A UK modified Delphi consensus on the clinical utility of triplet therapy in patients with metastatic hormone-sensitive prostate cancer (mHSPC)

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Why this UK consensus is needed?[1]

Which patients are suitable for triplet therapy?

- No direct head-to-head trials comparing triplet therapy with **DOCE + ADT + ARPI** vs **ADT + ARPI**
- Lack of clear guidelines on how and when to use triplet therapy

Approach to gaining consensus[1]

1: Steering group meeting
Discuss, agree, draft

2: Statement agreement
Evaluate, feedback, ratify

3: Survey
Likert survey development, distribute to UK clinical community

4. Analysis and consensus agreement
Results analysed, steering group consensus level discussion, recommendation development

Consensus defined as high (≥75% agreement) and very high (≥90% agreement)

Agreed topics for consensus consideration[1]

Four main topics were identified and agreed upon by the committee:

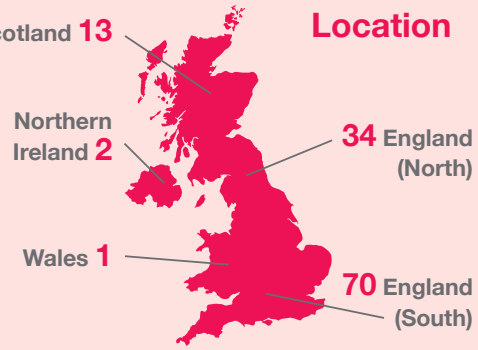
- The role and utility of treatment intensification including the option of chemotherapy in triplet therapy
- Identification of suitable patients to consider for treatment intensification including the option of chemotherapy in triplet therapy
- The role of patient education and shared decision-making
- Multidisciplinary working

Results: Responses received N=120[1]

Speciality

- Medical oncologist
- Consultant geriatrician
- Clinical oncologist
- Oncology nurse specialist
- Consultant urologist
- Hospital pharmacist

Location



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Results: Consensus statements*#1

92% — **Triplet therapy** should be **considered** in patients with **high-risk disease**†

82% — All **newly diagnosed mHSPC** patients suitable for **triplet therapy** should be offered it

94% — **Triplet therapy should be the preferred option** in patients with **high-volume disease suitable for chemotherapy**‡

96% — **Age alone is not a criterion for denying treatment intensification** with **triplet therapy**

88% — **Triplet therapy should be the preferred option** in **patients with visceral disease (liver or lung metastases) who are suitable for chemotherapy**

83% — If a patient is **offered treatment with docetaxel,** then **it should be in the context of triplet therapy**

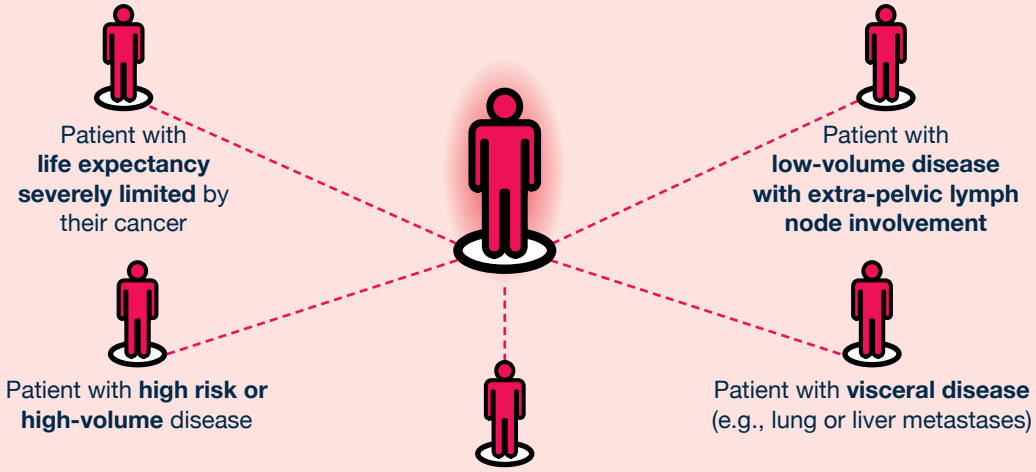
73% — **Triplet therapy should be considered** in patients with **low volume disease that have a significant disease burden and are suitable for chemotherapy**§

98% — There is evidence that **treatment intensification significantly delays time to castration resistance.** This is an important consideration

**A full list of defined consensus statements and corresponding levels of agreement can be found on page 3 of this document. †As defined by LATITUDE. ‡As defined by CHAARTED. §e.g., patients with multiple lymph node involvement.*
#The results of the STOPCAP M1 meta-analysis were not used to develop consensus statements as they were published after the initial literature review for the consensus had taken place.
Black = no consensus reached; Light green = high consensus; dark green = very high consensus.

