LB-OR01

The Fish Oil Inhibition of Stenosis in Hemodialysis Grafts (FISH) Study

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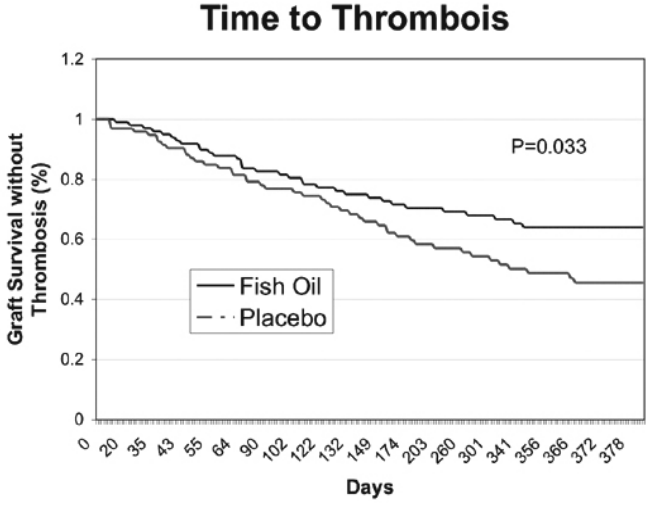
Background: Arteriovenous grafts are an important option for hemodialysis vascular access but are prone to stenosis and thrombosis.

Methods: We conducted a multi-centre, randomized, double-blind, placebo-controlled clinical trial to evaluate the effect of fish oil capsules on graft patency for patients with endstage renal disease. Two hundred and two patients from Canada and the United States requiring a new arteriovenous graft access for chronic hemodialysis were randomly assigned to receive daily fish oil capsules or a matching placebo. Loss of graft patency was defined by graft thrombosis or a radiological or surgical intervention during 12 months of follow-up after graft creation.

Results: During a median follow-up of 11.9 months, the risk of the primary outcome did not differ between fish oil and placebo recipients (48/99 [48%] vs 60/98 [61%]; relative risk 0.79 [95% CI, 0.60 to 1.04; P = 0.072]). However, the rate of graft failure was less in the fish oil group (3.43 versus 5.94 per 1,000 access days; P < 0.001). In the fish oil group, there were about half as many thrombosis events (1.71 versus 3.40 per 1,000 access days; P < 0.001); longer time to first thrombosis (P = 0.033); and fewer instances of radiological or surgical interventions (2.89 versus 4.91 per 1,000 access days; P < 0.001).



There were no differences in bleeding events or other significant complications between groups.

Conclusions: Provision of daily fish oil capsules to patients requiring a new hemodialysis graft access may be a safe and effective method to reduce the rate of thrombosis and the frequency of needed radiological or surgical interventions (ISRCTN 15838383).

Funding: Private Foundation Support, Government Support - Non-U.S.

LB-OR02

Reduced Rate of Cutaneous Squamous Cell Carcinomas after Conversion to Sirolimus-Based Immunosuppression in Stable Renal Transplant Recipients: A Randomized, Prospective, Open-Label Multicenter Study

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Background: Cutaneous squamous cell carcinomas (SCC) cause significant morbidity and mortality in renal transplant recipients (RTR). Available evidence suggests that conversion to a regimen with sirolimus may inhibit skin tumor growth. This randomized, prospective, multi-center trial investigated whether switching maintenance immunosuppression to sirolimus could diminish the recurrence rate of SCC.

Methods: One-hundred-fifty-five RTR in the Netherlands and the United Kingdom with at least one biopsy-confirmed SCC were randomized to sirolimus (n=74) or continuation of their original immunosuppression (n=81). They were evaluated every three months for 2 years by a dermatologist for SCC and for side effects of the treatment by a nephrologist.

Results: Survival analysis revealed that the time to recurrent SCC was delayed in the sirolimus group. The Risk of SCC recurrence in the sirolimus arm was significantly reduced (adjusted HR=0.54: CI 0.32-0.91; p=0.021). Also the total amount of SCC developing per follow up year differed in favor of sirolimus therapy (0.91 versus 2.50). The adjusted relative risk for developing new SCC per year was 0.36 (95% CI: 0.20-0.64), representing a 64% reduction in the risk of developing SCC with sirolimus compared with a non sirolimus-based regimen (p<0.001). Twenty-nine patients in the sirolimus treatment group stopped using sirolimus because of various adverse events.

Conclusions: Conversion to sirolimus-based immunosuppression in RTR delays the development of subsequent skin SCC and total number of skin SCC in those patients maintained on sirolimus.

Funding: Pharmaceutical Company Support

LB-OR03

Multicenter Randomized Controlled Trial Comparing Efficacy of Tacrolimus to Intravenous Cyclophosphamide in Children with Steroid Resistant Nephrotic Syndrome

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Background: While tacrolimus & IV cyclophosphamide (CP) are preferred therapies for steroid resistant nephrotic syndrome (SRNS), they have not been compared prospectively. Results of a multicentric RCT on their comparative efficacy & safety are presented. CTRI/2008/091/000215

Methods: Following ethics approval & parental consent, 131 new patients with idiopathic SRNS (1-16 yr) with minimal change (77) or focal glomerulosclerosis (FSGS, 53) & eGFR >60 ml/min/1.73m^2 were studied. They were stratified for initial (n=80) or late resistance (51) & randomized to therapy with tacrolimus (trough 5-8 ng/ml) for 12-months or IV CP (500 mg/m^2 monthly) for 6 doses. They also received prednisone (1.5 mg/kg alt.day, taper to 0.3 mg/kg) & enalapril for 12-mo. Primary outcome, at 6-mo, was proportion with complete (urine protein/creatinine, Up/Uc <0.2 mg/mg) or partial remission (Up/Uc 0.2-2; albumin >2.5 g/dl; no edema). Treatment failure was non-response/withdrawal of therapy (>1 serious infection;50% fall in GFR). Outcome at 12-mo was proportion with sustained remission or steroid sensitive nephrotic syndrome.

Results: Baseline features were comparable (Table). Therapy with tacrolimus led to significantly higher rates of complete & sustained remission at 6 & 12-mo. On multivariate regression, the odds of remission were significantly higher with tacrolimus (OR 6.1; 95% CI 2.6, 14.1); and lower with FSGS (OR 0.45; 0.2, 0.96). Treatment was withdrawn in 10 patients in CP group due to serious infections (8) & fall in GFR (2).

Baseline	**Tacrolimus, n=66**	**IV Cyclophosphamide, n=65**
Age, mo	62.1±39.1	74.5±43.9
Albumin, g/dl	2.2±0.7	2.3±0.7
Urine protein/creatinine ratio, mg/mg	6.5±4.8	5.3±2.9
Primary outcome, n (%)	n=63	n=60
Complete remission*	33 (52)	9 (15)
Partial remission	19 (30)	19 (32)
Treatment failure*	11(18)	32 (53)
Outcome @12-months	n=63	n=60
Remission/sensitive nephrotic syndrome (%)*	63.4	23.3
Reduction eGFR#, ml/min/1.73m^2	9.0	-1.8

P *<0.001, #0.2

Conclusions: Therapy with tacrolimus is effective & safe in inducing sustained remission, and should form the standard of care for children with steroid resistant nephrotic syndrome.

Funding: Government Support - Non-U.S.

LB-OR04

A Randomized Cross-Over Muticenter Trial of Mycophenolate Mofetil Versus Cyclosporin A in Children with Frequently Relapsing Nephrotic Syndrome

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Background: Treatment of children with frequently relapsing steroid sensitive nephrotic syndrome (FR-SSNS) is complicated by side effects of corticosteroids and cyclosporin A (CsA). We compared efficacy and safety of mycophenolate mofetil (MMF) and CsA in patients with FR-SSNS in a prospective randomized multicenter open-label crossover trial.

Methods: After obtaining remission, 60 patients with SR-SSNS (age 3.5-18) were randomized in two groups: the first group was treated with MMF at a starting dose of 1000 mg/m2 BSA/d, than adapted to trough level of mycophenolic acid (MPA) during the first year followed by CsA (target trough level 80 -100 ng/ml) in the second year. The second group was treated with CsA in the first year and with MMF in the second year. Primary endpoint: Frequency of relapses during treatment in both groups. Secondary endpoints: eGFR (cystatin C), mean systolic blood pressure on ambulatory blood pressure monitoring (ABPM), lipoprotein profile after 12 and 24 months. MPA-area under the curve (AUC) profiles were analyzed after 3 and 6 months.

Results: No relapses were observed in 84% of patients (13 relapses/ 9 patients) during CsA- therapy and in 64% (44 relapses/ 21 patients) during MMF- therapy (p=0.05). A low exposure to MMF was associated with more frequent relapses: MPA-AUC< 50g*h/ml = 1.3 relapses /patient; AUC > 50g*h/ml = 0.18 relapses/ patient. Patients with an MPA-AUC >50g*h/ml had a significantly longer initial remission time

Underline represents presenting author/disclosure.

than patients with a lower MMF exposure, which was not significantly different from initial remission time in CsA-treated patients. The GFR was higher (146 vs. 118 ml/min*1.73m2 BSA) and the triglycerides and cholesterol levels lower in the MMF group compared to the CsA group (TG 87 vs. 96 mg/dl; Chol 173 vs. 181 mg/dl); there was no significant difference in ABPM.

Conclusions: Treatment with CsA was superior to MMF in preventing relapses in patients with FR-SSNS. However, relapses on MMF treatment were associated with lower drug exposure, indicating the need for pharmacokinetic monitoring. Considering risks and benefits, lack of nephrotoxicity makes MMF a valuable option for treatment of FR-SSNS.

Funding: Pharmaceutical Company Support, Clinical Revenue Support

LB-OR05

Effects of Intensive Diabetes Therapy on Glomerular Filtration Rate in Type 1 Diabetes: Results from the DCCT/EDIC [Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications Study]

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Background: Impaired glomerular filtration rate (GFR) leads to end stage renal disease and increases risks of cardiovascular disease and death. Persons with type 1 diabetes are at high risk of kidney disease, but no interventions are proven to prevent the development of impaired GFR in this population.

Methods: The Diabetes Control and Complications Trial (DCCT) randomly assigned 1,441 persons with type 1 diabetes to intensive diabetes therapy, aimed at lowering glycemia as close to the non-diabetic range as safely possible, or conventional diabetes therapy, aimed at preventing symptoms of hyperglycemia, for a mean treatment duration of 6.5 years. Subsequently, 1,375 participants were followed in the observational Epidemiology of Diabetes Interventions and Complications Study (EDIC). Serum creatinine was measured annually throughout DCCT/EDIC, and GFR was estimated using the CKD-EPI formula. Impaired GFR was defined as estimated GFR < 60 mL/min/1.73m^2 on two consecutive study visits.

