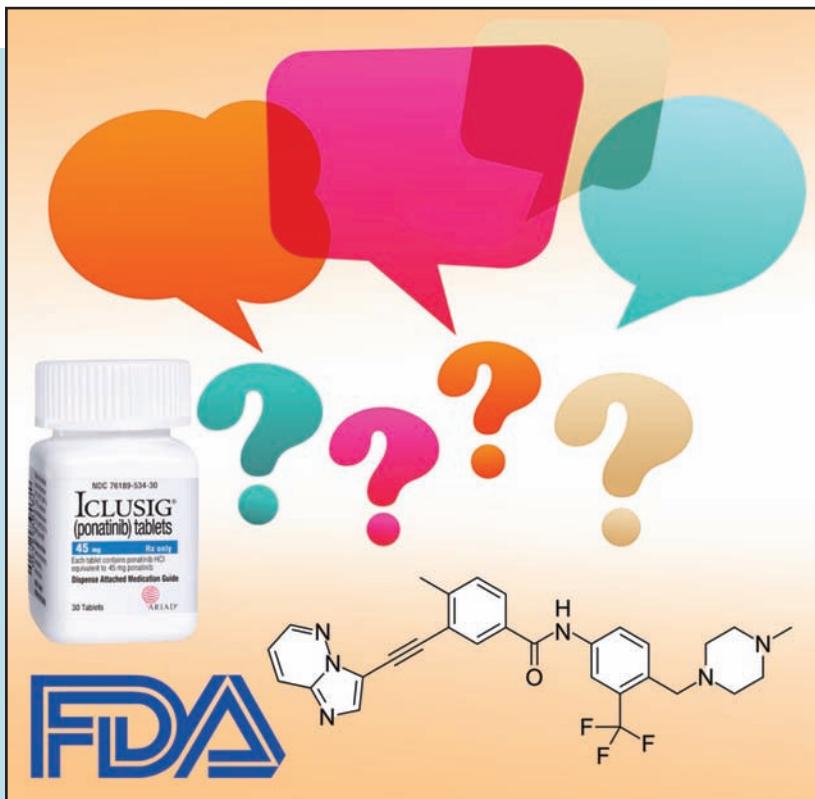


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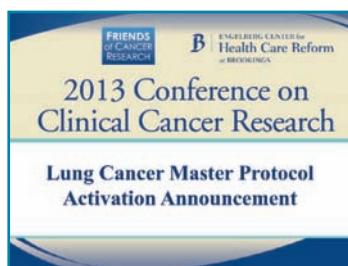


The Ponatinib Problem: Debating the FDA's Recent Market Suspension

BY SARAH DIGIULIO

Although promising early results led to the accelerated approval of the leukemia drug, recently reported longer follow-up data showed an increased risk of arterial thrombotic events—prompting the FDA to temporarily suspend marketing and sales of the drug. But, several experts told us that for some patients, the potential benefits may still outweigh the risks.

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Chronic GVHD and TBI Found to Affect Sexual Functioning After Transplantation

BY MARK FUERST

Nearly half of all survivors of hematopoietic cell transplantation (HCT) are not sexually active even by three years after transplant, primarily due to chronic graft-versus-host-disease (GVHD) in both sexes and transplant-related total body irradiation (TBI) in men. Those were the results of a prospective longitudinal study, one of the longest and most inclusive to date evaluating sexual well-being in transplant survivors. The study is now available online ahead of print in *Blood* (*doi: 10.1182/blood-2013-05-499806*).



Sexual satisfaction persistently declines in both men and women after HCT, with women reporting significantly worse sexual functioning than men, the study's senior author, Smita Bhatia, MD, MPH, Professor and Chair of the Department of Population Sciences at City of Hope National Medical Center, said in an interview.

"We were surprised that sexual functioning was so much lower among



SMITA BHATIA, MD, MPH: "Oncologists need to be more aware that HCT affects quality of life, and spend time with patients discussing this. Oncologists should find resources in the community, such as sexual dysfunction clinics and psychological support, and have a management plan in place if sexual problems develop among these patients."

HCT survivors than historical controls. Oncologists need to be more aware that HCT affects quality of life, and spend time with patients discussing this. Sometimes, oncologists gloss over or don't explore sexual concerns, which patients may be embarrassed to bring up. Oncologists should find resources in the community, such as sexual dysfunction clinics and psychological support, and have a management plan in place if sexual problems develop among these patients."

The study's lead author, F. Lennie Wong, PhD, Associate Professor in the

Departments of Population Sciences and Information Sciences at City of Hope, said that thanks

to improved transplant survival rates, researchers can now focus on examining how HCT affects key aspects of recipients' overall quality of life, including sexual health.

