High-titer anti-SARS-CoV-2 plasma improves outcome of severe COVID-19 in patients with hematologic and solid cancer - a randomized controlled trial

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RECOVER

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1. Background and methods

Background:
- High COVID-19 morbidity and mortality in cancer patients
- Few therapies in severe COVID-19 [1, 2]
- Lack of data from randomized controlled trials for convalescent and/or vaccinated plasma in high-risk patients [3, 4]

Methods:
- Randomized controlled multicenter trial (Germany), protocol [5]
- Inclusion of
  - hospitalized patients with COVID-19 (PCR-confirmed)
  - with oxygen saturation ≤94% under ambient air
  - and belonging to defined risk-groups:
    Group 1, hematologic or solid cancer
    Group 2, immunosuppression
    Group 3, lymphopenia (<0.8G/l) or D-dimers (>1µg/ml)
    Group 4, age >75 years
- Randomization into
  a) administration of convalescent/vaccinated plasma with live virus neutralization titer ≥1:80 on day 1+2 (PLASMA)
  b) Standard of Care (CONTROL, SOC), possible cross-over on day 10
- Primary endpoint: time to improvement of 2 points on a clinical 7-point ordinal scale or live hospital discharge
- Secondary endpoint: overall survival, antibody dynamics

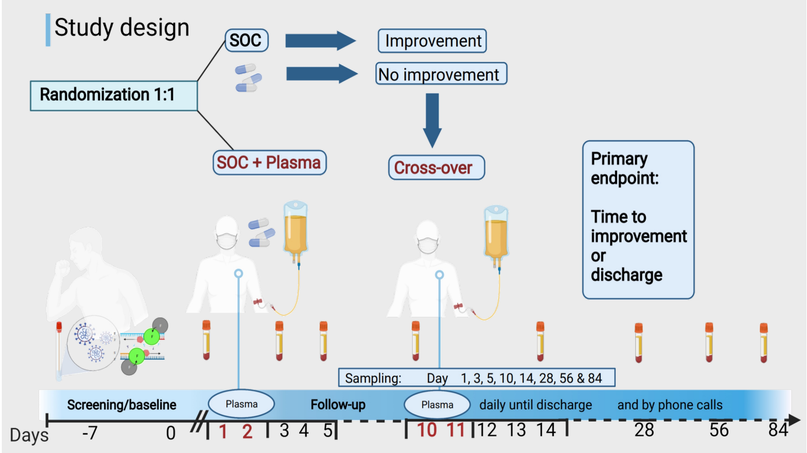

Fig.1: Study flow
Timeline from max. -7 days from symptom onset until randomization. Plasma donation from 2 different donors on day 1 and 2 in PLASMA group or on day 10 and 11 in CONTROL group in case of cross-over; SOC = standard of care

2. Population

- Total patients n=134, group 1 n=56 (42%), group 2 n=16 (12%), group 3 n=36 (27%), group 4 n=26 (19%).
- Group 1: B cell lymphoma/leukemia (36%), other hematological malignancies (48%), solid cancers (16%)
- Median time symptom onset to randomization: 7 days, IQR 4,10
- PLASMA: n=68, CONTROL n=66, cross-over n=10
- Adverse effects related to plasma were similar in PLASMA and CONTROL.

