Transplantation is the organ replacement therapy of choice, but immunological problems like preformed donor-specific antibodies or a high degree of immunization complicate the outcome of deceased or living donor transplantation. Postoperatively additional problems can limit the therapeutic success of transplantation, e.g. antibody-mediated rejections or drug-related side effects of the medication like the calcineurin inhibitor-induced thrombotic microangiopathy. Therapeutic strategies include a primary avoidance of immunization, careful patient selection, a meticulous immunological workup and a proper follow-up. In the event of an antibody-mediated disease, therapeutic apheresis is a cornerstone of management. Several techniques are available, but each technique is characterized by specific advantages as well as disadvantages for particular clinical problems. Due to the considerable costs and based on these characteristics, a careful selection of the procedure is mandatory but often not easy to accomplish. This overview will describe indications for therapeutic apheresis in the field of transplantation, illustrate the application of the available techniques to these indications by patient case studies and will provide a critical evaluation of the available techniques for therapeutic apheresis in respect to indications, evidence and costs.

Key words: plasmapheresis, immunoadsorption, ABO-incompatible, desensitization, antibody-mediated rejection, donor specific antibody, kidney transplantation, Luminex, costs

Therapeutische Apherese in der Transplantationsmedizin: Kritische Beurteilung der verfügbaren Verfahren hinsichtlich Indikationen, Evidenz und Kosten

Die Durchführung einer Transplantation als beste Organsatztherapie wird erschwert durch immunologische Probleme wie präformierte donoreigen spezifische Antikörper oder eine ausgeprägte Immunisierung des Empfängers. Die Organfunktion und das Organüberleben sind nach erfolgter Transplantation durch donordispersivische Antikörper, eine antikörperspezifische Abstoßung oder die durch Immunsuppressiva induzierte, thrombotische Mikroangiopathie gefährdet und einschränkt. Die therapeutische Strategie bei Risikotransplantationen beinhaltet die Vermeidung der Empfängersensibilisierung, eine sorgfältige immunologischen Evaluation, kritische Patientenauswahl und eine
individualised Nachsorge. Im Falle von antikörpervermittelten
Erkrankungen oder Problemen ist die therapeutische Apherese ein
unerwartbarer Bestandteil der Therapie. Verschiedene Verfahren
mit spezifischen therapeutischen Effekten, Vor- und Nachteilen sind
hierfür verfügbar. Die Auswahl des Therapieverfahrens sollte auf-
grund der signifikanten Kosten hinsichtlich der Verfahrenscharak-
teristika, Evidenz und Indikation für die vorliegende Indikation
ergünstig erfolgen.
Diese Übersicht führt die transplantsrelevanten Indikationen auf;
illustriert den Einsatz der verschiedenen Verfahren anhand
von klinischen Fallbeispielen und beurteilt die verfügbaren Ver-
fahren hinsichtlich Evidenz und Kosten.

**Schlüsselwörter:** Plasmapherese, Immunoadsorption, ABO-inkom-
patibel, Desensibilisierung, Antikörper-vermittelte Abstoßung,
Nierentransplantation, Lumine, Kosten

