

# Dr. Krishnansu Tewari: my journey as a Gynecological Oncologist

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## Editor's note

*The Clinical Gynecologic Oncology* 9th edition, released in 2017 is regarded as a must-have, readable and most comprehensive reference for the diagnosis and treatment of gynecologic cancers. The 6th and 8th edition of this book have been translated into Chinese, and have aroused tremendous attention in the field of gynecologic oncology in China. To benefit the physicians and patients in China and to further the communication in the field, we have launched a project which uncovers the stories and ideas behind the book, with the aim to share the thoughts and insights of the recognized leaders in the field.

During this project, we were honored to conduct an interview with Dr. Krishnansu Tewari, who is a full professor with Tenure and Director of the Division of Gynecology Oncology at the University of California, Irvine and the director of The Gynecologic Oncology Program at St Joseph's Center for Cancer Prevention and Treatment in Orange, California and the Chair of the National Cancer Institute's NRG Oncology Publications Committee and a voting member of the NRG Oncology Cervical Cancer Committee and NRG Oncology Translational Science/Phase I Committee (*Figure 1*). He is an author of the 9th *Clinical Gynecologic Oncology* and is going to be the 10th *Clinical Gynecologic Oncology*. He shared his insight on a Gynecological Oncologist, the treatment of ovarian cancer in the USA, and some stories about working on the book as an author.

## Expert's introduction

Krishnansu S. Tewari, MD, FACOG, FACS, FRSM is a Full Professor with Tenure and Director of the Division of Gynecologic Oncology at the University of California, Irvine. He is also the Director of the Gynecologic Oncology Program at St Joseph's Center for Cancer Prevention and Treatment in Orange, California. Dr. Tewari is the Chair of the National Cancer Institute's NRG Oncology Publications Committee and a voting member of the NRG Oncology Cervical Cancer Committee and NRG Oncology



**Figure 1** Krishnansu S. Tewari, MD, FACOG, FACS.

Translational Science/Phase I Committee.

Dr. Tewari earned his Bachelor's of Science in Molecular Biology at the University of California, Berkeley in 1990, and his MD at the University of California, Irvine School of Medicine in 1994. He completed both Residency in Obstetrics & Gynecology and Fellowship in Gynecologic Oncology at UC Irvine. He is Certified by the American Board of Obstetrics and Gynecology in both Obstetrics & Gynecology and Gynecologic Oncology. In 2017, Dr. Tewari was inducted into the Royal Society of Medicine in London, England. In 2018, Dr. Tewari was accepted to two physician leadership training courses at the American Academy of Medical Colleges in Washington, DC, and at the Harvard University T. H. Chan School of Public Health in Boston.

Dr. Tewari has published over 160 peer reviewed journal articles. In addition, he has written numerous book chapters including Invasive Cervical Cancer and Cancer in Pregnancy for the most recent three editions of DiSaia & Creasman's *Clinical Gynecologic Oncology* (#1 textbook in Gynecologic Oncology worldwide) and Ovarian Cancer for the latest edition of DeVita's *Principles and Practice of Oncology* (#1 textbook in Oncology worldwide). He is funded by the National Institute's of Health to study drug resistance in cervical cancer through a R21 award. Dr. Tewari is the Study Chair/Principal Investigator for Gynecologic Oncology Group protocol 240 (GOG-0240), the practice-changing phase III randomized clinical trial which demonstrated that compared to chemotherapy alone,

the addition of the anti-angiogenesis drug, bevacizumab, significantly improved overall survival, progression-free survival, and overall response without a significant deterioration in health-related quality of life (Tewari *et al.*, *New England Journal of Medicine* 2014 and Tewari *et al.*, *The Lancet* 2017). This pivotal clinical trial directly led to regulatory approval of bevacizumab for advanced cervical cancer by the United States Food and Drug Administration (August 2014), and the European Medicines Agency for citizens of the European Union (March 2015). Currently, based solely on this clinical trial, bevacizumab has been approved for women with advanced cervical cancer in 60 countries on six continents. Dr. Tewari is the Global Study Chair/Principal Investigator of the ongoing GOG 3016, a phase III randomized clinical trial studying checkpoint inhibition immunotherapy using cemiplimab as a second-line option in advanced cervical cancer. In addition, Dr. Tewari is one of the U.S. lead investigators for KEYNOTE-826, the confirmatory, phase III, randomized trial of chemotherapy with and without pembrolizumab as a first-line option for women with recurrent/metastatic cervical cancer. Finally, Dr. Tewari is the Chair of the Data Safety Monitoring Board for C-145-04, the phase II, multi-center study of autologous tumor infiltrating lymphocytes in patients with recurrent/metastatic cervical cancer.

Dr. Tewari has been listed for nine consecutive years as one of the Top Doctors in Orange County and has been designated a Best Doctors of America for the past 7 years. He maintains a very busy clinical practice in Southern California and performs five to eight life-saving cancer operations every week. Dr. Tewari has trained numerous undergraduate students, medical students, and Ob/Gyn residents over the preceding two decades at UC Irvine, and at least 20 Gynecologic Oncology Fellows. As a recognized expert in robotic surgery, for the past 6 years he travels overseas on an annual basis to serve as Director of a Robotics Surgery Workshop to train international Gynecologic Oncologists who care for women with early stage cervical and endometrial cancer in different hospitals in India. Dr. Tewari has won several Resident Teach Awards (most recently in 2018), and during July 2018 he travelled with 11 UC Irvine rising second year medical students to screen nearly 850 women for cervical cancer in the Mwanza district of Northern Tanzania.

Dr. Tewari's wife, Meagan Moore, MD, is an obstetrician-gynecologist in private practice in Orange County. They live with their three children, Sujata [17], Jeremy [14], and Rowan [11], three dogs, two pigs, a rabbit

and a little aquatic turtle, in Newport Beach, California.

