



SYNERGY
ORANGE
PAPER

RESEARCH REPORT

CLINICAL TRIALS IN EUROPE

ANNUAL 2018

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FOREWORD

The Orange Paper is a free publication produced by Synergy Research Group for the pharmaceutical industry since 2007. It pulls together data from numerous public sources into a single brief document to aid decision makers planning to conduct clinical trials. It is produced quarterly, with an annual summary at the close of each year.



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EXECUTIVE SUMMARY

During the year 2018 the official FDA website showed approvals for initiation of 25,186 new clinical trials of all types Worldwide, including local and bioequivalence studies. 9,371 of those studies were initiated in 18 leading European countries. That represents an overall year on year decline of 18,5%.

Interventional clinical trials are the dominant type of research with 82% market share worldwide, 90% in USA and 82% in Europe. The most prevalent phase of clinical trials conducted worldwide by number of studies was Phase II. The dominant phase of clinical trials conducted across European sites by number of studies and patients was Phase III.

In Europe the top-10 Sponsors combined account for 19% of total number of studies conducted in Y 2018. In comparison, in the U.S. the top-10 Sponsors combined account for only 8% of total number of studies.

During the year 2018 the Center for Drug Evaluation and Research (CDER) of the FDA approved 132 new drugs, including new molecular entities (NME), new dosages, combinations or manufacturers.

The Committee for Medicinal Products for Human Use (CHMP) of the European Medicine Agency (EMA) evaluated 78 new drugs, including 16 generics and 6 biosimilar drugs. Eight drugs were withdrawn, while 70 drugs received positive opinions and were approved to marketing.

According to the FDA data, 38 FDA inspections were conducted in investigative sites located in leading European countries during 2018. Countries which received the most inspections were Poland (9 inspections), Germany (6 inspections) and France (5 inspections).

The top tech trends in the Pharmaceuticals industry during 2018 were:

- Improving quality of Patient Relationship with patient-faced services like Medication Adherence apps, AI-based Diagnostic apps and Telemedicine services;
- Improving quality, speed and cost-efficiency in Clinical trials with Patient Engagement services, Remote Monitoring tools, Clinical Decision Support systems and In-Silico Drug Discovery approach;
- Improving speed and cost-efficiency in Clinical Practice of Healthcare Providers with AI-powered automated Diagnostic tools and voice-powered Physician's Assistant tools.





WORLDWIDE CLINICAL TRIALS

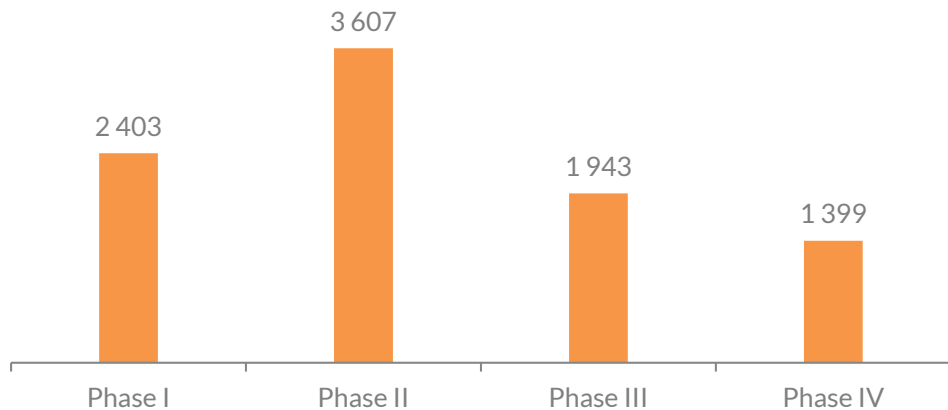
Trial Data

During the year 2018 the official FDA website showed approvals for initiation of 25,186 new clinical trials of all types worldwide, including local and bioequivalence studies with an overall year on year growth rate of 15% driven in large by an increasing number of trials in developing countries.