---

**Introduction**

**Terminology and Technical Considerations**

Therapeutic apheresis can be applied using a variety of devices and procedur-
al approaches. Plasmapheresis (PS) eliminates the patients’ plasma whereas the
cellular parts of the blood are rein-
fused together with a substitution fluid. Plasma separation is achieved either by
capillary separator (membrane PS, MPS) or with the use of a centrifuge.
Indications for PS are the elimination of a well-defined part of the plasma (e.g.
antibodies) or the necessity to adminis-
ter a plasma component in large quanti-
ties of plasma (e.g. ADAMTS13 in pa-
tients with thrombotic microangiopa-
thy). In the former case plasma substi-
tution is achieved by using isoosmotic albumin or fresh frozen plasma (FFP),
in the latter FFP is the substituted. This technique is simple to use, does not require
expensive secondary columns and can be used in different clinical situations.
The disadvantage is the elimination of useful proteins, the limitation to
1-1.5 plasma volumes (PV) as treating
dose [1] (thereby limiting the efficiency of each session) and the potential for in-
fected complications such as HIV or hepatitis B or C transmission if plasma
is used as substitution fluid.
Immunoadsorptive techniques have no risk for infectious transmission, can be
either unselective, semi-selective or highly selective for the protein targeted
for removal, and the specific secondary adsorbers are available for single use or
can be regenerated. If a regenerative system is used, the amount of treated
plasma has no limit, thereby qualifying as the technique with the highest effi-
ciency for each single treatment. Disad-
vantages are the high cost of the sec-
condary column and, in most cases, the
need for a specialized device. Another
relevant aspect is the higher degree of complement activation with the larger
extracorporeal circuit and the adsorber.
Due to the advantages of a theoretically unlimited treatment dose and treatment
number regenerative systems are used for indications requiring multiple treat-
ments like antibody-mediated rejection (AMR) or desensitization protocols.
Table 1 provides an overview of the available products for immunoadsorption
used with transplantation indications.
A double-lumen vascular access (AV-
fistula or catheter) is recommended to
limit the treatment duration, but single
needle devices also exist. The apheresis
protocol for PS is characterized by re-
placement of 1-1.5 PV per session, sub-
stituting the plasma partly with 0.9%
saline (e.g. in the case of hyperviscosi-
ity), 5% albumin or FFP. Anticoagula-
tion is usually achieved using heparin.
Regional anticoagulation with citrate
can be an alternative in special circum-
stances. With immunoadsorption usually
up to three PV per session can be
processed according to the adsorber
characteristics. For immunoadsorption
anticoagulation with citrate and heparin
is usually used to limit adverse events
due to complement activation by the
larger extracorporeal circuit and the ad-
sorber. Since contact of blood with the
materials used in the extracorporeal cir-
cuit may lead to a significant generation
of bradykinine it is necessary to stop
treatment with an ACE-inhibitor for at
least three days before starting imm-
unoadsorption to avoid potentially
live threatening events (shock, bru-
dykinine syndrome) due to inhibited
bradykinine degradation.
Treatments are usually scheduled ini-
tially daily to remove quickly the major
burden of antibodies, followed by alter-
ate day treatments to compensate for
redistribution, but different approaches
can be dictated by clinical needs. Mon-
itoring of coagulation parameters (INR,
PTT, fibrinogen) and immunoglobulins
detects significant depletion of these
components by apheresis and can promp
timely prophylactic substitu-
tion.

**Indications for Therapeutic Apheresis in Transplantation Medicine**

In the following section the indications
for therapeutic apheresis in a transplant
candidate or transplanted patient are
presented.

**I. Desensitization – ABO-incompatible (ABOi) Transplantation**

After the blood group barrier had been
successfully crossed in Japan in the
1980s [2,3], various protocols were de-
developed for ABO-incompatible kidney
transplantation and the procedure has
gained widespread acceptance and has
been implemented in multiple trans-
plant centers as a standard procedure.
Immunosuppression typically consists
of tacrolimus, mycophenolate and
steroids together with induction therapy
with an IL-2-receptor blocking agent.
The isoagglutinine antibodies against
the donor can be eliminated using a
stepwise approach. Firstly, the
CD19/20-positive pre-B-cells are elimi-
nated with a single infusion of ritux-
imab four weeks prior to transplantation.
Novel sensitization and production
of antibodies is thereby efficiently pre-
vent. In a second step, the already existing antibodies are depleted using different therapeutic apheresis modalities. PS was successfully applied in the initial protocol published by Gloor and colleagues [4]. Tyden reported the use of selective immunoabsorption with sepharose columns binding selectively anti-A or anti-B antibodies [5]. This technique allows the processing of a much higher plasma volume (typically three PV) instead of 1.5 PV with PS. The high costs of the only available product for highly selective adsorption (Glycosorb™), which is licensed only for single-use, has prompted various groups to use unselective IgG-immunoabsorption with regenerative columns (personal communication). Using PS limits treatment efficiency per session, depletes the patient of other immunoglobulins but also of other valuable proteins (e.g. coagulation factors) and is therefore not the best option. Due to its selectivity, treatment with the Glycosorb™ column has no relevant side effects, is the treatment of choice but is very expensive, especially for patients who require an intense apheresis schedule to eliminate a high titer of isoagglutinine antibodies. It has to be examined whether the use of semi-selective IgG-adsorption is equally effective and safe, and whether this regimen requires the administration of a high dose of IVIG.

