# $^{177}$Lu-PSMA-617 for treating PSMA-positive hormone-relapsed metastatic prostate cancer after 2 or more therapies

**For public** – contains no confidential information

**Technology appraisal committee B [12 January 2023]**

**2nd Committee Meeting (ACM2)**

**Chair:** Baljit Singh

**Lead team:** Nigel Westwood, David McAllister, Gabriel Rogers

**Evidence assessment group:** School of Health and Related Research Sheffield (ScHARR), University of Sheffield

**Technical team:** Summaya Mohammad, Eleanor Donegan, Janet Robertson

**Company:** Advanced Accelerator Applications, a Novartis company

# $^{177}$Lu vipivotide tetraxetan is not recommended

## Committee conclusions at ACM1

**Committee noted high uncertainty in the cost effectiveness estimates caused by:**

- **Clinical uncertainties:**
  - No evidence comparing $^{177}$Lu with radium-223 dichloride for people with symptomatic bone metastases only
  - No clinical evidence when taxanes are medically unsuitable (population excluded from VISION trial)
  - High levels of withdrawal from VISION
  - High uncertainty in the network meta-analysis
- **Uncertainty in cost-effectiveness:**
  - Cost of PSMA testing not included in the modelling
  - Modelling cabazitaxel overall survival
  - Uncertainty in utility estimates



Abbreviations: $^{177}$Lu: lutetium-177 vipivotide tetraxetan; ACM: Appraisal committee meeting; PSMA: prostate-specific membrane antigen

# Key issues

**Impact on ICER:** Small / Large / Unknown

| Issue at ACM1 | Resolved? | Committee | |
|---|---|---|---|
| **PSMA testing** | Partially | • PSMA imaging will be necessary to determine $^{177}$Lu eligibility<br>• ***What % PSMA testing should be used in the model? SPECT, PET-CT or both?*** |  |
| **Broadening population including people for whom taxanes are unsuitable** | No further evidence | • Appropriate to consider whole marketing authorisation<br>• ***Should $^{177}$Lu be considered for this population given there is no evidence for this population?*** |  |
| **Excluding radium-223 as a comparator for people with bone metastases** | No further evidence | • May be relevant comparator; subgroup analysis comparison<br>• ***Should radium-223 be considered for this population given there is no evidence for this subgroup?*** |  |
| **Company's NMA**<br>• Fixed- vs. random effects model<br>• Studies included in the NMA | No | • Using IPCW-adjusted estimates from VISION in NMA<br>• Exploring all studies in baseline-risk adjusted model<br>• ***Which NMA is best to model $^{177}$Lu vs cabazitaxel?*** |  |
| **Overall survival estimates for cabazitaxel in the model** | No | • RWE on survival with cabazitaxel as reference group for absolute event estimates, applying hazard ratio from NMA for $^{177}$Lu survival<br>• ***Is the updated company approach appropriate?*** |  |
| **Cabazitaxel utility values** | No | • Utilities are uncertain; account for withdrawals using IPCW<br>• ***Are utilities modelled appropriately?*** |  |
| **Pre-medication and concomitant medication costs for cabazitaxel** | Partially | • Using ERG's costs in the model to better reflect NHS practice<br>• ***Is the committee satisfied with G-CSF duration costs?*** |  |

Abbreviations: $^{177}$Lu: Lu vipivotide tetraxetan; G-CSF: granulocyte colony-stimulating factor; IPCW: inverse probability of censoring weighting; NMA: network meta-analysis; PET-CT: Positron emission tomography computerised tomography; PSMA: prostate-specific membrane antigen; rPFS: radiographic progression-free survival; SPECT: single-photon emission computerized tomography

# Re-cap from 1st committee meeting

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# RECAP – Background

Metastatic hormone-relapsed prostate cancer associated with poor outcomes and low quality of life

**Prostate cancer**

- 45,885 new cases in England and Wales in 2019-20; 13% with metastatic disease at diagnosis

**PSMA-positive**

- Prostate cancers can express a transmembrane protein – prostate-specific membrane antigen (PSMA)
- PSMA expression is increased in poorly differentiated, metastatic, and hormone-relapsed prostate cancers

**Prognosis**

- 10-20% people with prostate cancer develop hormone-relapsed cancer after ~ 5 years of follow-up
- mCRPC is associated with significant negative impacts on health-related quality of life
- Prostate cancer mortality is associated with increasing age and metastatic disease
- Skeletal involvement in mCRPC is common – significant morbidity and mortality
- People with visceral metastases are likely to have worse prognosis than those with bone metastases alone

**Unmet need:**

- $^{177}$Lu gives an option for people who have exhausted current therapies, especially with bone and soft tissue metastases
- $^{177}$Lu can increase quality of life because it is precise, has a novel mechanism and can target lymph nodes

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Abbreviations: mCRPC: metastatic castration-resistant prostate cancer

# RECAP – Lutetium-177 prostate-specific membrane antigen-617 (Pluvicto, Advanced Accelerator Applications)

| | |
|---|---|
| **Marketing authorisation** | "Adult patients with PSMA-positive mCRPC who have been treated with androgen receptor pathway inhibition and taxane-based chemotherapy or who are not medically suitable for taxanes"<br>• MHRA August 2022 |
| **Mechanism of action** | $^{177}$Lu binds to a protein called PSMA (prostate specific membrane antigen) that is found on the surface of prostate cancer cells. Radiation is emitted from $^{177}$Lu causing prostate cancer cells to die |
| **Eligibility** | People should be identified by PSMA imaging |
| **Administration** | • 7400 MBq intravenous injection, approximately every 6 weeks for up to a total of 6 doses<br>• Monitoring before and after treatment needed<br>• $^{177}$Lu only used in special controlled areas in hospital, administration by people who are trained and qualified to use it safely |
| **Price** | • List price: £20,000 per vial<br>• Confidential simple patient access scheme discount is applicable |

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Abbreviations: $^{177}$Lu: lutetium-177 vipivotide tetraxetan; MBq: megabecquerel; mCRPC: metastatic castration-resistant prostate cancer; MHRA: Medicines and Healthcare products Regulatory Agency

# RECAP – Treatment pathway

Taxane

ARPI

Androgen deprivation therapy (ADT) continues despite hormone-relapsed; docetaxel can be offered twice; abiraterone OR enzalutamide once; so fewer options

| | Hormone sensitive | Hormone relapsed | | |
|---|---|---|---|---|
| **Non-metastatic** | ADT<br>Radical therapy- surgery or radiotherapy | Progression → ADT<br>~~Enzalutamide + ADT in high risk (TA580)~~<br>Darolutamide + ADT in high risk (TA660)<br>Apalutamide + ADT in high risk (TA740) | | |
| **Metastatic** | ADT (NG131)<br>Docetaxel + ADT (NG131)<br>~~Abiraterone + ADT in high risk (TA720)~~<br>Apalutamide + ADT (TA741)<br>Enzalutamide + ADT (TA712) | **Chemotherapy 'not yet indicated'**<br>Abiraterone (TA387)<br>Enzalutamide (TA377)<br>Watchful waiting | **Chemotherapy indicated**<br>Docetaxel (TA101) – Karnofsky performance score 60% or more<br>Olaparib (no prior taxane) - ongoing | **Post-docetaxel**<br>Abiraterone (TA259)<br>Enzalutamide (TA316)<br>Cabazitaxel (TA391)<br>Radium-223* (TA412)<br>Docetaxel re-treatment<br>Olaparib (prior taxane) - Ongoing appraisal<br>**$^{177}$Lu vipivotide tetraxetan** |

