International Journal of Clinical Trials
Chawan VS et al. Int J Clin Trials. 2016 May;3(2):68-71
http://www.ijclinicaltrials.com
pISSN 2349-3240 | eISSN 2349-3259

DOI: http://dx.doi.org/10.18203/2349-3259.ijct20161413

Research Article

Analysis of randomized clinical trials leading to new drug approvals in India and USA

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Received: 24 March 2016
Accepted: 16 April 2016

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ABSTRACT

Background: To analyse the number of randomized clinical trials and subsequent new drug approvals in India and USA.
Methods: Data was collected for completed randomized clinical trials done by multinational in India and USA from www.clinicaltrials.gov during the period from 1/1/2009 to 31/08/2014 and the subsequent new drug approvals from 1/1/2010 to 31/10/2015 for India obtained from Central Drugs Standard Control Organization (CDSCO) (www.cdsco.nic.in.) website and for USA obtained from United States Food and Drug Administration (USFDA) (www.fda.gov) website. Results were measured in terms of percentage of completed randomized clinical trials for investigational medicinal products (IMP) leading to new drugs approvals in India and USA.
Results: A total of 163 randomized clinical trials fulfilled the eligibility criteria. Regrouping them for the same sponsor and IMP resulted in a total of 93 randomized clinical trials. In India, 13 drugs (13.93%) were approved by CDSCO, whereas in USA, 35 drugs (37.62%) were approved by USFDA out of a total of 93 randomized clinical trials. High number of randomized clinical trials were conducted for cancer (17.20%) while less number of randomized clinical trials were conducted for gastrointestinal conditions (3.22%).
Conclusions: This study revealed that, there exists a wide gap between the new drug approvals permitted by USFDA and CDSCO. Thus there is disparity in the number of clinical trials conducted and market availability of new drugs in India showing that India is lagging behind the USA in approval of new drugs. The regulatory authorities, investigators and institutional review boards should ensure the availability of new drugs in India after they have been researched in the population.

Keywords: Randomized clinical trials, Investigational medicinal product, New drug approvals, India, USA

INTRODUCTION

Drugs are marketed and made available for all after conducting randomized clinical trials mainly because of contribution of the study participants. Clinical trials have led to the development of novel treatment modalities in medicine. Multinational Clinical trials are sponsored by pharmaceutical companies and conducted by research teams of doctors and other medical professionals. Clinical trials are gold standard in the field of evidence based medicine.[1,2] Recently, there has been a shift in clinical trial sites from developed countries like the United States of America (USA) and the European countries to developing countries like India and South American countries.[3] India is expected to have tremendous growth potential in clinical research due to its huge disease

prevalence and treatment-naïve patient population. India has a vast genetically diverse population, well-equipped hospitals, and qualified English-speaking investigators making it a preferred destination for conducting global clinical trials. The contract research and manufacturing services are ever increasing in India.[4-7]

Due to this changing scenario, it becomes mandatory to explore whether these increase in randomized clinical trials in India have led to the availability of new drugs to Indian population. This study analyzed the relationship between the number of randomized clinical trial conducted and subsequent new drug approvals in India and USA. A comprehensive database of randomized clinical trials done in India and USA was collected from clinicaltrials.gov website during the period from January 2009 to August 2014 and evaluated for subsequent new drug approvals for the period January 2010 to October 2015 obtained from the websites www.cdsco.nic.in and www.fda.gov.in.[8-10]

METHODS

All multinational randomized clinical trials from www.clinicaltrials.gov website conducted during the period from 1st January 2009 to 31st August 2014 for the same investigational medicinal product (IMP) in India and USA were eligible and selected for the study.

Data was collected from www.clinicaltrials.gov website to identify clinical trials conducted by global sponsors in India and USA for the same investigational medicinal product. Interventional, phase II and III randomized clinical trials, funded by industry, registered, conducted and completed between 1st January 2009 and 31st August 2014 was selected for the study. As the sponsor has to submit clinical study report within 12 months to the regulatory authorities, it was decided that a period of 14 months was adequate for the sponsor to file a New Drug Application (NDA). On this basis, data was obtained from www.cdsco.nic.in and www.fda.gov for new drug approvals in India and USA respectively, from 1st January 2010 to 31st October 2015. We compared the number of new drug approvals made in India and USA for the same randomized clinical trials with the same investigational medicinal product.

The following information was assessed

Title of the trial, sponsor, indication and investigational medicinal product. The new product approval date was obtained from the new product approval database. Final data was compiled for the same sponsor, same trial and same investigational medicinal product to avoid miscounting the total number of randomized clinical trials. Figure 1 gives the details of generation of data.

Data was analyzed in terms of percentage of completed randomized clinical trials for investigational medicinal products (IMP) leading to new drug approvals in India and USA.

RESULTS

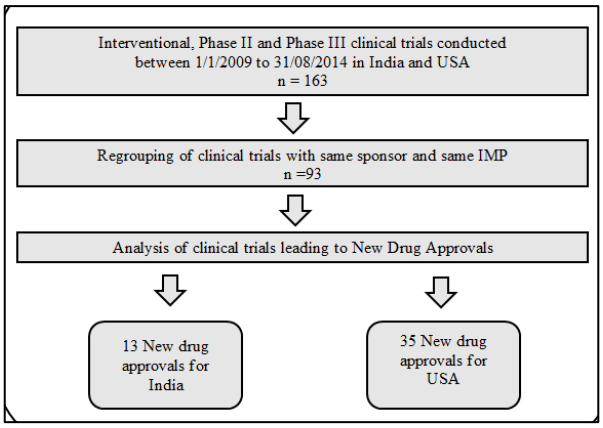

Figure 1: The flowchart illustrating the new drug approval.

