

New antibiotics clinical research

The data provided for this analysis have been retrieved from the National Observatory on Clinical Trials on Medicine (OsSC), managed and coordinated by the Italian Drug Agency (Office of Clinical Trials). Data given are of the trials approved by the Ethics Committee, during the period 1 January to 31 December 2007.

The drugs examined, in the field of general antimicrobials for systemic use (ATC J), are the antibacterial and the antimycotics (2nd level ATC, J01 and J02), exclusively present in the “experimental” branch of the studies analysed, either as a single drug, or in combination with others.

The results of the analysis show that during the mentioned period, 165 trials were recorded mainly regarding antibacterial / antimycotics (81.8%). The number of studies made for antibacterial/antimycotics was about 18.2%. The studies were principally made on the following molecules, levofloxacin, linezolid, amoxicillin and enzymatic inhibitors for the J01 class, caspofungin and amfotericina for the J02 class.

Over half of the studies were Phase III (58.8%) that is, the studies preceding registration, while Phase II and Phase IV (post-marketing) studies were at 21.8% and 13.3% respectively. Phase I and the Bioequivalence / Bioavailability phase studies were both at 3.0%.

The multicentric trials that represent 79.9% of all studies were for the greater part internationally performed (62.3%). The monocentric typology was present in 20.1% of the studies. This signifies that Italian research in this field was closely integrated with that of international research.

The research on antibacterial and antimycotics was supported (77.0%) principally by profit making organisations (drug companies). The residual 23.0%, were independent organisations not industrialists, specifically research hospitals and general hospitals.

The main areas of therapeutic study included immunology and infective diseases (32.7%), followed by respiratory diseases (24.2%).

The number of experimental centres, with reference to their distribution among the regions included Lombardia as the principal region, followed by Lazio, Toscana, Veneto and Liguria.

The experimentation took place at 300 centres among which *Policlinico S. Matteo* Institute of Pavia, the mostly frequently involved as a coordinating centre or satellite unit. Other centres include *Policlinico Universitario Gemelli* of Rome, *S. Martino* the university hospital of Genova, *Pisana* university hospital of Pisa and *S. Orsola Malpigli* polyclinic university hospital of Bologna.

Details of the analysis performed are available in the following tables.

Trials per year*

Total trials: 165

Year	No. Trials	%
2000	29	17,6
2001	22	13,3
2002	8	4,8
2003	25	15,2
2004	17	10,3
2005	16	9,7
2006	27	16,4
2007	21	12,7
Total	165	100,0

* Indicates the year of evaluation of the Clinical Trials (CTs) by the central coordinator of the Ethics Committee

Trials in each experimental phase

Total trials: 165

Phase	No. Trials	%
Phase III	97	58,8
Phase II	36	21,8
Phase IV	22	13,3
Phase I	5	3,0
Bioequivalence / Bioavailability	5	3,0
Total	165	100,0

Trials per year and trial phase

Total trials: 165

Year	No. Trials	% Phase I	% Phase II	% Phase III	% Phase IV	% Bioeq / Bioav	% Total
2000	29	0,0	13,8	75,9	6,9	3,4	100,0
2001	22	0,0	13,6	72,7	0,0	13,6	100,0
2002	8	0,0	0,0	87,5	12,5	0,0	100,0
2003	25	0,0	24,0	64,0	12,0	0,0	100,0
2004	17	5,9	11,8	52,9	29,4	0,0	100,0
2005	16	12,5	31,3	37,5	18,8	0,0	100,0
2006	27	3,7	40,7	44,4	11,1	0,0	100,0
2007	21	4,8	23,8	42,9	23,8	4,8	100,0
Total	165	3,0	21,8	58,8	13,3	3,0	100,0

Trials by therapeutic classification ATC (up to 2nd level)
Principal Anatomic Group (PAG): J – general Antimicrobial for systematic use
 Total Trials: 165

ATC (up to 2nd level)	No. Trials	%
Antibiotics – antibacterial systematic use	135	81,8
Antibiotics – antimycotic systematic use	30	18,2

The trial totals do not correspond to the experimentation total number, as each trial could involve other studies with other drugs.