The illustrative case 1 demonstrates the titer reduction using a Glycosorb™ column to prepare a patient for ABOi transplantation.

Illustrative Case 1: ABO incompatible transplantation

A 56 year-old patient with end stage renal disease due to nephrosclerosis presented after three years on dialysis with his wife as a living donor for ABO-incompatible kidney transplantation. The blood group constellation of donor and recipient was A/O. An anti-A isoagglutinine titer measured against the donor erythrocytes of 1:64 was quantified using the gel card technique (titers course triangles with line in plot). The crossmatch was negative and the HLA A/B/DR mismatch constellation was 0-1-2. After conditioning with a single administration of rituximab four weeks prior to the scheduled transplantation date, he was readmitted for therapeutic apheresis on day -10. Triple immunosuppression with tacrolimus, mycophenolate and prednisone was begun and immunoabsorptions with the specific anti-A Glycosorb™ column depleted the patient of the isoagglutinine titer in six sessions (isolated triangles in plot). Three plasma volumes were processed with citrate/heparin anticoagulation. The preoperative titers were 1:4/1:1 for IgG/IgM and surgery was successfully performed. After primary graft function the creatinine levels fell rapidly and the patient was discharged with stable renal function and an eGFR (MDRD) of 59 ml/min/1.73m² and a serum creatinine of 1.34 mg/dl (dot plot). The postoperative antibody titers remained well below the threshold for repeated IA (first week 1:8, second week 1:16 for IgG, horizontal line in plot) and no additional IA were necessary.

II. Desensitization – Donor-specific Antibodies (DSA)

Patients with preformed HLA-antibodies, i.e. a high percentage of panel reactive antibodies, accumulate on the waiting list for kidney transplantation and can experience a substantially longer waiting time (e.g. 10-15 years in comparison to 5-7 years in the Eurotransplant region [6]). The Eurotransplant acceptable mismatch program [6] or center-specific desensitization protocols for a patient in case of an organ offer [7] or while being on the waiting list [8] were developed in order to transplant these highly immunized patients within a reasonable time frame.

The transplantation procedure is problematic with deceased donor organs as the time for preconditioning of the recipient is extremely limited and the accompanying procedures are difficult to perform in time, especially if the transplantation happens at night. If transplantation from a living donor is planned and DSA are detected, various protocols were published to desensitize the recipient. These strategies [7-11] require an intensive procedure, mostly consisting of the administration of IVIG of intensified immunosuppression, pre- and postoperative plasmapheresis or immunoabsorption and carry a higher risk for antibody-mediated rejection.

To remove DSA or multiple HLA-antibodies, therapeutic apheresis can be applied in all forms. The same considerations described above in regard to the choice of the apheresis subtype apply here. In this setting, no superselective secondary adsorber exists and the selectivity for immunoglobulins would be considered the best option today. Whether a constant immunological surveillance and preemptive regular therapeutic apheresis sessions are necessary in the postoperative period needs to be investigated. More than one treatment is usually needed to deplete the recipient of the DSA- or anti-HLA titer. Regenerative or selective apheresis methods would therefore be the treatment of choice and should be used together with a relevant immunological monitoring. Anticoagulation, vascular access and amount of treated plasma follows the basic protocol described above.

The illustrative case 2 demonstrates the desensitization of a patient with DSA against the living donor using a crypto-
Illustrative Case 2: Desensitization

A patient scheduled for living donor transplantation was sensitized against HLA-A24 due to a blood transfusion. Unfortunately, the donor carried this surface antigen. The desensitization procedure consisted of one immunoadsorption, two IVIG and two rituximab administrations over a period of 30 days. After a waiting period of another thirty days the crossmatch was negative and a triple immunosuppression was begun. ATG induction was started on the day of transplantation. Perioperatively four immunoadsorptions were scheduled. The titer of the donor-specific antibody to HLA-A24 was quantified with the Luminex assay. After the initial immunoadsorption the titer fell below the level of significance for the local assay. After the additional waiting period of thirty days for security reasons after the completion of desensitization procedures, the titer increased but was almost eliminated by the immunoadsorption preceding transplantation. The graft function reached its best value on day six after transplantation 1.09 mg/dl, eGFR MDRD 78 ml/min/1.73m². During follow-up no signs of rejection occurred and the graft function stabilized with a serum creatinine of 1.59 mg/dl (eGFR MDRD 51 ml/min/1.73m²) with 244 days of follow-up.

