MRCT Center

Return of Aggregate Results to Participants

Toolkit

Framework

MULTI-REGIONAL CLINICAL TRIALS

THE MRCT CENTER of BRIGHAM AND WOMEN'S HOSPITAL and HARVARD

Version 3.1

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1. Introduction to the MRCT Toolkit for Return of Results

The Multi-Regional Clinical Trials Center of Brigham and Women's Hospital and Harvard (MRCT Center) Return of Results workgroup is a multi-stakeholder group comprised of 53 members from industry, academia, patient advocacy and non-profit centers.

The workgroup developed this resource to accompany the *MRCT Return of Aggregate Results Guidance Document*. While the Guidance Document addresses basic principles, organizational process, logistics, and content of return of results summaries, this toolkit provides practical examples to sponsors and investigators. The Toolkit includes concrete samples of templates for return of results summaries, descriptions of endpoints in plain language, neutral language guidance, a checklist for Plain Language Summary (PLS) reviewers and ethics committees, forms for notification to third party, and sample return of results summaries. For Version 3.0, the headings of the "Template for Communication of Study Results" and the "Checklist for Plain Language Summary Reviewers" have been updated to correspond to the EU Guidelines on Summaries of Clinical Trial Results for Laypersons and some examples from external sources have been updated.

The Guidance Document makes note when to refer to the Toolkit for practical examples on the concepts and recommendations it addresses. This Toolkit is meant to be a hands-on instrument for implementing the recommendations of the Guidance Document to be used as templates making adaptations as needed to best fit your particular situation.

The MRCT Center encourages broad dissemination of this Toolkit along with the Guidance Document. The MRCT Center appreciates feedback and additional contributions (addressed to MRCT@bwh.harvard.edu) so that we can continuously improve this Toolkit. If these materials are used in their entirety or in part, attribution should list the "MRCT Return of Aggregate Results Toolkit" and version date.

2. Template for Communication of Study Results

SPONSORS: This template helps create clear summaries of clinical trials. Replace the *[guidelines in red brackets]* with your text; delete this heading.

[If written to study participants, include the following:]

Thank you for participating in this study.

As a clinical study participant, you belong to a large community of participants around the world. You help researchers answer important health questions and help them discover new medical treatments.

The sponsor (researcher) of this study thinks it is important for you to know the results. We hope it helps you understand and feel proud of your key role in medical research. If you have questions about the results, please speak with the doctor or staff at your study site.

Here we describe the results of this study.

[If written for the general public, start here:]

This summary was completed on *[month/year]***.** Newer information since this summary was written may now exist. This summary includes only results from one single study. Other studies may find different results.

1. **Study name**

[Place a simple title or purpose of the study in the box above. Sponsors may consider using the same simple title as in the registry. If drug names are used, list both generics and also where brand names® can be found.]

Phase 1 Study

This study searched for a safe dose of *[interventions/treatments]* for people with *[disease/condition.]*

Phase 2 and 3 Studies

This study compared *[interventions/treatments]* for people with *[disease/condition.]*

This study is officially known as *[All identifying numbers that patients will most likely use (e.g. protocol number, federal number(s), other IDs), followed by the official title of the study.]*

2. **Who sponsored this study?**

This study was sponsored by *[list name of sponsor]*.

If you have questions, please contact *[list appropriate contact information and/or resources available]* about the study.

3. **General information about the clinical trial**

This study started on *[mo./year]* and ended on *[mo./year]*. The study was run in *[country(ies) that enrolled patients]* and *[states or regions, if desired]*. This study may finish before other studies that also study this. When they are all done, the researchers will look at the results across the studies.

[Report the purpose or main objective of the study:]

Phase 1 Study

This was the first time this *[treatment/drug/device/intervention]* was studied in humans. This study was done to find the highest *[dose/amount]* of the drug/treatment that people could take without having severe side effects. Side effects include unexpected medical issues that happen during the study, even if they may not be caused by the *[drug(s)/device(s)/treatments/interventions]* in the study.

[If some companion studies are not known yet, include:] There are also ongoing studies that may give more information later.

- *[No information regarding clinically relevant endpoints should be included in a Phase 1 study. It may be helpful to add this sentence.]* This study was not designed to test whether the drug was useful or effective.

Phase 2 and 3 Studies

This study was called a Phase *[2/3]* study. *[use the statement that applies or draft a similar, appropriate statement for the trial to be reported on:]*

This Phase 2 study was done to find out if patients' conditions improved by using the *[drug(s)/device(s)/treatments/interventions]*. -or-

This Phase 3 study compared a new *[drug(s)/device(s)/treatments/interventions]* to the standard treatment used for *[disease/condition]*.

