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Cryopreservation of Oocytes

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THE AUTHORS REPLY: As stated in our conclusion, the overall survival benefit was observed in the entire population receiving ADT and docetaxel. This benefit at the early analysis appears to be driven primarily by men with high-volume disease. Although definitions intended to characterize disease volume have limitations, two other phase 3 trials have yielded similar findings on overall survival when our definitions of disease volume were applied.^{1,2} It is also clear that prostate cancer is a heterogeneous disease, and we agree that the development of molecular biomarkers is very important. To this end, we agree that biologic characterization of patients and their tumors, including quality-of-life data, could be of value.

With longer follow-up, the potential benefit of up-front chemotherapy for men with low-volume disease will be better defined. At this time, patient preference and physician judgment should determine who (including those with low-volume disease) receives chemotherapy. However,

in a disease with a longer natural history, deaths not related to prostate cancer could affect overall survival. At this stage, there are no data to support the use of progression-free survival as a surrogate end point for overall survival.

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Since publication of their article, the authors report no further potential conflict of interest.

1. Gravis G, Boher J-M, Joly F, et al. Androgen deprivation therapy (ADT) plus docetaxel (D) versus ADT alone for hormone-naïve metastatic prostate cancer (PCa): Long-term analysis of the GETUG-AFU 15 phase III trial. *J Clin Oncol* 2015;33:140. abstract.

2. Hussain M, Tangen CM, Berry DL, et al. Intermittent versus continuous androgen deprivation in prostate cancer. *N Engl J Med* 2013;368:1314-25.

DOI: 10.1056/NEJMc1511800

Cryopreservation of Oocytes

TO THE EDITOR: In his review on cryopreservation of oocytes (Oct. 29 issue),¹ Schattman recommends that “the possibility of elective cryopreservation of oocytes should be discussed with all women who are in their early 30s.” We question this assertion. Although age-related infertility is of concern to many women, the evidence for successful pregnancy outcomes associated with elective oocyte cryopreservation is still limited, and the procedure carries potential risks for healthy women. The American Society for Reproductive Medicine no longer considers this procedure “experimental,” but it also recognizes the paucity of evidence with respect to safety, efficacy, ethics, emotional risks, and cost-effectiveness of oocyte cryopreservation for nonmedical indications.² Elective cryopreservation is expensive, and there is currently little objective and independent information to guide individual decision making. Discussions about oocyte cryopreservation usually take place with service providers who stand to gain a direct financial benefit. We are concerned that this universal clinical recommendation may fuel women’s anxiety about

age-related infertility and promote the commercial business of oocyte cryopreservation, without assisting clinicians in providing advice for women who are making complex decisions that affect their reproductive choices.

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No potential conflict of interest relevant to this letter was reported.

1. Schattman GL. Cryopreservation of oocytes. *N Engl J Med* 2015;373:1755-60.

2. Practice Committees of American Society for Reproductive Medicine, Society for Assisted Reproductive Technology. Mature oocyte cryopreservation: a guideline. *Fertil Steril* 2013;99:37-43.

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TO THE EDITOR: With regard to a woman concerned about her future fertility, Schattman describes in detail the indications for cryopreservation of

oocytes, the process of cryopreservation, and the outcome for the preserved oocytes. He also advises that women who opt for this procedure should be counseled about the increased risks of pregnancy among older women, the immediate risk of the ovarian hyperstimulation syndrome, and “the potentially harmful effects on their future fertility.” Unfortunately, he does not mention any other potential long-term health risks among women who undergo ovarian stimulation. Population studies have suggested that there is an increased risk of various malignant conditions among women who undergo ovarian stimulation because of infertility or because they are concerned about their future fertility.¹ For another group of young women — those who undergo ovarian stimulation to donate or sell their ova — data on the potential long-term medical risks are lacking.² In the United States, these women are predominantly anonymous donors, and registries that would enable studies of the potential long-term risks of this procedure are not maintained. All women who undergo ovarian stimulation, especially more than once, should be told that their long-term health risks are unknown.

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No potential conflict of interest relevant to this letter was reported.

1. Calderon-Margalit R, Friedlander Y, Yanetz R, et al. Cancer risk after exposure to treatments for ovulation induction. *Am J Epidemiol* 2009;169:365-75.
2. Schneider J. Fatal colon cancer in a young egg donor: a physician mother's call for follow-up and research on the long-term risks of ovarian stimulation. *Fertil Steril* 2008;90(5):2016.e1-2016.e5.

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THE AUTHOR REPLIES: As clearly pointed out by Hickey et al., age-related infertility is a great concern to many women. I agree that the recommendation that “elective cryopreservation of oocytes should be discussed with all women who are in their early 30s” might have been better phrased to make clear that the effects of aging on reproduction should be discussed with all women when they are in their early 20s and 30s and that the option of oocyte cryopreservation can be offered to women who are considering delaying childbearing until later in their reproductive years.

The comment by Hickey et al. regarding the expense of oocyte cryopreservation does not take into account the costs in the longer term; oocyte cryopreservation at 35 years of age has been shown to result in a 48% greater probability of having a live birth than the probability associated with waiting until 40 years of age to attempt to conceive, as well as with a 27% lower cost per live birth.¹

Although Schneider states as a fact that there is an increased risk of various malignant conditions among women who undergo ovarian stimulation and specifically refers to an unfortunate case of fatal colon cancer in a woman who previously donated oocytes, such findings cannot prove cause and effect. Women with infertility have a higher baseline risk of specific cancers even without exposure to ovarian stimulation.² A recent meta-analysis of data from 182,972 women who were exposed to ovarian stimulation showed “no convincing evidence of an increase in the risk of invasive ovarian tumors with fertility drug treatment.”³ Further evidence from a study that linked data from an assisted reproductive technology database to state cancer registries also showed that women treated with assisted reproductive technology had an overall lower incidence of all cancers than women who were never treated with assisted reproductive technology (standardized incidence ratio, 0.78; 95% confidence interval, 0.73 to 0.83).⁴ These observations may provide reassurance to women who desire to preserve their future fertility about the long-term safety of undergoing one or two cycles of treatment.

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Since publication of his article, the author reports no further potential conflict of interest.

1. Devine K, Mumford SL, Goldman KN, et al. Baby budgeting: oocyte cryopreservation in women delaying reproduction can reduce cost per live birth. *Fertil Steril* 2015;103:1446-53.
2. Brinton LA, Westhoff CL, Scoccia B, et al. Causes of infertility as predictors of subsequent cancer risk. *Epidemiology* 2005; 16:500-7.
3. Rizzuto I, Behrens R, Smith L. Risk of ovarian cancer in women treated with ovarian stimulating drugs for infertility. *Cochrane Database Syst Rev* 2013;8:CD008215.
4. Luke B, Brown MB, Spector LG, et al. Cancer in women after assisted reproductive technology. *Fertil Steril* 2015;104:1218-26.

DOI: 10.1056/NEJMc1515128