

Outcomes of Moderate-to-Severe Pneumocystis Pneumonia Treated with Adjunctive Steroid in Non-HIV-Infected Patients Mi Moon S et al Antimicrob. Agents Chemother. 2011, 55(10)

Hintergrund

- Wir empfehlen bei Non-HIV Patienten mit PCP-Pneumonie konkomitante Steroidtherapie bei arteriellem $\text{PaO}_2 < 10 \text{ kPa}$ ($< 70 \text{ mmHg}$)
- etablierte Methode bei HIV-Patienten, verbessert outcome, aber limitierte Daten bei Non-HIV
Pareja et al Chest 1998: Mortalitäts- und Ventilationsreduktion mit Steroiden aber kein Unterschied in-hospital mortality (retrospektiv, n=30), Delclaux CID 1999: kein Unterschied in Mortalität/Ventilation (retrospektiv, n=31, ohne Steroide: n=18)

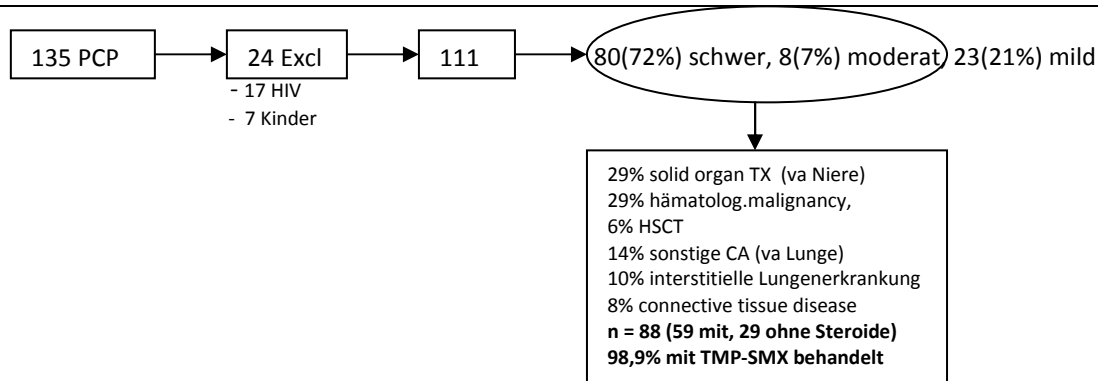
Methode und Definitionen

- **Study population:** Südkorea zwischen Januar 2007 und Dezember 2010 Einschluss von Patienten ≥ 16 jährig die Bronchoskopie wegen Vd.a PCP erhalten hatten, nur erste Bronchoskopie wurde analysiert
Ausschluss: Patienten mit bekannter HIV-Erkrankung
- **Mikrobiologie:** Diagnose einer PCP mikrobiologisch durch Immunfluoreszenz (zusätzlich bakterielle Kultur, Pilnachweis/kultur, Mykobakterienkultur, Virus[Immunfluor. für RSV, Influenza, Adeno, Parainfluenza, CMV-Kultur])
- Design: Klinische Daten **retrospektiv** gesammelt, O₂ Sättigung vor Bronchoskopie
Einteilung gemäss PaO_2 in Raumluft:
 - milde ($\text{PaO}_2 > 70 \text{ mmHg}$)
 - moderate ($\text{PaO}_2 \leq 70 \text{ mmHg}$)
 - schwere ($\text{PaO}_2 < 60 \text{ mmHg}$) PCP
- **Corticosteroide** = Gebrauch von Steroiden innerhalb 72h nach PCP Therapiebeginn bei moderate-severe. Minimum 40mg Prednison-aquivalent 2x/dfür 5Tage (unabhängig vom Tapering-Schema)
- **vorgängiger Steroidgebrauch** = $> 0.3 \text{ mg/kgKG/Tag}$ über 3Wochen im Monat vor PCP Diagnose
- **PCP-outcome:**
 - *respiratory failure* (mech.Ventilation $> 48 \text{ h}^*$) *48h damit initiale Ventilation für Bronchoskopie wegfällt
 - 30-Tage all cause mortality
 - 90-Tage all cause mortality ☹

☹ = Limitationen

Statistik: kategorische Variablen: chi-square, Fisher's exact, kontinuierliche Variablen: Mann-Whitney U, Time to event analysis: Kaplan-Meier, log rank

