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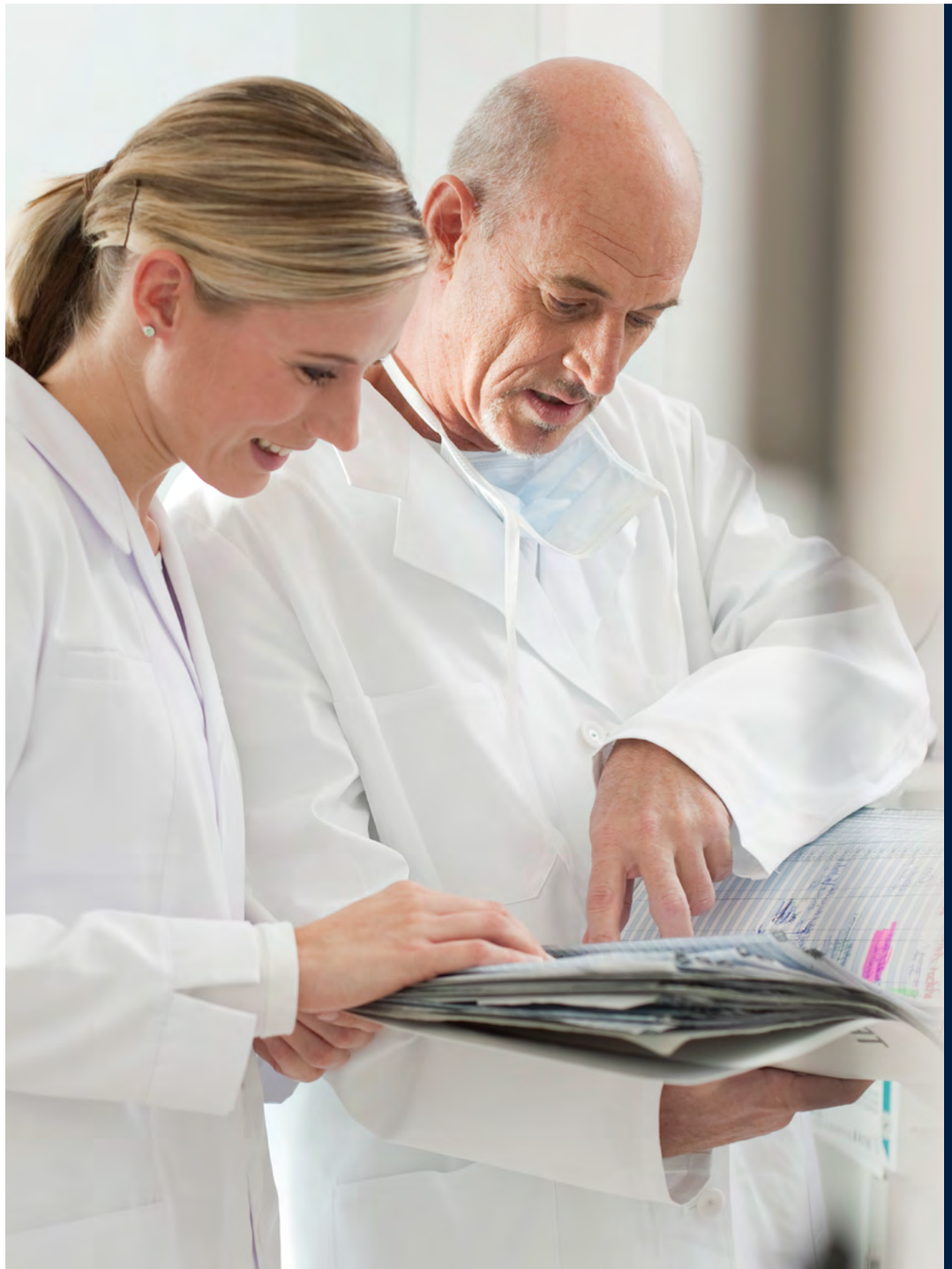


Effectiveness of double column immunoadsorption in a wide range of indications

Outcomes and impact of the IANIS study

Presented by Fresenius Medical Care

Contents

How important is immunoadsorption in your practice?

IANIS
Real-world treatment data

How is it different to many existing observational studies?

Most of the existing publications on immunoadsorption are limited to small studies due to:

- ethical reasons (severity of patients' illness)
- lack of power (low patient numbers)

→ **Large prospective randomised trials or placebo-controlled studies not possible**

What is the value of the multicentre IANIS study?

- Data from large patient cohort
- Observation of clinical effectiveness and safety of high dose Immunoadsorption
- Broad spectrum of autoimmune-mediated diseases covered
- Protocols on treatment patterns in practice identified

The IANIS study

"Performance, clinical effectiveness, and safety of immunoadsorption in a wide range of indications"

Fuchs K et al. Ther Apher Dial. 2022; 26(1):229-241.[1]

Note: This study was funded by Fresenius Medical Care.

IANIS
Objective

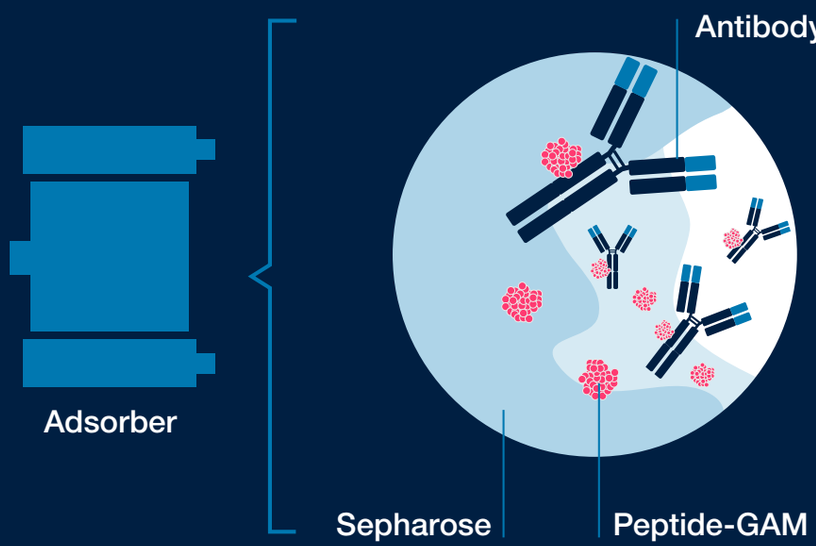
Assessment of the performance of both immunoadsorbers, Protein-A ligand (Immunosorba)* and peptide GAM ligand (GLOBAFFIN):

- immunoglobulin reduction (IgG, IgA, IgM)
- clinical effectiveness
- safety
- tolerability

Immunoadsorption is a specific extracorporeal blood purification procedure that selectively removes pathogenic antibodies, mainly IgG, as well as immune complexes from the blood while retaining important plasma constituents such as albumin.

Read more on the selectivity and effectiveness of immunoadsorption ❯

Removal of pathogenic substances



*Highly selective Protein-A ligand double adsorber system for selectable plasma volume results in predetermined IgG elimination. Immunosorba is no longer available on the market.