III. Rejection Treatment – Vascular Rejection/Abdom Mediated Rejection (AMR)

HLA antibodies are involved in AMR, and AMR and cellular vascular rejection can coexist. The renal biopsy often cannot rule out one cause or the other with sufficient certainty, leaving the clinician with the decision how to treat vascular rejection that can be caused by antibodies or cellular infiltration. Therapeutic apheresis, accompanied by T-cell depletion (ATG, ALG or OKT3), conversion to a tacrolimus-based immunosuppression and pulsed steroids, are used to limit the interstitial and vascular damage [12]. In the setting of AMR the use of immunoadsorption targeted against IgG has been used successfully [13]. Due to conflicting and limited data, general recommendations in regard to the treatment of choice, i.e. PS or IA, the number of apheresis sessions and the best immunosuppressive therapy are difficult to make [13-16]. If possible, a screening for donor-specific antibodies should be performed to monitor the antibody titer during treatment. In our center, we typically schedule 10 sessions with daily treatments initially followed by apheresis every other day in a patient with vascular rejection (Banff IIb-III or AMR). The illustrative case 3 demonstrates the application of PS in a patient with antibody-mediated rejection.

IV. Thrombotic Microangiopathy (TMA)

Recurrence or de novo TMA in the transplant patient is seen rarely with the use of calcineurin inhibitors or mTOR inhibitors or acute vascular rejection. Infectious diseases such as HIV, CMV, parovirus B19, an inhibited or decreased activity of the von Willebrand factor-cleaving metalloprotease ADAMTS13 or mutations in complement receptors may also trigger microangiopathy with either limited or systemic manifestations. If switching to a different immunosuppressive regimen or the treatment of an underlying infection does not lead to resolution of the TMA, plasma exchange can be attempted to ameliorate the course of the disease and subsequent graft damage [17,18], although the level of evidence is low. The treatment regimen is comparable to TMA in non-transplanted patients. The treatment volume is usually one PV with solely fresh frozen plasma as substitution fluid and anticoagulation with heparin on a daily basis until platelet count and lactate dehydrogenase have normalized. Up to 50% of patients demonstrate a prompt exacerbation if daily PS is stopped. Continuation of PS on an alternate day strategy for at least two additional treatments can reduce the recurrence rate [19,20]. Nevertheless TMA reduces graft survival both in recurring or de novo TMA and treatment might not alter the progression of the disease [21]. Immunoadsorption so far is experimental in the treatment of post-transplantation TMA but a few cases in other clinical settings have been reported [22,23].

V. Posttransplantation Anti-glomerular Basement Membrane (GBM) Disease

Goodpasture syndrome or anti-GBM disease can occur de novo in patients following transplantation or as a manifestation of underlying Alport disease, but is rare (e.g. 3% of transplanted male Alport patients [24]). In the latter instance, the recipient’s immune system is exposed to a collagen component carried by the transplanted organ that is lacking in Alport patients and, consequently, the patient might develop antibodies against this antigen in the glomerular basement membrane. These antibodies may then induce post-transplantation anti-GBM disease [25,26]. The treatment of this condition and of de novo disease is identical to the strategy applied to non-transplanted patients. Therapeutic apheresis is used in
order to remove the causative antibody. Both PS and IA have been shown to deplete the patient effectively of antibodies and halt disease progression [27-29]. A direct comparison is lacking in the published literature, but due to theoretical considerations, IA with its ability to treat a larger plasma volume might be the first option. If a patient presents with pulmonary hemorrhage precautions should be taken to interfere with coagulation, so it is recommendable to use FFP in the case of PS or choose an adsorber that does not relevantly adsorb fibrinogen (see Table 1). The treatment strategy aims to a rapid removal of the antibody with daily treatments. Treatment frequency should be tapered later according to antibody titer measurements. Apheresis is accompanied by an intensified immunosuppressive regimen to suppress further antibody formation [27].