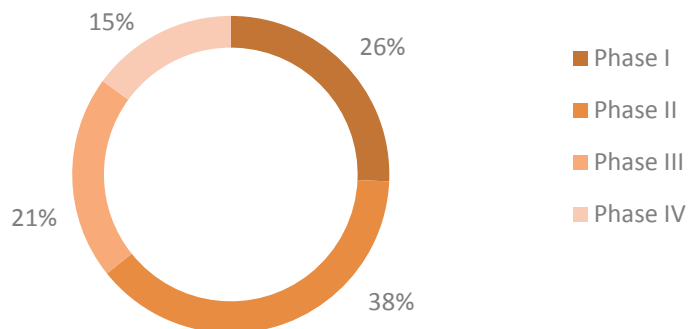
The combined market share of USA and European countries by number of initiated studies reached 71% in 2018, with the USA having 34% and Europe having 37%.

80% of all clinical trials initiated in 2018 were Interventional Clinical Trials.

Breakdown of Worldwide Clinical Trials by Phase in 2018



Percentage Breakdown of Clinical Trials by Phase in 2018 (worldwide)

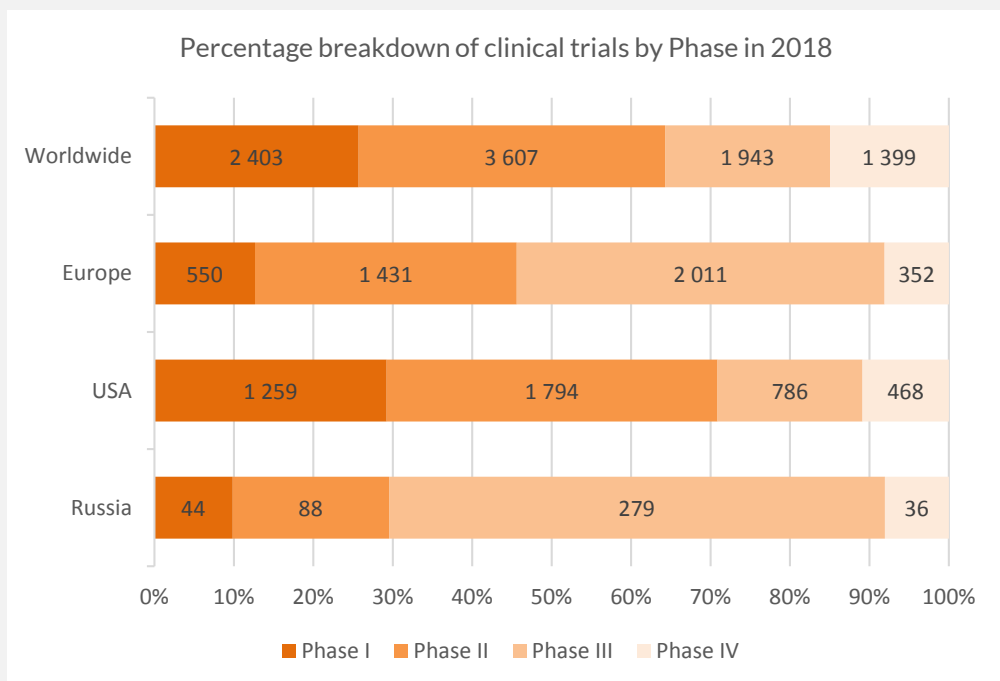
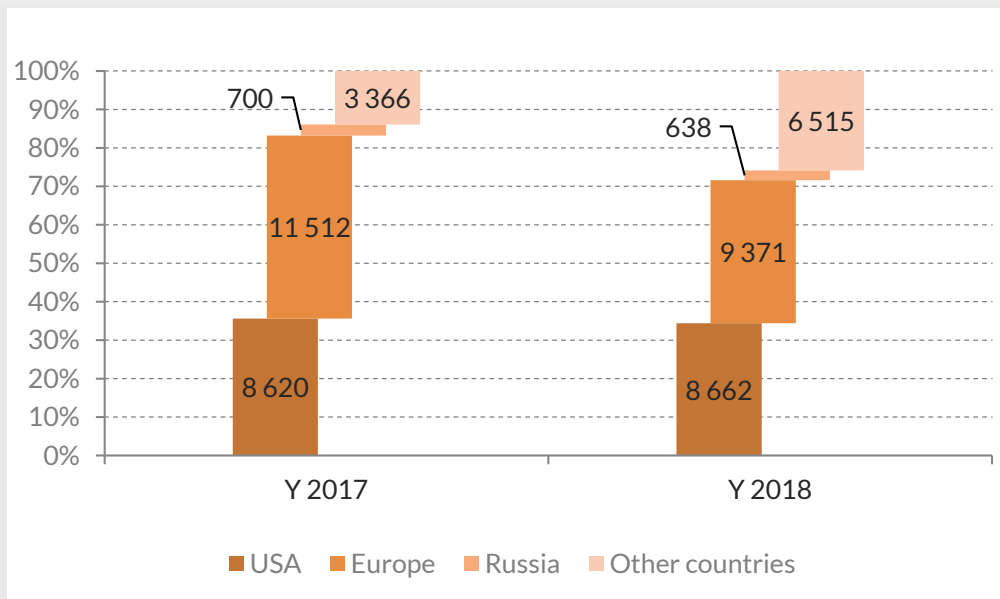


