Evaluating safety reporting in paediatric antibiotic trials 2000-2016: a systematic review and meta-analysis

Subheading: Safety reporting in paediatric antibiotic clinical trial 2000-2016

Drugs

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SEARCH STRATEGY

Medline (Ovid MEDLINE(R) without Revisions 1996 to June Week 1 2016). Searched on 02/06/2016

1. anti?bioti*.mp.
2. antibiotic.mp. or exp Anti-Bacterial Agents/
3. exp Anti-Bacterial Agents/ or exp Anti-Infective Agents/ or anti infective.mp.
4. antimicrobial.mp.
5. anti microbial.mp.
6. (anti?biot* or anti?infect* or anti?bact* or anti?microb*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
7. 1 or 2 or 3 or 4 or 5 or 6
8. randomized controlled trial.pt.
9. controlled clinical trial.pt.
10. randomized.ab.
11. placebo.ab.
12. clinical trials as topic.sh.
13. randomly.ab.
14. trial.ti.
15. 8 or 9 or 10 or 11 or 12 or 13 or 14
16. exp animals/ not humans.sh.
17. 15 not 16
18. exp Safety/ or exp Patient Safety/ or safety.mp.
19. exp "Drug-Related Side Effects and Adverse Reactions"/ or drug reaction.mp. or exp Drug Hypersensitivity/
20. side effect.mp.
21. adverse effect.mp.
22. toxicity.mp.
23. exp Anaphylaxis/ or anaphylaxis.mp.
24. adverse event.mp.

25. Product Surveillance, Postmarketing/ or pharmacovigilance.mp. or exp Adverse Drug Reaction Reporting Systems/ or exp Pharmacovigilance/ or Drug Monitoring/

26. 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25

27. 7 and 17 and 27

28. limit 27 to (yr="2000 - 2016" and "all child (0 to 18 years)")

29. malaria.mp. or exp Malaria/

30. exp HIV/ or HIV.mp.

31. exp Tuberculosis/

32. 29 or 30 or 31

33. 28 not 32

CENTRAL (Issue 6 of 12, June 2016). Searched on 02/06/2016

1. MeSH descriptor: [Anti-Bacterial Agents] explode all trees
2. (anti* near (infect* or biotic* or bacter* or microb*))
3. MeSH descriptor: [Safety] explode all trees
4. MeSH descriptor: [Drug Hypersensitivity] explode all trees
5. MeSH descriptor: [Drug-Related Side Effects and Adverse Reactions] explode all trees
6. "toxicity":ti,ab,kw (Word variations have been searched)
7. "anaphylaxis":ti,ab,kw (Word variations have been searched)
8. MeSH descriptor: [Anaphylaxis] explode all trees
9. MeSH descriptor: [Pharmacovigilance] explode all trees
10. "pharmacovigilance":ti,ab,kw (Word variations have been searched)
11. "adverse drug event":ti,ab,kw (Word variations have been searched)
12. 1 or 2
13. 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11
14. 12 and 13
15. 14 limited to Publication Year from 2000 to 2016, in Trials

Clinicaltrials.gov. Searched on 02/06/2016

Ongoing trials

(antibiotic OR antibacterial OR antiinfective OR antimicrobial) AND (safety OR drug hypersensitivity OR adverse reaction OR side effects OR hypersensitivity OR toxicity OR pharmacovigilance OR anaphylaxis) AND EXACT ("Recruiting" OR "Not yet recruiting" OR "Available") [OVERALL-STATUS] AND EXACT "Interventional" [STUDY-TYPES] AND EXACT Child [AGE-GROUP] AND ("01/01/2000" : "06/02/2016") [FIRST-RECEIVED-DATE]

Closed in the last 5 years

(antibiotic OR antibacterial OR antiinfective OR antimicrobial) AND (safety OR drug hypersensitivity OR adverse reaction OR side effects OR hypersensitivity OR toxicity OR pharmacovigilance OR anaphylaxis) AND EXACT NOT ("Recruiting" OR "Not yet recruiting" OR "Available") [OVERALL-STATUS] AND EXACT "Interventional" [STUDY-TYPES] AND EXACT Child [AGE-GROUP] AND ("01/01/2011" : "06/02/2016") [FIRST-RECEIVED-DATE]

eTable 1 Included studies and quality assessment

Study Reference	Country	Study period	Funded by pharmaceutical	Safety endpoint	Condition	Intervention	Population N	Age	Quality assessment[a]
Abdel-Hady, 2011 [1]	Egypt	03/2007-01/2008	no	Secondary	Neonatal Sepsis	Open label RCT 1:1 to • Amikacin OD • Amikacin BID	30	Neonates	44
Adler, 2000 [2]	Europe, South Africa and Australia	nr	yes	Secondary	URTI	Open label RCT 1:1:1 to • Cefdinir OD • Cefdinir BID • Amoxicillin	752	6 m - 12 y	67
Afrinest, 2015 [3]	Democratic Republic of Congo (DRC), Kenya and Nigeria	04/2011-03/2013	no	Primary	Unspecified BI	Open label RCT 1:1 to • Procaine penicillin OD • Gentamicin OD & Amoxicillin BID	2,196	0 - 59 d	80
Afrinest, 2015 [4]	Democratic Republic of Congo (DRC), Kenya and Nigeria	04/2011-2013	no	Primary	Unspecified BI	Open label RCT 1:1:1:1 to • Gentamicin OD (7 days) + Procaine penicillin OD (7 days) • Gentamicin OD (7 days) + Amoxicillin BID (7 days) • Gentamicin OD (7 days) + Procaine penicillin OD (2 days) + Amoxicillin 5 days • Gentamicin OD (2 days) & Amoxicillin BID (2 days) + Amoxicillin BID (5 days)	3,564	0 - 59 d	70
Aguilar, 2000 [5]	Worldwide	07/1998-07/1999	yes	Secondary	URTI	Double blind RCT 1:1 to • Amoxicillin BID • Amoxicillin TID	516	2 - 12 y	78
Arguedas, 2005 [6]	Chile, US, Costa Rica and Finland	09/2002-07/2003	yes	Secondary	URTI	Double blind RCT 1:1 to • Azithromycin OD • Amoxicillin BID (High dose)	306	6 – 30 m	78
Arguedas, 2009 [7]	Colombia, USA, Slovenia, Chile, Peru, Spain, Romania, South Africa, Malaysia, Brazil, Guatemala, Venezuela, Germany, Singapore	2002-2003	yes	Primary and Secondary	UTI, SSTI, LRTI	Double blind RCT 3:1 to • Ertapenem OD or BID • Ceftriaxone OD or BID	403	3 m - 18 y	80

