Research Data Request: Efficacy of Crohn's Disease Treatment Stratified by Disease Phenotype

Vivli ID: 00004949

Research Team

Lead Investigator and Statistician

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Education or Qualifications
MD, PhD, Postdoctoral Fellow in Clinical Data Science, clinical speciality in IBD

Conflicts of Interest and Plan for Management
None

Additional Researchers

Research Proposal

General

Title of Proposed Research
Efficacy of Crohn's Disease Treatment Stratified by Disease Phenotype

Narrative summary explaining the relevance of the project to science and public health
Crohn's Disease is a heterogenous disorder encompassing distinct clinical phenotypes which arise from different biological pathways. Preclinical and clinical studies suggest that the efficacy of different agents does vary by disease phenotype, including anatomical location. Although these data are commonly collected in clinical trials, they have not been uniformly analyzed by strata nor meta-analyzed across studies by phenotype. As such, clinicians are left to recommend treatments based on best guess of efficacy rather than high-quality evidence. Therefore, we propose to meta-analyze this existing trial data as an important first step towards realizing precision medicine for Crohn's Disease.

Aims/Objectives and Hypotheses

Hypothesis: This study is an estimation study rather than one that aims to perform specific statistical hypothesis testing. However, as previously mentioned, the hypothesis that motivates this study is the hypothesis that currently approved Crohn's treatments will differ in efficacy when assessed within specific subgroups.

Objective: To optimally position current therapy for Crohn's disease by quantifying treatment efficacy stratified by disease phenotype, including anatomic location, behavior, and prior medication use (including a history of anti-Tumor Necrosis Factor-alpha failure). The latter will be stratified by shared treatment mechanism.

An exploratory objective is the analysis of treatment safety. We will assess the fitness of the data set to support an analysis of safety stratified by disease subgroups, although suspect that the number of included trials/patients, length of follow-up, and number of subgroups may severely curtail the statistical ability to detect many clinically-important signals.

An additional secondary objective is perform comparative effectiveness (e.g. ranking of efficacy for each given subgroup). Network meta-analysis may be more appropriate for this objective but may be hampered by limited trial number and patient numbers. While we plan to explore the potential of this methodology to yield useful results, achieving the first goal alone would represent a more than satisfactory outcome of this study.

Aims: We plan to quantify treatment efficacy by stratification along the lines of disease phenotype, including anatomic location, behavior (e.g. structuring, penetrating), and history of prior medication failure including anti-Tumor Necrosis Factor-alpha agents. To estimate treatment efficacy with maximal statistical power and minimal bias, we will perform a meta-analysis of randomized clinical trials.

Purpose of Analysis

NewResearchTreatmentEffectiveness
ConfirmingResearchTreatmentEffectiveness
ParticipantLevelDataMetanalysis

Study Design

Brief Description
Crohn's Disease (CD) is an idiopathic and morbid syndrome of gastrointestinal inflammation with risidurcurative or preventative strategies. It is a heterogeneous disease entity that encompasses multiple clinical phenotypes arising from a variety of underlying biological pathways. Although treatment options for CD historically have been limited, recent advances in novel agents with well-defined molecular targets. At the present time, patient response to any of these treatments remains largely unpredictable. Therefore, the choice of treatment largely lies in other factors such as side-effect profile and predicted efficacy.

Clinical experience, limited clinical trials[2], and preclinical models[3] all suggest that treatment response varies by disease phenotype. Although disease phenotypic classification – most commonly the Montreal Classification[4] – is collected on an individual patient level in all modern trials, it has gone without dedicated subgroup analysis in most of the pivotal trials that led to FDA approval.

As a result, clinicians are presently unequipped to make evidence-based treatment recommendations to their patients who encompass the full phenotypic spectrum of Crohn's disease. This therapeutic imprecision invariably leads to suboptimal disease control, excess exposure to medication-related risks, and increased healthcare costs.

Therefore, we propose to meta-analyze existing placebo-controlled clinical trial data in order to prioritize FDA-approved therapeutic candidates stratified by disease phenotype and help advance precision medicine for this morbid disease.

