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The life cycle of the vascular access: from creation to ligation

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Chapter 5

A Randomized Trial of Liposomal Prednisolone (LIPMAT) to Enhance Radiocephalic Fistula Maturation: A Pilot Study

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Abstract

Introduction Maturation failure of radiocephalic arteriovenous fistulas (RCAVF) is a significant clinical issue. Vascular inflammation after AVF surgery is associated with non-maturation.

Objective To evaluate whether liposomal prednisolone improves RCAVF maturation in end-stage renal disease (ESRD) patients.

Methods The LIPMAT-study was a multi-center, double-blind, 1:1 randomized, placebo-controlled trial. Subjects were enrolled after RCAVF creation and treated with placebo or 150 mg of liposomal prednisolone at days 1 and 15 after AVF surgery. The primary end point was the juxta-anastomotic diameter of the cephalic vein at 6 weeks after surgery. Secondary end points were the diameter of the cephalic vein, brachial and radial artery at 6 weeks and 3 months after surgery as well as AVF flow and functional use for hemodialysis. Adverse events were compared to assess safety.

Results 29 subjects were included of which 13 received placebo and 16 received liposomal prednisolone. The juxta-anastomitic cephalic vein diameter at 6 weeks was 3.9 mm (95% confidence interval 2.7 – 5.8 mm) in the placebo group and 3.7 mm (95% confidence interval 3.0 – 5.3 mm) in the liposomal prednisolone group ($p=0.88$). No significant differences in secondary end point parameters were observed. Treatment of end-stage renal disease patients with liposomal prednisolone was not associated with significant side effects.

Conclusion Liposomal prednisolone treatment of ESRD patients was safe, but did not result in enhanced RCAVF maturation.

Introduction

Patients on maintenance hemodialysis (HD) require a reliable vascular access; however, only half of newly created radiocephalic arteriovenous fistulas (RCAVF) can be used for HD without additional procedures to promote maturation and up to 25% fail to provide adequate vascular access for HD ¹. The need for subsequent creation of upper arm arteriovenous fistulas (AVFs) and arteriovenous grafts may decrease if maturation can be improved. Currently, no pharmacological treatments have been proven to improve clinical maturation of AVFs.

Although the underlying pathophysiology of nonmaturation is incompletely understood, impaired outward remodeling and neointimal hyperplasia in the venous outflow tract seem to contribute ². Studies in murine and porcine models of AVF failure revealed a pronounced inflammatory response in the venous outflow tract in the early phase after AVF surgery ³. Recent studies suggest that this inflammatory response impairs AVF maturation ⁴.

Pegylated liposomes have emerged as an attractive tool to facilitate selective delivery of drugs to inflamed tissues with a highly permeable microvasculature, where liposomes are being phagocytized by macrophages. It has a potent and long-lasting anti-inflammatory effect at sites of inflammation, while minimizing exposure of noninflamed tissues. In a murine model of AVF failure, we have demonstrated that liposomal prednisolone inhibits inflammation of the juxta-anastomotic vein and improves outward remodeling of the venous outflow tract ⁵.

We hypothesized that maturation of RCAVFs in humans can be improved by inhibition of juxta-anastomotic inflammation using liposomal prednisolone. In the Liposomal Prednisolone to Improve Hemodialysis Fistula Maturation (LIPMAT) study, we aimed to assess if liposomal prednisolone improves maturation of RCAVFs and if it can be safely administered to patients with end-stage renal disease. The design of this multicenter randomized placebo-controlled trial has been reported earlier in detail ⁶.

Methods

Study design

The Liposomal Prednisolone to Improve Hemodialysis Fistula Maturation (LIPMAT) was a phase 2, investigator-initiated, multi-center, double-blinded, randomized, placebo-controlled trial. Subjects were recruited in 11 participating hospitals in the Netherlands. Patients were

