containing sCD89-IgA1 or free sCD89 from patients induced mesangial cell proliferation *in vitro*. Recombinant (r) sCD89 induced mesangial cell proliferation *in vitro* that was inhibited by rCD71 or rapamycin. Injection of rsCD89 induced marked glomerular proliferation and proteinuria in human IgA1 transgenic mice.
Conclusions: In conclusion, free and IgA1-complexed sCD89 are key players in mesangial proliferation. These findings reveal a new role for sCD89 in cIgAN, making it a potentially useful biomarker and therapeutic target.

OP-19 PREDICTORS OF RENAL OUTCOME IN CHILDREN WITH ANCA ASSOCIATED VASCULITIS: RESULTS OF THE ERKNET/ESPN/IPNA SURVEY

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Introduction: ANCA associated vasculitis (AAV) is a rare condition in children and data are limited on its treatment and renal outcomes. We aimed to determine clinical predictors of adverse renal outcome in children with AAV.
Material and methods: Retrospective international survey conducted through professional paediatric nephrology organisations from December 2019 to March 2020. Paediatric nephrologists were asked to anonymously enter demographic and clinical data through an online form on all children presenting with AAV to their centre.
Results: Adequate data were collected for 337 patients (from 41 countries, 72% female). Mean age at presentation 12.4 years, mean duration of follow-up 42 months. Mean peak serum creatinine at presentation was 377umol/L (4.26mg/dl) falling to a mean of 95umol/L (1.07mg/dl) at latest follow up in those not on KRT. 42% were classified as microscopic polyangiitis, 31% as granulomatosis with polyangiitis. 63% were from high income countries, 29% from upper-middle income countries (GNP 2019). There was an 5% mortality in this cohort, with 41% of patients requiring kidney replacement therapy (KRT) at any point. In multivariate mixed regression modelling, significant predictors of adverse renal outcome (requirement for KRT) included higher peak serum creatinine at presentation ($p<0.001$), ANCA-MPO positivity ($p=0.002$) and neurological involvement at presentation ($p=0.02$). Additionally, receiving plasma exchange as part of induction treatment was associated with a higher risk of having an abnormal creatinine at latest follow up in those not requiring KRT ($p=0.0004$).
Conclusions: This large international cohort of children with AAV demonstrates the significant risk of chronic kidney disease and requirement for KRT in those presenting to paediatric nephrologists. Clinical predictors of adverse renal outcome at presentation are identified but further prospective research is required to determine the impact of treatment on clinical outcomes.

OP-20 KIDNEY TRANSPLANT REJECTION AND SURVIVAL IN ADOLESCENTS – THE ROTTERDAM EXPERIENCE

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Introduction: Several registries report a higher risk of kidney transplant loss in adolescence compared to other age groups. The objectives of this study were to evaluate:
1. -if adolescents have a higher risk of acute rejection
2. -if adolescents have (early) transplant loss due to acute and/or chronic rejection.
Material and methods: This retrospective study was performed in pediatric and young adult kidney transplant recipients, receiving a first

transplant between 1990-2018, at the age of 6-25 years(y), in the Erasmus MC Rotterdam. Patient files were searched for all for-cause graft biopsy reports, and cause of transplant failure and/or death. Biopsies were reevaluated according to the 2017 Banff Classification.

Results: In 65(54%) of all pediatric and 85(65%) of all adult patients at least one transplant biopsy was obtained. Sixty seven (45%) patients had an acute rejection episode (ARE) in at least one biopsy, with the highest incidence in the 20-25y age group (27%, n=20) and the lowest incidence in the 6-10y group (16%, n=5).

ARE-free survival was best in the 6-10y group (n=32): 90% at 2y and 86% at 8y post-transplant, followed by the 10-15y group (n=49): 86% and 81%. Older recipients showed a poorer ARE-free survival: in 15-20y group (n=94) of 86% at 2y and 68% at 8y post-transplant, and in the 20-25y group(n=75) of 84% and 65% (p=0.063).

Subsequently graft losses due to acute and/or chronic rejection were studied. Transplant survival was superior in the 6-10y group: 97% at 2y and 89% at 8y at post-transplant, followed by the 20-25y group: 97% and 85%. Inferior transplant survival was seen in the 10-15y group (96% and 67%) and in the 15-20y group (93% and 67%) (p=0.073).

Conclusions: The youngest(6-10y) kidney transplant recipients had the lowest incidence of ARE, the oldest(20-25y) recipients the highest. Inferior transplant survival due to rejection was seen in the adolescent (10-20y) groups.