VI. Recurrence of Primary FSGS after Kidney Transplantation

Primary focal segmental glomerular sclerosis recurs with an uncertain incidence after kidney transplantation (presumably 20%). A circulating factor is assumed to play a causative role and therapeutic apheresis has been successfully applied in patients with recurrent FSGS. In patients treated with a regenerating protein adsorption column or plasma exchange, a dramatic but usually transient reduction in proteinuria has been observed [30]. This effect was greater with the use of IA, but more prolonged remissions were reported with the use of PS with or without combination with cyclophosphamide [31,32]. PS and protein A IA are applied using the standard parameters as described above. Treatment duration is 6-10 sessions with PS (median 9).

Critical Evaluation of Modalities of Efficacy, Evidence and Costs

Therapeutic apheresis is a valuable treatment option in transplantation medicine and is available in different technical variants. Despite the increasing use of immunoadsorption in the treatment of transplantation-associated conditions, the evidence for effective and safe treatment is largely on the side of plasmapheresis. This method can be safely applied in every circumstance but has a limited efficiency of clearance due to the limitations in treated plasma volume per session in comparison to a regenerative immunoadsorption. However, this disadvantage is relative, as e.g. the IgG clearance follows an exponential curve, and, thus, an increase of treatment volume induces increasingly smaller additional protein reduction. IA, on the other side, is attractive due to its advantageous side effect profile, the

Illustrative Case 3: Antibody-mediated rejection

A 54 year-old patient with end stage renal disease due to malignant hypertension received a blood group compatible organ from a deceased donor (donor/recipient CMV positive/positive; HLA A/B/DR 2-1-1 mismatch). The immunosuppressive therapy consisted of cyclosporine A, mycophenolate and prednisone. An allograft biopsy on day 8 demonstrated an antibody-mediated rejection (glomerulitis, acute tubular necrosis, activated endothelium in interlobular arteries, C4d positivity of the peritubular capillaries) together with a Banff 1a cellular rejection. Rejection treatment consisted of pulsed steroids, switching cyclosporine to tacrolimus, 10 days of ATG (initial dose 2.5 mg/kg body weight/day, subsequent doses adjusted to the CD3-cell count aiming for less than 50 cells/ml) and plasmapheresis (due to non-availability of protein A immunoadsorption, treatment parameters: 1.5 PV, substitution with 5% albumin, anticoagulation with heparin). Donor-specific antibodies could not be monitored. Graft function stabilized and a control biopsy on day 27 demonstrated minimal residual signs of endothelialitis and cellular infiltrates. On this day rituximab was given (375 mg/m²). The creatinine improved to 3.8 mg/dl.

Tab. 1: Adsorber characteristics for immunoadsorption in transplantation

<table>
<thead>
<tr>
<th>Adsorber</th>
<th>Manufacturer</th>
<th>Targeted protein</th>
<th>Ligand</th>
<th>selective</th>
<th>special device necessary</th>
<th>single use</th>
<th>regenerative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immunosorba TR 350</td>
<td>Diamed</td>
<td>IgG/CIC</td>
<td>Tryptophane</td>
<td>unselective</td>
<td>no</td>
<td>yes</td>
<td>no</td>
</tr>
<tr>
<td>Glycoareb</td>
<td>Glycoen</td>
<td>lseaaglutamin A/B/AB</td>
<td>Blood group antigen A/B/A-sepharose</td>
<td>highly selective</td>
<td>no</td>
<td>yes</td>
<td>yes</td>
</tr>
<tr>
<td>Globamin</td>
<td>Fresenius Medical Care</td>
<td>IgG/CIC</td>
<td>synthetic peptide GAM</td>
<td>semi-selective</td>
<td>yes²</td>
<td>no</td>
<td>yes</td>
</tr>
<tr>
<td>Immunosorba</td>
<td>Fresenius Medical Care</td>
<td>IgG/CIC, IgA, IgM</td>
<td>SPA-sepharose</td>
<td>semi-selective</td>
<td>yes²</td>
<td>yes</td>
<td>yes</td>
</tr>
<tr>
<td>Theracorb IgG</td>
<td>Milteny Biotech</td>
<td>IgG/CIC, IgA, IgM, IgE</td>
<td>SPA-sepharose</td>
<td>semi-selective</td>
<td>yes²</td>
<td>yes</td>
<td>yes</td>
</tr>
</tbody>
</table>