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Key facts

Study design	Prospective, noncomparative, noninterventional multicentre cohort study
Study period	July 2013 – April 2018
Number of treated patients	81
Number of centres	6
Examined adsorbers	Protein-A ligand (Immunosorba*) and peptide GAM ligand (GLOBAFFIN)
Examined indications	Multiple sclerosis, myasthenia gravis, inflammatory polyneuropathies, dilated cardiomyopathy, desensitisation before or after transplantation, further neurological or other indications
Result	**Immunoadsorption represents an additional therapeutic option for therapy-refractory immune disorders.**

* Highly selective Protein-A ligand double adsorber system for selectable plasma volume results in predetermined IgG elimination. Immunosorba is no longer available on the market.

IANIS Study

Notes:
The chapters presenting the IANIS study are a summary of: Fuchs K et al. Ther Apher Dial. 2022; 26(1):229–241.
The IANIS study chapters reflect the results of the study and the views and opinions of its authors only.

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Patients and methods

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Immunoadsorption treatments and documented parameters

Immunoadsorption treatments

- **Plasma separation:**
  centrifugation or plasma filtration
- **Initiation of anti-coagulation:**
  heparin and/or citrate
- **Administration of immunoadsorption:**
  alternating double column adsorber system

Documented parameters

- **Performance of immunoadsorption:**
  pre- to post-treatment reduction rates of IgG, IgA, and IgM
- **Clinical effectiveness:**
  improvement, stabilisation or deterioration of the clinical status
- **Safety and tolerability:**
  pre- and post-treatment laboratory parameters; documentation of adverse device effects (ADEs)

Patient follow-up lasted up to two years if possible.

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Results

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Study population

Neurology (patients)

17	10	9	8	3	18
Multiple sclerosis	Myasthenia gravis	Autoimmune encephalitis	Inflammatory polyneuropathies	Guillain-Barré syndrome	Further neurological / other indications

Cardiology (patients)

8

Dilated cardiomyopathy

Transplantation (patients)

8

Transplant organ rejection
HLA-incompatible transplantation
AB0-incompatible transplantation

81 patients in total

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Treatment patterns of immunoadsorption

Immunoadsorption treatments

- **Peptide GAM ligand:** 156 treatments
- **Protein-A ligand:** 443 treatments
- **Average treated plasma:** 2.2-fold volume/session

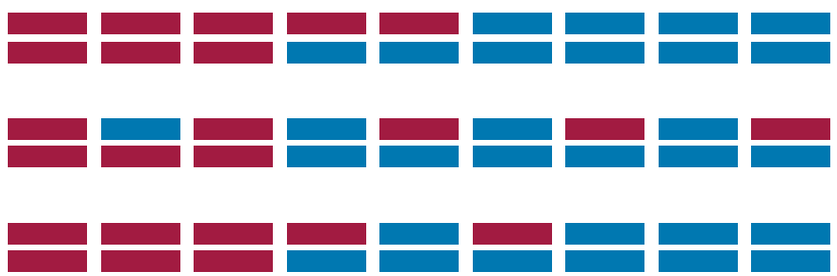
Plasma preparation and anticoagulation

- **Main plasma separation method:**
  centrifugation (91.4 %)
- **Preferred anticoagulant:**
  citrate (ACD-A solution or the combination of both ACD-A and heparin)

Treatment patterns

- Identified for DCM, multiple sclerosis and myasthenia gravis
- Strong overall reduction of plasma IgG levels with a regimen on consecutive days

Identified treatment patterns of immunoadsorption (Examples)



Identified treatment patterns of immunoadsorption (Examples)

Dilated cardiomyopathy

8 patients received 3–5 treatments within 5 consecutive days

Multiple sclerosis

14 out of 17 patients received 3–5 treatments within 3–9 consecutive days

Myasthenia gravis

8 out of 10 patients received 3–5 treatments within 3–6 consecutive days

Graph adapted from
Fuchs K et al. Ther Apher Dial. 2022;
26(1):229–241.

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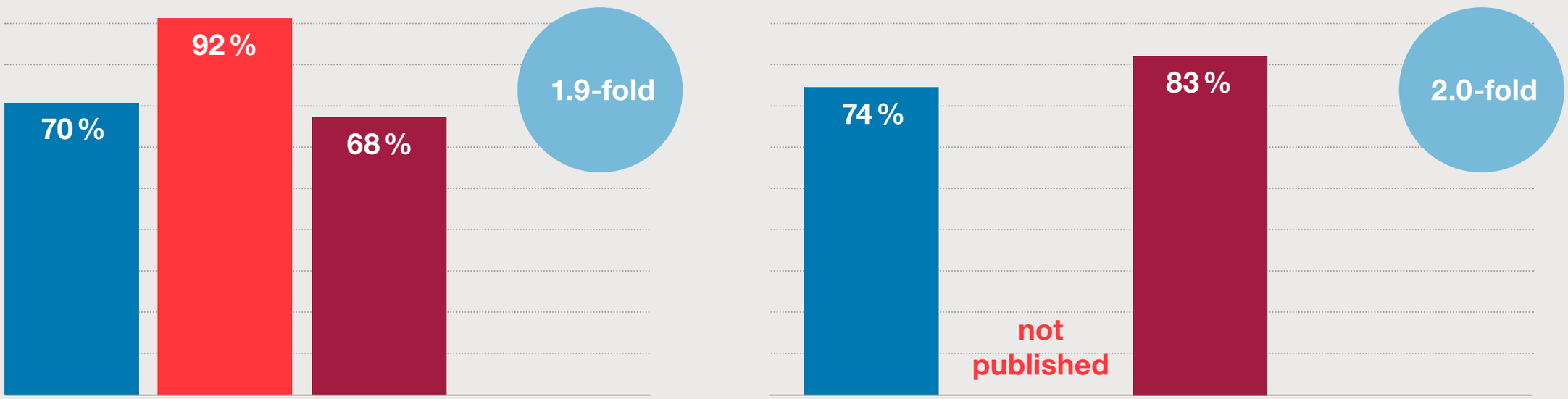
Performance of immunoadsorption

Check on safety profile here ❯

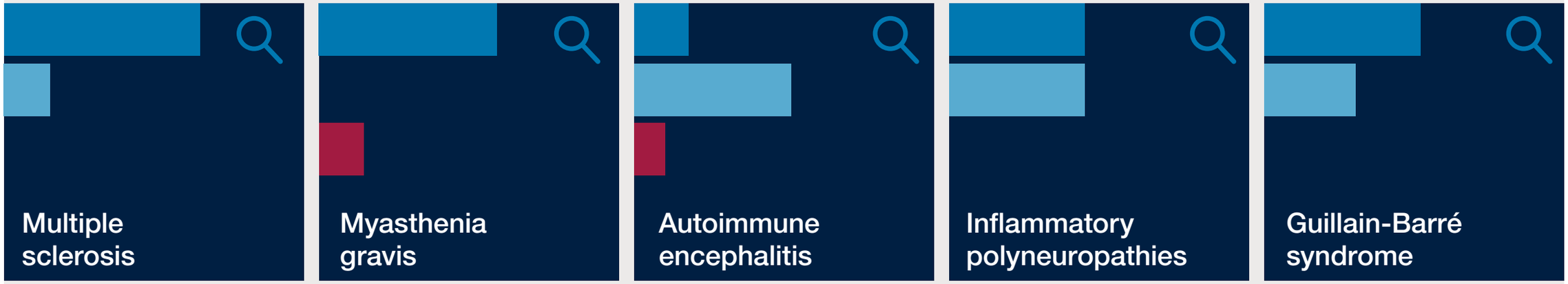
Comparable effectiveness in IgG reduction with a high binding affinity*



