Supplementary material - list of content

Supplementary Table S1. Criteria for inclusion and exclusion

	Inclusion
1	Anti-GBM antibodies detected by Enzyme-Linked Immunosorbent Assay (ELISA) above a level that is considered toxic (using local laboratory) by the investigator. Patients double-positive for anti-GBM and ANCA may be entered in the trial, but only if their level of anti-GBM antibodies fulfil the criteria above
2	eGFR < 15 ml/min/1.73 m2 (by MDRD equation) or if the patient is non-responsive to standard treatment, and has lost >15 ml/min/1.73 m2 after start of treatment
3	Hematuria on dipstick and/or urinary sediment
4	Male or female patients aged at least 18 years; Female patients of childbearing potential must be willing to accept birth control methods which are considered as highly effective birth control methods according to CTFG (clinical trial facilitation group) guidance 2014
5	Willing and able to give written Informed Consent and to comply with the requirements of the study protocol; and
6	Judged to be otherwise healthy by the Investigator, based on medical history, physical examination, and clinical laboratory assessments. Patients with clinical laboratory values that are outside of normal limits (other than those specified in the Exclusion Criteria) and/or with other abnormal clinical findings that are judged by the Investigator not to be of clinical significance, may be entered into the study
	Exclusion
1	Anuria for more than 48 hours (defined as; less than 200 ml last 48 h)
2	Dialysis dependency for more than 5 days (defined as; maximum 3 dialysis sessions before signing informed consent)
3	Ongoing moderate to severe pulmonary hemorrhage (or having ceased within the last two weeks), defined as; requiring assisted ventilation, oxygen or blood transfusions
4	Pregnancy
5	Symptomatic congestive heart failure (NYHA class 2-4) and requiring prescription medication or clinically evident peripheral edema of cardiac origin
6	Myocardial infarction, unstable angina or stroke within 3 months prior to screening
7	Ongoing bacterial infection requiring antibiotic therapy or viral infection with Hepatitis B, C or HIV (up to 3 months old negative test results are accepted) or active tuberculosis as indicated by chest x-ray
8	Patients should not have received investigational drugs within 30 days prior to screening or within 4 half-lives (whichever is longer); and
9	History or presence of any medical condition or disease which, in the opinion of the Investigator, may place the subject at unacceptable risk for study participation

Supplementary Table S2. Steroid dosing

	Rec[a] dose for 50-75 kg, *mg*	**Actual dose (n=6), mg median (range)**	**Rec[a] dose, for >75 kg, *mg***	**Actual dose (n=9) mg, median (range)**	**Below rec dose n *(%)***	**Above rec dose, *n (%)***
Study visit	..	..	..	..	..	..
Day 7	*50 - 75*	60 (50-70)	*60 - 80*	75 (30-80)	0	1 (7%)
Day 15	*50 - 75*	42.5 (40-50)	*60 - 80*	60 (30-80)	0	7 (47%)
Day 22	*30 - 45*	35 (30-40)	*40 - 60*	40 (30-80)	1 (7%)	2 (13%)
Day 29	*25 - 45*	27.5 (20-40)	*30 - 60*	40 (20-80)	1 (7%)	3 (20%)
Day 50	*17.5 - 30*	25 (17.5-30)	*20 - 40*	20 (16-60)	1 (7%)	0
Day 93	*10 - 15*	16.25 (7.5-20)	*12.5 - 15*	15 (6-25)	4 (29%)	4 (29%)
Day 135	*7.5*	5 (5-20)	*7.5 - 10*	5 (0.5-25)	3 (21%)	9 (64%)
Day 180	*5 - 7.5*	10 (0-15)	*7.5 - 10*	5 (0-12.5)	4 (29 %)	4 (29%)

[a]Rec= Dose recommended in protocol

Supplementary Table S3. Plasma exchange in relation to anti-GBM levels.

