

The 2008 European School of Oncology Inside Track Conference, “Predictive Modeling in Prostate Cancer”^{*}

Riccardo Valdagni, MD, PhD¹; Peter T. Scardino, MD²; and Louis Denis, MD³

The European School of Oncology (ESO) Inside Track Conference, “Predictive Modeling in Prostate Cancer,” the first event ever dedicated to prediction in prostate cancer, was organized in collaboration with the Prostate Program of Milan National Cancer Institute and the American Italian Cancer Foundation in the wonderful scenario of the Excelsior Lido Hotel in Venice on April 17 through 19, 2008. More than 240 participants from 23 countries attended this 3-day conference, which convened an exceptional group of experts from all over the world whose presentations provided a framework for understanding the state of the art in predictive modeling of prostate cancer and displayed future research trends in the uro-oncologic community. **Cancer 2009;115(13 suppl):3035-8. © 2009 American Cancer Society.**

KEY WORDS: prostate cancer, predictive modeling, quality of life, TNM classification.

Introductory Remarks

The Inside Track Conference “Predictive Modeling in Prostate Cancer,” the first event ever dedicated to the topic of prediction in prostate cancer, was organized by the European School of Oncology in collaboration with the Prostate Program of Milan National Cancer Institute and the American Italian Cancer Foundation and took place April 17 through 19, 2008 in the wonderful scenario of the Excelsior Lido Hotel in Venice (Fig. 1). The conference attracted strong attendance. More than 240 participants from 23 countries attended this 3-day conference, which convened an exceptional group of experts from all over the world, included Chris Bangma and Monique Roobol from Rotterdam, the Netherlands; Joaquim Bellmunt Molins from Barcelona, Spain; Michael J. Donovan from New York, NY; Phillip G. Febbo from Durham, NC; Claudio Fiorino from Milan, Italy; Michael Kattan from Cleveland, Ohio; Rodolfo Montironi from Ancona, Italy; Francesco Montorsi and Alberto Briganti from Milan, Italy; Carla Ripamonti from Milan, Italy; Mack Roach III from San Francisco, Calif; Ash Tewari from New York, NY; Karim Touier from

Corresponding author: Riccardo Valdagni, MD, PhD, Director, Prostate Program, Scientific Directorate, National Cancer Institute, Via Venezian 1, 20133, Milano, Italy; Fax: (011) 39-02-23903015; riccardo.valdagni@istitutotumori.mi.it

¹Prostate Program, Scientific Directorate, National Cancer Institute, Milan, Italy; ²Department of Surgery, Memorial Sloan-Kettering Cancer Center, New York, New York; ³Oncology Center Antwerp, Antwerp, Belgium

Presented at the Inside Track Conference, “Predictive Modeling in Prostate Cancer,” organized by the European School of Oncology, Venice, Italy, April 17-19, 2008.

**Predictive Modeling in Prostate Cancer, Supplement to Cancer*

Received: September 22, 2008; **Accepted:** January 20, 2009

Published online: June 19, 2009 © 2009 American Cancer Society

DOI: 10.1002/cncr.24342, www.interscience.wiley.com

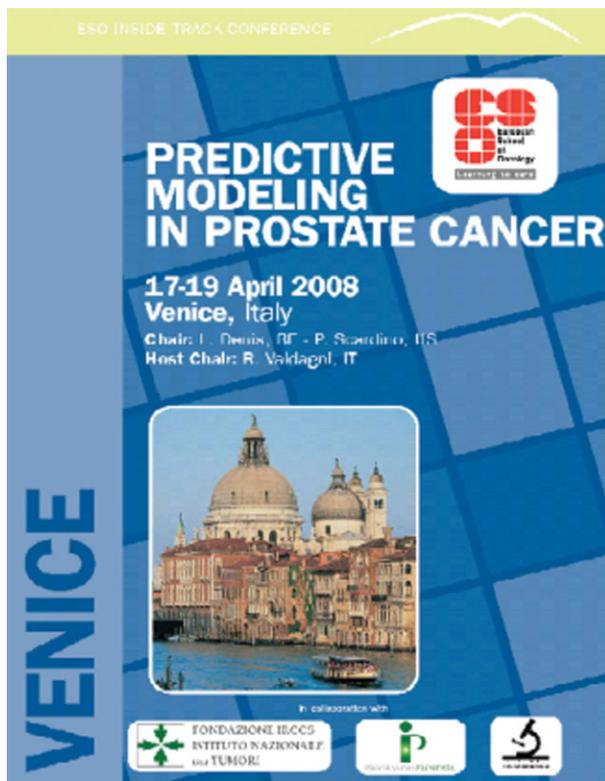


FIGURE 1. The European School of Oncology (ESO) Inside Track Conference, "Predictive Modeling in Prostate Cancer."