Results: Over 22 years median DCCT/EDIC follow-up, 24 participants assigned to intensive therapy and 46 assigned to conventional therapy developed impaired GFR (risk reduction 50%, 95% confidence interval 18%, 69%, p=0.006). Of these, 8 and 16 developed end stage renal disease, respectively. Compared to conventional therapy, intensive therapy reduced mean estimated GFR by 1.7 mL/min/1.73m^2 during the DCCT but slowed rate of GFR loss and increased mean estimated GFR by 2.5 mL/min/1.73m^2 during EDIC (each p<0.0001). The beneficial effect of intensive therapy on impaired GFR was fully explained by lower hemoglobin A1c and lower albumin excretion rate.

Conclusions: Intensive diabetes therapy reduced the risk of developing impaired GFR in type 1 diabetes. Small short-term reductions in GFR within the normal range were followed by long-term GFR preservation.

Funding: NIDDK Support

LB-OR06

Vitamin D Therapy and Cardiac Structure, Function, and Cardiovascular Events

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Background: Vitamin D has been associated with cardiovascular risk, yet the role of vitamin D therapy in preventing cardiovascular disease is not known. We tested whether an active vitamin D compound attenuates cardiac hypertrophy, improves diastolic function, and lowers cardiovascular events.

Methods: We randomly assigned 227 patients (from 11 countries) with mild to moderate left ventricular hypertrophy, normal ejection fraction, and chronic kidney disease (estimated glomerular filtration rate 15 to 60 ml per minute per 1.73m2) to 48 weeks of treatment with oral paricalcitol (19-nor-1,25-(OH)2-vitamin D2) 2 mg per day or placebo. The primary endpoint was a change in left-ventricular mass index by cardiovascular magnetic resonance. Secondary endpoints included echocardiographic measures of diastolic function, cardiovascular related events, and changes in cardiac biomarkers.

Results: Treatment with paricalcitol lowered parathyroid hormone levels within 4 weeks, and in this group levels remained within the normal range for the study duration.

The remaining Results will be presented.

Conclusions: The Conclusion will be presented. (Funded by Abbott Laboratories; ClinicalTrials.gov number, NCT00497146)

Funding: Pharmaceutical Company Support

LB-PO3142

Immunogenicity of Investigational HEPLISAV Compared with Licensed Hepatitis B Vaccine (Engerix-B) in Patients with Chronic Kidney Disease (CKD)

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Background: Hemodialysis patients are at increased risk of hepatitis B virus (HBV) infection and CKD patients are commonly hypo-responsive to HBV vaccines. Current recommendations for CKD patients require 4 double-doses (2x20 mcg rHBsAg) of Engerix-B (EB).

Methods: A multicenter, observer-blinded, phase 3 study was conducted among 516 patients 18-75 years of age with CKD (GFR ≤ 45 mL/min/1.73 m2), comparing 3 doses of HEPLISAV (20 mcg rHBsAg + 3000 mcg 1018 immunostimulatory sequence, a toll-like receptor 9 agonist) given at 0, 1, and 6 months to 4 double-doses of EB (2x20 mcg rHBsAg) given at 0, 1, 2, and 6 months. The primary objective was to determine if HEPLISAV is non-inferior to EB by comparing seroprotection rates (SPR = anti-HBs ≥ 10mIU/mL) 4 weeks after the last dose of vaccine (Month 7) and if non-inferior, to determine if HEPLISAV was superior to EB. Safety is being evaluated for one year after the first study injection. Eligible subjects had no previous HBV infection or vaccination and were judged to be clinically stable. Beginning in September 2009, subjects were recruited at 69 sites in the US, Canada, and Germany and were randomized 1:1 to receive HEPLISAV or EB (stratified by site and GFR [≤ 15, 16-30, and 31-45 mL/min/1.73 m2]). An immunogenicity analysis for the primary endpoint and an interim safety analysis were performed after the last subject completed their Month 7 visit.

Results: Among 467 subjects in the modified intent-to-treat population (225 HEPLISAV; 242 EB), the mean age and gender distribution was similar in both groups. At Month 7, the SPR in the HEPLISAV group was 89.8% (95% CI: 85.1%, 93.4%) and in the EB group was 81.8% (95% CI: 76.4%, 86.5%). The difference in SPRs (HEPLISAV minus EB) was 8.0% (95% CI: 1.6%, 14.2%). The lower limit of the CI was above the pre-specified non-inferiority criterion of -10% and superiority criterion of 0%. The incidence of post-injection reactions and adverse events were similar in both groups.

Conclusions: In CKD patients, HEPLISAV given as 3 doses induced a superior immune response to EB given as 8 doses and had a similar safety profile.

Funding: Pharmaceutical Company Support

LB-PO3143

A Randomized Controlled Trial of Gentamicin/Citrate Versus Heparin Locks for Central Venous Catheters in Maintenance Hemodialysis Patients

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Background: The major complications of central venous catheters (CVC)as vascular access in hemodialysis are catheter-related bloodstream infection (CRBSI) and clotting in the catheter lumen. An ideal locking solution would prevent both complications.

Methods: Parallel group randomized multicenter clinical trial, with patients blinded to study intervention.

Setting & Participants: 16 free-standing dialysis facilities in Northern California. It included 303 patients using a tunneled cuffed CVC for vascular access.

Intervention: The treatment group received a lock containing gentamicin 320 µg/mL in 4% sodium citrate; the control group received heparin 1,000 U/mL. Both groups received triple antibiotic ointment on the catheter exit site at dressing changes with each dialysis.

Outcomes: CRBSI and catheter clotting

Measurements: CRBSI was defined as the occurrence of symptoms of bacteremia together with positive blood cultures in the absence of another obvious source of infection. Catheter clotting was measured as the rate of thrombolytic agent usage to maintain adequate blood flow.

Results: The rate of CRBSI was 0.91 episodes and 0.28 episodes per 1,000 catheter-days in the control and treatment groups respectively (p = 0.003). The time to the first episode of bacteremia was significantly delayed (p = 0.005). The rate of tPA usage was similar in the control and treatment groups, 3.42 vs. 2.36 per 1,000 catheter-days, respectively (p = 0.2).

Results

Group	Control	Treatment	P value
Patient number	148	155	
Total days of follow-up	32,933	39,827	
Days at risk per patient	222.9	256.9	0.2
Episodes of bacteremia	30	11	
Episodes of bacteremia/1,000 catheter days	0.91	0.28	0.003
tPA usage/1,000 catheter days	3.42	2.36	0.2

Conclusions: Gentamicin 320 µg/mL in 4% sodium citrate markedly reduces the incidence of CRBSI, and is as effective as heparin 1,000 U/mL in preventing catheter clotting.

Funding: Clinical Revenue Support

Underline represents presenting author/disclosure.

LB-PO3144

Safety and Efficacy of the Vasopressin V_2-Receptor Antagonist, Lixivaptan, in Outpatients with Euvolemic Hyponatremia

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Background: Historically, treatments for chronic hyponatremia have been limited by poor efficacy, tolerability, and potential safety concerns. Vasopressin receptor antagonists (AVP-A) have shown promise in the treatment of the condition. However, their use has been limited by their approved labeling requiring in-hospital initiation/re-initiation of therapy and costs.

Methods: In this multicenter, randomized, double-blind, placebo-controlled, phase 3 study, the efficacy, safety, and tolerability of chronic oral lixivaptan, a selective V_2 AVP-A, were evaluated for treatment of non-hospitalized subjects with euvolemic hyponatremia (sodium <135 mmol/L). Subjects received placebo (n=52) or lixivaptan (n=154) at 25–100 mg/day for a maximum of 24 weeks. Therapy was initiated in an outpatient setting and titrated based on daily serum sodium measurements. The population included approximately 40% of elderly subjects in chronic care.

Results: Serum sodium concentrations (sNa) increases from baseline to Day 7 (primary efficacy endpoint) were 3.2±0.5 mmol/L for lixivaptan vs 0.8±0.6 mmol/L for placebo (p <0.001). The effects were maintained over the entire 24-week treatment period in spite of significantly lower need for fluid restriction in the lixivaptan arm. A significantly greater proportion of subjects receiving lixivaptan achieved normalized sNa by Day 7 relative to placebo (39.4% vs 12.2%; p <0.001). SNa decreased within 7 days of discontinuation of study drug to the PBO levels.

Conclusions: Oral lixivaptan was well tolerated and can be safely initiated in the outpatient setting while effectively increasing sNa in euvolemic hyponatremia.

Funding: Pharmaceutical Company Support

LB-PO3145

Efficacy of Cinacalcet Combined with Low Dose Vitamin D in Incident Hemodialysis Subjects with Secondary Hyperparathyroidism

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Background: Incident dialysis patients have a high prevalence of SHPT and initial treatment typically includes vitamin D, calcium supplements, and phosphate binders. Cin therapy is commonly used later in the course of the disease in patients who are not adequately controlled with vitamin D.

Methods: To evaluate the efficacy of Cin+LDVD initiation in incident HD subjects, we conducted a randomized, open-label trial in subjects on dialysis for 3-12 months with SHPT (PTH>300 pg/mL). Subjects (N=309) were randomized 1:1 to either Cin+LDVD (=2.0 mcg IV paricalcitol or equivalent per dialysis session if prescribed) or, flexible dosing of vitamin D (if prescribed) alone (Flex-D). Randomization was stratified by PTH at screening (300-450, >450-600, and >600 pg/mL) as well as by the use of vitamin D at enrollment. The total treatment duration was 12 months, whereas the primary efficacy endpoint was assessed at 6 months.

Results: Baseline characteristics were well balanced between treatment arms. Mean (SD) dialysis vintage at enrollment was 7.2 (2.7) months. Of note, 54% of study subjects were not on vitamin D at enrollment representing a subset of relatively treatment naïve subjects. There was a statistically significant difference (p<0.0001) in achievement of the primary endpoint (≥30% PTH reduction at 6 months) between subjects treated with Cin+LDVD (63%) and the Flex-D (38%) group. Results favoring Cin+LDVD were observed across all PTH strata. In addition, the magnitude of the reductions in PTH among Cin+LDVD treated subjects did not differ according to prior vitamin D use at enrollment. A greater proportion of subjects given Cin+LDVD (57%) compared with Flex-D (35%) achieved PTH£300 pg/mL at 6 months (p=0.0002).

Conclusions: These results indicate that cinacalcet with low dose vitamin D provides a more effective treatment approach than flexible doses of vitamin D alone for SHPT in incident HD patients regardless of disease severity.