eligible for enrolment if RCAVF creation was planned based on local hospital protocols, including a baseline ultrasound examination, as recommended by the Dutch Vascular Access Guidelines ⁷. Treating physicians identified eligible patients based on the in- and exclusion criteria (Supplementary Materials). Patients who provided written informed consent were then assessed for eligibility at a screening visit by the investigators, using medical history, physical examination and laboratory investigations. If an RCAVF could be successfully created, patients were enrolled and randomized stratified per hospital 1:1 to two infusions of each 150mg liposomal prednisolone or matching placebo in 500ml normal saline. Treatments were administered at 1 (\pm 1) day and 15 (\pm 2) days after surgery. Although the plasma half-life of liposomal prednisolone is 3 days, previous studies in humans revealed a therapeutic effect of 2 weeks after a single dose of 150 mg liposomal prednisolone ⁸. Therefore, we anticipated that the treatment regime in our study would result in an anti-inflammatory effect that would last 4 weeks. All patients were pre-treated with paracetamol and clemastine before each infusion to mitigate any allergic responses. Blinding methods have been described previously in detail, the investigators and patients were blinded to treatment allocation ⁶. The protocol was approved by the ethics committee of the Leiden University Medical Center and the Institutional Review Boards of all participating hospitals and the study was performed in accordance with the principles of the Declaration of Helsinki.

End points

The primary end point was the juxta-anastomotic diameter of the cephalic vein, measured by ultrasonography at 1cm downstream from the arteriovenous anastomosis at 6 weeks (\pm 5 days) after surgery. Secondary end points were the diameter of the cephalic vein at the elbow and mid upper arm and blood flow in the upstream radial and brachial arteries at 6 weeks and 3 months (\pm 14 days). The 6-week and 3-month time points chosen for AVF evaluation are similar to other studies evaluating the effect of pharmaceutical interventions on AVF maturation ^{9,10}. Ultrasound examinations were performed by qualified personnel in the participating hospitals. In case of AVF occlusion, diameters and flow were analysed as 0 mm and 0 ml/min respectively. Adverse events were recorded up to 3 months after surgery. Adverse events were classified as 'severe' if these met the criteria for Serious Adverse Events according to Good Clinical Practice guidelines, stating that an adverse event is serious if it is fatal, and/or is life-threatening for the subject, and/or makes hospital admission or an extension of the admission necessary, and/or causes persistent or significant invalidity or work disability, and/or manifests itself in a congenital

abnormality or malformation, and/or could, according to the person that carries out the research, have developed to a serious undesired medical event, but was however prevented due to premature interference. Functional outcomes were assessed in December 2018 for all subjects.

Statistical analysis

In a pilot cohort, a 1.5 mm standard deviation of the 6-week distal cephalic vein diameter was observed. A difference of 1.0 mm between the treatment and control group was considered clinically relevant. The sample size was calculated at 40 patients per group, allowing for a drop-out of 10%. The non-normally distributed end points were described as median and interquartile range (IQR) and were tested for significance using the Mann-Whitney U-test. The proportions of AVF occlusions were reported as percentages per treatment group. The study was not powered to demonstrate differences in AVF occlusions, side effects and functional outcomes and no statistical analysis was performed for these parameters.

Results

Study Population

From April 2016 through May 2018, 109 patients were planned for RCAVF creation and assessed for study eligibility. A total of 64 patients were excluded for known exclusion criteria from their medical history ($n = 24$), not consenting to study participation ($n = 34$), or late referral ($n = 6$, Figure 1). Of the remaining 45 patients who provided informed consent, 32 were randomized (Table 1). Reasons for dropout are shown in Figure 1. After randomization, but before treatment, 2 patients experienced clinical events constituting exclusion criteria. The remaining 30 patients received the study treatment. The trial was stopped prematurely in May 2018 because of slow enrollment.