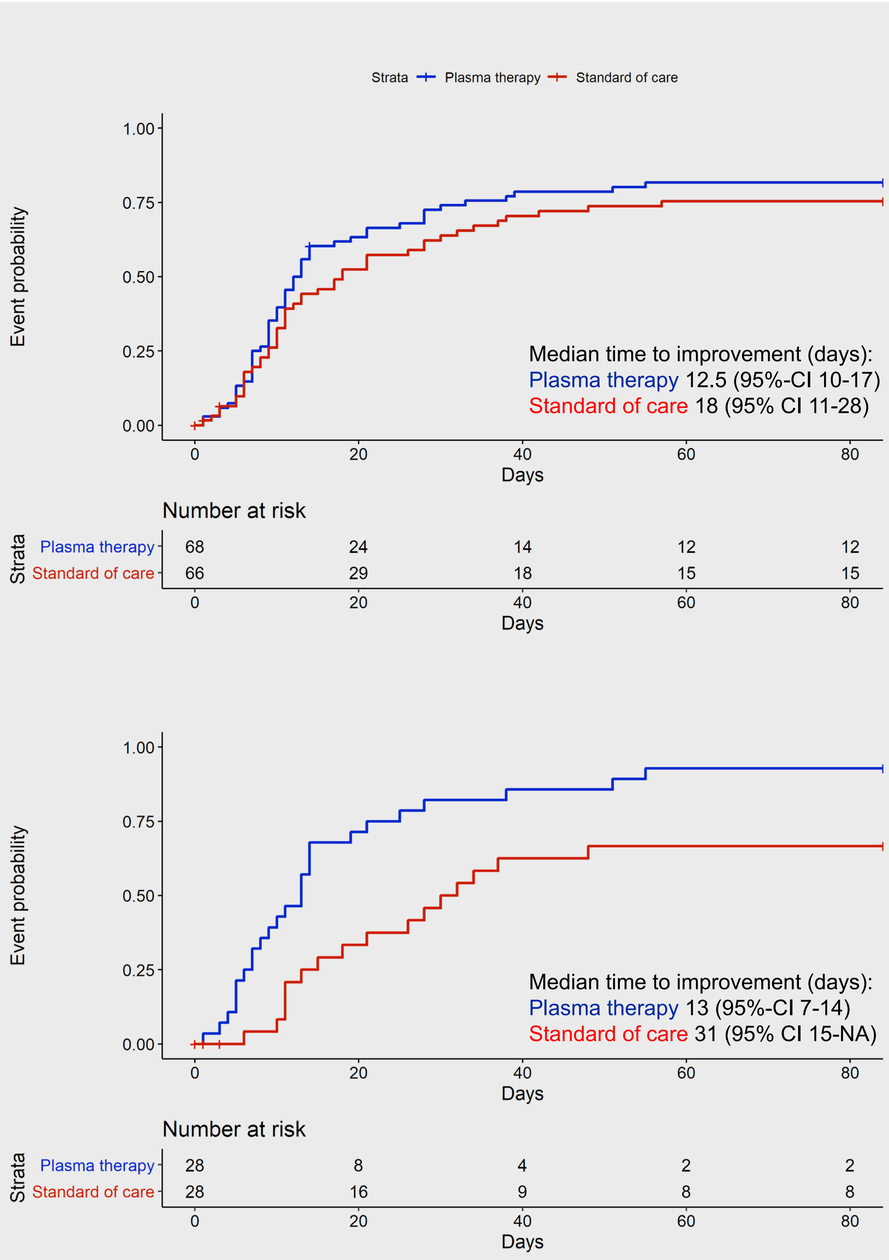

Fig.2: Primary endpoint - Time to discharge or improvement of 2 points in the 7-point ordinal scale or live hospital discharge; Kaplan Meier curve by PLASMA (blue) and CONTROL (red) with number of subjects at risk
Top: all groups; bottom: group 1 (cancer)

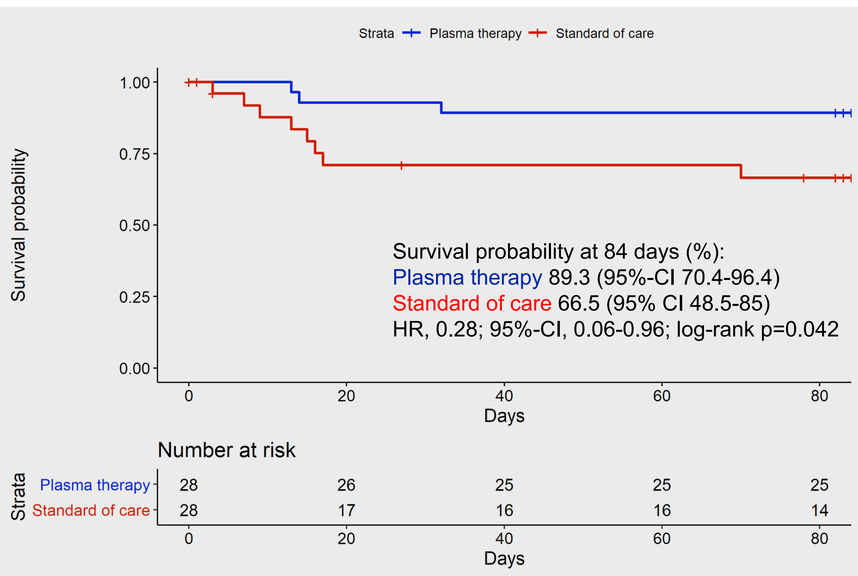

Fig.3: Overall survival probability for subgroup for group 1 (cancer), Kaplan Meier curve by PLASMA (blue) and CONTROL (red) with number of subjects at risk