TRIAL DATA



Breakdown by region of origin

The proportions between different regions (USA, Europe, Russia, Other Countries) for trials conducted in 2018 changed in comparison to 2017. Notably, the market share of leading European countries by number of initiated studies dropped down to 37% (from 47% in the year 2017).



TRIAL DATA

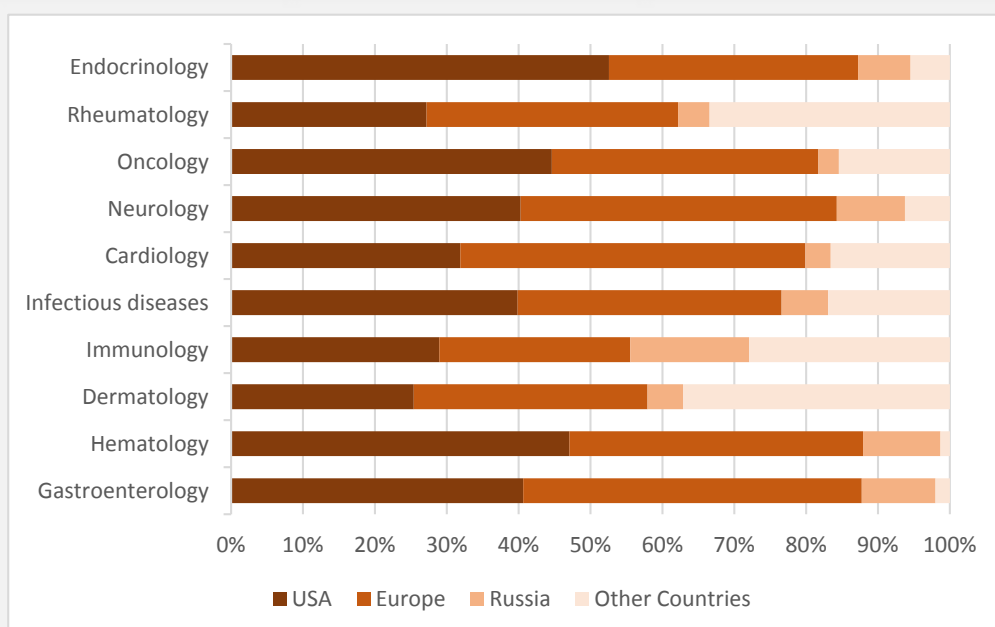
Therapeutic areas of clinical trials worldwide



In the year 2018, the largest number of studies were initiated in Oncology (4681 studies), Cardiology (1386 studies), and Infectious Diseases (803).

More than one therapeutic area could be assigned to a trial. BE studies were not included in any therapeutic area group.

Therapeutic Area	No. studies in Q4 2018	No. studies in Y 2018
Oncology	1 137	4 681
Cardiology	390	1 386
Infectious Diseases	208	803
Rheumatology	193	640
Dermatology	76	606
Neurology	201	591
Endocrinology	140	548
Gastroenterology	148	497
Hematology	91	306
Immunology	51	290
Other	4 136	14 838





WORLDWIDE CLINICAL TRIALS

Sponsor Data

The Top-10 list of global Sponsors of clinical trials worldwide remains unchanged for the past 5 years – this fact may be explained by the significant and continuously increasing amount of investment required for research and development of new drugs.

However, it's remarkable that the combined market power of these leading pharmaceutical corporations accounts for 40% of all patients enrolled in interventional clinical trials where the study Phase has been identified.