Funding: Pharmaceutical Company Support

LB-PO3146

A Prospective Multicenter Study of Vitamin E Bonded Polysulfone Membrane for Erythropoiesis Stimulation Agents in Hemodialysis Patients (VEESA-STUDY) by Vitamembrane Study Group

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Background: Hemodialysis patients with renal anemia are required for an administration of Erythropoiesis Stimulation Agents (ESA) to maintain Hb level. Some reports exhibited the positive effects of biocompatible dialyzers to reduce ESA dosage. However, the effects of dialyzers are not confirmed by multicenter randomized controlled trial (RCT).

Methods: We conducted a RCT with multicenter design to improve effectiveness of vitamin E bonded polysulfone dialyzer (VPS) for managements of anemia conditions of hemodialysis patient. Inclusion criteria were (1) TSAT is more than 20%, (2) hemoglobin level is from 10.0 to 12.0 g/dL, (3) epoetin beta or darbepoetin alfa is administered, and (4) high flux polysulfone dialyzers were used before enrollment.

Results: 305 patients of 48 centers were enrolled. The subjects were divided in 2 groups (A:VPS, B:control PS). Interim analysis showed that ESA index significantly decreased at more than 7 month treatment period in VPS group compare to the control PS group in the patients subgroup with hemoglobin range from 11.0 to 12.0 g/dL.

Conclusions: Vitamin E bonded PS dialyzer might have positive effect to manage anemia condition for the hemodialysis patients by reducing ESA index.

The trial was registered in UMIN clinical trial registed system (UMIN 000001285).

LB-PO3147

Results of a Phase 2 Study Evaluating the Safety and Efficacy of KAI-4169, A Novel Peptide for the Treatment of Chronic Kidney Disease-Mineral and Bone Disorder in Hemodialysis Subjects

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Background: KAI-4169, a novel, long-acting peptide agonist of the calcium sensing receptor (CaSR), is being evaluated in hemodialysis (HD) subjects as a treatment for chronic kidney disease-mineral and bone disorder (CKD-MBD). This Phase 2 randomized, double-blind, placebo-controlled, dose escalation study evaluated the safety and efficacy of KAI-4169 administered thrice weekly by IV bolus during HD. The primary endpoint was the mean percent change from baseline in intact parathyroid hormone (iPTH).

Methods: Seventy-eight subjects (10, 42 and 26 in Cohorts 1, 2 and 3, respectively) were randomized and treated. Subjects were treated for 2 weeks in Cohort 1 (5 mg) and 4 weeks in Cohorts 2 (10 mg) and 3 (5 mg). Main inclusion criteria: serum iPTH ≥350 pg/mL, cCa ≥9.0 mg/dL and stable doses of vitamin D. Subjects on cinacalcet discontinued treatment ≥2 weeks prior to screening.

Results: KAI-4169 treatment was well-tolerated. No drug-related GI AEs were reported. No subject developed symptomatic hypocalcemia or discontinued due to an AE. KAI-4169 at 5 mg and 10 mg resulted in 33% and 49% reduction from baseline in iPTH at the end of the treatment period (P <0.05 vs. placebo).

Mean Serum iPTH (pg/mL)

	Cohort 1 (2 weeks)		Cohort 2 (4 weeks)		Cohort 3 (4 weeks)	
	Placebo	KAI-4169 5 mg	Placebo	KAI-4169 10mg	Placebo	KAI-4169 5 mg
Baseline	636	588	602	765	619	662
End of Treatment	648	462	734	376	608	517
% Change from Baseline	0.3%	-19%	28%	-49%	2.3%	-33%

In the 10 mg cohort, 76% of subjects achieved ≥30% reduction in iPTH and 67% of subjects achieved an iPTH £300 pg/mL at the end of the treatment period. The mean % change in serum calcium was -6% and -13% in the KAI-4169 5 mg and 10 mg treatment groups, respectively.

Conclusions: KAI-4169, a novel CaSR peptide agonist resulted in profound, sustained, dose-dependent reductions in iPTH without significant hypocalcemia or GI adverse events. KAI-4169 represents a novel therapeutic approach for the treatment of CKD-MBD.

Funding: Pharmaceutical Company Support

LB-PO3148

HFR-Aequilibrium International Multicentric Study (AIMS): Focus on Intradialytic Cardiovascular Stability

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Background: Intradialytic hypotension (IDH) is still a major clinical problem for hemodialysis patients (pts). Hemodiafiltration, including a variant with endogenous ultrafiltrate reinfusion (HFR) seems to reduce the incidence of IDH. The sodium kinetic biofeedback HFR-Aequilibrium (HFR-Aeq) allows the achievement of a preset final plasma sodium (Na) level by a continuous Na measurement (Natrium sensor) and its control by dialysate conductivity and uf rate.

Aim of this cross-over randomized study was the evaluation of HFR-Aeq on intradialytic cardiovascular stability and nurse intervention.

Methods: Fifty hypotension-prone pts on thrice-weekly hemodialysis were enrolled. After a month run-in period, patients were randomized to two treatments lasting 2 months each: HFR-Aeq or HFR, followed by a month of HFR (wash-out), then switched to the other treatment. Blood pressure was measured every 30 minutes during the session. Intradialytic symptoms and nurse interventions were assessed. ANOVA for repeated measurement, Wilcoxon or Chi-square tests were used as appropriate.

Results: IDH episodes and nurses interventions were significantly reduced in HFR-Aeq while systolic blood pressure resulted more stable on higher values (Table I; Data expressed as mean±SEM).

Underline represents presenting author/disclosure.

Treatment tolerance

Primary end-point			
All pts. (N=43)	HFR	HFR-Aeq	Wilcoxon
IDH episodes	31±4%	23±3%	p=0.03
Odds ratio analysis			
All pts. (N=43)		HFR-Aeq/HFR	Chi-square
IDH		0.74	p=0.04
Other symptoms		0.62	p=0.01
Interventions		0.67	p=0.01
Average Blood pressures over dialysis			
All pts. (N=43)	HFR	HFR-Aeq	Wilcoxon
SBP, mmHg	115±4	118±3	p=0.01
DBP, mmHg	62±2	63±1	p=0.08

Dry weight (68.0±2.0 kg in HFR and 68.5±2.0 kg in HFR-Aeq) and weight loss (2.4±0.1 kg in HFR and 2.5±0.1 kg in HFR-Aeq) didn't vary significantly. Pre-dialysis average plasma Na was 138.6±3.0 in HFR and 139.4±3.4 in HFR-Aeq (p=ns).

Conclusions: We found that HFR-Aeq can significantly affect the daily dialysis practice by reducing IDH occurrence and the consequent clinical interventions.

Funding: Government Support - Non-U.S.

LB-PO3149

A Randomized Trial Comparing Buttonhole to Standard Needling in Conventional Hemodialysis Patients

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Background: Apprehension and fear of needling among hemodialysis (HD) patients is common and may impact choice of vascular access. Buttonhole needling (BN), a technique adopted from nocturnal dialysis patients, uses a constant site for arterial and venous needles in a fistula. Repeated needling forms an epithelial track that accommodates a blunt buttonhole needle. Studies report that BN is associated with less pain than standard needling (SN), which rotates needling sites. We undertook a randomized trial to compare BN and SN techniques on patient perceived pain and fistula complications.

Methods: 140 conventional HD patients on thrice weekly in-centre HD using a fistula, were randomized to BN (n=70) or SN (n=70) techniques. The primary outcome was patient perceived pain with needling at 8 weeks. Perception of pain was obtained by an individual blinded to the needling using a validated 10 cm visual analogue scale at baseline (3 dialysis runs at week 1) and again at week 8 (3 dialysis runs). Secondary outcomes included fistula complications of hematoma, nursing difficulty with needling and infection.

Results: Of the 140 study patients 131 completed the study: 66 SN and 65 BN. All patients were included in the intention to treat analyses. The mean pain score at 8 weeks was similar for BN and SN (2.10 vs 1.73, p=0.572). More patients developed a hematoma in SN (25/70, 36%) than BN (12/70, 17%), p=0.0127. Difficulty of needling was significantly higher for both arterial (0.47 vs 0.11, p=0.0008) and venous needles (0.20 vs 0.55, p=0.0008) in BN vs SN. Signs of potential infection (erythema, pus or swelling of the fistula) were similar for SN 25/70 and BN 16/70, p=0.094. There was one episode of bacteremia (staphylococcal aureus) at week 6 in BN and none in SN. After study completion, 6 BN and no SN patients developed a bacteremia.

Conclusions: We found no difference in patient perceived pain with BH or SN needling techniques. While fewer patients develop a hematoma with [A name=_ GoBack][/A]BN, there was an increased risk of bacteremia. Routine use of buttonhole in conventional HD does not reduce pain and may result in an increased risk of bacteremia.

Funding: Government Support - Non-U.S.

LB-PO3150

Visit-to-Visit Blood Pressure Variability Is a Strong Predictor of Cardiovascular Events in End-Stage Renal Disease: Insights from the Fosinopril in Dialysis (FOSIDIAL) Study

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Background: Optimal blood pressure (BP) targets are still controversial in End-stage renal disease (ESRD). Recent data have highlighted shortcomings of the usual BP hypothesis in other patient populations, and emphasized the importance of visit-to–visit variability of BP in predicting cardiovascular events (CVE). The Fosinopril in Dialysis (FOSIDIAL) study failed to demonstrate the efficacy in preventing CVE (composite primary endpoint) of two-year angiotensin-converting enzyme inhibition with fosinopril versus placebo in 397 hemodialysis patients with left ventricular hypertrophy, but provided an opportunity to assess the influence of BP variability on CVE.

Methods: The variations in BP throughout the 17 visits were assessed by within-patient overall variability of systolic, diastolic and pulse pressures between adjacent readings (SDSBPV, SDDBPV, SDPPV), their corresponding coefficients of variation (CV: CVSBPV, CVDBPV, CVPPV), by within-patient overall variability of systolic/diastolic/pulse pressures [standard deviation of the series (SDSBP, SDDBP, SDPP) and their CV: CVSBP, CVDBP, CVPP], and the residual of the linear fit.

Results: Compared to our previous predictive model of CVE occurrence, the percentage of explained variance improved by 30.1% (R^2=0.141 to 0.184) when adding CVSBP. Usual BP parameters were neither CVE predictors, nor correlated to BP variability. Baseline antihypertensive medications, body mass index and history of stroke were modest predictors of CVSBP (R^2=0.051).

Conclusions: Visit-to-visit BP variability was extremely high in hemodialysis patients compared to other populations, and a major determinant of CVE. Such assessments should be prioritized for testing prevention strategies in ESRD.

LB-PO3151

A Randomized Controlled Crossover Trial for Nephropathic Cystinosis Demonstrates a Twice Daily Gastroresistant Cysteamine Is Not Inferior to Every Six Hour Cystagon

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Background: Cysteamine bitartrate immediate release (CBIR), is the only Rx for cystinosis that prevents/delays kidney failure & its other serious outcomes, but requires adherence to q6h dosing lifelong. This schedule and CBIR-associated side effects cause nonadherence, suboptimal treatment & ensuing kidney failure & other problems of disease progression. An efficacious delayed-release (DR) formulation would be desirable.

