UROLOGY

CARE™ PERSPECTIVES

ASCO GUCS 2018

Commentary and content provided by the CARE Urology Faculty

GUCS 2018 - GENITOURINARY CANCERS SYMPOSIUM **- SAN FRANCISCO, CALIFORNIA** - FEBRUARY 8-10

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CARE™ PERSPECTIVES

ASCO GUCS 2018

HIGHLIGHTS FROM ASCO GUCS 2018

Members of the CARE™ Urology Faculty recently attended the American Society of Clinical Oncology Genitourinary Cancers Symposium (ASCO GUCS 2018) on February 8th to 10th 2018 in San Francisco, California.

The ASCO GUCS is a multi-day, scientific education symposium focused on the multidisciplinary needs of physicians and other members of the cancer care and research community who diagnose, treat, and study genitourinary (GU) malignancies.

This issue of CARE™ Perspectives from ASCO GUCS provides updates on key news presented at the 2018 Genitourinary Cancers Symposium. Content is augmented with perspectives from Dr. Sebastien Hotte (McMaster University) and Dr. Anil Kapoor (McMaster University), as well as other CARE™ urology, radiation and medical oncology faculty who added new sequencing considerations to the CARE™ treatment algorithm for prostate cancer (PC). This algorithm is found at the end of this report.

Although the symposium features coverage on the full spectrum of GU diseases, this report focuses on PC.

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This report is based on the language in which the information was presented. The content and graphics included are drawn from the respective abstracts from ASCO GUCS 2018. Additional perspectives are provided by select members of the CARE™ Urology Faculty.

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MAJOR CLINICAL TRIALS

This section focuses on major clinical trials in prostate cancer and features updates on the PROSPER, SPARTAN, STAMPEDE and LATITUDE studies - augmented with CARE™ Faculty Perspectives.

THE PROSPER TRIAL

ASCO GUCS 2018. Abstract 3. PROSPER: A phase 3, randomized, double-blind, placebo (PBO)-controlled study of enzalutamide (ENZA) in men with nonmetastatic castration-resistant prostate cancer (M0 CRPC).

Hussain, M. et al.

Background: Men with M0 CRPC and rapidly rising prostate-specific antigen (PSA) are at high risk of developing metastatic (M1) CRPC. ENZA improves overall survival (OS) and radiographic progression-free survival in men with M1 CRPC. We hypothesized that ENZA will improve metastasis-free survival (MFS) in men with M0 CRPC.

Methods: Eligible men with M0 CRPC, PSA doubling time ≤ 10 mo and PSA ≥ 2 ng/mL at screening continued androgen deprivation therapy (ADT) and were randomized 2:1 to ENZA 160 mg or PBO. The primary endpoint was MFS. Secondary endpoints included time to PSA progression, time to first use of new antineoplastic therapy, OS and safety.

Results: In 1401 men, ENZA significantly prolonged median MFS (36.6 mo vs 14.7 mo [P< .0001]), time to first use of new antineoplastic therapy (39.6 mo vs 17.7 mo [P< .0001]) and time to PSA progression (37.2 mo vs 3.9 mo [P< .0001]) compared to PBO. In the first interim analysis of OS there was a trend in favor of ENZA (hazard ratio [HR] = 0.80; P = .1519). Median duration of treatment was 18.4 mo vs 11.1 mo for ENZA vs PBO. Adverse events (AEs) were higher with ENZA vs PBO (any grade: 87% vs 77%; grade ≥ 3: 31% vs 23%; serious: 24% vs 18%); 10% with ENZA discontinued treatment due to AE vs 8% with PBO.

Conclusions: In men with M0 CRPC and rapidly rising PSA, ENZA treatment resulted in a clinically meaningful and statistically significant 71% reduction in the risk of developing M1 CRPC. AEs were consistent with the established safety profile of ENZA. Clinical trial information: NCT02003924

THE SPARTAN TRIAL

ASCO GUCS 2018. Abstract 161. SPARTAN, a phase 3 double-blind, randomized study of apalutamide (APA) versus placebo (PBO) in patients (pts) with nonmetastatic castration-resistant prostate cancer (nmCRPC).

Small, E.J. et al.

Background: Pts with nmCRPC are at risk for developing metastatic disease and cancer-specific mortality. There are no approved treatments for nmCRPC. APA is an orally administered next-generation androgen receptor inhibitor with antitumor activity in CRPC. SPARTAN evaluated the effects of APA on metastasis-free survival (MFS) in men with nmCRPC.