We have identified candidate studies for inclusion by systematic search of the clinicaltrials.gov database. The inclusion criteria are randomized, placebo-controlled, phase 2-4 clinical trials of biologics (anti-Tumor Necrosis Factor alpha, anti-alpha-4-beta-7-integrin, and anti-interleukin 12/23) approved for the treatment of Crohn’s Disease in the patient population of adults over the age of 18. The exclusion criteria include study termination due to poor enrollment, as well as studies/patients receiving non-FDA-approved doses or routes of administration. Most of the clinical trials data for FDA-approved biologics for Crohn's disease will be requested through the Vivli platform.

We will perform a mixed effects model meta-analysis, where treatment (active drug vs placebo), disease location, behavior, demographics (age, gender, race) and medication history (including anti-tumor necrosis factor failure) will be treated as fixed effects. Individual studies will be treated as random effects.

A secondary, exploratory goal of this work would be to perform comparative effectiveness (e.g. ranking of efficacy for each given subgroup). Network meta-analysis may be more appropriate for this objective but may be hampered by limited trial number and patient numbers. While we plan to explore the potential of this methodology to yield useful results, achieving the first goal alone would represent a more than satisfactory outcome of this study.

Outcome Elements Categorization/Definitions

The primary outcome measure will be treatment response as defined by the original study protocol. This will be dichotomized as a binary categorical variable for this study. The nearly all of the trials we have requested data from report this by an absolute or relative reduction in the Crohn's Disease Activity Index (e.g. "CDAI 150" defined as a CDAI score under 150, or "CR 70/100" defined by a 70 or 100 point reduction in CDAI score).

We are also requesting endoscopic scores and histologic results for each of the trials to the extent that this is available. In most of the trials we are requesting data on, this data has not been published but we suspect that the data exist and may be available insofar as it represents a common aspect of clinical care. Specifically, we would request scores corresponding to the baseline time (prior to trial start) as well as at the time of the primary endpoint.

We recognize that there are multiple endoscopic (e.g. CDEIS, SES-CD) and histologic (e.g. Geboes, Naini/Cortina, GHAS) scores and only some pairs of scores within each of these two categories have been formally studied from the standpoint of comparability/correlation. These variables would be treated as binary categorical variables as representing improvement or no improvement compared to baseline.

If the endoscopic or histologic data as above is not available, we do not foresee any limitations in our ability to proceed with this meta-analysis.

Main Predictor / Independent Variable

The main predictor variable is treatment assignment (e.g. Adalimumab, Vedolizumab, Placebo, etc.). These will each be defined as indicator/binary variables.

Other Variables of Interest

The phenotypic data we seek are disease location, behavior, age of onset, and the presence of perianal disease as defined by the Montreal classification, history of prior inflammatory-bowel disease medications (including antiTNF-alpha), number of prior biologic treatment failures, as well as reasons for treatment failure if available (e.g. primary or secondary loss of response, unacceptable side effects), concurrent medications at baseline (e.g. immunosuppressants, glucocorticoids, aminosalicylates, antibiotics), the presence of comorbid extraintestinal manifestations, demographics (age, gender, race/ethnicity, body mass index (or if unavailable, weight), duration of disease), smoking status at the time of the trial, history of prior intestinal surgery, history of prior C Diffcile infection, and baseline inflammatory biomarkers (C-Reactive Protein, Fecal Calprotectin, Erythrocyte Sedimentation Rate, and Albumin as available).

The clinical phenotypes listed above would be identified on the basis of what was documented by the physician/site investigator.

The above list of covariates adequately defines the desired phenotypes. Interactions will be explored in regression analysis but no unsupervised learning is planned.

Project Timeline

<table>
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<th>Target Analysis Start Date</th>
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https://search.vivli.org/myDataRequestDetailsRO/InProgress/bab8c4c4-2a0d-4fa8-8680-acd6b0cc5cf/RequestDetailsPrintView
Estimated Analysis Completion Date
10/24/20

Dissemination and Publication Plan

Plan
We suspect that this analysis will have broad interest within the gastroenterology community. When the work is complete we will submit abstracts for presentation at national gastroenterology meetings as well as to gastroenterology journals with a wide readership base. Specific target journals would be Gastroenterology, the American Journal of Gastroenterology, and Inflammatory Bowel Diseases.

