FORCE Testimony to ODAC on Application to FDA for Approval of Olaparib

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FORCE is the only national nonprofit organization devoted to people and families with a BRCA mutation, including those facing hereditary breast, ovarian, and related cancers (HBOC). We have been providing support, advocacy, education, and research to this community for over 15 years. Women with BRCA mutations face some of the highest known cancer risks of any population. Their cancers develop at younger ages and may occur in multiple family members, who pass the increased risk of cancer on to future generations. This community faces a disproportionate and tremendous cancer burden. Developing therapies that target how cancers develop in BRCA mutation carriers makes sense.

Our organization first learned about PARP inhibitors such as olaparib a decade ago; since that time, we have followed the research, educated our community about these agents, generated excitement about the research focus on HBOC, and facilitated clinical trial enrollment. For the HBOC community and the almost 1 million people in the US that FORCE represents, a drug targeted against BRCA-associated cancers offers hope. As a community, people with BRCA-associated cancers are very motivated to participate in research. Still, completion of PARP inhibitor studies has taken a long time and in the duration, many women who could not access PARP inhibitors and did not meet criteria for any clinical trial have died of hereditary cancers.

Ledermann and colleagues published the outcomes for BRCA-mutation carriers in the Phase II olaparib maintenance trials in Lancet Oncology. We are encouraged that the median progression-free survival for BRCA mutation carriers who received olaparib was 6.9 months longer than those on placebo and that the time to next treatment was 9.4 months longer in BRCA mutation carriers who took olaparib. Olaparib showed a significant effect on time to subsequent therapy in BRCA-mutation carriers, with the median time to subsequent therapy of 15.6 months in patients receiving olaparib versus 6.2 months in the placebo group. The adverse effects reported appear to be manageable. As of January 2014, 20 patients remained on study and of those, 19 were in the olaparib group. In addition, 18% of all patients in the olaparib group received the drug for over 3 years.

Women with BRCA-associated ovarian cancer cannot and should not have to wait another decade to have access to a PARP inhibitor. We ask that the FDA consider our community carefully when
reviewing this drug application and grant approval to olaparib for maintenance therapy in ovarian cancer patients who are BRCA positive based on the following points:

- This drug will improve the quality of life for women with recurrent ovarian cancer by affording them more disease-free time, and by extending their time off of toxic chemotherapy

- Platinum hypersensitivity or intolerance has been shown to occur in 20-40% of patients treated with cisplatin or carboplatin, increasing with repeated exposures, which limits the use of these agents even if the cancer itself remains platinum sensitive. Many patients have moderate to severe side-effects on platinum-containing drugs, suffering from painful neuropathy, nausea and compromised immune function among other adverse effects. It is imperative to have less toxic non-platinum treatment options available for women with platinum-sensitive ovarian cancer.

- The trend towards survival favors women who took olaparib, with 55% of patients in the placebo arm dying compared to 50%, with a reported hazard ratio of 0.73. We understand that confidence intervals are wide and the published study did not reach maturity. However, given the small subpopulations of women eligible for these trials, and the long timeline for completion of these studies, we are very concerned that completion of larger trials could take another decade.

Looking at the data on progression-free survival and time to subsequent first therapy, olaparib gives BRCA mutation carriers with ovarian cancer more time without disease and more time where they can avoid chemotherapy, translating to months or years with improved quality of life. How many more women will die or suffer the effects of advanced disease and chemotherapy while we are waiting for larger trials to be completed? Women fighting hereditary ovarian cancer do not have time to wait. FORCE strongly supports the approval of olaparib as a maintenance drug for BRCA-positive ovarian cancer. We urge the FDA to approve this agent, and firmly believe that approval will improve the lives of women with BRCA mutations fighting ovarian cancer.

I’d like to share a quote from a member of our community who received olaparib through an NIH trial.

“Olaparib worked very well for me with minimal side effects. I was on the trial for 15 months and might have continued longer but for how the protocol was written (no more than a small percentage of progression from the nadir was allowed and since olaparib had resulted in reducing my cancer load to almost nothing, the slightest growth was too much).

…I feel so strongly about the need to make promising avenues of treatment available to women with recurrent ovarian cancer. I have accepted that my disease is likely to be chronic and that I will be in treatment constantly. But I worry about running out of options. Olaparib worked well for me and could again, if I were able to get it. I would like to have that option.”

Her story has been echoed by others in the BRCA community. Please consider these women when making your decision on this long-awaited therapy.