Methods: Pts with nmCRPC and prostate-specific antigen doubling time (PSADT) of ≤ 10 mos were randomized 2:1 to APA (240 mg QD) or PBO. The primary end point was MFS, defined as the time from randomization to first radiographic distant metastasis (per blinded central review) or death. Secondary end points included time to metastasis (TTM), progression-free survival (PFS), time to symptomatic progression (SymProg), and overall survival (OS). Pts were eligible to receive study-provided abiraterone acetate plus prednisone after developing distant metastases. Second progression-free survival (PFS2, the time from randomization to disease progression or death after first treatment for metastatic CRPC) was also evaluated.

Results: 1207 pts were randomized. Baseline PSADT was < 5 mos in both groups. APA decreased the risk of distant metastasis or death by 72% (HR = 0.28; 95% CI, 0.23-0.35; p < 0.0001), with a median MFS of 40.5 vs 16.2 mos in the PBO group. Secondary end points (TTM, PFS, and SymProg) were all significantly improved. At an interim analysis for OS, there was a trend favoring APA. At a median follow-up of 20.3 mos, 61% of APA and 30% of PBO pts were still on treatment. Rates of discontinuation due to adverse events were low in both groups (10.7% APA, 6.3% PBO). Mean baseline health-related quality of life scores were maintained with treatment, with no difference between groups over time. Of those whose disease progressed, 80% of PBO and 56% of APA pts received therapy for metastatic CRPC. PFS2 was significantly longer for APA vs PBO.

Conclusions: APA significantly improved median MFS by 2 years in men with nmCRPC. APA also significantly increased TTM, PFS, SymProg, and PFS2. APA was associated with improved OS. These results support the addition of APA to androgen deprivation therapy in men with nmCRPC. Clinical trial information: NCT01946204

	PROSPER (ENZA+ADT VS. PLACEBO+ADT)	SPARTAN (APA+ADT VS. PLACEBO+ADT)
Patient Characteristics	• PSA doubling time ≤ 10 mo and PSA ≥ 2 ng/mL at screening • Enza+ADT vs. Placebo+ADT: 933 vs. 468 patents (randomized 2:1) • Median age of 74 years vs. 73 years • Serum PSA: 11.1 vs. 10.2 • PSA doubling time <6months: 77%	• PSA doubling time ≤ 10 mo (both groups had PSADT of <5 months) • 1207 patients randomized 2:1 (Apa+ADT vs. Placebo+ADT)
Patient Reported Data	1401 patients	1207 patients
MFS improvement Median (95% CI)	• 36.6 mo vs 14.7 mo [P< 0.0001] • HR: 0.29 (0.24-0.35) • 21.9 months improvement	• 40.5 mo vs. 16.2 mo • 24.3 months improvement • Reduced risk of metastases or death by 72% (HR = 0.28; 95% CI, 0.23-0.35; p < 0.0001)
Time to First Use of New Antineoplastic Therapy	• 39.6 mo vs 17.7 mo [P< 0.0001] • HR: 0.21 (0.17-0.26) • 21.9 months improvement	NA
Time to PSA Progression	• 37.2 mo vs. 3.9 mo [P< 0.0001] • HR: 0.07 (0.05-0.08) • 33.3 months improvement	• NR vs 3.7 mo (placebo) • HR: 0.06, p<0.0001
Median Duration on Treatment	18.4 mo vs 11.1 mo	NA
OS Improvement Median (95% CI)	• NR vs NR [P< 0.1519] • HR: 0.80 (0.58-1.09) • At first interim analysis there is an OS trend favouring enzalutamide	• NR • At first interim analysis there is an OS trend favouring apalutamide
Adverse Events	• Any grade: 87% vs 77%; • Grade ≥ 3: 31% vs 23% • Serious: 24% vs 18%	Serious: 25% vs 23%
Treatment Discontinuation Rate	10% vs. 8%	10.7% vs. 6.3%
PFS	NA	• 40.5 mo vs 14.7 mo • HR: 0.49, p<0.0001
PFS 2	NA	• NR vs 39 mo • HR: 0.29, p<0.0001
PQoL Reporting	NA	Health-related QoL scores maintained with treatment (no difference)
Additional Data	NA	• 80% of placebo arm patients and 56% of apalutamide arm patients received treatment for mCRPC • Abi+P offered in the treatment protocol as an option for mCRPC

OTHER ABSTRACTS OF INTEREST

In addition to updates in delaying metastasis, ASCO GUCS 2018 also featured prostate cancer abstracts that review the entire disease continuum - the options available at each stage and sequencing/progression considerations.

METASTATIC HORMONE SENSITIVE PROSTATE CANCER (mHSPC)

In addition to being investigated in pre metastatic disease (SPARTAN Trial), apalutamide is also being explored in metastatic hormone sensitive prostate cancer (mHSPC). The LACOG 0415 trial results may further inform the role of apalutamide, and other AR inhibitors in metastatic disease- potentially leading (eventually) to another approved indication.