- *[Purpose of the study: including primary endpoints as the general rule) See the Endpoint Table in the MRCT Return of Aggregate Results Toolkit].*

All Phases

[Provide a simple explanation that includes these points:]

- *[Why the trial is important to patients/people]*
- *[A **simple explanation** of the disease/condition and what standard treatments may exist (**translate** from IRB-approved materials, informed consent forms, medical websites, ICH E3 synopsis, publication introduction, etc.). Sponsors may want to create a glossary of conditions, source sites, etc. See "Sample Summaries" in the MRCT Return of Aggregate Results Toolkit for language examples].*
- *[A **simple, general** sentence that gives context of what is already known about the agent, molecular profile, etc. (e.g. from consent forms, other studies). All investigational products must be described in simple terms.]*

For Clinical Trials that Stop Early

This study was stopped earlier than planned. This can happen for many reasons.

This study stopped early because [*add one of the possible statements below, or your own **simple explanation**, to this sentence. If there is more than one reason, list all that apply.]*

… too many participants had side effects (see below).

… *[drug generic name]* did not improve patient results.

… *[drug generic name]* was not as effective as expected *[comparator]*.

… *[drug generic name]* was much more effective than expected. *[if applicable, add]* The study was stopped so all participants had a chance to take *[drug generic name]*.

… not enough people joined the study.

[Include a statement about what will happen next. This includes:

- *Change in return dates*
- *Where participants can get further information or answers if questions arise.]*
- *For **Side effects**: to whom participants should report ongoing events or issues, where to get more information, treatment, or prevention, if appropriate.*

- *For **Efficacy**: anticipated next steps for the compound/device or indication, and who is available to discuss potential access to the compound.*
- *For **Futility**: a clear interpretation for participants explaining that the drug/device was not likely to be more effective than the comparator with reasonable certainty, whether development will/will not continue, etc.*
- ***Low accrual**: potential reasons for low accrual, if evident.*
    - *NOTE: be careful with language - do NOT inadvertently "blame" participants.]*

4. What patients/people were included in this study?

*[Include the following **general** information and consider graphics that conform to health literacy, cultural, and numeracy principles (see Appendix 3 in the MRCT Return of Aggregate Results Guidance Document).]*

This study included:

- *[Specific patient population to whom this study applies, including healthy volunteers]*
- *[Provide a **simple explanation** of how participants were chosen, divided into groups, stratified, etc. OR if patients/physicians could choose which therapy they could have.]*
- *[Include pediatric regulatory details if appropriate]*

Phase 1 Study

[#] agreed to be part of this study.[1] *[#]* were treated at each dose. *[#]* left the study before it was done. [*If there are special circumstances (e.g. induction therapy, transplant), a brief simple description can be added.] [#]* patients came from *[list the # of participants from each country included in the study]*

Phase 2 and 3 Studies

[#] agreed to be part of this study.[1]*[#]* were in Group A and *[#]* were in Group B. *[Add additional groups (arms) if applicable. If there are special circumstances (e.g. induction therapy, transplant), a brief simple description can be added.] [#] left* the study before it was done. *[#]* patients came from *[list the # of participants from each country included in the study]*

[1] *[# patients/people (use "people" if healthy volunteers are used)]* were considered for this study. Some people did not participate because they did not meet the requirements for this study.

5. Which medicines [or vaccines] were studied?

*[Include the following **general** information:]*

- *All drugs, devices, therapies and interventions involved in the study, with generic names. This includes any supplemental/companion studies that have relevant results. In Phase 1 studies, rarely are any supplemental/companion studies performed.]*
- *[Include any molecular analysis and/or integral markers that impacted patient selection and/or intervention/treatment]*
- *[Include if a placebo was used.]*

Phase 1 Study

[For dose escalation, use this text] [# patients/people] were put into the first dose group (Group A) to make sure the dose was safe. *[#]* people received a higher dose until patients left the study due to too many side effects. Side effects include unwanted medical issues that happen during the study, even if they may not be related to the *[drug(s)/device(s)/treatments/interventions]* in the study. Side effects did not happen to all *[people/patients]* in this study.

[List a separate Group for each dose level, e.g. "Group A," "Group B"]

Group A got *[**simple explanation** of study visits and study procedures (especially those that help explain the endpoints) for first group of participants. Include medicine/regimens used to prevent/lessen side effects. Also include the timeframe for the treatment/intervention, and any response or endpoint measurement in plain language. See the Endpoint Table in the MRCT Return of Aggregate Results Toolkit.]*

- *[Minimize acronyms/medical terms; explain any that are used.]*

Optional box or image

for a specific information point, e.g. dates, locations, or number of participants.

[Consider a simple graphic that helps people/patients understand the study. This could include a simple schema, patient flow and other pertinent information.]

Phase 2 and 3 Studies

[If randomized, use this text] [Patients/People] in the study were put into *[#]* groups by chance (randomized) to reduce differences between the groups. Each patient had the same chance to be selected for any group in the study. *[If not randomized, list how many patients/people were in each group, and how this was determined.]*

[Create a separate Group listing for each arm in the trial. Template includes "Group A" and "Group B" below – add others if warranted.]