Arguedas, 2011 [8]	North America, Europe, Latin America	05/2003-05/2004	yes	Secondary	URTI	Double blind RCT 1:1 to • Azithromycin ER OD (1 day) • Amoxicillin/clavulanate BID (10 days)	902	3 - 48 m	56
Arrieta, 2003 [9]	US, Latin American	03/2001-03/2002	yes	Secondary	URTI	Double blind RCT 1:1 to • Azithromycin OD (3 days, high-dose) • Amoxicillin/clavulanate BID (10 days)	300	6 m-6 y	78
Balatsouras, 2005 [10]	Greece	(3 years)	no	Secondary	URTI	Open label RCT 1:1 to • Loracarbef BID (Low dose) • Loracarbef BID (High dose)	58	5 - 12 y	56
Baqui, 2015 [11]	Bangladesh	07/ 2009-06/2013	yes	Primary	Unspecified BI	Open label RCT 1:1:1 to • Procaine benzylpenicillin & gentamicin OD (7 days) • Gentamicin OD & Amoxicillin BID (7 days)	2,367	0 – 59 d	56
Baysoy, 2012 [12]	Turkey	10/2008-03/2010	no	Secondary	GII	Open label RCT 2:3 to • Amoxicillin & Clarithromycin & Lansoprazole (14 days) • Amoxicillin & Lansoprazole (5 days) + Clarithromycin & Ornidazole & Lansoprazole (5 days)	61	4 - 18 y	44
Begum, 2014 [13]	Bangladesh	01/2011-12/2011	no	Secondary	GII	Open label RCT 1:1 to • Azithromycin OD (7 days) • Cefixime BID (14 days)	60	children	33
Block, 2000 [14]	US	04/1992-08/1993	yes	Secondary	URTI	Double blind RCT 1:1:1 to • Cefdinir OD • Cefdinir BID	384	6 m - 12 y	89
Block, 2006 [15]	US	01/2005-05/2005	yes	Secondary	URTI	Double blind, phase 4 RCT 1:1 to • Cefdinir BID • Amoxicillin/Clavulanate BID (high dose)	318	6 m - 6 y	67
Boccazzi, 2000 [16]	Italy	11/1996-07/1998	no	Secondary	URTI	Open label RCT 1:1 to • Ceftibuten OD (5 days) • Azithromycin OD (3 days)	248	3 - 16 y	44

Bradley, 2007 [17]	Argentina, Brazil, Chile, Costa Rica, Mexico, Panama, and US	08/2002-06/2004	yes	Secondary	LRTI	Open label RCT 3:1 to • Levofloxacin BID • Comparator: - 6 months-5 years: Amoxicillin/ clavulanate BID or Ceftriaxone - 5-16 years: Clarithromycine or Ceftriaxone & erythromycin lactobionate q6h or clarithromycin BID	533	6 m - 16 y	78
Carapetis, 2001 [18]	Australia	03/1994-01/1997	no	Secondary	UTI	Open label RCT 1:1 to • Gentamicin OD • Gentamicin TID	179	1 m - 12 y	89
Cascio, 2001 [19]	Italy	06/1998-09/1998	no	Secondary	Unspecified BI	Open label RCT 1:1 to • Clarithromycin BID (7 days) • Chloramphenicol q6h (7 days)	51	0 - 14 y	56
Cascio, 2002 [20]	Italy	06/1999-09/2000	no	Secondary	Unspecified BI	Open label RCT 1:1 to • Clarithromycin BID (7 days) • Azithromycin OD (3 days)	87	0 - 14 y	78
Chanta, 2015 [21]	Thailand	06/2010-05/2013	no	Secondary	GII	Open label RCT 1:1 to • Azitromycin OD (3 days) • Comparator: - <8 years: IV chloramfenicol q6h; - > 8 years: Doxycycline BID (>5 days)	29	0 - 15 y	56
Chong, 2003 [22]	Singapore	01/2000-05/2001	no	Primary	UTI	Open label RCT 1:1 to • Gentamicin OD • Gentamicin TID	172	1 m - 13 y	78
Chotigeat, 2001 [23]	Thailand	08/1999-12/1999	no	Secondary	Unspecified BI	Open label RCT 1:1 to • Gentamicin BID • Gentamicin OD	54	Neonates	44
Cochereau, 2007 [24]	Guinea, Pakistan	01/2004-05/2004	yes	Secondary	Other BI	Double blind RCT 1:1:1 to • Azithromycin topical (2 days) • Azithromycin topical (3 days) • Azithromycin OD (3 days)	179	1 - 10 y	78
Cohen, 2001 [25]	France	11/1997-07/1998	yes	Secondary	URTI	Double blind RCT, 1:1:1 to • Azithromycin OD (3 days) • Azithromycin OD High dose (3 days)	499	2 - 12 y	67

Damrikarnler, 2000 [26]	Argentina, Brazil, Costa Rica, India, Kenya, Mexico, Morocco, Nigeria, Thailand, Turkey	08/1996-03/1998	yes	Secondary	URTI	Single blind RCT 1:1 to • Amoxycillin/clavulanate BID (7 or 10 days) • Amoxycillin/clavulanate TID (7 or 10 days)	415	2 m - 12 y	78
Demirjian, 2013 [27]	US	02/2011-01/2012	no	Secondary	Unspecified BI	Double blind RCT 1:1 to • Vancomycin loading dose + Vancomycin standard dose TID • Vancomicin standard dose TID	59	2 – 18 y	67
Deville, 2003 [28]	US, Mexico, South America	02/2001-12/2001	no	Primary	LRTI	Open label, phase 3 RCT 2:1 to • Linezolid TID • Vancomycin q6h or OD	62	0 - 12 y	78
English, 2004 [29]	Kenya	08/2000-02/2001	no	Secondary	Sepsis	Open label RCT 1:1 to • Gentamicin OD • Gentamicin MD (Multi-dose)	297	0 - 3 m	67
Eppes, 2002 [30]	US	1997–1999	no	Secondary	Other BI	Open label RCT 1:1:1 to • Cefuroxime axetil Low dose & Amoxicillin • Cefuroxime axetil High dose &Amoxicillin	42	6 m - 12 y	56
Esposito, 2002 [31]	Italy	11/1998-11/2000	yes	Secondary	URTI	Single blind RCT 1:1 to • Cefaclor BID (5 days) • Amoxicillin TID (10 days)	384	2 - 14 y	78
Ferwerda, 2001 [32]	The Netherlands	06/1995-12/1998	yes	Secondary	LRTI	Double blind RCT 1:1 to • Azithromycin OD (3 days) • Amoxicillin/clavulanate TID (10 days)	110	3 m - 12 y	89
Haczyński, 2003 [33]	Poland	nr	no	Secondary	URTI	Double blind RCT 1:1 to • Cefaclor BID (10 days) • Amoxicillin/clavulanate TID (10 days)	97	2 - 12 y	56
Jantaush, 2003 [34]	US, Mexico, South America	02/2001-12/2001	no	Secondary	LRTI, Sepsis	Open label, phase 3 RCT 2:1 to • Linezolid TID • Vancomycin q6h or OD	151	0 - 12 y	78
Kafetzis, 2000 [35]	Greece	nr	yes	Secondary	UTI	Open label RCT 2:1 to • Isepamicin BID (10–14 days) • Amikacin BID (10–14 days)	16	1 m - 12 y	67

