Supplemental Appendix 1. Questions and Expert Responses (N=38) From USPCC Sessions on ADT in Prostate Cancer, High-Risk Localized Prostate Cancer, Biochemical Recurrence, Metastasis-Directed Therapy, and mCSPC

1. ADT in Prostate Cancer

1.1 In clinical practice, what should be the target testosterone (T) level for a patient receiving an LHRH agonist/antagonist for androgen deprivation therapy (ADT)?		
Answer	**#**	**%**
<50 ng/dL	10	26
<30 ng/dL	1	3
<20 ng/dL	26	68
Not sure	1	3
Does not matter	0	0
Abstain	0	0

1.2 In your opinion, how important is it that LHRH agents be administered on time, ie, exactly 84 days for a 84-day preparation?		
Answer	**#**	**%**
It is important to deliver exactly on schedule	6	16
Within 2 weeks is acceptable	28	74
3 calendar months between doses is acceptable	3	8
Abstain	1	3

1.3 Do you monitor testosterone (T) levels regularly in your patients who are receiving ADT?		
Answer	**#**	**%**
Yes	28	74
No	2	5
Sometimes	6	16
Rarely	1	3
Abstain	1	3

1.4 When initiating ADT, when should T levels be measured?		
Answer	**#**	**%**
Before therapy and then every 3 months	20	53
Every 3 months until T remains less than 20 ng/dL	2	5
At 3 months, then when the PSA elevates	8	21
At 6 months, and then periodically, as needed	0	0
Variable depending on the individual patient	7	18
Abstain	1	3

1.5 Does failure to monitor T lead to an erroneous diagnosis of castration-resistant prostate cancer (CRPC)?		
Answer	**#**	**%**
Yes	28	74
No	6	16
Not sure	1	3
Abstain	3	8

1.6 Are randomized controlled trials (RCTs) necessary to evaluate any differences in efficacy or safety between LHRH agonists and antagonists?		
Answer	**#**	**%**
Yes	16	42
No	8	21
Any differences are small and not clinically relevant	13	34
Abstain	1	3

2. High-Risk Prostate Cancer

2.1 Do you believe that an updated risk stratification methodology is needed?		
Answer	**#**	**%**
The NCCN definitions for “high risk” and “very high risk” remain adequate	3	8
“High risk” should be defined based on multivariable clinical tools (eg,UCSF- CAPRA, STAR-CAP)	11	29
The definition of “high risk” should be based on clinical plus genomic characteristics	21	55
Not sure	1	3
Abstain	2	5

2.2 In your opinion, in high-risk prostate cancer, when should bone scan and CT be used?		
Answer	**#**	**%**
Bone scan and CT should only be used when prostate-specific membrane antigen (PSMA) PET/CT is not available	16	42
Bone scan and CT should still be used to define oligometastatic disease and to define “M1” in applying historical RCT findings	17	45
There is no role for bone scan or CT in 2023	3	8
Not sure	1	3
Abstain	1	3

2.3 Is PSMA PET/CT appropriate at diagnosis only in men with high-risk disease?		
Answer	**#**	**%**
Yes	21	55
No	14	37
Not sure	2	5
Abstain	1	3

2.4 Is PSMA PET appropriate at diagnosis for all men with unfavorable intermediate or high-risk disease?		
Answer	**#**	**%**
Yes	24	63
No	9	24
Not sure	5	13
Abstain	0	0

2.5 What should guide management of the pelvis?		
Answer	**#**	**%**
Pretreatment PSMA PET/CT	16	42
Clinical characteristics only	14	37
Not sure	4	11
Abstain	4	11

2.6 Is there a role for truly adjuvant radiation therapy (PSA < 0.1) for any subsets of patients after radical prostatectomy (RP)?		
Answer	**#**	**%**
Patients with very adverse pathology (eg, T3b, extensive surgical margin, pN+) should get adjuvant radiation	16	42
Postoperative radiation should only be used when PSA is detectable	13	34
Postoperative radiation should be solely guided by the Decipher score and/or PORTOS	4	11
Not sure	3	8
Abstain	2	5

2.7 How should genomic analysis of primary prostate tissue (biopsy or RP) guide intensification of perioperative systemic therapy?		
Answer	**#**	**%**
Therapy should be guided by gene mutational analysis (eg, FoundationOne CDx)	1	3
Therapy should be guided by gene expression analysis (eg, Decipher genomic risk classifier)	16	42
Therapy should be guided by patient preference, comorbidities and/or cost	11	29
Not sure	4	11
Abstain	6	16