Optional box or image

for a specific information point, e.g. dates, locations, or number of participants.

Group A got *[**simple explanation** of study regimen for first arm. Include medicine/regimens used to prevent/lessen side effects. Also include the timeframe for the treatment/intervention.]*

- *[Minimize acronyms/medical terms and explain any that are used.]*

Group B got *[**simple explanation** of study regimen for second arm. Include medicine/regimens used to prevent/lessen side effects. Also include the timeframe for the treatment/ intervention.]*

- *[Minimize acronyms/medical terms and explain any that are used.]*

[Consider a simple graphic that helps people/patients understand the study. This could include a simple schema, patient flow and other pertinent information. Sometimes this can be found in the clinical trial protocol and adapted here for use]

[*Provide **simple descriptions** of any companion studies, follow-up data, etc. that are included in the study or have clinically relevant, statistically significant results.]*

6. What were the side effects?

Common and serious medical issues that happened during the study are listed here. Not all *[people/patients]* in this study experienced side effects.

[List the most serious and/or most prevalent adverse events for each study drug(s) tested. Explain a cut-off used for common side effect, e.g., >5% of participants and link to full listing of adverse events. If possible, compare the number of people who had each event by dose level. Apply numeracy principles.]

[Plainly state any objectives or statistically valid endpoints that dealt directly with side effects. "Pre-specified" safety secondary endpoints may be one of the exceptions to the general rule of only reporting primary endpoints].

Phase 1 Study

Issues *[*in Group A*]* included:

- *[List events ≥5% or whatever percentage is used by the sponsor. Use numeracy and health literacy principles. See sample summaries for examples.]*
- *[Minimize acronyms/medical terms and explain any that are used.]*

Issues *[*in Group B*]* included:

Issues *[*in Group C*]* included:

[#] of side effects were seen in Group B, and *[#]* of side effects were seen in Group C. No higher doses were tested because of the number of side effects seen in Group C.

This study did not test the effects of the drug on patients. [*It did help us to understand what dose of the drug could be used in more studies.* Or: *It did help us to show that this drug should not be used in people in the way it was given here*.]

Phase 2 and 3 Studies

[Plainly state any objectives or statistically valid endpoints that dealt directly with side effects].

In this study, *[common or frequent* side effects *[list definition, e.g.]* "affected at least 1 in 20 patients". We also report serious side effects, even if rare.

Events *[*in Group A*]* included *[list for each study arm OR include comparison between arms for each event listed]*:

- *[List events ≥5% or whatever percentage is used by the sponsor. Use numeracy and health literacy principles. See Sample Summaries in the MRCT Return of Aggregate Resuulst Toolkit for examples.]*
- *[Minimize acronyms/medical terms and explain any that are used.]*

7. What were the overall results of the study?

For Studies that Close Early

Because this study was stopped early, we will not know answers to *[many/most/any]* of the questions that were studied. This is a summary of what was learned while the study was open. Study details are listed after the results for more information.

Phase 1 Study

[Results of a Phase 1 study usually include what the body does to the drug and what the drug does to the body. They also try to find the best dose that people can take safely.]

Phase 2 and 3 Studies

[Results can be grouped in different ways, including the medicine given, the side effects, the responses etc. If this is a randomized trial, a simple chart could also list statistically significant comparisons.]

All Phases

The study found that:

[NOTE: always use absolute factors, not relative hazards or risks.]

[If composite endpoints are used—which is unusual in a Phase 1 study—it may be better to include bolded headings for each endpoint, followed by a brief, simple explanation in one to two sentences.]

Optional box or image

If relevant

- *[# of # patients/people]* in **Group A** *[(list the intervention/treatment used in Group A, then include information for each additional cohort if applicable) Include each identified primary endpoint as a separate bullet and in **simple terms** with numeracy principles on how many people tolerated the dose, adverse events reported, etc. Include the primary endpoint and safety data that are important to the overall results of the trial.*

Phase 1 Study

[Note that in a Phase 1 study, no clinical impact will be reported.] The study was not designed to look at whether the drug worked. It studied which doses seem to be safe to use in future trials.

[Include a neutral conclusion only if there is a clear indication that an MTD or DLT was/was not found. See suggestions for neutral language in the MRCT Return of Aggregate Results Toolkit.]

Phase 2 and 3 Studies

*[*Refer to the complete list of outcomes for all endpoints which is available in the technical results summary*]*

8. How has this study helped patients and researchers?

These results are for [*the specific population that was studied, including age and gender breakdown. Include eligibility criteria, including specific genetic mutations (when appropriate).*

Results are limited to the particular people studied and cannot be assumed to be true for everybody. Not all participants in each part of the study had the same results.

Include this statement if volunteers are used: Phase 1 studies often involve healthy volunteers.

This research helps future patients and families by helping us understand more about each medicine being studied.