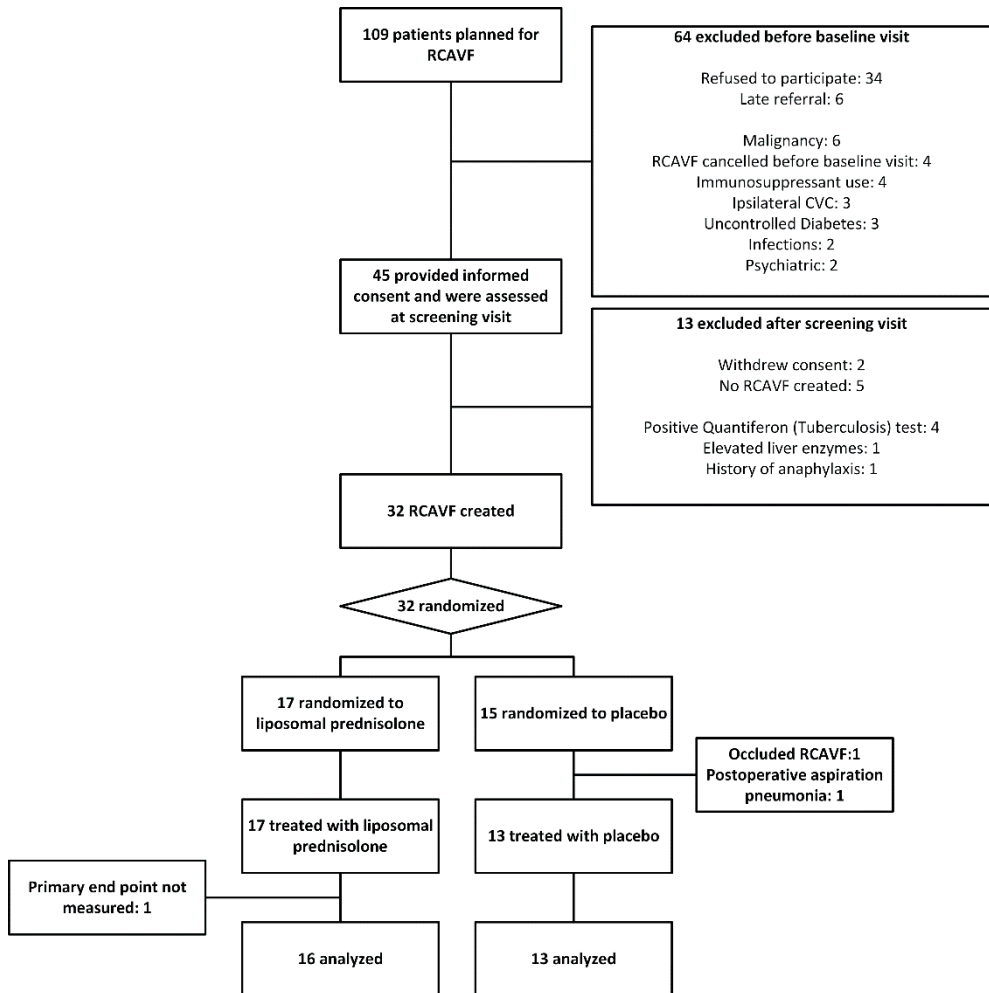


Figure 1 Study flowchart. CVC, central venous catheterization; RCAVF, radiocephalic arteriovenous fistula.

	Placebo (n=13)	Liposomal prednisolone (n=16)	Total (n=29)
Age, yrs	70 ± 8.5	65 ± 12	67 ± 11
Gender			
Female	5 (38%)	1 (6%)	6 (21%)
Male, no (%)	8 (62%)	15 (94%)	23 (79%)
Race			
Caucasian	11 (85%)	13 (81%)	24 (83%)
Hindustani Surinamese	1 (8%)	2 (13%)	3 (10%)
Moroccan	0 (0%)	1 (6%)	1 (3%)
Asian	1 (8%)	0 (0%)	1 (3%)
Cause of renal failure			
Diabetes mellitus	4 (31%)	6 (38%)	10 (35%)
Renal vascular disease	5 (39%)	4 (25%)	9 (31%)
Glomerulonephritis	3 (23%)	2 (13%)	5 (17%)
Interstitial nephropathy	1 (8%)	2 (13%)	3 (10%)
Cystic kidney disease	0 (0%)	2 (13%)	2 (7%)
Comorbidities			
Diabetes mellitus	7 (54%)	7 (44%)	14 (48%)
Coronary artery disease	6 (46%)	4 (25%)	10 (35%)
Peripheral artery disease	4 (31%)	3 (19%)	7 (24%)
Cerebrovascular disease	5 (39%)	4 (25%)	9 (31%)
Medication			
ACE inhibitor	1 (8%)	6 (38%)	7 (24%)
Angiotensin 2 receptor blocker	8 (62%)	5 (31%)	13 (45%)
Loop diuretic	8 (62%)	9 (56%)	17 (59%)
Aldosterone receptor antagonist	0 (0%)	1 (6%)	1 (3%)
Beta blocker	10 (77%)	8 (50%)	18 (62%)
Calcium channel blocker	8 (62%)	11 (69%)	19 (66%)
Platelet inhibitor	4 (31%)	10 (63%)	14 (48%)
Anticoagulant	2 (15%)	3 (19%)	5 (17%)
Vitamin D	12 (92%)	13 (81%)	25 (86%)

Table 1 Baseline characteristics of 29 patients in the LIPMAT study by treatment group. ACE, angiotensin-converting enzyme; LIPMAT, Liposomal Prednisolone to Improve Hemodialysis Fistula Maturation. Data are reported as mean ± SD or n (%).