Recommendations specifically related to triplet therapy

Triplet therapy improves OS compared to ADT + DOCE and should be considered in all patients, and is recommended (following assessment) in patients meeting at least one of the following criteria:



Recommendations for triplet therapy when considering treatment options

"All patients should be assessed for frailty and vulnerability, including life expectancy, comorbidities, age, personal circumstances, patient goals and preferences"

"All patients should have their fitness for treatment intensification with triplet therapy assessed and this should be optimised where appropriate and required"

"Shared decision making is key when considering treatment intensification, clinicians must consult with the patient and ensure they are educated on their treatment options"

For the full list of recommendations, please refer to the published article.

https://bmjopen.bmj.com/content/14/11/e090013

"Choosing the right treatment for our patients with metastatic hormone-sensitive prostate cancer can be challenging and we hope this might aid clinicians with their decision making."

Dr Hilary Glen, *Consultant in Medical Oncology*, Beatson West of Scotland Cancer Centre Glasgow

Full list of defined consensus statements and corresponding levels of agreement (percentages have been rounded to nearest decimal place)[1]

No:	Satement:	Strongly Agree	Tend To Agree	Tend To Disagree	Strongly Disagree	Agreement
Topic A. The role & utility of treatment intensification including the option of chemotherapy in triplet therapy						
1	There is level 1 evidence that treatment intensification in newly diagnosed mHSPC including doublet therapy (ADT + ARTA) improves PFS and OS vs ADT alone	53%	48%	0%	0%	100%
2	There is level 1 evidence that triplet therapy and early treatment intensification in the form of ADT + docetaxel + ARTA benefits mHSPC patients vs doublet therapy of ADT + docetaxel	43%	53%	4%	0%	96%
3	The evidence for treatment intensification in mHSPC with ADT + ARTA + chemotherapy is based on ARASENS	41%	48%	10%	1%	89%
4	The evidence for treatment intensification in mHSPC with ADT + ARTA is based on TITAN, ENZAMET, LATITUDE, ARCHES, and STAMPEDE	53%	41%	5%	1%	94%
5	ADT monotherapy is no longer acceptable standard of care for patients with mHSPC apart from patients in whom ARTA or docetaxel is contraindicated, if the patient is elderly/frail/unfit due to co-morbidity or if the patient declines additional treatment	58%	29%	13%	1%	87%
6	Ensuring equity of access across the UK to treatment intensification in appropriate patients is a priority	68%	28%	3%	0%	97%
7	In newly diagnosed mHSPC, the preferred doublet is ADT + ARTA rather than ADT + docetaxel	32%	49%	18%	1%	81%
8	If a patient is offered treatment with docetaxel, then it should be in the context of triplet therapy (ADT + ARTA + Chemotherapy)	30%	53%	15%	2%	83%
9	The inclusion of docetaxel to ADT + ARTA provides better overall free survival vs ADT + docetaxel	42%	52%	7%	0%	93%
10	There is evidence that treatment intensification significantly delays time to castration resistance. This is an important consideration in the management of mHSPC	46%	52%	3%	0%	98%
11	Treatment intensification is not associated with significant impact to quality of life at 1 year in clinical trials compared to the comparator arms	21%	52%	25%	3%	73%
Topic B. Identification of suitable patients to consider for treatment intensification including the option of chemotherapy in triplet therapy						
12	In metastatic disease a patient's prostate cancer is likely to be a determining factor of reduced life expectancy, and treatment intensification with triplet therapy should be considered	33%	58%	8%	1%	92%
13	Most patients should be assessed with a comprehensive multidisciplinary assessment (such as the comprehensive geriatric assessment) to identify suitability for treatment intensification with triplet therapy	63%	23%	13%	2%	86%
14	If a patient's life expectancy is significantly limited due to comorbidities (< 1-2 years), then treatment intensification with triplet therapy may not be appropriate	54%	39%	7%	0%	93%