Methods: We powered an open-label, randomized, controlled, crossover trial to show that a new DR ("gastroresistant") cysteamine bitartrate, RP103, was non-inferior to CBIR (Cystagon®), in maintaining a surrogate marker, WBC[cystine] at baseline or < 0.3 nmol ½ cystine/mg protein greater (non-inferiority margin). Subjects were stratified by their WBC[cystine] baseline value (0 to 1 or >1 to 2) before being randomized to Cystagon® or RP103, for 3wks, & then crossed over to the other Rx. Total daily dose (TDD) of RP103 = 70% of Cystagon® TDD at start & adjusted once based on WBC[cystine]. Patients stopped PPIs on RP103.

Results: 43 cystinosis pts & native kidney eGFR > 30 mL/minute/1.73 m2 were randomized. Using a mixed-effects model, the least-square-mean peak of WBC[cystine] after 12h under RP103=0.62±0.05 & after 6 hours under CBIR=0.54±0.05 nmol½cystine/mg protein; the difference=.08±.04 nmol½cystine/mg protein (95.8% confidence interval 0 to .16' p=NS). The mean TDD of RP103=82% of Cystagon® TDD. PK([cysteamine]) & PD (WBC[cystine]) profiles with RP103 (12h) were comparable to PK/PD profiles with Cystagon® (6h). No unexpected side effects were noted vs Cystagon®, & no difference in patient #s having GI side effects.

Conclusions: The gastroresistant Q12H formulation of cysteamine bitartrate is not inferior to marketed Q6H CBIR in maintaining low WBC[cystine] in patients with cystinosis, but at a lower TDD & with reduced use of PPIs.

Funding: Pharmaceutical Company Support

LB-PO3152

A Double-Blind, Randomized, Placebo-Controlled Multicenter Trial To Compare the Phosphate Lowering Efficacy of Different Doses of the Iron-Based Phosphate Binder SBR759 to Placebo

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Background: SBR759 is an iron-based oral phosphate binder that has been under development for use in CKD stage V patients with hyperphosphatemia.

Methods: CSBR759A2304 is a phase III, double-blind, placebo-controlled 4+2 week treatment/recovery trial to assess the phosphate lowering efficacy and dose response of 4 doses of SBR759 (3, 6, 9, and 12 g/day) compared to placebo.

Results: Tab-1 shows the results of the mean change from baseline(BL) in serum phosphate concentrations(PO4) in each SBR759 group over 4 weeks(W). In the 4 SBR759 groups, a significant PO4 reduction was achieved at W4 compared to placebo. A significant linear dose-response trend was demonstrated (p<0.001).

Table-1

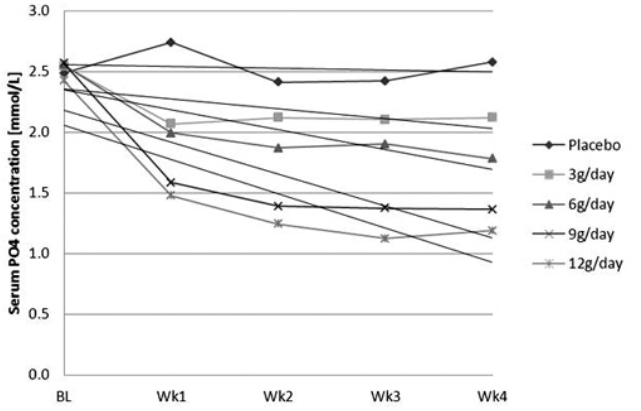
	Placebo	SBR759 (3g/d)	SBR759 (6g/d)	SBR759 (9g/d)	SBR759 (12g/d)
LS Mean (SE)	0.190 (0.0969)	-0.409 (0.0931)	-0.809 (0.0970)	-1.205 (0.0933)	-1.209 (0.0977)
Difference		-0.599	-0.998	-1.395	-1.398
Linear trend test p<0.001					

ANCOVA of change from baseline in serum phosphate concentration (mmol/L) to week 4

The evolution of mean PO4 by treatment and visit is displayed in Fig-1.

Underline represents presenting author/disclosure.

Fig-1 Evolution of mean serum phosphate concentrations by treatment and visit



Following treatment withdrawal a relevant increase in PO4 re-confirmed efficacy of SBR759. Overall, no deaths occurred during study conduct; SAEs were observed in 2 SBR759 patients (3g, 12g/day) and 3 AEs leading to study drug discontinuation. Most frequent AE were GI disorders, including discolored feces, diarrhea and vomiting. AE were equally distributed and similar in SBR759 and placebo treated patients.

Conclusions: Study CSBR759A2304 demonstrates dose-dependent and significant phosphate lowering efficacy of SBR759 compared to placebo confirming favorable safety and tolerability that is almost similar to placebo.

Funding: Pharmaceutical Company Support

LB-PO3153

Dialysate Consumption and Dialysis Dose in On-Line Hemodiafiltration with Automated Coupling Dialysate/Blood Flow Function (Autoflow Function)

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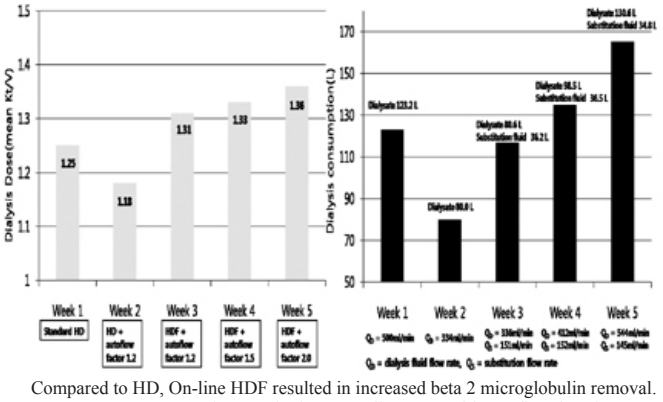
Background: The purpose of this study is to compare concerning dialysate consumption and dialysis dose between standard hemodialysis (HD) and pre-dilutional hemodiafiltration (HDF) with autoflow function.

Methods: Eighteen dialysis patients were treated with F60S and HF80S dialyzers (88.9% and 11.1%, 5008S machine) for 5 weeks. The patients were consecutively treated as follows: 1) week 1: standard HD, 2) week 2: HD with autoflow function(factor 1.2), 3) week 3: HDF with autoflow function (factor 1.2), 4) week 4: HDF with autoflow function (factor 1.5), 5) week 5: HDF with autoflow function(factor 2.0). The parameters were acquired from the machine displays: effective blood flow rate, mean dialysate flow rate, ultrafiltration rate/volume, cumulated blood volume, effective dialysis time, Kt/V(OCM). The pre/post-dialytic blood samples of beta 2 microglobulin were obtained at the end of each week.

Results: All of patients completed the study and 270 treatments were analyzed. In standard HD treatment (week 1), the mean delivered dose of dialysis and mean dialysate consumption for all patients was 1.25 ± 0.04 Kt/V and 123.2 ± 2.5L. By applying the autoflow factor 1.2 (week 2), mean dialysis dose and dialysate consumption decreased to 1.18 ± 0.04 Kt/V and 80.0 ± 3.8L. However, by using autoflow factor 1.2 in on-line HDF(week 3), mean dialysis dose increased 1.31 ± 0.06 Kt/V and dialysate consumption was 116.8 ± 3.4L(included dialysate and substitution fluid).



Compared to HD, On-line HDF resulted in increased beta 2 microglobulin removal.

Conclusions: Compared to standard HD, On-line HDF with autoflow function resulted in elevated dialysis doses(week 1 vs week 3, Kt/V: +4.8%, p<0.05), lower amounts of dialysate consumption(week 1 vs week 3, -5.2%, p<0.05).

LB-PO3154

Therapeutic Interventions To Control Blood Pressure, Proteinuria and Dyslipidemia for Delaying the Progression of Nephropathy in Type 2 Diabetic Subjects – Preliminary Report from BNDC Trial in BIRDEM, Bangladesh

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Background: In this study the efficacy of a prefixed, least expensive, drug regimen achieving control of blood glucose, blood poressure, prteinuria and dyslipidemia affecting the progression of renal function in diabetic CKD subjects was observed in an economically disadvantaged country.

Methods: The primary target was to keep eGFR increase <5ml/min/1.73m²/year by reducing BP<125/75 mmHg; UTP <0.5 g/day; HbA1c <7% and LDL<100mg/dl. In prefixed standard regimen Enalapril up to 40 mg or Losartan 100 mg (randomly), Atenolol 100 mg, sustained release Nifedipine 60 mg and diuretics added sequentially. Metformin 2 g and gliclazide 320 mg or insulin upto 1u/kg and Atorvastatin up to 20 mg were used.

Results: Primarily 204 patients were included. Their diastolic blood BP at 0 vs. end of 48week was 79±9 vs. 75±8, mmHg, (p<0.001); SCreatinine (SCr) 1.7±0.6 vs. 2.0±0.9 mg/dl, (p<0.001); CCr 55±30 vs. 48±29 ml/min/1.73m², (p<0.007); 24hrUTP 1.35±1.3 vs. 1.4±2.3 g/day; HbA1c 7.8±1.5 vs. 7.6 ± 1.4 % and LDL 98±47vs. 80±36 mg/dl, (p<0.001). Renal deterioration was progressive. Outcomes in Enalapril subgroup (n=110) at 0 vs. 48 week showed that SCr 1.6±0.5vs. 1.9±0.8 mg/dl, (p<0.001); UTP 1.6±1.3 vs. 1.3±1.5 g/day, (p<0.03) and CCr 58±30 vs. 52±31 ml/min/1.73m², (P=NS) indicating reduction in proteinuria was associated with stabling renal function. In Losartan group (n= 88) SCr 1.7±0.6vs. 2.0±0.8 mg/dl, (p<0.001); UTP 1.1±0.9 vs. 1.2±1.5 g/day, (P=NS) and CCr 54±31 vs. 45±25 ml/min/1.73m², (p<0.03) showing deterioration of renal function.Bivariate analysis also showed negative association of proteinuria with CCr (r=0.3, p<0.01).

Conclusions: It may be concluded that in our type 2 DN patients, standard therapeutic regimens are effective to control blood pressure and dyslipidemia only. The ACEI Enalapril seems to be more renoprotective. To have tighter control of blood sugar and further reduction in proteinuria, more aggressive multi dimensional approach is needed, although this would require more economic and infrastructural support.

