Uniplas – Das Einheitsplasma für jedermann

Petra Jilma, MD
Medical University of Vienna,
Vienna, Austria

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Universal plasma is a novel, blood group independent human pooled plasma and can be transfused irrespective of the patient's blood group.
OctaplasLG® / UniplasLG
Novel Manufacturing Process

<table>
<thead>
<tr>
<th>OctaplasLG®</th>
<th>UniplasLG®</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fast thawing and pooling of single-donor FFP according to specific blood group</td>
<td>Fast thawing and optimal mixing of single-donor FFP of blood groups A, B and AB</td>
</tr>
<tr>
<td>Complete cell removal</td>
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</tr>
<tr>
<td>S/D treatment [1-1.5 hours at +30±1°C]</td>
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<tr>
<td>Removal of S/D reagents</td>
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<tr>
<td>Prion protein removal</td>
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<tr>
<td>Sterile filtration</td>
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<tr>
<td>Aseptic filling and sealing of bags</td>
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<tr>
<td>Fast freezing and storage</td>
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<tr>
<td>Quality control and batch release</td>
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</tbody>
</table>

*OctaplasLG® plasma pool is prepared from only ABO blood group identical FFP units; while UniplasLG® (uniplas®) plasma pool is prepared by optimal mixing of specific parts of FFP blood group A, B and AB (i.e. 8.2:1 for European plasma and 5.5:4.5:1 for US plasma, respectively)*
IgM & IgG Antibody Titration

Optimal mixing of FFP in Europe: 8A, 2B, 1AB
Biochemical characterization of Uniplas compared to Octaplas and FFP

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Uniplas*</th>
<th>Octaplas(^\d) (n=12)</th>
<th>Quarantine FFP(^\d) (n=12)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total proteins [mg/ml]</td>
<td>57 (53-60)</td>
<td>55 (54-57)</td>
<td>57 (50-61)</td>
</tr>
<tr>
<td>Fibrinogen [mg/ml]</td>
<td>2.5 (2.3-2.9)</td>
<td>2.5 (2.4-2.6)</td>
<td>2.6 (1.9-3.6)</td>
</tr>
<tr>
<td>Factor II [IU/ml]</td>
<td>0.80 (0.74-0.84)</td>
<td>0.83 (0.79-0.86)</td>
<td>0.88 (0.77-1.18)</td>
</tr>
<tr>
<td>Factor V [IU/ml]</td>
<td>0.89 (0.60-1.00)</td>
<td>0.78 (0.75-0.84)</td>
<td>0.90 (0.73-1.50)</td>
</tr>
<tr>
<td>Factor VII [IU/ml]</td>
<td>1.03 (0.92-1.20)</td>
<td>1.08 (0.90-1.17)</td>
<td>0.95 (0.67-1.38)</td>
</tr>
<tr>
<td>Factor VIII [IU/ml]</td>
<td>0.75 (0.60-0.90)</td>
<td>0.68 (0.51-0.78)</td>
<td>0.76 (0.52-1.13)</td>
</tr>
<tr>
<td>Factor IX [IU/ml]</td>
<td>0.96 (0.70-1.19)</td>
<td>0.96 (0.86-1.06)</td>
<td>1.02 (0.82-1.28)</td>
</tr>
<tr>
<td>Factor X [IU/ml]</td>
<td>0.88 (0.73-0.97)</td>
<td>0.76 (0.75-0.80)</td>
<td>0.79 (0.62-0.99)</td>
</tr>
<tr>
<td>Factor XI [IU/ml]</td>
<td>1.10 (0.90-1.30)</td>
<td>0.99 (0.91-1.04)</td>
<td>1.13 (0.96-1.00)</td>
</tr>
<tr>
<td>Factor XII [IU/ml]</td>
<td>0.86 (0.85-0.93)</td>
<td>0.84 (0.74-0.89)</td>
<td>0.82 (0.45-1.12)</td>
</tr>
<tr>
<td>Factor XIII [IU/ml]</td>
<td>1.11 (0.99-1.23)</td>
<td>1.08 (1.05-1.11)</td>
<td>1.06 (0.68-1.69)</td>
</tr>
<tr>
<td>VWF (Rcof) [IU/ml]</td>
<td>0.74 (0.67-0.80)</td>
<td>0.76 (0.63-0.91)</td>
<td>0.89 (0.77-0.98)</td>
</tr>
<tr>
<td>aPTT [sec]</td>
<td>30.2 (30.0-33.0)</td>
<td>35.2 (33.8-36.9)</td>
<td>35.2 (31.7-42.5)</td>
</tr>
<tr>
<td>Protein C [IU/ml]</td>
<td>0.82 (0.71-0.88)</td>
<td>0.85 (0.81-0.87)</td>
<td>0.89 (0.79-1.05)</td>
</tr>
<tr>
<td>Protein S [IU/ml] activity</td>
<td>0.56 (0.42-0.62)</td>
<td>0.64 (0.55-0.71)</td>
<td>1.03 (0.71-1.39)</td>
</tr>
<tr>
<td>Plasmin inhibitor [IU/ml]</td>
<td>0.32 (0.27-0.34)</td>
<td>0.23 (0.20-0.27)</td>
<td>1.04 (0.95-1.18)</td>
</tr>
<tr>
<td>Anti-thrombin [IU/ml]</td>
<td>0.91 (0.88-0.95)</td>
<td>0.94 (0.90-0.97)</td>
<td>1.06 (0.77-1.23)</td>
</tr>
</tbody>
</table>

FFP, fresh-frozen plasma. VWF, von Willebrand factor. aPTT, activated partial thromboplastin time.
*Batch release data.