15	Patients' fitness should be assessed with treatment intensification of triplet therapy in mind, and optimised in readiness where appropriate and required	51%	43%	6%	0%	94%
16	Age alone is not a criterion for denying treatment intensification with triplet therapy	52%	44%	3%	1%	96%
17	Assessment for frailty and vulnerability is important in determining suitability for treatment intensification	70%	28%	3%	0%	98%
18	Tools such as G8, Charlson comorbidity index (CCI), frailty scores should be utilised in appropriate patients	32%	57%	11%	1%	88%
19	Triplet therapy should be considered in fitter patients e.g., ECOG 0-1	66%	28%	6%	1%	93%
20	Triplet therapy should be considered in patients with high-risk disease* * as defined by LATITUDE with having at least two of the three following high-risk factors: a Gleason score of 8 or more (on a scale of 2 to 10, with higher scores indicating more aggressive disease), at least three bone lesions, and the presence of measurable visceral metastasis	44%	48%	8%	1%	92%
21	Triplet therapy should be the preferred option in patients with high volume disease who are suitable for chemotherapy, as defined by CHAARTED* *presence of visceral metastases or four or more bone lesions with at least one beyond the vertebral bodies and pelvis	43%	51%	4%	2%	94%
22	Triplet therapy should be considered in patients with low volume disease that has a significant disease burden (e.g., with multiple lymph node involvement) who are suitable for chemotherapy	24%	49%	23%	3%	73%
23	Triplet therapy should be the preferred option in patients with visceral disease (liver or lung metastases) who are suitable for chemotherapy	48%	41%	11%	1%	88%
24	Approximately 30% of newly diagnosed mHSPC patients are potentially suitable for treatment intensification with triplet therapy	31%	57%	12%	1%	88%
25	All newly diagnosed mHSPC patients suitable for triplet therapy should be offered it	34%	48%	12%	7%	82%
Topic C. The role of patient education and shared decision making						
26	Identifying and understanding patient goals is critical to the shared decision-making process	74%	23%	2%	0%	98%
27	Shared decision making is vital for decisions regarding treatment intensification in mHSPC	82%	16%	3%	0%	98%
28	Shared decision making improves compliance and adherence to treatment	75%	21%	4%	0%	96%
29	Shared decision making is important in minimising a patient's post treatment regret	77%	23%	1%	0%	99%
30	Patient education is important to provide the tools for patients to mitigate or respond to side effects during treatment	73%	27%	1%	0%	99%
31	Patient understanding of the disease and their treatments is important	73%	26%	1%	0%	99%
Topic D. Multidisciplinary working						
32	Categorisation of patients by volume & risk should be done for all patients by the MDT	48%	44%	8%	0%	93%
33	The prostate cancer MDT pro-forma should contain all relevant patient details including all comorbidities and functional status	71%	26%	3%	1%	97%
34	Physical and psychological prehabilitation should be an integral part of management of patients with mHSPC	43%	48%	7%	2%	92%
35	Education is an ongoing process of the prostate cancer team and should be integrated into the work programme	52%	46%	3%	0%	98%
36	Multidisciplinary working has been shown to improve outcomes in cancer patients	60%	36%	3%	1%	96%
37	All patients with mHSPC should have a named CNS throughout their prostate cancer journey	65%	30%	5%	0%	95%
38	CNS staffing levels are currently inadequate to provide optimal patient support in prostate cancer	58%	33%	7%	3%	90%
39	Lack of chemotherapy suite capacity should not be a reason in decision making regarding triplet therapy	48%	40%	12%	0%	88%

Advanced Prostate Cancer Consensus Conference (APCCC 2024) on the management of patients with advanced prostate cancer

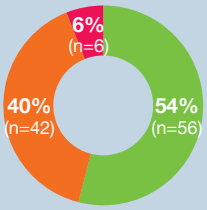
APCCC consensus methods[2]

The Advanced Prostate Cancer Consensus Conference (APCCC) was initiated to **provide a forum to debate current questions on the clinical management** of men with advanced prostate cancer, with a special focus on areas for which there is sparse or low-level evidence to support clinical decision-making. Consensus was a priori defined as ≥75% agreement, with strong consensus defined as ≥90% agreement.

