

Axumin for functional imaging of prostate cancer recurrence

Medtech innovation briefing

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Summary

- The **technology** described in this briefing is Axumin, a radiopharmaceutical agent. It is intended for use in positron emission tomography (PET) to detect suspected prostate cancer recurrence in people who have elevated prostate-specific antigen levels after primary curative treatment. It is currently the only licensed PET tracer indicated for use in recurrent prostate cancer.
- The **innovative aspects** are that it is a prostate cancer-specific PET tracer with a novel mechanism of action based on amino acid transport. Its longer half-life and shorter uptake period may allow use in more people with suspected prostate cancer recurrence compared with other PET tracers.
- The intended **place in therapy** is in addition to bone scans or MRI to detect suspected prostate cancer recurrence in adults. It may be used as an alternative to choline or prostate-specific membrane antigen PET/CT in centres where these scans are available.
- The **main points from the evidence** summarised in this briefing are from 1 meta-analysis and 5 studies (2 randomised trials and 3 non-randomised observational studies) including more than 1,200 men with suspected prostate cancer recurrence. The evidence reported that Axumin PET/CT detected prostate cancer recurrence with good diagnostic accuracy and frequently led to changes in patients' management plans.

- **Key uncertainties** around the evidence or technology are the lack of comparative studies with other PET tracers. There are no head-to-head studies comparing Axumin with ^{18}F -choline. Also, the effects of Axumin PET on earlier diagnosis and on quality of life have not been evaluated.
- The per-patient cost for a single dose of Axumin tracer is £950 (excluding VAT), plus transport costs estimated at £50 to £250 per shipment. The **resource impact** would be a cost increase per scan. The technology has the potential to free up resources if it reduces the number of imaging tests needed to confirm diagnosis or if fewer people are referred for radiotherapy.

The technology

Axumin (Blue Earth Diagnostics Ltd) is a molecular imaging agent. It is intended for use in positron emission tomography (PET) to detect whether prostate cancer has returned in people whose blood prostate-specific antigen (PSA) levels have risen after primary curative treatment. Axumin is given as an intravenous injection in the arm 3 to 5 minutes before a PET scan. A CT scan is used to provide information about the patient anatomy and the combined scan is termed PET/CT.

Axumin contains the active ingredient ^{18}F -fluciclovine (anti-1-amino-3- ^{18}F -fluorocyclobutane-1-carboxylic acid or FACBC). This is a radiolabelled synthetic amino acid that is taken up into cells by transporters (LAT-1 and ASCT2) known to be present in high numbers on the surface of prostate cancer cells. Once inside the cancer cells, it emits radiation that is detected on the PET scan, with the aim of identifying local and distant areas of recurrence. The preferential uptake of the tracer into prostate cancer cells compared with the surrounding non-cancerous tissue enables cancerous areas to be reliably located.

Innovations

Axumin is the only PET tracer currently licensed for clinical use in recurrent prostate cancer. Prostate-specific membrane antigen (^{68}Ga -PSMA) and choline-based (^{11}C - and ^{18}F -labelled) PET tracers are available only on a special licence basis or for use in research. Expert advice indicates that these tracers are increasingly used in UK practice and that ^{18}F -choline PET/CT is currently the only scan commissioned by NHS England in the national PET/CT tender. Axumin is designed to more effectively identify recurrent disease across a wide range of PSA levels compared with standard-of-care imaging (pelvic CT or MRI and bone scans). These lack the sensitivity and specificity to detect prostate cancer when PSA levels are low ([Mottet et al. 2017](#); [Cornford et al. 2017](#)). The short uptake period for Axumin allows scans to be done 3 to 5 minutes after administration, compared with alternative PET tracers, which may need about 1 hour for optimal

tracer uptake. Also, the technology's shelf life of 7 to 10 hours may offer potential for wider use compared with ^{11}C -choline. This has a half-life of 20 minutes, meaning that it can only be done in PET centres with on-site cyclotron and radiopharmacy facilities.

Current care pathway

NICE's guideline on [prostate cancer: diagnosis and management](#) recommends routine follow-up to identify recurrent disease in men who have had treatment for localised prostate cancer. According to the guideline, methods of monitoring disease control and detecting recurrence include physical examination, PSA blood tests and imaging investigations. It recommends that PSA levels are checked in everyone having curative-intent (or radical) treatment 6 weeks or more after treatment, at least every 6 months for the first 2 years and then at least once a year. To detect areas of local recurrence or metastatic lesions, it recommends imaging techniques such as MRI or bone scans in people with a rising PSA (biochemical relapse [BCR]) after curative-intent treatment, and who are considering second-line therapy. However, it recommends MRI only after salvage radiotherapy, and an isotope bone scan only if symptoms suggest metastasis. An [update](#) to this guideline is currently in process (expected publication date April 2019). In the draft of this update, several previous recommendations on imaging have been deleted, including the recommendation against using PET scans for prostate cancer in routine clinical practice (1.2.15). No new recommendations for managing relapse after radical treatment have been added.

The [2017 European guidelines on prostate cancer](#) recommend routine follow-up of people who are asymptomatic at 3, 6 and 12 months after treatment, then every 6 months until 3 years, and then annually. Imaging to detect local recurrence is only recommended if it affects treatment planning. It also recommends that other imaging modalities should not be routinely offered to people who are asymptomatic if there are no signs of BCR. It states that re-staging should be considered irrespective of PSA levels if there is bone pain or other symptoms of progression. It also recommends the use of choline or PSMA PET/CT imaging in people with BCR after radical prostatectomy with PSA levels of 1 ng/ml or more. In people with low baseline PSA levels (that is, less than 1 ng/ml), no imaging is recommended. In people with BCR after radiotherapy, choline PET/CT imaging is recommended to rule out lymph nodes or distant metastases in patients fit enough for curative salvage treatment. It also states that bone scans and abdominopelvic CT should only be considered in patients with BCR after radical prostatectomy or radiotherapy who have a high baseline PSA (greater than 10 ng/ml) or adverse PSA kinetics (PSA doubling time less than 6 months or PSA velocity greater than 0.5 ng/ml/month).