## Interview

### *About the journey of Gynecological Oncologist*

**GPM: What aspects have influenced you as a surgeon in the specialty of gynecology oncology?**

**Dr. Tewari:** The ability to continue to expand my surgical armamentarium and repertoire has been important to me as a Gyn Oncology surgeon. From laparoscopy to robotics, from ultra-radical pelvic surgery to upper abdominal surgical cytoreduction, and also being able to introduce sentinel lymphatic mapping for patients with vulvar, cervical and endometrial cancer—all of this has been critical in my growth as a cancer surgeon.

**GPM: How do you manage operations effectively and safely?**

**Dr. Tewari:** When indicated I obtain pre-operative medical clearance and optimize medical co-morbidities and correct malnutrition when possible. Patients with a deep venous thrombosis or recent history of pulmonary embolus will get a greenfield filter pre-operatively and those with malignant pleural effusion undergo thoracentesis before surgery. Appropriate antimicrobial prophylaxis is administered and re-dosing during surgery according to the accepted guidelines for specific antibiotics is also important to prevent post-operative wound infection. Finally, pre-operative subcutaneous low molecular weight heparin prophylaxis and sequential compression devices are also liberally employed. All of these things optimize patient safety. As for effective surgery, I always need to see a path forward, the proverbial light at the end of the tunnel—if I can't see a way forward at all times, then the life-saving cancer operation is less likely to be effective.

**GPM: What major changes have you observed in your career over the last decade?**

**Dr. Tewari:** More robotic surgery for endometrial cancer and as of the recent study by Ramirez *et al.*, I no longer offer minimally invasive surgery for cervical cancer. Other changes include more upper abdominal surgery for advanced ovarian cancer including upper para-aortic lymphadenectomy, liver mobilization, and full-thickness diaphragm resection. I've also incorporated sentinel lymph node identification in my patients with early stage vulvar, cervical, and endometrial cancer with the caveat that the

women with cervical and endometrial cancer also undergo lymphadenectomy. I have also learned to perform robotic radical trachelectomy and full-thickness skin grafts for McIndoe neovagina.

**GPM: What would you comment on the current treatment of ovarian cancer in the USA?**

**Dr. Tewari:** In the past 5 years in the U.S. there have been 9 new treatment/maintenance indications in ovarian cancer, three of which are biomarker driven. We have learned to successfully incorporate anti-angiogenesis therapy and PARP inhibitors into the management of patients with newly diagnosed disease as well as those with platinum-sensitive and platinum-resistant recurrent disease.

**GPM: You are conducting several ovarian cancer clinical trials at UC Irvine Chao Family Comprehensive Cancer Center. Which one do you think is the most exciting? Why?**

**Dr. Tewari:** The most exciting trials are the ones in which novel combinations are being studied such as the DUO-O study and ATHENA.

**GPM: Looking forward, what advances do you anticipate as a result of ovarian cancer?**

**Dr. Tewari:** I believe we will find a role for immunologic checkpoint inhibition for ovarian cancer in the near future, most probably in combination with other targeted agents (e.g., bevacizumab and/or PARP inhibitors).

*About the book Clinical Gynecologic Oncology*

**GPM: When did you know this foremost textbook Clinical Gynecologic Oncology?**

**Dr. Tewari:** I was a medical student at the University of California, Irvine and since Dr. DiSaia was also at UC Irvine, all medical students were naturally aware of this fantastic textbook when we did our Gyn Oncology rotation during our third year of medical school. I believe in 1992 when I was a third-year medical student the 3rd edition of the book had come out. Today (in 2019) we are preparing to put together the 10th edition.

**GPM: What you have contributed to this textbook as an author in the 9th edition?**

**Dr. Tewari:** For the 7th, 8th, and 9th editions of the textbook I wrote the Invasive Cervical Cancer chapter and I also wrote the Cancer in Pregnancy chapter. The Invasive

Cervical Cancer chapter was co-authored by my mentor, Dr. Bradley J. Monk.

**GPM: What was the most difficult part when you were writing chapter(s) in the 9th edition?**

**Dr. Tewari:** There were no difficult areas to write for the 9th edition because I had written the same chapters for both the 7th and 8th editions. I just needed to perform a new literature search and incorporate any new data that had been published on my subjects.

**GPM: What are the features of the 9th Clinical Gynecologic Oncology?**

**Dr. Tewari:** The features that make this text unique are the disease-site chapters in which sufficient details are included but by no means does the level of detail go overboard. The beauty of this textbook is that it has been developed with not only the practicing Gyn Oncologist in mind, but more importantly, the student of Gyn Oncology—mainly Obstetrics & Gynecology residents, but also for medical students and even Gynecologic Oncology fellows.

**GPM: Is there any content you would like to add to the 10th edition?**

**Dr. Tewari:** Yes, now that pembrolizumab has been approved for PD-L1+ platinum-refractory cervical cancer I will include immunologic checkpoint inhibition. Studies are also in place looking at the activity of ribonucleoside reductase inhibitors, therapeutic vaccines, adoptive T cell therapy, and antibody-drug conjugates so I will also include all of these in the Cervical Cancer chapter. I think it's important to note that although I am now going to be one of the Associate Editors of the textbook for the 10th Edition, I am still planning to write the Invasive Cervical Cancer chapter with Dr. Bradley J. Monk and the Cancer in Pregnancy chapter.

**GPM: Any advice that you would like to give to the readers of the book?**

**Dr. Tewari:** Readers awaiting the 10th Edition should expect something very special. In honor of Dr. DiSaia who passed away on Sept 27, 2018, Dr. Creasman has told me that this will be a very emotionally difficult edition to write, but it will also be celebratory.

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