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*Radium-223: For symptomatic bone metastases and no known visceral metastases



Abbreviations: $^{177}$Lu: Lu vipivotide tetraxetan; ADT: androgen deprivation therapy; ARPI: androgen receptor pathway inhibitor; NG: NICE guideline; TA: technology appraisal

# Clinical effectiveness evidence

- **$^{177}$Lu vipivotide tetraxetan vs standard of care**
- $^{177}$Lu vipivotide tetraxetan vs cabazitaxel

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# RECAP – Clinical trial evidence: VISION

VISION informs key evidence for $^{177}$Lu vs standard care but concern with risk of bias

| | |
|---|---|
| **Design** | International, multi-centre, phase 3 RCT, prospective, open-label including UK sites – FDA approved education measure implemented mid-trial to reduce withdrawal rates |
| **Population** | mCRPC, progressed after treatment with ≥1 ARPI and 1 or 2 taxane regimens |
| **Intervention** | $^{177}$Lu vipivotide tetraxetan plus standard of care |
| **Comparator** | Standard of care |
| **Duration** | Final data-cut: January 2021; median follow-up: 20.9 months |
| **Primary outcome** | Overall survival; radiographic progression-free survival |
| **Key 2$^{0}$ outcomes** | Time to first symptomatic skeletal event; adverse events; health related quality of life |
| **Other 2$^{0}$ outcomes** | Overall response rate; disease control rate; duration of response |

**ERG:** Company use LDH as control for tumour burden but ERG concerned it is not a robust prognostic marker and not routinely collected for people with mCRPC in NHS

- Imbalances between arms due to withdrawals – even after education measure intervention
- Open-label trial – result in risk of bias as may affect some outcomes (not overall survival)

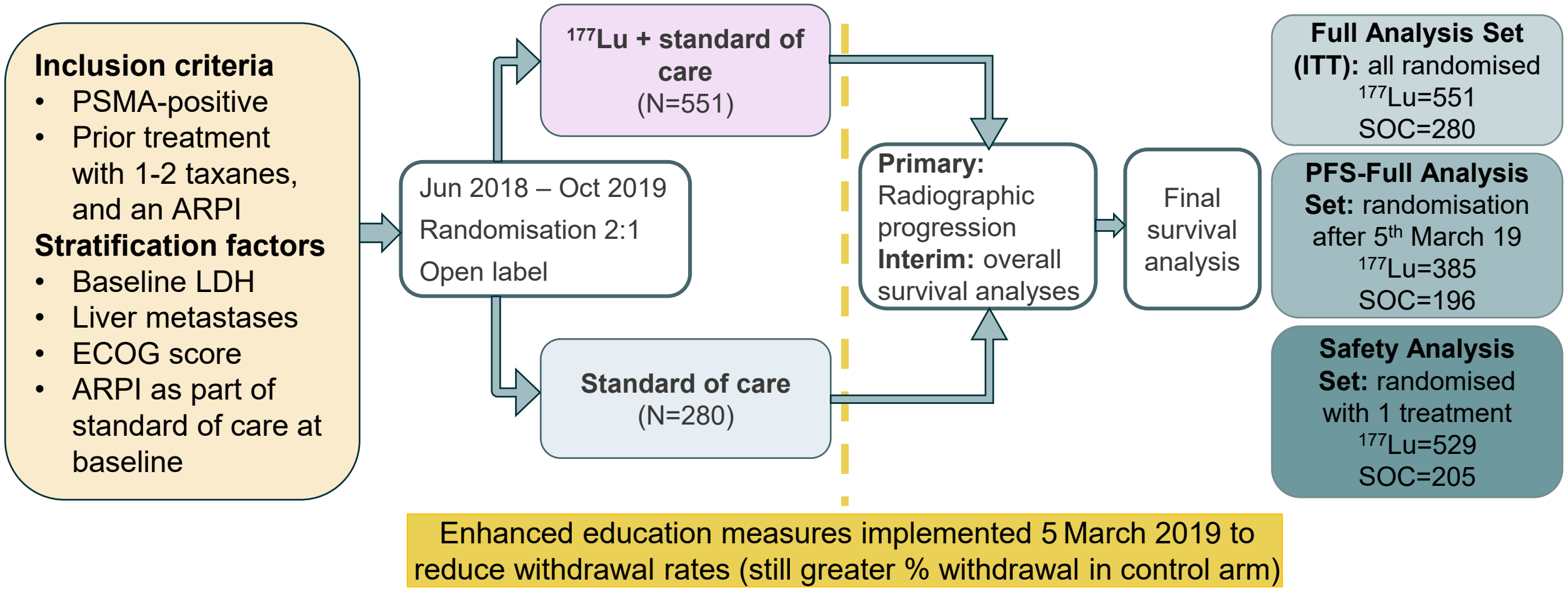
**Clinical experts:** In VISION people could have 2 androgen receptor targeted agents but NICE approval is 1 – likely benefits of $^{177}$Lu in NHS setting could be more than in VISION



Abbreviations: $^{177}$Lu: Lu vipivotide tetraxetan; ARPI: androgen receptor pathway inhibitor; CRD: Centre for Reviews and Dissemination; LDH: lactase dehydrogenase; mCRPC: metastatic castration-resistant prostate cancer; RCT: randomised controlled trial; RoB: risk-of-bias

# RECAP – VISION study design

Phase 3, open-label, randomised controlled trial; completed January 2021




Abbreviations: $^{177}$Lu: Lu vipivotide tetraxetan; ARPI: androgen receptor pathway inhibitor; ECOG: Eastern Cooperative Oncology Group; ITT: intention-to-treat; LDH: lactate dehydrogenase; PFS: progression-free survival; PSMA: prostate-specific membrane antigen; SOC: standard of care

# RECAP – VISION primary outcome results: Overall survival and radiographic progression-free survival

| | Full analysis set (ITT population) | | PFS Full Analysis Set (after withdrawal intervention) | |
|---|---|---|---|---|
| | $^{177}$Lu + SOC (N=551) | SOC (N=280) | $^{177}$Lu + SOC (N=385) | SOC (N=196) |
| **Primary endpoint:** overall survival – Jan 2021 | | | | |
| **Events, n (%)** | 343 (62.3) | 187 (66.8) | [redacted] | [redacted] |
| **Median, months (95% CI)** | 15.3 [redacted] | 11.3 [redacted] | [redacted] | [redacted] |
| **Hazard ratio (95% CI)** | 0.62 (0.52, 0.74) | | [redacted] | |
| **Alternative primary endpoint:** radiographic progression-free survival – Jan 2021 | | | | |
| **Events, n (%)** | | | 254 (66) | 93 (47.4) |
| **Median, months (99.2% CI)** | | | 8.7 [redacted] | 3.4 [redacted] |
| **Hazard ratio (99.2% CI)** | | | 0.40 (0.29, 0.57) | |

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Abbreviations: $^{177}$Lu: Lu vipivotide tetraxetan; ITT: intention-to-treat; OS: Overall survival; PFS: Progression-free survival

# Clinical effectiveness evidence

- $^{177}$Lu vipivotide tetraxetan vs standard of care
- **$^{177}$Lu vipivotide tetraxetan vs cabazitaxel**

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# RECAP – Cabazitaxel direct evidence: TheraP phase 2 trial