Kafetzis, 2004 [36]	Greece	12/1999-04/2002	no	Secondary	URTI	Open label RCT 1:1:1 to • Penicillin V TID (10 days) • Clarithromycin BID (10 days)	265	3 - 14 y	67
Kaplan, 2003 [37]	US, Latin America	02/2001-12/2001	yes	Secondary	Unspecified BI	Open label RCT 2:1 to • Linezolid TID • Vancomycin q6h or OD	312	0 - 12 y	100
Khan, 2005 [38]	Bangladesh	nr	no	Secondary	LRTI, GII	Open label RCT 1:1 to • Gentamicin OD & Ceftriaxone OD • Gentamicin TID & Ceftriaxone OD	310	6 m - 5 y	67
Langley, 2004 [39]	Canada, US	1995-1998	yes	Secondary	URTI	Open label RCT 1:1 to • Azithromycin OD (5 days) • Erythromicyn TID (10 days)	477	6 m - 16 y	78
Lebel, 2001 [40]	Canada	07/1995-071998	yes	Secondary	URTI, LRTI	Single blind RCT 1:1 to • Clarithromycin BID (7 days) • Erythromicyn TID (14 days)	153	1 m - 16 y	89
Lee, 2008 [41]	Taiwan	nr	no	Secondary	LRTI	Open label RCT 1:1 to • Clarithromycin BID (10 days) • Erytromycin q6h (10 days)	99	0 - 15 y	78
Marild, 2009 [42]	Sweden	06/1996-02/2001	yes	Secondary	UTI	Open label RCT 2:1 to • Ceftibuten OD (10 days) • TMP-SMX BID (10 days)	461	1 m - 12 y	78
McCarty, 2000 [43]	US	11/1996-03/1997	no	Secondary	URTI	Double blind, phase 3 RCT 1:1 to • Clarithromycin BID (10 days) • Penicillin V TID	528	6 m - 12 y	78
Nizic, 2012 [44]	Slovenia	01/2004-12/2005	no	Secondary	Other BI	Open label RCT 1:1 to • Clarithromycin BID (14 days) • Amoxicillin TID (14 days)	130	0 - 15 y	89
Noel, 2008 [45]	Argentina, Brazil, Chile, Costa Rica, Panama, US	10/2002-05/2005	yes	Secondary	URTI	Double blind RCT 1:1 to • Levofloxacin BID (10 days) • Amoxicillin/Clavulanate BID (10 days)	1,607	6 m - 2 y	67
Pareek, 2008 [46]	India	11/2006-02/2008	yes	Secondary	LRTI	Open label RCT 1:1 to • Cefotazime-sulbactam TID (7 days) • Amoxicillin/clavulanic TID (7 Days)	102	3 m - 12 y	89

Perez, 2011 [47]	Costa Rica	04/2005-02/2006	no	Primary	GII	Double blind RCT 1:1 to • Amikacin TID & Clindamycin q6h • Amikacin OD & Clindamycin q6h	100	2 - 12 y	78
Pichichero, 2000 [48]	US, Canada	nr	no	Secondary	URTI	Double blind RCT A- 1:1:1 to • Cefdinir OD (10 days) • Cefdinir BID (10 days) • Penicillin V q6h (10 days) B- 1:1 to • Cefdinir BID (5 days) • Penicillin V q6h (10 days)	1,273	6 m - 12 y	67
Poachanukoon, 2008 [49]	Thailand	nr	no	Secondary	URTI	Double blind RCT 1:1 to • Cefditoren pivoxil BID (14 days) • Amoxicillin/Clavulanate BID (14 days)	138	1 – 15 y	89
Portier, 2001 [50]	France	06/1997-10/1998	no	Secondary	URTI	Open label RCT 1:1 to • Josamycin BID (5 days) • Penicillin TID (10 days)	324	3 - 12 y	56
Saez-Llorens, 2002 [51]	US, Latin America, Egypt, South Africa and Hungary	04/1998-07/1999	no	Secondary	CNS infection	Open label RCT 1:1 to • Alatrofloxacin BID • Ceftriaxone OD +/- Vancomycin q6h	162	3 m - 12 y	78
Sakata, 2008 [52]	Japan	06/2006-02/2007	no	Secondary	URTI	Open label RCT 1:1:1 to • Cefcapene–pivoxil TID (5 or 10 days) • Amoxicillin TID (10 days)	236	6 m - 13 y	44
Shahid, 2008 [53]	Malaysia	04/2004-08/2005	no	Secondary	LRTI	Open label RCT 1:1 to • Cefepime BID • Ceftazidime TID	30	0 – 12 m	33
Sher, 2005 [54]	Costa Rica, US	03/2001-06/2002	no	Secondary	URTI	Double blind RCT 1:1 to • Gatifloxacin OD (10 days) • Amoxicillin/Clavulanate BID (10 days)	349	6 m - 7 y	44
Tiwari, 2009 [55]	India	05/2005-03/2006	no	Secondary	Unspecified BI	Open label RCT 1:1 to • Gentamicin OD • Gentamicin BID or TID	400	0 - 12 y	56