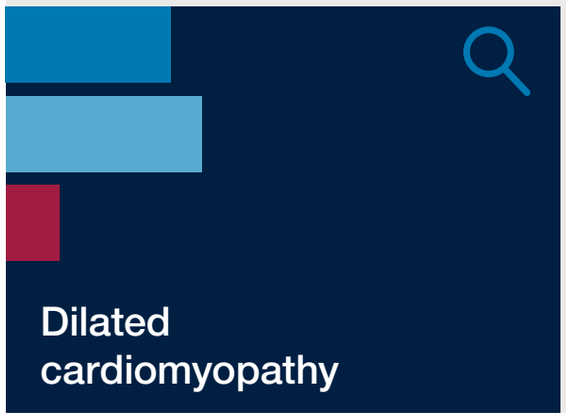
Graphs adapted from Fuchs K et al. Ther Apher Dial. 2022; 26(1):229-241.
*The immunoglobulins IgA and IgM also adsorb to the immunoadsorbers but to a markedly lower extent than IgG.

IANIS
Clinical effectiveness of immunoadsorption

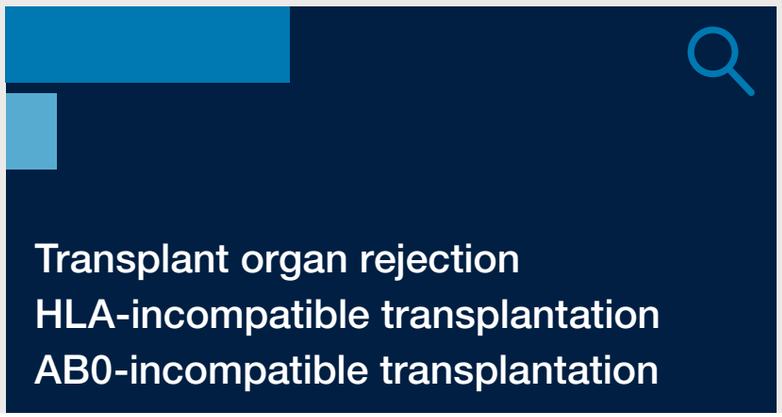
Neurology



Cardiology



Transplantation

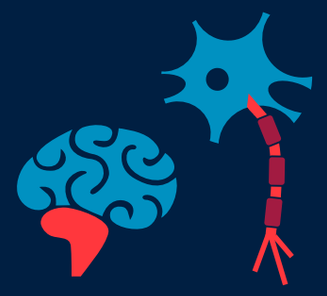


Improvement
No change
Deterioration

81 patients in total

IANIS

Patients with multiple sclerosis



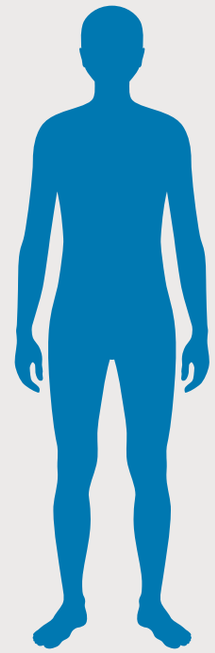
After the immunoadsorption treatment regimen:

94 %

of patients experienced clinical improvements

6 %

experienced no change



17

patients

Motor improvements of various type: nine

Improvement of visual acuity and/or eyesight: seven

No change in the clinical status: one

Any deterioration: zero

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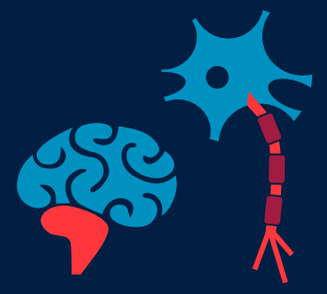
Patients with myasthenia gravis



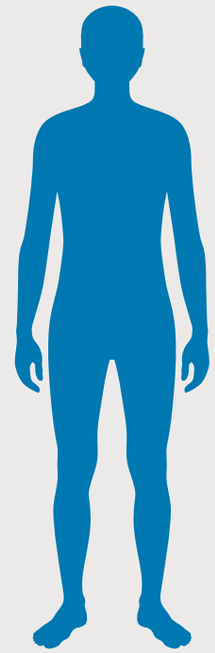
After the immunoadsorption treatment regimen:

80 %

of patients experienced clinical improvements

20 %

deterioration occurred



10

patients

Improvement of paresis: three

Improvement of symptoms of
dysphagia, dyspnea, and dysarthria: five

Deteriorations of symptoms of dysphagia, dyspnea,
and dysarthria together with double images and/or ptosis: two

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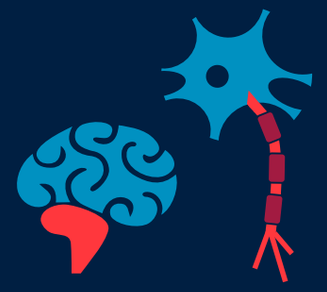
Patients with autoimmune encephalitis



After the immunoadsorption treatment regimen:

22 %

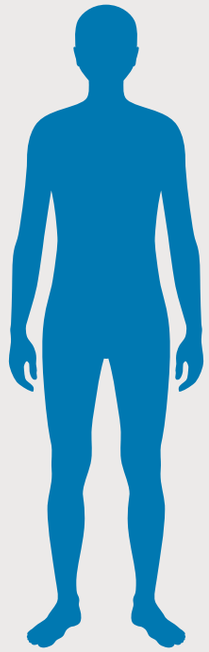
of patients experienced clinical improvements

67 %

stabilised with no worsening of the symptoms

11 %

deterioration occurred



9 patients

Improvements of cognitive abilities and gait disorders: two

No change observed: six

Deterioration of clinical status
(motor activity, incontinence): one

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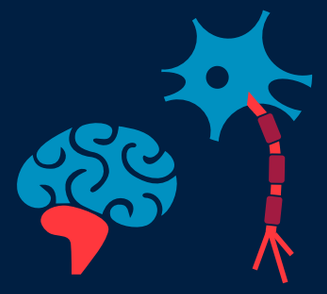
Patients with inflammatory polyneuropathies



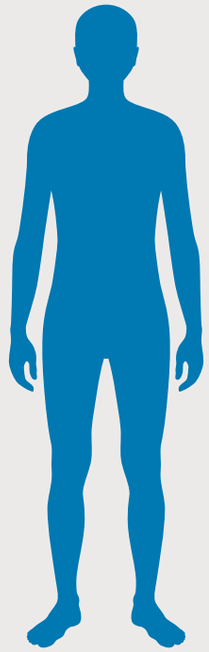
After the immunoadsorption treatment regimen:

50 %

of the patients with an improvement of motor function, sensitivity or walking capacity

50 %

patients with no change of clinical status



8

patients

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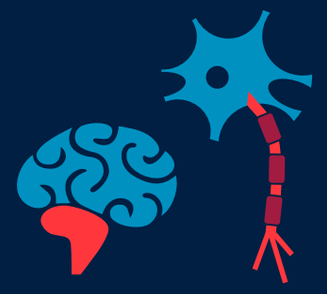
Patients with Guillain-Barré syndrome