²limited IgG3-adsorption, ²²ad libitum, ²²²CITRAMO™ or ADAsorb™, ²²²²LIFE18™, SPA denotes staphylococcal protein A, IC denotes immunocomplexes.
opportunity to treat large plasma volumes without the necessity of plasma transfusion and the selective character. The selectivity, however, is not always needed and also not always wanted. There are only special circumstances, e.g. the removal of isoaaglutinine antibodies in ABO-incompatible transplantation, where a single defined plasma component is responsible for the disease and the adsorption of this fraction is possible. But even in this case, various centers use PS in the event of insufficient titer reduction even after intense specific IA and achieve a significant improvement with PS, suggesting pleiotropic effects like, for example, complement depletion. In other conditions where no specific target protein is known, the unreflected use of IA can be detrimental, as good head to head comparisons are missing and one cannot extrapolate PS findings (even in the case of an antibody-mediated disease) to IA and hope for identical immunological or clinical outcomes.

In economic terms, a PS with albumin is the cheapest treatment option, followed by PS with a small fraction of FFP. Depending on the negotiations with the manufacturer and the insurance companies, an IA with a single use column (e.g. tryptophane) can be identical in terms of costs as PS with FFP. The Glycosorbt™ column used in ABOi-transplantation is strikingly expensive for a single use column reflecting the missing alternative. IA with regenerative columns is very expensive but amortizes with multiple use. In cases of scheduled repeated treatments (e.g. antibody-mediated rejection with 8-15 treatments) the use of this variant can be encouraged. Recommendations on the choice of apheresis technique can be found in Table 2.

Unfortunately, the financial aspects of therapeutic apheresis are a matter of regional negotiation and preference. To simplify reimbursement, transplant centers should define their common needs, aim for a standard reimbursement and try to limit price variations. The structure of reimbursement codes (ZE2008-13) in Germany, for example, was adjusted in 2008. As a result, three different codes and thus three different prices had to be negotiated. The first is the code for a single IA with a non-regenerative column (OPS 8-821.0), the second is the code for the first treatment with a regenerative column (OPS 8-821.10) and the third is the code for each following treatment with a regenerative column (OPS 8-821.11). It is advantageous to achieve the agreement, that the first treatment with a regenerative IA receives the main bulk of the refund, whereas the following treatments receive lesser refund. Thereby the danger is minimized that a premature cessation of treatment results in a monetary deficit. The overview about the financial aspects of the different methods in Table 3 highlights the importance of knowing the in-house costs and reimbursements to avoid a large deficit.

**Summary**

The application of therapeutic apheresis in transplantation medicine is a cornerstone of therapy for several conditions such as AMR or ABO-incompatible transplantation, and enables clinicians to develop strategies to provide the best organ replacement to patients with a high degree of immunization or pre-formed DSA thereby expanding the use of living donation. The standard method has been plasma separation but it is currently more and more replaced by the more selective treatment provided by immunoadsorption. Due to the considerable costs of immunoadsorption the selection and application of an adsorb and device for immunoadsorption should be preceded by a judicious effort to characterize and plan the treatment procedure for the patient. The specific characteristics of the clinical problem, the capabilities of the choices available and the current evidence have to be known to avoid high costs or inadequate therapy. Unfortunately, robust evidence is scarce and more clinical research with a high standard of quality is needed to define the role of each therapeutic apheresis method for the clinical problems that occur in transplantation medicine.