Here are the top-10 global sponsors by total number of studies initiated in Y 2018

No	Company Name	No. studies	No. patients
1	Novartis	89	19 962
2	Pfizer	78	21 862
3	Hoffman-La Roche	62	17 954
4	Merck	57	27 818
5	Bayer	59	668 121
6	Eli Lilly	55	18 557
7	AbbVie	46	11 688
8	Janssen	45	4 468
9	GlaxoSmithKline	41	19 356
10	AstraZeneca	40	15 707
Combined market share of top-10 companies		2%	40%

Note: Observational clinical trials and clinical trials without U.S. FDA-defined Phases (from I to IV) were not included within this ranking.



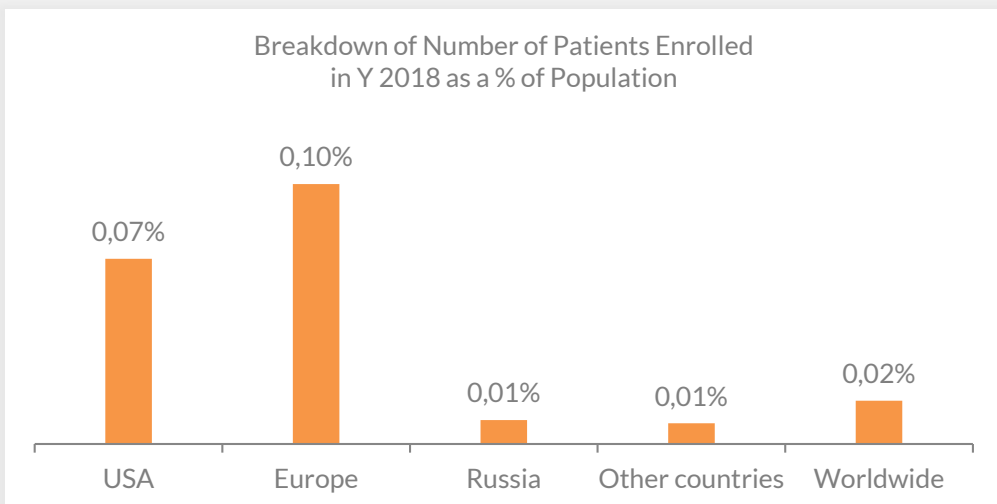
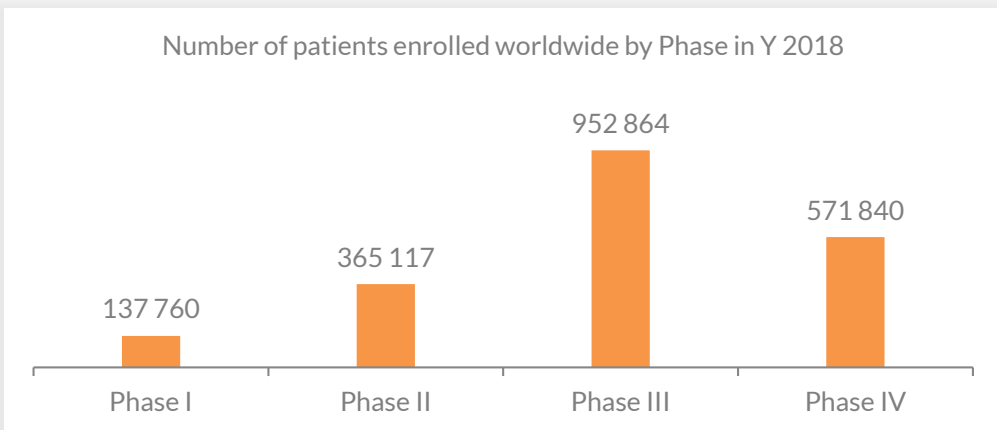


WORLDWIDE CLINICAL TRIALS

Patient Data

The total number of patients enrolled in Clinical trials of all types in the year 2018 exceeded 2 million individuals.

The majority of patients were enrolled in Phase III trials, and the largest proportion of the global patient population were Europeans. However, the share of patients participating in clinical trials remains extremely low in comparison with overall size of the population - with approximately 0,02% Worldwide.



