Supplementary Online Content

Uranga A, España PP, Bilbao A, et al. Duration of antibiotic treatment in community-acquired pneumonia: a multicenter randomized clinical trial. *JAMA Intern Med.* Published online July 25, 2016. doi:10.1001/jamainternmed.2016.3633.

This supplementary material has been provided by the authors to give readers additional information about their work.

eTable 1. Vital Signs at Day 5 in the Per-Protocol Population

	Control group	**Intervention group**	**P value**
Body temperature, °C	36.3 (0.5)	36.4 (0.7)	.43
Systolic blood pressure, mmHg	129.9 (24.8)	125.6 (18.7)	.43
Respiratory rate, breaths/min	20.1 (5.0)	21 (3.0)	.10
Heart rate, beats/min	81.7 (17.2)	77.5 (13.4)	.26
Oxygen saturation, %	94.6 (2.8)	94.9 (2.1)	.92

All data are presented as mean (SD).
SD: standard deviation.

eTable 2. Distribution of Causative Microorganism in 63 Patients With CAP in the Per-Protocol Population

	Control group (n=35)	**Intervention group (n=28)**	**P value**
Streptococcus pneumonia	29 (82.9)	21 (75)	.44
Legionella pneumophila	4 (11.4)	7 (25)	.19
Haemophilus influenzae	1 (2.9)	0 (0)	>.99
Escherichia coli	1 (2.9)	1 (3.6)	>.99
Streptococcus pyogenes	1 (2.9)	0 (0)	>.99
Coxiella burnetti	1 (2.9)	1 (3.6)	>.99
Mycoplama	1 (2.9)	1 (3.6)	>.99
Chlamydia	1 (2.9)	1 (3.6)	>.99
Virus[a]	1 (2.9)	1 (3.6)	>.99

All data are presented as number (percentage) of study participants.
[a] The same patient was positive for more than one virus.

eTable 3. Results for Primary Study Outcomes by Type of Antibiotics [a]

	Intention-to-treat			**Per-protocol**		
Quinolones alone or in combination	**Control group (n=119)**	**Intervention group (n=128)**	**P value**	**Control group (n=109)**	**Intervention group (n=117)**	**P value**
Clinical success, n (%)						
At day 10	54 (46.5)	71 (56.3)	.13	51 (48.1)	67 (58.2)	.13
At day 30	103 (87.2)	117 (92.1)	.21	99 (91.6)	110 (94.8)	.34
CAP-Symptom questionnaire score[b], mean (SD)						
At day 5	24.2 (11.7)	27.1 (12.0)	.06	23.7 (11.5)	26.8 (11.4)	.04
At day 10	18.5 (9.3)	17.5 (7.4)	.62	18.0 (8.7)	17.4 (7.2)	.82
Beta-lactams + macrolides	**Control group (n=11)**	**Intervention group (n=13)**	**P value**	**Control group (n=10)**	**Intervention group (n=13)**	**P value**
Clinical success, n (%)						
At day 10	6 (54.5)	10 (76.9)	.39	6 (60)	10 (76.9)	.65
At day 30	10 (90.9)	12 (92.3)	>.99	10 (100)	12 (92.3)	>.99
CAP-Symptom questionnaire score[b], mean (SD)						
At day 5	25.3 (8.7)	24.0 (17.5)	.53	24.9 (9.0)	24.0 (17.5)	.60
At day 10	16.9 (7.3)	14.8 (8.7)	.44	15.6 (6.2)	14.8 (8.7)	.62
Beta-lactams	**Control group (n=20)**	**Intervention group (n=19)**	**P value**	**Control group (n=18)**	**Intervention group (n=16)**	**P value**
Clinical success, n (%)						
At day 10	11 (57.8)	9 (47.3)	.52	10 (58.8)	9 (56.2)	.88
At day 30	19 (95)	16 (88.8)	.59	17 (94.4)	14 (93.3)	>.99

CAP-Symptom questionnaire score[b], mean (SD)						
At day 5	27 (11.2)	28.5 (11.1)	.87	27.7 (11.6)	27.5 (11.5)	.53
At day 10	20.3 (7.6)	21.7 (6.4)	.42	20.1 (8.0)	21.1 (5.8)	.48

Abbreviation: CAP, community-acquired pneumonia.

[a] Data are presented as number (percentage) or mean (SD). Percentages exclude patients with missing data.

