TH-PO365

Adherence to Treatment among Children and Adolescents with Chronic Kidney Disease Rita Rosicker,[1] Sudha Chennasamudram,[2] Tetyana L. Vasylyeva.[2] *[1]Department of Family Medicine, Texas Tech University Health Sciences Center, Amarillo, TX; [2]Department of Pediatrics, Texas Tech Unviersity Health Sciences Center, Amarillo, TX.*

Background: Adherence to a prescribed treatment regimen reduces morbidity and mortality among patients with chronic renal diseases (CKD).Children often fail to adhere adequately to their medication plans.This report addresses behavioral functioning and child self-reporting of medication adherence among 10-21 year old patients with CKD.

Methods: The objective of this study was to examine patient-perceived factors that impact adherence to treatment using a qualitative descriptive individual interview approach.The questionnaire included 20 questions, answered by total of 12 children and was administered anonymously.

Results: Children admitted that they skipped their medications an average 1.6 days/ week. One third of the patients "did not like all of their medications." One of the least "favorite" medications was prednisone. Two-thirds of the patients felt either "upset" or "sometimes upset" by taking medications. Although 91.6% were frustrated by having their condition, only 25% stated that taking medications interferes with their daily lives, while 50% stated that taking medications did NOT interfere with their daily lives, and the other 25% were not sure. Most adolescents (66.6%) did not care what their friends think of them having a condition requiring medication. Interestingly, we discovered that the biggest problem in taking medications existed at home, not at school. Thus, 75% forgot to take medications at home, and just 16.6% forgot to take medications at school. The patients surveyed also were more likely to forget to take medications during the week (42%) versus the weekend (33%). As for ideas to help adolescents remember to take their medications, the most popular idea was a pill box with 66.6% saying it would help, while only 33.3% said that a reminder alarm would help, and 25% thought that a better tasting medicine would help.

Conclusions: Adherence to medications among pre-adolescents and adolescents with CKD is a serious medical problem which affects treatments and quality of life and requires developing a systematic approach.

TH-PO366

Ph II Study of Eculizumab (ECU) in Patients (PTS) with Atypical Hemolytic Uremic Syndrome (aHUS) Receiving Chronic Plasma Exchange/Iinfusion (PE/PI) Christoph Licht,[1] Petra Muus,[2] Christophe M. Legendre,[3] Kenneth Douglas,[4] Maryvonne Hourmant,[5] Yahsou Delmas,[6] Maria Herthelius,[7] Antonella Trivelli,[8] Timothy Goodship,[9] Camille Bedrosian,[10] Chantal Loriat.[11] *[1]Hosp for Sick Children; [2]Radboud Univ Nijmegen Med Ctr; [3]Hop Necker; [4]Beaston W Scotland Cancer Ctr; [5]CHU Hotel Dieu-Nantes; [6]CHU Pellegrin; [7]Karolinskia Univ Hosp; [8]Inst G. Gaslini; [9]Newcastle Univ; [10]Alexion Pharm; [11]Hop Debre.*

Background: Permanent uncontrolled complement activation drives systemic thrombotic microangiopathy (TMA) and life threatening complications in aHUS. Despite PE/PI, >50% of pts develop ESRD/die within 1yr of diagnosis. We report final 26wk and follow-up data for pts with aHUS receiving ECU, a terminal complement inhibitor.

Methods: Pts ≥12 yrs with aHUS, receiving PE/PI enrolled in a controlled, open-label, single-arm, PhII trial (pts enrolled 2009-2010). Prim endpt: TMA event-free status (≥12 consecutive wks stable platelet count, no PE/PI, no new dialysis). Sec endpts included TMA intervention rate (# plasma and new dialysis events/pt/day), renal function safety. We report the final 26wk and follow-up results as of data cut-off (10/10).

Results: 20pts received ECU thru wk26. 19pts continued into an extension. Median time from diagnosis to screening=48mths (range:.66-286). ECU median treatment (Tx) duration =40wks (26-52) at time of analysis. Median age=28yrs. Prim & sec endpts were achieved with high clin & stat. significance.

Key Endpoints	Wk 26	Follow-up (ECU=40 wks)
PRIMARY TMA event-free status, n (%)	16* (80)	16* (80)
SECONDARY Median TMA intervention rate (pre-Tx [0.23])	Post-Tx: 0 (*P*<.0001)	Post-Tx: 0 (*P*<.0001)
CKD improvements ≥1 stage, n (%)	7 (35)	7 (35)
Point estimate change in QoL	0.11 (*P*<.0001)	0.12 (P=.001)
Pts achieving a minimally important difference (MID)	8/11 (73%)	8/11 (73%)

*The 4 pts who did not achieve TMA-event free status had normal platelet count at study entry and maintained platelet count ≥150x10^9/L throughout. However, at certain time points, plt count in these pts was >25% change from baseline.
MID= change of at least 0.08 on the US Time Trade-off Value

ECU was similarly effective in pts w/wo identified complement mutations and was well tolerated; only 6pts had AEs deemed related to drug.

Conclusions: Continued ECU Tx resulted in sustained TMA suppression and led to permanent discontinuation of chronic PE/PI. Sustained ECU Tx resulted in stabilized/ improved renal function, was well tolerated and demonstrates potential as the new SOC for aHUS.