New York, NY; and Nadia Zaffaroni from Milan, Italy. The meeting was chaired by Louis Denis from Antwerp, Belgium; Peter T. Scardino from New York, NY; and Riccardo Valdagni from Milan, Italy.

Prediction has always fascinated mankind, with fortune tellers, magicians, prophets, sibyls, oracles, and Cassandra trying to forecast events and anticipate the future. For several decades, the standard classification in oncology has been anatomic staging known as the International Union Against Cancer/American Joint Committee on Cancer TNM classification. The introduction of biologic prognostic factors has complemented the staging and stage grouping in most tumors, and the development of sophisticated mathematical models in the past 15 years has enabled the evaluation of tumor variables and response to treatments. So far, starting from the first attempts to assess the risk of positive lymph nodes before pelvic irradiation (developed at Stanford University in 1987) and the clinical and pathologic tumor and lymph node characteristics before surgery studied by Partin and colleagues in 1993, more than 80 mathematical predictive models have been formulated.

At the meeting, Philip G. Febbo presented the genomic approaches to outcome prediction and highlighted the role for genomic technologies in evaluating molecular modifiers of prostate cancer risk and behavior and the construction of predictive models that anticipate the development of prostate cancer, prostate cancer progression, and response to therapy.

Nadia Zaffaroni lectured on the biomolecular approaches to outcome prediction developed to date, stressing the need for novel molecular markers that are associated specifically with biologically aggressive disease for improved staging and prognostication and also for providing mechanistic information to facilitate treatment selection.

Rodolfo Montironi discussed the predictive models in histopathology and the importance of a diagnostic decision support system, defined as a methodology that provides guidance in situations involving complex decision sequences and resulting in a systematic, ordered, and exhaustive evaluation of evidence and weighting of individual items as they are combined to form the basis for a final decision.

Michael J. Donovan presented the systems pathology approach for building predictive models, going through the novel approaches with molecular diagnostics and predictive testing for guiding therapy and overall patient management and discussing how a systems pathology program, which includes image analysis and quantitative biomarker assessment with machine learning analytics, has transformed the clinical paradigm of personalized medicine.

Ash Tewari lectured on predictive models in prostate cancer diagnosis. He focused on a study aimed at predicting the incidence and risk of Gleason score upgrading between biopsy and final pathology after prostatectomy using a novel, biopsy-based variable: cancer density. Cancer density proved to be a better predictor of Gleason score upgrading from biopsy to prostatectomy than total serum prostate-specific antigen.

Monique Roobol talked about predictive models in diagnosing indolent cancer and the experience of the Rotterdam section of the European Randomized Study of Screening for Prostate Cancer, which constructed an ad-hoc predictive tool.

Karim Touijer presented the Memorial Sloan-Kettering Cancer Center experience with predictive models

before surgery, starting with the nomogram developed by Kattan et al in 1998 and predicting the risk of disease recurrence after radical prostatectomy for clinically localized prostate cancer, and after surgery, by extending Kattan's preoperative nomogram to postoperative data in 1999, with inclusion of information available postoperatively. He also made a survey of possible new nomograms that are being developed for prostate cancer prostatectomy with the inclusion of image-analysis variables and molecular markers.

Mack Roach III lectured on predictive models in external radiotherapy that have been designed to help physicians and patients understand which outcomes may be expected for patients who have specific pretreatment clinical features, focusing on the prediction of biochemical failure, the risk of metastasis and/or death, and the importance of predicting pathologic features (ie, seminal vesicles, extracapsular extension, lymph node involvement) to optimize the selection of targets for radiation.

Michael Kattan talked about predictive models in brachytherapy and the possibility of individualizing the treatment plan. He presented a nomogram predicting 5-year freedom from recurrence that is based on pretreatment prostate-specific antigen, Gleason sum, clinical stage, and the presence of external beam radiotherapy along with a subsequent nomogram that takes into account the quality of the brachytherapy implant. His conclusions underline the finding that brachytherapy nomograms are rare and that heterogeneity across centers plays an important role in treatment outcome. Predictive accuracy appears to be lower with brachytherapy nomograms, although they provide better predictions than the alternatives.

