CERTARA

Quantify CD Clinical Outcomes Database

Summary Information

The current version of the database contains information from randomized controlled trails on all current biologic and small molecule drugs that are evaluated for moderate-to-severe Crohn's disease in patients that failed conventional treatment.

Table 1. Summary information

Parameter	Description
format	Excel or KEEP format
indications	cd, cd in children
references	91
trials	77
trial.arms	211
patients	16,595
data.rows	8,210
compounds	abatacept, adalimumab, alicaforsen, apilimod mesylate, azathioprine, ccx282-b, certolizumab, ciprofloxacin, etanercept, hydrocortisone, infliximab, lenalidomide, natalizumab, ni-0401, onercept, placebo, rhuil-10, rifaximim-eir, sargramostim, secukinumab, semapimod, teduglutide, tofacitinib, ustekinumab, vedolizumab
key.efficacy.endpoints	anti-drug antibodies positive, cdai score, cdeis score, clinical remission, clinical response, crp, ibdq score
key.safety.endpoints	abdominal distension, abdominal pain, abscess, ae any, ae drug related, ae serious, ae serious drug related, anemia, arthralgia, asthenia, back pain, bronchitis, cd exacerbation, cough, death, demyelination, diarrhea, dizziness, dropout ae, dropout loe, dropout other, dropout total, dyspepsia, fatigue, flatulence, headache, hypersensitivity reaction, infection any, infection serious, influenza, infusion reaction, injection site pain, injection site reaction, insomnia, lupus-like reaction, malignancy, nasopharyngitis, nausea, nausea/vomiting, opportunistic infection, pain, pharyngitis, pharyngolaryngeal pain, pyrexia, rash, sinusitis, tuberculosis, upper respiratory tract infection, urinary tract infection, vomiting

Features and Benefits

Databases can be delivered as Excel files or through a web-based access platform.

General features of the database:

- **Comprehensive:** includes information for marketed drugs; data sources include journal publications, conference posters, regulatory reviews, etc.
- **Ease of tracking**
- **Flexibility:** the database design allows for quick updates as well as expansions to include additional indications/drugs/endpoints/trials
- **Analysis-ready:**
  - Background treatments are categorized
  - Missing covariates are imputed
  - Endpoint data are calculated when applicable
  - Units are normalized
- **Customizability**

Benefits of the web-based access tool:

- **Instant access to up-to-date data:**
  - Database will be updated throughout the year, with timestamps for each record which help users to keep track of new updates
  - Web platform acts as a single point of access to all clinical trial databases
- **User-friendly interface:** users can explore and visualize data through a web interface with no requirement for software installation
- **Easy to communicate data and analysis results:** data summary, plotting functions are embedded

Potential Applications

Understand relative efficacy and safety profiles

This type of analysis is important and frequently done, especially for compounds in crowded markets. However, large trial-to-trial variations make direct numbers comparison less compelling and sometimes even meaningless. Clinical outcomes databases capture a broad range of trial-specific information, which enables comparative efficacy and safety analysis NORMALIZED by variants such as existing therapy, placebo response, patient characteristics, etc.