TH-PO367

Continued Improvements in Renal Function with Sustained Eculizumab (ECU) in Patients (PTS) with Atypical Hemolytic Uremic Syndrome (aHUS) Resistant to Plasma Exchange/Infusion (PE/PI) Laurence A. Greenbaum,[1] Sunil Babu,[2] Richard Furman,[3] Neil Sheerin,[4] David J. Cohen,[5] A. Osama Gaber,[6] Frank Eitner,[7] Yahsou Delmas,[8] Chantal Loriat,[9] Camille Bedrosian,[10] Christophe M. Legendre.[11] *[1]Emory Univer; [2]Fort Wayne Med; [3]Weill Cornell Med Coll; [4]Newcastle Univ; [5]Columbia Univ Med Center; [6]Methodist Hosp; [7]Univ Aachen; [8]CHU Pellegrin-Bordeaux; [9]Hopital Robert Debre; [10]Alexion Pharmacetuicals, Inc; [11]Universite Paris Descartes & Hopital Necker.*

Background: aHUS is a genetic, devastating, systemic disease, caused by permanently uncontrolled complement activation, resulting in thrombotic microangiopathy(TMA). Despite PE/PI, >50% of pts develop ESRD/die within 1 yr of diagnosis. We report longer follow-up data from a phase II trial of ECU, a terminal complement inhibitor.

Methods: Pts ≥12 yrs with aHUS and persistent TMA despite ≥4 PE/PI sessions 1 wk before screening were enrolled in a 26-wk, controlled, open-label, single-arm phase II trial (2009-2010). Prim. Endpoint: change in platelet (plt) count (a measure of TMA) (73x109/L; p=0.0001). Sec. endpoint: 15/17 pts (88%) achieved TMA event-free status (≥12 wks of stable plt count, no PE/PI and no new dialysis). 4/5 pts on dialysis permanently discontinued dialysis. ECU was well tolerated (Legendre. ASN 2010). We report follow-up results as of data cut-off (10/2010).

Results: 17 pts enrolled (2 discontinued; SLE and an AE unrelated to ECU, respectively). Median time from diagnosis to screening =10mo (range:<1-236). Median age=28 yrs. ECU median duration~38 wks (range: 26-64 wks) at time of analysis. 13 pts entered the extension study. 13 pts with low platelets at baseline had plt normalization at week 26 and continued to maintain normal levels at data cut-off. Renal function improved (≥1 CKD stage=10 pts and ≥25% decrease in creatinine from baseline=11 pts). ECU was well tolerated; 10 pts with adverse events deemed related to ECU (generally mild/moderate). Longer follow-up (>1 yr) will be presented.

Conclusions: In this early intervention study, sustained treatment with ECU prevented TMA and improved renal function. These data further strengthen the evidence for ECU as standard of care for aHUS.

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TH-PO368

Neutrophil Gelatinase-Associated Lipocalcin (NGAL) and Alternate Pathway of Complement (APC) Factors as Biomarkers of Response to Treatment in Patients with Focal Segmental Glomerulosclerosis (FSGS) Howard Trachtman,[1] Prasad Devarajan,[2] Michael R. Bennett,[2] Joshua M. Thurman,[3] Milena Radeva,[4] Debbie S. Gipson,[5] Frederick J. Kaskel,[6] Aaron L. Friedman,[7] Marva M. Moxey-Mims,[8] Suzanne M. Vento.[1] *[1]Pediatrics, Cohen Children's Medical Center, New Hyde Park, NY; [2]Pediatrics, Cincinnati Children's Medical Center, Cincinnati, OH; [3]Medicine, University of Colorado Denver School of Medicine, Aurora, CO; [4]Quantitative Health Sciences, Cleveland Clinic Foundation, Cleveland, OH; [5]Pediatrics, University of Michigan, Ann Arbor, MI; [6]Pediatrics, Albert Einstein College of Medicine, Bronx, NY; [7]Pediatrics, University of Minnesota, Minneapolis, MN; [8]NIDDK, KUH, Bethesda, MD.*

Background: The FSGS-Clinical Trial evaluated a 12-month course of cyclosporine (CSA) *versus* combination dexamethasone (DEX) and mycophenolate mofetil (MMF) in 138 patients with steroid-resistant FSGS. This ancillary study evaluated the use of NGAL and APC factors as biomarkers of response to treatment.

Methods: Urine and plasma were obtained at weeks 0, 26, 52, and 78. NGAL and APC factors -- Ba and Bb, and soluble C5b-9 -- were determined by ELISA. Outcomes were defined by a 6-ordinal scale (1, complete remission, 6 no reduction in Up/c). Results are provided as mean±SEM.

Results: 19 patients (10M:9F) were included, 7 received CSA and 12 DEX/MMF. There were no differences between these two groups. There was a decline in plasma sC5b-9 in response to DEX/MMF (P\<0.001); however, there were no therapy-related differences in urinary NGAL or APC levels (ng/mg creatinine). Baseline urinary NGAL excretion correlated with primary outcome at 52 wk (P=0.08). When pooled by outcome, 1-3 *versus* 4-6, baseline urinary NGAL (54±17 vs 227±190) and sC5b-9 (168±36 vs 450±181) levels were numerically lower in those with a favorable response. Urine Ba excretion at the end of treatment correlated with outcome (P<0.01).

Conclusions: Urinary excretion of NGAL and select APC factors may be useful indices for patient stratification to predict outcome and to assess adequacy of response to treatment in patients with primary steroid resistant FSGS.

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