

## Mini Review

# A Current Trend of Clinical Trials on Endometrial Cancer in India

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## Abstract

Humanized monoclonal antibody called dostarlimab is developed as PD1 receptor antagonist to treat various malignancies. Jemperli, Glaxosmithkline (Dostarlimab) just received approval in the USA and EU for the treatment of adult patients with defective genes, (progressive endometrial cancer) based on results from the garnet trial. Clinical research depends on Treatment research, prevention research, diagnostic research, screening research, quality of life research, and genetic studies. A phase of clinical trial on dostarlimab is performed at Memorial Solan Kettering Cancer centre in Manhattan, USA. After platinum-based chemotherapy, it was observed that the drug is safe for the patients with defective gene. Statistical analysis was executed on 8<sup>th</sup> July to 9<sup>th</sup> August, 2019. Safety and efficacy results were outlined. Approximately 15000 patients in the United States and 11000 patients in the European Union are examined every year with latest or repetitive endometrial cancer. At first stage, endometrial cancer may be treated by surgery or it can be treated with radiotherapy, chemotherapy called platinum-based chemotherapy. At the end of the clinical trial, it was observed that no people died or effected.

**Keywords:** Clinical trials; Endometrial cancer; Dostarlimab; Chemotherapy

## Introduction

Clinical research can be defined as the study of health and illness in people. Clinical research is the way we learn how to prevent, diagnose and treat various pathological conditions. Clinical research describes various elements of scientific investigation. It involves human participants and helps in transition of basic research (done in labs) into new treatments and information to benefit patients. Clinical trials as well as research in epidemiology, physiology and pathophysiology, health services, education, and mental health can all come under the clinical research umbrella [1,2].

Various types of clinical research are used which depends on what the researchers are studying. Some different kinds of clinical research are as follows:

- Treatment Research: It normally involves an intervention such as psychotherapy, new devices, medications or new approaches to radiation therapy and surgery.
- Prevention Research: It continuously looks for superior techniques to avert various disorders from developing or returning. Various kinds of prevention research may study medicines, vaccines, vitamins, minerals, or lifestyle alterations.
- Diagnostic Research: It refers to the techniques of researching

for superior ways to identify a specific condition or disorder.

- Screening Research: Its main objective is to find the optimum techniques to detect specific health conditions or disorders.
- Quality of Life Research: It explores methods to improve comfort and quality of life for individuals who have a chronic illness.
- Genetic studies: Genetic studies help to improve the prognosis of disorders by studying how genes and illnesses may be interconnected. These studies may lead to the development of personalized medicines based on a patient's genetic make-up.
- Epidemiological studies: Epidemiological studies seek to recognise the causes, patterns, and control of disorders in groups of people.

Some clinical research is "outpatient," which means that the subjects under study do not stay overnight at the hospital. Some clinical research is "inpatient," which means that the test subjects under study will need to stay for at least one night in the hospital or research centre [3].

Prior to the approval given by U.S. Food and Drug Administration (FDA) for a clinical trial to begin, researchers carry out laboratory tests and studies in animals to evaluate a prospective therapy's safety and efficacy. If these studies show desirable outcomes, the FDA gives approval for the intervention to be tested in human subjects [4-6].

Cancer treatment is getting improved in medical sciences and so many drugs are discovered. Clinical trials are performed for marketing a new drug, which helps to treat the cancer patients. Now days, clinical trials are going on various drugs, endometrial cancer treatment is one of them. Doctors use diagnostic test to find out the cancer stage. Doctors and researchers are national leaders in clinical trials for addressing metastatic colon cancer. There are so many types of clinical trials which are followed:

Pilot studies, prevention trial, screening trial, treatment trial,

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cohort studies, case control studies and cross-sectional studies. Avastin, Bevacizumab, Cetuximab, Eloxatin are approved drugs for colorectal cancer. Dostarlimab-gxly injection is the monoclonal antibody effective for colorectal cancer. FDA approved this drug on 17<sup>th</sup> August, 2021 as the brand name 'Jemperli'. This targeted monoclonal antibody is discovered by Tesaro. In this way Cancer treatment is getting improved in India [7,8].