ASCO GUCS 2018. Abstract 404. Phase II randomized study of abiraterone acetate plus ADT versus apalutamide versus abiraterone and apalutamide in patients with advanced prostate cancer with non-castrate testosterone levels. (LACOG 0415).

Maluf, F. et al.

CARE™ FACULTY PERSPECTIVES: THE PROSPER AND SPARTAN TRIALS

Non-metastatic castration resistant prostate cancer (nmCRPC or M0 CRPC) is a disease state without approved therapies or accepted standard of care. In CRPC, metastatic disease is most often observed in men with a PSA doubling time of less than 10 months. The average bone metastasis free survival is 25-30 months. Prolonging time to metastases is likely clinically relevant – potentially delaying overall morbidity and increasing overall survival. The PROSPER and SPARTAN Clinical trials focused on prolonging metastasis in patients with CRPC. Considering that approximately 90% of patients will experience bone metastasis (Kirby, M. The International Journal of Clinical Practice, 2011) and that metastatic disease is uniformly fatal, (median survival ~2.5 years) this disease stage holds potential promise for extending life.

THE PROSPER TRIAL

The PROSPER Trial, met its primary endpoint. Hypothesizing that enzalutamide plus ADT therapy would delay metastasis development in M0 CRPC was the basis of the PROSPER trial. This hypothesis was supported by the results of the PREVAIL and STRIVE trials which suggested that enzalutamide improved PFS in the chemotherapy naïve, M1 CRPC and M0 CRPC patients respectively.

In PROSPER, enzalutamide plus ADT therapy was successful in delaying time to metastasis in M0 CRPC-producing statistically significant and clinically relevant results.

Enzalutamide + ADT also improved the study's secondary endpoints (time to PSA progression) and produced an adverse event profile consistent with that of other enzalutamide clinical trials. Although data is immature, and results were not statistically significant, enzalutamide plus ADT also appeared to reduce the relative risk of death by 20% (compared to the placebo cohort). Results of the PROSPER trial suggest that the enzalutamide plus ADT therapy is efficacious in the non-metastatic CRPC and may lead to approval of enzalutamide for this indication.

THE SPARTAN TRIAL

The results of the SPARTAN trial suggest that the addition of apalutamide to ADT significantly extends:

- Metastasis free survival (MFS)
- Time to metastasis
- Progression Free Survival (PFS)

Apalutamide was also well tolerated, maintained HRQoL and possibly improved OS, although data is immature and not yet statistically significant.

Apalutamide, a next generation androgen signaling inhibitor (ASI) should be considered as a new standard of care for men with high risk nmCRPC. A number of questions do remain such as, will either treatment have an impact on overall survival, what will be the usefulness and impact of subsequent therapy, what will be the clinical behavior of the disease once metastases occur and what will be treatment options at that point?

“ RESULTS OF THE SPARTAN TRIAL SUGGEST THAT THE ADDITION OF APALUTAMIDE TO ADT SIGNIFICANTLY EXTENDS METASTASIS FREE SURVIVAL, TIME TO METASTASIS AND PFS. ”

THE STAMPEDE TRIAL

ASCO GUCS 2018. Abstract 162. Addition of docetaxel to first-line long-term hormone therapy in prostate cancer (STAMPEDE): Long-term survival, quality-adjusted survival, and cost-effectiveness analysis.

James, N.D. et al.

Background: Results from large randomised controlled trials have shown that adding docetaxel to standard of care (SOC) in men initiating hormone therapy for prostate cancer prolongs survival for those with metastatic disease and prolongs time to treatment failure for those without metastatic disease. We report on the impact of docetaxel on health related quality of life (HRQoL), resource use and cost-effectiveness for men treated in the STAMPEDE trial.

Methods: Health outcomes and costs in the UK NHS were modelled using EuroQol (EQ-5D)and resource use data collected within the STAMPEDE trial (STAMPEDE enrolled men advanced prostate cancer starting first line hormone therapy. SOC was hormone therapy for ≥2 years and radiotherapy in some patients. Docetaxel (75 mg/m2) was administered alongside SOC for six 3-weekly cycles with prednisolone 10 mg daily. Lifetime predictions of costs, changes in predicted survival duration, quality adjusted life years (QALYs), and incremental cost effectiveness ratios (ICERs) were calculated.