Joaquim Bellmunt Molins discussed predictive models in medical oncology, pointing out the importance of capturing clinically relevant and measurable variables for routine use to inform patients, improve palliation and treatment decisions, and create homogeneous prognostic strata for randomized comparative trials of therapeutic agents.

Carla Ripamonti dealt with predictive models in palliative care with reference to the prognostication of life expectancy and the appropriate therapy for symptom control.

Karim Touijer went through predictive models of toxicity in surgery, pointing out that the objective of

modern prostatectomy is the complete removal of the prostate, seminal vesicles, and pelvic lymph nodes with minimal perioperative morbidity, no blood transfusions, and an early return to normal activities with no positive surgical margins and no long-term loss of continence or potency. He reported the Memorial Sloan-Kettering Cancer Center experience on recording and grading erectile dysfunction and urinary incontinence after prostatectomy and also compared laparoscopy with prostatectomy.

Claudio Fiorino introduced the dosimetric issues of predictive models of toxicity in external radiotherapy, analyzing predictive tools like single/multiple dose-volume constraints and Equivalent Uniform Dose or Normal Tissue Complication Probability models. He analyzed literature-based knowledge as well as new, unpublished results about dosimetric predictors of toxicity for all the critical organs involved in prostate irradiation: rectum, bladder, bowel, and regions suspected to cause radiation-induced erectile dysfunction. An accurate knowledge of the dose-volume relations concerning the side effects of the organs at risk is of paramount importance to drive the optimization of the treatment in minimizing the risk of complications.

Riccardo Valdagni presented the clinical issues of modeling toxicity in external radiotherapy, introducing the first sets of nomograms for predicting the rectal syndrome. Nomograms are expected to increase the predictive accuracy of models based on dosimetric issues, because they take important clinical factors into account (ie, comorbidities, concomitant use of drugs, androgen deprivation, and the presence of previous abdominal surgery). The careful prediction of treatment-related morbidity may help patients in the decision-making process and may help clinicians tailor treatments better to patient's characteristics.

Mack Roach III highlighted the use of predictive models of toxicity in brachytherapy. In this field, a few dosimetric issues are known concerning rectal, urethra, and bladder doses, and the development of new models that take clinical factors into account is needed.

Alberto Briganti discussed predictive models in andrology, analyzed the literature, and presented a nomogram that estimated the risk of developing erectile dysfunction based on patient age, Charlson comorbidities index, preoperative International Index of Erectile

Function score, the quality of rehabilitation therapy, and the quality of bilateral nerve-sparing prostatectomy.

Ash Tewari lectured on predictive models of long-term survival, providing a review of the basic and advanced statistical techniques of predictive modeling, underlining the most common clinical decision tools available in prostate cancer (eg, nomograms, look-up tables, and artificial neural networks), and highlighting their potential shortcomings and merits with their application in clinical practice.

Michael Kattan forecast the future of predictive models and presented the take-home messages. He stated that the existing prediction models need to be categorized around actionable decisions so that clinicians will know which tool to use for a particular problem. He used a diabetes example to illustrate how nomograms should be used to predict good and bad outcomes for any difficult treatment decision.

The faculty's presentations provided a framework for understanding the state of the art in predictive modeling of prostate cancer and displayed future research trends in the uro-oncologic community. The discussions that

followed each session highlighted the importance of the multidisciplinary approach to the disease; of stimulating further collaboration among specialists; and of integrating basic, translational, and clinical research to optimize outcomes for patients with prostate cancer patients and to improve their quality of life.

This supplement is meant to be a collection of the outstanding lectures presented in Venice and the elaboration of future trends and perspectives. The obvious success of the conference; the evaluative questionnaires from conference participants; and, above all, the strong feeling that this conference will contribute to the advancement of the diagnosis, treatment, and quality of life of patients with prostate cancer have convinced the Chairs and the European School of Oncology to schedule the conference biannually. The next edition will present proceedings from the meeting to be held in 2010.

Conflict of Interest Disclosures

Sponsored by ASTRA Zeneca and the European School of Oncology.