Uijtendaal, 2001 [56]	The Netherlands	nr	no	Primary	Unspecified BI	Open label RCT 1:1 to • Gentamicin OD • Gentamicin multiple daily	40	1 m - 16 y	78
Vasquez-Mendoza, 2007 [57]	Mexico	10/2001-08/2003	no	Primary	Neonatal Sepsis	Double blind RCT 1:1 to • Amikacin OD & Ampicillin • Amikacin BID & Ampicillin	120	0 - 28 d	100
Wang, 2003 [58]	Taiwan	02/2000-04/2002	no	Secondary	URTI	Open label RCT 1:1 to • Amikacin OD • Amikacin BID	109	3 m- 6 y	67
Wible, 2003 [59]	US, Canada, Mexico, Argentina, Brazil, Chile and Peru.	06/2000-02/2001	yes	Secondary	SSTI	Double blind RCT 1:1 to • Linezolid BID • Cefadroxil BID	494	5 - 17 y	78
Yellin, 2007 [60]	US, Mexico, Brazil	03/2002-01/2004	no	Primary	GII, other BI	Open label RCT 3:1 to • Ertapenem BID • Ticarcillin/clavulanate q6h or q4h	105	2 - 17 y	78
Yogev, 2003 [61]	US, Mexico, South America	02/2001-12/2001	no	Secondary	SSTI	Open label RCT 2:1 to • Linezolid BID • Vancomycin q6h or OD	119	0 - 12 y	78
Zimbasa Dysentery Study Group, 2002 [62]	Zimbabwe, South Africa, Bangladesh	05/1996-06/2000	yes	Secondary	GII	Double blind RCT 1:1 to • Ciprofloxacin BID (3 days) + placebo • Ciprofloxacin BID (5 days)	252	12 m - 11 y	67
NCT01400867 [63]	US, Argentina, Chile, Georgia, Latvia, Lithuania, Poland, Romania, South Africa, Spain	12/2011-07/2014	yes	Primary	Other BI	Single blind, phase 2, phase 3 RCT • Ceftaroline fosamil • Vancomycin +/- Aztreonam or Cefazolin +/- Aztreonam • Cephalexin or Clindamycin or Linezolid	163	2 m - 17 y	na
NCT01530763 [64]	US, Argentina, Bulgaria, Georgia, Greece, Hungary, Poland, Spain, Ukraine	09/2012-07/2014	yes	Primary	Other BI, LRTI	Single blind, phase 2, phase 3 RCT • Ceftaroline fosamil • Amoxicillin/clavulanate	161	2 m - 18 y	na
NCT01551394 [65]	Italy, Spain, Greece, Lithuania, Estonia	09/2012-12/2014	yes	Secondary	Sepsis	Open label RCT to • Meropenem (11±3 days) • Ampicillin/Gentamicin or Cefotaxime/Gentamicin	272	0 - 90 d	na

NCT01669980 [66]	US, Argentina, Georgia, Ukraine	10/2012-08/2014	yes	Primary	Other BI, LRTI	Single blind, phase 4 RCT • Ceftaroline fosamil • Ceftriaxone & Vancomycin	40	2 m - 18 y	na
NCT01707485 [67]	Canada	11/2012-05/2014	no	Secondary	LRTI	Double blind, phase 4 RCT • Amoxicillin TID (5 days) • Amoxicillin TID (10 days)	60	1 - 10 y	na
NCT01728376 [68]	Argentina, Australia, Brazil, Chile, Colombia, Greece, Guatemala, Hungary, Israel, Italy, Malaysia, Panama, Romania, Spain, Taiwan, Thailand, Ukraine, US	11/2012-01/2016	yes	Primary	Sepsis	Open label, phase 4 RCT • Daptomycin OD • SOC: Vancomycin, Semi-synthetic penicillin, First-generation cephalosporins, Clindamycin	82	1 - 17 y	na
NCT01922011 [69]	Argentina, Australia, Brazil, Bulgaria, Chile, Colombia, Estonia, France, Georgia, Germany, Greece, Guatemala, Hungary, Israel, Italy, Korea, Republic of, Latvia, Malaysia, Moldova, Republic of, New Zealand, Panama, Peru, Romania, Russian Federation, Serbia, South Africa, Spain, Turkey, Ukraine, UK, US	09/2013-ongoing	yes	Secondary	Other BI	Double blind RCT to • Daptomycin OD • Vancomycin q6h, or nafcillin q6h	144	1 - 17 y	na
NCT01994993 [70]	US, Canada	12/2013-ongoing	no	Secondary	GII	Double blind RCT to • Ampicillin & Metronidazole & Gentamicin • Ampicillin & Gentamicin & Clindamycin • Gentamicin and Piperacillin- tazobactam • Standard of care antibiotics and Metronidazole • Metronidazole & clindamycin or peracillin-tazobactam	284	0 - 120 d	na
NCT02258763 [71]	Malaysia	09/2014-ongoing	no	Secondary	LRTI	Double blind, phase 4 RCT • Amoxicillin/Clavulanate BID (10 days) • Amoxicillin/Clavulanate BID (3 days)	300	3 - 59 m	na

NCT02276482 [72]	US, Argentina, Bulgaria, Chile, Czech Republic, Georgia, Germany, Latvia, Lithuania, Panama, Poland, Slovenia, South Africa, Spain	03/2015-ongoing	yes	Primary	SSTI	Single blind, RCT to • Tedizolid Phophate (6 days) • Antibiotic comparator	162	12 - 17 y	na
NCT02334124 [73]	Australia	01/2015-ongoing	no	Primary and Secondary	SSTI	Single blind, RCT to • Ceftriaxone • Flucloxacillin	188	6 m - 18 y	na
NCT02380352 [74]	Canada	03/2016-ongoing	no	Secondary	LRTI	Double blind RCT • Amoxicillin TID (5 days) • Amoxicillin TID (10 days)	270	6 m - 10 y	na
NCT02475733 [75]	Argentina, Chile, Czech Republic, Greece, Hungary, Poland, Romania, Russia, Spain, Taiwan, Turkey, US	05/2015-ongoing	yes	Primary	GII	Single blind, phase 2 RCT 3:1 to • Ceftazidime -avibactam TID & metronidazole TID • Meropenem TID	102	3 m - 18 y	na
NCT02497781 [76]	Czech Republic, Greece, Hungary, Poland, Romania, Russia, South Korea, Taiwan, Turkey, US	06/2015-ongoing	yes	Primary	UTI	Single blind, phase 2 RCT 3:1 to • Ceftazidime-avibactam TID • Cefepime	102	3 m - 18 y	na
NCT02503761 [77]	Egypt	06/2015-ongoing	no	Secondary	Neonatal Sepsis	Open label, phase 3 RCT • Meropenem TID (infused over 4 hours) • Meropenem TID (infused over 30 minutes)	100	0 - 28 d	na
NCT02554383 [78]	US	02/2016-ongoing	no	Secondary	URTI	Double blind, placebo controlled RCT to • Amoxicillin-clavulanate (10 days) • Placebo	688	2 - 11 y	na
NCT02605122 [79]	US, Hungary	11/2015-ongoing	yes	Primary	LRTI	Open label, phase 2, phase 3 RCT • Solithromycin • SOC (intravenous ceftriaxone, ampicillin, and amoxicillin and oral amoxicillin and amoxicillin-clavulanic acid)	400	2 m - 17 y	na