TheraP not included in model and not powered for OS; ERG assess high risk of bias

| TheraP multicentre, open-label, Phase 2, randomised controlled trial | |
|---|---|
| **Population** | mCRPC progressed after prior docetaxel and ARPI |
| **Intervention** | $^{177}$Lu vipivotide tetraxetan (N=99) – dose 6.0-8.5 GBq |
| **Comparator** | Cabazitaxel (N=101) |
| **Outcomes** | **Primary:** PSA response (reduction of PSA ≥50% from baseline)<br>**Secondary:** rPFS; response rates; pain; prognostic biomarkers |
| **Duration** | Median follow-up 18.4 months |
| **Pre-treatment withdrawals** | 16% (16/101) for cabazitaxel; 1% (1/99) for $^{177}$Lu |

| $^{177}$Lu vs cabazitaxel | Results |
|---|---|
| **PSA response** | 66% vs 37% (95% CI: 16-42%) |
| **rPFS** | HR: 0.64 (95% CI: 0.46, 0.88) |
| ***OS (restricted mean to 36 months)** | 19.1 vs 19.6 (95% CI: -3.7, 2.7) |
| **Adverse events** | • $^{177}$Lu: More Grade 1-2 (54% vs 40%);<br>• Cabazitaxel: More Grade 3-4 (53% vs 33%) |

**Company:** TheraP not included in NMA or model because:

- Differences in diagnostic process, $^{177}$Lu production/dose, and patient stratification
- Not powered for OS

**ERG:** High-risk of bias

- Imbalances and missing data between arms – leading to high risk of bias in at least 1 domain
- Open-label trial – can affect outcomes

*OS is from extended follow-up (Hofman et al., 2022, Journal of Clinical Oncology)

Abbreviations: ARPI: androgen receptor pathway inhibitor; GBq: giga-becquerel; HR; Hazard Ratio; mCRPC: metastatic castration-resistant prostate cancer; NMA: network meta-analysis; OS: overall survival; PSA: prostate specific antigen; rPFS: radiographic progression-free survival; SOC: standard of care

# RECAP – Cabazitaxel real-world evidence

## RWE comparable to VISION but OS for cabazitaxel shorter than SOC in VISION

Company did retrospective RWE study which combined data from major UK databases, identifying people with mCRPC 2009-18 (population most likely aligned with post-ARPI, post-taxane population)

- Datasets: NCR, SACT, Hospital Episode Statistics, Diagnostic Imaging Dataset and Radiotherapy Dataset
- Study assessed characteristics, current standard of care, clinical outcomes and healthcare resource usage
- Comparison then made with the VISION patient population

| Baseline characteristics | RWE Cabazitaxel (N=[redacted]) | VISION (FAS) (N=831) |
|---|---|---|
| Median age*, years | [redacted] | [redacted] |
| White British† % | [redacted] | [redacted] |
| ECOG ≤1, n (%) | [redacted] | [redacted] |
| Bone metastases, n (%) | [redacted] | [redacted] |

*RWE reported age at diagnosis, not cabazitaxel initiation
†VISION did not specify 'British'

**Results: (no rPFS results)**

- Median OS cabazitaxel: [redacted]
- Restricted mean OS: [redacted]

**Company:** Median OS for cabazitaxel in RWE shorter than median OS in SOC arm of VISION ([redacted] vs 11.3 months)

- People have enhanced monitoring with more visits to healthcare professionals and imaging, so may have longer OS compared to real-world

**ERG:** Argument of enhanced care in clinical trials applies equally to both treatment arms in VISION

- PSWA analyses from company post TE, results in similar OS estimates but prognostic factors may not be included

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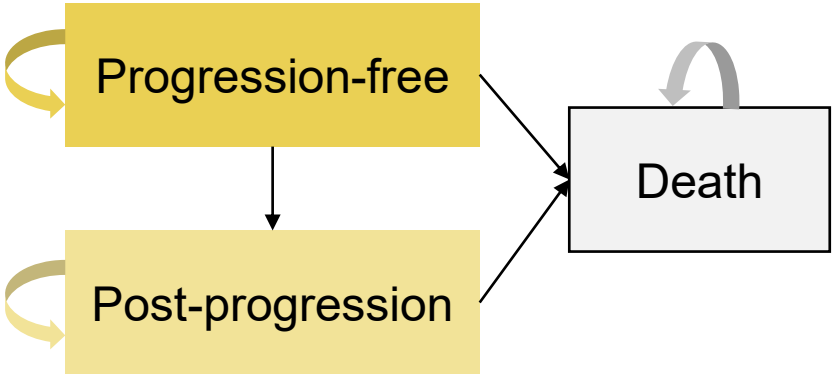
Abbreviations: $^{177}$Lu: Lu vipivotide tetraxetan; ECOG: eastern Cooperative Oncology Group; mCRPC: metastatic castration-resistant prostate cancer; NCR, National Cancer Registry; OS: overall survival; PSWA: propensity score weighted analysis; rPFS: radiographic progression-free survival; RWE: real-world evidence; SOC: standard of care; SACT, Systemic Anticancer Therapy

# RECAP – Company's model structure – cost utility analysis

## Partitioned survival model for $^{177}$Lu compared with cabazitaxel and standard of care

**Model structure:**

- Partitioned survival model; 3 health states




| | |
|---|---|
| **Intervention** | $^{177}$Lu vipivotide tetraxetan |
| **Comparators** | Cabazitaxel, standard of care |
| **Cabazitaxel OS** | Real-world evidence |
| **Mean age** | [redacted] years |
| **Cycle length** | Weekly. No half-cycle correction |
| **Time horizon** | 10 years |
| **Utilities** | EQ-5D-5L mapped to 3L |
| **Price year** | Unit costs: 2019/2020 prices; Drug costs: 2021 |
| **Discount rate** | 3.5% per year for cost and health effects |
| **Treatment costs** | $^{177}$Lu from VISION; cabazitaxel from CARD |

**ERG:** Company present 1 cost-effectiveness analysis covering all patients in $^{177}$Lu indication; only relevant comparator differs across subgroups:

- When further taxane treatment is possible (cabazitaxel)
- When further taxane treatment after docetaxel is not possible (standard of care)
- When taxane treatment is medically unsuitable (standard of care)

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Abbreviations: $^{177}$Lu: Lu vipivotide tetraxetan; mCRPC: metastatic castration-resistant prostate cancer; EQ-5D-5L: EuroQol-5-Dimension 5-level; OS: overall survival

# Company's model overview

## $^{177}$Lu affects:

### Costs

- Increasing treatment costs compared with cabazitaxel & standard of care
- For standard of care – some costs offset by reduced concomitant treatments use (depends on company assumption of concomitant treatment costs for standard care only)

### QALYs

- Increasing pre- and post-progression-free survival compared with cabazitaxel and standard of care
- Post-progression increase vs cabazitaxel depends on company using RWE for cabazitaxel survival

## Assumptions with greatest ICER effect

### $^{177}$Lu vs cabazitaxel

- RWE or NMA used to model cabazitaxel OS
- Evidence directly comparing $^{177}$Lu and cabazitaxel from TheraP in NMA for rPFS
- Evidence used in NMA to compare cabazitaxel and ARPI subgroup
- Utilities used for pre- and post-progression health states & cumulative incidence of SSE from trials rather than extrapolating time-to-first SSE data
- G-CSF use during cabazitaxel treatment

### $^{177}$Lu vs standard of care

- Costs for concomitant treatments during $^{177}$Lu treatment in VISION
- Utilities for pre- and post-progression health states & cumulative incidence of SSE from trials rather than extrapolating time-to-first SSE data



