Background

There will be an estimated 248,530 new cases of prostate cancer (PCa) diagnosed in the U.S. in 2021. While only 3-5% of patients will be diagnosed with frank metastatic disease, there will be nearly 35,000 (34,130) deaths from PCa in 2021.1 The import of these statistics is magnified in the southeastern region of the U.S. where death rates from PCa in many southern states exceed the national rate with the exceptions of Florida and West Virginia. Nonetheless, the death rates in the southeastern U.S. as a region are amongst the highest rates in the country.

The imperative for managing individuals with PCa with best practice and the best available evidence comes from two key points. First, PCa is consistently the leading cause of cancer-specific deaths in men in the U.S., second only to lung/bronchial cancer deaths. Concern increased amongst clinicians following the publication of a controversial study by Weiner et al from Northwestern University, who concluded that the incidence of metastatic PCa has increased dramatically in the U.S. between 2004 and 2013, particularly in men in the 55-69 years of age cohort.2 The authors suggest that the increase may be related to an increase in the development of more aggressive cancers. There is considerable evidence to suggest that PCa patients who benefit most from systemic therapies are those with higher risk disease.

Second, and perhaps more importantly, only 50% of men who die of PCa have metastatic disease at diagnosis, suggesting that timely deployment of best practices might convert some of those men otherwise destined to develop metastatic disease to become long term survivors. Recent studies suggest that systemic intervention for men with high risk M0 disease may offer some clinical benefit. Early results from the STAMPEDE trial, a multi-arm, multistage (MAMS) platform design which included a cohort of men with M0 disease, suggests that the addition of effective agents to standard of care (SOC) androgen deprivation therapy (ADT) as first line therapy in M1 and select M0 men, can improve outcomes. Subjects with M0 disease who had docetaxel added to ADT did have a statistically significant improvement in failure-free survival at 4 years (22 to 30%; P< 0.0001) despite a failure to demonstrate the same level of benefit in overall survival.3 Longer follow up reported for the androgen deprivation therapy (ADT) alone vs ADT + Abiraterone arms of the STAMPEDE trial has seen clear benefit in patients with metastatic disease and increasing separation of the Kaplan-Meier overall survival curves in patients with non-metastatic disease with longer follow up in favor of abiraterone + ADT, although results remain immature.4

The approval of several new agents for use in hormone sensitive PCa (HSPC), M0 castrate-resistant PCa (CRPC) and mCRPC as well as advances in understanding the molecular drivers of PCa itself as well as the resistance to treatment, emphasizes that the treatment of PCa is at an inflection point.

Landscape of Prostate Cancer Care in the Community

OPTIMIZING PROSTATE CANCER CARE IN COMMUNITY PRACTICE, 2021

ABSTRACT

A white paper presented by the Duke Cancer Network in collaboration with the Duke Cancer Institute focusing on emerging trends that impact the care of prostate cancer patients in the community setting.

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The Duke Cancer Network (DCN), in collaboration with the Duke Cancer Institute, engaged oncology practitioners in the community to understand the current state of practice and optimize care of PCa patients across environments of care. The project was funded by an educational grant from Astellas, Inc. The DCN has affiliate relationships with a dozen or more independent organizations throughout the eastern United States. The affiliations focus on iteratively improving the care of cancer patients across the healthcare spectrum. Prostate cancer is one of the most commonly diagnosed cancers in the U.S.

Need for Education and Collaboration in the Management of Advanced Prostate Cancer

The landscape of evidence-based management of advanced PCa continues to expand with ongoing emergence of practice changing data. However, a number of factors suggest that clinicians may be unaware of latest clinical advances in the treatment of PCa, for example, the treatment of non-metastatic castrate resistant PCa, or the role of radiotherapy in recurrent or advanced disease - resulting in suboptimal outcomes for patients with PCa.

The burden of maintaining knowledge of best practice(s) for the individual clinician is enormous, particularly for those in general medical oncologic or urologic practice. The sheer volume of material and the barriers a clinician must overcome to access, review, and digest evolving data in order to understand the nuances that define best practice precludes effective learning and the consequent changes in practice without the assistance of guided education opportunities.