[Include a general comment on what this study contributed to the relevant area of research and potential next steps to build on that knowledge. Mention if further studies are planned. See suggestions for neutral language and the Endpoint Table in the MRCT Return of Aggregate Results Toolkit.]

Findings from this study will be used *[add general next steps to this sentence to help explain context. Suggestions include:* "in other studies to compare this drug with other treatments for *[patients with condition/disease];*" "to combine with other treatments in *[patients with condition/disease],*"to seek approval from the *[EMA/FDA/other agency]*;" "inform doctors about a new way to treat people"*.]*

9. Are there plans for further studies?

[Include whether other related trials are ongoing, or if further trials are planned.]

10. Where can I find more information about this study?

To learn more about this study, visit *[provide URL link for this protocol here, e.g. on clinicaltrials.gov, EudraCT]* (if applicable: Phase 1 studies are not required to be on clinicaltrials.gov but are required on *EudraCT*). More information may also be available by looking up the official number or title, or by going to *[list any websites that may have plain language information, non-scientific articles, etc.].*

You can also find more details about this study at:

- *[List all applicable citations and websites that are not listed in clinicaltrials.gov or EudraCT. This can include resources as well as articles.]*
- This study was sponsored by *[List each sponsor, including company, government, consortium, and/or private funders]. [Sponsor(s) is/are]* available at *[list contact information]*.

For more information about the disease/condition:

- *[List any resources or links that may list additional publications or information about the disease/condition.; avoid links to promotional language]*

For general information about research studies, go to *[list appropriate sites, e.g., https://www.clinicaltrials.gov/ct2/about-studies/learn, http://www.fda.gov/drugs/resourcesforyou/consumers/ucm143534.htm, http://www.ema.europa.eu/ema/index.jsp?curl=pages/special_topics/general/general_content_000489.jsp&mid=WC0b01ac058060676f]*

[If written to study participants, include the following:]

This research was important. Thank you for helping us understand more about *[drug generic name(s) or intervention studied]*. If you have questions, please talk to your *[study doctor, trial designee, whomever the plan states, or, if that person is no longer available, talk to your family doctor]*.

Thanks again for being part of this study.

We do research to try to find the best ways to help patients, and you helped us to do that.

Optional box or image

Logo, icon or other image if relevant or helpful.

3. Checklist for Plain Language Summaries (PLS) Reviewers

As of March 1, 2015, this checklist includes at a minimum elements listed in Appendix 5 p. 63 of the EMA "Functional specifications for the EU portal and EU database to be audited" EMA / 641479/2014 issued January 20, 2015 and additional elements the MRCT team believed beneficial to return to study participants.

This checklist is meant to assist the people who are responsible for reviewing PLS before they are finalized.

Checklist for Review of Content for Aggregate Plain Language Summary

The summary document **should** contain (in accordance with EU Guidance):

- Name of research study and identifying number; simple title of the study
- Sponsor of the study
  - List of study sponsors and contact information (companies, foundations, public funding, academic institutions, etc.)
- General information about the study
  - Countries in which study conducted
  - Start and stop dates, with mention of early discontinuation if appropriate
  - A simple description of the objectives that were measured (primary endpoint, safety data relevant to the overall results of the trial)
  - How the study worked (protocol flow description, etc.)
  - Randomization and blinding information
- Study participants:
  - Number of participants per country
  - Characteristics of study population including age and gender breakdown
  - Eligibility criteria
  - Pediatric regulatory details (if appropriate)
- Description of investigational product used
- Side effects,
  - Frequency and severity (use cut-off for common and state what it is and where to find the full list of adverse events)
  - Occasionally, results may have safety implications for individual participants; if so, individual communication may be more appropriate. The summary may advise monitoring or care plans for the future
- Overall results of the study
  - A simple description of the outcomes (primary endpoints by trial arm) using numeracy principles for statistics and data presentation

- How the study helped patients and researchers
    - Clear statement that results are relevant for this population, no other population with different characteristics, symptom or diseases.
    - Result analysis state (including dates of intermediate analysis date, interim/final analysis stage, global end of trial date)
    - Clear statement that results may not reflect individual results
- Plans for future studies
- Where to find more information
    - Where further information may be obtained (e.g. websites, publications, ClinicalTrials.gov, etc.).
    - Contact person for more information;

In addition, we recommend:

- A simple thank you to the study participants
- Date summary was prepared and disseminated
- The document follows principles of health literacy. If medical terms must be used, a simple explanation is included.

The summary document **should not** contain:

Claims, explicit or implicit that:

- The drug, biologic or device is safe or effective for the purposes under investigation
- The test article (drug, biologic, device) is known to be equivalent or superior to any other drug, biologic or device
- References to "new treatment", "new medication" or "new drug" without explaining that the drug, biologic or device is investigational.

4. Endpoint Table with Simple Language

The following table lists common clinical trial endpoints. Terms are defined with general descriptions, followed by examples of simple, plain language that can be used in Plain Language Summaries (PLS).