Resultate



BASELINE (das wichtigste) und OUTCOME Steroid vs kein Steroid

Characteristic	Adjunctive steroid therapy (n = 59)	No adjunctive steroid therapy (n = 29)	P value
Demographics			
→ Age, median years (IQR) ^b	59 (45–69)	54 (39–60)	0.01
→ Male gender	38 (64.4)	18 (62.1)	0.83
Underlying disease			
→ Solid-organ transplant recipient	12 (20.3)	14 (48.3)	0.007
Hematologic malignancy	21 (35.6)	5 (17.2)	0.08
Immunosuppressive agents use, previous month			
→ Steroid	23 (39.0)	11 (37.9)	0.92
→ T-cell immunosuppressant	16 (27.1)	15 (51.7)	0.02
Anticancer agent	27 (45.8)	10 (34.5)	0.31
Initial treatment regimen			
Trimethoprim-sulfamethoxazole	59 (100)	28 (96.6)	0.33
Change to second-line regimen			
→ Due to treatment failure	24 (40.7)	7 (24.1)	0.13
→ Due to adverse reaction	19 (32.2)	6 (20.7)	0.26
	5 (8.5)	1 (3.4)	0.66
Respiratory failure	37 (62.7)	17 (58.6)	0.71
30-day all-cause mortality	18 (30.5)	10 (34.5)	0.71
90-day all-cause mortality	28 (47.5)	12 (41.4)	0.59

^a Data are numbers (%) of patients, unless otherwise indicated.

^b IQR, interquartile range.

^c BAL, bronchoalveolar lavage.

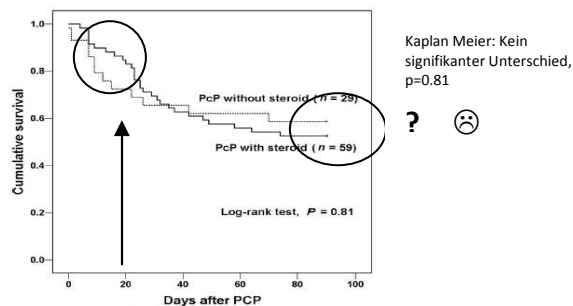


FIG. 1. Kaplan-Meier survival curves in patients with moderate-to-severe *Pneumocystis jirovecii* pneumonia (PCP) with or without adjunctive steroid therapy.

OUTCOMES Subgruppen

Outcomes of moderate-to-severe *Pneumocystis jirovecii* pneumonia with and without adjunctive steroid therapy according to age^a

	Younger than 56 years-old			Older than 56 years-old		
	Adjunctive steroid therapy (n = 26)	No adjunctive steroid therapy (n = 19)	P value	Adjunctive steroid therapy (n = 33)	No adjunctive steroid therapy (n = 10)	P Value
Respiratory failure	16 (61.5)	9 (47.4)	0.34	21 (63.6)	8 (80.0)	0.46
30-day all-cause mortality	6 (23.1)	5 (26.3)	0.99	12 (36.4)	5 (50.0)	0.48
90-day all-cause mortality	10 (38.5)	6 (31.6)	0.63	18 (54.5)	6 (60.0)	0.99

^a Data are numbers (%) of patients.

TABLE 1. Outcomes of moderate-to-severe *P. jirovecii* pneumonia according to underlying disease^a

Underlying disease	Respiratory failure	30-day all-cause mortality	90-day all-cause mortality
Solid-organ transplant recipient (n = 26)	15 (57.7)	5 (19.2)	6 (23.1) ^b
Hematologic malignancy (n = 26)	17 (65.4)	4 (15.4)	10 (38.5)
Non-hematologic malignancy (n = 12)	6 (50.0)	5 (41.7)	8 (66.7)
Interstitial lung disease (n = 9)	6 (66.7)	5 (55.6)	7 (77.8)
Connective tissue disease (n = 7)	6 (85.7)	4 (57.1)	4 (57.1)
Others (n = 8)	4 (50.0)	5 (62.5)	5 (62.5)
Total (n = 88)	54 (61.4)	28 (31.8)	40 (45.5)

^a Data are numbers (%) of patients.

^b P values of <0.05 between patients with a given underlying disease and all other underlying diseases.