Trials by typology: monocentric/multicentric
 Total trials: 165

Typology	No. Trials	%
Multicentric	132	80,0
Monocentric	33	20,0
Total	165	100,0

Trials by active principal

The lists gives the active principals tested in Italy in the period 2000-2007. Certain trials were conducted for the registration of new products and/or enhanced action properties (of products already on the market).

ATC	Active Principals	No. CTs
Antibiotics–Antibacterial systematic use		
J01MA12	LEVOFLOXACIN	13
J01XX08	LINEZOLID	12
J01CR02	AMOXICILLINA AND ENZYMATIC INHIBITORS	10
J01MA17	PRULIFLOXACIN	10
J01MA14	MOXIFLOXACIN	9
J01XA01	VANCOMYCIN	9
J01FA09	CLARITHROMYCIN PRULIFLOXACIN	8
J01FA10	AZITHROMYCIN	8
J01MA02	CIPROFLOXACIN	8
J01AA02	DOXYCYCLINE	6
J01DH03	ERTAPENEM	6
J01FA15	TELITROMICINA	6
J01CR05	PIPERACILLIN AND ENZYMATIC INHIBITORS	5
J01CA04	AMOXICILLIN	4
J01DA13	CEFTRIAZONE	4
J01CR01	AMPICILLIN AND ENZYMATIC INHIBITORS	3
J01DH02	MEROPENEM	3
J01BA02	THIAMPHENICAL	2
J01DA11	CEFTAZIDIME	2
J01DC04	CEFACLOR	2
J01DD04	CEFTRIAZONE	2
J01DF01	AZTREONAM	2
J01GB01	TOBRAMYCIN	2
J01GB06	AMIKACIN	2
J01MA16	GATIFLOXACIN	2
J01XB01	COLISTIN	2
J01XX49	VARIOUS	2
J01AA08	MINOCYCLINE	1
J01DA04	CEFAZOLIN	1
J01DA06	CEFUROXIME	1
J01DA24	CEFEPIME	1
J01DB04	CEFAZOLIN	1
J01DD13	CEFPODOXIME	1
J01FA12	ROKITAMYCIN	1
J01XD01	METRONIDAZOLE	1

ATC	Active Principals	No. CTs
Antibiotics – antimycotic systematic use		
J02AX04	CASPOFUNGIN	12
J02AA01	AMPHOTERICIN	10
J02AC03	VORICONAZOLE	6
J02AA01	AMPHOTERICIN B	1
J02AC02	ITRACONAZOLE	1
J02AX06	ANIDULAFUNGIN	1

Trials by promoter typologies

Total Trials: 165

Total Promoters: 57

Typology	No. CTs	%	No. Promoters
Drug Companies	128	77,0	36
IRCCS public and private	16	9,7	5
Clinics and hospitals	12	7,3	8
Scientific associations	5	3,0	5
Universities	4	2,4	3
Total	165	100,0	57

Trials by therapeutic fields

Total trials: 165

Therapeutic field	No. CTs	%
Immunology and infective diseases	54	32,7
Respiratory diseases	40	24,2
Dermatology/plastic surgery	11	6,7
Haematology	11	6,7
Nephrology/Urology	11	6,7
Pharmacology/Toxicology	7	4,2
Otorhinolaryngology	7	4,2
Neurology	6	3,6
Urinary System	4	2,4
Gastroenterology	3	1,8
Gynaecology and obstetrics	2	1,2
Ophthalmology	2	1,2
Oncology	2	1,2
Cardiology/Vascular diseases	1	0,0
Musculoskeletal diseases	1	0,0
Oral and maxillofacial surgery	1	0,0
Paediatrics/Neonatology	1	0,0
Traumatology and emergency medicine	1	0,0
Total	165	100,0

Trials by region and participants
(only the analysis of CE approved centres were considered)