Endpoint	Description of the type of endpoint	Example in simple, plain language
Composite	A **composite endpoint,** as the primary endpoint, combines multiple outcomes (e.g. death, getting sick again (relapse), serious event) and test results into one measure of how well the drug/therapy/device works. This is useful when there are many different outcomes that can happen during a trial. This can also be called a **combined** or **multi-part endpoint**.	"The XXX study measured *[patients/people]* to see if those in Group A (ABC treatment) or Group B (XYZ treatment) lived longer, had fewer heart attacks, or fewer hospital visits for heart failure. These events were measured together (combined) because each one is quite rare. Researchers also wanted to see if the drug worked in patients who had all 3 conditions. The study found that there was no change in the number of events for [*patients/people*] in Group A or Group B."
Dose Escalation	Dose escalation is used in phase 1 studies to measure safety. People in the study start with a low dose of the medicine (drug). If that dose does not cause safety problems, then more people are given a higher dose until there are too many side effects. The highest dose that is tolerated is called the maximum tolerated dose (MTD) or dose limiting toxicity (DLT).	"This study was done to find the highest *[dose/amount]* of treatment that people could take without having too many side effects."

Endpoint	Description of the type of endpoint	Example in simple, plain language
Exploratory Biomarker / Genomics Markers	A characteristic that is objectively measured and evaluated as an indicator of normal biological processes, pathogenic processes or pharmacologic responses to a therapeutic intervention."	"Certain markers in the body (biomarkers) can be used as clues to see how cells behave. This Alzheimer's study measured changes in many biomarkers in a body fluid found in the brain and spine. Each of these biomarkers are known to be [involved/ [active/turned on (activated)/turned off, etc.] in Alzheimer's Disease. The amount of xxx biomarker got lower over time in about 1 in 5 patients (20%) in Group A. xxx biomarker did not change for most (4 in 5) patients (80%) in Group B. It is not yet known if the biomarker changes mean the disease changed. More studies are needed before these biomarkers can help doctors and patients decide about treatment."
Mortality / Overall Survival	The goal of this trial was to see if patients who took Treatment ABC or Treatment XYZ with *[disease/condition]* lived longer.	"This trial compared patients in Group A (Treatment ABC) to those in Group B (Treatment XYZ) to see who lived longer. **If there was NO EFFECT** – **"**Patients in both groups lived about the same amount of time, no matter what treatment they got." **If there was an EFFECT** – "The times given include the middle (average) amount of time that *[patients/people]* in this study lived. Some *[patients/people]* lived for a shorter time and some lived longer. People in Group A (ABC treatment) lived about 15 months. People in

		Group B (XYZ treatment) lived about 12 months. This means that people in Group A (ABC treatment) lived about 3 months longer than people in Group B."
Endpoint	**Description of the type of endpoint**	**Example in simple, plain language**
Morbidity	Morbidity endpoints are those that measure the severity of disease or when a new disease begins.	"People with diabetes were put into 2 groups by chance (randomized). This was done because no one knew if one treatment was better than another. Group A received drug X, Group B followed a diet and exercise program. All people were followed for heart and blood effects, including stroke, high blood pressure and coronary heart disease. EFFECT – Both groups had similar health conditions and outcomes. There was no difference in the health of their heart for patients in Group A (Drug X) compared to patients in Group B (diet and exercise)." "People with diabetes were put into 3 groups by chance (randomized) to reduce differences between the groups. *[If the study was double blinded, also add the following wording]* This study was also "double blinded" – this means that neither patients nor doctors knew who was given which treatment/drug. This was done to make sure that the study results were not influenced in any way.

		[If the study was single blinded, use the following words]This study was single blinded, this means the patient did not know who was given which treatment/drug but the doctor did know. A single blinded trial may mean that the results may be biased by knowing who received each treatment. *[If not randomized, list how many patients/people were in each group, and how this was determined.]*
Endpoint	**Description of the type of endpoint**	**Example in simple, plain language**
Non-Inferiority	Non-inferiority endpoints are designed to show that a new treatment or drug is not worse than the control (or other comparison drug) by a pre-specified amount (also termed the non-inferiority margin). Efficacy can, in fact, be worse if there are other benefits (e.g., fewer side effects).	[Need to include some specific comparisons between the arms before stating the following sentence.] "This study showed that Group A (insulin A) was not different than Group B (standard insulin therapy) in lowering the level of red blood cells in Type 1 diabetic patients. Patients in Group B had fewer side effects of upset stomach and nausea than those in Group A."
Patient-Reported Outcomes	This study asked patients about their [list the main purpose of the questionnaire: e.g., symptoms, activity level, quality of life, income and/or happiness] and if the measurement changed based on whether a patient got A or B. The primary endpoint is less XXX based on the YYY scale. This scale measures ZZZ and how this changes over time.	"Patients answered questions to measure pain, stiffness, and how well people climbed stairs, stood or bent over. Questions were asked during each study visit. About 50 in 100 people (50%) in Group A had less knee pain. About 25 in 100 people (25%) in Group B had less knee pain.

