Eileen M. O'Reilly, MD
Associate Director for Clinical Research
David M. Rubenstein Center for Pancreas Cancer
Memorial Sloan Kettering Cancer Center
Professor of Medicine
Weill Cornell Medical College
New York, New York

What new subcategories of pancreatic cancer have emerged that are allowing for a biomarker-driven approach to therapy?

Hi, my name is Dr. Eileen O'Reilly, and I am going to focus for the next couple of minutes on defining what are the new subcategories of pancreas cancer that have been identified, which might allow opportunities for biomarker-directed therapies. There has been a lot of work in this context, trying to see if the heterogeneous group of people that represent pancreas cancer can be defined from either a pathologic or biomarker perspective. This may provide opportunity for stratification, for example, for part of clinical trials or for identification of subgroups of patients that are more likely to respond to a particular treatment approach.

There has been a number of major articles in the last couple of years, and one in particular comes from Andrew Biankin's group. This study looked at about 460 people with pancreas cancer and did an extensive genomic analysis looking at whole genome and deep exome sequencing, copy number alteration, and RNA expression profiles and identified what appeared to be four subgroups, one being a squamous subgroup that is characterized, for example, by P53, KDM6A mutations, and typically has a poor prognosis. Another is a subgroup that may be immunogenic, which is characterized by T and B cells being infiltrated, PD-1, PDL-1 expression, and more immune favorable microenvironment, and this is a subgroup, for example, where immune targeting may have opportunity. There is another subgroup which is the apparently differentiated endocrine and exocrine component which may be a different group that has some endocrine features; and then a larger group which is the more classic setting of ductal adenocarcinoma.

As yet, these are not readily available for prospective use, and many other groups are going back trying to refine these subcategories and build on them and see if there may be characterizable biomarkers for each of these subgroups that, again, could help with patient stratification. Let's say, this is another, very exciting area in terms of

understanding the biology of pancreas cancer and beginning to get the opportunity for treatment refinement, which for the most part, have not succeeded in pancreas cancer, although there are now biomarkers that are becoming available in the clinic that do identify subgroups of patients. An example of this would be patients with defects in DNA repair strategies; for example, germline BRCA and somatic BRCA deleterious mutations may predict for patients who could have exceptional benefit from platinum therapies and experimental PARP inhibitors. There are trials underway examining these opportunities in pancreas cancer, and we will hopefully have some randomized data for this subset of patients in the next couple of years that again will help with treatment selection and refinement for a subgroup of patients.