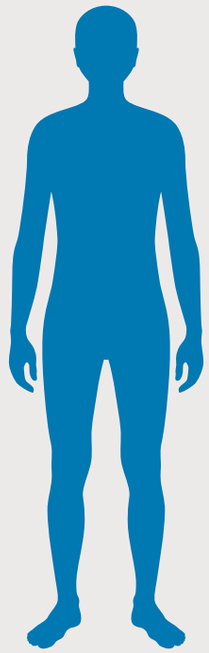
After the immunoadsorption treatment regimen:

67 %

Improvement of clinical status (gait disorders and paraparesis of the lower extremities) **in two patients**

33 %

No change in one patient



3 patients

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Patients with dilated cardiomyopathy (DCM)

After the immunoadsorption treatment regimen:

37.5 %

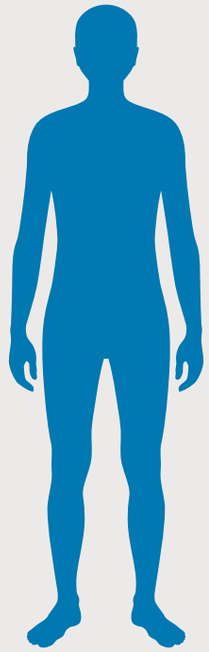
Clinical status improved in three out of eight patients
(physical capacity; NYHA status and left ventricular function)

50 %

In four patients, the clinical status was stabilized

11.5 %

In one patient, the clinical status deteriorated



8 patients

During the follow-up period of up to one year:
- Improved NYHA status and left ventricular ejection fraction (LVEF): two
- No change of NYHA status and either no change of LVEF or variable values: four
- Worsened NYHA status and LVEF: two

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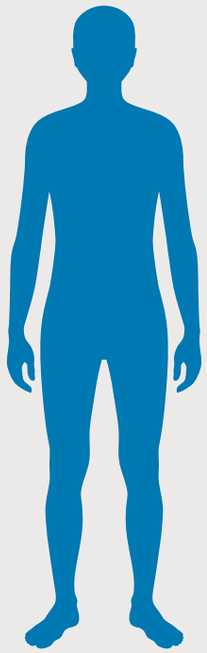
Patients with transplantation

Clinical outcome after immunoadsorption and transplantation:



Acute kidney graft rejection (two patients)

- ↑ One patient improved
- → One patient experienced a slight deterioration

AB0-incompatible kidney transplantation (two patients)

- ↑ The clinical effectiveness of both patients improved

Acute heart graft rejection (three patients)

- ↑ Stabilisation of cardiopulmonary condition, res. improvement in terms of pump power

HLA-incompatible heart transplantation (one patient)

This patient could not be assessed, since an infection precluded organ transplantation

8 patients

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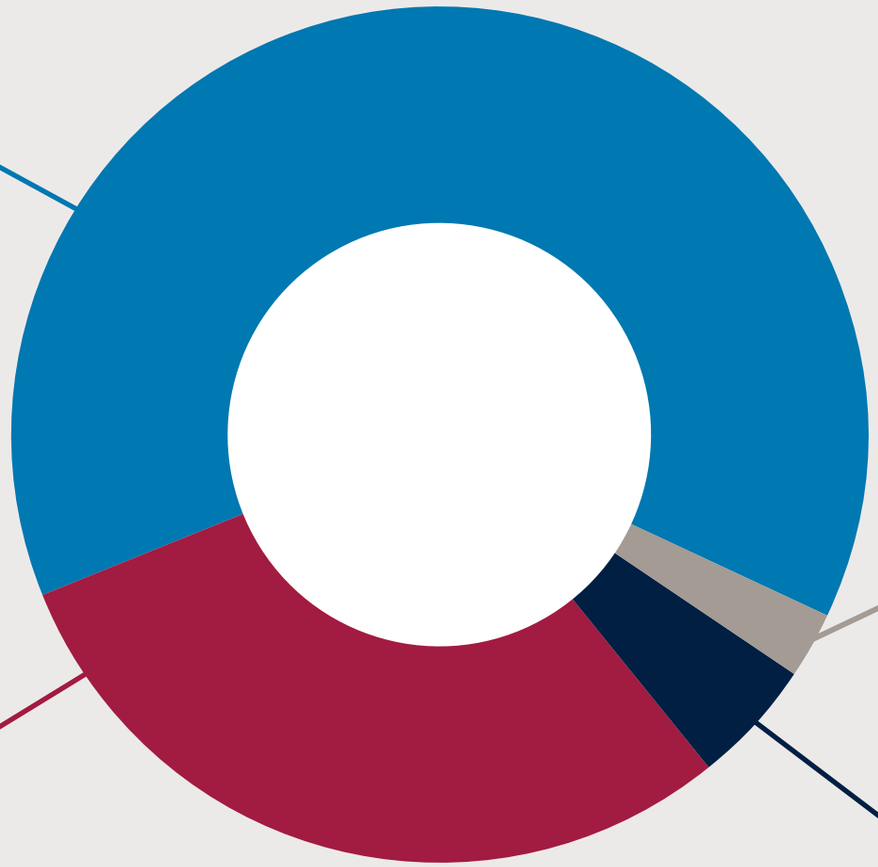
Clinical effectiveness of immunoadsorption*



63.0 %
Improved status

29.6 %
Stabilised status

2.5 %
Not assessable

4.9 %
Deteriorated status

About two thirds of the patients experienced an improvement of their clinical status; approximately 30 % were stabilised.

*Evaluated after each patient's last immunoadsorption session

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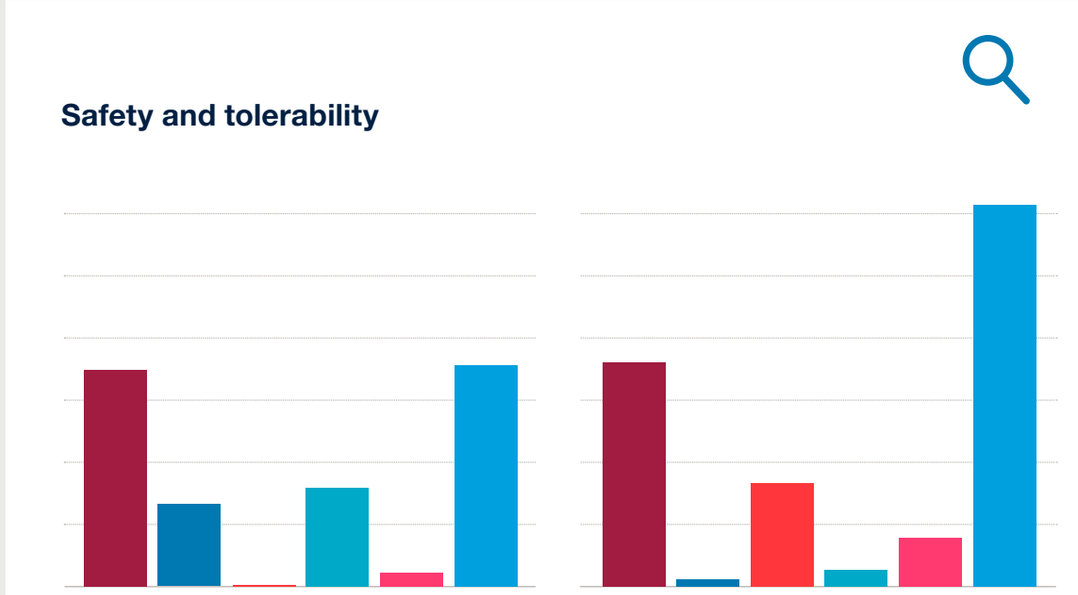
Safety and tolerability