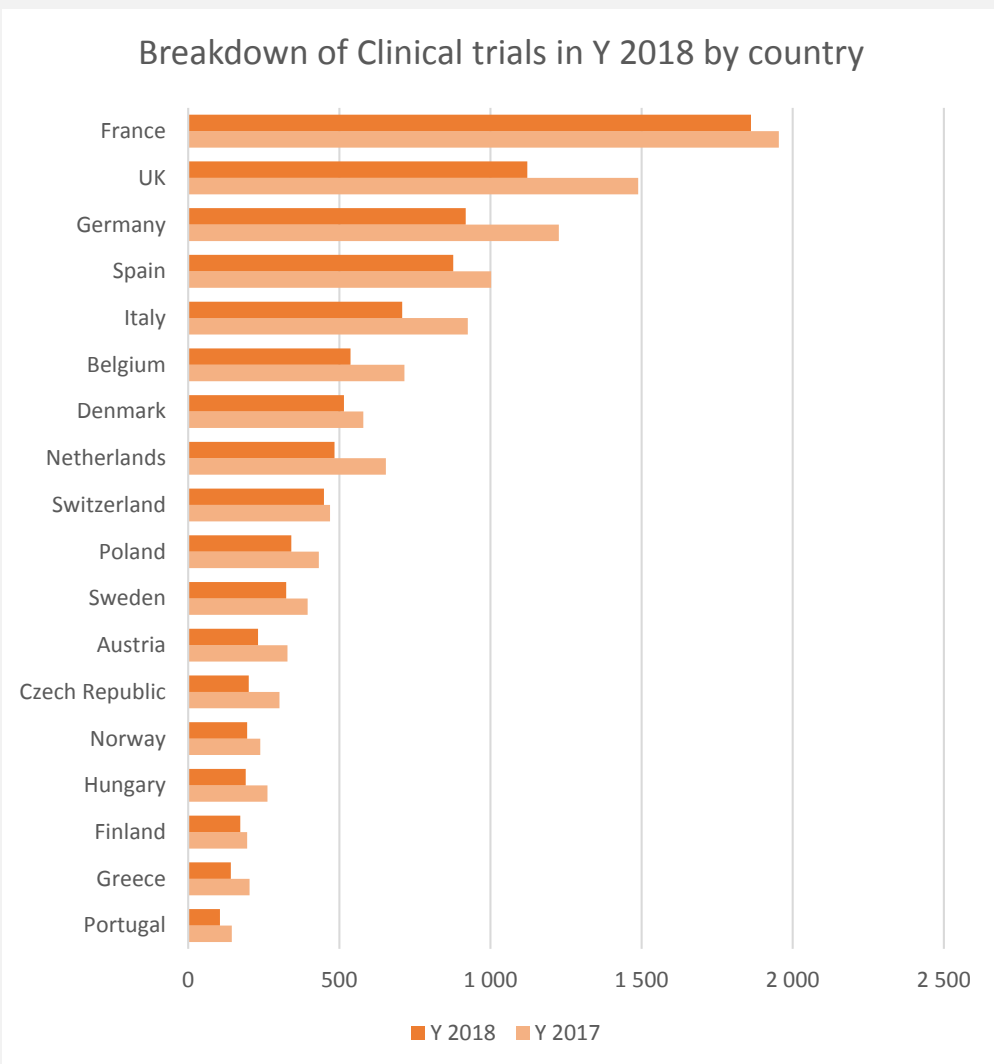


CLINICAL TRIALS IN EUROPE

Trial Data

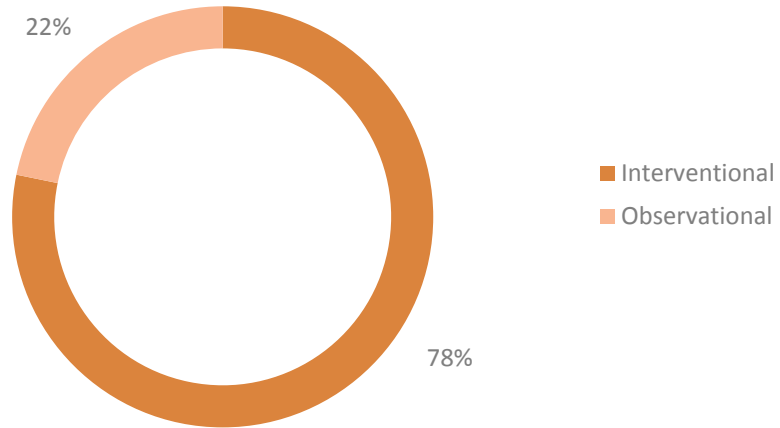
According to FDA data, 9,371 clinical trials were initiated in the 18 leading European countries during the year 2018 (we set a threshold of minimum 20 Clinical trials conducted in any quarter of 2018 as including criteria for European countries), including local and bioequivalence studies with an overall year on year decrease of 18,5%.

