

Online Supplementary Appendix

Figures and Screenshots (from 1 February 2018)

Figure S1: Accessing Archival Versions of a ClinicalTrials.gov Study Record via “History of Changes.” (A) Click on the History of Changes link near the bottom of a study record in the “Study Details” format to access previously posted versions of that record. (B) On the ClinicalTrials.gov archive site, select the two versions to view and click “Compare.” By default, the record as initially registered (i.e., “Version 1”) and the most recent version that is currently displayed on the public site are selected.

ClinicalTrials.gov archive

History of Changes for Study: NCT00136318

Escitalopram for the Prevention of PEGASYS-associated Depression in Hepatitis C Virus-infected Patients

[Latest version on ClinicalTrials.gov](#)

- A study version is represented by a row in the table.
- Select two study versions to compare. One each from columns A and B.
- Choose either the “Merged” or “Side-by-Side” comparison format to specify how the two study versions are to be displayed. The Side-by-Side format only applies to the Protocol section of the study.
- Click “Compare” to do the comparison and show the differences.
- Select a version’s date link to see a rendering of the study for that version.
- Edits or deletions will be displayed in **red** and additions will be displayed in **green**.
- The yellow choices in the table indicate the study versions currently compared below. A yellow row indicates the study version being viewed.

Compare Study Version A to B

Version	A	B	Date	Changes
1	<input checked="" type="radio"/>	<input type="radio"/>	August 26, 2005	Nothing (earliest Version on record)
2	<input type="radio"/>	<input type="radio"/>	November 1, 2005	Study Status and Study Identification
3	<input type="radio"/>	<input type="radio"/>	November 3, 2005	Conditions and Study Status
4	<input type="radio"/>	<input type="radio"/>	November 21, 2005	Eligibility, Study Description and Study Status
5	<input type="radio"/>	<input type="radio"/>	December 12, 2005	Study Status
6	<input type="radio"/>	<input type="radio"/>	May 22, 2006	Contacts/Locations, Study Status and Oversight
7	<input type="radio"/>	<input type="radio"/>	July 24, 2006	Contacts/Locations and Study Status
8	<input type="radio"/>	<input checked="" type="radio"/>	March 20, 2013	Study Status, Contacts/Locations, Arms and Interventions, Study Design, Study Identification, Eligibility, Oversight, Results, Outcome Measures, Study Description and Sponsor/Collaborators

Compare Comparison Format: Merged Side-by-Side

Figure S2: Viewing Changes in Archival Versions of a ClinicalTrials.gov Study Record.

Entries and text displayed in the earlier version but deleted from the later version are shown with red strikethrough. Those displayed in the later version only are shown in green-highlighted, italicized font. For example, under the second bullet of the Primary Outcome Measure, “Hamilton Depression Rating Scale” was changed to “Montgomery Asberg Depression Scale.” [See Zarin & Tse (2013)]

Changes (Merged) for Study: NCT00136318
August 26, 2005 (v1) -- March 20, 2013 (v8)

Changes in: [Study Status](#), [Contacts/Locations](#), [Arms and Interventions](#), [Study Design](#), [Oversight](#),
[Study Identification](#), [Eligibility](#), [Conditions](#), [Results](#), [Outcome Measures](#), [Study Description](#) and
[Sponsor/Collaborators](#)

Study Description

Brief Summary: ~~Primary Endpoints~~ *Primary end points*

- *incidence of depression defined as a Montgomery Asberg Depression Scale Score (MADRS) of 13 or higher during antiviral therapy (up to 48 weeks, depending on genotype)*
- effect of an antidepressive pre-treatment over two weeks and a continuously concomitant treatment with Escitalopram (*S-citalopram*) on frequency and severity of depression in patients with chronic hepatitis C (HCV) treated with Peg-interferon alfa-2a (PEGASYS) and ribavirin. ~~The occurrence of moderate to severe depression is~~,
measured by the ~~Hamilton~~ *Montgomery Asberg* Depression Rating Scale ~~24 weeks after starting interferon therapy.~~

Figure S3: Viewing Changes in Outcome Measures of a ClinicalTrials.gov Study Record via the “Tabular View.” The Tracking Information section of a study record in the “Tabular View” format displays for outcome measures the (A) original entry as first registered and (B) the most recent (current) entry and the date on which it was submitted. In this example, no secondary outcome measures were submitted during the initial registration.