Citations

Statistical Analysis Plan

General Plan

Missing Values: For missing values corresponding to the primary endpoint we will perform non-responder imputation. For missing data corresponding to other variables we will perform group mean imputation. We will repeat the analysis using exclusion of missing data and perform sensitivity analysis to assess the robustness of our conclusions to these methods.

Statistical Procedure:
We will perform a mixed effects linear model meta-analysis and weight individual study effect sizes using the DerSimonian-Laird method. Treatment (active drug vs placebo), as well as aforementioned covariates (e.g. disease location, behavior, demographics (age, gender, race) and medication history including anti-tumor necrosis factor failure) will be treated as fixed effects. Individual studies will be treated as random effects.

We will also explore network meta-analysis methods if the size of the available data will permit this.

Measures to Adjust for Multiplicity, Confounders, Heterogeneity:
We will assess study heterogeneity using Q and I-squared statistics. We will adjust for multiple testing using the Benjamin-Hochberg method to maintain a false discovery rate at the 0.05 level.

Sensitivity Analysis: We will assess the sensitivity of our model to intention-to-treat vs per-protocol analysis, inclusion vs exclusion of patients receiving non-FDA approved dosing, as well as statistical significance with and without multiple hypothesis correction. We will also test the sensitivity of our model using leave-one-out tests, and interactively perform the meta-analysis with n-1 studies to test if the result are influenced by one particular study.

QC Plan: We anticipate that many of the requested patient-level datasets have already undergone data-cleaning activities as a part of the study database lock process in the course of carrying out the trial. Our data-cleaning activities will focus on harmonizing the data between data-sets to facilitate meaningful meta-analytic cross-comparison and usage of the statistical software.

Programming Plans: We will be performing all data visualization and statistical analysis in the R programming environment. We will use the following statistical computing packages:
tidyverse
data.table
stringr
MICE
caret
lme4
metafor
plotly
DT
survminer
descTools
heatmap.2
lubridate
survival
RMarkdown
FrontierMatching
gemtc
netmeta