Results: Compared to patients allocated SOC, docetaxel was estimated to extend predicted survival by an average of 0.89 years for M1 patients and 0.78 years for M0 patients. Docetaxel was estimated to extend discounted QALYs by 0.51 years in M1 patients and 0.39 years in M0 patients. QALY gains in M0 patients were driven by the beneficial effect of delayed and reduced relapse. Docetaxel was cost-effective both in M1 patients (ICER = £5,514/QALY vs. SOC) and M0 patients (higher QALYs, lower costs vs. SOC). The probabilistic sensitivity analysis indicated a very high probability (> 99%) that docetaxel is cost-effective in both M0 and M1 patients. Docetaxel remained cost effective in M0 patients even when no survival advantage was assumed due to reductions and delays in relapse.

Conclusions: Docetaxel improves overall HRQoL, delays time to, and reduces the need for, subsequent therapy, and is cost-effective, amongst patients with both non-metastatic and metastatic disease. Clinicians should consider whether the evidence is now sufficiently compelling to support docetaxel use in non-metastatic patients. Clinical trial information: ISRCTN78818544.

THE LATITUDE TRIAL

Although it was not presented during Oral Abstract Session A, The LATITUDE clinical trial is an important phase 3, multinational, multicenter randomized, double blind, placebo-controlled study. LATITUDE began in 2013 and seeks to investigate the effectiveness of abiraterone acetate (AA) plus low dose prednisone when added to ADT in prostate cancer patients. The results of the LATITUDE Trial presented at ASCO GUCS 2018 suggest that AA+P added to ADT is a safe, efficacious and resource sustainable treatment for metastatic prostate cancers.

ASCO GUCS 2018. Abstract 286. Efficacy and safety of abiraterone acetate (AA) and low-dose prednisone (P) in Japanese patients with newly diagnosed, metastatic, hormone-naïve prostate cancer (mHNPC): Subgroup analysis of LATITUDE trial.

Fukasawa, S. et al.

ASCO GUCS 2018. Abstract 201. Medical resource utilization (MRU) of abiraterone acetate plus prednisone (AAP) added to androgen deprivation therapy (ADT) in metastatic castration-naive prostate cancer: Results from LATITUDE.

Li, T. et al.

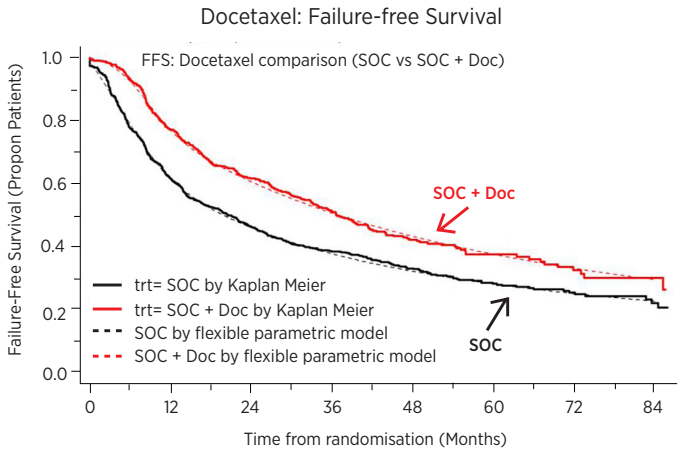
> **“ THE RESULTS OF THE LATITUDE TRIAL PRESENTED AT ASCO GUCS 2018 SUGGEST THAT AA+P ADDED TO ADT IS A SAFE, EFFICACIOUS AND RESOURCE SUSTAINABLE TREATMENT FOR METASTATIC PROSTATE CANCERS. ”**

CARE™ FACULTY PERSPECTIVE: THE STAMPEDE TRIAL

Although docetaxel is a chemotherapy which is widely used for first-line metastatic (M1) CSPC, its usefulness in the non-metastatic setting (M0) is still not well elucidated and controversial.

The STAMPEDE trial results suggest a possible benefit of docetaxel for all men with CSPC, both metastatic (M1) or non-metastatic (N+M0 or N0M0 high risk disease) In this updated analysis and cost-effectiveness modeling exercise, the use of docetaxel in high risk, non-metastatic prostate cancer was associated with cost effective improvement in HRQoL and reduction in treatment failure in both metastatic and non-metastatic disease forms. The authors concluded that docetaxel would be cost effective even if it may not improve survival given the increased time spent in the hormone sensitive state (without treatment failure) and less time with CRPC (particularly M0 patients), which would delay and decrease the use of more expensive oral agents such as Enzalutamide and/or abiraterone.