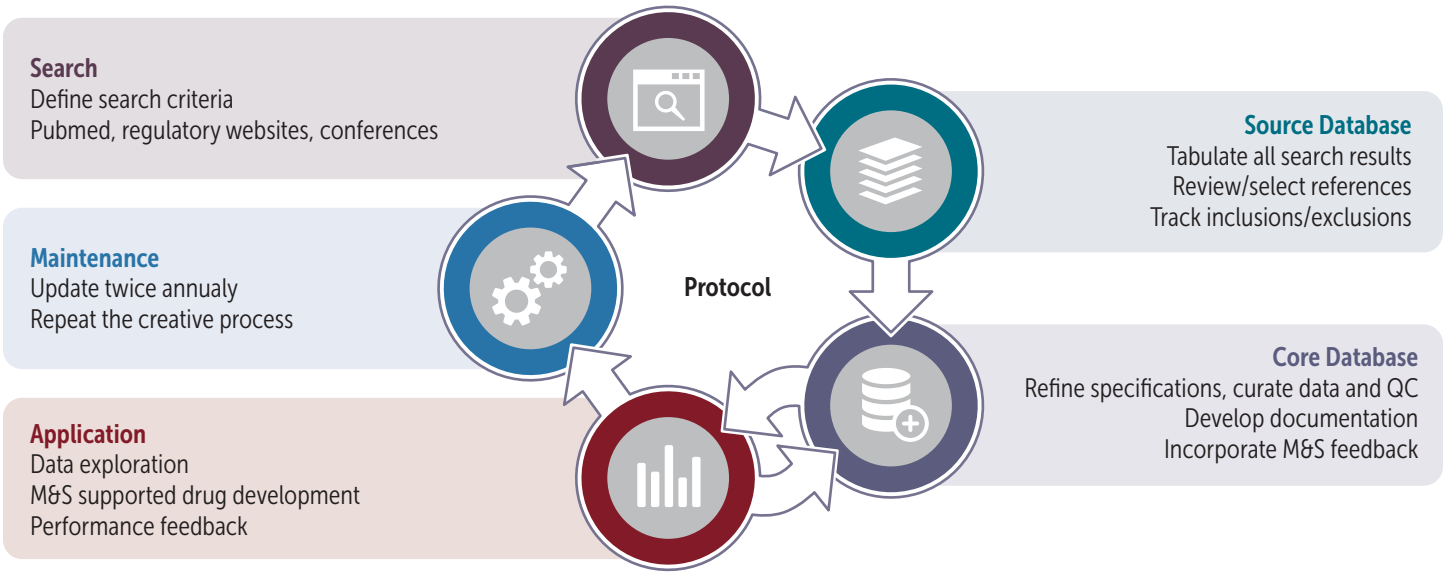
Link/Scale different endpoints or indications

Clinical outcomes databases aggregate endpoint data from tens of thousands of patients, making it possible to make reasonable predictions of clinical outcomes from existing data. For example, clinical teams find it valuable to predict a compound's performance in late phase development based on early development results.

Organization and Structure

This product consists of two databases, the source database and the clinical outcomes database (core database), developed for CD. The source database is a database that maintains the sources of information identified by searches and reviewed for inclusion or exclusion from the database. The clinical outcomes database contains the information on trial, treatment and patients characteristics and safety and efficacy results of the trials identified for inclusion in the database.

The following is a flowchart showing the process with which databases are created, optimized and updated.



Overview of the CD Source Database

The primary data sources were controlled clinical trials published in the medical literature. A secondary source of information was published abstracts or presentations of clinical trial data from conferences and corporate websites.

363 references were identified and documented in the source database of which a total of 91 references for CD were selected for inclusion in the database after careful review of the abstracts. The detailed reference information as well as reasons for exclusion is recorded to facilitate potential future expansion of the database. The 91 references selected for inclusion in the database provide information on 77 unique trials.

Overview of the CD Clinical Outcomes Database

The clinical outcomes database contains information from 77 trials, representing 211 unique treatment arms and over 16,595 patients. There are a total of 8,210 rows in the database. The table below provides an overview of the available data for randomized treatments, ie, treatments that were started at time of randomization and not present as background therapy. The tables below show the number of treatment arms and the number of patients for each study drug.

Table 2. Number of trials, treatment arms and patients by drug

randomized.drug	trials	arms	patients
abatacept	2	4	367
adalimumab	10	16	1382
alicaforsen	5	11	516
apilimod mesylate	1	2	44
azathioprine	2	2	193
azathioprine+infliximab	1	1	169
ccx282-b	2	4	438
certolizumab	7	13	1588
ciprofloxacin	1	1	11
etanercept	1	1	23
hydrocortisone	1	1	23
infliximab	17	28	1016
infliximab+azathioprine	1	1	67
infliximab+mtx	1	1	11
lenalidomide	1	2	58
natalizumab	6	8	1413
ni-0401	1	6	33
onercept	1	4	170
placebo	64	64	5164
rhuil-10	2	8	335
rifaximim-eir	1	3	308
sargramostim	2	2	168
secukinumab	1	1	39
semapimod	2	4	109
teduglutide	1	3	75
tofacitinib	1	3	105
ustekinumab	6	9	595
vedolizumab	5	8	1769
TOTAL	**77**	**211**	**16189**

