	Height median (range)	-	
	Weight (kg) median (range)	SD-FFP: 69,4 (16,8) FFP: 70,8 (18,8), p=0,4	
	Baseline PTs	SD-FFP: 20,7 (8,2) FFP: 23,3 (10,2), p=0,18 Normal range: 11,3-13,0	
	Baseline Fibrinogen mg/dl	SD-FFP: 369,3 (163,5) FFP: 398,3 (169,6), p=0,29 Normal range: 200-400	
	Pretreatment diagnosis	SD-FFP: liver disease:7, warfarin therapy11,vitamin K def 2, combined 1, other 1 FFP: liver desease: 7, warfarin therapy 11, vitamin K def 0, combined 4, other1	
	Infusion: *mean number of units per patient* *mean number of infusions per patient* *mean dose per infusion ml/kg*	SD-FFP 2,6 (0,7) 1,5 (0,6) 7,8	FFP 2,3 (0,7) 1,7 (0,8) 8,0
Method	*Criteria for inclusion* *As described by the authors*	PTs > 15 s, correctable by normal plasma in vitro, due to liver disease, vitamin K deficiency (determined by medical history) or warfarin therapy. Patients treated on study required plasma therapy for either active bleeding, surgical prophylaxis or warfarin overdose	
	Criteria for exclusion	Exclusion criteria consisted of a platelet count < 130,000 /µl, history of IgA deficiency, clinical congestive heart failure so that transfusion of a volume of 400ml of plasma could not be tolerated, history of serious allergic reactions to plasma infusion, previous history of receipt of experimental plasma, and receipt of any other experimental products	
	Analysis by intention to treat	Not reported	
	Main statistical analysis *Power calculation description*	For PT data were analyzed by X_2 analysis to determine stat. sign. (P=0.05) of observed difference between SD-FFP and FFP. Correlational analysis was udes to determine relationships between numbers of units of either SD-FFP or FFP infused and cessation of bleeding, achievement of PT less than 15, and change from baseline PT. The sample size was based on a number of patients who could be enrolled over a 2,5 year period. Large standard deviation of the PT required a significantly larger number of subjects to detect or obtain a small difference in PT	
Results	*Primary endpoint of study*	Outcomes: changes in PT, APTT, TT, fibrinogen and other factors Test for viral markers:HBV, HCV and HIV	
	Endpoints and effect estimate (RR/OR/Rate ratio/Hazard ratio 95% CI); p-value	See table	
	Adverse effects	No serious, severe or unexpected advers events during study. 4 adverse events: 2 FFP patients developed fever 1 SD-FFP patients had chest - and back pain during infusion 1 SD-FFP patient had diarrhea during treatment Seroconversion HBV, HCV and HIV: none 8 deaths in each group, but these were not related to transfusion	
	Drop-out analysis	None	
Comments			

Studie 5	**Williamson, L.M. 1999** **A Randomized trial of solvent/detergent-treated and standrard fresh frozen plasma in the coagulopathy of liver disease and liver transplantation - *equal population baseline characteristics between the intervention groups***	
Study description	*First Author*	Williamson, L.M.
	Year of publication	1999
	Reference no.	
	Setting	Hospital patients at three centres
	Country	UK
	Aim (as described in the article)	To examine clinical tolerance, efficacy, and viral status in 49 pateints with liver disease (LD, n=24) or undergoing liver transplantation (LT, n=25, se article above Freeman) who prospectively were randomly assigned to receive either FFP or SD-FFP
	Study design	RCT
	Inclusion period (year start-year end)	
	Mean / median /minimum / max period of follow-up	
Intervention	***Plasma transfusion (SD-FFP vs FFP)***	
	Specify procedures	Plasma was obtained either by apheresis or from wholeblood donations from voluntary blood groups O and A donors meeting UK Transfusion Service criteria FFP or SD-treated plasma was given at the initial recommended dose of 12 to 15 mL per kg. Subsequent administration was on the basis of coagulation results, and patients received the same product or component to which they were randomly assigned for the first 24 hours of treatment. Clinicians but not the patients were aware which product was being used
	N total	Total: 49; LT, n=25 previously described in Freeman 1999 ref 2. Total LD patients: 24
	N control	FFP: 11
	N intervention	SD-FFP:13
	N lost to follow-up	None (in the LD group)
Population characteristics	**LD patients were included if FFP was clinically indicated for correction of coagulopathy prior to elective invasive procedures, such as liver biopsy, and LD patients were entered into the study only if the PT was prolonged by >4 seconds**	
	Age, median (range)	FFP: 52 (26-66) SD-FFP: 50 (30-69)
	Sex, women /men	FFP:3/8 SD-FFP:3/10
	Height median (range)	-
	Weight (kg) median (range)	-
	Plasma dose (ml)	-
	Plasma dose (ml/kg of body weight)	FFP: 13 (11-17) SD-FFP: 12 (11-15)