## Drugs Used for the Treatment of Endometrial Cancer

Recently launched drug for the treatment of endometrial cancer is Dostarlimab.

### Ongoing clinical trials on dostarlimab in India

Clinical trials are performed under different conditions, adverse reaction rates which are noticed in clinical trials of a drug that cannot be directly correlated with the clinical trials of another drug. The safety population which are used for analysis of safety, adverse events, toxicity and laboratory evaluations are mentioned in WARNINGS AND PRECAUTIONS which speculate that 444 patients are exposed to the drug "JEMPERLI" (brand name of Dostarlimab) with latest or repetitive solid tumours, multicohort GARNET study was conducted in 268 patients with Endometrial cancer and 176 patients with other solid tumours [9]. JEMPERLI is a drug and it was administered through intravenous route at doses of 500 mg every 3 weeks for 4 doses ensued by 1,000 mg every 6 weeks until severe disease or chronic toxicity occurs. Among the 444 patients, 38% were exposed for >6 months and 12% were subjected for >1 year [10].

Dostarlimab was approved on 17<sup>th</sup> August, 2021 for the treatment of endometrial cancer. The clinical trial on this drug was subsidized by GlaxoSmithKline. The cost of Dostarlimab per dose is Rupees 8.55 lakh. FDA approved this drug to treat the adult patients with latest or repetitive solid tumours [11]. Recently MSK (Memorial Sloan Kettering Cancer Center) in Manhattan, US performed the trial on Dostarlimab. At the end of the trial the cancer was detected through some physical and medical tests like PET Scans, MRI Scans. Dostarlimab kills the cancer cells and helps the immune system present in our body to detect and destroy them [12-14].

Some important phases of clinical trial at Memorial Sloan Kettering Cancer Center:

- The trial was conducted at Memorial Sloan Kettering Cancer Center in Manhattan, US on a group of 18 patients. They were fighting against the endometrial cancer.
- In all of them, the cancer was provincially upgraded. This means that cancer had spread within the rectum and also to the lymph nodes and it had not spread to the other organs of our body.
- Dostarlimab was given to the patients for six months. Then it was prescribed as a dosage form of every three weeks.
- At the last stage of trial, Cancer was examined or unchecked through some physical or medical tests like PET Scans, MRI Scans.
- Dostarlimab acts by exposing the cancer cells which help the immune system to find and kill the cancer cells.
- The endometrial cancer study was influenced by a clinical trial performed by Dr. Luis A. Diaz of Memorial Sloan Kettering

Cancer Center in 2017.

- Patients participated in the trial had to go through some prior treatments like chemotherapy, radiation and invasive surgery to control their stage of cancer.
- Post treatment complications will not be observed in the patients after the completion of clinical trial.

### Function of dostarlimab in endometrial cancer treatment

Dostarlimab is a monoclonal antibody of IgG4 isotype and it binds with PD-1 receptor i.e., programmed death receptor-1 and it can block the interaction of PDL-1 and PDL-2 ligands and it inhibits the immune response which is known as antitumor immune response [15] (Figure 1).

### Results

Screening started on 10<sup>th</sup> April 2017, 129 and 161 patients with latest endometrial cancer where registered in cohort A1 and A2. It was investigated that, time required for cohort A1 was investigated that, time required for cohort A2 was 11.5 months [16-20]. The Overall Response Rate (ORR) was 43.5% which comprised of 11 complete responses and 36 partial responses. In case of cohort A2 study, the overall response rate was 14.1% which comprised of 3 complete responses and 19 limited responses [21-26]. The Duration of Response (DOR) was not observed in cohort A1 and Cohort A2 study, treatment related adverse events was 75.5% which includes 17.6% fatigue, 13.6% diarrhoea and 13.8% nausea [27-30]. At the end of the study side effects are observed but no fatal condition or death observed in people, participated in the trial. Half-life of Dostarlimab: The elimination half-life of dostarlimab is 25 days (Figure 2).

