



POSITIVE *Progress*



Luc, a POSITIVE baby from Switzerland with love!

The baseline characteristics of POSITIVE participants published in the scientific journal *The Breast*: A very interesting overview across four continents.



Who are the women who enrolled in the POSITIVE trial: A global study to support young hormone receptor positive breast cancer survivors desiring pregnancy*

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ABSTRACT

Background: Premenopausal women with early hormone-receptor positive (HR+) breast cancer receive 5–10 years of adjuvant endocrine therapy (ET) during which pregnancy is contraindicated and fertility may wane. The POSITIVE study investigates the impact of temporary ET interruption to allow pregnancy. **Methods:** POSITIVE enrolled women with stage I–III HR+ early breast cancer, ≤42 years, who had received 18–30 months of adjuvant ET and wished to interrupt ET for pregnancy. Treatment interruption for up to 2 years was permitted to allow pregnancy, delivery and breastfeeding, followed by ET resumption to complete the planned duration. **Findings:** From 12/2014 to 12/2019, 518 women were enrolled at 116 institutions/20 countries/4 continents. At enrolment, the median age was 37 years and 74.9 % were nulliparous. Fertility preservation was used by 51.5 % of women. 93.2 % of patients had stage I/II disease, 66.0 % were node-negative, 54.7 % had breast conserving surgery, 61.9 % had received neo/adjuvant chemotherapy. Tamoxifen alone was the most prescribed ET (41.8 %), followed by tamoxifen + ovarian function suppression (OFS) (35.4 %). A greater proportion of North American women were <35 years at enrolment (42.7 %), had mastectomy (59.0 %) and received tamoxifen alone (59.8 %). More Asian women were nulliparous (81.0 %), had node-negative disease (76.2 %) and received tamoxifen + OFS (56.0 %). More European women had received chemotherapy (69.3 %). **Interpretation:** The characteristics of participants in the POSITIVE study provide insights to which patients and doctors considered it acceptable to interrupt ET to pursue pregnancy. Similarities and variations from a regional, sociodemographic, disease and treatment standpoint suggest specific sociocultural attitudes across the world.

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POSITIVE Facts

Trial Progress

as of 21 July 2021

Accrual (target: 500 patients)	
· Patients enrolled in the main study	518
· Patients enrolled in the Psycho-Oncological Companion Study (POCS)	236
Number of patients who have become pregnant	351
Number of babies born	307
Patients withdrawn but providing recurrence status	17
Patients withdrawn, no further participation	35
Number of patients lost to follow-up	9

Participation

Continents	4
Countries	20
Centers	203
Collaborative Groups	11

The IBCSG Data Safety and Monitoring Committee (DSMC)

The IBCSG Data and Safety Monitoring Committee (DSMC) is a standing committee of independent experts, including medical oncologists, a statistician and a patient representative not involved in the study. The mandate of the DSMC is to safeguard the interest and safety of the study participants and the scientific integrity of the study. The committee meets every 6 months to monitor patient accrual and study conduct.

To monitor patient safety, 3 interim analyses are planned prior to reaching the primary analysis on safety, thus providing the opportunity for the DSMC to recommend an early termination of the trial if the observed breast cancer recurrence risk is higher

than anticipated. To protect the integrity of the study, only the recommendation of the DSMC is shared with study investigators, not the details of the interim analyses.

The DSMC met on 10 June 2021 and recommended that the POSITIVE Trial continue as planned.

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POSITIVE Psycho-oncological Companion Study (POCS) Web Application

By Poonam Jani, Trial Coordinator and Data Manager at IBCSG Data Management Center

"Necessity is the mother of invention." This quote became a reality when the COVID-19 pandemic hit us, and we all were under lockdown restrictions. POCS questionnaire submission decreased as patients were not visiting the sites and could not complete the paper forms as they used to do in normal circumstances. We realized there was something we needed to do to improve the POCS questionnaire submission. After looking into various alternative solutions, we decided to develop a web application to facilitate data submission. We chose this option as it is user-friendly, fast, secure, and accessible through the internet from any remote location.