Countries where analysis will be conducted

| USA

Funding
General

Government Funding
YES
NIH NIDDK T32 DK007007, NIH/NCATS UCSF-CTSI TL1 TR001871

Employment Contracts
NO

Additional Contracts or Consultancies
NO

Commercial Funding
NO

Other Information

This is a revision of a previously submitted proposal with a number of important questions raised by our data contributors. We have made in-line edits to the document in an attempt to address each of these concerns; however some did not responses did not lend themselves naturally to the available categories of this document. For the sake of completeness and ease of review we will include all specific responses here: 1. A hypothesis is missing. Hypothesis: This study is an estimation study rather than one that aims to perform specific statistical hypothesis testing. However, as previously mentioned, the hypothesis that motivates this study is the hypothesis that currently approved Crohn’s treatments will differ in efficacy when assessed within specific subgroups. 2. The Outcome Elements Categorization doesn’t provide outcome specifics. 2.1. What outcome elements would be assessed? 2.2. How will differences in outcome measures used across studies be handled? The primary outcome measure will be treatment response as defined by the original study protocol. This will be dichotomized as a binary categorical variable for this study. The nearly all of the trials we have requested data from report this by an absolute or relative reduction in the Crohn’s Disease Activity Index (e.g. “CDAI 150” defined as a CDAI score under 150, or “CR 70/100” defined by a 70 or 100 point reduction in CDAI score). Although there may be slight differences in the precise outcome measure assessed across studies, our underlying model is that these are interchangeable proxies of the underlying latent (unmeasurable) variable of interest -- Disease Activity. Therefore, we plan to pool these outcomes. We have intentionally selected studies that include efficacy as a primary endpoint; so we anticipate that this data should be widely available. We are also requesting endoscopic scores and histologic results for each of the trials to the extent that this is available. In most of the trials we are requesting data on, this data has not been published but we suspect that the data exist and may be available insofar as it represents a common aspect of clinical care. Specifically, we would request scores corresponding to the baseline time (prior to trial start) as well as at the time of the primary endpoint. We recognize that there are multiple endoscopic (e.g. CDEIS, SES-CD) and histologic (e.g. Geboes, Naini/Cortina, GHAS) scores and only some pairs of scores within each of these two categories have been formally studied from the standpoint of comparability/correlation. We do not know what precisely has been collected and what scoring systems (if any) have been used. However, if the result of this data request indicates that most trials have this data available, then we will evaluate its fitness to support an analysis of drug efficacy measured by endoscopic improvement, the subject of a separate proposal. If the endoscopic or histologic data as above is not available, we do not foresee any limitations in our ability to proceed with this meta-analysis. 3. How will the differences in study designs be handled? 3.1. How will studies with induction phases, or with patients in maintenance be handled? 3.2. How will studies with different induction doses be handled? 3.3. Will the analysis distinguish between phase 2 and phase 3 studies? 3.4. How will differences in patient enrollment criteria be addressed? We recognize that there are some differences in study design both within and across medications. Prior to computing any pooled effect-size estimates that would combine data across studies, we will first assess the subgroup-level efficacy within individual studies, as well as compute the degree of heterogeneity using the I-squared statistic. Other measures we plan to take are as follows: 1) We are limiting our analysis to those patients who received either FDA-approved doses of the drug vs placebo, and will be looking purely at the endpoints pertinent to treatment efficacy as highlighted above (e.g. Clinical Response, CDAI, endoscopic histologic scores as available). Beyond this, however, we are not planning to treat Phase 2 or Phase 3 data any differently. 2) We will separately assess treatment effect for both induction and maintenance. These estimates will be pooled within each category (e.g. treatment response for maintenance at week 40 in one study with treatment response for maintenance at week 52). 3) We are otherwise not planning to make any adjustments for differences in patient enrollment criteria. Overall, we believe that these studies reflect the best efforts of different investigators to measure the same underlying latent variable -- treatment response -- and that some degree of heterogeneity will improve the robustness and generalizability of the meta-analytic effect size estimation we propose to do in this work. Our group has extensive expertise in performing meta-analysis – see Hu et al 2018 (https://www.sciencedirect.com/science/article/pii/S2211124718310805) as one example. 4. The varying types of response and the varying study designs makes results difficult to interpret. Even if response definition and study designs were harmonized, it is unclear how the proposed meta-analysis could achieve the objective to “optimally position current therapy for Crohn’s disease” – that sounds like an attempt to get at comparative effectiveness, where a network meta-analysis might be more appropriate, but the limited number active-controlled trials may preclude this. Please address. Our primary goal is to identify pairs of patient subgroups for which identified drugs are most likely to be beneficial. We hope to achieve this via the mixed-effect meta-analytic process as previously outlined. A secondary, exploratory goal of this work would be to perform comparative effectiveness (e.g. ranking of efficacy for each given subgroup). We agree that network meta-analysis may be more appropriate for the latter, and limitations to the success of such an analysis include limited trial and patient numbers as has been mentioned. Nevertheless, we feel that achieving the first goal alone would represent a more than satisfactory outcome of this study, and would provide tremendous value to the community of researchers and clinicians. 5. What is the approach for handling missing values? Will missing data be either excluded or imputed? Missing Values: For missing values corresponding to the primary endpoint we will perform non-responder imputation. For missing data corresponding to other variables we will perform group mean imputation. We will repeat the analysis using exclusion of missing data and perform sensitivity analysis to assess the robustness of our conclusions to these methods. 6. How will data from part of the Qc Plan be performed on datasets from studies which have already undergone data cleaning activities as part of the sponsors’ routine study database lock process? We anticipate that many of the requested patient-level datasets have already undergone data-cleaning activities as a part of the study database lock process in the course of carrying out the trial. Our data-cleaning activities will focus on harmonizing the data between data-sets to facilitate meaningful meta-analytic cross-comparison and usage of the statistical software. 7. Regarding phenotypes: 7.1. What phenotype scoring method will be used? Montreal? 7.2. What parameters are used to identify the phenotypes? This will help Sponsors confirm if the necessary parameters are available in each of the studies requested. 7.3. Are the phenotypes clinically validated? 7.4. How will they be stratified & analyzed? 7.5. How will the response rate for phenotypes in the active and placebo arms be analyzed? We requesting as much of the below disease phenotypic data as is available from all data contributors, and plan to assess and perform a subgroup analysis if these covariates are widely available across studies. The phenotypic data we seek are disease location, behavior, age of onset, and the presence of perianal disease as defined by the Montreal classification, history.
of prior inflammatory-bowel disease medications (including anti-TNF-alpha) as well as reasons for treatment failure if available (e.g. primary vs secondary loss of response), concurrent medications at the time of the trial (e.g. thiopurines, steroids), the presence of comorbid extraintestinal manifestations, demographics (age, gender, race/ethnicity, body mass index), smoking status at the time of the trial, history of prior intestinal surgery, history of prior C Difficile infection, and baseline inflammatory biomarkers (C-Reactive Protein, Fecal Calprotectin, Erythrocyte Sedimentation Rate). The clinical phenotypes listed above would be identified on the basis of what was documented by the physician upon study enrollment. These features are all well-known and commonly-studied covariates in the Inflammatory Bowel Disease clinical research literature. Most of the above would be naturally classified as binary/categorical variables and would be stratified as such.