Kein signifikanter Unterschied in der Inzidenz von respiratorischem Versagen entsprechend der Grundkrankheit

TABLE 4. Outcomes of moderate-to-severe *P. jirovecii* pneumonia with and without adjunctive steroid therapy in solid-organ transplant recipients^a

Outcome	Adjunctive steroid therapy (n = 12)	No adjunctive steroid therapy (n = 14)	P value
Respiratory failure	6 (50.0)	9 (64.3)	0.46
30-day all-cause mortality	3 (25.0)	2 (14.3)	0.64
90-day all-cause mortality	4 (33.3)	2 (14.3)	0.37

^a Data are numbers (%) of patients.

Outcomes of moderate-to-severe *Pneumocystis jirovecii* pneumonia with and without adjunctive steroid therapy according to the use of T-cell immunosuppressants^a

	Use of T-cell immunosuppressants			No use of T-cell immunosuppressants		
	Adjunctive steroid therapy (n = 16)	No adjunctive steroid therapy (n = 15)	P value	Adjunctive steroid therapy (n = 43)	No adjunctive steroid therapy (n = 14)	P value
Respiratory failure	8 (50.0)	9 (60.0)	0.58	29 (67.4)	8 (57.1)	0.53
30-day all-cause mortality	5 (31.3)	3 (20.0)	0.69	13 (30.2)	7 (50.0)	0.20
90-day all-cause mortality	6 (37.5)	3 (20.0)	0.43	22 (51.2)	9 (64.3)	0.58

^a Data are numbers (%) of patients.

TABLE 3. Demographics, clinical characteristics, and outcomes of moderate-to-severe *P. jirovecii* pneumonia with and without adjunctive steroid therapy in non-HIV-infected patients with or without recent steroid use^a

Characteristic	Recent steroid use			No recent steroid use		
	Adjunctive steroid therapy (n = 23)	No adjunctive steroid therapy (n = 11)	P value	Adjunctive steroid therapy (n = 36)	No adjunctive steroid therapy (n = 18)	P value
Underlying disease						
Solid-organ transplant recipient	2 (8.7)	1 (9.1)	0.99	10 (27.8)	13 (72.2)	0.002
Hematologic malignancy	3 (13.0)	3 (27.3)	0.36	18 (50.0)	2 (11.1)	0.005
Hematopoietic stem cell transplant recipient	1 (4.3)	1 (9.1)	0.99	3 (8.3)	0 (0)	0.54
Nonhematologic malignancy	3 (13.0)	1 (9.1)	0.99	6 (16.7)	2 (11.1)	0.70
Interstitial lung disease	6 (26.1)	3 (27.3)	0.99	0 (0)	0 (0)	—
Connective tissue disease	5 (21.7)	1 (9.1)	0.64	1 (2.8)	0 (0)	0.99
Others	4 (17.4)	2 (18.2)	0.99	1 (2.8)	1 (5.6)	0.99
Immunosuppressive agents use, previous month						
T-cell immunosuppressant	5 (21.7)	2 (18.2)	0.99	11 (30.6)	13 (72.2)	0.004
Anticancer agent	7 (30.4)	5 (45.5)	0.46	20 (55.6)	5 (27.8)	0.054
Respiratory failure	15 (65.2)	6 (54.5)	0.71	22 (61.1)	11 (61.1)	0.99
30-day all-cause mortality	11 (47.8)	4 (36.4)	0.72	7 (19.4)	6 (33.3)	0.32
90-day all-cause mortality	12 (52.2)	6 (54.5)	0.90	16 (44.4)	6 (33.3)	0.43

Diskussion

Grösste (retrospektive) Studie mit dieser Fragestellung bisher

Fazit der Autoren: zusätzliche Steroidgabe verbessert outcome bei non-HIV patienten wbs nicht. Prospektive Studien notwendig

Limitationen ☹

- retrospektiver Charakter, sample sizes zu klein
- etliche „Subgruppenanalysen“... zu kleine sample size um Subgruppen wie hämatologische Malignitäten, andere Krebsarten, connective tissue diseases, interstitielle Lungenerkrankungen zu analysieren
- Dosis von Bactrim wird nicht erwähnt
- Keine Info bzgl Bactrim Prophylaxe (immerhin viele Patienten mit Immunsuppressiva)
- mind 38% hatten vorgängig Steroide
- Verlauf Kaplan-Meier Kurve: bei End of Treatment (d21) besseres outcome bzgl survival bei denen mit zusätzlicher Steroidgabe.

FAZIT: Steroide zusätzlich noch geben bis bessere Daten verfügbar.