Abbreviations: $^{177}$Lu: Lu vipivotide tetraxetan; ARPI: androgen receptor pathway inhibitor; G-CSF: granulocyte colony-stimulating factor; NMA: network meta-analysis; OS: overall survival; RWE: real world evidence; SSE: symptomatic skeletal event

# ACD consultation responses

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# ACD consultation responses

**NICE received consultation responses from:**

- **Company: Advanced Accelerator Applications**
  - Responded to committee conclusions, new base case, increased patient access scheme discount
- **Stakeholders:**
  - Bayer
  - British Nuclear Medicine Society
  - Prostate Cancer Research
  - Prostate Cancer UK
  - TACKLE
  - UK MRT Consortium
- **Web comments**

# PSMA testing (1)

## PSMA testing should be included in economic modelling

**ACM1: Diagnostic resources to identify PSMA-positive were not included in company or ERG model**

**ACD:** Variability in clinical practice and access to PSMA PET-CT scans. Not standard but necessary for $^{177}$Lu eligibility

- PSMA test costs should be included; scenarios for up to 75% of people having PET-CT/SPECT scans
- Costs should reflect proportion of PSMA-positive cancer in relevant population to account for PSMA-negative cancer

**Consultation:**

**Company: Update base case to include PSMA testing costs for 25% of people in $^{177}$Lu arm**

- Consider excluding PSMA testing better reflects current and near-future NHS practice.
- PSMA scans assumed SPECT, as a weighted average of NHS Reference Costs commonly used in NHS
- Cost of PSMA testing adjusted proportionally to rate of PSMA positivity (from VISION)
- Scenario for 100% people having PSMA testing costs – limited impact

**ERG: Update base case assuming 100% have PSMA testing**

- Company's PSMA testing impact may be underestimated because it does not use PET-CT scans (generally more expensive)
- Scenario where 25% have PSMA testing



Abbreviations: $^{177}$Lu: lutetium-177 vipivotide tetraxetan; PSMA: prostate-specific membrane antigen

# PSMA testing (2)

## Summary ACD responses: stakeholders and web comments

### Stakeholders

- **BNMS:** Need to reduce geographical inequality and improve infrastructure to deliver this treatment and diagnostic test
- **Prostate Cancer Research:** Limited access to PSMA imaging – provision of access to targeted treatments e.g. $^{177}$Lu could be a driver for service improvement
- **TACKLE:** Patients report difficulty in accessing PSMA scanning and PET scanning in general – but improvement
  - Eligibility for $^{177}$Lu can be done by SPECT – clinical experts indicate more widely available
- **UK MRT Consortium:** IR(ME)R and CQC report PSMA treatment dosimetry is necessary and accounted for on costings and recommendations

### Web comments

- Cost for imaging and patient dosimetry should be included (required to meet IR(ME)R and ARSAC recommendations) – unnecessary treatments will be avoided
- Screening and post-therapy imaging should be used to optimise selection and monitor response
- Combining PSMA imaging with other molecular imaging agents e.g. FDG-PET should be considered
- Evidence that PSMA testing is better than choline and other alternatives

Abbreviations: $^{177}$Lu: lutetium-177 vipivotide tetraxetan; ARSAC: Administration of Radioactive Substances Advisory Committee; BNMS: British Nuclear Medicine Society; IR(ME)R: Ionising Radiation Medical Exposure Regulations; FDG-PET: fluorodeoxyglucose (FDG)-positron emission tomography (PET); PSMA: prostate-specific membrane antigen

# Exclusion of radium-223 as a comparator (1)

Is Radium-223 a relevant comparator for mCRPC with bone, but no visceral metastases?

**ACM1: Company and ERG disagree whether radium-223 is a relevant comparator**

- **Company** didn't consider radium-223 relevant comparator/limited comparability with $^{177}$Lu (small subgroup of symptomatic bone metastases but no visceral); used to treat bone pain (vs. tumour/metastases for $^{177}$Lu); limited OS benefit
- No suitable evidence for radium-223 in post ARPI, post-taxane setting → prevents indirect comparison
- **ERG:** minority have radium-223 in post-ARPI and taxane setting but lack of comparative evidence

**ACD: Considered radium-223 as comparator for people with bone metastases**

- Radium-223 has different mechanism of action to $^{177}$Lu, palliative treatment for bone pain
- Acknowledge lack of evidence for $^{177}$Lu vs. radium-223 but not reason to exclude as a comparator
- Radium-223 may be a relevant comparator for some people but limited information available about the size of the relevant population → **Committee wanted to see comparative evidence for this group**

**Consultation**: **No additional analysis of $^{177}$Lu vs radium-223**

- **Company** reiterate radium comparator for small subgroup (RWE [redacted] of all mCRPC had radium-223; [redacted] had prior ARPI + taxane). Audit data 80% had radium at 1st or 2nd line – earlier in treatment pathway
- **ERG** maintain radium-223 relevant in people with bone metastases / no visceral metastases with no new evidence from company

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Abbreviations: $^{177}$Lu: Lu vipivotide tetraxetan; ARPI: androgen receptor pathway inhibitor; mCRPC: metastatic castration-resistant prostate cancer; OS: overall survival; RWE: real-world evidence

# Exclusion of radium-223 as a comparator (2)

## Summary ACD responses: Stakeholders and web comment

**Comments**

**Bayer (manufacturer of radium-223)**

- Estimate approx. **30% of people with mCRPC would be eligible for radium-223** – substantial
- Radium-223 is not just 'palliative' – improves survival and targets underlying mechanism of condition
- Overall survival in ALSYMPCA trial (radium-223 vs. placebo) shows significant improvement
- Indirect treatment comparison between radium-223 and $^{177}$Lu with ALSYMPCA should be explored
- Symptomatic bone metastases (for radium-223 eligibility) is broader than bone pain and includes:
  - *Hypercalcaemia*
  - *Pathological fracture*
  - *Newly or increased fatigue/generalised weakness*
  - *Impaired mobility*
  - *Anaemia, neutropenia, thrombocytopenia*
  - *Pain and discomfort; back pain (spinal cord compression)*
  - *Reduced activity of daily living or sleep disturbance because of pain*

- **BNMS:** Radium-223 should **not be considered a comparator** – ALSYMPCA and VISION populations are different; $^{177}$Lu and radium-223 are different – sequential treatments possible until direct evidence
- **PCUK:** Limited comparability with $^{177}$Lu , e.g. 21% ineligible for radium-223 in VISION (visceral metastases). A subgroup analysis with statistically powered evidence difficult because small sample size
- **Prostate Cancer Research:** Radium-223 may be a comparator for some, but no evidence – not consider
- **TACKLE:** $^{177}$Lu can be used at all metastases sites – 'superior' mode of action
- **Web:** More use of $^{177}$Lu will mean less use of radium-223 and cabazitaxel



Abbreviations: $^{177}$Lu: lutetium-177 vipivotide tetraxetan; ACD: Appraisal consultation document; BNMS: British nuclear medicine society; mCRPC: metastatic castration-resistant prostate cancer; PCUK: prostate cancer UK

# Population for whom taxanes are unsuitable (1)

Subgroup that would benefit from added treatment option but no evidence of efficacy

**ACM1: Company include people for whom taxanes are unsuitable in MA; ERG acknowledge VISION not representative of this subgroup**