Table 3. Number of trials, treatment arms and patients by efficacy endpoints
(For endpoints that are reported by more than 3 trials)

endpoint	trials	arms	patients
abdominal abscess	3	6	585
abdominal distension	6	16	499
abdominal pain	38	98	10451
abdominal tenderness	4	14	1115
abscess	6	18	1779
ae any	52	140	13603
ae drug related	16	42	4931
ae serious	50	130	14090
ae serious drug related	13	32	3450
ae severe	3	6	290
alanine aminotransferase elevation	3	7	352
alopecia	3	8	291
anemia	7	16	1659
anti-dna antibodies positive	4	8	892
anti-drug antibodies positive	12	27	4839
anti-nuclear antibodies positive	5	10	1554
anxiety	3	8	243
arthralgia	33	85	8610
asthenia	6	14	1022
back pain	14	40	3289
basal cell carcinoma	3	6	1082
bronchitis	6	18	1069
cd exacerbation	22	50	5973
cdai score	41	119	8925
cdeis score	11	38	1634
chills	3	13	510
clinical relapse	5	11	446
clinical remission	64	171	15042
clinical response	57	156	14209
congestive heart failure	4	9	457
constipation	4	12	501
cough	8	19	1926
crohn's disease	4	10	743
crp	32	88	7485
death	28	79	7168
demyelination	5	11	968
diarrhea	13	42	3956
dizziness	21	58	4086
dropout ae	50	139	12458
dropout loe	32	89	7080
dropout other	19	57	4301
dropout total	43	120	9526
dyspepsia	9	23	1667
dyspnea	4	10	372

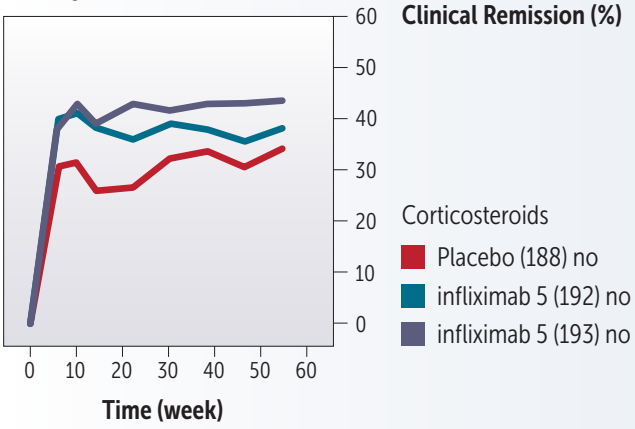
esr	4	10	162
fatigue	30	77	7951
fistula closure	3	6	798
flatulence	6	18	771
gastroenteritis	3	6	341
gastrointestinal disorder	3	12	620
headache	49	133	13170
hematologic ae	3	6	329
herpes simplex	3	8	1104
herpes zoster	3	8	407
hospitalization	4	9	1535
hypersensitivity reaction	5	10	2159
ibdq - bowel function	8	18	2401
ibdq - emotional function	7	16	2272
ibdq - social function	7	16	2272
ibdq - systemic function	8	18	2401
ibdq score	33	91	7492
infection any	31	82	8942
infection serious	25	60	7356
influenza	13	35	3383
infusion reaction	11	28	3619
injection site bruising	4	11	1531
injection site pain	9	21	2933
injection site reaction	16	43	3959
insomnia	7	19	609
leukopenia	3	7	579
lupus-like reaction	7	17	1476
lymphocyte count	3	6	129
lymphoma	5	14	1367
malignancy	12	28	1444
mouth ulceration	3	10	680
myalgia	4	13	559
nasopharyngitis	29	73	8281
nausea	28	80	8790
nausea/vomiting	16	40	3774
neoplasm	3	10	667
opportunistic infection	13	31	2161
pain	7	17	1773
pancreatitis	3	6	334
perianal abscess or fistula	4	8	554
pharyngitis	7	22	1667
pharyngolaryngeal pain	6	12	1457
pneumonia	4	10	908
pruritus	5	11	1042
pyrexia	28	74	8253
rash	15	36	3110
rectal haemorrhage	3	10	810