3. Biochemically Recurrent Prostate Cancer

3.1 For the patient with prior RP, when do you recommend salvage radiotherapy (RT)?		
Answer	**#**	**%**
As early as possible (PSA <0.2 ng/mL)	18	47
PSA 0.2-1 ng/mL	19	50
PSA 1-5 ng/mL	1	3
Not sure	0	0
Abstain	0	0

3.2 When do you recommend ADT with salvage RT?		
Answer	**#**	**%**
Always	8	21
Never	0	0
Only for those patients with high risk according to polygenic risk score assay	6	16
Only for those with high risk by multivariable clinical tools	19	50
Not sure	4	11
Abstain	1	3

3.3 Which of the following is the primary parameter you use when initiating BCR therapy postprostatectomy and salvage RT?		
Answer	**#**	**%**
PSA doubling time (DT) ≤ 9 months and a PSA ≥ 1 ng/mL (if post-RP) or PSA ≥ 2 ng/mL (if post-RT)	25	66
Original Gleason score (GS) ≥8 OR Gleason grade group ≥ 4	1	3
Time until PSA recurrence (BCR) < 6 months	1	3
Time until PSA recurrence < 12 months	2	5
PSA ≥ 1 ng/mL (if post-RP) or PSA ≥ 2 ng/mL (if post-RT)	1	3
Abstain	8	21

3.4 Which of the following is the optimal diagnostic imaging test for BCR evaluation?		
Answer	**#**	**%**
CT abdomen/pelvis	1	3
CT chest/abdomen/pelvis	0	0
Tc bone scan	0	0
PSMA PET scan	34	89
Bone scan and CT	2	5
Not sure	1	3
Abstain	0	0

3.5 Will conventional imaging still be routinely utilized in clinical practice in 5 years?		
Answer	**#**	**%**
Yes	15	39
No	21	55
Abstain	2	5

3.6 Which of the following end points would prove ADT plus an androgen receptor inhibitor (ARI) was superior to ADT alone for the treatment of nmHSPC?		
Answer	**#**	**%**
6-month delay in PSA progression	0	0
6-month benefit in metastasis-free survival (MFS)	7	18
12-month benefit in MFS	16	42
Increase in overall survival (OS)	9	24
12-month delay to CRPC	2	5
24-month delay to CRPC	0	0
Abstain	4	11

3.7 Germline testing is currently recommended for all men with high-risk, very high-risk, and metastatic prostate cancer. Do you recommend germline testing for men with BCR?		
Answer	**#**	**%**
No, I only order if there are metastases	4	11
No, I generally do not order germline testing unless there is a strong family history, or the patient is from a high-risk population	14	37
Yes, BCR is between very high-risk and metastatic disease, so germline testing is clearly indicated	20	53

3.8 When considering the results from FORMULA 509 in the context of the RADICALS HD results, what approach to ADT do you recommend for men receiving Salvage radiation therapy after RP and a PSA >0.5?		
Answer	**#**	**%**
ADT x 6 months	13	34
ADT x 24 months	15	39
ADT + Abiraterone + apalutamide x 6 moths	2	5
Radiotherapy alone without ADT	1	3
Other	4	11
Abstain	3	8

3.9 When considering the results from FORMULA 509 in the context of the RADICALS HD results, what approach to ADT do you recommend for men receiving Salvage radiation therapy after RP and a PSA [<0.5]?[a]		
Answer	**#**	**%**
ADT x 6 months	15	41
ADT x 24 months	4	11
ADT + Abiraterone + apalutamide x6 moths	3	8
alone without ADT	10	27
Other	2	5
Abstain	3	8

[a]During the live PROST8CON meeting, the version of question 3.9 pushed to panel members errantly omitted the PSA level shown in square brackets. Verbal instructions were given to all attendees to consider the question for patients with PSA levels less than 0.5 ng/mL.