"Previous findings point to the unfortunate fact that, while recipients may physically recover, their sexual health might not rebound as much or as quickly. Data have been limited on this point, prompting us to take a closer look at this issue in a larger, more diverse group of autologous and allogeneic transplant survivors over an extended period."

Sexual Health Survey

The team of City of Hope researchers surveyed 277 adult patients (152 men, 125 women) with a median age of 48 who underwent HCT (131 allogeneic, 146 autologous) there for blood cancers. Participants completed two questionnaires that together evaluated specific areas of sexual function (sexual cognition/fantasy, sexual arousal, sexual behavior/experience, orgasm, and drive/relationship) as well as sexual satisfaction at a median time of 17 days pre-transplant and at six, 12, 24, and 36 months post-transplant. A third questionnaire assessed overall health-related quality of life.

"Our analysis of the questionnaire results confirmed previous studies in demonstrating a definitive impact of HCT on survivors' post-transplant sexual activity," Wong said. Before HCT, about two-thirds of men and about one-third of women were sexually active (defined as having sex with a partner at least once in the preceding month).



F. LENNIE WONG, PHD: "Previous findings point to the unfortunate fact that, while recipients may physically recover, their sexual health might not rebound as much or as quickly. Data have been limited, prompting us to take a closer look at this issue in a larger, more diverse group of autologous and allogeneic transplant survivors over an extended period."

The three-year prevalence declined to 54 percent for men but increased to 52 percent for women. This increase in sexual activity among women may be explained by a corresponding improvement in female psychological quality-of-life post-transplant, said Bhatia, who is also Associate Director for Population Research at City of Hope Comprehensive Cancer Center.

Despite the fact that their sexual activity increased over the three-year period, the women surveyed suffered significantly worse effects overall, she noted.

In addition to further crystallizing transplantation's impact on survivors' sexual health, the study data specifically associated diminished sexual function and satisfaction with transplant-related TBI in men.

"The most important finding is that TBI has an effect on men," said Bhatia. "Early orgasm is the most affected, and drives all other domains of function for men."

The researchers observed a nearly 18 percent decline in sexual function in men who had received TBI. The same group also reported an approximate 32 percent decrease in sexual satisfaction, 26 percent decrease in sexual behavior/experience, 26 percent

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Sexual satisfaction was found to persistently decline in both men and women after HCT, with women reporting significantly more problems than men.

→SIMONE

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more or less, but as time goes by contact information is lost—and at our ages, there are inevitable deaths. Thus, the chance to bring together "The First 25" was a joyful

experience, just like a family reunion with a lot of catching up to do and people to hug and question about their families. It was certainly worth the effort. So many of the staff in that era made it possible for me and my colleagues to do some very special work on behalf of children with cancer.

For that I am eternally grateful to all of my First 25 colleagues and staff of St. Jude; they all made me and my colleagues look good—all the time being good friends who really loved one another. That is a priceless gift that will never be forgotten by any of us. 📷

New CML Registry to Better Understand Patients' Social and Emotional Needs

The Cancer Support Community Research and Training Institute and The Leukemia & Lymphoma Society have together launched the Cancer Experience Registry: Chronic Myeloid Leukemia (CML)—CancerExperienceRegistry.org. The project is an extension of the general Cancer Experience Registry, a global online survey that collects information about the experiences of people living with cancer to better

understand the social and emotional needs of those patients.

"CML patients are living longer, fuller lives due to treatment advances, but we believe that survivorship comes with an array of physical and psychosocial issues. Patients will tell us more about these issues and their impact



through the Cancer Experience Registry," Louis DeGennaro, PhD, LLS's Chief Mission Officer, said in a news release.

Patients who participate will answer a series of questions about their experiences including questions about the patient-medical team dialogue, side effect management, cancer care

planning, financial concerns, and the emotional and social effects of their cancer experiences. Participants will instantly be able to compare their responses with those of others in the community after completing the survey—as well as be connected to support and resources that meet their needs from the two organizations.

Pfizer Oncology is the inaugural sponsor of the registry, and continues to provide funding. 

→POST-TRANSPLANT SEXUALITY

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"The most important finding is that TBI has an effect on men. Early orgasm is the most affected, and drives all other domains of function for men."

decrease in the quality of orgasm, and 17 percent decrease in sex drive/relationship in the time since transplantation.

"TBI studies show physiological effects in men, primarily due to the effect on vascular function in the penis," Wong said. TBI had no such reported effect in women—again because of the inherent physiologic differences in the pathogenesis of sexual dysfunction among men and women, Bhatia added.