Funding: Pharmaceutical Company Support

LB-PO3155

Direct Comparison of Ferric Carboxymaltose vs. Venofer in 2500 Patients with Iron Deficiency Anemia and Impaired Renal Function (REPAIR-IDA)

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Background: Ferric carboxymaltose (FCM; Injectafer®) is a non-dextran intravenous iron that permits a single infusion of up to 750 mg iron.

Methods: This trial compared FCM to iron sucrose (Venofer® [VEN]) in patients with CKD (not on dialysis) with a screening hemoglobin (Hb) ≤ 11.5 g/dL. Patients were randomized to receive FCM (2 x 750 mg iron) or VEN (5 x 200 mg iron). The primary safety endpoint was an adjudicated composite of death, MI, stroke, unstable angina, congestive heart failure, arrhythmia, and protocol defined hypertensive (PDHH) or hypotensive (PDHL) events up to Day 120.

Results: Of the 2584 subjects enrolled, 2561 received at least 1 dose of iron (safety population) arm. Baseline Hb was 10.3 g/dL (+/-0.83) in both arms and change to highest Hb during the first 56 days (the primary efficacy endpoint) was 1.1 g/dL in the FCM arm vs. 0.9 g/dL in the VEN arm (difference [diff] 0.21 g/dL; 95% CI 0.13, 0.28). In the FCM arm, 175/1276 subjects (13.7%) had one of the composite safety events vs. 156/1285 subjects (12.1%) in the VEN arm (diff 1.6%; 95% CI -1.1, 4.3). Death due to any cause was observed in 15 patients receiving FCM vs. 18 patients receiving Venofer. Excluding PDHH and PDHL events, 5.5% and 5.4% of subjects experienced a composite event in the arms receiving FCM and VEN, respectively (diff 0.1; 95% CI -1.7, 2.0). While subjects receiving FCM were less likely to experience a PDHL event compared with subjects receiving VEN (1.8 vs. 3.2%, diff -1.4%, 95% CI -2.7%, -0.1%) they were more likely to experience a PDHH event (7.5 vs. 4.4%, diff 3.1% 95% CI 1.2%, 5.0%). PDHH events were mostly transient systolic excursions occurring immediately post dose with resolution by 30 minutes with no observed relationship to any of the other cardiovascular safety endpoints.

Conclusions: Therefore, two 750 mg doses of FCM are more effective at raising Hb than five 200 mg doses of VEN. This is the largest head to head study of IV iron in CKD patients demonstrating comparable safety profiles of the two preparations.

Funding: Pharmaceutical Company Support

Underline represents presenting author/disclosure.

LB-PO3156

The FIRST Head-to-Head Comparison Study (Ferumoxytol Compared to Iron Sucrose Trial) of the Safety and Efficacy of Ferumoxytol with Iron Sucrose for the Treatment of Iron Deficiency Anemia (IDA) in Patients with Chronic Kidney Disease (CKD)

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Background: Few randomized controlled trials have compared IV iron preparations head-to-head in CKD patients (pts) with IDA. This open-label study compared the efficacy and safety of two marketed IV irons (ferumoxytol [FER] and iron sucrose [IS]) in pts with CKD.

Methods: Pts were randomized 1:1 to either 1.02 g FER (2 x 510 mg injections) or 1.0 g IS (10 x 100 mg slow injections or infusions for hemodialysis [HD] pts and 5 x 200 mg slow injections or infusions for nondialysis pts). Main inclusion criteria included hemoglobin (Hgb) <11.0 g/dL and TSAT <30%. Pts with a history of allergy to IV iron and Hgb ≤7g/dL were excluded.

Results: Overall, 162 pts were randomized (80 FER; 82 IS). Demographics were balanced between the two treatment groups; approximately 43% of pts were on HD. Key adverse event (AE) categories are presented below.

Summary of Adverse Events

AE Category	Ferumoxytol (N=80)			Iron Sucrose (N=82)		
	Events	Pts [N(%)]	Events per pt	Events	Pts [N (%)]	Events per pt
All AEs	86	38 (48)	2.3	161	53 (65)	3.0
Related AEs	8	8 (10)	1.0	46	13 (16)	3.5
SAEs	8	7 (9)	1.1	11	6 (7)	1.8
Related SAEs	1	1 (1)	1.0	1	1 (1)	1.0
AEs of special interest[1]	1	1 (1)	1.0	4	2 (2)	2.0
AEs leading to drug discontinuation	1	1 (1)	1.0	7	4 (5)	1.3

[1]acute moderate-to-severe hypotension and hypersensitivity reactions

The mean change in Hgb from Baseline to Week 5 for FER-treated pts was 0.71 g/dL vs 0.61 g/dL for IS-treated pts. Additionally, 50% of pts treated with FER achieved a ≥1 g increase in Hgb from Baseline to Week 5 compared to 42% of IS-treated pts.

Conclusions: In this randomized controlled trial, FER demonstrated comparable efficacy and a favorable safety profile relative to IS. The lower rate of AEs in the FER group may relate to fewer IV iron exposures required to deliver 1 gram of iron with FER relative to IS (2 vs 5 or 10). The fewer administrations with FER may translate into clinical resource savings.

Funding: Pharmaceutical Company Support

LB-PO3157

Cyclosporine C_2 Monitoring for Frequent-Relapsing Nephrotic Syndrome in Children: A Multicenter Randomized Controlled Trial

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Background: It is still unclear if C2 management of cyclosporine is effective and safe in children with frequent-relapsing nephrotic syndrome (FRNS).

Methods: Japanese Study Group of Kidney Disease in Children (JSKDC) conducted an open-label multicenter randomized controlled trial (JSKDC03, JPRN-C000000008). Ninety-three children with FRNS from 15 centers in Japan were randomly assigned to the treatment A group (n=46) or treatment B group (n=47). Treatment A consisted of C2 monitoring with a target level of 600-700 ng/ml for the first 6 months and a target level of 450-550 ng/ml for the next 18 months. Treatment B consisted of C2 monitoring with a target level of 450-550 ng/ml for the first 6 months and a target level of 300-400 ng/ml for the next 18 months. The primary endpoint was a sustained remission rate. The decision rule was as follows; if treatment A was more than 8% higher than treatment B, select treatment A, otherwise select treatment B.

Results: The sustained remission rate at month 24 was 64.4% with treatment A and 50.0% with treatment B. Although the hazard ratio for relapse was 0.57 (95% CI: 0.29-1.11; P=0.094), the posterior probability that treatment A was 8% superior for sustained remission rate was 70.8%. The progression (to FRNS)-free survival at month 24 was 88.1% for treatment A and 68.4% for treatment B. The hazard ratio for progression to FRNS was 0.33 (95% CI: 0.12-0.94; P=0.028). The time of relapse was lower in treatment A group than that in treatment B group (0.410 vs. 0.945 times/person-years; ratio: 0.434; 95% CI: 0.190-0.841; P=0.016). The ratio and severity of adverse events including chronic cyclosporine nephrotoxicity in both treatment groups were similar.

Conclusions: We consider that treatment A should be the standard treatment C2 monitoring of cyclosporine for children with FRNS.

Funding: Government Support - Non-U.S.

LB-PO3158

Exploratory Analysis from the EXIST-1 Study: Everolimus Therapy for Angiomyolipoma in Patients with Subependymal Giant Cell Astrocytomas Associated with Tuberous Sclerosis Complex

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Background: We evaluated everolimus, an oral mTOR inhibitor, for treating angiomyolipoma (AML) in patients with subependymal giant cell astrocytomas (SEGAs) associated with tuberous sclerosis complex (TSC).

Methods: EXIST-1 (NCT00789828), a prospective double-blind, randomized, placebo-controlled phase 3 study, evaluated everolimus in patients with SEGA associated with TSC. Patients demonstrating serial SEGA growth from pre-baseline to baseline scans were eligible. Patients were randomized 2:1 (stratified by enzyme-inducing anti-epileptic drug use) to receive everolimus (n=78) or placebo (n=39). Oral everolimus was initiated at 4.5 mg/m²/d and titrated to attain a blood trough level of 5-15 ng/mL based on tolerability. An exploratory analysis was performed in a patient subset who also had ≥1 target AML (lesion longest diameter ≥1 cm) at baseline (n=30 everolimus; n=14 placebo). Kidney CT/MRI was performed at 12, 24, and 48 weeks after study treatment initiation, then annually. AML response rate was defined as the proportion of patients with confirmed AML response (reduction in sum of target AML volumes of ≥50% relative to baseline).

Results: AML response rate was 53.3% (16/30) for everolimus patients vs 0% of placebo patients (0/14). Only everolimus patients had AML reductions of ≥50% at weeks 12, 24, and 48 (56.5%, 78.3%, 80.0%, respectively). Higher percentages of everolimus patients had AML reductions of ≥30% (82.6%, 100%, 100%, respectively) than placebo patients (8.3%, 18.2%, 16.7%, respectively).

Conclusions: Everolimus treatment elicited AML response in patients with AML and SEGAs associated with TSC. Everolimus may be a pharmacologic treatment option for AML in patients with SEGA associated with TSC.

Funding: Pharmaceutical Company Support

LB-PO3159

Everolimus Therapy for Angiomyolipoma in Patients with Tuberous Sclerosis Complex or Sporadic Lymphangioleiomyomatosis: Final Results from EXIST-2

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Background: We evaluated everolimus, an oral mTOR inhibitor, for treating angiomyolipoma (AML) in patients with tuberous sclerosis complex (TSC) or sporadic lymphangioleiomyomatosis (sLAM).

Methods: EXIST-2 (NCT00790400) is a prospective, international, randomized, double-blind, placebo-controlled, phase 3 study. Patients (≥1 AML, longest diameter ≥3 cm) were stratified by (i) enzyme-induced anti-epileptic drug (EIAED) use, (ii) TSC and EIAED non-use, (iii) sLAM and randomized 2:1 to receive everolimus 10 mg daily (n=79) or placebo (n=39). Kidney CT/MRI was performed at baseline, at 12, 24, and 48 weeks, and then annually. Primary efficacy endpoint was the proportion of patients with AML response (best overall confirmed ≥50% reduction in sum of volumes of all target AML relative to baseline). Adverse events (AE) were monitored every visit. Core phase results (6 months from last patient randomized) are presented.

Results: Patient characteristics were balanced across the 2 groups; median patient age was 31 years. Median treatment duration was 38.1 weeks on everolimus and 34.0 weeks on placebo. Everolimus best overall response rate (41.8%) was superior to placebo (0%) for the primary efficacy endpoint (difference = 41.8%; 95% CI: 23.5, 58.4; p<0.0001). Everolimus was associated with an acceptable safety profile consistent with previous reports in TSC, with most AEs being grade 1 or 2. Serious AE incidence was similar in the treatment arms (everolimus 19.0% vs. placebo 17.9%). Final analyses including biomarkers will be presented.