4. Metastasis-Directed Therapy

4.1 Do you offer treatment with MDT to patients with oligometastatic de novo mHSPC treated with standard of care systemic therapy and radiotherapy to the primary site?		
Answer	**#**	**%**
Usually	22	58
Sometimes	11	29
Never	4	11
Abstain	1	3

4.2 What is your preferred type of MDT for extrapelvic metastatic disease (ie, bone, lung, para-aortic lymph nodes)?		
Answer	**#**	**%**
Radiotherapy (ie, stereotactic ablative radiotherapy [SABR]/ stereotactic body radiation therapy [SBRT])	36	95
Surgical resection/lymphadenectomy	0	0
Cryotherapy	0	0
I do not recommend MDT in these patients	0	0
Abstain	2	5

4.3 Would you order a PSMA PET/CT prior to starting therapy for a patient diagnosed with oligometastatic de novo mHSPC based on CT and bone scan (assuming insurance coverage)?		
Answer	**#**	**%**
Usually	22	58
Sometimes	13	34
Never	2	5
Abstain	1	3

4.4 If all sites of metastatic disease are treated with MDT, the primary site is treated with radiotherapy, and the patient receives optimal systemic therapy (ie, ADT plus androgen receptor signaling inhibitor [ARSI]), what is the duration of systemic therapy you would use?		
Answer	**#**	**%**
I do not recommend systemic therapy	2	5
6 months	8	21
12 months	3	8
24 months	15	39
Treat to progression	6	16
Abstain	4	11

4.5 Do you offer treatment with MDT for patients with oligorecurrent mHSPC diagnosed by conventional imaging (CT/bone scan)?		
Answer	**#**	**%**
Usually	15	39
Sometimes	20	53
Never	3	8
Abstain	0	0

4.6 How many metastatic sites are needed for you to diagnose oligometastases?		
Answer	**#**	**%**
1 site	2	5
2 sites	1	3
3 sites	10	26
4 sites	3	8
5 sites	12	32
> 5 sites	6	16
Abstain	4	11

4.7 Do you offer treatment with MDT for patients with oligorecurrent mHSPC diagnosed by molecular imaging, such as PSMA, choline, FACBC PET/CT?		
Answer	**#**	**%**
Usually	16	43
Sometimes	20	54
Never	1	3
Abstain	0	0

4.8 What is your preferred method of delivering MDT?		
Answer	**#**	**%**
Radiotherapy (ie, SABR/SBRT)	33	89
Surgical resection/lymphadenectomy	0	0
Cryotherapy	0	0
I never recommend MDT	1	3
Abstain	3	8

4.9 Do you consider ADT-free interval/survival a meaningful end point for patients?		
Answer	**#**	**%**
Yes	28	76
No	8	22
Abstain	1	3

4.10 Do you routinely add ADT (ie, LHRH agonist or antagonist) to MDT?		
Answer	**#**	**%**
Usually	17	46
Sometimes	19	51
Never	1	3
Abstain	0	0

4.11 How long do you usually recommend ADT if you are adding it to MDT?		
Answer	**#**	**%**
I don't recommend ADT with MDT	2	5
4-6 months	15	41
12 months	5	14
24 months	7	19
Lifelong	2	5
Abstain	6	16

4.12 How long do you usually recommend ADT if you are adding it to MDT?[a]		
Answer	**#**	**%**
I don't recommend ADT with MDT	3	8
4-6 months	14	38
12 months	4	11
24 months	6	16
Lifelong	2	5
Abstain	8	22

[a]Question 4.12 was unintentionally a repeat of question 4.11. Because the responses differed between the questions, both sets are included here.

4.13 Do you intensify systemic therapy with ADT plus ARSI when offering MDT?		
Answer	**#**	**%**
Usually	19	51
Rarely	8	22
Never	5	14
Abstain	5	14

4.14 If intensifying systemic therapy with ADT plus ARSI and MDT, how long do you give systemic therapy for?		
Answer	**#**	**%**
I do not recommend systemic therapy intensification	5	14
4-6 months	10	27
12 months	6	16
24 months	10	27
Lifelong	2	5
Abstain	4	11

5. mHSPC

5.1 Should triplet therapy be given to all patients with mHSPC?		
Answer	**#**	**%**
Yes	2	5
No	17	46
Only high-risk patients as defined by ARASENS and PEACE1	5	14
Only high-risk patients as defined by volume and de novo vs metachronous metastases	9	24
Only high-risk as defined by clinical criteria and next generation sequencing (NGS)	2	5
Abstain	2	5
Not sure	0	0

5.2 If you choose triplet therapy in addition to ADT plus docetaxel, which AR pathway inhibitor would you prescribe?		
Answer	**#**	**%**
Abiraterone/prednisone	5	14
Darolutamide	15	41
Enzalutamide	1	3
Apalutamide		
Whichever one is covered by insurance with the lowest co-pay and no medical contraindications	13	35
Abstain	3	8

5.3 Which type of imaging do you prefer to determine extent of disease?		
Answer	**#**	**%**
Conventional imaging (CT plus bone scan)	16	43
PSMA PET imaging	17	46
Other	3	8
Abstain	1	3