Exceptions include age and BMI, which would be classified by quartile and by the WHO classification respectively. The response rates for active and placebo arms would be by the primary outcome measure of efficacy specified by the original study protocol, as previously specified. 8. In the Outcomes section, a parallel analysis is mentioned. Please provide more information about this. This section has been revised. 9. It is not clear which studies will be part of this metaanalysis 9.1. What was the criteria by which the studies requested were identified? We have identified candidate studies for inclusion by systematic search of the clinicaltrials.gov database. The inclusion criteria are randomized, placebo-controlled, phase 2-4 clinical trials of biologics (anti-Tumor Necrosis Factor alpha, anti-alpha-4-beta-7-integrin, and anti-interleukin 12/23) approved for the treatment of Crohn’s Disease in the patient population of adults over the age of 18. The exclusion criteria are study termination by the trial sponsor due to poor enrollment, and studies/patients receiving non-FDA-approved doses or routes of administration. 9.2. In the Narrative, it is mentioned that this proposed meta-analysis will prioritized FDA-approved therapeutic candidates. However, all FDA approved products for CD are not represented in the study list (missing: infliximab, certolizumab pegol, ustekinumab). Conversely, 3 tofacitinib studies were initially listed as included in the analysis, however tofacitinib is not FDA approved for CD (which have subsequently been declined to be shared by Pfizer and no longer part of the study design, however, does still leave the question stated above as to what criteria was used to identify the requested studies ) Most of the clinical trials data for FDA-approved biologics for Crohn’s disease will be requested through the Vivli platform. Infliximab, Certolizumab Pegol, and Ustekinumab clinical trials data are not available through Vivli, however, and therefore will be requested from the YODA platform (yoda.yale.edu). 10. How will safety be assessed, as the warnings with the drugs vary. We will assess the fitness of the data set to support an analysis of safety stratified by disease subgroups, although suspect that the number of included trials/patients, length of follow-up, and number of subgroups may severely curtail the statistical ability to detect many clinically-important signals. Other relevant notes are listed below: 1) Our institution does not require IRB approval for this proposed study. 2) We will be performing all data visualization and statistical analysis in the R/RStudio programming environment. We will use the statistical computing packages: tidyrse data table stringr MICE caret lme4 metafor plotly DT survmir desctools heatmap.2 lubridate survival RMarkdown FrontierMatching gemtc netmeta

Requested Studies

A Multicenter, Randomized, Double-Blind, Placebo Controlled Study to Evaluate the Efficacy and Safety of Adalimumab for the Induction and Maintenance of Clinical Remission in Chinese Patients With Moderately to Severely Active Crohn’s Disease and Elevated High-Sensitivity C-reactive Protein