**Company:** High unmet need, no treatment options for this subgroup; 42% eligible for $^{177}$Lu at 2$^{nd}$ line

- Performance status; comorbidities; patient choice; all reasons why taxanes may be medically unsuitable
- Lack of clinical evidence in this group but no reason for different $^{177}$Lu efficacy and safety
- Potential to explore managed access routes: PSMAfore RCT (no taxanes in past 12 months)
- **ERG:** Company modelling uses evidence from trials where people with mCRPC have had both ARPIs and taxanes and no evidence of similar efficacy in this population

**ACD: Appropriate to consider whole MA including when taxanes are medically unsuitable**

- People for whom taxanes are medically unsuitable would be able to have $^{177}$Lu ( but worse prognosis)
- Request scenario analyses: same relative treatment effect as wider population /higher baseline risk (worse overall survival)

**Consultation**: **No additional analysis for subgroup for whom taxanes are medically unsuitable**

- **Company:** Consider base case generalisable for this subgroup – prognosis may be better than having docetaxel too
- **ERG:** Maintain view on uncertainty on relative treatment effects of $^{177}$Lu for this subgroup – no evidence to support same benefit as in VISION (at least 1 taxane)



Abbreviations: $^{177}$Lu: Lu vipivotide tetraxetan; ARPI: androgen receptor pathway inhibitor; ECOG: Eastern Cooperative Oncology Group; MA: marketing authorisation; mCRPC: metastatic castration-resistant prostate cancer; RCT: randomised controlled trial

# Population for whom taxanes are unsuitable (2)

Summary ACD responses: stakeholders and web comments

## Stakeholders

- **BNMS:** This subpopulation has an unmet need – $^{177}$Lu would address this and reduce inequality
  - People with non-painful bone metastases after chemotherapy (if tolerable) would have no treatment options → overall inequality in mCRPC patient care – can be perceived discriminatory
- **PCUK:** Statistically powered data when taxanes are medically unsuitable for a taxane-based chemotherapy population is limited
  - Small subset of mCRPC and unlikely well represented in clinical trials – VISION not designed for this either
  - People without bone metastases only would have no alternative treatment options – only small number of people with bone metastases eligible for radium-223
- **Prostate Cancer Research:** Give further consideration to benefits of $^{177}$Lu vs SOC, given for 42%, taxanes may not be suitable
- **TACKLE:** Pleased committee recognised all patient needs irrespective of prior taxane treatment – potential equality issue otherwise
- **UK MRT:** Myelosuppression with cabazitaxel is dose limiting – not seen with $^{177}$Lu or febrile neutropenia needing hospital admission; gastro-intestinal toxicity/fatigue with cabazitaxel negligible with 177Lu

## Web comments

- Unmet need - no real comparator (especially when taxanes unsuitable), unless suitable for radium-223



Abbreviations: $^{177}$Lu: lutetium-177 vipivotide tetraxetan; ACD: Appraisal consultation document; BNMS: British nuclear medicine society; mCRPC: metastatic castration-resistant prostate cancer; PCUK: prostate cancer UK: SOC: standard of care

# RECAP – Studies included in the network meta-analysis

Company and ERG have different preferences for inclusion/exclusion of TROPIC, COU-AA-301, AFFIRM, Sun et al., 2016 and TheraP trials in network meta-analysis

| | Company NMA | ERG NMA | Study Population (all mCRPC) | Intervention (per arm) | Prior ARPI? | N |
|---|---|---|---|---|---|---|
| **TROPIC** | ✓ | | Refractory to hormone therapy and previous treatment with docetaxel | **Mitoxantrone** + prednisone vs. **cabazitaxel** + prednisone | No | 755 |
| **COU-AA-301** | ✓ | | Previous docetaxel treatment | **Abiraterone** + prednisone/prednisolone vs. **placebo** + prednisone/prednisolone | No | 1195 |
| **AFFIRM** | ✓ | | Previous docetaxel treatment | **Enzalutamide** vs. **placebo** | No | 1199 |
| **Sun et al. 2016** | ✓ | | ≥ 18 years old | **Abiraterone** + prednisone vs. **placebo** + prednisone | No | 214 |
| **CARD** | ✓ | ✓ | Progressive and previously treated with 3 or more cycles of docetaxel | **Cabazitaxel** vs. **enzalutamide** or **abiraterone** + prednisone | 1 | 255 |
| **VISION** | ✓ | ✓ | Pre-treated with taxane regimens - subpopulation of patients who received ARPI as part of SOC | **$^{177}$Lu vipivotide tetraxetan** + **SOC** vs. **SOC** | 1 or more | 831 |
| **TheraP** | | ✓ | Pre-treated with taxane regimens | **$^{177}$Lu vipivotide tetraxetan** vs. **cabazitaxel** | 1 or 2 | 200 |

**ACD:** Use adjusted estimates from VISION (inverse probability of censoring weighting analysis)

- Explore using a baseline risk-adjusted network meta-analysis including all the studies
- Prefer including TheraP direct evidence

Abbreviations: $^{177}$Lu: Lu vipivotide tetraxetan; ARPI: androgen receptor pathway inhibitor; mCRPC: metastatic castration-resistant prostate cancer; NMA: network meta-analysis; SOC: standard of care

# Post ACM1: Network meta-analysis (1)

## Company updated fixed-effects NMA; ERG prefer random-effects

**Company: Updated network meta-analysis using fixed-effect model in base case but prefer results from PSW RWE study for cabazitaxel**

- Updated fixed effects NMA: For OS using IPCW-adjusted VISION data; for rPFS using interval imputed VISION data and TheraP (and scenario analysis excluding TheraP)
- Baseline risk-adjusted NMA for OS and rPFS to account for heterogeneity between trials did not improve model fit (no improvement in residual deviance and no significant reduction in DIC)
- PSW RWE study for cabazitaxel preferred because potential bias in treatment effect from heterogenous CARD and VISION in NMA

**Company VISION OS and rPFS outcomes adjusted for informative censoring in updated NMA**

| ARPI subgroup | | Hazard ratio (95% CI) |
|---|---|---|
| Overall survival | No adjustment | [redacted] |
| | IPCW | [redacted] |
| rPFS | No adjustment | [redacted] |
| | Interval imputation | [redacted] |

**ERG's additional NMA including company adjustments**

| Direct evidence to inform cabazitaxel vs ARPI | |
|---|---|
| Overall survival | 1.00 (0.44 to 2.24) |
| rPFS | 0.77 (0.47 to 1.20) |

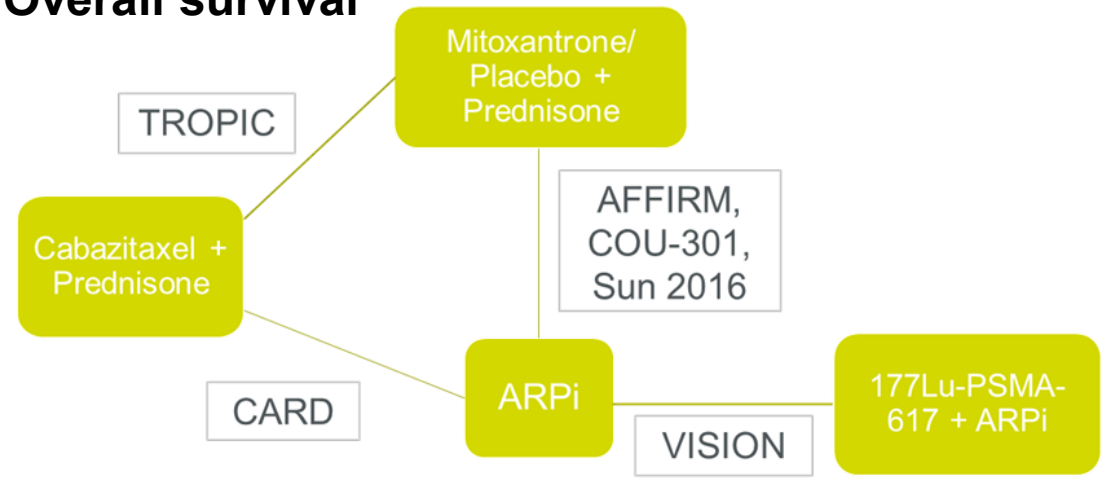
**ERG: Prefer random-effects NMA with trials for ARPI experienced people (CARD, VISION, TheraP)**