NCT02635191 [80]	China	03/2014-ongoing	no	Secondary	GII	Open label RCT to • Proton Pump Inhibitor & two antibiotics (Amoxicillin BID, Clarithromycin BID, Metronidazole BID) • Omeprazole BID & Amoxicillin BID & Clarithromycin BID	200	4 - 18 y	na
NCT02783859 [81]	Australia, Malaysia	06/2016-ongoing	no	Secondary	LRTI	Double blind, placebo controlled RCT to • Amoxicillin-clavulanic Acid BID (8 days) • Placebo	314	3 m - 5 y	na
NCT02790996 [82]	UK, Estonia, Italy, Spain, Greece	05/2016-ongoing (Not yet recruiting)	no	Secondary	Sepsis	Open label RCT to • Vancomycin (Optimised Regimen) • Vancomycin (Standard Regimen)	300	0 - 90 d	na
NCT02795793 [83]	Australia	05/2016-ongoing (Not yet recruiting)	no	Secondary	GII	Open label, RCT to • Piperacillin tazobactam TID • Appendectomy	226	5 - 16 y	na

[a]proportion of items of the CONSORT 2004 on safety quality reporting [Ref] checklist that were adequately reported. UTI: Urinary tract infections, LRTI: Low Respiratory Tract Infection, URTI: Upper Respiratory Tract Infection, SSTI: Skin and Soft Tissue Infection, GI: Gastrointestinal Infection, BI: Bacterial Infection, na: not applicable

eTable 2 Patients distribution per drug class in included trials

Drug class	Number of patients (%) [N = 27,693]	Number of trials (%) [N = 83]
Penicillins	11,408 (41.2)	23 (27.7)
Aminoglycosides	9,852 (35.6)	15 (18.1)
Cephalosporins	4,014 (14.5)	25 (30.1)
Penicillins and β-lactamase inhibitor	3,617 (13.1)	18 (21.7)
Macrolides	3,292 (11.9)	21 (25.3)
Fluoroquinolones	1,920 (6.9)	5 (6.0)
Lincosamides	1,429 (5.2)	3 (3.6)
Oxazolidinone	764 (2.8)	6 (7.2)
Carbapenems	646 (2.3)	5 (6.0)
Glycopeptides	585 (2.1)	7 (8.4)
Sulfonamides and trimethoprim	152 (0.5)	1 (1.2)
Imidazole derivates	133 (0.5)	2 (2.4)
Lipopeptides	113 (0.4)	2 (2.4)
Cephalosporins and β-lactamase inhibitor	50 (0.2)	1 (1.2)
Amphenicols	25 (0.1)	1 (1.2)

eTable 3 Overall and specific reported Adverse Events (AEs) per drug class

Drug class	N patients	Overall AEs	Sum of specific AEs	Discontinuation due to AEs (11,566)*	Systemic[a]	Nephro toxicity (2,223)*	Oto toxicity (1,576)*	Gastro Intestinal	Neurological	Respiratory	Dermatologic	Muscolo-skeletal	Infusional	Laboratory (5,064)*
Penicillins	3,019	333	205	49	7	3	0	145	6	0	22	0	6	16
Aminoglycosides	1,308	129	90	nr	0	75	6	0	9	0	0	0	0	0
Cephalosporins	2,462	507	470	53	10	0	0	316	11	56	52	0	6	19
Macrolides	2,931	802	640	34	34	0	0	511	0	3	79	0	0	13
Penicillins + β-lactamase inhib	2,566	1,394	1325	50	84	0	4	758	0	175	281	22	1	0
Fluoroquinolones	1,920	1,304	916	44	89	0	0	388	0	202	119	56	0	62
Carbapenems	385	122	111	6	0	0	0	27	0	0	0	0	42	42
Linezolid	683	398	357	10	9	0	0	81	20	25	9	0	2	215
Glycopeptides	265	192	181	8	48	5	0	23	1	0	21	0	0	84
Sulfonamides + trimethoprim	152	7	7	4	2	0	0	4	0	0	1	0	0	0
Amphenicols	25	1	1	0	0	0	0	1	0	0	0	0	0	0
Total	**15,716**	**5,189**	**4,308**	**258**	**283**	**83**	**10**	**2,254**	**47**	**461**	**584**	**78**	**57**	**451**

***Population in which this parameter was evaluated; [a]including fever, anaphylaxis and Red Man Syndrome. Patients on combination of Aminoglycosides/Penicillin were included in Aminoglycosides only when class specific AEs (Nephrotoxicity and Ototoxicity) were reported.**

References

1. Abdel-Hady E, Hamamsy M, Hedaya M, Awad H. The efficacy and toxicity of two dosing-regimens of amikacin in neonates with sepsis. J Clin Pharm Ther 2011; 36(1):45-52.

2. Adler M, McDonald PJ, Trostmann U, Keyserling C, Tack K. Cefdinir vs. amoxicillin/clavulanic acid in the treatment of suppurative acute otitis media in children. Pediatr Infect Dis J 2000; 19(12 Suppl): S166-70.

3. African Neonatal Sepsis Trial group, Tshefu A, Lokangaka A, et al. Oral amoxicillin compared with injectable procaine benzylpenicillin plus gentamicin for treatment of neonates and young infants with fast breathing when referral is not possible: a randomised, open-label, equivalence trial. Lancet 2015; 385(9979): 1758-66.

4. African Neonatal Sepsis Trial group, Tshefu A, Lokangaka A, et al. Simplified antibiotic regimens compared with injectable procaine benzylpenicillin plus gentamicin for treatment of neonates and young infants with clinical signs of possible serious bacterial infection when referral is not possible: a randomised, open-label, equivalence trial. Lancet 2015; 385(9979): 1767-76.

5. Aguilar A, Tinoco JC, Macias M, et al. Clinical and bacteriologic efficacy of amoxycillin b.d. (45 mg/kg/day) versus amoxycillin t.d.s (40 mg/kg/day) in children with group A beta-hemolytic streptococcal tonsillopharyngitis. J Chemother 2000; 12(5): 396-405.

6. Arguedas A, Emparanza P, Schwartz RH, et al. A randomized, multicenter, double blind, double dummy trial of single dose azithromycin versus high dose amoxicillin for treatment of uncomplicated acute otitis media. Pediatr Infect Dis J 2005; 24(2): 153-61.

7. Arguedas A, Cespedes J, Botet FA, et al. Safety and tolerability of ertapenem versus ceftriaxone in a double-blind study performed in children with complicated urinary tract infection, community-acquired pneumonia or skin and soft-tissue infection. Int J Antimicrob Agents 2009; 33(2): 163-7.

8. Arguedas A, Soley C, Kamicker BJ, Jorgensen DM. Single-dose extended-release azithromycin versus a 10-day regimen of amoxicillin/clavulanate for the treatment of children with acute otitis media. Int J Infect Dis 2011; 15(4): e240-8.