The application allows the collection of the Decisional Conflict Scale (48-POCS-DCS), Hospital Anxiety and Depression Scale (48-POCS-HADS), and Reproductive Concerns After Cancer Scale (48-POCS-RCAC) Forms by individual patients in an anonymous fashion. It is available in several supported languages (English, French, German, Italian, Portuguese, and Spanish). Centers provide patients with the URL to this web application, their Patient ID, and a patient-specific access code. If the forms are due for the visit as per the protocol, patients complete the POCS questionnaires via the web application. Data are transmitted to IBCSG DMC and stored in DFExplore, our Electronic Data Capture (EDC) system.

The web application can be accessed via any electronic device and maintains a comprehensive audit trail for all data received. All the applicable regulatory guidelines and best practices have been followed during the development of this tool. This application is already utilized by all the Centers participating in POCS. We have already received POCS questionnaires successfully completed by patients from remote locations.

To date, electronic submission of patient questionnaires via web application is unique to the POSITIVE

Trial because of its distinctive design and young patient population. Recognizing that nowadays, advancement in electronic platforms is changing the way trials were being managed in the past, we are pioneering this electronic tool with our POSITIVE Trial which sets an example for future trials in IBCSG.



Poonam Jani, Trial Coordinator and Data Manager, IBCSG DMC

"With the POSITIVE Trial, we are pioneering a web application to facilitate patient questionnaires collection."



Robert Starkweather, Deputy Director of Software Engineering, IBCSG DMC



Jacob Kachelmeyer, Programmer/Analyst, IBCSG DMC



Rosita Kammler, IBCSG Head TR Coordination

FFPE Tumor Block Submission and Central Pathology Review

By Rosita Kammler, IBCSG Head Translational Research Coordination

better understanding of the overall results of the POSITIVE Trial. In addition, correlating the results of the Central Pathology Review with the clinical data of POSITIVE will enable future molecular subtyping to better tailor treatment in this population and help future patients fulfill their motherhood wish, without risking breast cancer relapse.

FFPE tumor block submission

On behalf of International Breast Cancer Study Group (IBCSG), we thank and congratulate all Centers that have submitted FFPE tumor blocks to the IBCSG 48 POSITIVE Trial. Primary tumor blocks for 92% of the patients are submitted to the IBCSG Biobank.

The so far collected FFPE tumor blocks represent almost the entire study population, and is an important milestone for the POSITIVE Trial. We encourage all remaining Centers to submit FFPE tumor blocks for 100% of their patients.

Central Pathology Review

The IBCSG Central Pathology Office and Lab are in the midst of assessing levels of ER, PR, Ki67 and HER2 expression, TILs, and tumor cellularity by staining and scoring the FFPE tumor tissue, and performing quantitative analysis. It is an exceptional opportunity to investigate the biology of breast cancer in young patients, a subset that is well-known to be biologically distinct, yet poorly studied, particularly at the molecular and genomic level. The Central Pathology Review is a crucial component of IBCSG multicenter tumor trials, and allows IBCSG to review tumor biological characteristics (such as ER, PR, Ki67 and HER2, TIL's) alone and in combination with clinical-pathological parameters (grade of tumor, size of tumor, nodal status and patient age). The aim is to evaluate whether treatment interruption for some women with high-risk tumors may be detrimental and whether pregnancy might modify the risk of cancer relapse.

The data obtained will therefore permit the individualized assessment of patient outcomes according to the biological characteristics of the tumor, as well as allow a

The IBCSG Central Pathology Office and Laboratory of the IBCSG is located in the premises of the Department of Pathology of the European Institute of Oncology, Milan, Italy. Prof. Giuseppe Viale is the Chairman of the Department and of the Central Pathology Office and Laboratory of the IBCSG, and is an internationally-recognized breast cancer Pathologist.

