Protocol Title: Open-Label, Multicenter, Multinational, Phase II Study Exploring the Efficacy and Safety of Neratinib Therapy in Patients with Solid Tumors with Activating HER2, HER3, or EGFR Mutations or with EGFR Gene Amplification

Target Population: Patients with Malignant Solid Tumors Harboring Somatic Human Epidermal Growth Factor Receptor (EGFR, HER2, HER3) Mutations or EGFR Amplification.

Summary: Open-label, Multicenter, Multinational, Phase 2 Study exploring the efficacy and safety of Neratinib therapy in patients with Solid Tumors with Activating HER2, HER3, or EGFR Mutations or with EGFR Gene Amplification. The trial will consist of a screening period, a treatment period, and an end of treatment visit occurring when Neratinib is discontinued for any reason, a safety follow-up visit occurring 28 to 42 Days after the last dose of Neratinib and a survival follow-up period lasting for a maximum of 12 Months for each patient after their last dose of Neratinib or until initiation of additional anti-cancer therapy.

Key Inclusion Criteria:
- Histologically confirmed cancers in patients with activating ERBB Mutations and/or EGFR Amplifications and who are refractory to standard therapy or for which standard or curative therapy does not exists.
- Documented HER2 Mutation.
- At least one measurable lesion.
- Female patients with cancers known to secrete β-Human Chorionic Gonadotropin (hCG) are eligible if the pattern of serum β-hCG is suggestive of the malignancy and the pelvic ultrasound is negative for pregnancy.
- Left Ventricular Ejection Fraction (LVEF) ≥50% measured by Multiple-Gated Acquisition Scan (MUGA) or Echocardiogram (ECHO).

Key Exclusion Criteria:
- Prior treatment with any pan-HER / ERBB2-directed TKI (e.g., Lapatinib, Afatinib, Dacomitinib, Neratinib).
  - Exception: NSCLC patients who may have received Afatinib remain eligible.
- Patients who are receiving any other anticancer agents.
  - Exception: Patients on a stable dose of Bisphosphonates or Denosumab or Sex Hormone therapy in the case of Breast, Prostate, or Gynecological Cancers.
- Symptomatic or Unstable Brain Metastases.
- Demonstrates a QTc Interval >450 ms for men or >470 ms for women, or known history of Congenital QT-Prolongation or Torsades de Pointes (TdP).
- Significant chronic gastrointestinal disorder with diarrhea as a major symptom.
- Patients bearing certain Somatic ERBB Mutations, such as those that are subclonal in nature or resulting in the expression of truncated proteins including alterations that result in a premature stop codon or a change in reading frame.

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For additional information: https://clinicaltrials.gov/ct2/show/NCT01953926