Similar safety profile of both adsorbers

Immunoadsorption with both Protein-A ligand (Immunosorba*) and peptide GAM ligand (GLOBAFFIN) is tolerated generally well:

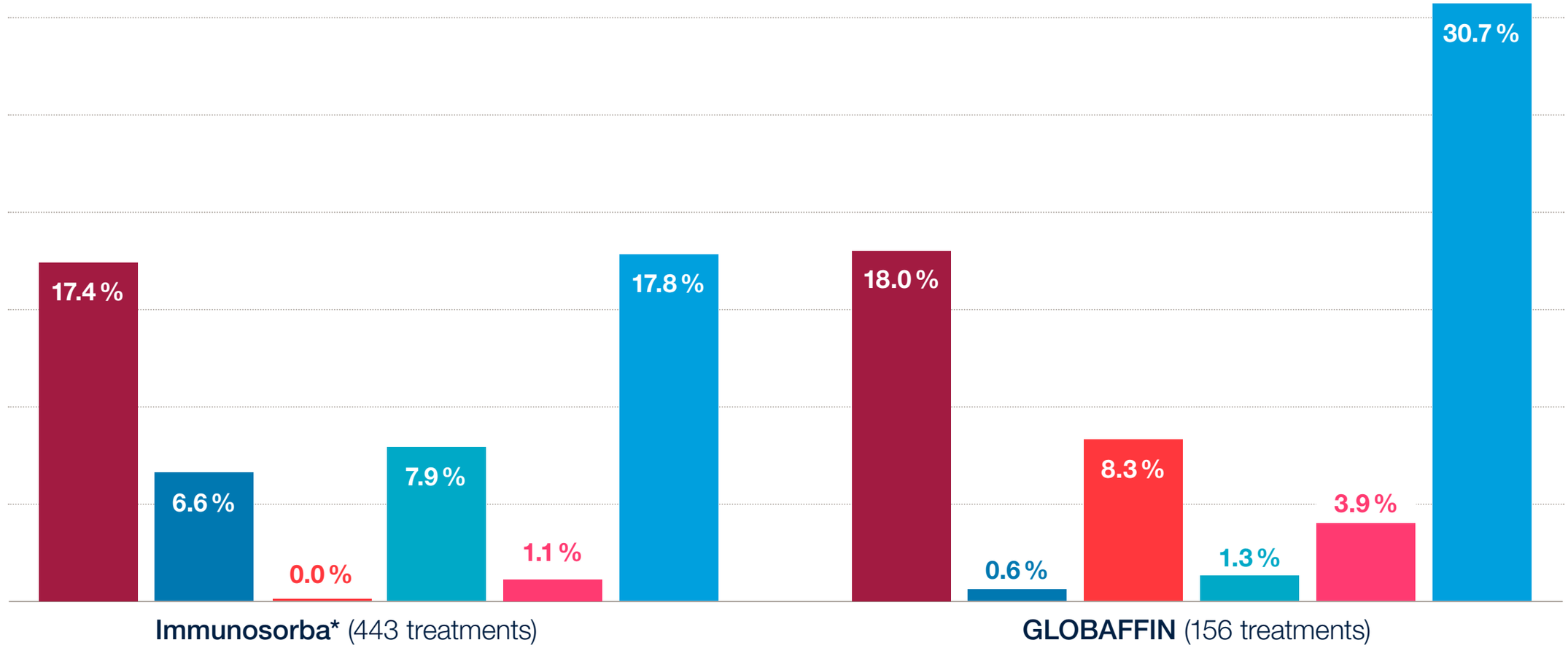
- Classification of fibrinogen, thrombocytes, and albumin mostly noncritical
- Treatments overall well tolerated
- 36 patients out of 81 experienced a total of 143 ADEs, with observed side effects reflecting the usual pattern as seen with extracorporeal therapies
- No difference in the safety profile of both adsorbers



*Highly selective Protein-A ligand double adsorber system for selectable plasma volume results in predetermined IgG elimination. Immunosorba is no longer available on the market.

Back to performance of immunoadsorption

Safety and tolerability



Graph adapted from Fuchs K et al. Ther Apher Dial. 2022;26(1):229-241.[1]
Frequency of sessions with any ADE are reported as well as the frequencies of the two most frequent ADEs in each of the adsorbers.

*Highly selective Protein-A ligand double adsorber system for selectable plasma volume results in predetermined IgG elimination. Immunosorba is no longer available on the market.

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Discussion

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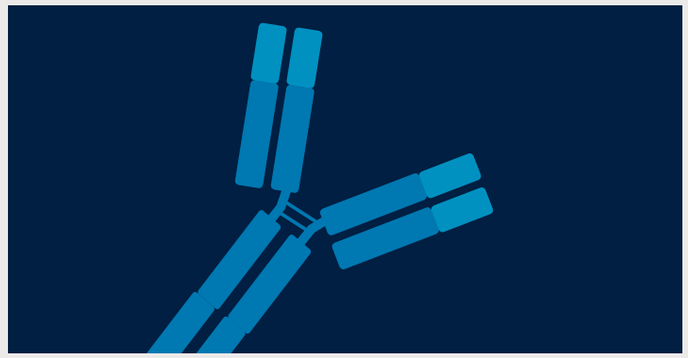
Discussion

Comparable effectiveness in reducing IgG levels for both adsorbers could be proved

- Protein-A ligand and peptide GAM ligand demonstrated a comparable effectiveness in reducing IgG levels with a high binding affinity to IgG.



Antibody reduction depends mainly on treated plasma volume

- Double column system allows Immunoadsorption as long as needed.

Frequent treatments on consecutive days are possible

- Successful suppression of autoantibody rebound
- Lowering of pre-treatment IgG levels
- Strong overall reduction of plasma IgG levels

IANIS
Discussion

Treatment patterns could be identified for DCM, multiple sclerosis and myasthenia gravis

- Frequently a short interval regimen on consecutive days, associated with a greater overall reduction of plasma IgG levels compared to longer treatment periods

About two thirds of the patients experienced an improvement of their clinical status

- Approximately 30 % of the treated patients stabilised

Immunoadsorption is regarded as an option for transplant patients

- Patients who need desensitisation for
  - AB0-incompatible transplantation
  - HLA-incompatible transplantation
  - Antibody-mediated rejection

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Conclusion

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Conclusion

Immunoadsorption with adsorbers Protein-A ligand (Immunosorba*) and peptide GAM ligand (GLOBAFFIN)

Was effective in reducing IgG antibodies and in improving the clinical status.

Represents an additional therapeutic option for therapy-refractory immune disorders.

Was overall tolerated well with pattern of side effects resembling that of other extracorporeal therapies.

*Highly selective Protein-A ligand double adsorber system for selectable plasma volume results in predetermined IgG elimination. Immunosorba is no longer available on the market.