"Other" responses:

- I prefer both
- Sometimes PSMA and conventional
- Both

5.4 Do you consider discontinuation of therapy in long-term responders?		
Answer	**#**	**%**
Yes	20	54
No	1	3
Maybe	15	41
Abstain	1	3

5.5 What criterion do you use for treatment discontinuation?		
Answer	**#**	**%**
Complete response (CR) at 6 months	2	5
CR at 1 year	2	5
CR at 2 years	18	49
CR at 5 years	3	8
None of the above	6	16
Abstain	6	16

5.6 Which method do you use to assess burden of disease to guide treatment of the primary site?		
Answer	**#**	**%**
Number of bone metastases	3	8
Low vs high volume of disease per CHAARTED (high volume defined as the presence of visceral metastases or ≥ 4 bone lesions with ≥ 1 beyond the vertebral bodies and pelvis)	25	68
Low vs high risk per LATITUDE (high risk defined as ≥ 2 of the 3 following high-risk factors associated with poor prognosis: a Gleason score of ≥ 8 [on a scale of 2 to 10], ≥ 3 bone lesions, and the presence of measurable visceral metastasis)	1	3
None of the above	6	16
Abstain	2	5

5.7 Do you recommend the treatment of the primary site in patients with de novo mHSPC and a low burden of disease?		
Answer	**#**	**%**
Usually	32	86
Sometimes	3	8
Never	1	3
Abstain	1	3

5.8 Which treatment method do you most commonly recommend for treatment of the primary site in patients with de novo mHSPC and a low volume disease?		
Answer	**#**	**%**
Radiotherapy (lower doses per STAMPEDE)	16	43
Radiotherapy (higher doses used in localized prostate cancer)	14	38
Surgery with or without postoperative radiotherapy	3	8
Other ablative therapies (ie, cryotherapy)	2	5
I do not recommend treatment of the primary site in these patients	1	3
Abstain	1	3

5.9 Do you recommend treatment of the primary site in patients with de novo mHSPC and a high volume of disease?		
Answer	**#**	**%**
Usually	2	5
Sometimes	23	62
Never	11	30
Abstain	1	3

5.10 Which treatment do you most commonly recommend for treatment of the primary site in patients with de novo mHSPC and a high volume of disease?		
Answer	**#**	**%**
Radiotherapy (lower doses per STAMPEDE)	9	24
Radiotherapy (higher doses used in localized prostate cancer)	7	19
Surgery with or without postoperative radiotherapy	3	8
Other ablative therapies (ie, cryotherapy)	1	3
I do not recommend treatment of the primary in these patients	16	43
Abstain	1	3

5.11 Is it clinically meaningful to patients if treatment of the primary site could improve failure-free survival, analogous to time to development of mCRPC, without an increase in bothersome toxicity?		
Answer	**#**	**%**
Yes	29	78
No	2	5
Not sure	5	14
I do not recommend treatment of the primary in these patients	0	0
Abstain	1	3

5.12 How many bone metastases do you use as a threshold to not offer treatment of the primary site?		
Answer	**#**	**%**
3	4	11
5	21	57
7	3	8
9	2	5
I do not recommend treatment of the primary site or do not use a certain number of bone metastases to influence my recommendation	4	11
Abstain	3	8

5.13 STAMPEDE demonstrated benefit of treatment of the primary site with EBRT in patients treated with ADT or ADT plus docetaxel. If a patient is treated with ADT plus ARSI, does this change your recommendations of adding treatment of the primary site for patients with low-volume/oligometastatic disease?		
Answer	**#**	**%**
Yes, I am more likely to offer treatment of the primary site with ADT plus ARSI, given the synergy of AR inhibition and EBRT	11	30
Yes, I am less likely to offer treatment of the primary with ADT plus ARSI	3	8
No, the use of ARSI or docetaxel does not impact offering treatment of the primary site	20	54
Abstain	3	8

5.14 What treatment would you recommended to add to ADT for patients at high risk for financial toxicity and/or treatment noncompliance for oligometastatic/low burden de novo mHSPC?		
Answer	**#**	**%**
Docetaxel	7	19
Abiraterone until progression	10	27
Treatment of the primary	10	27
None of the above	5	14
Abstain	5	14

5.15 How would you classify a Patient who is low volume on conventional imaging and high volume on PSMA PET CT?		
Answer	**#**	**%**
Low Volume	25	69
High Volume	8	22
Abstain	3	8