Trial 1 – GIST Study Description

Prepared by Replica Analytics using the study sponsor's trial description

Background

Gastrointestinal stromal tumors (GIST) are the most common mesenchymal tumor of the gastrointestinal tract with an estimated annual incidence of 3,000-4,000 individuals in the United States[1]. Surgical removal is the most common initial treatment of GIST, with tumor size affecting the disease specific survival rates of patients. However, an estimated 90% of patients who receive surgeries that successfully remove the complete tumor, experience recurrence. This was suspected to be due to microscopic tumor dissemination.

This trial was designed to test if post-surgery receipt of imatinib could reduce the recurrence of GIST. Imatinib is an FDA approved protein-tyrosine kinase inhibitor that is approved for treating certain cancers of the blood cells. This drug is hypothesized to be effective against GIST as imatinib inhibits the kinase which experiences gain of function mutations in up to 90% of GIST patients[2]. At the time of this trial the efficacy of imatinib for GIST as well as the optimal dosage for treatment of GIST was unknown.

Study Design

This study was a phase III double-blinded two-armed randomized placebo-controlled trial. Patients were randomized to receive either 400mg study drug or placebo per day for 12 months. Randomization was stratified according to tumor size, and participants with histologically confirmed recurrence during the follow-up period were allowed to either cross-over from the placebo to the study drug or double the dose of the study drug. Recruitment for this study sought patients with histologically confirmed GIST who have undergone a successful surgery in the past 70 days. Patients could be excluded from the study if they received additional post-operative cancer treatments (i.e. chemotherapy, radiation therapy, etc.), had previously received the study drug, were pregnant or breastfeeding, had an infection or cardiac disease.

The study was originally designed to detect a clinically meaningful increase (deemed to be 35%) in overall survival for participants randomized to receive the study drug. Based on projected accrual rates, this design recommended enrolling 380 participants over a period of 3.8 years with 3 years of follow-up to achieve 90% power to detect a clinically meaningful increase in overall survival. The study design was revised to account for a higher than expected accrual rate, and a change in the primary end point from overall survival to recurrence free survival. This led to a desired sample size of 732 patients over 4.36 years with 3 years of follow-up. These design modifications were vetted by simulation and also achieve 90% power to detect a clinically meaningful difference.

Main Findings

This study stopped randomizing participants early as there was sufficient evidence to show that the study drug had significantly increased recurrence free survival. Additionally, this study concluded that the study drug at this dosage was safe for most participants on the basis of adverse events observed between treatment groups. Currently imatinib is a cornerstone of treatment for GIST[3].

References

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