Victoria Rodriguez Week 2: Research Design Draft HHA 506

**Research Question**: In U.S. female patients with HER2-positive breast cancer aged 30-65, how could nano therapy interventions compare to traditional trastuzumab chemotherapy in regards to more effective breast cancer treatment beginning 30-60 days after initial diagnosis?

**Research Design**: Prospective Crossover Study Design

**Research Methods**:

1. Description of Study Design

This research study will utilize a prospective crossover study design in order to compare the effects of tyrosine kinase lapatinib nano therapy and traditional trastuzumab chemotherapy treatment for patients with HER2-positive breast cancer. Crossover studies consist of participants being randomly assigned into two groups where each group undergoes the same two treatment options at different time intervals for direct comparison where a participant serves as their own control variable. In this study, the participants will be initially receiving either the lipid nano therapy intervention or trastuzumab chemotherapy for the first 3-month long session. Afterwards, a “washout period” will take place where participants will not be receiving either of the treatment options for a two- week period. After this period, the two groups will switch and undergo the other treatment option for another 3-month long session. This study is considered a prospective study because the participants would not have had previous exposure to any form of cancer treatment, except for their initial surgery. This study will also be a closed study because all participants will remain the same until the end of the study.

Research Study Timeline

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| **Introduction**  **(2 Meetings at the beginning and end of the opening week, e.g. Monday and Friday of same week)** | Selected participants are randomly assigned to Group A or Group B, described the conditions and protocols for the research study, and provided information on both treatment types to independently go over and read thoroughly. Questions or concerns can be discussed in scheduled joint meetings. |
| **First Session**  **(First 3 months of treatment)** | Group A is given traditional trastuzumab chemotherapy and Group B is given the tyrosine kinase lapatinib nano therapy for HER2 breast cancer for a 3- month long period. |
| **“Washout Period”**  **(2 weeks of no treatment)** | During this period, both groups will not undergo any form of treatment for 2 weeks. Participants will be interviewed to see how they are feeling after the first session and data will be collected. |
| **Second Session**  **(Second 3 months of treatment)** | For the second session, Group A and Group B will switch treatment options for the next 3-month long period. |
| **Conclusion**  **(2-3 weeks to conduct interviews, analyze results, and draw up conclusions)** | After the second session, the research study will end. Participants will be interviewed once more and results will be analyzed. Participants will then have the option to continue with the most effective treatment option, if they wish. |

1. Location
2. This research study is going to take place at the Baylor College of Medicine Lester and Sue Smith Breast Center in Houston, TX for all of the sessions enlisted above. During the individual sessions, the participants will stay in the center as admitted patients for the Baylor medicine hospital system.
3. Participants and Criteria
4. Recruitment method: The recruitment process for this research study will primarily focus on gathering female patients that have recently been diagnosed with HER-2 positive breast cancer in Houston, Texas. Online postings via social media platforms, digital and physical newspaper articles, as well as potential partnerships with nearby centers or hospitals providing breast cancer treatment will assist in gathering the desired population for this study. Those interested have the opportunity to contact a hotline provided in the social media advertisements and newspaper articles for the study, and after expressing interest will be advised to provide an email or phone number to discuss further steps. A link to create an appointment for a consultation with our research team’s providers will be sent to those who provided an email or a representative will contact those who provided a phone number to set up a consultation. After participants of interest have been seen by our provider and the variables needed for the study have been met, those selected will be contacted and given information to attend the introductory session of the study. The total number of participants desired for this study is 12, for an equal distribution between the two sessions and for smoother follow ups thereafter.
5. Inclusion Criteria

* Participants must be females living in Houston, TX within the 30-65 age range who have been recently diagnosed with HER2- positive breast cancer
* Participants need to have been diagnosed or gotten initial surgery no later than 60 days before study
* Participants need to be willing to stay within the research facility for the entire duration of the study

1. Exclusion Criteria

* Participants who have either had a form of breast cancer or received some form of breast cancer treatment in the past
* Participants who smoke or drink regularly