9. Arrieta A, Arguedas A, Fernandez P, et al. High-dose azithromycin versus high-dose amoxicillin-clavulanate for treatment of children with recurrent or persistent acute otitis media. Antimicrob Agents Chemother 2003; 47(10): 3179-86.

10. Balatsouras DG, Korres S, Rallis E, Eliopoulos P, Ferekidis E. Twice-daily dosing of loracarbef 15 mg/kg versus 30 mg/kg in the treatment of children with acute sinusitis. Drugs Exp Clin Res 2005; 31 Suppl: 1-5.

11. Baqui AH, Saha SK, Ahmed AS, et al. Safety and efficacy of alternative antibiotic regimens compared with 7 day injectable procaine benzylpenicillin and gentamicin for outpatient treatment of neonates and young infants with clinical signs of severe infection when referral is not possible: a randomised, open-label, equivalence trial. Lancet Glob Health 2015; 3(5): e279-87.

12. Baysoy G, Saltik Temizel IN, Uslu N, et al. Ornidazole-based sequential therapy is not effective in Helicobacter pylori eradication in children. Turk J Gastroenterol 2013; 24(5): 382-6.

13. Begum B, Haque MA, Ahmed MS, et al. Comparison between azithromycin and cefixime in the treatment of typhoid fever in children. Mymensingh Med J 2014; 23(3): 441-8.

14. Block SL, McCarty JM, Hedrick JA, et al. Comparative safety and efficacy of cefdinir vs amoxicillin/clavulanate for treatment of suppurative acute otitis media in children. Pediatr Infect Dis J 2000; 19(12 Suppl): S159-65.

15. Block SL, Schmier JK, Notario GF, et al. Efficacy, tolerability, and parent reported outcomes for cefdinir vs. high-dose amoxicillin/clavulanate oral suspension for acute otitis media in young children. Curr Med Res Opin 2006; 22(9): 1839-47.

16. Boccazzi A, Tonelli P, De'Angelis M, Bellussi L, Passali D, Careddu P. Short course therapy with cefitbuten versus azithromycin in pediatric streptococcal pharyngitis. Pediatr Infect Dis J 2000; 19(10): 963-7.

17. Bradley JS, Arguedas A, Blumer JL, Saez-Llorens X, Melkote R, Noel GJ. Comparative study of levofloxacin in the treatment of children with community-acquired pneumonia. Pediatr Infect Dis J 2007; 26(10): 868-78.

18. Carapetis JR, Jaquiery AL, Buttery JP, et al. Randomized, controlled trial comparing once daily and three times daily gentamicin in children with urinary tract infections. Pediatr Infect Dis J 2001; 20(3): 240-6.

19. Cascio A, Colomba C, Di Rosa D, Salsa L, di Martino L, Titone L. Efficacy and safety of clarithromycin as treatment for Mediterranean spotted fever in children: a randomized controlled trial. Clin Infect Dis 2001; 33(3): 409-11.

20. Cascio A, Colomba C, Antinori S, Paterson DL, Titone L. Clarithromycin versus azithromycin in the treatment of Mediterranean spotted fever in children: a randomized controlled trial. Clin Infect Dis 2002; 34(2): 154-8.

21. Chanta C, Phloenchaiwanit P. Randomized Controlled Trial of Azithromycin versus Doxycycline or Chloramphenicol for Treatment of Uncomplicated Pediatric Scrub Typhus. J Med Assoc Thai 2015; 98(8): 756-60.

22. Chong CY, Tan AS, Ng W, Tan-Kendrick A, Balakrishnan A, Chao SM. Treatment of urinary tract infection with gentamicin once or three times daily. Acta Paediatr 2003; 92(3): 291-6.

23. Chotigeat U, Narongsanti A, Ayudhya DP. Gentamicin in neonatal infection: once versus twice daily dosage. J Med Assoc Thai 2001; 84(8): 1109-15.

24. Cochereau I, Goldschmidt P, Goepogui A, et al. Efficacy and safety of short duration azithromycin eye drops versus azithromycin single oral dose for the treatment of trachoma in children: a randomised, controlled, double-masked clinical trial. Br J Ophthalmol 2007; 91(5): 667-72.

25. Cohen R, Reinert P, De La Rocque F, et al. Comparison of two dosages of azithromycin for three days versus penicillin V for ten days in acute group A streptococcal tonsillopharyngitis. Pediatr Infect Dis J 2002; 21(4): 297-303.

26. Damrikarnlert L, Jauregui AC, Kzadri M. Efficacy and safety of amoxycillin/clavulanate (Augmentin) twice daily versus three times daily in the treatment of acute otitis media in children. The Augmentin 454 Study Group. J Chemother 2000; 12(1): 79-87.

27. Demirjian A, Finkelstein Y, Nava-Ocampo A, et al. A randomized controlled trial of a vancomycin loading dose in children. Pediatr Infect Dis J 2013; 32(11): 1217-23.

28. Deville JG, Adler S, Azimi PH, et al. Linezolid versus vancomycin in the treatment of known or suspected resistant gram-positive infections in neonates. Pediatr Infect Dis J 2003; 22(9 Suppl): S158-63.

29. English M, Mohammed S, Ross A, et al. A randomised, controlled trial of once daily and multi-dose daily gentamicin in young Kenyan infants. Arch Dis Child 2004; 89(7): 665-9.

30. Eppes SC, Childs JA. Comparative study of cefuroxime axetil versus amoxicillin in children with early Lyme disease. Pediatrics 2002; 109(6): 1173-7.

31. Esposito S, Marchisio P, Bosis S, et al. Comparative efficacy and safety of 5-day cefaclor and 10-day amoxycillin treatment of group A streptococcal pharyngitis in children. Int J Antimicrob Agents 2002; 20(1): 28-33.

32. Ferwerda A, Moll HA, Hop WC, et al. Efficacy, safety and tolerability of 3 day azithromycin versus 10 day co-amoxiclav in the treatment of children with acute lower respiratory tract infections. J Antimicrob Chemother 2001; 47(4): 441-6.

33. Haczynski J, Chmielik M, Bien S, et al. A comparative study of cefaclor vs amoxicillin/clavulanate in pediatric pharyngotonsillitis. Med Sci Monit 2003; 9(3): PI29-35.

34. Jantausch BA, Deville J, Adler S, et al. Linezolid for the treatment of children with bacteremia or nosocomial pneumonia caused by resistant gram-positive bacterial pathogens. Pediatr Infect Dis J 2003; 22(9 Suppl): S164-71.

35. Kafetzis DA, Maltezou HC, Mavrikou M, et al. Isepamicin versus amikacin for the treatment of acute pyelonephritis in children. Int J Antimicrob Agents 2000; 14(1): 51-5.