The screenshot shows the 'Tracking Information' section of a study record in 'Tabular View'. The 'Tabular View' tab is circled in red. The section contains two rows of information:

B	<p>Current Secondary Outcome Measures <small>ICMJE</small> (submitted: March 20, 2013)</p>	<ul style="list-style-type: none"> • Proportion of Patients Without Depression (Defined as a MADRS Score of 13 or Higher) [Time Frame: Pat therapy] Number of patients who did not develop at any time of antiviral treatment (up to 48 weeks) a MADRS sco • Incidence of Major Depression Defined by Diagnostic and Statistical Manual IV (DSM-IV) Criteria [Time Fra therapy] • Severe Depression Defined as a MADRS Score of 25 or Higher [Time Frame: severe depression during 24 • Health Related Quality of Life (HRQOL) Measured by the Short Form 36 (SF-36) [Time Frame: assessed 2 • Sustained Virologic Response [Time Frame: assessed 24 weeks after end of antiviral treatment] (negative Polymerase Chain Reaction (PCR) 6 months after the end of antiviral treatment) • Tolerability [Time Frame: assessed 2,4,12,24 and for genotype 1 and 4, 48 weeks of antiviral treatment] • Safety [Time Frame: assessed 2,4,12,24 and for genotype 1 and 4, 48 weeks of antiviral treatment]
A	<p>Original Secondary Outcome Measures <small>ICMJE</small></p>	<p><i>Not Provided</i></p>

Figure S4: ClinicalTrials.gov Basic Fielded Search Form. Provides several key search fields.

Find a study (all fields optional)

Recruitment status ⓘ

Recruiting and not yet recruiting studies

All studies

Condition or disease ⓘ (For example: breast cancer)

Other terms ⓘ (For example: NCT number, drug name, investigator name)

Country ⓘ

United Kingdom

City ⓘ **Distance** ⓘ

[Advanced Search](#)

[Help](#) | [Studies by Topic](#) | [Studies on Map](#) | [Glossary](#)

Figure S5: ClinicalTrials.gov Advanced Search Form. Provides many more search fields.

Advanced Search

Fill in any or all of the fields below. Click on the label to the left of each search field for more information or read the [Help](#)

[Help](#)

Condition or disease:

Other terms:

Study type: All Studies

Study Results: All Studies

Recruitment status:

<p>Clinical study:</p> <input type="checkbox"/> Not yet recruiting <input type="checkbox"/> Recruiting <input type="checkbox"/> Enrolling by invitation <input type="checkbox"/> Active, not recruiting <input type="checkbox"/> Suspended <input type="checkbox"/> Terminated <input type="checkbox"/> Completed <input type="checkbox"/> Withdrawn <input type="checkbox"/> Unknown status	<p>Expanded Access:</p> <input type="checkbox"/> Available <input type="checkbox"/> No longer available <input type="checkbox"/> Temporarily not available <input type="checkbox"/> Approved for marketing
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Eligibility Criteria:

Age: years OR Age Group: Child (birth-17) Adult (18-65) Senior (66+)

Sex: All

Accepts Healthy Volunteers: Healthy volunteers may participate in the study

Targeted Search:

Intervention/treatment:

Title / Acronym:

Outcome Measure:

Sponsor / Collaborator: Exact match

Sponsor (Lead): Exact match

Study IDs:

Figure S6: Download the Search Results Panel. After conducting a search, (A) clicking on “Download” opens (B) a new window that provides options for downloading the retrieved records including number of study records, data elements, and file format.

