Antiangiogenesis Therapy Improves Overall Survival for Patients with Advanced Cervical Carcinoma

PHILADELPHIA, PA — Final analysis results of the NRG Oncology/GOG-0240 clinical trial corroborated that the addition of the US Food and Drug Administration (FDA)-approved antiangiogenesis drug bevacizumab to chemotherapy contributed to clinically significant increase in overall survival for patients with advanced cervical cancer. The findings of this National Cancer Institute (NCI)-sponsored study represent a proof-of-concept of the efficacy and tolerability of antiangiogenesis therapy in the treatment of this patient population. These results were published online in *The Lancet* on July 27, 2017. The study was conducted under the Cooperative Research and Development Agreement between Genentech and NCI for bevacizumab.

“The extended follow up of this trial shows that the final overall survival analysis is consistent with the initial findings at the study’s second interim analysis reported in 2014 in the *New England Journal of Medicine*: that the addition of bevacizumab to chemotherapy significantly improves the outcomes for patients with advanced cervical cancer in a clinically meaningful way,” stated Krishnansu S. Tewari, MD, Interim Division Director of Gynecologic Oncology at the University of California, Irvine, lead author of this NRG Oncology study.

NRG Oncology/GOG-0240 is a phase 3, randomized, open-label trial that enrolled and surveyed 452 eligible patients with metastatic, persistent, or recurrent cervical carcinoma from 81 centers within the United States of America, Canada, and Spain. Four treatment groups were randomly assigned: two groups received chemotherapy with bevacizumab and two groups received chemotherapy alone. The second interim analysis of this trial established that overall survival duration was significantly increased for the patients treated on the chemotherapy with bevacizumab arms. When NRG Oncology/GOG-0240 reached its cutoff for final analysis at 348 patient deaths, the two chemotherapy with bevacizumab treatment arms continued to show a significant increase in overall survival.

Patients on NRG Oncology/GOG-0240 were randomized 1:1:1:1 to intravenous chemotherapy of either cisplatin and paclitaxel or topotecan and paclitaxel with or without intravenous bevacizumab until disease progression, unacceptable toxic effects, voluntary withdrawal by the patient, or complete response. At the final protocol-specified analysis, median overall survival for the bevacizumab and chemotherapy arms was 16·8 months versus 13·3 months in the chemotherapy-alone arm.

“This study has served as a proof of concept of targeted therapy for women struggling with advanced cervical cancer. As a consequence, several clinical trials are now planned in this space both within and outside of NRG Oncology. We are hopeful that this increase of support for trials and new innovative therapeutics will lead to more significant improvements in survival,” stated Larry J. Copeland, MD, Deputy Group Chair (Scientific Conduct) of NRG Oncology and co-author of the GOG-0240 study.

Also reported for the first time, the median overall survival among patients not receiving previous pelvic radiotherapy was 24·5 months versus 16·8 months and post-progression median overall survival was not statistically significantly different between arms. Fistulas of any grade were reported in 15% of the chemotherapy and bevacizumab treated patients versus 1% of patients treated with chemotherapy alone and grade 3 fistulas developed in 6% of the chemotherapy and bevacizumab treated patients versus less than 1% of the patients treated with chemotherapy. All fistulas (in both...
arms) occurred only among patients who had received previous pelvic radiotherapy. Both bevacizumab-containing triplet regimens are listed as Category 1 in the National Comprehensive Cancer Network guidelines for management of cervical cancer. NRG Oncology/GOG-0240 has led to regulatory approval of bevacizumab for advanced cervical cancer in at least 60 countries on six continents.

“Two additional key points from this study were 1) the post-progression survival showed no observed negative rebound effects after bevacizumab treatment ceased; and 2) among the radiation-naïve patients, median OS was 24.5 mos with bevacizumab vs 16.8 mos without and although this was not statistically significant, it highlights a subpopulation (i.e, stage IVB) for whom treatment with bevacizumab is effective and associated with a fistula rate of 0%”, added Bradley J. Monk, MD, Chairman of the NRG Oncology Cervical Cancer Committee and senior author on the GOG-0240 publications.

Citation:

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NRG Oncology conducts practice-changing, multi-institutional clinical and translational research to improve the lives of patients with cancer. Founded in 2012, NRG Oncology is a Pennsylvania-based nonprofit corporation that integrates the research of the NSABP Foundation, the Radiation Therapy Oncology Group (RTOG), and the Gynecologic Oncology Group (GOG). The research network seeks to carry out clinical trials with emphases on gender-specific malignancies, including gynecologic, breast, and prostate cancers, and on localized or locally advanced cancers of all types. NRG Oncology’s extensive research organization comprises multidisciplinary investigators, including medical oncologists, radiation oncologists, surgeons, physicists, pathologists, and statisticians, and encompasses more than 1,300 research sites located world-wide with predominance in the United States and Canada. NRG Oncology is supported primarily through grants from the National Cancer Institute (NCI) and is one of five research groups in the NCI’s National Clinical Trials Network.