The leading countries by the number of clinical trials initiated in 2018 were France, UK, Germany, Spain, Italy, Belgium and Denmark.

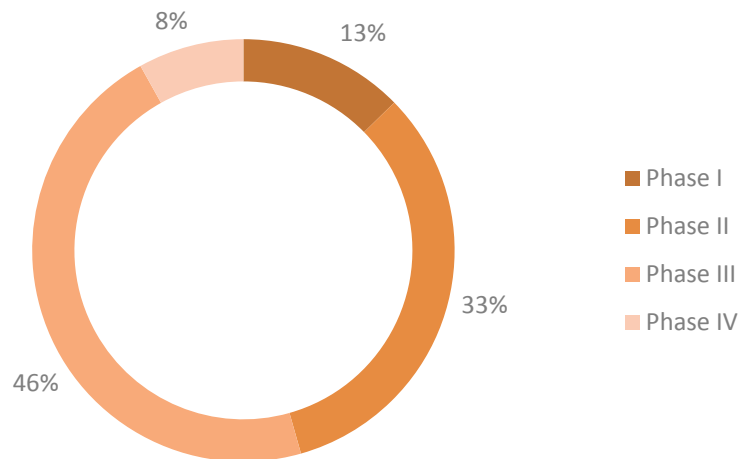


The most prevalent type of clinical trials conducted across European sites were interventional studies. The most frequent phase of clinical trials conducted across European sites by total number of studies was Phase III.

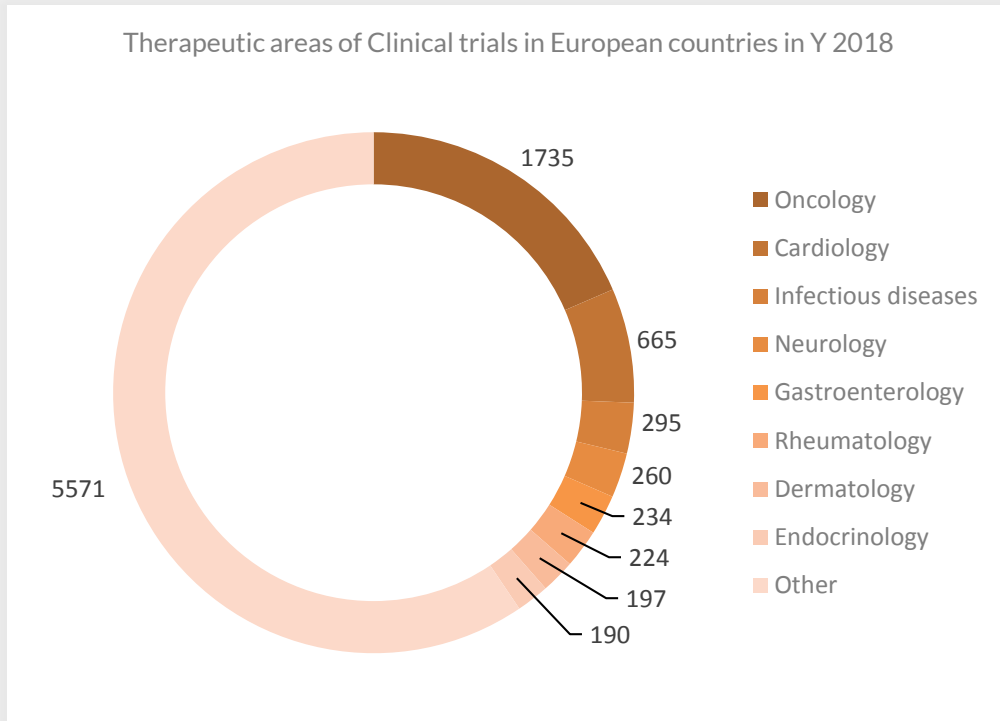
Interventional vs Observational studies in Europe in Y 2018



Breakdown of Clinical trials in Europe by Phase



The largest number of clinical trials initiated in the 18 leading European countries in Y 2018 were related to Oncology (1,735 studies), Cardiology (665 studies), Infectious Diseases (295 studies) and Neurology (260 studies). Other popular areas include Gastroenterology, Rheumatology, Dermatology and Endocrinology.