OP-21 PHARMACOKINETICS OF TACROLIMUS IN RENAL TRANSPLANTATION RECIPIENTS DURING ADOLESCENCE

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Introduction: Adolescents have the highest risk of kidney transplant failure of all age groups. The objective of this study is to investigate the relation between puberty and the pharmacokinetic properties of tacrolimus after kidney transplantation.

Material and methods: This study is part of the larger multicentre cohort study Adolesce-NT. Kidney transplant recipients aged between 8 -30 years were enrolled between 2012-2021. The study contains a pre-transplant and post-transplant patient group at time of inclusion. The variability of tacrolimus levels was calculated with all measurements from 6 months till 1 year after transplantation in the pre-transplant group and from inclusion till 1 year later in the post-transplant group. For each trough level we calculated the tacrolimus dose adjusted for weight.

Our primary outcome parameters are the dose-adjusted trough level and the intrapatient variability. We compared these pharmacokinetic parameters to puberty staging and gender, and corrected for confounders (including eGFR, steroid use, CYP3A4 and CYP3A5 polymorphisms).

Results: 25 patients were included in the pre-transplant and 39 patients in the post-transplant group. When corrected for confounders, we found a significant correlation between puberty staging and the dose-adjusted trough level (p= 0.017). There was a linearly increase of the dose-adjusted trough levels by increasing age.

Dose-adjusted trough levels increased linearly with increasing age, with higher increase for females compared to males. Intrapatient variability did not correlate significantly with stages of puberty (p=0.122) or gender (p=0.287).

Conclusions: Our preliminary results indicate that the dose requirement to reach tacrolimus target levels is lower in adolescents, and in females. We did not find a relationship between intrapatient variability as a measure of drug adherence and pubertal development. As we are in the process of including more patient data and adding data on drug compliance, future evaluations are expected to provide more information.

OP-22 RANDOMIZED, PLACEBO-CONTROLLED, PHASE 3B TRIAL OF TOLVAPTAN IN THE TREATMENT OF CHILDREN AND ADOLESCENTS WITH AUTOSOMAL DOMINANT POLYCYSTIC KIDNEY DISEASE (ADPKD): 1-YEAR DATA

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Objectives: To evaluate the vasopressin V2 receptor antagonist tolvaptan for pharmacodynamic activity and preliminary efficacy and safety in children/adolescents with early manifesting ADPKD.

Methods: Phase 3b, 2-part trial (EudraCT 2016-000187-42). Phase A (reported here) was a 1-year (y), randomized, double-blind, placebo-controlled, multicenter trial; Phase B is an ongoing, 2-y, open-label extension. Eligibility criteria: ADPKD (renal cysts with family history and/or genetic diagnosis), eGFR ≥60 mL/min/1.73m^2, body weight ≥20 kg. The target population was age 12-17y; subjects 4-11y could also enter if eligible. Tolvaptan/placebo were titrated based on body weight and tolerability. Co-primary endpoints: changes from baseline in spot urine osmolality (Uosm) and specific gravity (SG) at Week 1. Additional endpoints: 12-month changes in height-adjusted total kidney volume (htTKV) and eGFR, safety/tolerability. Statistical comparisons were exploratory and post hoc.

Results: Of 91 subjects enrolled (66 age 12-17y; 25 age <12y), 48 were randomized to tolvaptan and 43 to placebo. Mean reduction (±SD) from baseline to Week 1 (tolvaptan vs placebo): 386 (284) vs 93 (332) mOsm/kg for Uosm (P<.001) and 0.009 (0.007) vs 0.002 (0.008) for urine SG (P<.001). In subjects 12-17y, mean %htTKV increase from baseline to Month 12 was 2.3% (8.8) for tolvaptan and 6.1% (7.5) for placebo (P=.14). Mean eGFR change from Day 7 to Month 12 (all subjects) was 2.7 (10.7) mL/min/1.73m^2 for tolvaptan, -3.2 (10.9) mL/min/1.73m^2 for placebo (P=.10). Most frequent adverse events over 12 months (tolvaptan/placebo): polyuria (25.0/2.3%), elevated serum creatinine (18.8/4.7%), pollakiuria (18.8/0.0%), cough (14.6/11.6%), and nocturia (14.6/4.7%). No elevated transaminases or drug-induced liver injury. Serious adverse events in 1 tolvaptan (viral pericarditis) and 6 placebo, none treatment-related. One discontinuation due to pollakiuria (tolvaptan), 1 due to dizziness (placebo).