Conclusions: Everolimus treatment produced a clinically and statistically significant reduction in AML volume compared with placebo and showed a safety profile consistent with previous reports. Everolimus represents the first pharmacologic treatment option for patients with AML.

Funding: Pharmaceutical Company Support

Underline represents presenting author/disclosure.

LB-PO3160

Effects of Rapamycin on Angiomyolipoma in Tuberous Sclerosis
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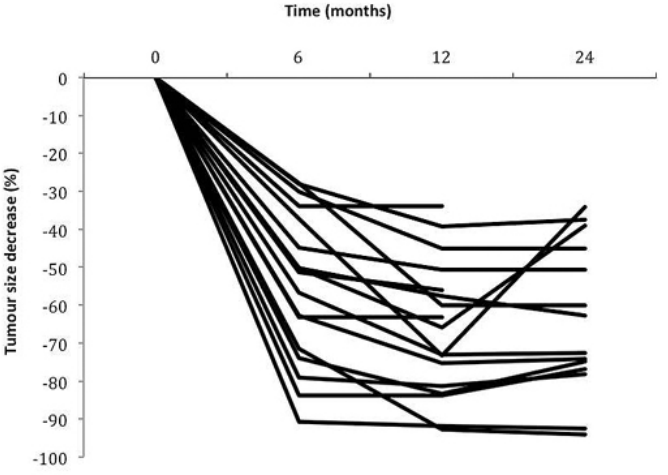
Background: Renal angiomyolipoma (AML) is a benign tumour, frequent in Tuberous Sclerosis (TS). Its morbidity is high, as the tumour can lead to spontaneous haemorrhage and, albeit more rarely, arterial hypertension and kidney failure. To date, the main therapeutic options are embolization, elective surgery, and emergency nephrectomy. The objective of the present study was to demonstrate if mTOR inhibitors are safe and effective to reduce the volume of AML in patients with TS.

Methods: This trial was a 24-month prospective phase III study (ClinTrials.gov: NCT0121712, EudraCT: 2007-005978-30), single-centre, noncontrolled and nonblinded to test a new therapeutic indication in a marketed drug.

Primary objective: evaluate the effect of rapamycin on the size of AML. Study population: 17 TS patients who had at least 1 renal AML >2 cm in diameter. Target rapamycin plasma levels: 4-8 ng/ml. Abdominal MRI was performed at 6, 12 and 24 months.

Results: The percentage decrease in the volume of the AML at 6, 12 and 24 months of treatment for each participant is shown in Figure 1.



After 6 months, the mean volume decrease was 55.18% (SE 5.01) p<0.001 and 66.38% (SE 4.41) at 1 year p<0.001 (ITT based). There was no significant decrease between one and 2 years. Two patients showed severe adverse events (nephrotic range proteinuria and exacerbation of erythema nodosum) and several showed minor adverse events.

Conclusions: The results of this study show that mTOR inhibitors are a relatively safe and efficacious therapeutic alternative in the management of AML in patients with TS, less aggressive than currently available options and, above all, preserve renal function.

Funding: Government Support - Non-U.S.

LB-PO3161

A Cluster Randomized Trial of an Enhanced eGFR Laboratory Prompt in Chronic Kidney Disease
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Background: The use of evidence-based interventions in chronic kidney disease(CKD) is low, suggesting the significance of CKD may not be recognized. We did a cluster randomized trial to evaluate the effect of adding recommendations for management of CKD to serum creatinine results ordered by primary care physicians.

Methods: We randomized 93 primary care practices to receive a standard (no recommendations) or enhanced (recommendations provided) laboratory prompt for patients with CKD (eGFR<60 ml/min/1.73m2). Patients were followed for one year to assess outcomes; data on medication use was available in elderly patients (aged 66 years).The primary outcome was the proportion of elderly CKD patients with diabetes or proteinuria in whom an ACE inhibitor (ACEi) or angiotensin receptor blocker (ARB) was used. (ISRCTN26610787)

Results: 5,444 elderly CKD patients with diabetes or proteinuria were eligible for assessment of the primary outcome. ACEi or ARB use was 77.1% and 76.9% in the standard and enhanced prompt groups, respectively (RR 1.00; 95%CI 0.96 to 1.04). In the subgroup of elderly patients with eGFR<30 ml/min/1.73m2, ACEi or ARB use was higher in the enhanced prompt group (RR 1.13; 95%CI 1.03 to 1.24). Among all 22,092 patients with CKD, there was no difference in the likelihood of a composite clinical outcome (death, end stage renal disease, doubling of serum creatinine, or hospitalization for myocardial infarction, heart failure, or stroke)(RR 1.00; 95%CI 0.89 to 1.12) over a median of 2.1 years.

Conclusions: In elderly patients with reduced eGFR and an indication for ACEi or ARB, use of an enhanced eGFR laboratory prompt did not increase their use. These data suggest that enhanced management-based eGFR laboratory prompts cannot currently be recommended for routine use in all patients with CKD, and has implications for eGFR reporting guidelines.

Funding: Pharmaceutical Company Support, Government Support - Non-U.S.

LB-PO3162

Effect of Renal Revascularization on Cardiac Structure and Function in Atherosclerotic Renovascular Disease
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Background: The ASTRAL study reported on the effect of renal revascularization on clinical outcomes in 2009. A sub-study examined cardiac structure and function using magnetic resonance imaging (MRI) in 45 patients randomised to revascularization (Revas) or medical therapy (Med) within the trial.

Methods: Cardiac MRI was performed at baseline and 1 year. Variables collected were left ventricular (LV) and right ventricular (RV) end diastolic volume (EDV), end systolic volume (ESV), ejection fraction (EF) and mass (M). A power calculation indicated that 25 patients in each arm would identify significant changes in one or more of these. Median changes in MRI variables between baseline and 1 year were compared between Revas and Med using the Wilcoxon 2-sample test.

Results: 44 patients completed the study (Med n=21, Revas n=23). Characteristics were similar between the 2 groups: age 70 v 72 years, BMI 30 v 26 kg/m2, diabetes 40% v 32%, ischemic heart disease 56% v 68%, blood pressure 148/71 v 143/74 mmHg, eGFR 42 v 43 ml/min, mean renal artery stenosis 75% in both. Baseline MRI data were similar in the 2 groups. At 1 year there was no difference in the median changes between the 2 groups for any variable. The median change between baseline and 1 year were (Med v Revas) LVEDV -1.9 v -5.8ml p=0.4; LVESV -2.1 v 0.3ml p=0.7; LVM -5.4 vs -6.3 g p=0.8; LVEF -1.5 v -0.8% p=0.7; RVEDV 0.2 v 1.7ml p=0.7; RVESV 2.1 v -0.9ml p=0.8; RVM 0.2 v -2.5 p=0.6 and RVEF -1.5 v 1.2% p=0.6. Multivariate modelling showed that at 1 year higher baseline blood pressure was significantly associated with greater LVEDV, and more severe stenosis and renal dysfunction associated with higher LVMI.

Conclusions: Renal revascularization did not lead to substantial cardiac changes in patients with ARVD. Some patients may benefit from renal revascularization, but this sub-study was inadequately powered to investigate effects in sub-groups.

Funding: Government Support - Non-U.S.

LB-PO3163

Early Intervention in the CKD-MBD Affects Vascular Function
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Background: The cardiovascular morbidity and mortality of CKD is causally linked to the CKD-MBD. Since Pi may be a cardiovascular risk factor, we hypothesized that early treatment of the CKD-MBD might have efficacy.

Methods: *Fosrenol In CKD* is a double blind placebo controlled trial in 40 patients, mean age 62, with CKD 3 using 1000mg of LaCO3 with meals. The primary endpoint was a composite of changes in cardiac and vascular function over 12 mos.

Results: The eGFR was 47 at baseline in the LaCO3 group and 45 in the placebo group, and did not change during the study. Serum Pi was 3.5 and 3.3 and 3.3 and 3.2 at baseline and at 12mos in the LaCO3 and placebo groups respectively, while the **TRP was** 76 and 74 and **77 and 71**. Cardiac function was reduced in the cohort overall (Max DP/DT of 860), but LV function tended to improve in both groups during the study with Sm (cm/s) and Max DP/DT significantly improving in the placebo group while diastolic function parameters revealed a significant reduction in E/Em ratio, demonstrating "the clinic effect". Diastolic BP significantly decreased during the study. Vascular function assessed by **pulse wave velocity was significantly reduced in the LaCO3 group** but not the placebo group at 12 mos compared to baseline. Aortic calcium scores were 3773± 8195 and 2445±2669 in the LaCO3 and placebo groups respectively at baseline and were not significantly changed during the study. PTH levels were not increased, but FGF23 levels were mildly elevated (66 and 75, nl 48) at baseline and did not change during the study. Sclerostin and DKK1 levels were elevated at baseline and neither changed. Bone Mineral Density of the lumbar spine was significantly greater in the LaCO3 group at 12 mos compared to placebo.

Conclusions: LaCO3 was well tolerated. Weaknesses of the present study are the small size, the variability in cardiac function and vascular calcification, and the 12 mo duration. Use of a Pi binder is safe, may reduce the rate of fall in the TRP, improve BMD and decrease vascular stiffness. Novel biomarkers of CKD are elevated in CKD 3.

Funding: NIDDK Support, Pharmaceutical Company Support

Underline represents presenting author/disclosure.

LB-PO3164

VTP-27999 Increases Renal Plasma Flow More than Aliskiren

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Background: Renal Plasma Flow (RPF)is a biomarker of renal vascular function. Drugs that slow the progression of chronic kidney disease (CKD) increase rates of RPF.

Methods: We performed a RPF study in salt restricted normal volunteers (10 mEq Na^+/d) using infusion of para-aminohippurate to measure RPF. This dose-ranging study compared the effects on RPF of four doses of a new renin inhibitor, VTP-27999 (75, 150, 300, 600 mg), versus either vehicle or 300 mg of Aliskiren (maximum approved clinical dose) as active comparator. Baseline RPF values were obtained over 60 minutes prior to dosing. RPF was then measured hourly over 5 hours after administration of drug. Nine to 12 subjects were studied in each dose group. The respective changes in RPF (± SEM), compared to the baseline value, were as follows: vehicle -8.9 ± 5.3 mL/min/1.73m2, Aliskiren 62.6 ± 14.5, VTP-27999 75 mg 17.2 ±12.0, VTP-27999 150 mg 63.1± 15.6, 300 mg 97.5 ± 20.3, and 600 mg 115.2 ± 20.6.

Results: Both VTP-27999 and Aliskiren increased RPF significantly. VTP-27999 also increased RPF in a clear, dose-dependent manner. The increase in RPF with Aliskiren at 300 mg was comparable in magnitude to the increase with 150 mg of VTP-27999. In addition, the 300 mg and 600 mg doses of VTP-27999 increased RPF more than Aliskiren.