**References**


**Table 2: Indications and recommendations for therapeutic apheresis**

<table>
<thead>
<tr>
<th>Indication</th>
<th>Targeted protein</th>
<th>Preferable apheresis method</th>
<th>Number of treatment sessions</th>
<th>Treatment volume</th>
<th>Substitution fluid</th>
<th>Anticoagulation</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABOi</td>
<td>ABO incompatibility</td>
<td>Selective immunoadsorption</td>
<td>depending on isoagglutinintiter, mean 6</td>
<td>2.5 PV (IA)/3 PV (PS)</td>
<td>None</td>
<td>Heparin</td>
<td>[30]</td>
</tr>
<tr>
<td>AMR</td>
<td>HLA-antibodies</td>
<td>Immunoadsorption/PS</td>
<td>0.9-1.6 (A)/1.4 (PS)</td>
<td>None</td>
<td>None</td>
<td>Heparin</td>
<td>[15-19]</td>
</tr>
<tr>
<td>Desensitization</td>
<td>LLC-antibodies</td>
<td>Immunoadsorption/PS</td>
<td>One to three cycles of two to seven 1-day association/PS (median 3)</td>
<td>None</td>
<td>None</td>
<td>Heparin</td>
<td>[27-29]</td>
</tr>
<tr>
<td>recurrent FSGS</td>
<td>unknown permeability factor</td>
<td>PS</td>
<td>14 (±2)/14 (PS)</td>
<td>2.5 PV (IA)/3 PV (PS)</td>
<td>None</td>
<td>Heparin</td>
<td>[27-29]</td>
</tr>
<tr>
<td>anti-GBM disease</td>
<td>anti-GBM peptide</td>
<td>Immunoadsorption/PS</td>
<td>3 PV = 4200 ml</td>
<td>Tissue plasmavolume (PV in ml = kg body weight x 40)</td>
<td>5% albumin: 100-150 €/liter; 1 FFP (250 ml): 80-100 €</td>
<td>300-500 €</td>
<td>800-1.300 €</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>NA</td>
<td>900-1.300 €</td>
<td>NA</td>
<td>1.300-1.600 €</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>1.000-1.400 €</td>
<td>NA</td>
<td>NA</td>
<td>1.000-1.400 €</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>1.000-1.400 €</td>
<td>NA</td>
<td>NA</td>
<td>1.000-1.400 €</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>1.000-1.400 €</td>
<td>NA</td>
<td>NA</td>
<td>1.000-1.400 €</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>1.000-1.400 €</td>
<td>NA</td>
<td>NA</td>
<td>1.000-1.400 €</td>
<td></td>
</tr>
</tbody>
</table>

**Tab. 3: Costs projections for therapeutic apheresis**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Treatment regimen</th>
<th>Substitution with 5% albumin</th>
<th>Consumables</th>
<th>AdSORber</th>
<th>Costs per treatment</th>
<th>Reimbursement</th>
</tr>
</thead>
<tbody>
<tr>
<td>PS</td>
<td>1.5 PV x 4200 ml</td>
<td>5% albumin: 100-150€/mL, 1 FFP (250 ml): 80-100 €</td>
<td>800-1000 €</td>
<td>NA</td>
<td>800-1300 €</td>
<td>1.300 €</td>
</tr>
<tr>
<td>IA</td>
<td>single use column</td>
<td>1.5 PV x 4200 ml</td>
<td>NA</td>
<td>400-600 €</td>
<td>900-1300 €</td>
<td>1.300-1.600 €</td>
</tr>
<tr>
<td></td>
<td>regenerative</td>
<td>1.5 PV x 4200 ml</td>
<td>NA</td>
<td>500-1000 €</td>
<td>1000-1600 €</td>
<td>3.500-5.000 €</td>
</tr>
<tr>
<td></td>
<td>single use GlycoSorb</td>
<td>1.5 PV x 4200 ml</td>
<td>NA</td>
<td>400-600 €</td>
<td>3.500-5.000 €</td>
<td>3.500-5.000 €</td>
</tr>
</tbody>
</table>

Treatment parameters calculations are based on a 70 kg Patient with a normal hematocrit and using the Kaplan-formula for calculation the plasmavolume (PV in ml = kg body weight x 40) with a shunt or double lumen shalden catheter

Financial data are based on real data with rounding of numbers (inhouse data and personal communication)

All treatments immunoadsorption, PV plasma volume; GA Glanzendorf, NA not applicable
sions, splenectomy, and double-filtration plasmapheresis. Transplantation 74: 1207-10

Sven Teschner, M.D.
Transplant Center Cologne and Renal Division
Department of Medicine
University Hospital Cologne
50924 Cologne
Germany
sven.teschner@uk-koeln.de