PI:
Sponsor: AbbVie
Study ID: NCT02499783
IRP/Approver: AbbVie
Data Request ID: 00004949
Sponsor ID: M14-233

A Phase 3, Randomized, Placebo-Controlled, Blinded, Multicenter Study of the Induction of Clinical Response and Remission by Vedolizumab in Patients With Moderate to Severe Crohn’s Disease

PI:
Sponsor: Takeda
Study ID: NCT01224171
IRP/Approver: Wellcome Trust
Data Request ID: 00004949
Sponsor ID: C13011

A Phase 3, Randomized, Placebo-Controlled, Blinded, Multicenter Study of the Induction and Maintenance of Clinical Response and Remission by Vedolizumab (MLN0002) in Patients With Moderate to Severe Crohn’s Disease

PI:
Sponsor: Takeda
Study ID: NCT00783692
IRP/Approver: Wellcome Trust
Data Request ID: 00004949
Sponsor ID: C13007

A Multi-Center, Randomized, Double-blind, Placebo-controlled Study of Adalimumab for the Induction of Clinical Remission in Japanese Subjects With Crohn’s Disease

PI:
Sponsor: AbbVie
Study ID: NCT00445939
IRP/Approver: AbbVie
Data Request ID: 00004949
Sponsor ID: M04-729

A Multi-Center, Randomized, Double-blind, Placebo-controlled Study of Adalimumab for the Maintenance of Clinical Remission in Japanese Subjects With Crohn’s Disease

PI:
Sponsor: AbbVie
Study ID: NCT00445432
IRP/Approver: AbbVie
Data Request ID: 00004949
Sponsor ID: M06-837

A Multicenter, Randomized, Double-Blind, Placebo-Controlled Study of the Human Anti-TNF Monoclonal Antibody Adalimumab Endoscopy Trial to Evaluate the Effects on Mucosal Healing in Subjects With Crohn’s Disease Involving the Colon

PI:
Sponsor: AbbVie
Study ID: NCT00348283
IRP/Approver: AbbVie
Data Request ID: 00004949
Sponsor ID: M05-769
ACCENT I - A Randomized, Double-blind, Placebo-controlled Trial of Anti-TNFα Chimeric Monoclonal Antibody (Infliximab, Remicade) in the Long-term Treatment of Patients With Moderately to Severely Active Crohn's Disease

PI:
Sponsor: Centocor, Inc.
Study ID: NCT00207662
IRP/Approver: Johnson & Johnson
Data Request ID: 00004949
Sponsor ID: CR004771

A Multi-Center, Randomized, Double-Blind, Placebo-Controlled Study of the Human Anti-TNF Monoclonal Antibody Adalimumab for the Induction of Clinical Remission in Subjects With Moderate to Severe Crohn's Disease Who Have Lost Response or Are Intolerant to Infliximab

PI:
Sponsor: AbbVie
Study ID: NCT00105300
IRP/Approver: AbbVie
Data Request ID: 00004949
Sponsor ID: M05-591

Multicenter, Randomized, Double-Blind, Active Controlled Trial Comparing REMICADE® (Infliximab) and REMICADE Plus Azathioprine to Azathioprine in the Treatment of Patients With Crohn's Disease Naive to Both Immunomodulators and Biologic Therapy

PI:
Sponsor: Centocor Ortho Biotech Services, L.L.C.
Study ID: NCT00094458
IRP/Approver: Johnson & Johnson
Data Request ID: 00004949
Sponsor ID: CR004804

A Phase III, Multicenter, Double-Blind, Placebo-Controlled Study of the Safety and Efficacy of Intravenous Antegren(TM) (Natalizumab) in Subjects With Moderately to Severely Active Crohn's Disease With Elevated C-Reactive Protein

PI:
Sponsor: Biogen
Study ID: NCT00078611
IRP/Approver: Biogen
Data Request ID: 00004949
Sponsor ID: ELN100226-CD307