	Pretreatment diagnosis	Liver disease
Method	*Criteria for inclusion* *As described by the authors*	LD patients were included if FFP was clinically indicated for correction of coagulopathy prior to elective invasive procedures, such as liver biopsy, and LD patients were entered into the study only if the PT was prolonged by >4 seconds
	Criteria for exclusion	Patients were not entered into the study if pregnant or lactating, or if they were known to have antibodies to IgA. As SD-treated plasma is not Rh-specific, D-negative patients were excluded if preexisting anti-D was present. To minimize the possibility of viral infection from other sources, intravenous drug users were excluded
	Analysis by intention to treat *Main statistical analysis* *Power calculation description*	No ITT analysis Data in the two arms of the study were shown to be skewed by a determination of Sk values and the plotting of frequency histograms. The Sk value is calculated by using the following formula: Sk value = 3 × (mean – median) /SD Because of a lack of normality, comparisons of variables in patients receiving FFP or SD-treated plasma were made with the Mann-Whitney two-tailed nonparametric test using a statistical package (Minitab, Stoke College, PA) at the 5-percent level of significance. The variables compared were baseline coagulation values and improvement over baseline values after treatment.
Results	*Primary endpoint of study*	PT (PT values were converted to an International Normalised Ratio (INR)) APTT (APTT values were expressed as the difference between the clotting times (in sec) of the test plasma and the laboratory control) Fibrinogen Coagulation factors Test for viral markers:HBV, HCV and HIV
	Endpoints and effect estimate (RR/OR/Rate ratio/Hazard ratio 95% CI); p-value	See table
	Adverse effects	In LD patients, temperature, pulse, blood pressure, and the presence or absence of skin changes were noted before treatment and at 30, 60, and 120 minutes and 4 hours from the start of the infusion. Adverse events in these patients had been defined as a rise in temperature of >1°C above baseline, an increase in pulse rate of >10 beats per minute, a drop in blood pressure of >10 mm Hg, rigors occurring during or within 4 hours of the end of the infusion, or any skin changes occurring within 24 hours of the infusion. No side-effects reported Seroconversion HBV, HCV and HIV: none
	Drop-out analysis	None
Comments		

Studie 6	**Fisher NC 1997 - se Williamson 1999 (Studie 5) og Fisher 1998 (Studie 2) – ABSTRACT Fresh-frozen plasma in clinical usage – a comparison of Octaplas and standard FFP**	
	First Author	Fisher, NC

Study description	*Year of publication*	1997
	Reference no.	
	Setting	Hospital patients in one centre
	Country	UK
	Aim (as described in the article)	To evaluate the correction of coagulopathy achieved by infusing recommended doses of FFP and compared standard FFP with Octaplas (SD) in patients with liver disease (LD) to prevent bleeding
	Study design	RCT
	Inclusion period (year start-year end)	NR
	Mean / median /minimum / max period of follow-up	24 hours
Intervention	***Plasma transfusion (SD-FFP vs FFP)***	
	Specify procedures	Patients with stable liver disease and coagulopathy were randomized to receive either FFP or SD-FFP prior to elective procedures.
	N total	Total: 21
	N control	FFP: 9
	N intervention	SD-FFP:12
	N lost to follow-up	none
Population characteristics	*Age, median (range)*	NR
	Sex, women /men	NR
	Height median (range)	NR
	Weight (kg) median (range)	NR
	Plasma dose (ml)	NR
	Plasma dose (ml/kg of body weight)	Dosage 12-15 mls/Kg over 20-30 rains??
	Pretreatment diagnosis	LD
	Pretreatment PT, median	FFP:21s (range 17-28) SD-FFP: 30,5s (range 18-60) – *there is a difference between groups, but p value not reported*
Method	*Criteria for inclusion* *As described by the authors*	Patients with stable liver disease and coagulopathy
	Criteria for exclusion	NR
	Analysis by intention to treat *Main statistical analysis*	NR
	Power calculation description	NR
Results	*Primary endpoint of study*	Blood samples for prothrombin time (PT) and partial thromboplastin time (PTT) were taken before treatment, after 400 mls FFP or SD-FFP, after full dose and at 3, 6 and 24 hours