Made possible by generous grant from the Rising Tide Foundation

Central Pathology Review has been made possible because of the generous grant by the Rising Tide Foundation. IBCSG is deeply grateful to the Rising Tide Foundation for the generous grant that supports the currently ongoing central pathology review.

“The so far collected FFPE tumor blocks represents almost the entire study population. This is an exceptional opportunity to investigate the biology of breast cancer in young patients.”



The IBCSG Central Pathology Office and Laboratory in Milan, Italy

Prof Giuseppe Viale, Chairman of the IBCSG Central Pathology Office and Laboratory



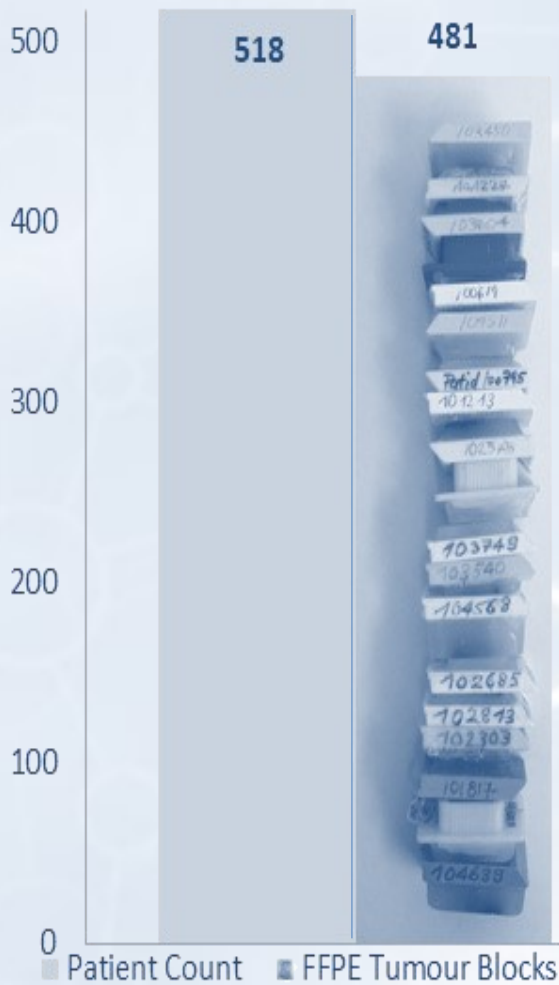
Stefania Andrichetto, Coordinator



Laura Arrigoni, Data Entry/Secretary



Elvira Benini, Data Manager



Leila Russo, Pathologist



Cinzia with Luc

Patient Voices

Cinzia and Luc, Switzerland

" Our son Luc is our greatest gift and miracle. We are thankful every day to have him with us and enjoy immensely being mom and dad. When I look at him and think about the past, all the stresses and strains of cancer treatments have been worth it! Every now and then, Luc's happiness moves me to tears..."

" When I look at him and think about the past, all the stresses and strains of cancer treatments have been worth it! "

Aubrey, Joe and Kelly, USA

Aubrey Ann was born at 7:31am on 3/13/2020 to Joe & Kelly. Kelly was diagnosed at age 27 with Invasive Ductal Carcinoma, and subsequently discovered she carries a BRCA1 mutation. Kelly completed surgeries and treatments at Dana Farber Cancer Institute (DFCI) after undergoing fertility preservation. Due to her BRCA1 status, Kelly and Joe had their embryos tested to screen for the mutation. Kelly and Joe are grateful to have been able to participate in the POSITIVE Trial, which allowed them to fulfill their dreams of becoming parents sooner than they thought they would after Kelly's cancer journey. Joe, Kelly, and Aubrey are healthy and happy!



Kelly with Aubrey and Joe

Welcome POSITIVE Dads!

Partners of women with breast cancer also experience a variety of psychological, emotional and relationship consequences during survivorship. They play a critical role in both the decision making and the challenging journey through pregnancy. We wish to recognize them by giving them a voice.