Within the treatment paradigms of many cancers, systemic therapy has traditionally fallen within the portfolio of the Medical Oncologist. However, the management of PCa has been somewhat different. The engagement of medical oncologists in the care of PCa patients lags far behind that of other malignancies, limiting the ability of patients to benefit from multidisciplinary care. True multidisciplinary care in PCa is too often limited to academic centers. Indeed, a review of utilization of medical oncology services amongst Medicare beneficiaries published in 2008 revealed that the vast majority of PCa patients did not see a medical oncologist until the last 12 months of life, when 52.7 % of patients with PCa compared with 70% of patients with any cancer were seen by medical oncology.5 This suggests that urologists continue to play a major role in the management of PCa throughout the entire clinical course of individual patients.

The introduction of oral systemic therapies, compared with intravenous therapies (e.g. chemotherapy) that require considerable infrastructure support, creates the opportunity for clinicians in any specialty to prescribe oral medications such as abiraterone or enzalutamide. Indeed, a recent analysis of Medicare Part D data for use of abiraterone or enzalutamide between 2013-2015 indicated that while at least 75% of prescriptions for these agents were written by medical oncologists; a small but rising proportion were written by urologists.6 Furthermore, the successful management of patients being treated with these new therapies is highly nuanced, requiring an understanding of the consequences of agent selection and sequencing.
An informal survey of medical oncologists in select community oncology practices suggests that there is a general lack of awareness of the impact of prior therapies on the effectiveness of subsequent PCa interventions. (Personal communication) Despite awareness of the positive impact on overall survival from abiraterone, enzalutamide, sipuleucel –T, and other therapies, there was limited awareness among clinicians surveyed of the rationale for sequencing.

Emerging evidence supports thoughtful selection and sequencing of therapies and integration with data on molecular markers for optimal patient outcomes. Multivariate analysis of data for 161 patients with castrate resistant PCa (mCRPC) treated with abiraterone in the Prostate Clinical Research Information System at the Dana Farber Cancer Institute revealed that longer duration of abiraterone use (and presumably benefit) occurred when patients had not received prior ketoconazole. Conversely, in univariate analysis, men who had received prior ketoconazole had shorter duration of subsequent abiraterone use – as was seen in other phase II clinical trials. A recent review of chemotherapy in PCa by Quinn and colleagues highlights the evidence for possible, yet not completely understood, cross-resistance between taxanes and androgen receptor- and CYP 17- targeted agents. Furthermore, cross-resistance may not be intuitive. One might predict that patients who had been treated with one taxane might be resistant to a second taxane. However, the TAXYNERGY phase II trial demonstrated that subjects with metastatic castrate-resistant prostate cancer (mCRPC) who failed to respond to initial treatment with docetaxel or cabazitaxel benefitted from an early switch to the alternate taxane.

Clinicians’ awareness of the factors that support the choice of one anticancer treatment over another in the management of metastatic castrate resistant or castrate-sensitive PCa is limited. Oncologists asked to provide a rationale for choosing one agent over another indicated that the choice was based on personal experience with individual agents rather than evidence-based. There is limited information regarding community urologists’ awareness of or implementation of best practices with regard to systemic therapies.

Data on current practice patterns are difficult to obtain for a variety of reasons. But prior studies in related areas suggest the need for education specifically designed to reach the community practitioner. The Medicare Modernization Act of 2003 targeted the overuse of therapeutics such as drugs covered under Medicare Part B; including the GnRH agonists. By 2005, although GnRH overuse declined 34%, ~26% of men for whom use was not recommended were still receiving this treatment. Urologists who continued to prescribe the GnRH for men outside of the recommended guidelines were more likely to be in solo practice, unaffiliated with a medical school, and caring for a more vulnerable population (racial minorities). Combined with the data that a significant number of patients with advanced PCa do not see a Medical Oncologist, the possibility that management of PCa patients not involving multiple disciplines may lead to less than optimal outcomes mandates education targeting a broad swath of clinicians caring for patients with PCa.
In order to understand the existing practice patterns in the community, DCN/DCI conducted a survey of the clinical care landscape for patients with PCa within the 14 organizations affiliated with DCN at the time. Following the Landscape of Care survey, a program of choreographed educational activities were developed to engage community providers and target educational needs.

**Landscape of Care Survey**
The Landscape of Care survey was sent to all the medical oncologists and urologists at all DCN affiliates. There were 15 respondents: 10 Oncologists and 5 Urologists. All the providers were board certified in the respective discipline and practiced in the community. One of the oncologists did not provide care for patients with metastatic PCa and those responses were removed from the reported survey results.