487 Studies found for: **Recruiting Studies | Interventional Studies | Cancer | stem cell**
 Also searched for **Neoplasm, Malignancy, Progenitor Cell** and more. [See Search Details](#)

Applied Filters: Recruiting Interventional

List By Topic On Map Search Details

Show Filters

Showing: 1-50 of 487 studies 50 studies per page

Row	Saved	Status	Study Title
1	<input type="checkbox"/>	Recruiting	Hematopoietic Cell Transplantation for Patients With Hematologic Malignancies Using Related, HLA-Haploidentical Stem Cell Transplantation, Milan, Italy

Interventions Locations

amide • European Institute of Oncology Milan, Italy

Download Subscribe to RSS Show/Hide Columns

Download the search results for:
Recruiting Studies | Interventional Studies | Cancer | stem cell (487 records)
 Need help? See [Downloading Content for Analysis](#)

Number of Studies: Top 100 Studies

Download Table Contents (1 row per study)

Select table columns: Displayed Columns

Select file format: PDF

Download **Cancel**

For Advanced Users: Full Study Record XML Download

- Download** a zip file of the full study records in XML for all studies in the search results table (max 10000)
- To download the XML for all public study records in our database; See [Downloading All Study Content for Analysis](#)

Table S7: Content of a ClinicalTrials.gov Record for Interventional Studies: Overview of Minimum Information Requirements for (A) Registration and (B) Results Reporting by Data Element*

(A) Required Registration Data Element
<p>Trial Identification and Key Dates</p> <ul style="list-style-type: none"> • Brief Title, Acronym, Official Title^{WHO} • Study Type^{WHO} • Key Dates <ul style="list-style-type: none"> ○ Study Start Date^{WHO} ○ Primary Completion Date ○ Study Completion Date^{WHO}
<p>Key Protocol Details</p> <ul style="list-style-type: none"> • Brief Summary • Study Design <ul style="list-style-type: none"> ○ Primary Purpose, Study Phase, Interventional Study Model, Number of Arms, Masking, Allocation, Enrollment^{WHO} • Arm Information – for each: Arm Title, Arm Type^{WHO} • Primary Disease or Condition^{WHO} • Interventions – for each: Intervention Type, Intervention Name, Intervention Description^{WHO} • Primary and Secondary Outcome Measures – for each: Title, Description, Time Frame^{WHO}
<p>Oversight Information</p> <ul style="list-style-type: none"> • Responsible Party, by Official Title • Studies a U.S. FDA-regulated Drug Product • Studies a U.S. FDA-regulated Device Product, Device Product Not Approved or Cleared by U.S. FDA, Pediatric Postmarket Surveillance of a Device Product • U.S. Food and Drug Administration IND or IDE, FDA Center, IND/IDE Number, IND Serial Number (Not publicly displayed) • Availability of Expanded Access, Expanded Access Record NCT Number • Product Manufactured in and Exported from the U.S. • Human Subjects Protection Review Board Status
<p>Recruitment Information</p> <ul style="list-style-type: none"> • Overall Recruitment Status, Why Study Stopped^{WHO} • Eligibility Criteria^{WHO} <ul style="list-style-type: none"> ○ Sex/Gender Based ○ Age Limits ○ Accepts Healthy Volunteers ○ Inclusion and Exclusion Criteria • Central Contact Person (or Facility Contacts at each location) • Facility Information – for each facility: <ul style="list-style-type: none"> ○ Name and Address^{WHO} ○ Individual Site Status ○ Facility Contact (or Central Contact Person)^{WHO}
<p>Administrative Information</p> <ul style="list-style-type: none"> • Unique Protocol Identification Number^{WHO} • Secondary IDs and Type^{WHO} • Name of the Sponsor^{WHO} • Record Verification Date