A Multi-Center Randomized, Double-Blind, Placebo-Controlled Study of the Human Anti-TNF Monoclonal Antibody Adalimumab for the Induction and Maintenance of Clinical Remission in Subjects With Crohn's Disease

PI:
Sponsor: AbbVie
Study ID: NCT00077779
IRP/Approver: AbbVie
Data Request ID: 00004949
Sponsor ID: M02-404

A Phase II Study of the Human Anti-TNF Antibody Adalimumab for the Induction of Clinical Remission in Subjects With Crohn's Disease

PI:
Sponsor: AbbVie
Study ID: NCT00055523
IRP/Approver: AbbVie
Data Request ID: 00004949
Sponsor ID: M02-403

A Multi-Center, Randomized, Double-Blind, Placebo-Controlled Study of the Human Anti-TNF Monoclonal Antibody Adalimumab for the Maintenance of Clinical Remission in Subjects With Crohn's Disease

PI:
Sponsor: AbbVie
Study ID: NCT00055497
IRP/Approver: AbbVie
Data Request ID: 00004949
Sponsor ID: M02-433

A Phase 3 International, Multicenter, Double-blind, Placebo-controlled Study of the Safety, Efficacy, and Tolerability of Intravenous Antegren (Natalizumab) in Subjects With Moderate to Severely Active Crohn's Disease

PI:
Sponsor: Biogen
Study ID: NCT00032799
IRP/Approver: Biogen
Data Request ID: 00004949
Sponsor ID: CD301


PI:
Sponsor: Biogen
Study ID: NCT00032786
IRP/Approver: Biogen
Data Request ID: 00004949
Sponsor ID: CD303

A Phase 3, Randomized, Double-blind, Placebo-controlled, Parallel-group, Multicenter Study to Evaluate the Safety and Efficacy of Ustekinumab Induction Therapy in Subjects With Moderately to Severely Active Crohn's Disease (UNITI-2)

PI:
Sponsor: Janssen Research & Development, LLC
Study ID: NCT01369342
IRP/Approver: Johnson & Johnson
A Phase 3, Randomized, Double-blind, Placebo-controlled, Parallel-group, Multicenter Study to Evaluate the Safety and Efficacy of Ustekinumab Induction Therapy in Subjects With Moderately to Severely Active Crohn's Disease Who Have Failed or Are Intolerant to TNF Antagonist Therapy (UNITI-1)

PI:
Sponsor: Janssen Research & Development, LLC
Study ID: NCT01369329
IRP/Approver: Johnson & Johnson
Data Request ID: 00004949
Sponsor ID: CR018415

Prospective, Multicenter, Randomized, Double-Blind, Placebo-Controlled Trial Comparing REMICADE (Infliximab) and Placebo in the Prevention of Recurrence in Crohn's Disease Patients Undergoing Surgical Resection Who Are at Increased Risk of Recurrence

PI:
Sponsor: Janssen Biotech, Inc.
Study ID: NCT01190839
IRP/Approver: Johnson & Johnson
Data Request ID: 00004949
Sponsor ID: CR017080

A Phase 2b, Multicenter, Randomized, Double-blind, Placebo-controlled, Parallel Group Study to Evaluate the Efficacy and Safety of Ustekinumab Therapy in Subjects With Moderately to Severely Active Crohn's Disease Previously Treated With TNF Antagonist Therapy

PI:
Sponsor: Centocor, Inc.
Study ID: NCT00771667
IRP/Approver: Johnson & Johnson
Data Request ID: 00004949
Sponsor ID: CR005287

A Placebo-Controlled, Dose-Ranging Study Followed by a Placebo-Controlled, Repeated-Dose Extension of Anti-TNF Chimeric Monoclonal Antibody (cA2) in the Treatment of Patients With Active Crohn's Disease

PI:
Sponsor: Centocor, Inc.
Study ID: NCT00269854
IRP/Approver: Johnson & Johnson
Data Request ID: 00004949
Sponsor ID: CR006256

ACCENT II - A Randomized, Double-blind, Placebo-controlled Trial of Anti-TNF Chimeric Monoclonal Antibody (Infliximab, Remicade) in the Long Term Treatment of Patients With Fistulizing CROHN'S DISEASE