Comparison of vWF multimeric pattern and of ADAMTS13 levels in different plasma products

Normalplasma: lanes 1, 11
Octaplas (USA: A, B, O, AB): lanes 2-5
Octaplas (Europe: A, B, O, AB): lanes 6-9
Uniplas: lane 10

Normal levels of ADAMTS13 and factor H are present in the pharmaceutically licensed plasma for transfusion (Octaplas) and in the universally applicable plasma (Uniplas) in development. Heger A, Kannicht C, Römisch J, Svae TE. *Vox Sang*. 2007 Apr;92(3):206-12.
Two studies in open-heart surgery

Uniplas has a similar effect as Octaplas in the treatment of bleeding in patients undergoing open-heart surgery:

![Table showing bypass times, chest drainage, and number of revisions due to bleeding in the four study groups.](image)

Universal solvent/detergent-treated fresh frozen plasma (Uniplas®) – rational and clinical properties


Safety of Uniplas in open-heart surgery:

- Complement activation is not increased after Uniplas or Octaplas transfusion
- No haemolytic reactions
- No viral transmissions

Universal fresh frozen plasma (Uniplas): a safe product in open-heart surgery

One study in adult patients undergoing elective liver resection

122 patients were enrolled, 81 required plasma transfusions (mostly due to intraoperative bleeding) : 64 received Uniplas

- no increase of complement activation after Uniplas (C3b)
- 3 patients: change from negative to intermittently positive DAT with no signs of hemolysis (Hb, haptoglobin or free Hb)
- no viral transmission (HIV, Hep. B, C)
- INR, aPTT and protein C levels were maintained after transfusion

We compared the safety and tolerability of a novel universal plasma (Uniplas LG) with an ABO matched plasma (Octaplas LG®).
Study population

Inclusion criteria:
  healthy male or female volunteers (age > 18 yrs, n=30);
  blood group: A, B or AB

Exclusion criteria:
  ● history of hyper-sensitivity reaction, bleeding or coagulation disorder,
  ● transfused with blood products within the last 6 months, IgA deficiency,
  ● seropositivity for HBsAg, HCV or HIV1/2
Study design: randomized double blind

V1: Screening
V2: Plasmapheresis 1 followed by transfusion of 6U Uniplas LG (A) or Octaplas LG (B), blood sampling

V3: 24 h after plasmapheresis 1: blood sampling
V4: 1 week after PPh 1: blood sampling

V5: at least 4 weeks after V2 plasmapheresis 2 followed by transfusion of Uniplas LG (B) or Octaplas LG (A), blood sampling

V6: 24 h after plasmapheresis 2: blood sampling
V7: 1 week after plasmapheresis 2: blood sampling
V8: 12 weeks after V5

Cross over after 4 weeks wash out
Study parameters

1) **Primary safety outcome:**
   change in Hb conc.

2) **Secondary safety outcomes:**
   Direct antiglobulin test, free Hb, haptoglobin, indirect bilirubin
   complement activation

3) **Evaluation of efficacy:**
   coagulation parameters
Time course of Hb-Concentration

[Graph showing the time course of Hb-Concentration with different treatments.]
Clinical Equivalence OctaplasLG® vs. Uniplas

\[ n = 14 \text{ in phase I/cross-over} \]

Apheresis 600 ml

Plasma 1,200 ml

Albumin 750 ml 5% +
450 ml 0.9% NaCl
Time course of aPTT

![Graph showing the time course of aPTT with lines representing different treatment groups.](image)
Time-course of pro-thrombin time

[Graph showing the time-course of pro-thrombin time with different treatments indicated by lines for Uniplas LG and Octaplas LG, with time points at Pre-PPh, Post PPh, 15min POST, 2h POST, and 24h POST.]
Adverse events

Adverse events (AEs):
- no serious AEs
- no difference in frequency or severity of AEs between groups
- about 40% of AEs were considered treatment related: urticaria, paresthesia, headache (19 in Uniplas, 18 in Octaplas period)

Viral safety
- 1 subject seroconverted for B19 and remained positive, most likely due to sub-clinical infection - not caused by plasma transfusion
Conclusion

1. **No HTR** occurred after transfusion of Uniplas: no difference in laboratory parameters, no positive DAT or any signs or symptoms of hemolysis.

2. UniplasLG was **equivalent** to OctaplasLG® with respect to safety and tolerability, and recovery of coagulation factors.
GENERAL CONCLUSIONS

UNIPLAS

• Eliminates risk of mismatch errors due to ABO incompat.
• Offers improved convenience vs. blood group specific plasma
  - Simplified logistics in emergency situations
• Equivalent to well-established Octaplas/OctaplasLG® with regard to efficacy and tolerability
  ▪ Standardised content of coagulation factors
  ▪ Octaplas has been used in more than 2 Mio patients
• Highest standards in plasma safety
  ▪ Virally inactivated by S/D treatment
  ▪ Enhanced prion safety due to unique Ligand-Gel technology (LG)
  ▪ No risk of TRALI: plasma pools for optimal dilution or neutralisation of HLA / human anti-neutrophil antibodies
Thank you for your attention
...to answer any questions

- NOW or
- ...LATER petra.jilma@meduniwien.ac.at