J Antimicrob Chemother 2019; **74**: 2394–2399
doi:10.1093/jac/dkz202 Advance Access publication 18 May 2019

Journal of Antimicrobial Chemotherapy

Four versus six weeks of antibiotic therapy for osteoarticular infections after implant removal: a randomized trial

Mohamed Benkabouche[1]†, Guillaume Racloz[2,3]†, Hervé Spechbach[1], Benjamin A. Lipsky[4], Jean-Michel Gaspoz[1] and Ilker Uçkay [2,4,5]*

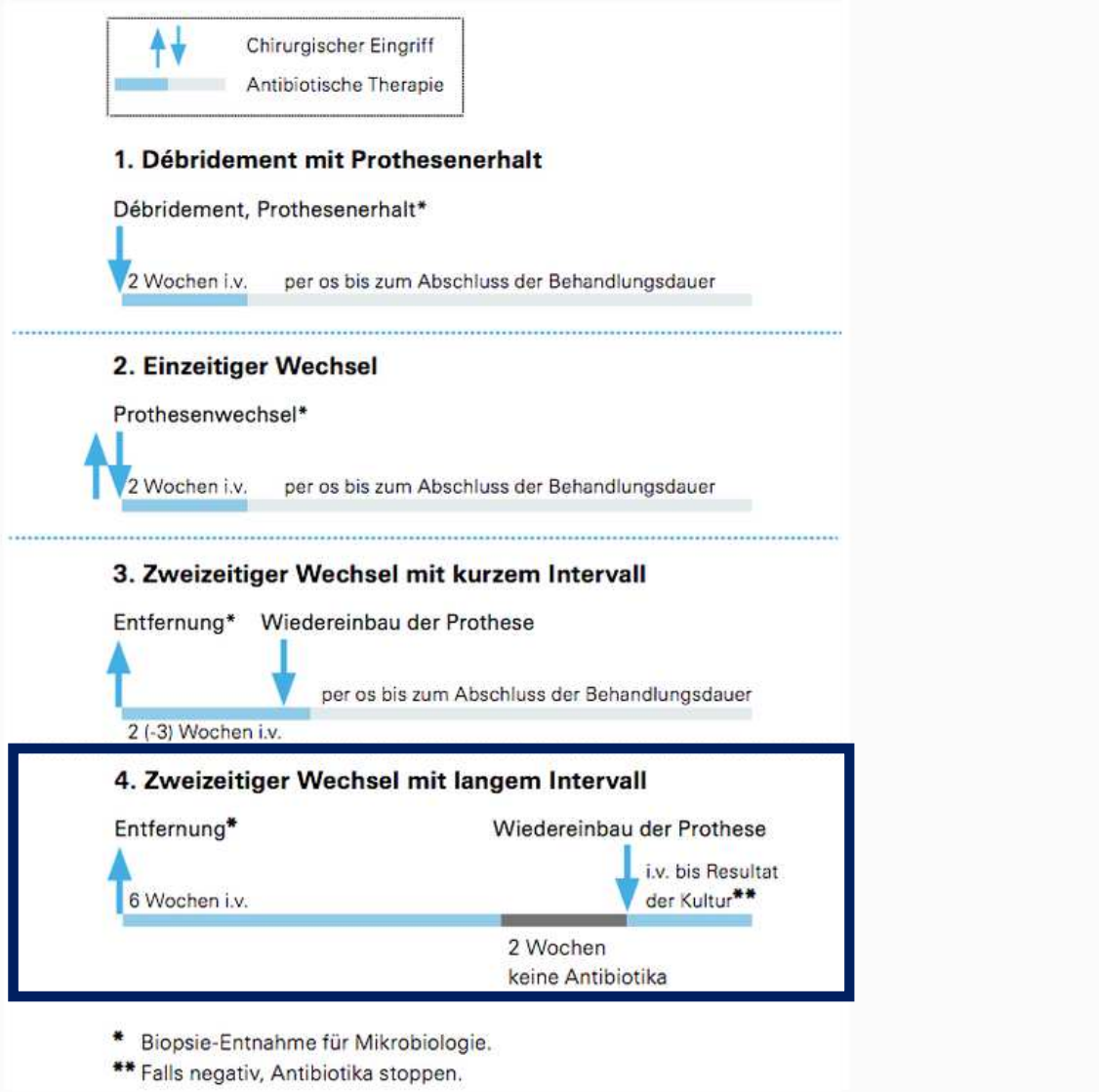
[1]Department of Community Medicine, Geneva University Hospitals and Faculty of Medicine, Geneva, Switzerland; [2]Orthopaedic Surgery Service, Geneva University Hospitals and Faculty of Medicine, Geneva, Switzerland; [3]Orthopaedic Service of Surgery, Pourtales Hospital, Neuchâtel, Switzerland; [4]Service of Infectious Diseases, Geneva University Hospitals and Faculty of Medicine, Geneva, Switzerland; [5]Infectiology, Balgrist University Hospital and Faculty of Medicine, Zurich, Switzerland