(B) Required Results Reporting Information
<p>Participant Flow, by arm</p> <ul style="list-style-type: none"> • Started – Number of participants that entered the study • Completed – Number of participants that finished the study • [Not Completed – Computed number of participants that started but did not complete the study (e.g., dropped out of the study)]
<p>Baseline Characteristics, by arm and overall</p> <ul style="list-style-type: none"> • Age • Sex/gender • Race and ethnicity (if collected under the protocol) • Other study-specific measures
<p>Outcome Measures – For each pre-specified primary and secondary outcome measure:</p> <ul style="list-style-type: none"> • Name of Measure – for each: Type, Title, Description • Unit of Measure • Time Frame – Time point(s) at which the measurement was assessed for the specific metric used • Total and by arm: <ul style="list-style-type: none"> ○ Outcome data ○ For continuous measures, also measures of central tendency, measure of dispersion/precision ○ For categorical measures, also name of category, value for each category <p>Statistical Analyses per Outcome Measure– For each provided:</p> <ul style="list-style-type: none"> • Overview: Comparison groups selected for comparison, Type of statistical test (e.g., superiority, non-inferiority) • Either of: <ul style="list-style-type: none"> ○ Statistical Test of Hypothesis (<i>if provided</i>): P-value, Method name (e.g., ANCOVA, chi-squared) OR ○ Method of Estimation (<i>if provided</i>): Estimation parameter name (e.g., Cox proportional hazard, mean difference (final values), Confidence interval)e.g., 95%, Number of sides (1 or 2), Lower limit, Upper limit)
<p>Adverse Event Information All-cause mortality, by arm:</p> <ul style="list-style-type: none"> • Total number of participants who died due to any cause • Total number of participants included in the assessment of deaths due to any cause (i.e., denominator for calculating frequency of all-cause mortality) <p>For each serious adverse event:</p> <ul style="list-style-type: none"> • Adverse event term • Organ system • Collection approach (systematic or non-systematic assessment) • Adverse event data, by arm: <ul style="list-style-type: none"> ○ Number of participants affected ○ Number of participants at risk <p>Other adverse events:</p> <ul style="list-style-type: none"> • Frequency Threshold for Reporting, by arm (e.g., 5%) • For each other adverse event: <ul style="list-style-type: none"> ○ Adverse event term ○ Organ system

<ul style="list-style-type: none"> ○ Collection approach (systematic or non-systematic assessment) ○ Adverse event data, by arm: <ul style="list-style-type: none"> ▪ Number of participants affected ▪ Number of participants at risk
<p>Uploaded Study Documents For each document saved as a PDF/A file:</p> <ul style="list-style-type: none"> • Document type (e.g., study protocol) • Document date and subtitle • Document
<p>Other Information</p> <ul style="list-style-type: none"> • Results point of contact • Certain agreements that restrict PIs from discussing the results of a study after completion

*For a complete listing, see Data Element Definitions, Templates, and Checklists (<https://clinicaltrials.gov/ct2/manage-recs/resources#DataElement>)

^{WHO}Data elements also required by the WHO ICTRP Trial Registration Data Set.

Table S8: Key Changes to the Structure and Requirements for Selected Data Elements

Data Element	Description of Change in Structure or Requirement	Data Element Status	Month/Year
Primary and Secondary Outcome Measures	First introduced as a free-text field	Optional	September 2004
	Definitional changes, including adding information about the timeframe	Optional	May 2005
	Split up into 3 distinct sub-elements: <ol style="list-style-type: none"> 1. Outcome Measure 2. Time Frame: "The duration of making measurements" 3. Safety Issue (Y/N): "Is this outcome measure assessing a safety issue" 	Optional	December 2007
	"Description" free-text field added as sub-element	Optional	February 2010
	Change in status: Title and Time Frame sub-elements required "for records first released on or after December 1, 2012"	Required (Title and Time Frame)	December 2012
	Change in status: Description sub-element required "if Study Start Date is on or after January 18, 2017"	Required (Title, Description, and Time Frame)	January 2017
Primary Completion Date	First introduced as "Completion Date" with Month/Year format	Optional	December 2007
	Renamed "Primary Completion Date"	Optional	January 2008
	Change in status: required "for records first released on or after December 1, 2012"	Required	December 2012
	Format changed to Month/Day/Year	Required	January 2017
Study Start Date	First introduced as "Start Date" with Month/Year format	Optional	September 2004
	Name changed to "Study Start Date"	Optional	October 2004
	Change in status: required "if Study Start Date is on or after January 18, 2017" and format changed to Month/Day/Year	Required	January 2017

Box S9: Helpful Hints for Researchers. Practical and technical tips for applying the 10 issues to consider and examples.