	Endpoints and effect estimate (RR/OR/Rate ratio/Hazard ratio 95% CI); p-value	See comments
	PT median after full FFP dosage:	FFP: 18s (16-23) SD-FFP: 22,5s (17-32) Improvement in PT correlated with PT prolongation pre-treatment (r=0.96, p<0.001 linear regression analyses). After correction for this effect, no significant difference in efficacy between the 2 agents. Serial trend towards pre-treatment values occurred in follow-up samples. Similar observations were made for PTT measure-ments (data not shown).
	Adverse effects	No serious adverse effect or evidence of transmitted disease
	Drop-out analysis	None
Comments	Authors conclude with: Even at full recommended doses, the efficacy of FFP as measured by PT and PTT appears limited and is proportionately greater in those with more severe coagulopathy. 2. Octaplas (SD) may be an effective alternative to standard FFP.	

Studie 7	**Wieding, J.U. 1999 ABSTACT** **Prospective Randomized and Controlled study on Solvent/detergent (SD-FFP) versus Methylene Blue/Light virus inactivated plasma (MB-FFP)**	
Study description	*First Author*	Wieding, J.U.
	Year of publication	1999
	Reference no.	
	Setting	?
	Country	Germany
	Aim (as described in the article)	The efficacy and tolerance of of SD-VIP versus MB-VIP was examined in patients undergoing cardiopulmonary bypass surgery in a prospective randomized controlled study
	Study design	RCT
	Inclusion period (year start-year end)	NR
	Mean / median /minimum / max period of follow-up	NR
Intervention	***Plasma transfusion (MB-FFP vs SD-FFP)***	
	Specify procedures	Fibrinogen and other factor measured before and 120 min after transfusion
	N total	71
	N control	MB-FFP:36
	N intervention	SD-FFP: 35
	N lost to follow-up	NR
Population characteristics	***Patients undergoing cardiopulmonary by-pass surgery***	
	Age, median (range)	NR
	Sex, women /men	NR
	Height median (range)	NR
	Weight (kg) median (range)	NR
	Plasma dose (ml)	36 patients received 4.3 units MB-FFP 35 patients received 4.2 units SD-FFP on average (á 200 ml)

Summary of findings:

FFP compared to SD-FFP for plasma transfusion

Patient or population: blood transfusion, RCT Lerner 2000
Settings:
Intervention: FFP
Comparison: SD-FFP

Out-comes	Anticipated absolute effects* (95% CI)		Rela-tive ef-fect (95% CI)	№ of parti-cipants (Studies)	Quality of the evidence (GRADE)	Com-ments
	Risk with SD-FFP	Risk with FFP				

5. wide confidence intervals
6. incomplete blinding (RCT)

Planlagte og pågående studier

ID (Start og slutt dato)	Navn på studie (type studie)	Populasjon (N)	Intervensjon	Kontroll	Utfall
NCT02037373 Startet januar 2014 Beregnet ferdig mai 2017 Sponsor: Octap-harma	Post-Marketing Re-quirement to Evalu-ate the Safety of Octaplas™ Versus Plasma in Patients Undergoing Ortho-topic Liver Trans-plantation With Spe-cial Emphasis on Hyperfibrinolysis. Prospektiv kohort-studie	Coagulopathy Endstage Liver Disease N= 300	Octaplas™	FFP and other approved plasma prod-ucts	Hyperfibino-lysis
NCT02007473 Startet novem-ber 2013 Beregnet ferdig april 2015 Sponsor: Maco Productions	A Prospective Non-interventional Study to Evaluate the Safety of Methylene Blue Plasma Prospektiv observa-sjonsstudie	Inpatients re-quiring plasma trans-fusion N=80	Patients requir-ing transfusion with plasma Recipients who have received a transfusion with Methylene Blue plasma pro-duced using the THERAFLEX MB-Plasma pro-cedure from MacoPharma.	-	Incidence of transfusion reactions fol-lowing ad-ministration of Methylene Blue Plasma