*Corresponding author. Balgrist University Hospital, Forchstrasse 340, 8008 Zurich, Switzerland. Tel: +41-44-386-1111; Fax: +41-44-386-3709;
E-mail: Ilker.Uckay@balgrist.ch orcid.org/0000-0002-5552-0973
†Equal contribution as first authors.

Received 4 December 2018; returned 20 February 2019; revised 26 March 2019; accepted 8 April 2019

Journal Club 09.09.2019

3.2 Therapeutischer Ablauf anhand der verschiedenen chirurgischen Optionen



* Biopsie-Entnahme für Mikrobiologie.
** Falls negativ, Antibiotika stoppen.

Weissbuch, Stand April 2019

Methods

- Single-centre
- Prospective, unmatched, unblinded, randomized, interventional study
- March 2015 – March 2018

Methods

- Inclusion criteria:
  - ≥ 18 years
  - First episode of infection
  - Having undergone complete removal of the infected implant without immediate re-osteosynthesis
- Exclusion criteria:
  - Recurrent infection
  - Allergies to multiple antibiotics
  - Primary native joint septic arthritis
  - Left-side endocarditis
  - Incomplete debridement or persistent foreign material in the infected area
  - Long-lasting antibiotic therapy: mycobacteria, fungi, brucellosis, nocardiosis, mycoplasma

Methods

- primary outcome: remission of infection at the operative site
- secondary outcome: occurence of any adverse events related to antibiotic therapy