Conclusions: The ability of VTP-27999 to influence RPF offers the potential for VTP-27999 to slow the progression of CKD to a greater extent than Aliskiren.

Funding: Pharmaceutical Company Support

LB-PO3165

VTP-27999: A Potent and Efficacious Inhibitor of Renin in the Kidney

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Background: The RAAS pathway is important in CKD, and ACE inhibitors and ARBs slow progression of CKD. Increased blockade of the RAAS in kidney, which can be achieved by inhibition of the activity of renin, is expected to provide even greater renal protection. Renin is the rate-limiting enzyme in RAAS, and virtually all renin is made in kidney. Its synthesis and secretion is induced by inhibition of renin through decreased interaction of Ang II with the AT_1 receptor. Thus, the level of induction of plasma renin concentration (PRC) following inhibition of renin indicates the degree of inhibition of renin in kidney. There is also accumulating evidence prorenin is secreted in an active form, and provides additional enzymatic activity at its site of secretion. Thus, one needs to inhibit both renin and active prorenin to fully inhibit renin activity.

Methods: VTP-27999 (VTP) is a new renin inhibitor (IC_{50} 0.30 nM, aliskiren IC_{50} 0.53 nM). HMC-1 cells (human mast cell line which secretes renin) were used to study inhibition of intracellular renin activity and secreted renin and prorenin. In addition, in order to study renin inhibition in humans, Na^+ depleted normal volunteers (NV) (10 meq/d for 7 days) were dosed qd for 10 days with placebo, VTP (75, 150, 300, or 600 mg), or aliskiren (300 mg).

Results: In HMC-1 cells, VTP is 7X more potent than aliskiren in inhibiting intracellular renin activity (IC_{50} 27 nM vs 171 nM), and it potently inhibits both renin and prorenin. This is consistent with VTP providing superior inhibition of both renin and active prorenin. In NV studies, plasma renin activity (PRA) was inhibited to a similar extent by all doses of both drugs. In contrast, there was a dose response for induction of PRC; at day 10 VTP induced PRC levels 350X at 600 mg and 100X at 300 mg, while 300 mg aliskiren induced PRC 50X. This is consistent with VTP providing greater inhibition of renin activity in kidney.

Conclusions: VTP-27999 is an efficacious inhibitor of kidney renin and prorenin, and is a more potent inhibitor than aliskiren. VTP-27999 has the potential to be superior at preventing and slowing progression of CKD.

Funding: Pharmaceutical Company Support

LB-PO3166

Efficacy and Safety of Sitagliptin vs. Glipizide in Patients with Type 2 Diabetes and Moderate to Severe Chronic Renal Insufficiency

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Background: This 54-week (wk) study assessed the efficacy and safety of sitagliptin (SITA) vs. glipizide (GLP) in patients (pts) with type 2 diabetes (T2D) and moderate (mod) or severe (sev) chronic renal insufficiency (CRI).

Methods: Eligible pts: ≥30 years old, A1C 7-9%, and not on dialysis[A name=OLE_LINK4]. [/A]Pts were randomized (1:1) to SITA or GLP, stratified by: renal status (mod [eGFR 30-<50 mL/min/1.73 m^2] or sev CRI [eGFR <30 mL/min/1.73 m^2]); history of cardiovascular disease (yes or no); and history of heart failure (yes or no). The SITA dose was 50 mg q.d. for pts with mod CRI and 25 mg q.d. for pts with sev CRI; the dose was adjusted downward (from 50 to 25 mg q.d.) for pts whose renal status changed from mod to sev based on confirmed eGFR values. The GLP dose was 2.5 mg q.d., and could be titrated ↑ or ↓ by the investigator, up to 10 mg b.i.d. The primary efficacy endpoint was the mean change from baseline in A1C. The primary safety endpoint was the incidence of adverse events (AEs) of symptomatic hypoglycemia.

Results: There were 426 pts randomized (SITA = 213; GLP = 213). At Wk 54, LS mean changes from baseline (7.7% and 7.8%, respectively) were -0.75% in the SITA group and -0.64% in the GLP group; SITA was non-inferior to GLP (between-group difference [95% CI] = -0.11% [-0.29%, 0.06%] in the per-protocol population) since the upper bound of the 95% CI < the pre-specified non-inferiority margin (0.4%). The SITA group had a lower incidence of symptomatic hypoglycemia AEs than the GLP group (6.2% and 17.0%, respectively; p=0.001). SITA treatment resulted in a LS mean decrease in body weight (-0.6 kg) versus a LS mean increase (1.2 kg) with GLP treatment (between-group difference, -1.8 kg; $p<0.001$).

Conclusions: In pts with T2D and CRI, SITA and GLP produced clinically meaningful improvements in glycemic control; SITA was non-inferior to GLP. SITA had a significantly lower incidence of symptomatic hypoglycemia AEs vs. GLP. Treatment with SITA resulted in a decrease in body weight compared with an increase with GLP.

Funding: Pharmaceutical Company Support

LB-PO3167

Efficacy and Safety of Sitagliptin vs. Glipizide in Patients with Type 2 Diabetes and End-Stage Renal Disease on Dialysis

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Background: This study assessed the efficacy and safety of sitagliptin (SITA) vs. glipizide (GLP) in pts with type 2 diabetes (T2D) and end-stage renal disease (ESRD) on dialysis. SITA is mainly renally excreted. To achieve similar plasma concentrations to those in pts with normal to mildly-impaired renal function taking 100 mg of SITA, pts with ESRD should receive 1/4 of the usual clinical dose or 25 mg qd.

Methods: In a 54-week (wk), double-blind study, pts ≥30 years (ys) old with T2D, ESRD on dialysis, and A1C 7-9%, were randomized (1:1) to monotherapy with SITA (25 mg qd) or GLP (2.5 mg qd, titrated ↑ or ↓ by the investigator, to up to 10 mg bid). Primary endpoints: 54-wk change in A1C from baseline and safety and tolerability with SITA.

Results: In total, 129 pts were randomized, 64 to SITA (63% male, mean age 61 ys, A1C 7.9%, median duration of T2D 19 ys, 72% on haemodialysis) and 65 to GLP (57% male, mean age 59 ys, A1C 7.8%, median duration of T2DM 17 ys, 65% on hemodialysis). Overall, 71% of pts completed the 54-wk study (73% SITA, 69% GLP). After 54 wks, the least squares (LS) mean change (95% confidence interval [CI]) from baseline in A1C was -0.72% (-0.95, -0.48) with SITA and -0.87% (-1.11, -0.63) with GLP (difference [95% CI] = 0.15% [-0.18, 0.49]). There were 10 deaths (4 [6.3%] SITA, 6 [9.2%] GLP). The incidences (between-group difference [95% CI]) of hypoglycaemia and severe hypoglycaemia were 6.3% vs. 10.8% (-4.8 [-15.7, 5.6]) and 0% vs. 7.7% (-7.8 [-17.1, -1.9]) in the SITA and GLP groups, respectively. There were higher incidences of adverse experiences of cellulitis and headache in the SITA group relative to the GLP group (6.3% vs. 0%, respectively, for both). Mean change in body weight from baseline was -0.3 kg with SITA and 1.2 kg with GLP.

Conclusions: Treatment with SITA or GLP monotherapy was effective and well tolerated over 54 wks in pts with T2D and ESRD on dialysis.

Funding: Pharmaceutical Company Support

LB-PO3168

CMX001 Was Well Tolerated and without Nephrotoxicity in Renal Transplant (RT) and Hematopoietic Stem Cell Transplant (HSCT) Recipients with BK Virus (BKV) Infection in a Prospective, Randomized, Double-Blind Study

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Background: CMX001 is an oral lipid-antiviral-conjugate that delivers high intracellular levels of the active antiviral agent cidofovir (CDV)-diphosphate with potent activity against dsDNA viruses including BKV, CMV and adenovirus (AdV). No evidence of CDV-like nephrotoxicity has been observed in non-clinical studies. The effect of CMX001 on renal function was evaluated in a safety and tolerability study in RT and HSCT recipients with BKV infection.

Methods: RT and HSCT recipients with BKV infection received 5 weekly doses of 40mg CMX001 or placebo randomized 2:1. RT recipients were at least 28 days post-transplant and on stable immunosuppression. HSCT recipients were at least 3 days post-engraftment. Enrolled subjects had a GFR of >30mL/min and were to be discontinued if GFR decreased by ≥ 50% or to < 20mL/min. GFR was calculated using the MDRD formula.

Results: 12 RT and 11 HSCT recipients were enrolled and completed the treatment phase of the study. Mean GFRs at baseline and Day 35 (7 days post-treatment) are shown below.

Underline represents presenting author/disclosure.

Mean (SD) GFR (mL/min/1.73m²)

	RT recipients		HSCT recipients	
	CMX001 (n=8)	Placebo (n=4)	CMX001 (n=7)	Placebo (n=4)
Day 0/Baseline	55.5 (11.1)	49.8 (8.3)	83 (31.2)	66.5 (20.2)
Day 35	54.4 (10.5)	44.2 (4.7)	79.9 (32.3)	69.8 (40.5)
Change from Baseline	-1.1 (2.8)	-5.5 (4.8)	-3.1 (29.2)	3.2 (32.1)

There were no drug-related SAEs, remarkable AEs or significant changes in serum creatinine, BUN or proteinuria. Effectiveness in treating BKV infection could not be assessed in this small study.

Conclusions: Five weekly oral doses of CMX001 40mg in RT and HSCT recipients with BKV infection were well tolerated without adverse renal effects. This is consistent with results from other CMX001 clinical trials and experience with subjects treated under EINDs. Further evaluation of CMX001 as an anti-BKV therapy is planned.

Funding: Pharmaceutical Company Support

LB-PO3169

Bioequivalence of CellCept and Generic Mycophenolate Mofetil: A Randomized, Two-Period, Crossover Study in Pediatric Renal Transplant Patients

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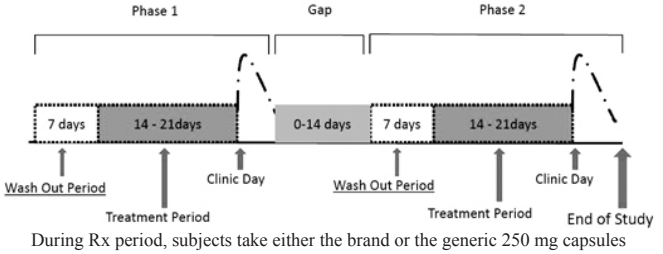
Background: Transplanted children have different metabolism of immunosuppressants when compared to adults. No published studies have compared the bioequivalence of CellCept and generic MMF in pediatric transplant patients.