[b] On the CAP symptom questionnaire score, which is a specific and validated patient-reported outcome measure based on 18 items, higher scores indicated more severe CAP-related symptoms (range: 0 to 90).

eTable 4. Results for Primary Study Outcomes by Hospitals [a]

	Intention-to-treat			**Per-protocol**		
HOSPITAL A	**Control group (n=65)**	**Intervention group (n=81)**	**P value**	**Control group (n=61)**	**Intervention group (n=75)**	**P value**
Clinical success, n (%)						
At day 10	44 (67.6)	58 (72.5)	.53	43 (70.4)	58 (78.3)	.29
At day 30	60 (92.3)	75 (93.7)	.75	59 (96.7)	71 (95.9)	>.99
CAP-Symptom questionnaire score[b], mean (SD)						
At day 5	26.0 (12.6)	30.5 (15.2)	.09	25.2 (12.2)	29.3 (14.8)	.13
At day 10	15.2 (8.9)	15.9 (7.5)	.42	14.3 (7.1)	15.6 (7.5)	.36
HOSPITAL B	**Control group (n=49)**	**Intervention group (n=37)**	**P value**	**Control group (n=42)**	**Intervention group (n=29)**	**P value**
Clinical success, n (%)						
At day 10	19 (41.3)	19 (52.7)	.30	16 (41.0)	16 (57.1)	.19
At day 30	42 (87.5)	32 (88.8)	>.99	37 (90.2)	27 (96.4)	.64
CAP-Symptom questionnaire score[b], mean (SD)						
At day 5	27.7 (9.7)	27.6 (6.9)	.82	28.3 (10.2)	27.5 (7.0)	.75
At day 10	23.5 (7.0)	24.5 (4.7)	.32	23.8 (7.5)	24.1 (4.1)	.64
HOSPITAL C	**Control group (n=26)**	**Intervention group (n=37)**	**P value**	**Control group (n=26)**	**Intervention group (n=36)**	**P value**
Clinical success, n (%)						
At day 10	6 (24)	10 (27.0)	.79	6 (24)	10 (27.7)	.74
At day 30	22 (84.6)	33 (89.1)	.71	22 (84.6)	32 (88.8)	.71

CAP-Symptom questionnaire score[b], mean (SD)						
At day 5	17.3 (7.7)	21.1 (6.6)	.05	17.3 (7.7)	21.4 (6.5)	.04
At day 10	19.0 (7.8)	17.4 (6.2)	.53	19.0 (7.8)	17.7 (5.9)	.62
HOSPITAL D	**Control group (n=10)**	**Intervention group (n=7)**	**P value**	**Control group (n=8)**	**Intervention group (n=6)**	**P value**
Clinical success, n (%)						
At day 10	2 (20)	3 (42.8)	.59	2 (25)	2 (33.3)	>.99
At day 30	8 (80)	7 (100)	.49	8 (100)	6 (100)	>.99
CAP-Symptom questionnaire score[b], mean (SD)						
At day 5	21.6 (9.9)	19.4 (8.3)	.81	20.6 (10.4)	21 (7.9)	.66
At day 10	18.4 (10.8)	11.5 (6.6)	.24	18.1 (10.3)	12.3 (6.8)	.32

Abbreviation: CAP, community-acquired pneumonia.

[a] Data are presented as number (percentage) or mean (SD). Percentages exclude patients with missing data.

[b] On the CAP symptom questionnaire, which is a specific and validated patient-reported outcome measure based on 18 items, higher scores indicated more severe CAP-related symptoms (range: 0 to 90).

eTable 5. Results for Secondary Outcomes in Intent-to-Treat Analysis[a]

	Control group (n=150)	**Intervention group (n=162)**	**P value**
Time, median (IQR), d			
Taking antibiotics	10 (10-11)	5 (5-9)	<.001
Not taking antibiotics	21 (10-27)	25 (5-31)	.0011
Taking intravenous antibiotics	2 (2-4)	3 (2-4)	.24
Until clinical improvement, median (IQR)	12 (8 – 18)	12 (8 – 15)	.50
Return to normal activity, median (IQR)	17 (9 – 24)	15 (10 – 21)	.58
Radiographic resolution at day 30	93 (66.4)	122 (79.2)	.01
In-hospital mortality	2 (1.3)	3 (1.8)	>.99
30-Day mortality	3 (2)	3 (1.8)	>.99
Recurrence by day 30	6 (4)	4 (2.4)	.53
Readmission by day 30	10 (6.7)	2 (1.8)	.03
In-hospital complications			
Pleural effusion	11 (7.3)	6 (3.7)	.16
Treatment failure[b]	3 (2)	3 (1.8)	>.99
Respiratory failure[c]	26 (17.3)	32 (19.7)	.58
Severe Sepsis[d]	7 (4.6)	11 (6.7)	.42
Renal failure[e]	5 (3.3)	8 (4.9)	.49
ICU admission	2 (1.3)	1 (0.6)	.61
Use of invasive mechanical ventilation	2 (1.3)	1 (0.6)	.61
Use of non-invasive mechanical ventilation	3 (2.0)	2 (1.2)	.67
Need for vasopressors	2 (1.3)	3 (1.8)	>.99
Antibiotic adverse effects by day 30	19 (12.6)	18 (11.1)	.69