### Conclusion

From the results of GARNET trial Dostarlimab is an effective drug for the treatment of endometrial cancer. This drug is more effective and its safety profile is acceptable. By analyzing the results, the protocol of the GARNET trial has been rectified to continue registering the patients with Dmmrec (DNA Mismatch Repair Deficient). Apart from other trials Immune Checkpoint Inhibitors (ICI) therapies Safety analysis should be carefully monitored for immune-related adverse events to determine the risk and predictive markers for adverse events. Dostarlimab should be the treatment of option for patients with new MMRd EC (Mismatch Repair-Deficient Endometrial Cancer) in advancement after a platinum-containing drug administration. Dostarlimab is an investigative humanized anti PD-1 that is advanced both in monotherapy as well as combination therapy, for gynecological tumours and also for lung cancer. The

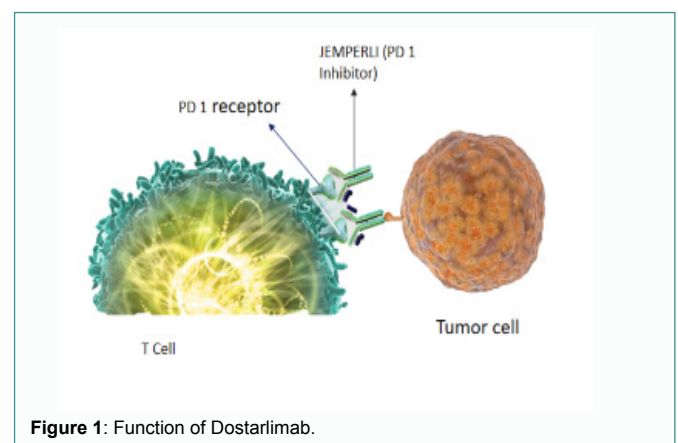
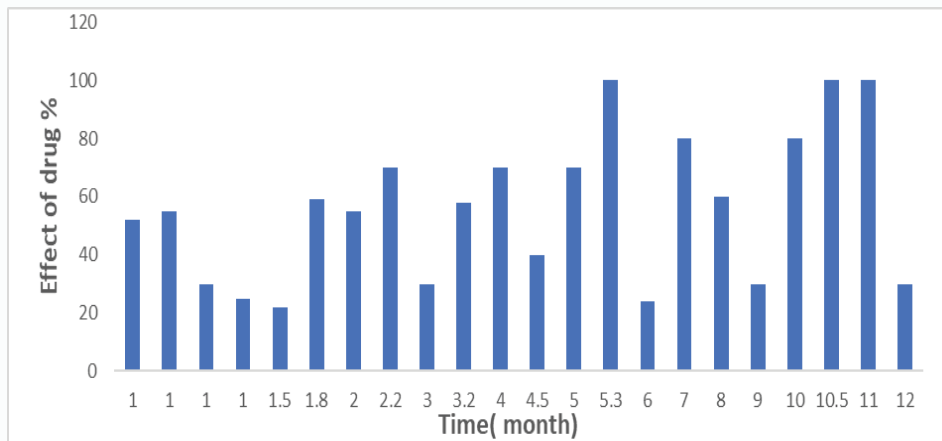


Figure 1: Function of Dostarlimab.



**Figure 2:** Trend in effect of drug (dostarlimab) on endometrial cancer.

GARNET trial shows particularly effective in endometrial cancer. It is highly effective against PD-1 in motivating clinical activity. So, Dostarlimab is connected with considerable survival compared with other treatments for women with repeated dMMR endometrial cancer. Here we outlined the development of this compound. Current preclinical and clinical data showed potential future development.

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