CTLA4 targeted therapy plus PD-1 targeted therapy could benefit women with ovarian cancer

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An analysis of the NRG Oncology clinical trial NRG-GY003 suggests that adding ipilimumab, a monoclonal antibody that targets the protein receptor CTLA-4, to a regimen with the checkpoint inhibitor nivolumab could improve the proportion with tumor response and progression-free survival hazard rates for women with recurrent epithelial ovarian cancer. These results were presented as a late-breaking abstract oral presentation at the 17th Biennial Meeting of the International Gynecological Cancer Society (IGCS) in Kyoto, Japan. This trial was sponsored by the Division of Cancer Treatment and Diagnosis, National Cancer Institute (NCI) and the agents were provided to NCI by Bristol Myers Squibb under the cooperative research and development agreements between Bristol Myers Squibb and NCI for the development of nivolumab and ipilimumab.

NRG-GY003 assessed the difference in tumor response proportions in 100 women between two treatment regimens over a period of six months. Participants on this trial were randomly assigned to either the first treatment arm (TA1) which received nivolumab alone, or the second arm (TA2) which received a combination of ipilimumab and nivolumab followed by maintenance nivolumab. Tumor response proportions were evaluated through RECIST 1.1 and secondary analyses included progression-free survival (PFS), overall survival (OS), and adverse events (AEs).

Within six months from randomization, 6 (12.2%) responses occurred in TA1 and 16 (31.4%) responses occurred in TA2 (the odds ratio is 3.28 with 85% confidence that it is greater than 1.90). Following the six-month evaluation period, one additional response appeared on TA2. The platinum-free interval stratified hazard ratio (HR) for progression-free survival was 0.528 (95% CI 0.339 to 0.821) and the respective HR for death was 0.789 (95% CI 0.439-1.418). Adverse events (grade 3 or higher) were more prevalent in TA2, however, there were no new safety signals and no treatment-related deaths.

"From my perspective, this is the first evidence that the addition of CTLA4 targeted therapy to PD-1 targeted therapy in patients with ovarian cancer may be more beneficial than PD-1 targeted therapy alone. Future directions could include a trial combining nivolumab and ipilimumab in front line therapy as an adjunct to standard chemotherapy," stated Robert A. Burger, MD, the abstract Lead Author and Professor of Obstetrics and Gynecology at the Perelman School of Medicine at the University of Pennsylvania.

The trial was not powered to detect a difference in overall survival, and there was no preliminary evidence to indicate a detrimental effect from TA2.

More information: Burger RA, Sill M, Zamarin D, Powell D, Frak I, Zivanovic O, Gunderson C, Ko E, Matthews C, Sharma S, Hagemann A, Khleif S, Aghajanian C. (2018, September). NRG Oncology Phase II Randomized Trial of Nivolumab with or without Ipilimumab in Patients with Persistent or Recurrent Ovarian Cancer. Abstract presented at the Biennial Meeting of the International Gynecologic Cancer Society (IGCS), Kyoto, JP.

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