- Company include trials where people are ARPI naïve → less generalisable to current practice
- Prefer random-effects model with informative prior due to heterogeneity

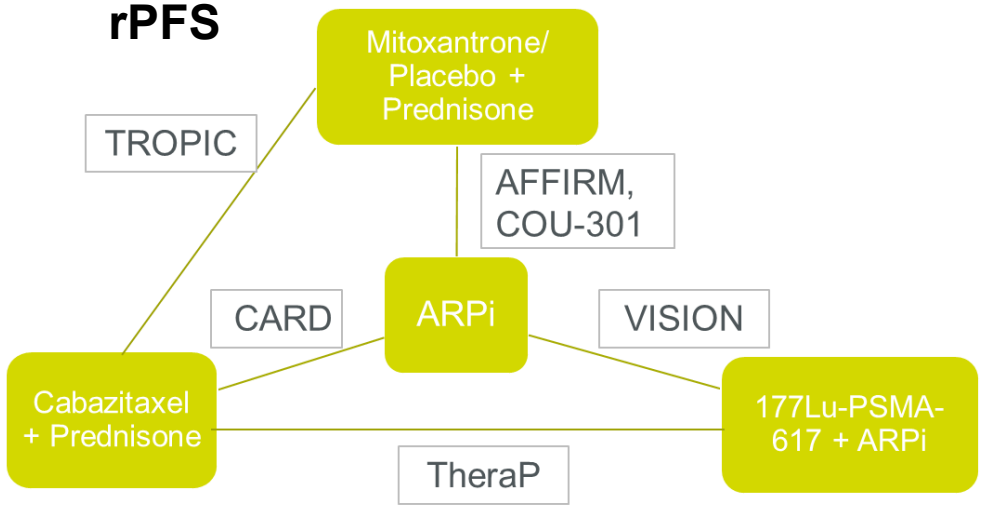
Abbreviations: ARPI: androgen receptor pathway inhibitor; DIC: deviance information criterion; IPCW: inverse probability of censoring weighting; OS: overall survival; rPFS: radiographic progression-free survival; NMA: network meta-analysis: PSW: propensity score weighting; RWE: real-world evidence

# Post ACM1: Company Network meta-analysis (2)

**Overall survival**




**rPFS**




**ERG:**

- Updated NMA results with adjusted OS and rPFS data from VISION used to inform OS and rPFS for cabazitaxel in updated base case
- Statistically significant difference in consistency test between direct (CARD) and indirect evidence (TROPIC, COU-AA-301, AFFIRM, Sun et al.) for cabazitaxel and ARPI comparison – may be because of ARPI naïve population in indirect evidence
- Prefer NMA including trials with ARPI experienced people (CARD, VISION and TheraP).



Abbreviations: OS: overall survival; rPFS: radiographic progression-free survival; NMA: network meta-analysis

# Post ACM1: Company's updated network meta-analysis (3)

**Company's updated NMA with adjusted VISION data**

| Hazard ratio of $^{177}$Lu vs: | | Cabazitaxel | ARPI | Mitoxantrone /placebo |
|---|---|---|---|---|
| **Overall survival** | Fixed effects | [redacted] | [redacted] | [redacted] |
| | Random effects | [redacted] | [redacted] | [redacted] |
| | DuMouchel priors | [redacted] | [redacted] | [redacted] |
| **rPFS (with TheraP)** | Fixed effects | [redacted] | [redacted] | [redacted] |
| | Random effects | [redacted] | [redacted] | [redacted] |
| | DuMouchel priors | [redacted] | [redacted] | [redacted] |
| **rPFS (no TheraP)** | Fixed effects | [redacted] | [redacted] | [redacted] |
| | Random effects | [redacted] | [redacted] | [redacted] |
| | DuMouchel priors | [redacted] | [redacted] | [redacted] |

**ERG:**

- Maintains that it is more appropriate to use a random effects model with informative prior, given heterogeneity among studies
- Company's NMA is less generalisable to current practice (using trials with ARPI naïve populations) where most have ARPI before cabazitaxel – and $^{177}$Lu marketing authorisation

Abbreviations: $^{177}$Lu: lutetium-177 vipivotide tetraxetan; ARPI: androgen receptor pathway inhibitor; rPFS: radiographic progression-free survival; NMA: network meta-analysis

# Cabazitaxel overall survival estimates

## Overall survival for cabazitaxel based on network meta-analysis

**ACM1: Company's** naïve comparison between $^{177}$Lu and cabazitaxel OS estimate from RWE increased uncertainty and potential bias – mean OS for cabazitaxel lower than SOC in VISION

- **ERG** concerns with company's comparison lacking face validity and appropriateness of prognostic covariates used in PSWA (adjusting baseline characteristics between VISION and RWE)

**ACD:** Appropriate to use RWE to estimate survival for people having cabazitaxel but relative treatment effect compared with $^{177}$Lu should come from re-analysed NMA

**Scenario:** Cabazitaxel RWE as reference OS estimate and deriving OS for $^{177}$Lu with NMA hazard ratio

**Company:** Targeted literature review for clinically important prognostic variables affecting survival (~25)

- 13 important prognostic factors – 9 not adjusted for because not available from RWE and VISION
- ACD suggested scenario introduces inconsistencies between source of OS and rPFS
- Address uncertainty in relative effect of $^{177}$Lu vs cabazitaxel: cabazitaxel OS based on NMA, and scenario for PSW RWE analysis

**ERG: Unchanged view on robustness of company's PSW RWE analysis**

- Company's focused search (rather than sensitive search) associated with limitations
- Unanchored ITC should adjust prognostic factors **and treatment effect modifiers** – no justification for whether appropriate effect modifiers were adjusted for
- ACD suggested scenario analysis likely better reflects true survival in current practice – company's scenario for cabazitaxel OS from RWE subject to same inconsistencies as ACD scenario

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Abbreviations: $^{177}$Lu: lutetium-177 vipivotide tetraxetan; ITC: indirect treatment comparison; OS: overall survival; PSW: propensity score weighting; rPFS: radiographic progression-free survival; NMA: network meta-analysis; RWE: real-world evidence

# Key issue: Cabazitaxel utility values (1)

**Company:** Prefer Treatment dependent utilities from VISION and TA391

| Health state utility | $^{177}$Lu | SOC | Cabazitaxel |
|---|---|---|---|
| Progression-free | [redacted] | [redacted] | [redacted] |
| Progressed disease | [redacted] | [redacted] | 0.627 |

