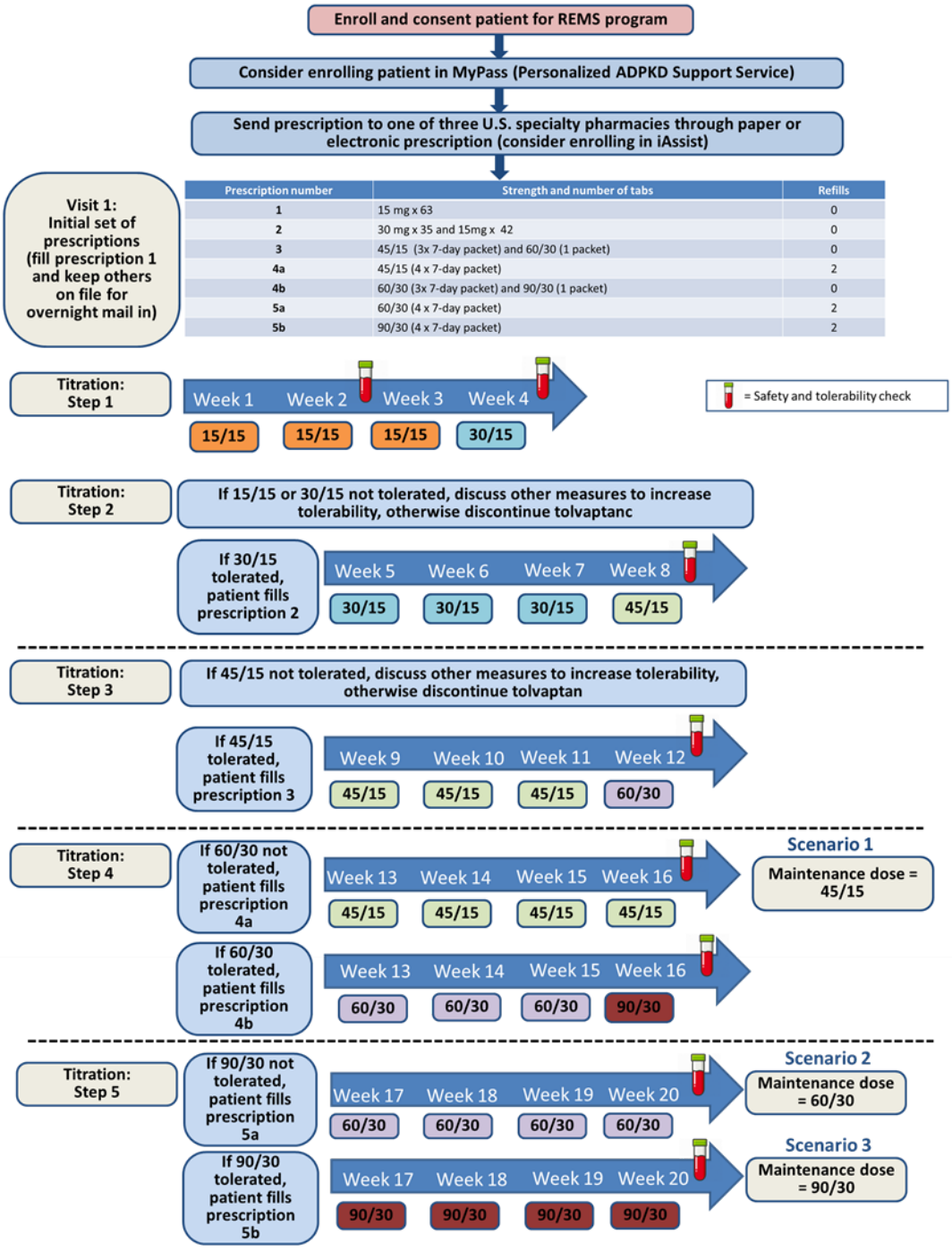
Supplemental Table of Contents



Supplemental figure 1: Classification of ADPKD cases based on imaging criteria. Typical cases constitute the majority of cases and are characterized by bilateral cystic burden where kidney cysts contribute equally to TKV. Class 1 is divided into 5 categories (A through E) based on TKV rate of growth. Class 2 or atypical cases represent 5% of the cases and have either focal disease or parenchymal atrophy. Examples of each of these classes are shown.



Supplemental figure 2a: Practical example for initiation and titration with currently available packaging of 45/15, 60/30 and 90/30. After consenting the patient and enrolling them in REMS, it is highly recommended to ask them to enroll in MyPass which includes several financial resources as well as services from the specialty pharmacy such as follow up phone calls and reminders to perform their REMS-mandated blood testing. An additional patient assistance form is available for patients without commercial insurance. Prescriptions could be sent through paper forms available from JYNARQUE REMS or electronically (Electronic medical records system or iASSIST which allows sending prescriptions and consenting patients under the same web-application). The provider can send to the specialty pharmacy a series of prescriptions to keep on file and hold until given instruction to fill them. This will ensure timely access of the patient to the right dose and avoid gaps in treatment during titration. Given that the pharmacy is allowed to dispense 4 weeks' worth of medications at a time, the first step is to start 3 weeks of 45/15 followed by one week of 60/30. The patients are educated about the expected aquaresis effect and methods to improve tolerability as delineated in step 8 of the manuscript. If the patient does not tolerate the 45/15 dosing, the therapy will be stopped unless other measures to improve tolerability have not been exhausted. Lower maintenance dose of 30/15 or 15/15 could be considered if these doses are able to lower Uosm to less than 280. In the second of titration, the dose is either increased to 60/30 if tolerated or if only 45/15 was tolerated, a maintenance dose of 45/15 is prescribed. In the third step of titration, the ability to increase to 90/30 is assessed and prescribed as maintenance dose if tolerated; otherwise the patient will continue 60/30 as a maintenance dose. Safety and tolerability check involves blood testing (LFTs, sodium and creatinine) as well as phone calls from supporting staff of provider to assess tolerability and encourage/advise patients to implement measures to improve tolerability.



Supplemental figure 2b shows a similar practical example starting with a lower dose for titration (15/15) which will likely improve tolerability.