The researchers also observed negative sexual effects among those who experienced chronic GVHD. Men surveyed who had developed this post-transplant complication reported a 21 percent decrease in sexual cognition/fantasy and a 24 percent decrease in the quality of orgasm since their transplant.

Similarly, there was a 27 percent decline in post-transplant sexual satisfaction among women surveyed who experienced chronic GVHD, with survey respondents also indicating a 27 percent decline in sexual arousal.

"We speculate that GVHD causes physical scarring of the genital tissue for both men and women," said Bhatia. "We see patients in the clinic who have GVHD who have difficulty during sex because of pain. Dyspareunia is very common among these women."

Discuss Sexual Function with Patients

The message for practicing oncologists is that sexual health after HCT is "an important and highly prevalent problem," she said. "Health care providers should not shy away from asking patients about this issue, and then should have resources available that they have identified in their community."

She noted that a handful of large survivorship clinics across the country take into account issues of sexual function and quality of life. "In a smaller transplant program, an oncologist can devote 10 minutes to openly discuss concerns related to sexual dysfunction and then refer patients to specialists who can help," Bhatia said.

Problem with Measurement Scales?

Asked for her opinion for this article, long-time sexuality in cancer researcher Leslie Schover, PhD, Professor in the Department of Behavioral Science, Cancer Prevention and Population Sciences, at the University of Texas MD Anderson Cancer

Center, said that the study adds to the literature showing that men and women who have HCT have high levels of sexual dysfunction. "However, the fact that the subscales of the sexual functioning self-report scale the researchers used do not correspond to how most people measure aspects of sexual dysfunction is a limitation. This confounds sexual desire and frequency of activity, and does not measure pain during sex.

"What I would expect to see, and appears to be buried in the data, is that men end up with increasing rates of erectile dysfunction due to aging, progressive vascular damage from TBI, and also possibly due to hypogonadism," she continued. "Many

"We speculate that GVHD causes physical scarring of the genital tissue for both men and women."

studies show that any type of pelvic radiation increases the risk of erectile dysfunction in patients with prostate, bladder, and colorectal cancer. Rates of hypogonadism are higher in men who have intensive chemotherapy, and the increase in sexual problems with decreasing body mass index may be a marker of that."

Men with GVHD sometimes complain that genital irritation makes sexual caressing and intercourse uncomfortable. Similarly, she said, the association of GVHD and sexual problems in women is probably almost all due to genital manifestations of GVHD, which can cause not only irritation, but also severe vaginal stenosis and adhesions.

Schover said that there was one unexpected finding: the increase in sexual activity over time in women. "Also, I wonder if TBI was not associated with problems in women because so many already had severe vaginal atrophy and pain from premature ovarian failure and GVHD, so an incremental additional problem from TBI might not be obvious. Again, in other studies, any type of radiation to the pelvis, including TBI, increases the risk of female sexual dysfunction."

Another issue, she pointed out, is that many women in their 40s and older lack a sexual partner because of being divorced or widowed, or because their partner is in ill health or has erectile dysfunction. This limits the ability of women to stay sexually



LESLIE SCHOVER, PHD: "Oncologists should designate someone on the team to talk to patients during treatment planning and at follow-up about the factors that can lead to sexual problems—and especially warn women who are about to have allogeneic transplantation to monitor for signs of genital GVHD. If this is not caught and treated early, it can literally obliterate the vagina."

active with aging, in major contrast to the opportunities for men.

Schover suggested that a multidisciplinary evaluation for sexual dysfunction should include an interview to assess psychosocial factors and a thorough review of medical systems, including a direct examination of the genital area, consideration of genital GVHD in men and women, and consideration of hormonal levels and potential need for vaginal estrogen in women or testosterone replacement in some men.

"Oncologists should designate someone on the team to talk to patients during treatment planning and at follow-up about the factors that can lead to sexual problems," she said. "They should offer patient education information, and especially warn women who are about to have allogeneic transplantation to monitor for signs of genital GVHD. If this is not caught and treated early, it can literally obliterate the vagina."

When problems occur, both brief sexual counseling and medical intervention should be offered. "Partners in a couple should be included in the entire process," Schover said. "This cohort was made up of relatively young patients, and the devastation of their sex lives can be seen, even when treated at an excellent center." 

Abstract Presented in 2008

An abstract of the study was presented at the 2008 American Society of Hematology Annual Meeting. Asked about the five-year delay until full publication, senior author Smita Bhatia, MD, PhD, said there was a considerable amount of refinement of the analyses that was done since the abstract. In addition, she said, the manuscript was originally submitted to another journal, and then the process of submission and resubmission to *Blood* also added to the time.