1. Variables
2. Progress during both treatment sessions will be monitored using imaging techniques and endoscopes to determine if detected tumor(s) or clusters of cancer cells are getting bigger, smaller, or staying the same size. More specifically, CT scans will be used to analyze the size and shape of the HER2 tumor(s) every 3 weeks throughout both sessions. PET scans will also be used to identify the presence of HER2 protein or receptors every 4 weeks throughout both sessions. These imaging times are spaced out to avoid an addition excess of radiation for participants.
3. The participants would need to have been recently diagnosed with HER2-positive breast cancer for the study, or have undergone initial surgery if needed, no later than 60 days before the study for the most optimal treatment period and analysis for the disease. Data suggests that the sooner a patient undergoes chemotherapy or cancer treatment after diagnosis or initial surgery, the better the outcome of the treatment. This is important for this study because comparing the two treatment options during the optimal time for a patient to improve in response to treatment would provide insightful data and results.
4. The stage of HER2- positive breast cancer or the size(s) of the tumors have not been identified because the participants will be their own controls. In other words, the selection process only includes females with HER2- positive breast cancer but does not specify the stage or size because this study is simply trying to determine which treatment option is better. Variety in regards to stages or sizes of tumors could potentially provide more insight into the treatment options by studying progress along multiple scopes or types of HER2 cases.
5. Data Sources and Measurement
6. As previously mentioned, imaging techniques (CT scans, PET scans, and endoscopes) will be used to track the progress of both treatment options for all participants during the two 3 month-long sessions. CT scans and PET scans will be conducted every 3-4 weeks (on separate days) to monitor if the tumor has grown larger, smaller, or stayed the same size. The dimensions of the tumors or cancer cell clusters (depending on stage) will be notated along with any distinguishing characteristics observed in either scans. At the end of each session, participants will comment on how they are feeling physically and data collected over the 3-month period will be analyzed for patterns or trends throughout the course of each treatment type.
7. There has been evidence to suggest that delaying breast cancer treatment for too long leads to an increase in risks, spread of the disease, and decreases the patient’s chance of survival. According to a population-based study conducted under JAMA Oncology, the majority of invasive breast cancer patients ranging from stage 1 to stage 3 started chemotherapy within 31-60 days after surgery, with the average time to chemotherapy being 46 days. No evidence of adverse outcomes was documented during the 31–60-day time frame but it was established that patients treated 91+ days had lower survival rates. Hence, this study will conduct two treatment options no later than 60 days to eliminate adverse outcomes as much as possible.
8. In this study, the participants will be their own controls when comparing the two treatment options. However for better guidance the stages must be identified during each participant’s initial consultation. Traditionally, stages were determined by the following criteria: size of the tumor, if the tumor has grown within tissue, the appearance of lymph nodes or lack thereof, and if the disease has spread to other areas besides the breast. However, recent changes have added the question of how much of the HER2 protein cells are being replicated when clarifying the stage of HER2-positive breast cancer. Using information from BreastCancer.org, the following table provides an easy-to-follow description of the breast cancer stages:

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| **Stage 0** | * Non-invasive * No evidence of cancer cells * Non-cancerous abnormal cells |
| **Stage 1A** | * Invasive * Tumor measures ~2cm * Cancer has not spread to areas besides the breast * No lymph nodes detected * Estrogen-receptor positive classified as this stage |
| **Stage 1B** | * Invasive   **Either:**  -No detected tumor in the breast but small groups of cancer cells >.2mm but also <2mm detected in lymph nodes  -Tumor in the breast <2cm and small groups of cancer cells >.2mm but <2mm   * **HER2 positive cancer** with a tumor between 2cm-5cm, found in 1-3 lymph nodes, and estrogen-receptor positive classified as this stage * **HER2 positive cancer** with a tumor more than 5cm across, found in 4-9 lymph nodes, “grade 2” and estrogen-receptor positive classified as this stage |
| **Stage 2A** | * Invasive   **Either:**  -No tumor in the breast but cancer detected in 1-3 lymph nodes or in lymph nodes near the breast bone  -Detected tumor measures ~2cm or less and has spread to lymph nodes  -Tumor is >2cm but <5cm and has not spread to lymph nodes   * **HER2 positive cancer** with a tumor more than 5cm across, found in 4-9 lymph nodes, “grade 3” and estrogen-receptor positive classified as this stage |
| **Stage 2B** | * Invasive * Inflammatory characteristics   **Either:**  -Tumor is >2cm but <5cm and smaller groups of cancer cells >.2mm but <2mm are in lymph nodes  -Tumor is >2cm but <5cm and cancer has spread to 1-3 lymph nodes or to lymph nodes near breast bone  -Tumor is >5cm but has not spread to any lymph nodes |
| **Stage 3A**  **Stage 3A (cont.)** | * Invasive   **Either:**  -No tumor found or tumor of any size detected with cancer cells in 4-9 lymph nodes or in lymph nodes near the breast bone  -Tumor >5cm or small groups of cancer cells >.2mm but <2mm found in lymph nodes  -Tumor >5cm and cancer has spread to 1-3 lymph nodes or lymph nodes near the breast bone   * **HER2 positive cancer** tumor of any size that has spread to more than 10 lymph nodes or lymph nodes near the collarbone or breastbone and estrogen-receptor positive classified at this stage |
| **Stage 3B** | * Invasive * Inflammatory breast cancer   **Either:**  -Tumor can be any size but has spread to the chest wall, breast skin and caused swelling or an ulcer  -Cancer spread to 9 lymph nodes or lymph nodes near the breast bone |
| **Stage 3C** | * Invasive   **Either:**  -May be no sign of cancer in the breast area  If a tumor is present, it can be any size and has spread to the chest wall, breast skin and has spread to 10+ lymph nodes  -Cancer has spread to lymph nodes above or below the collarbone  -Cancer has spread to lymph nodes near the breast bone |
| **Stage 4** | * Invasive * Metastatic * Breast cancer has spread beyond the breast and associated lymph nodes to other organs |