CLINICAL TRIALS IN EUROPE

Sponsor Data

The most prevalent countries of origin for pharmaceutical company sponsored clinical trials initiated in leading European countries in Y 2018 were the U.S (AbbVie, Bristol-Myers, Merck, Eli Lilly, Janssen), Switzerland (Hoffmann-La Roche, Novartis) and Denmark (Novo Nordisk).

No	Company Name	No. studies
1	Hoffman-La Roche	193
2	AbbVie	164
3	Janssen	133
4	Novartis	104
5	Merck	82
6	AstraZeneca	73
7	Bristol-Myers	41
8	Novo Nordisk	19
9	Celgene	16
10	Eli Lilly	15
Combined market share of these top-10 companies		19%



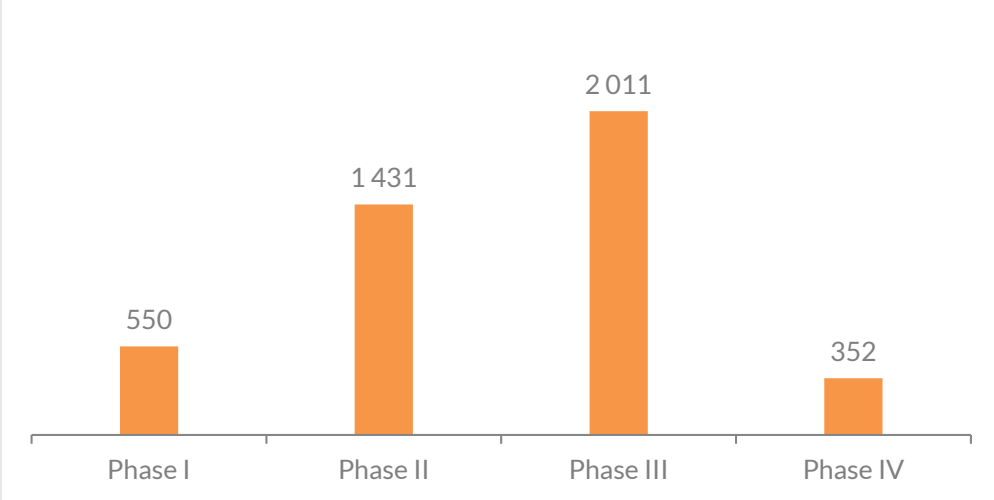


CLINICAL TRIALS IN EUROPE

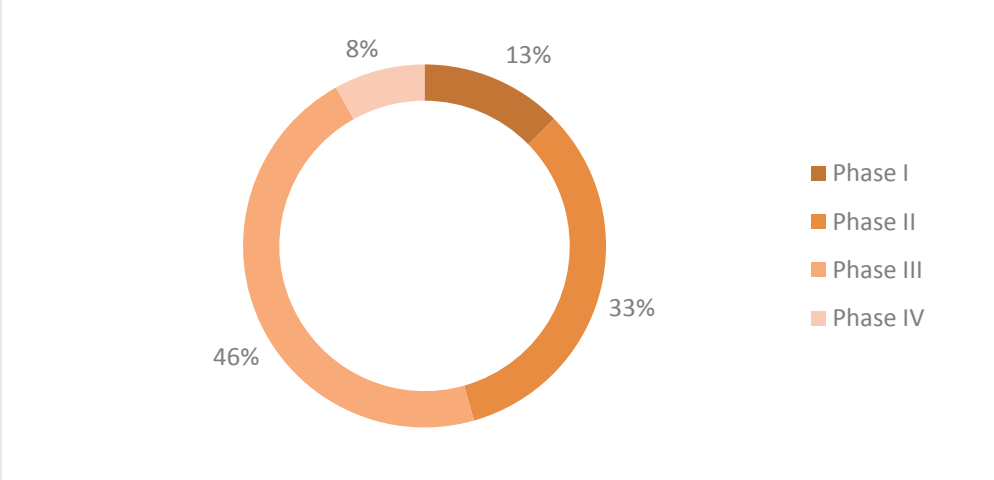
Patient Data

Overall the total number of patients involved in clinical trials initiated in leading European countries in Y 2018 exceeded 1 million individuals. The dominant phase by total number of patients enrolled during 2018 was Phase III.