PI:
Sponsor: Centocor, Inc.
Study ID: NCT00265122
IRP/Approver: Johnson & Johnson
Data Request ID: 00004949
Sponsor ID: CR018421

A Phase 3, Randomized, Double-blind, Placebo-controlled, Parallel-group, Multicenter Study to Evaluate the Safety and Efficacy of Ustekinumab Maintenance Therapy in Subjects With Moderately to Severely Active Crohn's Disease

PI:
Sponsor: Janssen Research & Development, LLC
Study ID: NCT01369355
IRP/Approver: Johnson & Johnson
Data Request ID: 00004949
Sponsor ID: CR018421

A Multicenter, Randomized, Phase 2a Study of Human Monoclonal Antibody to IL-12p40 (CNTO 1275) in Subjects With Moderately to Severely Active Crohn's Disease

PI:
Sponsor: Centocor, Inc.
Study ID: NCT00152490
IRP/Approver: Johnson & Johnson
Data Request ID: 00004949
Sponsor ID: CR005287

I would like to have access to the following R Packages in the R Studio software environment when performing this meta-analysis: tidyverse data.table stringr MICE caret lme4 metafor plotly DT survminer descTools heatmap.2 lubridate survival RMarkdown FrontierMatching

PI:
Data Contributor: I WILL BRING MY OWN
Study ID: Not Applicable
Data Request ID: 00004949
Sponsor ID: Not Applicable

A Phase III Multi-national, Multi-centre, Double-blind Placebo-controlled Parallel Group, 26 Week Study to Assess the Safety and Efficacy of the Humanised Anti-TNF PEG Conjugate, CDP870 400 mg sc, (Dosed at Weeks 0, 2, 4 Then 4-weekly to Week 24), in the Treatment of Patients With Active Crohn's Disease

PI:
Sponsor: UCB
Study ID: NCT00152490
IRP/Approver: Wellcome Trust
Data Request ID: 00004949
Sponsor ID: C87031

A Phase III Multi-national, Multi-centre, Double-blind Placebo-controlled Parallel Group, 26 Week Study to Assess the Maintenance of Clinical Response to Humanised Anti-TNF PEG Conjugate,
CDP870 400 mg sc. (Dosed 4-weekly From Weeks 8 to 24), in the Treatment of Patients With Active Crohn's Disease Who Have Responded to Open Induction Therapy (Dosed at Weeks 0, 2 and 4) With CDP870

PI:
Sponsor: UCB
Study ID: NCT00152425
IRP/Approver: Wellcome Trust
Data Request ID: 00004949
Sponsor ID: C87032

Phase IIb, Multinational, Randomized, Double-blind, Placebo-controlled Trial to Assess the Efficacy and Safety of Certolizumab Pegol, a Pegylated Fab' Fragment of a Humanized Anti-Tumor Necrosis Factor (TNF)-Alpha Monoclonal Antibody, Administered in Subjects With Moderately to Severely Active Crohn's Disease.

PI:
Sponsor: UCB
Study ID: NCT00552058
IRP/Approver: Wellcome Trust
Data Request ID: 00004949
Sponsor ID: C87085

A Phase II, Multi-center, Double-blind, Placebo-controlled, Parallel-group, Dose-response Study to Assess the Safety and Efficacy of CDP870/Certolizumab Pegol, Dosed Subcutaneously in Patients With Active Crohn's Disease

PI:
Sponsor: UCB
Study ID: NCT00291668
IRP/Approver: Wellcome Trust
Data Request ID: 00004949
Sponsor ID: C87037

Phase IIIb Open-label Induction and Double-blind Comparison of 2 Maintenance Schedules Evaluating Clinical Benefit and Tolerability of Certolizumab Pegol in Crohn's Disease Patients With Prior Loss of Response or Intolerance to Infliximab

PI:
Sponsor: UCB
Study ID: NCT00308581
IRP/Approver: Wellcome Trust
Data Request ID: 00004949
Sponsor ID: C87042

Attached Files

NO FILES IN PACKAGE