		This means that patients in Group A (x treatment) had less knee pain than patients in Group B (y treatment/placebo)."
Endpoint	**Description of the type of endpoint**	**Example in simple, plain language**
Prevention/ Incidence	The incidence endpoint tells how many new cases of XXX occurred over a given period of time.	"Women who had a bone fracture after they stopped having their monthly periods (menopause) were put into 2 groups by chance (randomized). This was done because no one knew if one treatment was better than another. 1 in 20 women (5%) in Group A (bisphosphonates) had a break in their back bone (vertebrae). 2 in 20 women (10%) in Group B (X Treatment) had a break in their back bone (vertebrae). This means that patients in Group A had fewer breaks in their back bone."
Progression-Free Survival (PFS)	Progression-free survival endpoints measure how much time it takes from the beginning of starting a drug/therapy/device until a patient has a sign that the disease has progressed/spread/gotten worse. The goal of this trial is to measure whether people given drug XXX had longer PFS than those that did not get drug XXX.	"Patients in this study were assigned to 2 groups by chance (randomized). This was done because no one knew if one treatment was better than another. The goal of the study was to measure the size of each breast cancer tumor to see if it shrunk, stayed the same, or grew in a 1 year period. 56 in 100 patients (56%) in Group A (ABC treatment) had tumors that stayed the same, while 12 in 100 patients (12%) had tumors that grew, and 32 in 100 patients (32%) had tumors that shrunk.

		33 in 100 patients (33%) in Group B (DEF treatment) had tumors that stayed the same, while 10 in 100 patients (10%) had tumors that grew, and 57 in 100 patients (57%) had tumors that shrunk. This means that more patients in Group B had tumors that shrunk."
Endpoint	**Description of the type of endpoint**	**Example in simple, plain language**
Surrogate	Surrogate markers may be used instead of a clear endpoint (i.e. overall survival) when it is hard to measure the outcome or the trial would take too long to complete. Surrogate markers measure participants' level of X over time. Doctors believe that measuring this level of X may show how severe the disease is or how likely something is to happen in the future.	"The main goal of this study was to see if the Drug X lowered pressure in the eye (called intra-ocular pressure). Higher eye pressure could mean that vision may be lost faster than with lower eye pressure. This study found that people in Group A (Drug X) had lower eye pressure at the end of the study than at the beginning. People in Group B (placebo) had no change in their eye pressure over the course of the study. Eye pressure may be linked to how much vision is lost to eye diseases that cause blindness (glaucoma). This is not yet known."

5. Neutral Language Guidance

Sponsors, as well as individuals and groups, that intend to communicate summary results to study participants and the public are sometimes concerned that the language used might be considered unduly positive, promotional, or serve a marketing purpose.

Below we offer terms to avoid and terms to consider that reflect objective, neutral descriptions of study results. Plain Language Summaries (PLS) may differ, depending on whether the drug has or has not been approved by the regulatory agency with jurisdiction (e.g. US FDA, EMA). If questions remain after every effort has been made to remove "promotional" language, the regulatory agency should be consulted.

The first column in the table below lists possible statements that might be considered promotional. The second column offers suggestions of neutral language that provides neutral and objective information.

Language that states data, such as "# of people with treatment X experienced Y," is acceptable, while language that makes a claim, such as "X is better than Y," should be avoided. Summaries should not include conclusions that have yet to be reviewed and approved by authorities.

Language to avoid	Language to consider
This study proved…	This study found that... This does not mean everyone in that group had these results.
This study proved that using <*drug A*> to prevent <*disease/condition*> is effective.	This study found that people with <*disease/condition*> who got <*drug A*> had <*primary endpoint*>.
The combination treatment of <*drug A and B*> may also help <*a different disease/condition than what was/was not studied elsewhere*> as observed in new small studies.	When <*Drug A and B*> are used together, people in this study had <*study endpoint*>. The drugs may be helpful in other diseases/conditions, but this was not studied here. Further studies in <*disease/condition*>will be necessary.
This means that <*Drug A*> is better than <*Drug B*>.	In this study, people who got <*drug A*> had more <*study endpoint*> than some people who got <*Drug B*> with the same health conditions.
<*Drug A*> works better than <*Drug B*>, but some people didn't tolerate it as well.	In this study, more people with <*study endpoint*> received or were treated with <*Drug A*>. They also had more side effects that interfered with their daily lives, like <*list specific adverse events*>.