End Points

The primary end point was assessed in 29 patients. The distal cephalic diameter was 3.9 mm (95% confidence interval, 2.7–5.8 mm) in the placebo group and 3.7 mm (95% confidence interval, 3.0–5.3 mm) in the treatment group ($p = 0.88$). No significant results were observed for secondary end points (Table 2).

	Placebo median (IQR)	Liposomal prednisolone median (IQR)	p (Mann Whitney U)
6 weeks			
Cephalic vein			
Juxta-anastomotic diameter	3.9 (2.7 – 5.8) mm	3.7 (3.0 – 5.3) mm	0.88
Elbow diameter	5.5 (4.7 – 6.7) mm	5.0 (4.0 – 6.1) mm	0.47
Mid upper arm diameter	4.0 (2.3 – 5.3) mm	4.8 (4.1 – 5.4) mm	0.22
Radial artery			
Juxta-anastomotic diameter	3.6 (2.9 – 4.2) mm	3.6 (3.0 – 4.0) mm	0.83
Flow	456 (277 – 688) ml/min	406 (300 – 772) ml/min	0.81
Brachial artery			
Flow	523 (342 – 985) ml/min	550 (417 – 1201) ml/min	0.79
3 months			
Cephalic vein			
Juxta-anastomotic diameter	4.2 (2.3 – 6.1) mm	4.9 (3.9 – 5.8) mm	0.43
Elbow diameter	6.2 (4.7 – 6.9) mm	5.7 (4.4 – 6.3) mm	0.35
Mid upper arm diameter	5.8 (2.8 – 4.5) mm	5.7 (3.6 – 6.2) mm	0.83
Radial artery			
Juxta-anastomotic diameter	4.0 (2.1 – 5.0) mm	3.6 (3.0 – 4.6) mm	1.00
Flow	546 (110 – 1037) ml/min	560 (334 – 970) ml/min	0.65
Brachial artery			
Flow	800 (434 – 1485) ml/min	798 (479 – 1019) ml/min	0.60

Table 2 Effect of liposomal prednisolone on primary and secondary end points in 29 patients in the LIPMAT study. IQR, interquartile range; LIPMAT, Liposomal Prednisolone to Improve Hemodialysis Fistula Maturation.

Functional Outcomes

At the time of assessment of the functional outcomes, 54% of AVFs in the placebo arm and 69% in the liposomal prednisolone arm were successfully used for HD ($p = 0.41$). Seven patients (44%) in the liposomal prednisolone arm and 4 patients (31%) in the placebo group underwent an endovascular or surgical procedure to achieve RCAVF maturation. During follow-up, in the placebo and liposomal prednisolone groups, respectively 23% and 13% of RCAVFs had failed ($p = 0.45$). The functional outcome could not be determined for 6 patients, because of loss to follow-up (2 patients who moved abroad) or not initiating HD (Table 3).

	Placebo (n=13)	Liposomal prednisolone (n=16)
AVF used		
Without procedures to improve maturation	3 (23%)	4 (25%)
With procedures to improve maturation	4 (31%)	7 (44%)
AVF not used		
Failed due to nonmaturation	3 (23%)	2 (13%)
Kidney transplantation	0 (0%)	1 (6%)
Did not reach ESRD	1 (8%)	1 (6%)
Deceased before ESRD	0 (0%)	1 (6%)
Loss to follow up	2 (16%)	0 (0%)

Table 3 Effect of liposomal prednisolone on functional outcomes of RCAVF in 29 patients in the LIPMAT study. Values are n (%). AVF, arteriovenous fistula; ESRD, end-stage renal disease; LIPMAT, Liposomal Prednisolone to Improve Hemodialysis Fistula Maturation.

Safety

No infusion reactions were observed except for 1 subject in the liposomal prednisolone arm who was known to have symptoms of orthostatic hypotension, and experienced mild dizziness without hypotension on postural change during the infusion. The incidence of symptoms related to progressive renal failure and cardiovascular events was similar in both treatment arms (Table 4).