The SPARTAN trial yielded the following results displaying docetaxel's superior ability to prolong treatment failure over standard of care (SOC):



CARE™ FACULTY PERSPECTIVE: THE LATITUDE TRIAL

Fukasawa et al. reported that abiraterone acetate plus prednisone (AA+P) was an effective treatment in the subset of Japanese men with mCNPC entered onto LATITUDE. Side effect profile and efficacy parameters were similar to the overall LATITUDE population.

An investigation conducted by Li et al. suggests that adding AA+P to ADT treatment does not increase medical resource utilization (MRU). Benefits experienced by adding AA+P to ADT appear to occur without an increased burden on the healthcare system (other than the cost of the drug itself).

OTHER ABSTRACTS OF INTEREST

METASTATIC CASTRATION RESISTANT PROSTATE CANCER (mCRPC)

Enzalutamide, abiraterone acetate (AA), abiraterone acetate +prednisone (AA+P), docetaxel and ADT continue to be explored in the metastatic castration resistant disease state (mCRPC). Hahn and colleagues found that - despite hypothesis - allele variations in the HSD3B1 gene (which encodes the enzyme 3β-hydroxysteroid dehydrogenase-1) could not predict patient response to first-line AA treatment in patient with mCRPC. The abstract presented by Grotto et al. represents data from the Canadian COSMiC study suggesting that therapy with AA+P maintained patient QoL and cognitive status over a 72 week treatment period. In a phase 2 study Bastos and colleagues found that AA+P provided PSA response - even in heavily treated patients – and showed clinical benefit, following hormonal therapy, in chemotherapy naïve mCRPC.

ASCO GUCS 2018. Abstract 173. Germline variant in HSD3B1 (1245 A>C) and response to abiraterone acetate plus prednisone (AA) in men with new onset metastatic castration-resistant prostate cancer (mCRPC).

Hahn, A. et al.

ASCO GUCS 2018. Abstract 196. Real-world evidence in patient-related outcomes (PROs) of metastatic castrate-resistant prostate cancer (mCRPC) patients treated with abiraterone acetate plus prednisone (AA+P).

Gotto, G. et al.

ASCO GUCS 2018. Abstract 235. Abiraterone acetate plus prednisone (AAP) in chemotherapy-naïve patients with metastatic castration-resistant prostate cancer (mCRPC) and prior diethylstilbestrol (DES) therapy: Preliminary results.

Bastos, D. et al.

EMERGING DIAGNOSTICS AND THERAPIES IN ADVANCED PROSTATE CANCER

While additional abstracts of interest are covered in the pages that follow, General Session 2 featured oral presentations on prostate cancer (PC) which have a strong potential to affect treatment. These presentation topics include:

- Emerging Immunotherapies in PC
- Managing Oligometastatic PC
- Incorporating Genomics into PC Treatment
- Molecular Therapies for Bone Metastasis

EMERGING IMMUNOTHERAPY STRATEGIES FOR CASTRATE RESISTANT PROSTATE CANCER

Padmanee Sharma, MD, PhD

Anti CTLA-4 blockade has opened a new field of therapy across a number of tumor areas. While immune oncology (IO) has changed the management of RCC and bladder cancer- recently reported studies using ipilimumab in men with CRCP have been negative. However, more recent preclinical work has shown that PDL-1 becomes increasingly expressed in men with CRPC who develop resistance to the novel androgen receptor targeted therapies such as enzalutamide. This has renewed the interest in IO therapy in these patients. The DynAMo trial is exploring which subsets might benefit from PD-1/PDL-1 and the VISTA trial is targeting men with mCRPC. (Goa et al Nature Medicine 2017). Anti-CTLA-4 (ipilimumab) plus anti-PD-1 (nivolumab) combination therapy is also being investigated in CRPC. We wait for more data and updates.

CARE Faculty Perspectives: The Canadian Cancer Trials Group (CCTG) is at the forefront of studying potential immunotherapy strategies for PC. The CCTG is conducting a phase 2 study of durvalumab (anti PDL-1 antibody) with or without tremelimumab (CTLA-4 targeting) in patients with mCRPC. NCT registration ID- NCT02788773. Accessible at: *https://clinicaltrials.gov/ct2/show/NCT02788773*

MANAGEMENT OF OLIGOMETASTATIC PROSTATE CANCER FROM IMAGING TO THERAPY

Felix Y. Feng, MD

Oligometastatic disease has been recognized as a distinct clinical state since 1995 and is typically characterized by the presence of 1 to 5 metastatic lesions. With advances in molecular imaging techniques (e.g. PSMA PET scanning) - the number of patients identified oligometastatic disease has increased.

Improvements in treatment strategies (such as directed intensification of radiation therapy) now allow specialists treating oligometastatic disease to potentially achieve a near complete response in selected prostate cancer patients. Increased diagnoses of oligometastatic PC hold particular relevance to radiation oncologists, as patients with this disease state often receive some form of radiation treatment. Ultimately better predictors of "less" aggressive vs "more" aggressive oligometastic disease are needed.