Figure 1 illustrates how the randomized clinical trials conducted in India and USA led to subsequent new drug approvals. Initially, 163 randomized clinical trials were obtained from www.clinicaltrials.gov registered in the period from 1st January 2009 to 31st August 2014. After regrouping the randomized clinical trials for same sponsor and for the same IMP resulted in 93 randomized clinical trials for India and USA. There were subsequent 13 new drug approvals for India and 35 new drug approvals for USA.

Figure 2 shows the percentage of completed randomized clinical trials leading to new drug approval in India and USA. 13.97% and 37.63% of randomized clinical trials resulted in new drug approvals for India and USA respectively. 86.03% and 62.37% of randomized clinical trials resulted in no new drug approvals for India and USA respectively.

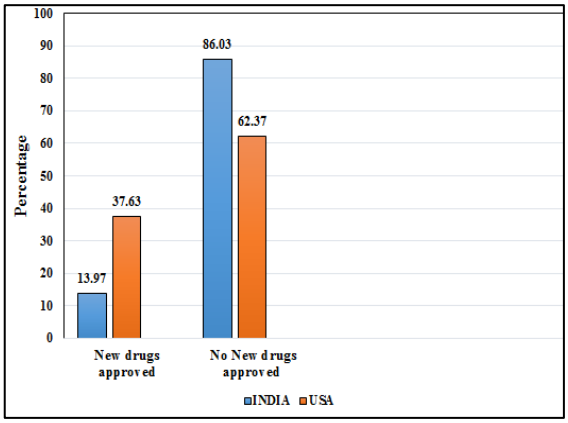

Figure 2: Percentage of randomized clinical trials leading to new drug approvals and no new drug approvals.

Table 1 shows the percentage of various randomized clinical trials done conducted for different clinical conditions. A large number of clinical trials were for cancer (17.20%), endocrine (16.12%) and neuropsychiatric diseases (15.55%). Least number of randomized clinical trials were for gastrointestinal diseases.

Table 1: Percentage of randomized clinical trials for different clinical conditions.

Clinical conditions	Percentage of clinical trials conducted
Cancer	17.20 %
Endocrine	16.12 %
Neuropsychiatry	15.55 %
Respiratory	10.75 %
Cardiovascular	7.50 %
Musculoskeletal	7.50 %
Infectious	5.37 %
Hematology	4.30 %
Gastrointestinal	3.22 %
Others	12.90 %

DISCUSSION

Randomized clinical trials conducted during the period from between January 2009 to August 2014 were identified and analyzed. The analysis showed that there is wide gap between number of randomized clinical trials conducted and number of new drug approvals in India. Out of 93 eligible randomized clinical trials, only 13 randomized clinical trials in India and 35 randomized clinical trials in USA resulted into new drug approvals. A high number of randomized clinical trials did not result in new drug approvals. Thus our study results show a wide variation in the number of new drug approvals in India and USA despite randomized clinical trials being conducted for the same investigational medicinal products. A low rate of new drug approvals reduces the availability of new drug for the treatment of various diseases.[11] Large randomized trials are required to provide reliable evidence based medicines. The current regulations and guidelines have increased trial complexity, creating barriers in their design and conduct.[12]

This study showed a high number of randomized clinical trials for cancer (17.20%), endocrine (16.12%), neuropsychiatry (15.55%), respiratory (10.75%), cardiovascular (7.5%), musculoskeletal diseases (7.5%), while few clinical trials were carried out for gastrointestinal diseases (3.2%).

As India is one of the developing countries, diseases such as high risk pregnancies, anemia, nutritional deficiencies are most prevalent. This study showed no randomized clinical trials being conducted for these conditions. The declaration of helsinki gives a clear guidance for research conducted in developing countries.[13] The 2000 version of the declaration of helsinki categorically states that at the end of any research study, every study subject should be assured of the best proven prophylactic, diagnostic and therapeutic methods identified by that study.[13] The World Medical Assembly emphasizes that medical research is justified if there is a reasonable likelihood that the population in which the research is carried out benefits from the results of the research.[13] The Indian drug regulatory authorities ask sponsors whether they will market the drug after conducting the trial in India.[14] However, the results of this study clearly shows that this regulation is not followed by sponsors even after they make a commitment with the regulatory authorities of India.

CONCLUSION

Clinical research done in developing countries should result in new drug approvals and subsequent use of these drugs for the population of that country. The goal of clinical research is to support and make new medicines available for the benefit of mankind. The study shows the research being done in a select few clinical conditions like cancer and endocrine diseases. This study shows that, there exists a wide gap between the new drug approvals in India and USA. Thus there is disparity in the number of clinical trials conducted and the subsequent availability of these new drugs in India. This study shows India to be lagging behind the USA regarding approvals of new drug following randomized clinical trials for same investigational medicinal product. The regulatory authorities, investigators and institutional review boards should ensure the availability of new drugs in India after they have been researched in the population.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

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Cite this article as: Chawan VS, Badwane SV, Gawand KV, Phatak AM, Naik MS. Analysis of randomized clinical trials leading to new drug approvals in India and USA. Int J Clin Trials 2016;3(2): 68-71.