Total centres: 293

Total trials: 165

Regions	No. CTs	% Total CTs(165)	No. centres	No. doctors CTs per centre	CT coord.	% CTs coord./totals
LOMBARDIA	110	66,7	53	4	59	53,6
LAZIO	60	36,4	22	4	15	25,0
TOSCANY	56	33,9	21	4	21	37,5
VENETO	52	31,5	23	3	8	15,4
LIGURIA	51	30,9	14	4	15	29,4
EMILIA ROMAGNA	48	29,1	21	3	9	18,8
SICILY	47	28,5	25	3	7	14,9
PIEMONTE	41	24,8	22	3	6	14,6
CAMPANIA	38	23,0	22	3	2	5,3
FRIULI VENEZIA GIULIA	32	19,4	9	4	6	18,8
PUGLIA	31	18,8	14	3	2	6,5
UMBRIA	30	18,2	8	4	10	33,3
SARDINIA	20	12,1	9	2	0	0,0
MARCHE	17	10,3	11	2	2	11,8
ABRUZZO	14	8,5	6	3	3	21,4
CALABRIA	14	8,5	6	2	0	0,0
BASILICATA	6	3,6	3	2	0	0,0
PROV. AUTON. BOLZANO	3	1,8	2	2	0	0,0
MOLISE	1	0,0	1	1	0	0,0
PROV. AUTON. TRENTO	1	0,0	1	1	0	0,0

Column totals “No. CTs” could result in being higher than the multicentric trials, as these were conducted at more centres and the same laboratory was used by the different regions.

In the column “No. CTs”, for some regions, the number of centres participating in the clinical studies was counted only once, even if involved in several studies.

For certain regions, the column “No. CTs per centre” is the average number of trials performed by the centre, obtained by the summation of the studies performed at the centres, divided by the number of centres taking part. (See the Table “Trials by participating centre”)

In the column “CT coord”, is the number of experiments that the coordinator assigned to the regions.

Trials by centre typology
Total no. of centres: 295
Total trials: 165

Typology	No. CTs	% total CTs(165)	No. centres involved
Hospitals	126	76,4	197
IRCCS public or private	83	50,3	25
Polyclinic universities	52	31,5	8
ASL	38	23,0	39
Universities	38	23,0	21
Nursing homes	3	1,8	4
Others	1	0,0	1

The totals in the columns "No. CTs" could result in being higher due to the multicentric trials being conducted at more than one centre that have different typologies.

Trials by participating centres
Total no. centres: 295
Total trials: 165

Item	Centres	No. CTs	% total CTs(165)	No. CTs coord.	% CTs coord./total
1	Polyclinic, <i>S. Matteo of Pavia</i>	42	25,5	24	57,1
2	University Polyclinic, <i>Gemelli of Rome</i>	30	18,2	10	33,3
3	University hospital, <i>S. Martino of Genova</i>	26	15,8	6	23,1
4	University <i>Pisana of Pisa</i>	23	13,9	8	34,8
5	University Polyclinic, <i>S. Orsola Malpighi of Bologna</i>	23	13,9	4	17,4
6	Hospital of <i>Padova</i>	19	11,5	3	15,8
7	Hospital, <i>Civili of Brescia</i>	18	10,9	3	16,7
8	Polyclinic of <i>Milan</i>	17	10,3	10	58,8
9	Hospital of <i>Perugia - Polyclinic Monteluce</i>	16	9,7	5	31,3
10	University <i>Careggi of Florence</i>	16	9,7	3	18,8
11	Institute, <i>S. Raffaele of Milan</i>	14	8,5	9	64,3
12	Hospital, <i>S. Gerardo dei Tintori of Monza (MI)</i>	14	8,5	0	0,0
13	Hospital <i>Niguarda Ca' Granda of Milan</i>	13	7,9	1	7,7
14	Hospital <i>Sacco of Milan</i>	13	7,9	3	23,1
15	University - Hospital <i>Consorziale Polyclinic of Bari</i>	12	7,3	1	8,3
16	University, <i>S. Giovanni Battista-Molinette of Turin</i>	12	7,3	3	25,0
17	University Hospital, <i>Riuniti of Foggia</i>	11	6,7	0	0,0
18	Hospital, <i>S. Paolo of Milan</i>	10	6,1	0	0,0
19	Hospital, <i>Riuniti of Bergamo</i>	10	6,1	0	0,0