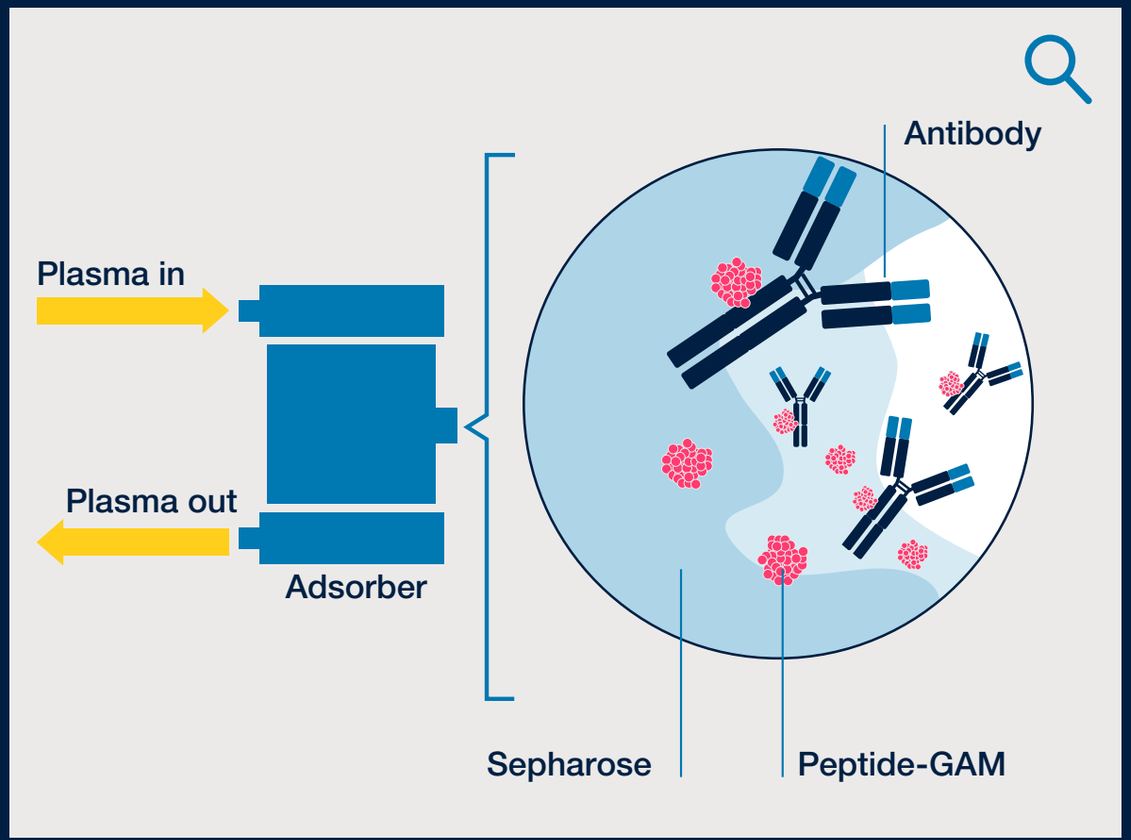
Immunoadsorption at a glance

Immunoadsorption at a glance

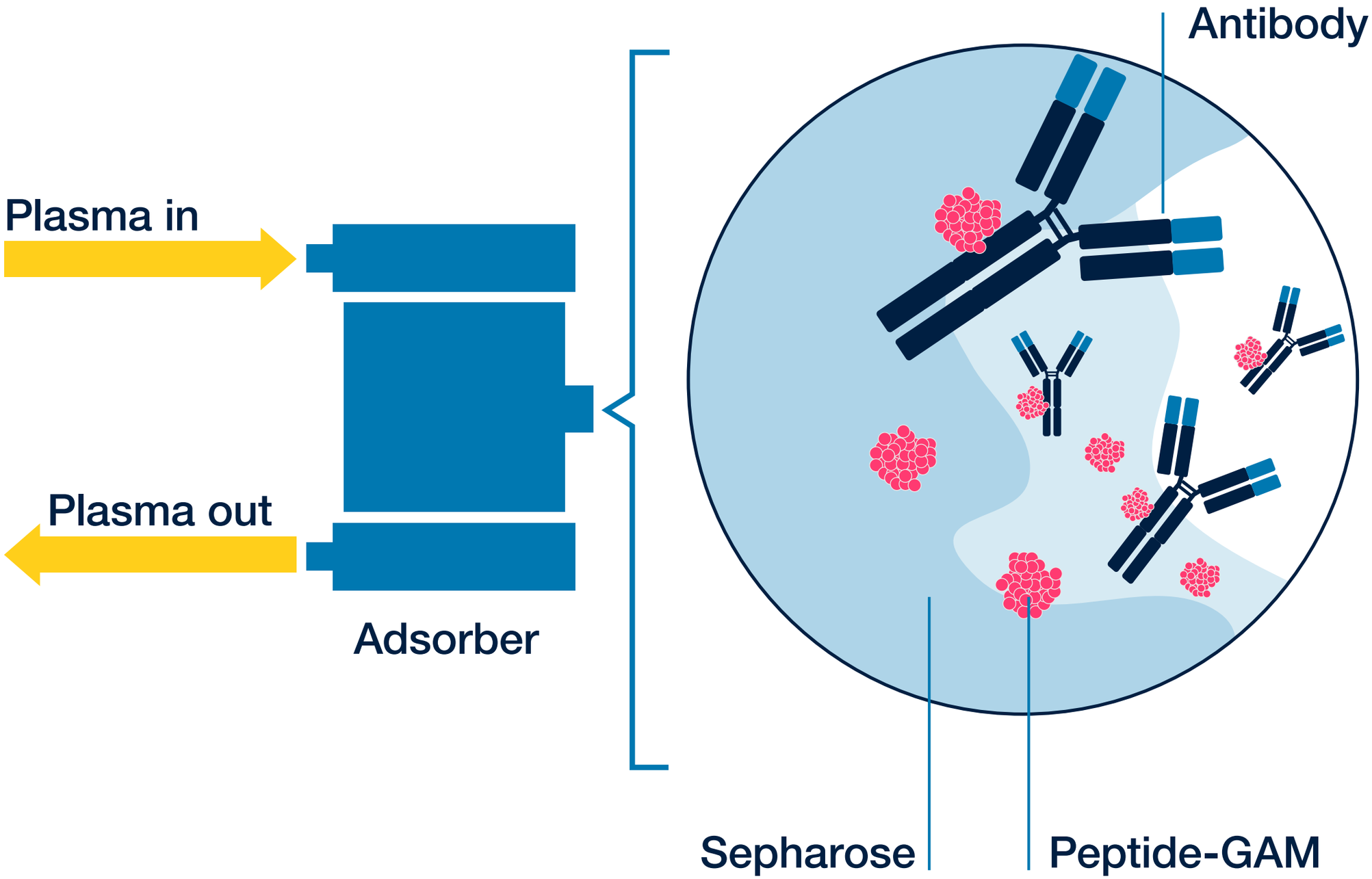
- Extracorporeal technology for the semi-selective removal of large numbers of IgG antibodies from the plasma [2,5,6]
- Retaining the largest share of important plasma constituents such as albumin [1]

Immunoadsorption is associated with some advantages over nonspecific plasma exchange:

- Allows treatments with higher plasma volume [1,4]
- Allows treatments on consecutive days [1,7]
- Replacement solutions like donor plasma or albumin become unnecessary

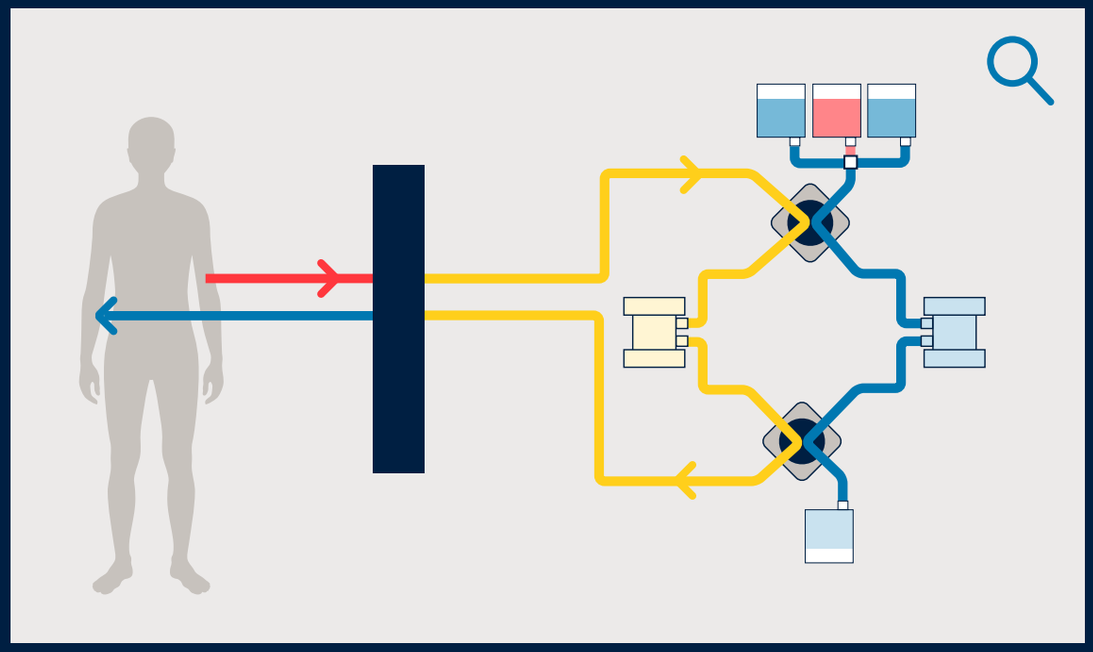


Specific binding of antibodies inside the adsorber



Immunoadsorption with a double adsorber system

- **Regenerative columns** – while one is adsorbing, the other is regenerated
- **Larger plasma volumes to be treated** than with plasma exchange
- **Effective removal of IgG antibodies**
- **No substitution solutions** like donor plasma or albumin required



Immunoadsorption with a double adsorber system

High antibody reduction with double columns

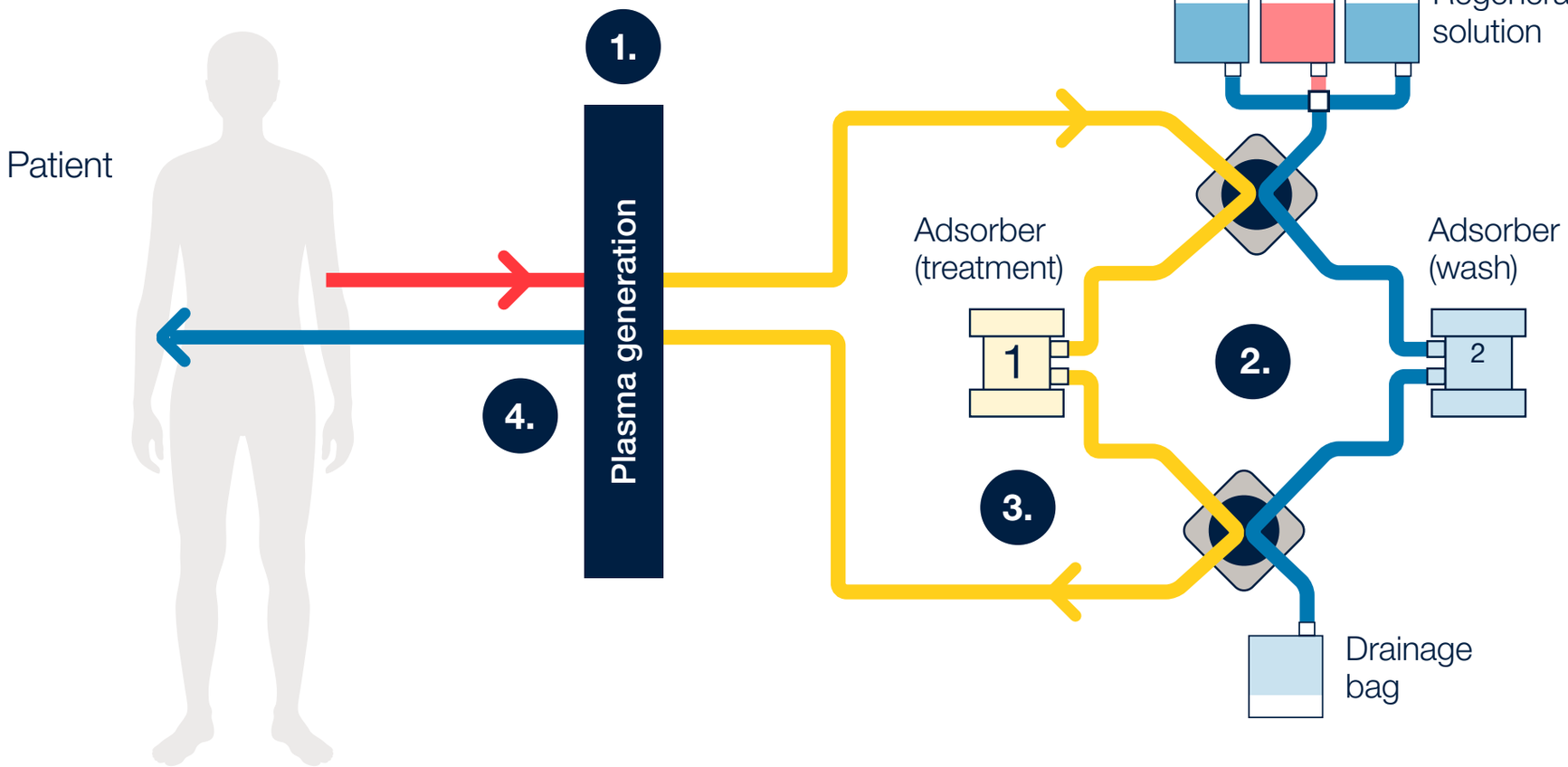
1. Separation of blood and plasma
2. Treatment of plasma
3. Antibody adsorption inside the adsorber
4. Return of plasma and blood