Results

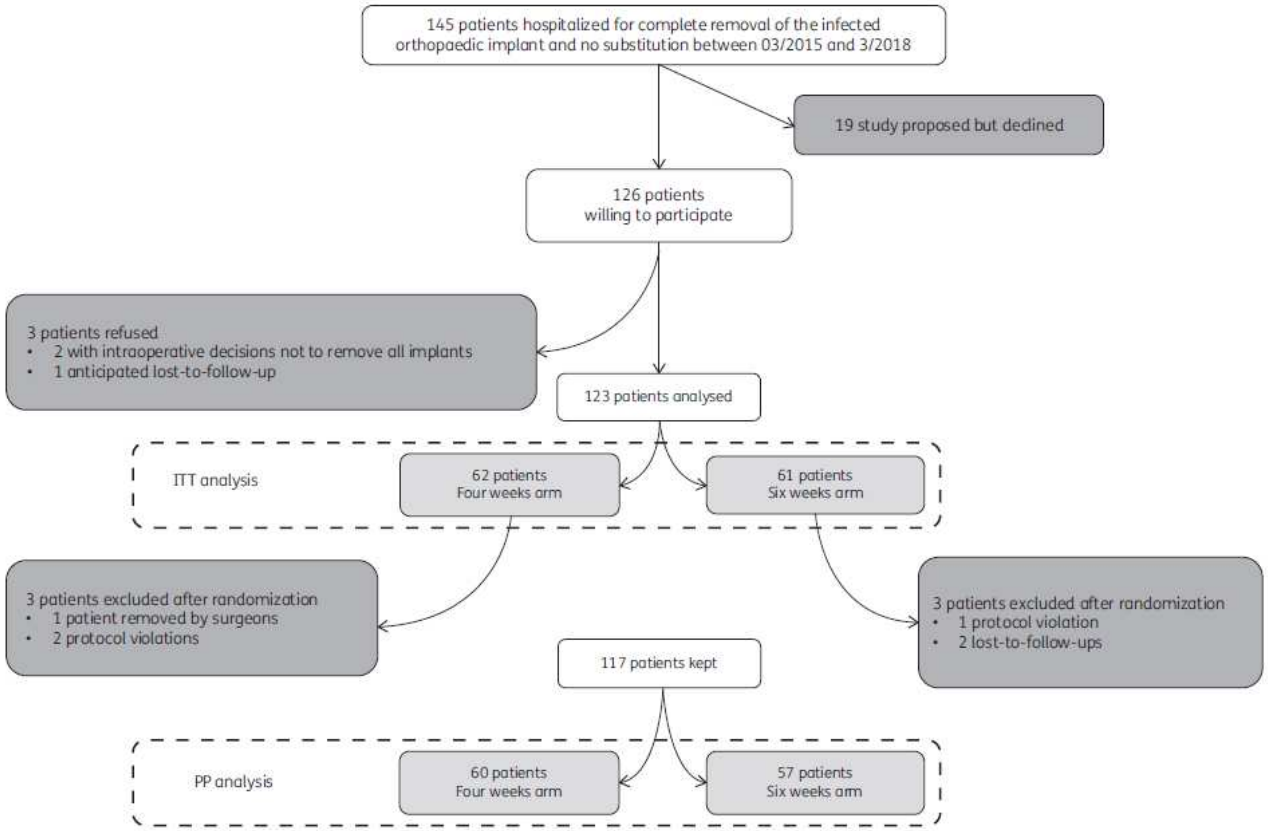


Figure 1. Study flow chart of patients.

Results

ITT analysis n = 123	**Six weeks** n = 61	**Four weeks** n = 62	*p*-value *	**PP analysis** n = 117	**Six weeks** n = 60	**Four weeks** n = 57	*p*-value *
Female sex	23 (37%)	25 (41%)	.67	Female sex	20 (35%)	25 (42%)	.47
Median age	65 years	62 years	.27	Median age	63 years	63 years	.36
Immune suppression[+]	18 (29%)	20 (33%)	.65	Immune suppression[+]	15 (26%)	20 (33%)	.41
Bacteraemia	8 (13%)	4 (7%)	.24	Bacteraemia	7 (12%)	4 (7%)	.30
Median ASA-Score[16]	2	2	.13	Median ASA-Score[16]	2	2	.22
Psychiatric co-morbidity	25 (40%)	24 (39%)	.91	Psychiatric co-morbidity	22 (39%)	24 (40%)	.88
Haematogenous origin of infection	9 (15%)	7 (11%)	.62	Haematogenous origin of infection	9 (15%)	7 (12%)	.52
Primary surgical site infections	23 (38%)	19 (31%)	.53	Primary surgical site infections	22 (37%)	18 (32%)	.36
Serum CRP level on admission (median)	37 mg/L	23 mg/L	.24	Serum CRP level on admission (median)	42 mg/L	23 mg/L	.35

Results

Origin of infection	
Surgical site infection	42 (34%)
Community-acquired infection	64 (52%)
Haematogenous seeding	16 (13%)
unknown	1
Types of implants and associated surgeries	
Two-stage exchange for prosthetic joint infection	39
Metal plate infection	44
Intramedullary nail infection	11
Infection of other osteosyntheses	30

Results (ITT)

	Four weeks arm N=62	Six weeks arm N=61	P-value
Recurrence of clinical infection Recurrence after median 55 days	4 (6.5%)	3 (4.9%)	0.74 1.5% (-9.8% to +6.8%)
Microbiological recurrence	2 (3.2%)	1 (1.6%)	0.57
Subgruppen Type of infection (explanted arthroplasties, plates, nales) Pathogen groups (Gram-negatives, staphylococci, streptococci, skind commensals)			 Not significant Not significant
Adverse Events 23 episodes (18.7%)			Not significant

