

Progress and Promise, Part V Panel Discussion

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INTRODUCTION

Biologic therapies are not only changing the way in which prostate cancer is treated, they are identifying new questions and opening up new areas of research that have the potential to improve outcomes in prostate cancer.

THE ROLE OF CHEMOTHERAPY IN AN ERA OF TARGETED THERAPY

All modalities—radiopharmaceuticals, aminomodulatory agents, chemotherapy, AR-targeted drugs—play a role in treating patients with prostate cancer. In order to identify patients who would benefit from chemotherapy, we need to better understand individual patients' tumors, which tumors are AR-driven, and how they respond to different treatments using all of tools discussed—organoids, circulating tumor cells, and imaging studies.

RADIUM-223

While we don't completely understand how radium-223 works, Dr. Morris was confident that the effects are biological, not physical and that delaying skeletal-related events may be a by-product of altering the cancer's behavior. Animal models are needed to help clarify what is happening and potentially develop a new platform beyond what is currently available. Researchers will most likely begin looking at combining radium-223 with other drugs.

CONSISTENCY WITH BIOMARKERS

In developing biomarkers, everybody needs to be on the same page in order to address the issue of reproducibility. PTEN is probably one of the most common deleted genes; however, for the same specimen, there will be very marked differences in the interpretations by pathologists. You need to make sure that everybody is using the same assay and getting the same result.

For circulating tumor cells, it is essential to establish consistency among relevant variables such as the type of antibody that is used, the conditions in which the antibody is incubated, and the specific counterstain that is used. The Epic platform, for example, generates 96 dif-

ferent parameters per cell, so if you have 100 cells, it is an enormous amount of information to wade through.

In developing imaging as a biomarker, you want to be sure that when you take the same picture on the same patient, the results are the same whether you use a machine in the United States or in Ireland.

CIRCULATING TUMOR CELLS AS PROGNOSTIC MARKERS

Circulating tumor cell clusters seem to be prognostic for poor outcomes in a number of different tumor types. They are often seen in late stage disease, in patients with very high tumor burdens.

BIOLOGIC AGENTS AND THE TREATMENT PROSTATE CANCER

With respect to hallmarks of the malignant process, the biologic drugs have shown that processes other than slowing tumor growth rates contribute to outcomes. Patients treated with biologic agents may live longer despite the fact that the tumor does not shrink or that PSA levels are not reduced. This means that we have to learn how to incorporate measurements of those processes in the way we evaluate drugs. One challenge is how to determine dosing for a biologic agent, since the traditional "more is better" approach does not necessarily apply, and may even be detrimental.

IN MEMORIAM



The Society for Translational Oncology is deeply saddened by the sudden passing of Professor John Fitzpatrick whose passion, dedication and drive ensured cancer research became a cornerstone in the fight against cancer. Prof. Fitzpatrick was one of European urology's most accomplished opinion leaders and highly respected by his peers in and outside Europe. His medical career spanned 44-years and included top positions in urology and major scientific honors.

FINANCIAL DISCLOSURES

Dr. Fitzpatrick discloses consultant relationships and receiving educational grants from Astellas, Ferring, GlaxoSmithLine, Janssen, Millenium, Sanofi and Takeda.

Dr. Chen discloses no financial relationships relevant to the content of this presentation.

Dr. Rathkopf discloses receiving research funding from Celgene, Exelixis, Janssen, Medivation/Astellas, Millenium/Takeda and Novartis; and serving as an advisor for Janssen, uncompensated.

Dr. Morris discloses serving as a consultant/advisor for Bayer, uncompensated; and receiving research funding directly paid to MSKCC from Agensys, Algeta, Bayer, Janssen, and Sanofi.

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