36. Kafetzis DA, Liapi G, Tsolia M, et al. Failure to eradicate Group A beta-haemolytic streptococci (GABHS) from the upper respiratory tract after antibiotic treatment. Int J Antimicrob Agents 2004; 23(1): 67-71.

37. Kaplan SL, Deville JG, Yogev R, et al. Linezolid versus vancomycin for treatment of resistant Gram-positive infections in children. Pediatr Infect Dis J 2003; 22(8): 677-86.

38. Khan AM, Ahmed T, Alam NH, Chowdhury AK, Fuchs GJ. Extended-interval gentamicin administration in malnourished children. . J Trop Pediatr 2006; 52(3): 179-84.

39. Langley JM, Halperin SA, Boucher FD, Smith B, Pediatric Investigators Collaborative Network on Infections in C. Azithromycin is as effective as and better tolerated than erythromycin estolate for the treatment of pertussis. Pediatrics 2004; 114(1): e96-101.

40. Lebel MH, Mehra S. Efficacy and safety of clarithromycin versus erythromycin for the treatment of pertussis: a prospective, randomized, single blind trial. Pediatr Infect Dis J 2001; 20(12): 1149-54.

41. Lee PI, Wu MH, Huang LM, Chen JM, Lee CY. An open, randomized, comparative study of clarithromycin and erythromycin in the treatment of children with community-acquired pneumonia. J Microbiol Immunol Infect 2008; 41(1): 54-61.

42. Marild S, Jodal U, Sandberg T. Ceftibuten versus trimethoprim-sulfamethoxazole for oral treatment of febrile urinary tract infection in children. Pediatr Nephrol 2009; 24(3): 521-6.

43. McCarty J, Hedrick JA, Gooch WM. Clarithromycin suspension vs penicillin V suspension in children with streptococcal pharyngitis. Adv Ther 2000; 17(1): 14-26.

44. Nizic T, Velikanje E, Ruzic-Sabljic E, Arnez M. Solitary erythema migrans in children: comparison of treatment with clarithromycin and amoxicillin. Wien Klin Wochenschr 2012; 124(13-14): 427-33.

45. Noel GJ, Blumer JL, Pichichero ME, et al. A randomized comparative study of levofloxacin versus amoxicillin/clavulanate for treatment of infants and young children with recurrent or persistent acute otitis media. Pediatr Infect Dis J 2008; 27(6): 483-9.

46. Pareek A, Kulkarni M, Daga S, Deshpande A, Chandurkar N. Comparative evaluation of efficacy and safety of cefotaxime-sulbactam with amoxicillin-clavulanic acid in children with lower respiratory tract infections. Expert Opin Pharmacother 2008; 9(16): 2751-7.

47. Perez V, Saenz D, Madriz J, et al. A double-blind study of the efficacy and safety of multiple daily doses of amikacin versus one daily dose for children with perforated appendicitis in Costa Rica. Int J Infect Dis 2011; 15(8): e569-75.

48. Pichichero ME, Gooch WM, 3rd. Comparison of cefdinir and penicillin V in the treatment of pediatric streptococcal tonsillopharyngitis. Pediatr Infect Dis J 2000; 19(12 Suppl): S171-3.

49. Poachanukoon O, Kitcharoensakkul M. Efficacy of cefditoren pivoxil and amoxicillin/clavulanate in the treatment of pediatric patients with acute bacterial rhinosinusitis in Thailand: a randomized, investigator-blinded, controlled trial. Clin Ther 2008; 30(10): 1870-9.

50. Portier H, Bourrillon A, Lucht F, et al. [Treatment of acute group A beta-hemolytic streptococcal tonsillitis in children with a 5-day course of josamycin]. Arch Pediatr 2001; 8(7): 700-6.

51. Saez-Llorens X, McCoig C, Feris JM, et al. Quinolone treatment for pediatric bacterial meningitis: a comparative study of trovafloxacin and ceftriaxone with or without vancomycin. Pediatr Infect Dis J 2002; 21(1): 14-22.

52. Sakata H. Comparative study of 5-day cefcapene-pivoxil and 10-day amoxicillin or cefcapene-pivoxil for treatment of group A streptococcal pharyngitis in children. J Infect Chemother 2008; 14(3): 208-12.

53. Shahid SK. Efficacy and safety of cefepime in late-onset ventilator-associated pneumonia in infants: a pilot randomized and controlled study. Ann Trop Med Parasitol 2008; 102(1): 63-71.

54. Sher L, Arguedas A, Husseman M, et al. Randomized, investigator-blinded, multicenter, comparative study of gatifloxacin versus amoxicillin/clavulanate in recurrent otitis media and acute otitis media treatment failure in children. Pediatr Infect Dis J 2005; 24(4): 301-8.

55. Tiwari S, Rehan HS, Chandra J, Mathur NN, Singh V. Efficacy and safety of a single daily dose of gentamicin in hospitalized Indian children: a quasi-randomized trial. J Antimicrob Chemother 2009; 64(5): 1096-101.

56. Uijtendaal EV, Rademaker CM, Schobben AF, et al. Once-daily versus multiple-daily gentamicin in infants and children. Ther Drug Monit 2001; 23(5): 506-13.

57. Guadalupe Vásquez-Mendoza M, Vargas-Origel A, Carmen Ramos-Jiménez A, Aguilar-Orozco G, Romero-Gutiérrez G. Efficacy and renal toxicity of one daily dose of amikacin versus conventional dosage regime. Am J Perinatol 2007; 24(2): 141-6

58. Wang CY, Lu CY, Hsieh YC, Lee CY, Huang LM. Intramuscular ceftriaxone in comparison with oral amoxicillin-clavulanate for the treatment of acute otitis media in infants and children. J Microbiol Immunol Infect 2004; 37(1): 57-62.

59. Wible K, Tregnaghi M, Bruss J, Fleishaker D, Naberhuis-Stehouwer S, Hilty M. Linezolid versus cefadroxil in the treatment of skin and skin structure infections in children. Pediatr Infect Dis J 2003; 22(4): 315-23.

60. Yellin AE, Johnson J, Higareda I, et al. Ertapenem or ticarcillin/clavulanate for the treatment of intra-abdominal infections or acute pelvic infections in pediatric patients. Am J Surg 2007; 194(3): 367-74.

61. Yogev R, Patterson LE, Kaplan SL, et al. Linezolid for the treatment of complicated skin and skin structure infections in children. Pediatr Infect Dis J 2003; 22(9 Suppl): S172-7.