Fully 80% (4/5) of urologists report providing prescriptions for PCa-directed therapeutics for patients with metastatic PCa and all report co-managing PCa patients with medical oncologists, while only 2 out of 9 medical oncologist report co-managing patients with urologists. Urologists report engaging medical oncology across the continuum of care with some engaging at the time of diagnosis and others engaging after 1st or 2nd line treatment. One urologist noted that the engagement was variable depending on the patients’ clinical status and goals. All of the responding urologists report prescribing agents such as abiraterone, enzalutamide and apalutamide in the mCRPC setting and 2/3 report using these agents in hormone-sensitive metastatic PCa (mHSPC) and in non-metastatic CRPC (nmCRPC).

Urologists were generally somewhat or extremely confident in their ability to educate patients about the diagnosis, discuss prognosis, participate in shared decision making and provide supplemental educational material to patients with non-metastatic PCa. Urologists were slightly less confident in their ability (75%, 60%, respectively) to identify clinical trials or discuss the cost benefit of various treatments for those with non-metastatic disease.

On the other hand, medical oncologists reported greater variability in their confidence to manage patients with non-metastatic disease. Most reported they were at least somewhat confident in educating patients about the diagnosis, the prognosis and eliciting patient preferences but only 63% were at least somewhat confident that they could supply supplemental educational materials for patients with non-metastatic PC. They too had less confidence in their ability to identify clinical trials or discuss the cost benefit of various treatments with this population of patients.

In the setting of metastatic PC, both urologists and medical oncologists reported a high degree of confidence in educating patients about the disease and discussing prognosis. There was less confidence in both groups in eliciting patient preferences and goals in making treatment decisions although a higher proportion of medical oncologists were extremely confident (75% versus 40% for urologists) about eliciting patient goal. All of the responding medical oncologists, compared with 80% of the urologists, were extremely confident in discussing treatment options for castration resistant metastatic PCa.
A significant proportion of urologists (2/3) and Medical Oncologists (3/7) felt that more research was needed in the management of CRPC post-docetaxel. A substantial proportion (43% or 3/7) of responding medical oncologists also felt that there was a significant unmet need in the management of patients with a rising PSA in the setting hormone-sensitive PCa.

A final note relating to the care of PCa pts is the lack of geriatric specialty support for a population that is largely, although not exclusively, elderly. A 2017 NCORP landscape survey of the capacity of care available to ~ 1000 community practices in the US revealed that of the 504 practices that participated, only about 5% had access to geriatric specialty care.12

**Educational Program**

Four (4) DCN affiliate sites chose to participate in a choreographed engagement between academic and community-based practitioners. Three of the 4 sites are located in socioeconomically and racially diverse communities in rural North Carolina. The remaining participating site was in a suburban area of a medium size city in South Carolina.

The engagement occurred in-person between sub-specialized academic physicians with clinical experience in the management of PCa and community-based clinicians participating in and facilitating discussion at site-based tumor conferences. The Tumor Conferences (TC) were held at the time regularly scheduled for site Tumor Boards and included a 30-minute live presentations augmented with a 15 min recorded presentation that focused on different selected portions of the care continuum. For example, if an academic urologist participated in the TC in person, a recorded presentation from an academic radiation or medical oncologist would be included. Finally, a brief presentation on the financial toxicity and barriers to care for PCa patients was offered. The presentations were followed by 25 minutes for site-based case presentations and discussions. The attendees were surveyed at the completion of the scheduled program.

Practicing clinicians made up nearly two thirds of the TC participants. The proportion and variety of disciplines represented at the TC are provided in the attached figure. (Administrators included Program Directors; APP included Nurse Practitioners and Physician Assistants; Nurses included Nurses and Navigators).
The participation of diverse disciplines in the TC afforded the opportunity to survey participants about practice patterns and the level of interaction on individual patient cases between the disciplines that was ‘usual’ and what would be anticipated following the educational event. The post-event surveys indicate that all of the 8 responding urology clinicians had regular interaction with medical oncologists regarding the care of PCa patients and 7/8 indicated that contact to be at least monthly. Given the high degree of reported engagement, it is somewhat surprising, but nonetheless encouraging, that all 8 responding urology practitioners expected the level of engagement to increase following the program. In addition, the majority of non-urology providers also reported at least monthly interaction with urologists (86%; 36/42 respondents), but the majority did not feel that was likely to increase.

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