120 clinicians from **36** countries including **11** clinicians from the UK, formed the expert consensus panel in 2024.

APCCC consensus on systemic therapy in mHSPC helps define the patient profile for triplet therapy[2]

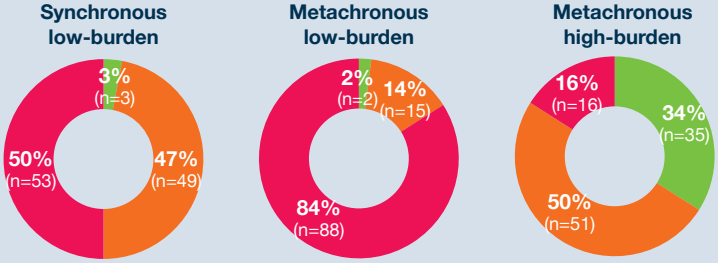
In patients with **high-burden** mHSPC that are **chemotherapy fit**, do you recommend the **triplet therapy DOCE + ADT + ARPI**?



abstain: n=2

- Yes, in the majority of patients
- Yes, but only in selected patients
- No, I usually do not recommend this combination

In patients with mHSPC that are **chemotherapy fit**, do you recommend the **triplet therapy DOCE + ADT + ARPI**?

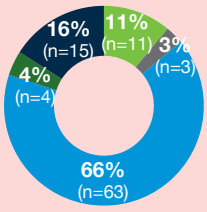


abstain: n=1 | abstain: n=1 | abstain: n=4

- Yes, in the majority of patients
- Yes, but only in selected patients
- No

APCCC consensus findings: ARPI selection[2]

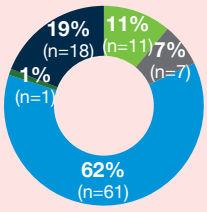
For the majority of patients **with advanced prostate cancer and a history of coronary artery disease and currently on oral anticoagulants and a statin**, what is your **preferred ARPI** (any treatment line, assuming all options are available)?



abstain: n=10

- Abiraterone
- Apalutamide
- Darolutamide
- Enzalutamide
- Any of the above

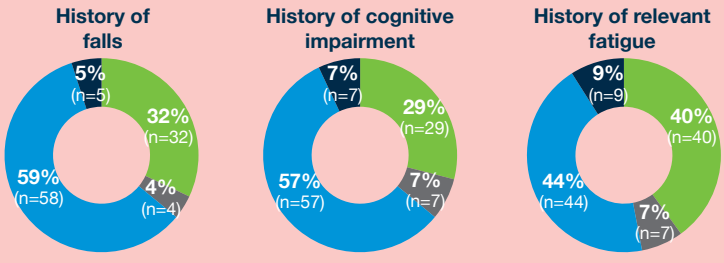
For the majority of patients with **mHSPC ≥75 years of age**, what is your **ARPI of choice in any line** with regards to efficacy and the safety profile in this patient population assuming all options are available?



abstain: n=8

- Abiraterone
- Apalutamide
- Darolutamide
- Enzalutamide
- Any of the above

For the majority of patients **with advanced prostate cancer and a history of comorbidities** (CNS related), what is your **preferred ARPI** (any treatment line, assuming all options are available)?



abstain: n=7 | abstain: n=6 | abstain: n=6

- Abiraterone
- Apalutamide
- Darolutamide
- Enzalutamide
- Any of the above

Abbreviations: ADT, androgen deprivation therapy; APCCC, Advanced Prostate Cancer Consensus Conference; ARPI, androgen receptor pathway inhibitor; CNS, central nervous system; DOCE, docetaxel; ECOG, Eastern Cooperative Oncology Group; mHSPC, metastatic hormone-sensitive prostate cancer; OS, overall survival; PFS, progression-free survival.

References: 1. Glen H, et al. A modified Delphi consensus regarding the clinical utility of triplet therapy in patients with metastatic hormone-sensitive prostate cancer patients in the UK. BMJ Open (in press); 2. Gillessen S, et al. Management of Patients with Advanced Prostate Cancer. Report from the 2024 Advanced Prostate Cancer Consensus Conference (APCCC). Eur Urol 2024:S0302–2838(24)02610–1.

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