sf36 - bodily pain scale	5	11	1755
sf36 - emotional scale	5	11	1755
sf36 - general health	4	9	1626
sf36 - mental component summary	6	14	1845
sf36 - mental health scale	6	16	2084
sf36 - physical component summary	4	9	1626
sf36 - physical function scale	6	16	2084
sf36 - physical role scale	4	9	1626
sf36 - social	4	9	1626
sf36 - vitality	3	7	1198
sinusitis	9	25	1835
skin disorders	4	9	395
small intestinal obstruction	4	11	885
stomatitis	3	6	487
surgery	3	8	1546
sustained clinical remission	7	18	2755
sustained clinical response	3	6	581
syncope	4	8	548
time to clinical response	3	7	818
time to loss of clinical response	3	5	678
transaminases increased	4	10	1069
tuberculosis	8	22	1499
ulceration	3	6	272
upper abdominal pain	3	6	237
upper respiratory tract infection	26	65	6397
urinary tract infection	15	39	5109
vaginal infection	3	10	564
viral infections	3	8	836
vomiting	20	54	6305
TOTAL	**77**	**211**	**419528**

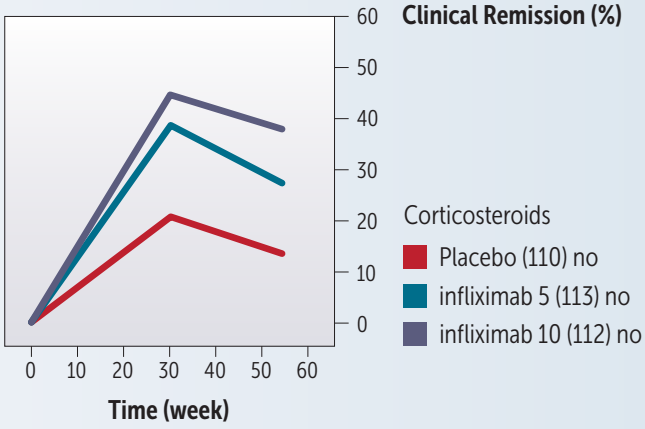
Example Plots of Actual Trial Data

The following graph shows examples of the time course data of clinical remission and mayo score, respectively, in selected trials.

Rutgeerts P 2004 (accent-1)



Hanauer SB 2002 (accent-1)



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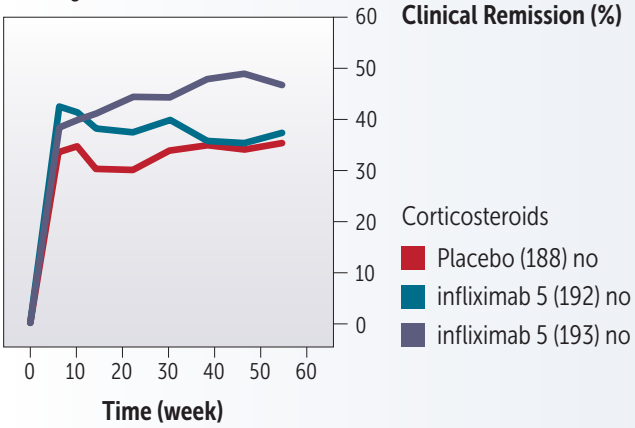
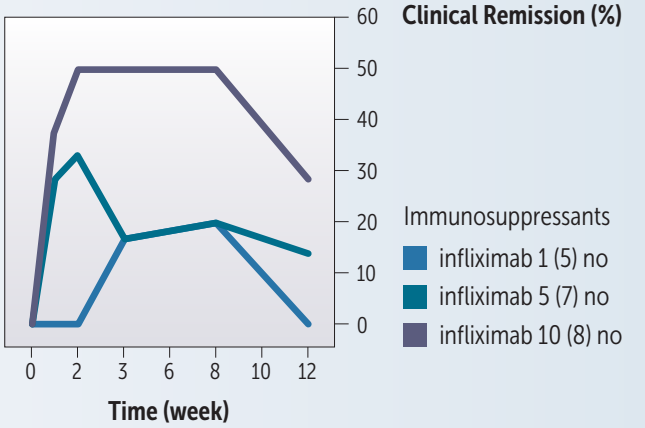
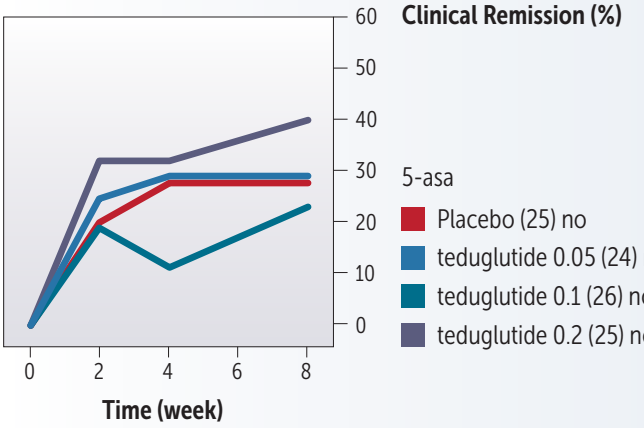