**ERG:** Prefer company's scenario using treatment-independent utilities for pre- and post-progression

- **Scenario:** Treatment-dependent utility assuming utility for cabazitaxel is average between utility for $^{177}$Lu vipivotide tetraxetan and utility for SOC

| | Company | | | ERG-preferred | | | Company updated (TE) | | | ERG exploratory | | | Company updated (ACD) | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | $^{177}$Lu | SOC | CBZ | $^{177}$Lu | SOC | CBZ | $^{177}$Lu | SOC | CBZ | $^{177}$Lu | SOC | CBZ | $^{177}$Lu | SOC | CBZ |
| **Utility** | | | | | | | | | | | | | | | |
| Pre-progression | [redacted] | [redacted] | [redacted] | [redacted] | [redacted] | [redacted] | [redacted] | [redacted] | [redacted] | [redacted] | [redacted] | [redacted] | [redacted] | [redacted] | [redacted] |
| Post-progression | [redacted] | [redacted] | 0.63 | [redacted] | [redacted] | [redacted] | [redacted] | [redacted] | 0.63 | [redacted] | [redacted] | [redacted] | [redacted] | [redacted] | [redacted] |
| **QALY losses (one-off)** | | | | | | | | | | | | | | | |
| Due to AE | - | - | - | [redacted] | [redacted] | [redacted] | - | - | - | - | - | - | - | - | - |
| Due to SSEs | - | - | - | [redacted] | [redacted] | [redacted] | - | - | - | - | - | - | - | - | - |

Abbreviations: $^{177}$Lu: lutetium-177 vipivotide tetraxetan; CBZ: cabazitaxel; SOC: standard of care; TE: technical engagement

# Key issue: Cabazitaxel utility values (2)

Company use treatment-dependent; ERG prefer treatment-independent utilities

**ACD:** Consider possibility to adjust for withdrawal in HRQoL results – applying IPCW – meaningful difference in results would reduce uncertainty of using treatment-dependent utilities

- Scenario analyses to address uncertainty in utilities; but treatment-independent utilities had higher face validity across treatments

**Company: Not feasible to adjust for withdrawal using IPCW; use treatment-dependent utilities**

- 3 sources of missing data in EQ-5D (dropouts, missed assessments, death) – unaware how to address
- To address uncertainties with treatment-dependent utilities: updated base case in line with ERG exploratory analysis where cabazitaxel utilities assumed average utilities for cabazitaxel and 177Lu
- No further analyses using treatment-independent utilities which does not account for psychological burden of chemotherapy and treatment burden with cabazitaxel

**ERG: Unchanged preference for treatment-independent utilities with QALY losses due to AE/SSEs**

- No detail around attempted IPCW from company; no analyses using treatment-independent utilities
- Company's updated approach for cabazitaxel utilities not consistent with ERG exploratory analysis – used utilities at technical engagement stage (associated with informative censoring)
- Scenario analysis: treatment-dependent utilities and assuming average of utilities for $^{177}$Lu and SOC for cabazitaxel pre- and post-progression health states



Abbreviations: $^{177}$Lu: lutetium-177 vipivotide tetraxetan; AE: adverse event; IPCW: inverse probability of censoring weighting; HRQoL: health-relate quality of life; SSE: symptomatic skeletal event; SOC: standard of care

# Key issue: Cabazitaxel pre-/concomitant medication costs (G-CSF)

Updated Company and ERG base case; company include additional costs for adverse events

**ACM1:**
**Company:** 7-9 days G-CSF use more appropriate – updated base case using 9 days
**ERG**: 5 days preferred approach but agree with risks associated with fewer days of G-CSF e.g. neutropenic sepsis → Did exploratory analysis using 7 days treatment

**ACD:** 7 days of G CSF treatment should have been used because this is the maximum commissioned by the NHS and would account for variations in clinical practice

**Consultation:**
**Company:** Updated base case to 7-day prophylactic treatment per 21-day cabazitaxel cycle

- Include costs for adverse events of neutropenic sepsis and febrile neutropenia from CARD (14 days G-CSF) to account for increased incidence of neutropenia-related adverse events using cabazitaxel
  - RWE (cabazitaxel in NHS): [redacted]% febrile neutropenia compared with 3.2% in CARD (grade 3 or 4)
  - No data on actual prophylactic G-CSF use in RWE
- **ERG:** Note company use incidence of neutropenic sepsis and febrile neutropenia from VISION ($^{177}$Lu) and CARD (cabazitaxel)
- Accept company approach in line with committee preferences including adverse event costs (small impact on costs/QALYs)

Abbreviations: $^{177}$Lu: Lu vipivotide tetraxetan; AE: adverse event; ASCO: American Society of Clinical Oncology; G-CSF: granulocyte-colony stimulating factor; SOC: standard of care

# End-of-life

1. *Treatment is indicated for patients with a short life expectancy, normally less than 24 months*
2. *Sufficient evidence to indicate the treatment has the prospect of offering an extension to life, normally a mean value of at least added 3 months, compared with current NHS treatment*

***Committee should be satisfied that:***

- *Estimates of the extension to life are sufficiently robust and can be shown or reasonably inferred from either progression-free survival or overall survival*
- *Assumptions used in the reference case economic modelling are plausible, objective and robust*

**ACD:** $^{177}$Lu meets end-of-life criteria compared with standard care but comparison with cabazitaxel is uncertain

- Committee did not see preferred estimates of $^{177}$Lu compared with cabazitaxel
- No evidence on comparison of $^{177}$Lu with radium-223



Abbreviations: $^{177}$Lu: Lu vipivotide tetraxetan

# Summary of company and ERG base case assumptions

| Assumption | Company | ERG |
|---|---|---|
| **Model errors** | Corrected some programming errors | All programming errors corrected |
| **Cabazitaxel pre/concomitant-medication costs** | Not updated | Costs preferred by committee (ERG costs) |
| **G-CSF treatment duration** | 7 days with additional adverse events costs | 7 days |
| **Utility values** | Treatment-specific (no AE or SSEs) and cabazitaxel utilities assumed average between $^{177}$Lu and SOC | Treatment-independent and decrements for AE and SSEs |
| **Cabazitaxel rPFS and overall survival HR estimates** | Fixed effects NMA using TROPIC, COU-AA301, AFFIRM, Sun et al., CARD, TheraP, VISION (adjusted overall survival and rPFS) | Random-effects NMA using CARD, TheraP, VISION |
| **PSMA test costs** | 25% people having test (SPECT not PET-CT) | 100% having test (either PET-CT or SPECT) |

**The ICERs are all above the level normally considered an effective use of NHS resources with or without end of life (comparator PAS discounts apply)**

Abbreviations: $^{177}$Lu: Lu vipivotide tetraxetan; AE: adverse event; G-CSF: granulocyte-colony stimulating factor; HR: hazard ratio; PSMA: prostate-specific membrane antigen; rPFS: radiographic progression-free survival; SSE: symptomatic skeletal event

# Cost-effectiveness results

All ICERs are reported in PART 2 slides because they include confidential comparator PAS and CMU discounts

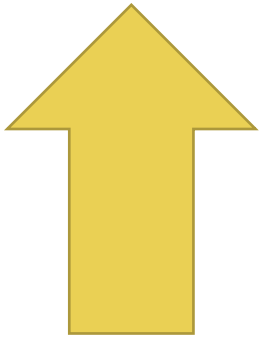
**Summary**

- The company and ERG ICERs are **higher** than would usually be considered an effective use of NHS resources, when confidential discounts are taken into account
- ERG's ICERs are **higher** than the company's:
  - ERG prefer a random effects network meta-analysis using direct evidence for relative effect of cabazitaxel and ARPI (VISION, CARD, TheraP trial)
  - Using treatment-independent utility decrements for adverse events and symptomatic skeletal events
  - Unit cost of PSMA testing for 100% of patients