<*Drug A*> is better tolerated than <*Drug B*>.	In this study, fewer patients who took <*drug A*> had *<list specific adverse events>* than patients who took <*drug B*>.
People taking <*drug A*> lived longer after they had <*therapy*> for <*disease/condition*>, even with more adverse events.	People who took <*drug*> had more time before their <*disease/condition*> came back and they lived longer. The patients who took the drug also had more side effect.
While the combined treatment of <*Drug A and B*> did not extend life over <*Drug A*> alone, people felt better and lived longer with the combined treatment.	People in both groups had the same kind of results (outcomes). People who took the combined treatment had fewer serious side effects like *<list specific adverse events>*.
Study groups had the same results. More studies are provided after acceptance for publication in a peer-reviewed journal.	There was no effect in the treatment groups/there was no difference between the groups. All groups still had pain and numbness in their fingers or toes (called neuropathy).
People in group <*1*> were able to tolerate the highest dose of <*Drug A*> so more studies will be done.	People in group 1 were able to take the highest dose of drug A without side effects so more studies will be done with drug A.

6. Ethics Committee Checklist for Aggregate Plain Language Summaries

In the course of a research study, investigators and sponsors may wish to provide participants with a summary of aggregate research results.

There are three different time frames in which investigators or sponsors may incorporate the concept of returning study results to participants: 1) the concept may be introduced in the initial protocol; 2) investigators or sponsors may choose to incorporate the return of aggregate study results into ongoing trials (this may require approval by the IRB/REC); and 3) investigators or sponsors may decide to provide a plain language summary of aggregate research results to participants for studies that are already completed and closed; this decision need not be reviewed or approved by the IRB/REC, as the committee no longer has oversight responsibilities.

This worksheet aims to assist Ethics Committees in their role to support the return of results to study participants. The U.S. regulatory criteria for IRB approval at 45 CFR 46.111(a)(1-7)(b) and 21 CFR 56.111(a)(1-7)(b) are used here. The worksheet may need to be adapted for other agency and governmental regulatory requirements, including those with oversight in international and transnational settings.

Regulatory Criteria for IRB Approval			
Determine whether the plan for return of results meets the regulatory criteria for approval. If YES, note protocol-specific information that supports your determination. If NO, note specific changes the investigator must make to meet this criterion. If DON'T KNOW (?), note additional information needed to help you decide whether the criterion is met.			
(1) Risks to participants are minimized by using procedures which are consistent with sound research design and which do not unnecessarily expose participants to risk. • Are procedures for communicating results respectful to the wishes of the participants? • Are privacy concerns adequately addressed?	☐ YES	☐ NO	☐ ?

(2) Risks to participants are reasonable in relation to anticipated benefits, if any, and the importance of the knowledge that may reasonably be expected to result. Risks include any physical, psychological, social, legal, and economic risks to participants. • Have risks been adequately addressed, and efforts to minimize risks maximized? Particular attention should be paid to privacy concerns and potential psychological stress. • Are benefits appropriate and not overly stated?	☐ YES	☐ NO	☐ ?
(3) Selection of participants for receipt of aggregate results is equitable. • Are all participants (e.g. enrolled, randomized) offered the information? • Are any participants excluded from access to information without appropriate justification?	☐ YES	☐ NO	☐ ?
(4) The participant has the ability to access the aggregate results or decline the information. Each prospective participant or their legally authorized representative may make an informed choice as to whether to receive the information • Are all participants able to opt-in or opt-out of receiving the information?	☐ YES	☐ NO	☐ ?
(5) If the research results involve more than minimal risk to participants, the communication plan makes adequate provision for how the participants should be monitored to ensure the safety of participants.	☐ YES	☐ NO	☐ ?
(6) There are adequate provisions to protect the privacy of participants and to maintain the confidentiality of individual participant data.	☐ YES	☐ NO	☐ ?
(7) When some or all of the participants are vulnerable (e.g. children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons) additional safeguards have been included in the study to protect the rights and welfare of these participants.	☐ YES	☐ NO	☐ ?

7. Sample Notification to Third Party Form

The following example can be used if the trial participant designates a third party to receive Return of Results of Plain Language Summaries (PLS).

Authorization for Third Party Receipt of General Research Results from *[trial title (can be simple title), include identifying numbers]*

Participant, patient, parent/Legal Guardian Name: _____

Participant's Name (if different):_____

Address:

_____

_____

Phone: _____

Date of Birth: _____

I request that information about this trial, and study results when available, be released to:

Name:

_____

Address:

_____

Phone:

_____

All records from (date) _____ to _____

Or only the following information:

_____

My signature below indicates that I understand what information will be released and the need for that information. *[If applicable:* I further understand that the information to be released may include information regarding drug and alcohol abuse or AIDS/HIV.*]*

I understand that I may revoke this consent in writing at any time, but that it will remain valid to the extent that action has already occurred based on this authorization.

Participant, Patient, Parent/Legal Guardian Signature Relationship Date

_____ _____

8. Other Examples from External Sources

Samples of existing, external Plain Language Summaries (PLS) are included as examples.

Examples include plain, simple language and various formats from different sponsors and organizations.