OTHER ABSTRACTS OF INTEREST

HIGH RISK LOCALIZED PROSTATE CANCER (PC)

In high risk localized prostate cancer, some abstracts focused on potentially efficacious treatments to combine with ADT and radiotherapy (RT) in order to delay metastasis and improve patient outcomes. Enzalutamide and AA+P both demonstrate a potentially synergistic combination with RT and ADT for the treatment of high risk localized disease.

ASCO GUCS 2018. Abstract 11. Phase II trial of 6 months ADT/abiraterone acetate plus prednisone (AAP) and definitive radiotherapy (AbiRT) for men with intermediate to high risk localized prostate cancer.

Koontz, B. et al.

ASCO GUCS 2018. Abstract 156. Randomised phase 3 trial of enzalutamide in androgen deprivation therapy (ADT) with radiation therapy for high risk, clinically localized prostate cancer: ENZARAD (ANZUP 1303).

Williams, S. et al.

INCORPORATING GENOMICS INTO THE MANAGEMENT OF SYSTEMIC THERAPY: ADVANCES AND PRACTICALITY

Kim N. Chi, MD, FRCPC

Liquid biopsies represent a minimally invasive blood test to determine the ratio of circulating tumor DNA (ctDNA) versus cell free DNA (cfDNA). The ratio of ctDNA versus cfDNA is associated with disease burden and proliferation.

This is important as:

- Baseline ctDNA alterations are associated with abiraterone and enzalutamide treatment outcomes.
- Alterations to the BRCA2 and ATM genes predict poor patient outcomes with abiraterone and enzalutamide treatment.

There has been interesting news on ipatasertib (an AKT inhibitor) plus abiraterone combination therapy, but more data is needed. Of note - loss of the phosphate and tensin homolog gene (PTEN) predicts a benefit with ipatasertib plus abiraterone.

The genomics of prostate cancer are likely to play a role in the treatment landscape of the future.

MOLECULAR THERAPIES IN BONE METASTASES

Joe M. O'Sullivan, MD, FRCR

Radium 223 is a powerful alpha particle emitter that offers short range and high payload. The ALYSMPCA trial has demonstrated that radium 223 is an effective agent in metastatic disease with relatively low AE's. Improving the therapeutic ratio of radium 223 can be accomplished through dose manipulation (increasing the number of cycles and/or increasing dose /personalizing the dose – dose intensity/dose density).

> "THE ALYSMPCA TRIAL HAS DEMONSTRATED THAT RADIUM 223 IS AN EFFECTIVE AGENT IN METASTATIC DISEASE WITH RELATIVELY LOW AE'S."

However, certain questions remain, such as:

- What is the value and safety of combining radium 223 with other therapies? E.g. abiraterone, enzalutamide, docetaxel or immunotherapies.
- How should response be assessed? E.g. whole body magnetic resonance imaging (WBMRI) or prostate specific membrane antigen (PSMA).
- What is optimal dosing?

OTHER ABSTRACTS OF INTEREST

METASTATIC CASTRATION NAÏVE PROSTATE CANCER (mCNPC)

In metastatic, castration naïve prostate cancer, the abstract presented by Feyerabend et al. suggests that patient reported outcomes (PROs) are superior with AA+P over docetaxel. The reported chances of AA+P leading to superior PRO results are between 92.3% and 100.0% in mCNPC.

ASCO GUCS 2018. Abstract 200. Indirect treatment comparison (ITC) of abiraterone acetate (AA) plus prednisone (P) and docetaxel (DOC) on patient-reported outcomes (PROs) in metastatic castration-naïve prostate cancer (mCNPC).

Feyerabend, S. et al.

METASTATIC CASTRATION RESISTANT PROSTATE CANCER (MCRPC)

Cabazitaxel is a common second line chemotherapy for mCRPC which may be efficacious in earlier settings and specific patient populations (informed by the TROPIC trial among others). With the use of hormonal therapies being explored in earlier stage disease (non-metastatic) - questions remain regarding how the development of castration (hormone) resistant disease forms will affect treatment sequencing. If patients on early hormone therapy become castration resistant, then the use of cabazitaxel, earlier in the treatment sequence (in replacement of ADT) could be efficacious. Though ASCO GUCS 2018 did not feature investigations on the use of cabazitaxel in early hormone resistance– It did feature other exciting updates on the use of cabazitaxel in mCRPC. The WeCabE study suggests that weekly cabazitaxel is effective in elderly patients (even those >80 years old) and has a manageable safety profile. CABACARE is a phase 2 study analyzing the effect of prednisone on cabazitaxel (safety and efficacy) while the CaBone study focuses on cabazitaxel's effect on bone metastasis- specifically, quality of life, bone turnover markers and time to the first skeletal related events (SREs). Results of the WeCabE, CABACARE and CaBone trials support the efficacy of cabazitaxel in mCRPC.