*Retrieved from* [*https://www.breastcancer.org/symptoms/diagnosis/staging#stage0*](https://www.breastcancer.org/symptoms/diagnosis/staging#stage0)

1. Bias

There could potentially be selection bias during the recruitment process since not all have access to social media platforms or mobile devices to email or contact a representative to express interest in the study. In this regard, technology illiteracy and broadband access could be another imbedded issue. Additionally, the recruitment process included possibly reaching out through partnerships with breast cancer treatment centers, which could also lead to bias depending on the demographic group(s) looking into treatment options in these centers.

1. Study Size
2. The recruitment process will terminate after 12 female participants within the age range of 30-65 with HER2- positive breast cancer living in Houston, TX have been identified. The maximum amount of participants in each of the randomly assigned groups will be 6. The combined two groups of 12 participants will be housed in the single floor of Baylor College of Medicine Lester and Sue Smith Breast Center dedicated to clinical trials.

**References**

Academy of Nutrition and Dietetics. (2021). “*Study Designs: Glossary of Terms Related to Research Design*”. AND Evidence Analysis Library. Retrieved from <https://www.andeal.org/study-designs>.

Baylor College of Medicine. (n.d.). “*Lester and Sue Smith Breast Center*”. Retrieved from <https://www.bcm.edu/academic-centers/lester-and-sue-smith-breast-center>

BreastCancer.org. (2021). “*Breast Cancer Stages*”. Retrieved from <https://www.breastcancer.org/symptoms/diagnosis/staging#stage0>.

BreastCancer.org. (2015). “*Timely Breast Cancer Treatment Improves Survival*”. Retrieved from <https://www.breastcancer.org/research-news/timely-treatment-improves-survival>.

Chavez-MacGregor, M., Clarke, C.A., Lichtensztajin, D.Y. & Giordano, S.H. (2016). “*Delayed Initiation of Adjuvant Chemotherapy Among Patients With Breast Cancer*”. Retrieved from <https://jamanetwork.com/journals/jamaoncology/fullarticle/2474437>.

Egan, T.K. (2000). “*Monitoring Patients Undergoing Cancer Therapy*”. pp.666-670. Retrieved from <https://academic.oup.com/labmed/article-pdf/31/12/666/24957721/labmed31-0666.pdf>.

Equator Network. (2021). “*The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: guidelines for reporting observational studies*”. Retrieved from <https://www.equator-network.org/reporting-guidelines/strobe/>.

Georgia State University Library Research Guides. (2021). “*Literature Reviews: Types of Clinical Study Designs*”. Retrieved from <https://research.library.gsu.edu/c.php?g=115595&p=755213>.

Sibbald, B. & Roberts, C. (1998). “*Understanding controlled trials Crossover trials*”. BMJ Clinical Research ed. Vol 316, 7146. pp. 1719-1720. Retrieved from <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1113275/>.

Tang, X., Loc, W.S., Dong, C., Matters, G., Butler, P.J., Kester, M., Meyers, C., Jiang, Y. & Adair, J. (2017). “*The use of nanoparticles to treat breast cancer*”. Nanomedicine London. Vol 12, 19. pp. 2367-2388. Retrieved from <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5612024/>.