Baldassano R 2003



Buchman AL 2010



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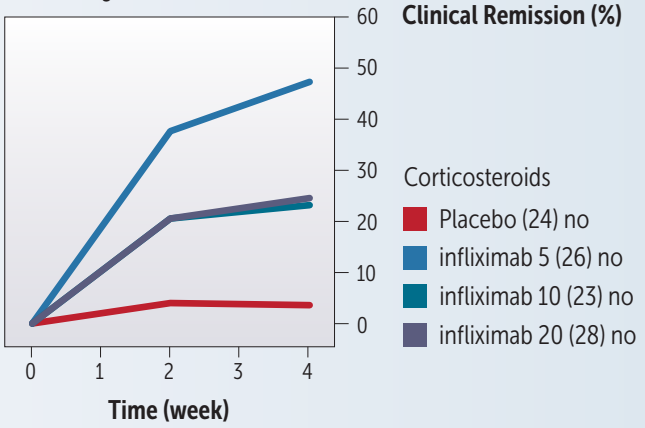
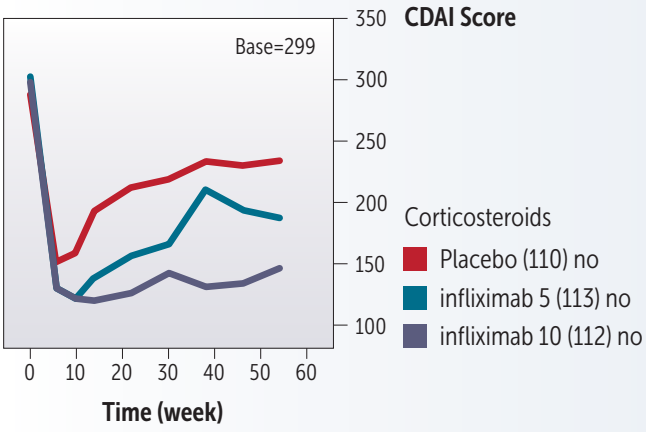
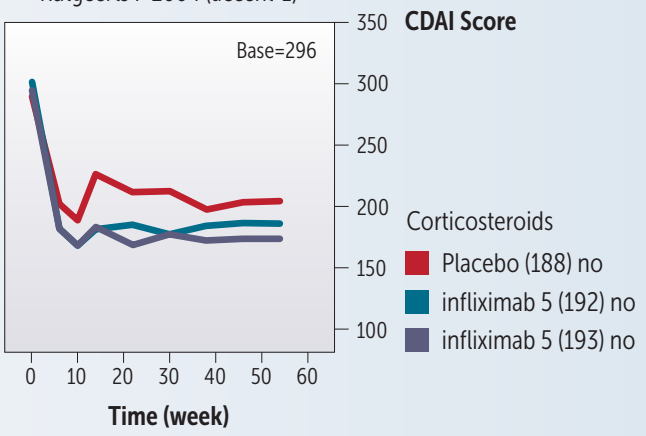