Time with antibiotic adverse effects, mean (SD), d	3 (2.7)	1.6 (2.0)	.17
Length of hospital stay, mean (SD), d	5.8 (3.0)	5.8 (2.7)	.71

Abbreviations: ICU, intensive care unit; IQR, interquartile range-

[a] Data are presented as number (percentage) of study participants unless otherwise indicated. Percentages exclude patients with missing data.

[b] Treatment failure was defined as clinical deterioration based on the presence of any of the following: hemodynamic instability, demonstrated respiratory failure or the appearance of it, need for mechanical ventilation, demonstrated radiographic progression of pneumonia or the appearance of a new infectious foci and absence or delay in achieving clinical stability after first 72 hours.

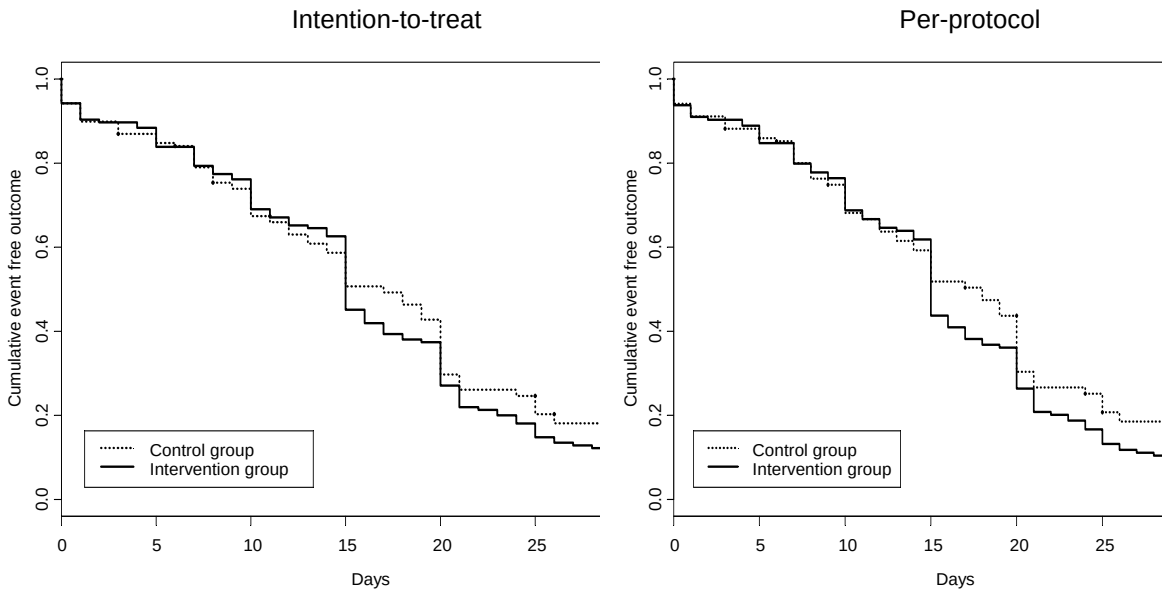
[c] Respiratory failure was defined as PaO_2 to fraction of inspired oxygen ratio less than 250 mmHg.

[d] Severe Sepsis was defined as sepsis associated with organ dysfunction and perfusion abnormalities. One of the following criteria had to be met: pH less than 7.30, systolic blood pressure less than 90 mmHg, pneumonia associated altered mental status, PaO_2 to fraction of inspired oxygen ratio less than 250 mmHg, acute renal failure >2 mg/dL (to convert to micromoles per liter, multiply by 88.4), disseminated intravascular coagulopathy or hematocrit less than 25%.

[e] Renal failure was defined as a creatinine greater than 2 mg/dL (to convert to micromoles per liter, multiply by 88.4).

eFigure. Kaplan-Meier Curves for Return to Normal Activity Until Day 30 in the Intent-to-Treat (A) and the Per-Protocol Population (B)

A) B)



The log-rank test did not detect statistically significant differences between the two groups (control group receiving conventional treatment and intervention group receiving antibiotic treatment with duration based on IDSA/ATS criteria; p=.38 in the intention-to trait and p=.16 in the per-protocol population).