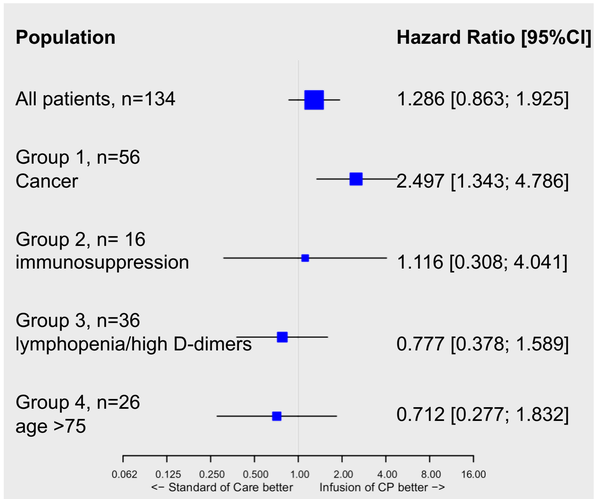

Fig.4: Primary endpoint - Time to discharge or improvement of 2 points in the 7-point ordinal scale or live hospital discharge; Forest plot for Hazard ratio for all groups and subgroups

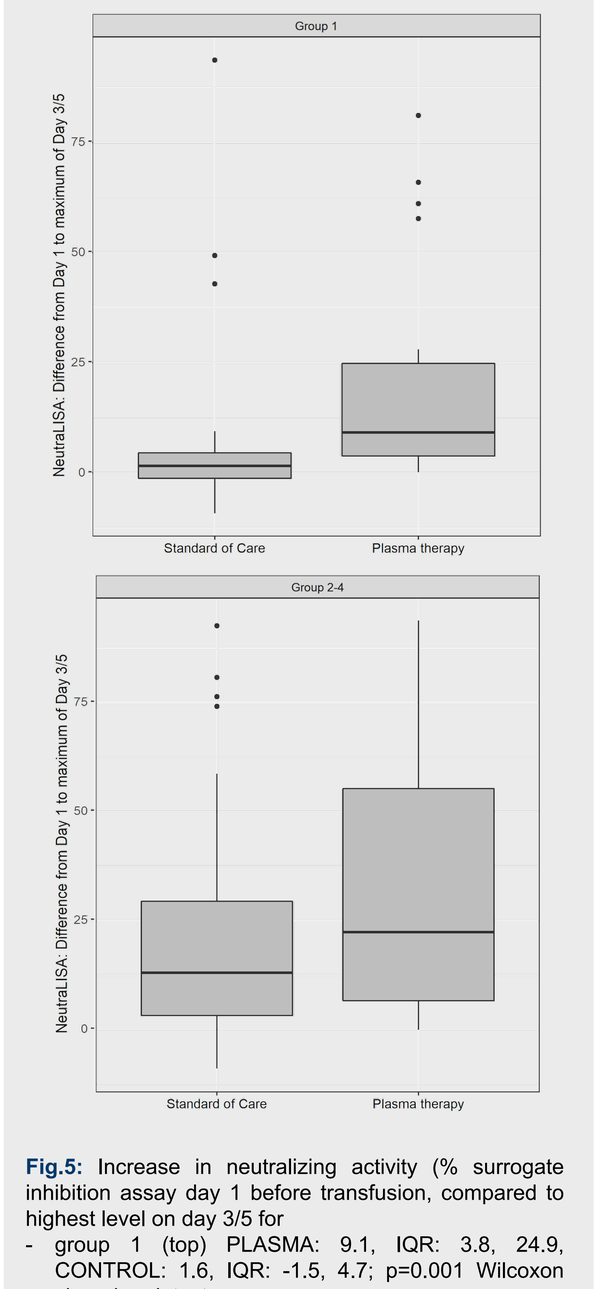

Fig.5: Increase in neutralizing activity (% surrogate inhibition assay day 1 before transfusion, compared to highest level on day 3/5 for
- group 1 (top) PLASMA: 9.1, IQR: 3.8, 24.9, CONTROL: 1.6, IQR: -1.5, 4.7; p=0.001 Wilcoxon signed rank test
- group 2-4 (bottom); no differences in neutralizing antibody activity

3. Conclusion and knowledge generated

- in group 1 (cancer patients) plasma therapy shortened time to improvement from 31 days to 13 days and improved overall survival
- in group 2 (immunosuppression), due to small numbers, no statistically significant effect could be shown → further trials needed
- in other high-risk groups (lymphopenia/elevated D-dimers, advanced age) no benefit was observed → specific effect
- likely mechanism: substantial increases in anti-SARS-CoV-2 neutralizing antibodies in cancer patients (low or absent levels at baseline) but not in other risk groups

Relevance: Convalescent/vaccinated plasma with high titers of neutralizing activity against SARS-CoV-2 may improve outcome in cancer patients with severe COVID-19

References

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