shared decision making, and ultimately improve meaningful outcomes, such as quality of patient care, quality of life, or quantity of life.

Several tissue-based prostate cancer biomarkers have been developed, commercialized, are widely available, and covered by insurance carriers. Decipher (GenomeDx Biosciences, Vancouver, BC, Canada), Onco*type* Dx (Genomic Health, Redwood City, CA), and Prolaris (Myriad Genetics, Salt Lake City, UT) are mRNA-based gene expression classifiers, and ProMark (Metamark Genetics, Waltham, MA) is a proteomic test amenable to formalin-fixed paraffin-embedded prostate biopsy or prostatectomy tissues. Several retrospective analyses have supported their potential to identify appropriate patients for active surveillance (Question 1) or predict adverse pathologic, biochemical, or cancer-specific survival outcomes (Question 2). These data could potentially improve confidence in management choice, especially in gray zone areas in which clinical variables are less certain, although high-quality prospective evidence, particularly in a randomized design, is currently lacking. The Decipher genomic expression score can also be helpful in selecting appropriate patients for adjuvant versus salvage radiation (Question 3). Identifying patients with poor prognosis may ultimately lead to therapy intensification, including the escalation of local therapy or addition of newer systemic agents, a focus of several ongoing trials.

Despite the promise of molecular biomarkers in addressing these important unmet clinical needs, there is currently insufficient evidence to recommend the routine use of these tests. The costs of testing and downstream therapy implications are considerable and currently not justified for routine use, financially or oncologically, based on available evidence. While these tissue-based tests may improve risk stratification, we recommend their use only in situations in which a specific assay result, when considered in combination with routine clinical factors, will clearly affect the management decision. These assays have not been prospectively tested nor shown to improve intermediate or long-term outcomes (eg, QOL, need for treatment, or survival). Rigorous and prospective clinical testing is warranted and strongly encouraged.

Although the routine use of molecular biomarkers is not recommended, the Expert Panel recognized that there may be scenarios in which biomarkers may be helpful to inform prognostication or to guide management decisions. For instance, men who are considering active surveillance of newly diagnosed prostate cancer with higher-risk features for progression (eg, high-volume Grade Group 1, low-volume Grade Group 2, or high PSA density) may benefit from a biomarker, although the committee recognizes that a relative minority of men will attain clear actionable data as test results are often equivocal in this scenario. For men struggling to determine whether adjuvant versus early salvage postprostatectomy RT is most appropriate, biomarker data may provide additional data to integrate into the final decision.

Which of the available commercial biomarkers is best (if any) in these settings cannot be determined as these assays have not been sufficiently compared head to head in properly designed studies. However, the extent of supporting data significantly varied among the assays. Furthermore, understanding their use in the context of MRI imaging is also of great importance (Question 4). There are insufficient data to support a consensus statement on the relative value of genomics versus MRI; however, for an individual patient, MRI or genomic testing may ultimately provide overlapping, complementary, or discordant information. Comprehensive studies with comparative data, costs, and clinical implications would be valuable.

Additional challenges exist for molecular biomarker development in prostate cancer. Tumor heterogeneity may occur within an individual, meaning two or more independent prostate cancer foci may exist within a patient, each harboring different characteristics. Identifying the most informative (eg, index or driver lesion) for biomarker testing may be a challenge, particularly given the known undersampling that occurs with prostate biopsy. Furthermore, molecular changes, as with any biologic process, are not always definitive or binary, as there is a biologic spectrum even within risk groups. Understanding if and how available assays complement other prognostic factors, such as germline DNA mutations (eg *BRCA1/2*, *MSH*, and others), may also influence future testing and management decisions. Studies including diverse racial and ethnic groups are essential to inform broader applicability of testing. Finally, cost-effectiveness analyses that incorporate the price of testing along with cost savings and quality of life gained from sparing ineffective treatment will be critical.

Despite several challenges ahead and the lack of current evidence to support a committee consensus for routine genomic biomarker testing, there is continued optimism regarding the potential for tissue-based biomarkers to inform decision making for certain men and, we hope, improve outcomes for men with prostate cancer.

SPECIAL COMMENTARY

In additional to the primary research questions, the following questions were also considered as the Expert Panel believed they warrant discussion despite the absence of evidence.

What Is the Optimal Approach for Tumor Selection and Processing for Molecular Testing?

In contrast to prostatectomy specimens, prostate biopsies offer unique challenges to molecular testing because of their small size, particularly in active surveillance populations, and their often limited volume of cancer. Furthermore, at the histopathologic level, prostatic adenocarcinoma is often intermingled with benign prostatic glands with variable