Pat	Local assay at diagnosis	Result local assay *(ref[g])*	Number PLEX before imlifidase	Anti-GBM[h] predose	Anti-GBM 6h[i]	Anti-GBM 24h[i]	Anti-GBM d3[j]	PLEX d3-d10[k]	Anti-GBM d10[j]	PLEX d11-d28[k]	PLEX d29-d183[k]
1	EliA[a]	**>680** *(<20)*	1	217	3	2	5	6	32	8	4
2	EliA	**18** *(<7)*	4	0	0	0	0	0	0	0	0
3	Oregentec[b]	**>200** *(<20)*	3	4	0	0	0	0	0	0	0
4	Biorad[c]	**5.5** *(<0.9)*	2	51	0	0	0	4	11	6	0
5	NOVA[d]	1/640 *(<1/20)*	4	21	0	0	0	0	3	5	0
6	EliA	**83** *(<10)*	2	7	0	nd[l]	1	4	5	12	1
7	Euroimmun[e]	**6.0** *(<5)*	1	17	0	0	0	0	0	3	0
8	Biorad	**3.2** *(<1)*	1	14	0	0	0	1	0	0	0
9	EliA	**246** *(<20)*	0	55	0	0	0	0	7	2	0
10	Biorad	**36** *(<1)*	1	66	0	0	0	0	7	2	0
11	EliA	**460** (<20)	2	29	0	0	0	0	0	0	0
12	Wieslab[f]	**108** (<10)	1	72	0	0	0	0	0	0	0
13	Wieslab	**36** *(<10)*	13	1	0	0	0	0	0	3	0
14	Biorad	**49.8** *(<1)*	1	84	0	0	0	3	2	1	0
15	EliA	**234** *(<10)*	1	66	0	0	1	5	11	9	0

[a] ThermoFisher EliA™; [b]Oregentec ELISA; [c]Biorad multiplex; NOVA Lite GBP slides for indirect immunofluorescence, [e]Euroimmun ELISA kit, [f]Wieslab ELISA kit, [g]reference range for local assay; [h]central laboratory analysis of anti-GBM values immediately prior to imlifidase analyzed by SVAR AB, using the Wieslab ELISA (ref <10); [i]Anti-GBM values at 6 and 24 hours after imlifidase treatment. [j]Anti-GBM values at study visit day 3. [k]Number of PLEX from day 3 to day 10, day 11 to day 28 and after day 28 until end of study. [l]Not done.

Supplementary Table S4. Putative prognostic factors

Factor	**Dialysis dependent[a]**	**Non-dialysis dependent**	**p value**
Gender *Males/Females n (%)*	5/0 (100/0)	4/6 (40/60)	0.044[b]
Age *years*	71.5 (19-77)	60 (32-74)	0.51
Dialysis at onset *n (%)*	5/5 (100)	5/10 (50)	0.101[b]
Oliguria at onset *n (%)*	4/5 (80)	1/10 (10)	0.017[b]
Berden class crescentic/ mixed/sclerotic *n (%)*	3/1/0	6/3/1	>0.99[c]
Normal glomeruli *%*	14 % (0-29)	11 % (0-35)	>0.99[d]
Interstitial fibrosis and tubular atrophy (IFTA) *%*	32 % (<10-60)	22 % (<10-45)	0.84[d]
Anti-GBM ELISA pre-dose *U/ml*	66 (17-217)	18 (0-66)	0.043[d]
Anti-GBM ELISA day 10 *U/ml*	7 (0-32)	0 (0-11)	0.12[d]
PLEX after rebound 0/1-5/>5	0/3/2	4/4/2	0.95[e]
ANCA *MPO/PR3/none*	2/1/2	2/1/7	0.33[f]
Anti-drug antibodies *mg/L*	10.2 (9.7-16.6)	6.1 (3.5-11.9)	0.023[d]

All parametric variables expressed as median (range). [a]The patient dying dialysis-dependent is included in this group, except for histological parameters as no biopsy was performed. [b]Fisher´s exact test; [c]Crescent class vs. non-crescentic class with Fisher´s exact test, [d]Mann-Whitney U-test, [e]Mann-Whitney U-test using actual count, [f]ANCA vs. no-ANCA with Fisher´s exact test.

Supplementary Table S4. Pharmacokinetic analyzes.

	Measurement	**Values**
Parameters	..	..
C_{max} *µg/mL* n=15	Geom. Mean (CV %) Median (range)	4.68 (34) 5.00 (2.59 – 7.97)
t_{max} *h* n=15	Geom. Mean (CV %) Median (range)	1.39 (72) 1.25 (0.75 – 6.58)
$t_{1/2}$ alpha *h* n=9	Harm. Mean Median (range)	53.0 59.5 (26.3 - 114)
AUC *(h*µg/mL)* n=9	Geom. Mean (CV %) Median (range)	158 (46) 178 (73.1 - 304)
V *(L/kg)* n=9	Geom. Mean (CV %) Median (range)	0.0484 (39) 0.0538 (0.0237 – 0.0949)
Vz *(L/kg)* n=9	Geom. Mean (CV %) Median (range)	0.130 (31) 0.128 (0.0718 - 0·210)
CL *(mL/h/kg)* n=9	Geom. Mean (CV %) Median (range)	1.58 (46) 1.40 (0.821 – 3.42)

AUC = area under the curve to infinite time; CL = clearance; Cmax = maximum plasma concentration; Tmax = the time of occurrence of Cmax; t1/2alpha = Alpha phase (distribution/elimination) half-life; Vz = volume of distribution during the elimination phase; V = volume of central compartment.