	Placebo (n=13)	Liposomal prednisolone (n=16)
AVF related events		
Angiography/angioplasty	3	6
Revision surgery	1	0
Coiling or ligation of collateral veins	1	2
Hematoma or bleeding	2	1
New AVF within 3 months	1	1
Nerve damage	1	0
Edema	1	0
Infusion related events		
Orthostatic symptoms (no hypotension)	0	1
Renal and metabolic		
Fluid overload	3	2
Gout	1	0
Uremia (worsening)	1	0
Anemia (worsening)	1	1
Cardiovascular		
Atrial fibrillation/flutter	2	4
Myocardial infarction	1	2
Angina pectoris (worsening)	0	1
Intermittent claudication (worsening)	1	0
Infectious		
AVF site infection	0	1
Cellulitis (non-AVF site)	0	1

Upper airway infection including rhinosinusitis	0	2
Septicemia	0	1
Dental	1	0
Other		
Accidental injury	3	2
Fatigue and sleep disorders	4	4
Liver enzyme abnormalities	2	2
Hyperthyroidism	0	1
Hair loss	1	0
Intoxication	0	1
Aspecific thoracic pain	0	1
Constipation	0	1
Sunburn	0	1
Melanoma	1	0
Gastric pain	0	1
Hematoma non-AVF site	0	1
Urinary catheter placement	0	1

Table 4 Adverse events reported in the LIPMAT study. Myocardial infarction includes non-ST-elevation myocardial infarction. AVF, arteriovenous fistula; LIPMAT, Liposomal Prednisolone to Improve Hemodialysis Fistula Maturation.

Infections

In the liposomal prednisolone arm, 5 infections were observed in the 3 months of follow-up. One subject was treated with antibiotics due to erythema in the AVF arm, without fever or systemic symptoms. One subject experienced 2 episodes of mild rhinosinusitis that resolved without specific treatment. One subject died 72 days after AVF surgery, because of progressive fluid overload, complicated by septicemia from a possible catheter-related infection or pneumonia. In the placebo group, 1 subject experienced a dental abscess 3 months after AVF surgery.

Discussion

In the LIPMAT study, we evaluated if liposomal prednisolone improves maturation of RCAVFs. The trial was terminated because of slow enrollment after inclusion of 30 of the 80 subjects initially aimed for. We present the study to investigate feasibility and to report preliminary outcomes. Liposomal prednisolone was safe and well-tolerated by patients with end-stage renal disease. No severe infusion reactions were observed and no severe infections were observed within the expected duration of effect of liposomal prednisolone. Liposomal prednisolone did not result in improved RCAVF maturation as measured by ultrasound at 6 weeks and 3 months after surgery. The 62% successful cannulation rate observed in the LIPMAT study was

comparable to previous studies on functional AVF maturation¹⁸. Although the nonsignificant result may be a mere result of a lack of power due to the small sample size, also no trend toward any difference between the treatment and control group was observed. Apart from a lack of statistical power, several factors might explain the lack of therapeutic efficacy of liposomal prednisolone to improve AVF maturation. First, the local concentration of liposomal prednisolone in the vessel wall of the AVF might not have been sufficient to exert a strong anti-inflammatory effect. The local accumulation of liposomal prednisolone could not be examined, as the AVFs could not be sacrificed for examination. In addition, no approved formulation of the compound was available to trace the liposomes *in vivo* in humans. Second, the inflammatory response in the RCAVF might have been too limited to induce significant local vascular accumulation of the liposomes. Previous clinical studies revealed substantial localization of liposomal prednisolone in the atherosclerotic arterial wall¹². As the prevalence of atherosclerosis was high in the LIPMAT subjects (Table 1), a significant proportion of liposomal prednisolone may therefore have accumulated in nontarget vessel walls instead of the AVF vein. In future studies, tissue samples of AVFs that failed early may be acquired during surgical revisions and analyzed for liposomal prednisolone content.

The extent and timing of venous inflammation after AVF surgery in humans is not fully known. To avoid potential detrimental effects on wound healing, liposomal prednisolone was not administered before surgery. As most of outward remodeling of AVFs has been shown to occur within the first 4 weeks after surgery¹³, we aimed to cover this interval by administering the drug at day 1 and 15 after surgery. This might have been too short, with significant inflammation persisting at 4 weeks after surgery.

Conclusion and Further Directions

The LIPMAT study was the first to study an anti-inflammatory strategy to improve AVF maturation in humans. We could not demonstrate a clinically significant impact on RCAVF maturation. Future studies are needed to elucidate the role of inflammation in AVF maturation and the clinical promise of liposomal formulations of anti-inflammatory drugs to promote AVF maturation.

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LIPMAT Study Group

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Data Safety Monitoring Board

Erasmus Medical Center: H.J.M. Verhagen, MD, PhD (Chair). University Medical Center Groningen: M.H. de Borst, MD, PhD. Leiden University Medical Center: S. le Cessie, PhD (statistician).