Step 1

Adsorber 1: Treatment
Adsorber 2: Wash

Step 2

Adsorber 1: Wash
Adsorber 2: Treatment



Click for Step 2

Immunoadsorption with a double adsorber system

High antibody reduction with double columns

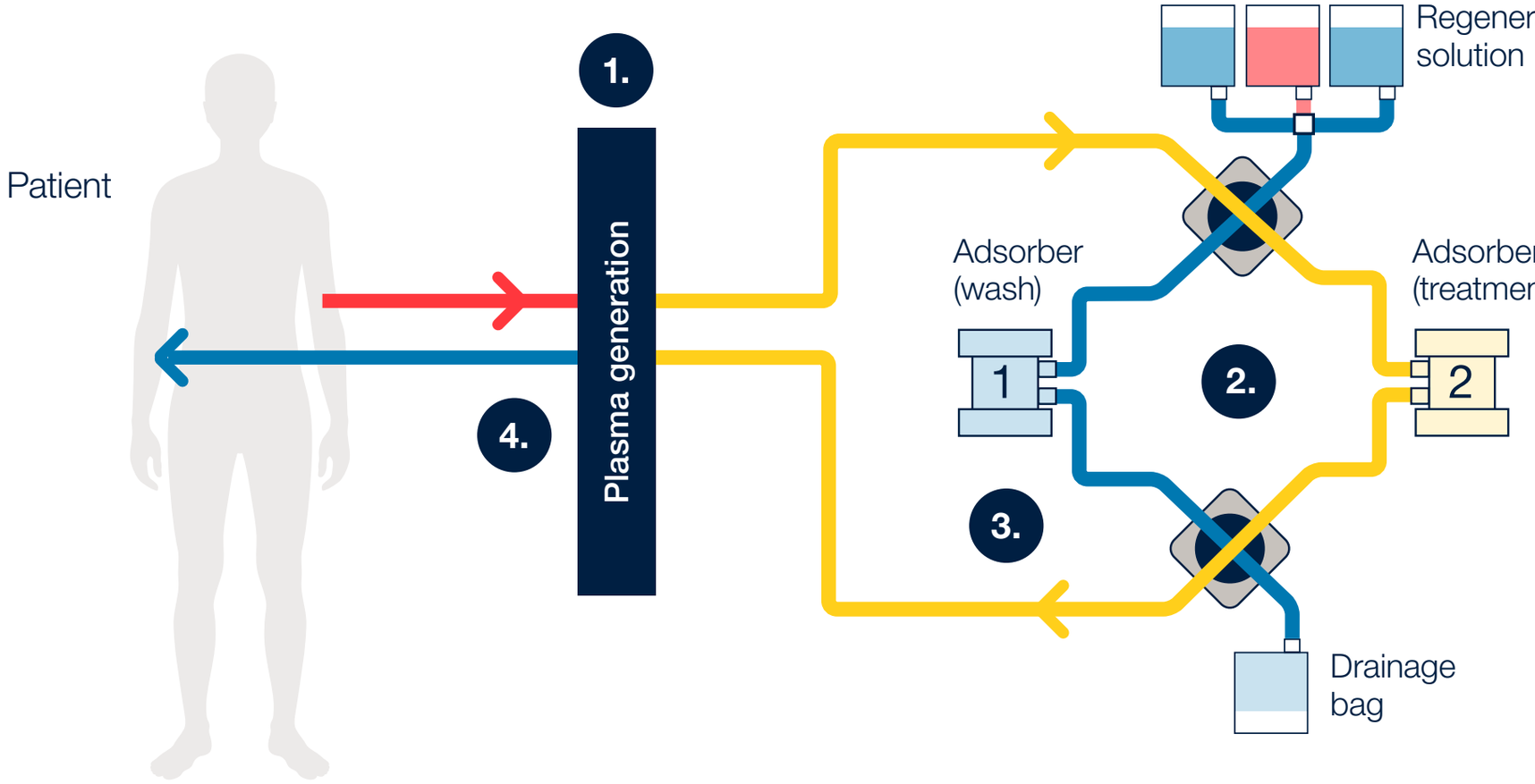
1. Separation of blood and plasma
2. Treatment of plasma
3. Antibody adsorption inside the adsorber
4. Return of plasma and blood

Step 1

Adsorber 1: Treatment
Adsorber 2: Wash

Step 2

Adsorber 1: Wash
Adsorber 2: Treatment



Click for Step 1

GLOBAFFIN
The first synthetic broad spectrum immunoadsorber[2]

Benefits

- First immunoadsorber with synthetic peptide GAM ligand[2]
- Selective and efficient removal of IgG immunoglobulins and immunocomplexes[3]
- Strong binding characteristics
- For the consistently high elimination of IgG immunoglobulins[1]
- Only small amounts of other essential plasma components are removed[1]
- Low reduction of plasma proteins allows for treatment on consecutive days[1]

For ordering information please contact your local Fresenius Medical Care sales representative.

Click here for product key features ›

GLOBAFFIN
Product key features

Matrix
Ca. 60 ml Sepharose
CL 4B Peptidligand, completely synthetic

Reusable
For the same patient

Regenerative
During an ongoing treatment (two-column system)

Housing
74 ml polycarbonate housing

Twin adsorber system
With multiple use and multiple pass characteristics[2]

References

1 Fuchs K et al. Ther Apher Dial. 2022; 26(1):229–241.

2 Rönspeck W et al. Ther Apher Dial. 2003; 7:91–7.

3 Eming et al. Dermatology. 2006; 212:177–87.

4 Maillard N et al. Blood Purif. 2015; 40(2):167–72.

5 Belak M et al. Transfus. Sci. 1994; 15:419–422.

6 Gjorstrup P and Watt RM. Transfus. Sci. 1990; 11:281–302.

7 Orlin et al. Blood. 1980; 56(6):1055-9.

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www.freseniusmedicalcare.com

Zkrácená informace o zdravotnickém prostředku

GLOBAFFIN – peptidová kolona pro imunoadsorpci
Kolona GLOBAFFIN je určena k odstraňování imunoglobulinů, imunitních komplexů a specifických protilátek z plazmy pacientů.
Léčbu pomocí GLOBAFFINu musí předepsat a dohlížet na ni kvalifikovaný lékař individuálně pro každého pacienta.

Možné nežádoucí účinky: Nespecifické nežádoucí účinky léčby spojené s mimotělním ošetřením krve. Specifické vedlejší účinky – důsledky snížení hladiny fibrinogenu a eliminace imunoglobulinů: ovlivnění krevního srážení, zvýšení náchylnosti k infekcím pro přechodné oslabení humorálního imunitního systému, hypoproteinemie; dále malé ztráty plazmy a přidání proplachovacího roztoku do plazmy; odstranění léků a/nebo jejich naředění v krvi. **Kontraindikace:** přecitlivělost nebo alergie na jakékoli použité materiály;
věk a fyzický nebo klinický stav neumožňující mimotělní léčbu; nesnášenlivost aferézní terapeutické procedury a přecitlivělost spojená s terapeutickou aferézou; nemožnost udržovat správnou antikoagulaci; hemoragická diatéza, závažné kardiovaskulární onemocnění, akutní systémová infekce.

Jedná se o zdravotnický prostředek (třída rizika IIb)

Pro detailní informace o správném používání, možných nežádoucích účincích, interakcích a kontraindikacích čtěte pozorně návod k použití.

Výrobce: Fresenius Medical Care AG & Co. KGaA, Else-Kröner-Straße 1, Bad Homburg, Německo.

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