

# OVERVIEW OF STUDIES OF CONVALESCENT PLASMA EFFECTIVENESS

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# OVERVIEW OF THE EVIDENCE

I'LL REVIEW SAFETY ISSUES FIRST

THEN DISCUSS THREE FORMS OF EVIDENCE  
OF EFFECTIVENESS

1. TREATMENT-CONTROL COMPARISONS
2. RANDOMIZED TRIALS
3. IMPACT OF ANTIBODY LEVEL IN PLASMA

# SAFETY ISSUES

- Some 4-5 million units of plasma are used in the US annually.
- Convalescent plasma differs from usual plasma only in its derivation from people who have recovered from COVID-19 and have been asymptomatic for at least 14 days.
- Residual virus in plasma after recovery does not seem to be a problem.
- Analysis of 20,000 Mayo patients:
  - TRALI = 0.10%
  - TACO = 0.18%
  - OTHER ALLERGIC REACTION = 0.19%
  - ALL OTHER POSSIBLY RELATED SEVERE ADVERSE EVENTS = 0.8%

# STUDIES COMPARING CP TO UNTREATED PATIENTS IN COUNTRIES OTHER THAN US

	1 <sup>st</sup> AUTHOR, LOCATION	CP DEATHS	CONTROL DEATHS	RISK RATIO
1	Rasheed, Iraq	1/21 = 4.8%	8/28 = 28.6%	0.125
2	Skrip, Burkina Faso	NA	NA	0.52
3	Perotti, Italy	3/40 = 7.5%	6/17 = 35%	0.15
4	Abolghasemi, Iran	17/114 = 14.8%	18/74 = 24.3%	0.61
5	Zeng, China	5/6 = 83.3%	14/15 = 93.3%	0.89
6	Duan, China	0/10 = 0%	3/10 = 30%	< 0.33
7	Xia, China	3/138 = 2.2%	59/1,371 = 4.1%	0.51
<b>POOLED (Skrip, Xia excluded)</b>		<b>26/191 = 13.6%</b>	<b>49/144 = 34.0%</b>	<b>0.40</b>

# US STUDIES COMPARING CP TO UNTREATED PATIENTS

	1 <sup>st</sup> AUTHOR, LOCATION	CP DEATHS	CONTROL DEATHS	RISK RATIO
1	Liu, NYC	5/39 = 12.8%	54/230 = 23.5%	0.49
2	Donato, NJ	11/47 = 23.4%	565/1340=42.2%	0.55
3	Hegerova, Seattle	2/20 = 10%	6/20 = 30%	0.22
4	Salazar, Houston	5/136 = 3.7%	19/251 = 7.6%	0.49
5	Rogers, Providence	8/64 = 12.5%	28/177 = 15.8%	0.79
<b>POOLED (Donato excluded)</b>		<b>31/306 = 10.1%</b>	<b>107/678 = 15.8%</b>	<b>0.64</b>

# RANDOMIZED TRIALS OF CONVALESCENT PLASMA

	<b>1<sup>st</sup> AUTHOR, LOCATION</b>	<b>DEATHS/ TREATED</b>	<b>DEATHS/ UNTREATED</b>	<b>RISK RATIO</b>
1	Li, China	8/51 = 15.7%	12/50 = 24.0%	0.75
2	Gharbharan, Holland	6/43 = 14.0%	11/43 = 25.6%	0.47
3	Avendano- Sola, Spain	0/38 = 0%	4/43 = 9.3%	< 0.25
4	Agarwal, India	34/235 = 14.6%	31/229 = 13.7%	1.06
	<b>1-3 POOLED</b>	<b>14/132 = 10.6%</b>	<b>27/136 = 19.9</b>	<b>0.53</b>
	<b>ALL 4 POOLED</b>	<b>48/367 = 13.1%</b>	<b>58/365 = 15.9</b>	<b>0.82</b>

# ANTIBODY FINDINGS

ANTIBODY LEVEL	MORTALITY		RISK RATIOS	
	7 DAY	30 DAY	7 DAY	30 DAY
ALL MAYO DATA (n = 3,082)				
LOW	13.7	29.6	<b>1.0</b>	<b>1.0</b>
MIDDLE	11.6	27.4	<b>0.85</b>	<b>0.93</b>
HIGH	8.9	22.3	<b>0.65</b>	<b>0.75</b>
TREATED WITHIN 3 DAYS (n = 1,097)				
LOW	13.2	25.3	<b>1.0</b>	<b>1.0</b>
MIDDLE	10.0	22.8	<b>0.76</b>	<b>0.9</b>
HIGH	6.1	16.7	<b>0.46</b>	<b>0.66</b>
(A small Israeli study found the RR for mortality in high-Ab transfused patients was 0.45 (2/19 vs 7/30))				

# CONCLUSIONS

- Even absent a large randomized trial, it is hard not to see powerful evidence of convalescent plasma efficacy in reducing mortality
- The data showing the dose-response relationship of antibody levels unknown at the time of treatment to mortality is hard to explain away.
- Early treatment is clearly better than waiting until disease is more severe and complications have ensued