Alliance for Clinical Trials in Oncology

All Alliance public study result summaries
https://www.allianceforclinicaltrialsinoncology.org/main/public/standard.xhtml?path=%2FPublic%2FResults

Alliance Sample Summary for a Non-Randomized Clinical Trial

https://www.allianceforclinicaltrialsinoncology.org/main/cmsfile?cmsPath=/Public/Results/files/N0821-results-03192015.pdf

Alliance Sample Summary for a Randomized Clinical Trial

https://www.allianceforclinicaltrialsinoncology.org/main/cmsfile?cmsPath=/Public/Results/files/N9831-results-03192015.pdf

Alliance Sample Summary for an Observational Study

https://www.allianceforclinicaltrialsinoncology.org/main/cmsfile?cmsPath=/Public/Results/files/89803-results-04132015.pdf

Dana Farber/Harvard Cancer Center Clinical Trials Summary

Title

DFCI # 03-311: Phase 2 trial of preoperative vinorelbine/trastuzumab (VH) or docetaxol/carboplatin/trastuzumab (TCH) in HER2+ breast cancer.

Plain Language Title

A clinical trial evaluating two pre-operative, Herceptin-based treatment regimens for patients with HER2-positive breast cancer, with or without cancer in the lymph nodes (stages II and III).

Why the Trial Was Done

The purpose of this trial was to evaluate the effectiveness of two treatments taken for 12 weeks, prior to surgery (Vinorelbine (navalbine)/Herceptin (trastuzumab): VH or Taxotere (docetaxol)/Carboplatin/Herceptin: TCH) in shrinking the breast cancer tumor. Although these two treatments had been used before to treat breast and other types of cancer, neither had been used before surgery to treat breast cancer. In addition to looking at how the treatments impact tumor shrinkage, another goal was to take a step toward individualizing treatments for future patients. Tissue samples (biopsies) were taken before, during and after treatment in order to learn about how the treatments affected each woman's tumor.

Trial Summary

This clinical trial was started in December 2003 and ended in August 2008. A total of 81 patients participated in the trial.

Results

The results of the study showed that **both** treatments were effective for treating early stage HER2-positive breast cancer. In both treatment groups, after treatment was completed just before surgery, a small number of patients had no evidence of breast cancer, and a larger number had tumors that decreased in size.

The two treatments were evaluated for safety by recording the number of occurrences of adverse events that were considered grade 3 (severe) or grade 4 (life-threatening). The grade 4 events in the two treatments had similar adverse events, with the most common being high neutrophil counts, reported in four patients in each group. Neutrophils are a type of white blood cell. Grade 3 adverse events occurring in two or more patients included high total white

cell count, fatigue, diarrhea, high liver function tests, anorexia, dehydration, and irregular menses.

This trial also contributed to an exciting new area of breast cancer research that involves studying the patient's tumor and looking particular features, called biomarkers, that can help identify whether a patient will benefit from one treatment over another. Such investigations are called translational research, as the work done in the lab (analyzing the tumor) will translate into how best to treat the individual patient in the clinic. The studies conducted in this clinical trial on the tumor tissue removed before and after the treatment resulted in new findings that will guide researchers down the path toward individualized medicine. Looking for certain biomarkers in patients who benefit from one or the other treatment will help determine which treatment patients should receive.

Here are the top three lessons learned from this clinical trial:

1. Both VH and TCH provided benefit in terms of reducing the size of the tumor. In the majority of patients the tumor became smaller. No patient had to stop treatment because her tumor(s) grew larger.
2. In some of the patients who still had tumor remaining at surgery, their tumors developed extra copies of a HER2-related gene called EGFR (also called HER1). Further studies are now looking at combining Herceptin with drugs that inhibit EGFR.
3. A protein called PI3Kinase is important for HER2 to function. Several of the patients who still had tumor remaining at surgery had the PI3Kinase mutation, but none of the patients who had no tumor remaining had the PI3Kinase mutation. This possible association of response to treatment with the PI3Kinase pathway is now being actively investigated through new clinical trials at Dana-Farber and elsewhere.

What does this mean for me?

This report describes the trial findings for the combined trial participants. At this time, we don't believe that any of the findings from this trial would impact your care. If you have questions about the trial findings, or your care, we encourage you to speak with your treating physician.

Study Sponsor

This study was designed by doctors at the Dana-Farber and Harvard Cancer Center. The study received financial support from Genentech and Aventis.

Scientific publications about the study

A full report of the study results has not yet been published. A short summary (abstract) of the early results, those summarized in this document, was published in the *Journal of Clinical Oncology*, 2010 ASCO Annual Meeting Proceedings (Post-Meeting Edition). Vol 28, No 15 suppl (May 20 Supplement), 2010: 549

Thank you again for your participation.

Eli Lilly and Pfizer Trial Results Summaries

https://www.ciscrp.org/our-programs/trial-results/results-summaries/

Trial Scope: Trial Results Summaries

https://www.trialsummaries.com