ASCO GUCS 2018. Abstract 300. Weekly cabazitaxel in elderly patients (EP) with metastatic castration resistant prostate cancer (mCRPC) progressing after docetaxel treatment: WeCabE, a phase II study.

Castagneto, B. et al.

ASCO GUCS 2018. Abstract 387. A randomized phase II study comparing cabazitaxel/prednisone to cabazitaxel alone for second-line chemotherapy in men with metastatic castrate resistant prostate cancer (mCRPC): CABACARE.

Buonerba, C. et al.

ASCO GUCS 2018. Abstract 405. Impact of cabazitaxel on metastatic bone health in patients with castration resistant prostate cancer previously treated with docetaxel: CaBone Study.

Santini, D. et al.

CARE™ PROSTATE CANCER TREATMENT ALGORITHM

The news and updates presented at ASCO GUCS 2018 represent potential changes to the prostate cancer (PC) treatment landscape in Canada. Members of the CARE™ Faculty (representing oncology/urology/radiation) recently met to discuss these news items and their effect on the diagnosis and management of PC. The goal of this CARE™ Faculty meeting was to refine the CARE™ Advanced Prostate Cancer Treatment Algorithm (last updated ESMO 2017) with new sequencing considerations. The CARE™ Faculty was not alone in meeting to discuss genitourinary updates, as other Canadian groups are also considering PC management.

With the news being presented on localized forms of prostate cancer, it is anticipated that specialty groups like urologists will manage patients in the localized (pre-metastatic) disease setting before referring the patient to another specialist if they experience metastasis. CARE™ is aware of the importance of managing localized PC, especially with regard to its effect on subsequent disease stages/therapy. CARE™ plans to expand the Prostate Cancer Treatment Algorithm to include earlier stages. The CARE™ Faculty will update the Prostate Cancer Treatment Algorithm at a working group meeting at CUA 2018 (June 2018). The CARE™ Algorithm included in this section features a visual depiction of where the updates can be expected.

Within this section is an abstract on how advanced PC treatments are sequenced based on data collected by the Canadian GU Research Consortium (GURC) followed by the CARE™ Advanced Prostate Cancer Treatment Guidance Algorithm which has been augmented with new sequencing considerations and portions where further updates are anticipated.

ASCO GUCS 2018. Abstract 321. Real world patterns of treatment sequencing in Canada for metastatic castrate-resistant prostate cancer.

Hotte, S. et al.

Background: The Canadian GU Research Consortium (GURC) was recently established to bring advanced prostate cancer centres together to collaborate on research, education, and adoption of best practices. As an initial step to inform the work of the GURC, an electronic questionnaire was designed to assess management of advanced prostate cancer care in Canada and how prostate cancer treatments are sequenced in a real-world setting.