*As the shimmer of dawn transforms the night
Into a blush of colour futured with delight,
The eyes of your new child awaken in you
A brightness that surprises your life.*

Poem by JoD, Canada



JoD with his beloved daughter



JoD with his beloved daughter

I ♥ ♥ ♥ ♥
♥ ♥ ♥ ♥ ♥
♥ ♥ ♥ ♥ ♥
♥ ♥ ♥ MY
daddy

Adapted from baxterboo.com

Supporters in action!

These images tell the beautiful and successful story of the long lasting and vital support of Pink Ribbon Switzerland to our POSITIVE Trial.

Again, in 2020 and 2021, the proceeds of their amazing Pink Ribbon Golf Tour in Northern Switzerland were donated to IBCSG to support the continuation of our study.

We are immensely honoured by the continuous commitment and support of Pink Ribbon Switzerland !



Pink Ribbon Golf Tour 2020. In the middle, Patricia, a POSITIVE participant with her husband and their cute son Sam, and M. Ruggeri



The Pink Ribbon Golf Tour 2021 sponsors with Nicole Zindel, Alexandra Sola and Monica Ruggeri



The Pink Ribbon dream team 2021. From the right: Joelle Zindel, Beatrice Wegmann, Nicole Zindel and Anja Flückiger



To show our appreciation, on Sept. 6, 2020, the IBCSG Pink Ladies participated in the Virtual Pink Ribbon Charity Walk from three different locations (Zurich, Bern and Uri).

"Although it was a stormy day and the pandemic forced us to separate, the sun was shining in our united hearts!" said one Pink Lady.

A BIG THANK YOU to our PINK LADIES for their amazing commitment!



From 1 October to 31 October 2020, the "One Note, One Donation" virtual participatory fundraising campaign took place, in collaboration with the French singer-songwriter Fanny Leeb, and with the support of the following Belgian sponsors: La Loterie Nationale (Belgian national lottery), Sogerim (real estate company), and Le Soir (newspaper).

For one month, we invited the BIG Against Breast Cancer community to sponsor notes from the song "Show them how it goes", an exclusive composition written especially for us by Fanny. For each donation of 11 euros, the notes of the song were "unlocked". This campaign, intended to support various studies conducted by BIG, will allow us to support 2 patients for one year in the POSITIVE Trial.



Our POSITIVE Supporters

-  *Breast International Group (BIG) with Baillet Latour Fund, Belgium*
-  *Frontier Science & Technology Research Foundation, Southern Switzerland (FSE)*
-  *Pink Ribbon, Switzerland and Norway*
-  *Estée Lauder, Switzerland*
-  *Swiss Cancer League, Switzerland*
-  *San Salvatore Foundation, Switzerland*
-  *Swiss Cancer Research Group (SAKK), Switzerland*
-  *Clinical Cancer Research Foundation of Eastern Switzerland (OSKK)*
-  *Rising Tide Foundation, Switzerland*
-  *Swiss Cancer Foundation, Switzerland*
-  *Piajoh Fondazione di Famiglia, Switzerland*
-  *Gruppo Giovani Pazienti "Anna dai Capelli Corti", Ticino, Switzerland*
-  *Bärgüf, Wallis, Switzerland*
-  *Schweizer Frauenlauf, Bern, Switzerland*
-  *Dutch Cancer Society, Netherlands*
-  *Norwegian Breast Cancer Society, Norway*
-  *Division of Cancer Prevention of the United States National Cancer Institute, USA*
-  *Gateway for Cancer Research, USA*
-  *Breast Cancer Research Foundation (BCRF), USA*
-  *Gilson Family Foundation, USA*
-  *RETHINK Breast Cancer, Canada*
-  *Canadian Cancer Society*
-  *Canada Foundation for Innovation*
-  *ELGC K.K., Tokyo, Japan*
-  *Pink Ring, Tokyo, Japan*
-  *Korea Breast Cancer Foundation, Seoul, South Korea*
-  *Mr. Yong Seop Lee, Seoul, South Korea*
-  *Other private donors*



Adapted frompostermywall.com

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