Methods: This is an on-going prospective study with two washout periods followed by randomization to two cross-over treatment (Rx) periods.



During Rx period, subjects take either the brand or the generic 250 mg capsules (300-450 mg/m2/dose) every 12 hours for 14 to 21 days. Blood samples are collected at 0 time, 0.5, 1, 2, 4, and 6 hours after the final morning dose to construct the pharmacokinetic profiles. The standard parameters of interest are the C-0, C-max, area under the concentration curve (AUC) calculated to AUC0-6, all at steady-state serum levels. Preliminary study has been conducted in 7 patients with α (two-tailed) = 0.05. $P < 0.05$ is considered significant.

Results: The 90% confidence intervals for test/ reference ratio of natural logarithm transformed values of pharmacokinetic parameters (AUC0-6 and C-max) are 80.0% to 164.4%, and, 61.2% to 256.5% respectively.

Table 1. The pharmacokinetic profile of TEVA MMF and CellCept

Parameters	90% confidence interval	
Log TEVA AUC0-6	80.0%	164.4%
Log TEVA Cmax	61.2%	256.5%

The correlation between AUC and trough MPA serum level was 0.33 in the generic MMF, compared to 0.79 in CellCept.

Conclusions: The bioequivalence of the tested generic MMF is out of the limits according to FDA standard (80% to 125%). Trough levels of MPA are good for CellCept steady serum level monitoring but not for the tested generic MMF. Pharmacokinetic studies may be required to allow proper and safe substitution of Cellcept with generic mycophenolate.

LB-PO3170

O104:H4 Shiga Toxin E.coli (STEC) Hemolytic Uremic Syndrome (HUS): Positive Outcome in 9/9 Patients (pts) after Early Treatment by Eculizumab (ECU)

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Background: STEC HUS is rare, life-threatening, and maybe driven by complement activation. Plasma exchange (PE) is used in adults, despite no randomized controlled trial (RCT) proven efficiency.

Monoclonal C5 antibody ECU has been reported as effective for STEC HUS with neurological involvement in children.

O104:H4 STEC has emerged as a cause of HUS in Germany. During the course of a different outbreak from O104:H4 STEC in our urban area, 9 pts with severe HUS were treated by ECU.

Methods: Diagnosis

STEC HUS diagnosis was based on association of hemolytic anemia, low platelet (Plt) count, and acute kidney injury. AKI definition: increasing serum creatinine levels (creat.), hematuria or proteinuria.

HUS-related main organ involvement was defined by

- coma, seizures, psychiatric, or other neurological symptoms : neuro
- troponin C levels > normal (NL) : heart
- transaminase levels > NL : liver
- hyperglycemia, lipase levels > NL : pancreas

Treatment

The first 3 pts were treated by PE. Because of no effect of PE on Plt and severe organ involvement, ECU was used when Plt <120,000/mL at 900mg/wk x 4, 1200mg at wk 5 and every 2 wk for 8 wks.

Results: Diarrhea occurred in 24 pts, with O104:H4 STEC in 15. In 9 pts (8 adults, 1 3.5 yr child), HUS developed 6 days (median; range 3-12) after diarrhea (2 household transmissions). Upon diagnosis of HUS, Plt was 46,000/mL (19-124,000), hemoglobin 11.3 g/dL (9.7- 14), LDH 800 IU/m/ (453-1981), creat. 1.67 mg/dL (0.53-5.72). 2 pts were treated by dialysis, 1 pt was artificially ventilated, 9 pts had extrarenal involvement: neuro 2 pts, heart 3 pts, liver 8 pts, pancreas 5 pts.

After failure of PE to increase Plt in 3 pts, ECU was used in all 9 pts. One pt received immunoadsorption because of severe neuro HUS.

Outcome was favorable in all pts, with no death. At day 60, creat. was 0.70 mg/dL (0.56-0.94), Plt, Hb, LDH and neuro status were NL. 3 pts were on antihypertensive therapy.

Conclusions: Early treatment of O104:H4 STEC HUS by ECU has been an efficient therapy in this experience. Further evaluation of ECU in STEC HUS is warranted.

Funding: Government Support - Non-U.S.

LB-PO3171

Characteristics of Soluble Urokinase Receptor as Focal Segmental Glomerulosclerosis Factor in Distinct Patient Cohorts

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Background: Soluble urokinase receptor (suPAR) has been recently identified as a cause of focal segmental glomerulosclerosis (FSGS) with elevated suPAR serum levels (>3000 pg/ml) in 71% of tested patients in a multicenter FSGS cohort (Wei et al, Nat Med 2011). We now analyzed the serum suPAR levels in a cohort of patients with steroid resistant disease who were enrolled in the multicenter FSGS Trial Consortium (Gipson et al, Kidney Int 2011).

Methods: suPAR was measured before and 26 weeks after randomly assigned treatment, cyclosporine (CSA, n=35) or mycophenolate/dexamethasone (MMF, n=35).

Results: We found that 87% patients had high suPAR level (>3000 pg/ml) before, compared to 84% after treatment; serum suPAR correlated with estimated glomerular filtration rate (eGFR, $r=-0.39$, $p<0.0001$), but not to the degree of proteinuria, and not to age of disease onset. No differences in suPAR, serum creatinine, eGFR were observed between male and female patients before or after treatment. We found a significant difference between CSA and MMF with regards to serum suPAR and eGFR 26 weeks after treatment. CSA treatment was associated with a 4% increase in serum suPAR and a 25% reduction in eGFR. In contrast, MMF decreased serum suPAR levels by 4% with creatinine and eGFR unaltered. We noted increased serum suPAR and decreased eGFR over the 26-week course in black FSGS patient regardless of the treatment. No significant change in serum suPAR, creatinine or eGFR was documented in Caucasians. In a second FSGS patient cohort from Europe (The PodoNet Consortium), we found a high level (>3000 pg/ml) of suPAR in 67 out of 109 (61.5%) children with FSGS. Similarly, serum suPAR correlated with serum creatinine ($r=0.37$, $p=0.0001$), but not with age of onset, gender, or extent of proteinuria. A significant decline in suPAR is associated with MMF, but not other treatments.

Conclusions: These data further substantiate the role of suPAR in FSGS as circulating glomerular disease factor.

Funding: Other NIH Support - FSGS Trial NIH supported and Divisional money

LB-PO3172

AP214 Improves Long-Term (3 Month) Outcome on Composite Endpoint of Death, Renal Replacement Therapy or Reduced Kidney Function in Patients Undergoing Cardiac Surgery in a Phase 2 Clinical Trial

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Background: More than 500,000 patients/year in the USA and EU undergo cardiac surgery, and a significant fraction develops kidney injury resulting in increased mortality, co-morbidity and prolonged hospitalization. Melanocortin receptor (MCr) agonists have shown marked immune modulating and organ protective effects in animal disease models. AP214 is a novel non-selective MCr agonist. Objective: Evaluation of efficacy and safety of AP214 for prevention of development of kidney injury and long term outcome (GFR or composite endpoint) in patients undergoing cardiac surgery on cardiopulmonary bypass.

Methods: Randomized, double-blind, placebo-controlled. AP214 was given at 2 dose-levels: 600 mcg/kg (low dose) and 800 mcg/kg (high dose), split into three i.v. bolus infusions. A total of 77 patients (5 USA and 3 Danish sites; AKI Study Group) were randomized: AP214 600 mcg/kg (n=25), AP214 800 mcg/kg (n=26) and placebo (n=26).

Underline represents presenting author/disclosure.

Results: AP214 at both dose levels was safe with a safety profile comparable to placebo. Preliminary efficacy analyses revealed that AP214 (high dose compared to placebo) resulted in lower incidence of acute kidney injury within 48 hours (AKIN score; 9/26 vs 17/26) or 7 days (RIFLE score; 11/26 vs 17/26). Moreover patients treated with AP214 (high-dose compared to placebo) had a significantly lower change in actual GFR at day 90 compared to baseline. AP214 at both dose-levels results in a better 90 day outcome on a composite endpoint (death, RRT or reduced kidney function) compared to placebo: placebo (15/26), AP214 low dose (6/25) and AP214 high dose (9/26).

Conclusions: AP214 is safe and efficacy data indicate that AP214 prevents post-operative kidney injury and improves long-term outcome in patients undergoing cardiac surgery on cardiopulmonary bypass.

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The Optimal Mode of Renal Replacement Therapy in Acute Kidney Injury (OMAKI): A Pilot Randomized Controlled Trial of CVVH vs CVVHD

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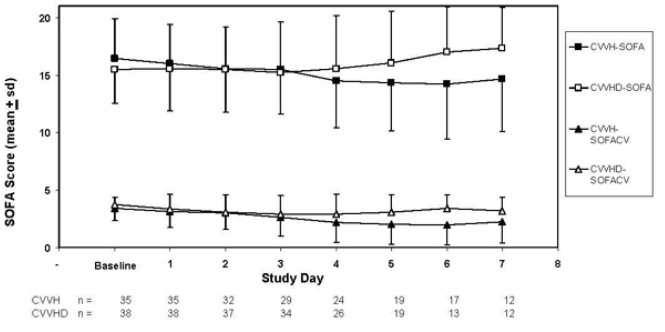
Background: Among critically ill patients with acute kidney injury (AKI) needing renal replacement, the effect of convective solute clearance (via continuous venovenous hemofiltration [CVVH]) vs diffusive clearance (via continuous venovenous hemodialysis [CVVHD]) on clinical outcomes is unclear.

Methods: We conducted a 6-centre unblinded randomized controlled trial of CVVH vs CVVHD in critically ill adults with AKI. Prescribed small solute clearance was 35 mL/kg/hr in both arms. The primary outcome was trial feasibility, defined by randomization of >25 % of eligible patients, delivery of >75% of the prescribed CRRT dose, and follow-up of >95% of patients to 60 days. A post hoc analysis using a mixed-effects model examined the impact of therapy on illness severity, as assessed by the Sequential Organ Failure Assessment (SOFA) score, over the first week.

Results: We randomized 77 patients (age 61.5 ± 14.2 y; 39% women; 23% had CKD, 82% had sepsis). Baseline SOFA scores (15.9 ± 3.2) and delivered doses (34.7 mL/kg/hr) were similar between groups. We recruited 55% of eligible patients, delivered > 80% of the prescribed dose in each arm, and followed all patients to 60 days. SOFA tended to decline more over the first week in CVVH patients (-0.8, 95% CI -2.1, +0.5) with a particular decline in the cardiovascular component. 60-day mortality (54% CVVH; 55% CVVHD) and dialysis dependence in survivors (25% CVVH; 19% CVVHD) were similar.



Conclusions: Our results suggest that a large trial comparing CVVH to CVVHD would be feasible. CVVH may confer an improvement in hemodynamic stability over the first week of treatment.

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