Abbreviations: $^{177}$Lu: Lu vipivotide tetraxetan; ICER: incremental cost-effectiveness ratio; PSMA: prostate-specific membrane antigen;

# Company's scenario analyses and ERG's exploratory analyses



**Company scenario analyses increasing ICER:**

- Random-effects network meta-analysis to inform cabazitaxel overall survival and rPFS
- Random-effects network meta-analysis with DuMouchel priors
- SPECT-CT PSMA scans for 100% patient population

**Company scenario analyses decreasing ICER:**

- Real-world evidence propensity score weighting study to inform cabazitaxel overall survival estimate
- Network meta-analysis excluding TheraP from rPFS network

**ERG exploratory analyses decreasing ICER:**

- Treatment-dependent utility assuming utility for cabazitaxel is average between utility for $^{177}$Lu and utility for standard of care
- PSMA test costs for 25% patient population

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Abbreviations: $^{177}$Lu: Lu vipivotide tetraxetan; PSMA: prostate-specific membrane antigen; rPFS: radiographic progression-free survival; SPECT: single-photon emission computerized tomography

# Key issues

**Impact on ICER:** Small / Large / Unknown

| Issue at ACM1 | Resolved? | Committee | |
|---|---|---|---|
| **PSMA testing** | Partially | • PSMA imaging will be necessary to determine $^{177}$Lu eligibility<br>• ***What % PSMA testing should be used in the model? SPECT, PET-CT or both?*** |  |
| **Broadening population including people for whom taxanes are unsuitable** | No further evidence | • Appropriate to consider whole marketing authorisation<br>• ***Should $^{177}$Lu be considered for this population given there is no evidence for this population?*** |  |
| **Excluding radium-223 as a comparator for people with bone metastases** | No further evidence | • May be relevant comparator; subgroup analysis comparison<br>• ***Should radium-223 be considered for this population given there is no evidence for this subgroup?*** |  |
| **Company's NMA**<br>• Fixed- vs. random effects model<br>• Studies included in the NMA | No | • Using IPCW-adjusted estimates from VISION in NMA<br>• Exploring all studies in baseline-risk adjusted model<br>• ***Which NMA is best to model $^{177}$Lu vs cabazitaxel?*** |  |
| **Overall survival estimates for cabazitaxel in the model** | No | • RWE on survival with cabazitaxel as reference group for absolute event estimates, applying hazard ratio from NMA for $^{177}$Lu survival<br>• ***Is the updated company approach appropriate?*** |  |
| **Cabazitaxel utility values** | No | • Utilities are uncertain; account for withdrawals using IPCW<br>• ***Are utilities modelled appropriately?*** |  |
| **Pre-medication and concomitant medication costs for cabazitaxel** | Partially | • Using ERG's costs in the model to better reflect NHS practice<br>• ***Is the committee satisfied with G-CSF duration costs?*** |  |

Abbreviations: $^{177}$Lu: Lu vipivotide tetraxetan; G-CSF: granulocyte colony-stimulating factor; IPCW: inverse probability of censoring weighting; NMA: network meta-analysis; PET-CT: Positron emission tomography computerised tomography; PSMA: prostate-specific membrane antigen; rPFS: radiographic progression-free survival; SPECT: single-photon emission computerized tomography

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# Thank you.

# Back-up slides

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# RECAP – VISION baseline characteristics

| Characteristic | | Full analysis set (N=831) | | PFS-full analysis set (N=581) | |
|---|---|---|---|---|---|
| | | $^{177}$Lu + SOC (N=551) | SOC (N=280) | $^{177}$Lu + SOC (N=385) | SOC (N=196) |
| Site of disease, n (%) | Lymph node | 274 (49.7) | 141 (50.4) | 193 (50.1) | 99 (50.5) |
| | Bone | 504 (91.5) | 256 (91.4) | 351 (91.2) | 179 (91.3) |
| | Lung | 49 (8.9) | 28 (10) | 35 (9.1) | 20 (10.2) |
| | Liver | 63 (11.4) | 38 (13.6) | 47 (12.2) | 26 (13.3) |
| Previous ARPI regimen, n (%) | 1 | 298 (54.1) | 128 (45.7) | 213 (55.3) | 98 (50) |
| | 2 | 213 (38.7) | 128 (45.7) | 150 (39) | 86 (43.9) |
| | >2 | 40 (7.3) | 24 (8.6) | 22 (5.7) | 12 (6.1) |
| Previous taxane therapy regimen, n (%) | 1 | 325 (59) | 156 (55.7) | 207 (53.8) | 102 (52) |
| | 2 | 220 (39.9) | 122 (43.6) | 173 (44.9) | 92 (46.9) |

NICE Abbreviations: $^{177}$Lu: Lu vipivotide tetraxetan; ARPI: androgen receptor pathway inhibitor; PFS: progression-free survival; PSA: prostate specific antigen; SOC: standard of care

# Summary of ACD response: stakeholder and web comments (1)

## Recommendation is disappointing

- Overall disappointment: fewer options available for people who have exhausted options – unmet need
- $^{177}$Lu shows clinical effectiveness – improved OS and better HRQoL
- "As a patient expert, I am very concerned at the committee's decision…this treatment has been successfully employed in Germany and Australia"
- "…It would be a tragedy for patients with advanced prostate cancer if this innovative therapy was not made available to NHS patients. It would also be a travesty for our healthcare system that it would be available to those who could afford it."

## $^{177}$Lu is innovative

- VISION is the first Phase 3 study showing value of targeted medicine for large population with mCRPC
- $^{177}$Lu is a novel and transformative therapy that improve survival and quality of life, if approved
- 'Theranostics' in treatment pathway is increasingly important strategy

## Adverse events

- "I am much stronger and I feel much calmer and more relaxed…Other than occasional dry mouth…my experience…has been extraordinary…"
- "Side-effects are minimal enabling me to continue my work and bike riding. I will be taking part in the stage 2 of the Tour de France"
- "I have been able to lead a full and active life for the past year with no additional treatment…$^{177}$Lu is a breakthrough therapy capable of lengthening and enhancing the lives…"

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Abbreviations: $^{177}$Lu: Lu vipivotide tetraxetan; HRQoL: health-related quality of life; mCRPC: metastatic castration-resistant prostate cancer

# Summary of ACD response: stakeholder and web comments (2)

## Costs

- Costs associated with cabazitaxel not sufficiently considered – Side effects neutropenia, febrile neutropenia, sepsis significantly less frequent in people having G-CSF → highly relevant to consider
- Service delivery cost should be fully considered – can be resource intensive compared with other radiotherapeutics
  - 390 people per year predicted eligible for PSMA-labelled treatment by 2029 in their region
  - Extrapolation to UK population: 7,800 people per year with up to 46,800 administrations
    - Total cost to NHS may be up to £1bn per year
- Ancillary costs include: nuclear medicine infrastructure, extra imaging costs, capacity, extra clinical space, lists, staff training and recruitment – administration costs does not cover this

## Other

- TheraP is more relevant than implied – improve PSA50 response compared with cabazitaxel
- Consider including post-therapy SPECT/CT imaging to identify people with low uptake in TheraP
- Consider mCRPC as 'particularly aggressive' in men of African background and diagnosed late
- Helpful to compare RWE on best supportive care vs trial arm best supportive care



Abbreviations: G-CSF: granulocyte colony-stimulating factor; CT: computerised tomography; mCRPC: metastatic castration-resistant prostate cancer; PSA: prostate specific antigen; PSMA: prostate-specific membrane antigen; RWE: real world evidence; SPECT: single-photon emission computerized tomography