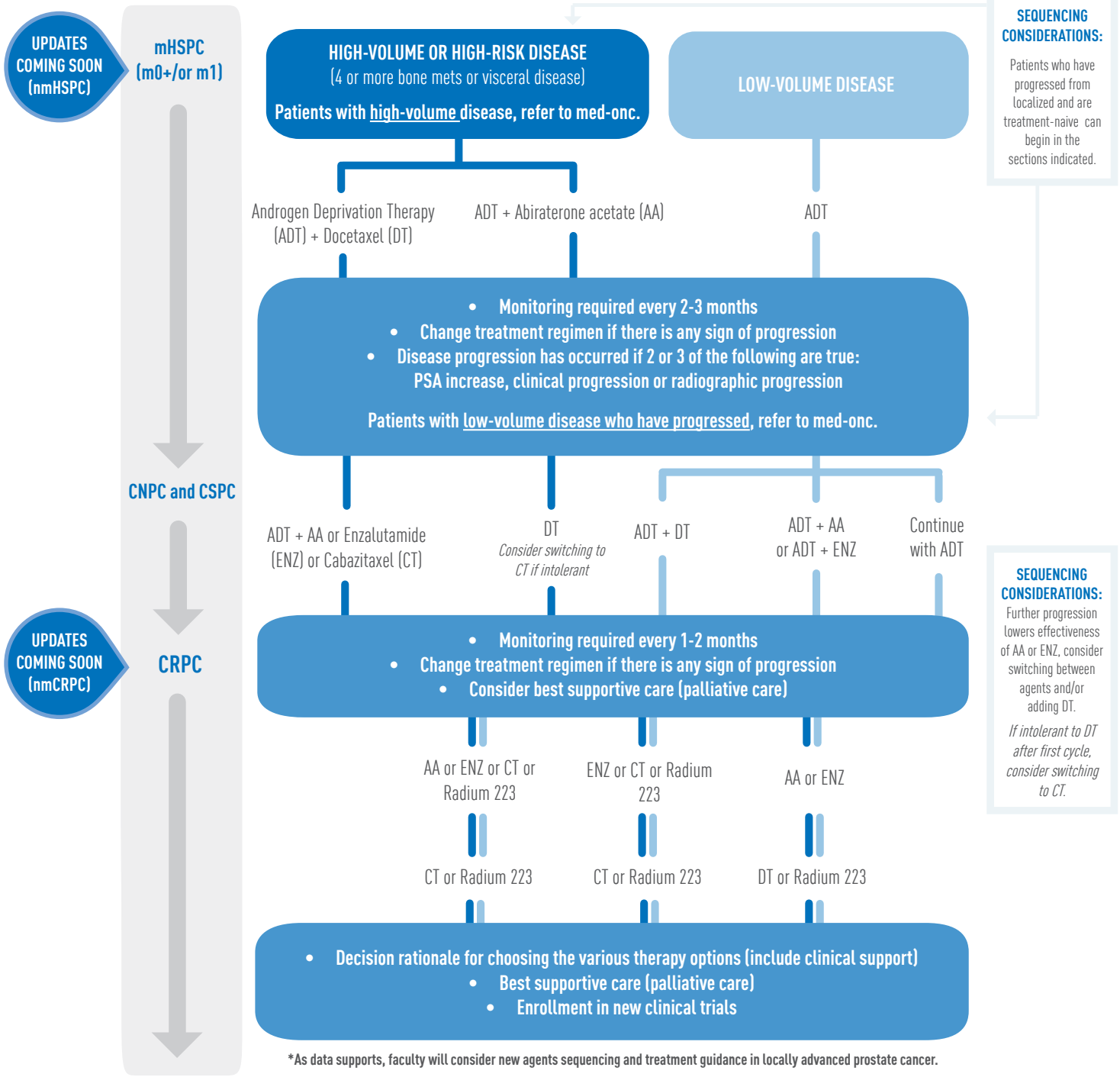
Methods: A 59-item online questionnaire was developed by a multidisciplinary scientific committee to measure physician practices, patterns of care, treatment sequencing, and management of mCRPC. After pre-testing, the online questionnaire was sent to 93 urologists, uro-oncologists, medical oncologists, radiation oncologists, and general practitioner oncologists who are actively involved in the treatment of prostate cancer.

Results: A total of 49 (53%) respondents completed the questionnaire between April 17, 2017 to May 17, 2017. Based on physician reports, the most frequently used treatment for first-line mCRPC was AR-targeted therapy (94%, n = 46 physicians) such as abiraterone acetate plus prednisone and enzalutamide. Among those 46 physicians, AR-targeted therapy was usually followed by docetaxel second-line therapy (57%, 31 physicians). The most common line 1 to line 3 treatment sequence for mCRPC was: AR-targeted therapy--Docetaxel--AR-targeted therapy (35%, 17 physicians), followed by AR-targeted therapy--Docetaxel--Radium 223 (14%, n = 7), Provincial differences were observed in the line 1 to line 3 treatment sequences, which aligned to variation in provincial policies for access to the treatments. In patients previously treated with docetaxel in the hormone sensitive setting, the most frequently used treatment for first-line mCRPC was AR-targeted therapy (76%, 37 physicians).

Conclusions: AR targeted therapy followed by docetaxel is the predominant pattern of practice for management of mCRPC, with variability beyond these lines of therapy. Prospective ongoing work through the GURC in research, education and best practices will aim to understand these practice patterns.

ADVANCED PROSTATE CANCER

TREATMENT GUIDANCE ALGORITHM



*As data supports, faculty will consider new agents sequencing and treatment guidance in locally advanced prostate cancer.

ABOUT THE CARE UROLOGY FACULTY

The CARE (Community. Academic. Research. Education) Faculty is a pan-Canadian group of leaders in their field who gather, discuss and address gaps in knowledge, to develop education initiatives that frame news from a Canadian perspective.

The vision of the CARE Faculty is to share opinions and update Canadian specialists with news and developments from key conferences framed in a Canadian perspective.

The mission of the CARE Faculty is to enhance medical education, with the explicit goal of improving patient outcomes.

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