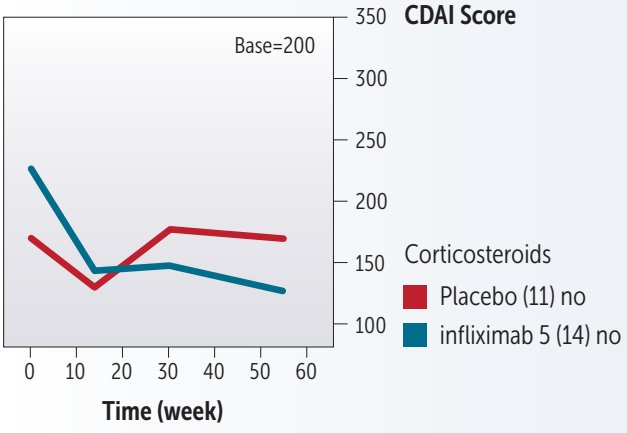
Hanauer SB 2002 (accent-1)



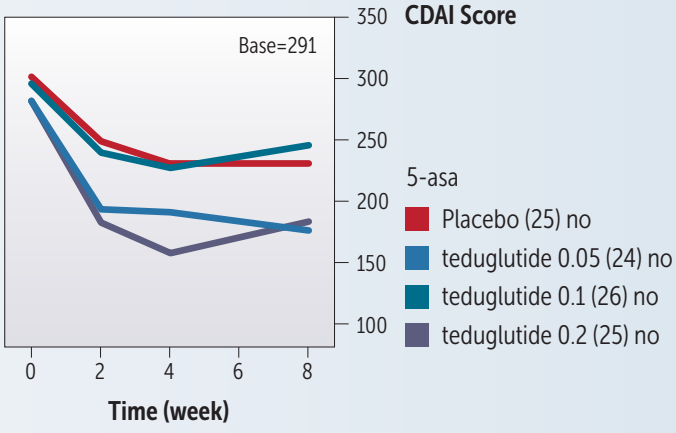
Rutgeerts P 2004 (accent-1)



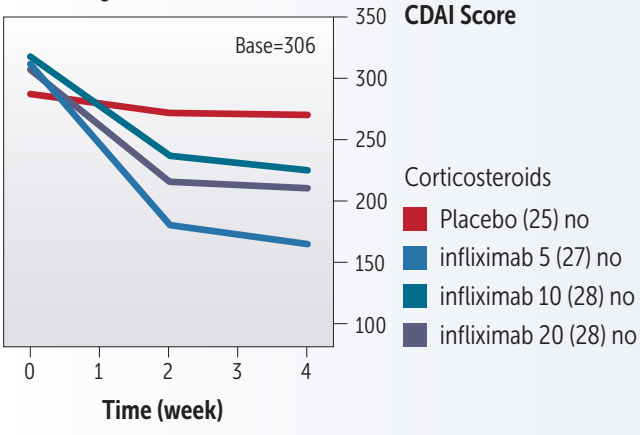
Sands BE 2004 (accent-2)



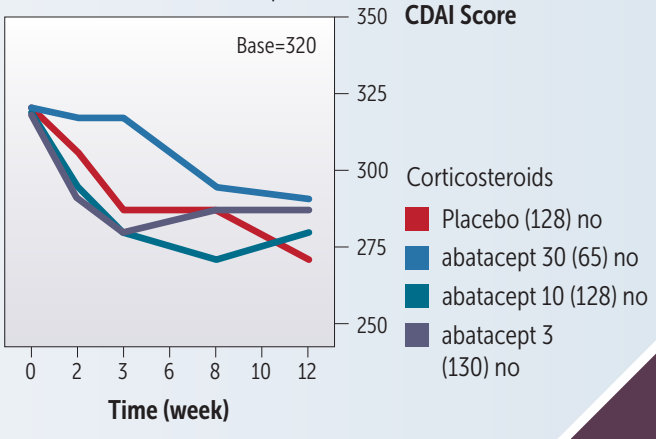
Buchman AL 2010



Targan SR 1997 (ca2)



Sandborn WJ 2012 (cd-ip)



About Certara

Certara is a leading provider of decision support technology and consulting services for optimizing drug development and improving health outcomes. Certara's solutions, which span the drug development and patient care lifecycle, help increase the probability of regulatory and commercial success by using the most scientifically advanced modeling and simulation technologies and regulatory strategies. Its clients include hundreds of global biopharmaceutical companies, leading academic institutions and key regulatory agencies.

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