Results

	Six weeks		**Four weeks**	
Pathogen group	Parenteral antibiotics	*Oral antibiotics*	Parenteral antibiotics	*Oral antibiotics*
MSSA, n=42	Flucloxacillin (n=4)	*Co-trimoxazole (n=3)*	Flucloxacillin (n=3)	*Co-trimoxazole (n=3)*
	Cefazolin (n=3)	*Clindamycin (n=8)*	Cefazolin (n=3)	*Clindamycin (n=10)*
	Co-amoxiclav (n=4)	*Quinolones (n=8)*	Co-amoxiclav (n=3)	*Quinolones (n=5)*
	Cefuroxim (n=3)	*Beta-lactams (n=4)*	Cefuroxim (n=1)	*Beta-lactams (n=6)*
	Daptomycin (n=1)	*Rifampicin (n=3)*	Daptomycin (n=0)	*Rifampicin (n=3)*
Streptococci, n=14	Cefuroxim (n=3)	*Levofloxacin (n=2)*	Cefuroxim (n=1)	*Levofloxacin (n=2)*
	Ampicillin (n=2)	*Clindamycin (n=2)*	Ampicillin (n=2)	*Clindamycin (n=2)*
	Vancomycin (n=2)	*Ampicillin (n=1)*	Vancomycin (n=1)	*Ampicillin (n=3)*
Gram-negatives, n=28	Cephalosporins (n=5)	*Quinolones (n=8)*	Cephalosporins (n=3)	*Quinolones (n=10)*
	Carbapenems/tazobactam (n=3)	*Co-trimoxazole (n=3)*	Carbapenems/tazobactam (n=2)	*Co-trimoxazole (n=2)*
Skin commensals*, n=43	Vancomycin/daptomycin (n=8)	*Ampicillin (n=4)*	Vancomycin/daptomycin (n=6)	*Ampicillin (n=3)*
	Aminopenicillins (n=7)	*Clindamycin (n=2)*	Aminopenicillins (n=4)	*Clindamycin (n=6)*
	Cephalosporins (n=9)	*Quinolones (n=8)*	Cephalosporins (n=3)	*Quinolones (n=6)*
		Tetracyclines (n=9)		*Tetracyclines (n=8)*
		Rifampicin (n=5)		*Rifampicin (n=3)*

*Skin commensals = coagulase-negative staphylococci, micrococci, corynebacteria, or cutibacteria

CLINICAL SCIENCE

Two weeks versus four weeks of ant after surgical drainage for native joi arthritis: a prospective, randomised, trial

Ergys Gjika,[1] Jean-Yves Beaulieu,[1] Konstantinos Vakalopou Cindy Bouvet,[1] Amanda Gonzalez,[1] Vanessa Morello,[1] Chri Stefanie Hirsiger,[1] Benjamin Alan Lipsky,[2,3] Ilker Uçkay[2,4]

ABSTRACT

Objective The optimal duration of postsurgical antibiotic therapy for adult native joint bacterial arthritis remains unknown.

Methods We conducted a prospective, unblinded, randomised, non-inferiority study comparing either 2 or 4 weeks of antibiotic therapy after surgical drainage of native joint bacterial arthritis in adults. Excluded were implant-related infections, episodes without surgical lavage and episodes with a follow-up of less than 2 months.

Results We enrolled 154 cases: 77 in the 4-week arm and 77 in the 2-week arm. Median length of intravenous antibiotic treatment was 1 and 2 days, respectively. The median number of surgical lavages was 1 in both arms. Recurrence of infection was noted in three patients (2%): 1 in the 2-week arm (99% cure rate) and 2 in the 4-week arm (97% cure rate). There was no difference in the number of adverse events or sequelae between the study arms. Of the overall 154 arthritis cases, 99 concerned the hand and wrist, for which an additional subgroup analysis was performed. In this per-protocol subanalysis, we noted three recurrences: one in the 2-week arm (97 % cure); two in the 4-week arm (96 % cure) and witnessed sequelae in 50% in the 2-week arm versus 55% in the 4-week arm, of which five (13%) and six (13%) needed further interventions.

Conclusions After initial surgical lavage for septic arthritis, 2 weeks of targeted antibiotic therapy is not inferior to 4 weeks regarding cure rate, adverse events or sequelae and leads to a significantly shorter hospital stay, at least for hand and wrist arthritis.

Trial registration number NCT03615781.

Discussion

- No difference in outcomes between 4 and 6 weeks
  → Änderung der Therapiedauer bei uns?
  → Optimale Therapiedauer weiterhin unbekannt!
- Clinical remission rate 94-98%
  → unerwartet hoch?
- Kurze intravenöse Therapiedauer von 4 Tagen
  → Anpassung bei uns möglich?
- Median follow-up 2.2 years, 8 % <1 year
  → Standard wäre min. 2 Jahre