1. ClinicalTrials.gov includes more than “clinical trials”

- Researchers can use a Filter on the Search Results page or the Advanced Search form to limit records by Study Type.
- Researchers should be aware, however, that searching by any parameter(s) without using the Study Type filter will retrieve records across all study types. For example, searching by a drug name will yield interventional, observational, and expanded access records.

2. Follow-on studies may be registered as separate records

- Researchers may find separate records for studies that might informally be referenced as a single “study” by the study sponsors. For example, protocol #01-M-0192 is registered as two separate records to represent both an “interventional” component (NCT03283930, a randomized controlled trial) and an “observational” component (NCT00018057, an observational study). The records represent studies in different populations and with different analyses for understanding anxiety in children and adolescents by the same researchers.
- Similarly, a single registered study may have results reported in multiple publications. For example, NCT00047385 (The National Lung Screening Trial or NLST) is linked to multiple publications, including articles reporting results from the initial screening examination, analysis of agreement in a retrospective reading of NLST screening chest radiographs, results of two incidence screenings, and a retrospective cohort analysis of NLST participants among others.

3. Incentives for reporting trials change over time

- Researchers should be familiar with the different reporting requirements (for more information, see links under “Key Policies” in Table 1 and Table 2)

4. ClinicalTrials.gov includes mandatory and optional data elements

- Researchers need to recognize when a data element (or sub-element) was added, changed, or deleted.

5. ClinicalTrials.gov conducts quality control review

- Researchers should understand the ClinicalTrials.gov quality control (QC) review criteria for making valid assessments about the studied records.
- Researchers should be aware that changes in QC review criteria may result in differences in specificity of the information submitted for data elements over time.

6. Records can be modified by the responsible party at any time

- The date on which ClinicalTrials.gov was searched and analyzed should be reported in any publications.
- Researchers who plan to reuse record information should download their analysis sample for future use and documentation.
- Researchers should consider whether the current version of each data element or some earlier version is most relevant to the analysis (e.g., the current primary outcome measure, which may incorporate updates since initial registration, or the version as originally registered).
- Researchers should understand how and what information might have changed within each study record during the study period.

7. ClinicalTrials.gov does not have all information for all studies

- Researchers need to assess the impact of the potential for missing studies from the CRE on the representativeness of any sample they choose.
- Researchers need to consider the impact of missing responses for data elements (e.g., whether or not the analysis population should include studies of interest that do not have responses for that data element)

8. ClinicalTrials.gov data can be accessed in several ways

- Researchers should consult the Downloading Content Analysis page (<https://clinicaltrials.gov/ct2/resources/download>) for more information.

9. Defining a sample of records to answer a specific question

- Researchers need to consider what type(s) of studies they want to include in their sample.
- Researchers need to consider to what degree the study type and design for studies of interest are covered by the scope of ClinicalTrials.gov, and how the scope has evolved over time. For instance, due to federal requirements, non-phase 1 trials of FDA-regulated drug, biological, and device products are represented more fully and systematically in ClinicalTrials.gov than other therapies, such as behavioral interventions, dietary supplements, and medical procedures.
- Researchers need to consider the reporting policies that apply to studies within a geographic region of interest. For example:
 - When analyzing trial locations, or considering changes over time to trials' geographic distribution, researchers should consider the evolution of rules and policies affecting reporting throughout the regions.
 - Additionally, sponsors and investigators can remove location information after a study ends, but information at the country level is maintained in the record's Tabular View (as "Removed Location Countries") and full facility information is available in the Archive site.
- Researchers should also consider which of the several potential date fields within the database are most appropriate and relevant to the research question and analyzed time-period, including the implications of each date (e.g., Primary Completion Date versus Study Completion Date).

10. Using the ClinicalTrials.gov results database

- Researchers should consult the following resources for more information:
 - About the ClinicalTrials.gov Results Database page (<https://clinicaltrials.gov/ct2/about-site/results>)
 - Results Data Element Definition document (<https://clinicaltrials.gov/ct2/manage-recs/resources#DataElement>)
 - Results QC Review Criteria document (<https://clinicaltrials.gov/ct2/manage-recs/resources#ReviewCriteria>)
 - How to Find Results of Studies page (<https://clinicaltrials.gov/ct2/help/how-find/find-study-results>)