Breakdown of Phases by number of patients enrolled during Y 2018



Percentage breakdown of Phases by number of patients enrolled during 2018





Regulatory Data

In Q4 2018 the Committee for Medicinal Products for Human Use (CHMP) of the European Medicine Agency (EMA) evaluated 8 new drugs. No drugs received negative opinion and as such 8 drugs received positive opinions and were approved for marketing.

Aprr.date	Drug (active ingredient)	Company
04/12/2018	Inovelon (Rufinamide)	Eisai
12/11/2018	Ameluz (5-Aminolevulinic Acid)	Biofrontera Bioscience
09/11/2018	Truxima (Rituximab)	Celltrion Healthcare
17/10/2018	Alecensa (Alectinib)	Roche
09/10/2018	Lucentis (Ranibizumab)	Novartis
02/10/2018	Movymia (Teriparatide)	STADA
02/10/2018	Terrosa (Teriparatide)	Gedeon Richter
01/10/2018	Jardiance (Empagliflozin)	Boehringer Ingelheim

Source: EMA



Inspection Data

According to the U.S. FDA data, 38 FDA inspections were conducted at investigative sites located in leading European countries. The greatest number of inspections were carried out most inspected countries were in Poland (9 inspections), Germany (6 inspections) and France (5 inspections). All of the inspections that were conducted during 2018 are listed below.

Country	Company / Investigator Site Firm Name	Outcome
Austria	J & P Medical Research Ltd.	NAI
Belgium	Sam Van Boxtael, M.D.	VAI
Belgium	Prof. Piet P.M.M. Geusens	VAI
Czech Republic	David Dolezil	NAI
Czech Republic	Robert Gurlich	NAI
Czech Republic	Yuliya Rizova, MD	NAI
Denmark	Anne-Sofie Krogsaa, MD	NAI
Denmark	Per Rathenborg	NAI
France	Ngai Liu	NAI
France	David Adams	NAI
France	Dominique Paul Germain, M.D.	VAI
France	SGS Cephac Europe	VAI
France	Benjamin Besse, M.D., Ph.D.	NAI
Germany	Profil Institut fuer Stoffwechselforschung Gmbh	NAI
Germany	Profil Mainz GmbH & Co. KG	NAI
Germany	Nuvisan GmbH	VAI
Germany	Hexal Ag	NAI
Germany	BioAgilytix	VAI
Germany	Fresenius Kabi	NAI



INSPECTION DATA

Country	Company / Investigator Site Firm Name	Outcome
Greece	Epaminondas Zakyntinos, M.D., PhD	NAI
Hungary	Peter Szabo, M.D.	NAI
Hungary	Renata Kun, M.D.	NAI
Italy	Angelo Iacobellis, M.D.	VAI
Italy	Rosario Pivonello	NAI
Poland	Magdalena Wieczorek-Rutkowska M.D.	NAI
Poland	Grazyna Bogutyn	NAI
Poland	Tomasz Sarosiek	NAI
Poland	Marta Banach, M.D.	NAI
Poland	Krzysztof Wilk, M.D., Ph.D.	VAI
Poland	Krzysztof Dynowski, MD	NAI
Poland	Edward Franek MD	NAI
Poland	Anna Kostera-Pruszczyk, MD, PhD	VAI
Poland	Piotr Kuna, M.D.	NAI
Spain	Enriqueta Felip Font, M.D.	NAI
Switzerland	Novartis Pharma AG	NAI
UK	York Bioanalytical Solutions (YBS)	NAI
UK	GW RESEARCH LTD	VAI
UK	Acacia Pharma Ltd.	NAI



About Synergy

With its unique prevolutionary mind-set, Synergy is now the World's First Agile Risk Based CRO.

Prevolution is the implementation of thoughtful premeditated change resulting from the anticipation and analysis of future trends before they happen – in other words, being 'one step ahead of evolution'.

The high recruitment rates of the emerging markets combined with innovative technology allows our clients conduct faster, cost-effective studies without sacrificing quality. We replace outdated R&D strategies by novel, more efficient approaches to clinical research.