Registration

The study was registered at ClinicalTrials.gov, identifier NCT02495662.

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Disclosure

EKH is a member of the Guideline Committee of the Dutch Federation of Nephrology. All the other authors declared no competing interests.

JMM is affiliated with Enceladus Pharmaceuticals which contributed financially to the work reported in this publication.

Supplementary materials

Supplementary materials are available at the *Kidney International Reports* website via <https://doi.org/10.1016/j.ekir.2020.05.030>

References

1. Voorzaat BM, van der Bogt KEAA, Janmaat CJ, van Schaik J, Dekker FW, Rotmans JI, et al. Arteriovenous Fistula Maturation Failure in a Large Cohort of Hemodialysis Patients in the Netherlands. *World J Surg.* 2018; 42(6): 1895–903.
2. Rothuizen TC, Wong C, Quax PHA, van Zonneveld AJ, Rabelink TJ, Rotmans JI. Arteriovenous access failure: more than just intimal hyperplasia? *Nephrol Dial Transplant.* 2013 May 1; 28(5): 1085–92.
3. Dundon BK, Torpey K, Nelson AJ, Wong DT, Duncan RF, Meredith IT, et al. The deleterious effects of arteriovenous fistula-creation on the cardiovascular system: a longitudinal magnetic resonance imaging study. *Int J Nephrol Renovasc Dis.* 2014 Jan; 7: 337–45.
4. Bezhaeva T, de Vries MR, Geelhoed WJ, van der Veer EP, Versteeg S, van Alem CMA, et al. Relaxin receptor deficiency promotes vascular inflammation and impairs outward remodeling in arteriovenous fistulas. *FASEB J.* 2018 Nov 8; 32(11): 6293–304.
5. Wong C, Bezhaeva T, Rothuizen TC, Metselaar JM, de Vries MR, Verbeek FPR, et al. Liposomal prednisolone inhibits vascular inflammation and enhances venous outward remodeling in a murine arteriovenous fistula model. *Sci Rep.* 2016; 6: 30439.
6. Voorzaat BM, van Schaik J, van der Bogt KEA, Vogt L, Huisman L, Gabreëls BATF, et al. Improvement of radiocephalic fistula maturation: rationale and design of the Liposomal Prednisolone to Improve Hemodialysis Fistula Maturation (LIPMAT) study – a randomized controlled trial. *J Vasc Access.* 2017 Mar 3;18(1_suppl): S114–7.
7. Guideline vascular access (“Richtlijn vaattoegang”) - Dutch Federation of Nephrology (“Nederlandse Federatie voor Nefrologie”). 2009.
8. van Assche G, Rutgeerts P, Ferrante M, Noman M, Fidler H, Oldenburg B, et al. Safety and efficacy of a novel IV targeted pegylated liposomal prednisolone product (Nanocort): results from a phase 2a study in patients with active ulcerative colitis. In: *European Crohn’s and Colitis Organisation.* 2016.
9. Peden EK, Leeser DB, Dixon BS, El-Khatib MT, Roy-Chaudhury P, Lawson JH, et al. A Multi-center, Dose-escalation Study of Human type I Pancreatic Elastase (PRT-201) Administered after Arteriovenous Fistula Creation. *J Vasc Access.* 2013 Apr 20; 14(2): 143–51.

10. Dember LM, Beck GJ, Allon M, Delmez JA, Dixon BS, Greenberg A, et al. Effect of clopidogrel on early failure of arteriovenous fistulas for hemodialysis: a randomized controlled trial. *JAMA*. 2008 May 14; 299(18): 2164–71.
11. Bleyer AJ, Scavo VA, Wilson SE, Browne BJ, Ferris BL, Ozaki CK, et al. A randomized trial of vonapanitase (PATENCY-1) to promote radiocephalic fistula patency and use for hemodialysis. *J Vasc Surg*. 2019 Feb; 69(2): 507–15.
12. der Valk FM van, van Wijk DF, Lobatto ME, Verberne HJ, Storm G, Willems MCM, et al. Prednisolone-containing liposomes accumulate in human atherosclerotic macrophages upon intravenous administration. *Nanomedicine*. 2015 Mar 17;
13. Robbin ML, Greene T, Cheung AK, Allon M, Berceci SA, Kaufman JS, et al. Arteriovenous Fistula Development in the First 6 Weeks after Creation. *Radiology*. 2016 May; 279(2): 620–9.