62. Zimbabwe BSADSG. Multicenter, randomized, double blind clinical trial of short course versus standard course oral ciprofloxacin for Shigella dysenteriae type 1 dysentery in children. Pediatr Infect Dis J 2002; 21(12): 1136-41.

63. Safety and Efficacy Study of Ceftaroline Versus a Comparator in Pediatric Subjects With Complicated Skin Infections. ClinicalTrials.gov Identifier: NCT01400867. https://clinicaltrials.gov/ct2/show/NCT01400867?term=NCT01400867&rank=1. Accessed Jan 20, 2017

64. Safety and Efficacy Study of Ceftaroline Versus a Comparator in Pediatric Subjects With Community Acquired Bacterial Pneumonia (CABP). ClinicalTrials.gov Identifier: NCT01530763. https://clinicaltrials.gov/ct2/show/NCT01530763?term=NCT01530763&rank=1. Accessed Jan 20, 2017

65. Efficacy, Pharmacokinetics and Safety of Meropenem in Infants Below 90 Days With Clinical or Confirmed Late-onset Sepsis (NeoMero-1). ClinicalTrials.gov Identifier: NCT01551394. https://clinicaltrials.gov/ct2/show/NCT01551394?term=NCT01551394&rank=1. Accessed Jan 20, 2017

66. Safety and Efficacy Study of Ceftaroline Versus a Comparator in Pediatric Subjects With Complicated Community Acquired Pneumonia (CABP). ClinicalTrials.gov Identifier: NCT01669980. https://clinicaltrials.gov/ct2/show/NCT01669980?term=nCT01669980&rank=1. Accessed Jan 20, 2017

67. Duration of Antimicrobial Therapy for Paediatric Pneumonia. ClinicalTrials.gov Identifier: NCT01707485. https://clinicaltrials.gov/ct2/show/NCT01707485?term=NCT01707485&rank=1. Accessed Jan 20, 2017

68. Comparative Evaluation of the Safety & Efficacy of Daptomycin Versus SOC in 1 - 17 Year Olds With Staphylococcus Aureus Bacteremia (MK-3009-005). ClinicalTrials.gov Identifier: NCT01728376. https://clinicaltrials.gov/ct2/show/NCT01728376?term=NCT01728376&rank=1. Accessed Jan 20, 2017

69. Safety and Efficacy Study of Daptomycin Compared to Active Comparator in Pediatric Participants With Acute Hematogenous Osteomyelitis (AHO) (MK-3009-006). ClinicalTrials.gov Identifier: NCT01922011. https://clinicaltrials.gov/ct2/show/NCT01922011?term=NCT01922011&rank=1. Accessed Jan 20, 2017

70. Antibiotic Safety (SCAMP). ClinicalTrials.gov Identifier: NCT01994993. https://clinicaltrials.gov/ct2/show/NCT01994993?term=NCT01994993&rank=1. Accessed Jan 20, 2017

71. Trial on the Ideal Duration of Oral Antibiotics in Children With Pneumonia. ClinicalTrials.gov Identifier: NCT02258763. https://clinicaltrials.gov/ct2/show/NCT02258763?term=NCT02258763&rank=1. Accessed Jan 20, 2017

72. Study of Tedizolid Phosphate in Adolescents With Complicated Skin and Soft Tissue Infection (cSSTI) (MK-1986-012). ClinicalTrials.gov Identifier: NCT02276482. https://clinicaltrials.gov/ct2/show/NCT02276482?term=NCT02276482&rank=1. Accessed Jan 20, 2017

73. Comparing the Intravenous Treatment of Skin Infections in Children, Home Versus Hospital (CHOICE). ClinicalTrials.gov Identifier: NCT02334124. https://clinicaltrials.gov/ct2/show/NCT02334124?term=NCT02334124&rank=1. Accessed Jan 20, 2017

74. Short-course Antimicrobial Therapy for Paediatric Respiratory Infections (SAFER). ClinicalTrials.gov Identifier: NCT02380352. https://clinicaltrials.gov/ct2/show/NCT02380352?term=NCT02380352&rank=1. Accessed Jan 20, 2017

75. Evaluation of Safety, Pharmacokinetics and Efficacy of CAZ-AVI With Metronidazole in Childern Aged 3 Months to 18 Years Old With Complicated Intra-abdominal Infections (cIAIs). ClinicalTrials.gov Identifier: NCT02475733. https://clinicaltrials.gov/ct2/show/NCT02475733?term=NCT02475733&rank=1. Accessed Jan 20, 2017

76. Evaluation of Safety, Pharmacokinetics and Efficacy of Ceftazidime and Avibactam (CAZ-AVI) Compared With Cefepime in Children From 3 Months to Less Than 18 Years of Age With Complicated Urinary Tract Infections (cUTIs). ClinicalTrials.gov Identifier: NCT02497781 https://clinicaltrials.gov/ct2/show/NCT02497781?term=NCT02497781&rank=1. Accessed Jan 20, 2017

77. Bolus Versus Prolonged Infusion of Meropenem in Newborn With Late Onset Sepsis (BVPIMNBLOS). ClinicalTrials.gov Identifier: NCT02503761. https://clinicaltrials.gov/ct2/show/NCT02503761?term=NCT02503761&rank=1. Accessed Jan 20, 2017

78. Efficacy of Antibiotics in Children With Acute Sinusitis: Which Subgroups Benefit? ClinicalTrials.gov Identifier: NCT02554383. Accessed Jan 20, 2017

79. Safety and Efficacy of Solithromycin in Adolescents and Children With Community-acquired Bacterial Pneumonia. ClinicalTrials.gov Identifier: NCT02605122. https://clinicaltrials.gov/ct2/show/NCT02605122?term=NCT02605122&rank=1. Accessed Jan 20, 2017

80. Tailored Therapy for Helicobacter Pylori in Children. ClinicalTrials.gov Identifier: NCT02635191. https://clinicaltrials.gov/ct2/show/NCT02635191?term=NCT02635191&rank=1. Accessed Jan 20, 2017

81. Hospitalised Pneumonia With Extended Treatment (HOPE) Study (HOPE). ClinicalTrials.gov Identifier: NCT02783859. https://clinicaltrials.gov/ct2/show/NCT02783859?term=NCT02783859&rank=1. Accessed Jan 20, 2017

82. Neonatal Vancomycin Trial (NeoVanc). ClinicalTrials.gov Identifier: NCT02790996. https://clinicaltrials.gov/ct2/show/NCT02790996?term=NCT02790996&rank=1. Accessed Jan 20, 2017

83. Non-operative Management for Appendicitis in Children (APRES). ClinicalTrials.gov Identifier: NCT02795793. https://clinicaltrials.gov/ct2/show/NCT02795793?term=NCT02795793&rank=1. Accessed Jan 20, 2017