Population, setting and intended user

Axumin is indicated for PET imaging to detect suspected prostate cancer recurrence in adults with elevated blood PSA levels after primary curative treatment. Axumin will be used in nuclear medicine or radiology centres of tertiary centres. It will be administered by radiographers and the resultant PET/CT images will be read by nuclear medicine physicians.

Costs

Technology costs

According to the company, the per-patient cost for a single dose of Axumin tracer is £950 (excluding VAT), plus transport costs estimated at £50 to £250 per shipment (a shipment may include more than 1 dose). This does not include the cost of the scan and other consumables.

Costs of standard care

The cost of an MRI is £114 to £163, a CT is £71 to £85 and a bone scan is £181 (based on National Tariff 2018/19 and include the cost of reporting). According to the national schedule of reference costs 2017/18, the average cost of a PET/CT scan is £586 (HRG code RN01A). This includes the cost of the tracer, shipment and scan, but the tracer it includes is not used for prostate cancer.

Resource consequences

If adopted, the technology would be used in addition to MRI and CT, but has the potential to replace bone scans and PET scans with specialised PSMA and choline-based tracers. Since equipment and staff needs would be comparable to those for PET scans used in other indications, there would only need to be minimal change to adopt the technology, and no facility or infrastructure modifications would be needed. Axumin, however, may potentially lead to an increase in the number of PET scans done, so may increase resource needs. Radiologists will need product-specific training on interpreting Axumin scans, and the company states that approved training programmes are available from the Medicines and Healthcare products Regulatory Agency and the Administration of Radioactive Substances Advisory Committee.

The use of Axumin PET is likely to be cost incurring compared with current standard care. However, because of increased detection compared with standard imaging, Axumin has the potential to be resource releasing by reducing the number of repeat scans done, and enabling earlier detection and subsequent treatment. In addition, Axumin may have the potential to influence subsequent treatment decisions, reducing the number of patients being under- or over-treated with salvage

radiotherapy. The company also claims that Axumin use has the potential to reduce the pre-patient scan time compared to alternative PET tracers.

The results of a US cost-consequence study ([Jensen et al. 2017](#), published as an abstract only) suggests that increased use of the technology for suspected prostate cancer recurrence may lead to better clinical outcomes while being cost neutral. Results from this study found that Axumin use reduced the number of imaging procedures by 27% and led to a 13% increase in correct diagnoses. There was a small cost increase of 3% per correct diagnosis from \$24,870 to \$25,589.

Regulatory information

Axumin was regulated for use in the EU on 22 May 2017 by the European Medicine Agency's Committee for Medicinal Products for Human Use.

Equality considerations

NICE is committed to promoting equality, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. In producing guidance and advice, NICE aims to comply fully with all legal obligations to: promote race and disability equality and equality of opportunity between men and women, eliminate unlawful discrimination on grounds of race, disability, age, sex, gender reassignment, marriage and civil partnership, pregnancy and maternity (including women post-delivery), sexual orientation, and religion or belief (these are protected characteristics under the Equality Act 2010).

People with a diagnosis of cancer are protected under the Equality Act 2010 from the point of diagnosis. Older people and people of African-Caribbean and African family origin are at higher risk of developing prostate cancer. Transgender women may also remain at risk of developing prostate cancer. Age, race, sex and gender reassignment are all protected characteristics under the Equality Act 2010.

Clinical and technical evidence

A literature search was carried out for this briefing in accordance with the [interim process and methods statement](#). This briefing includes the most relevant or best available published evidence relating to the clinical effectiveness of the technology. Further information about how the evidence for this briefing was selected is available on request by contacting mibs@nice.org.uk.

Published evidence

The evidence base for Axumin includes over 20 studies and case reports identified as being potentially relevant. One meta-analysis and 5 studies (2 randomised trials and 3 non-randomised studies), involving over 1,200 patients are included in this briefing based on relevance and quality of evidence. [Table 1](#) summarises the clinical evidence, as well as its strengths and limitations.

Overall assessment of the evidence

Overall, the evidence suggests that Axumin positron emission tomography (PET)/CT can detect prostate cancer recurrence with good diagnostic accuracy. The technology has been shown to detect local and distant areas of recurrence across a wide range of prostate-specific antigen (PSA) levels and is generally well tolerated.

Evidence shows that Axumin PET/CT can detect recurrence at low PSA levels (below 1 ng/ml) and that detection rates vary with PSA levels, improving as levels increase. In the LOCATE study, a detection rate of 31% was reported for patients with the lowest PSA (0 to 0.5 ng/ml), which rose to 50% and 66% for PSA ranges of 0.5 to 1 ng/ml and 1.0 to 2.0 ng/ml respectively. In [Bach-Gansmo et al. 2017](#), the detection rate in the lowest PSA quartile (below 0.79 ng/ml) was 41%; 30% of patients had recurrence detected outside of the prostate. Both of these studies included a mixed post-therapy population (men with biochemical relapse after radical prostatectomy, or radiotherapy or both). In another study involving men with biochemical relapse after radical prostatectomy only, the Axumin PET/CT detection rate was 72% when the PSA level was less than 1 ng/mL, but increased to 83% and 100% when the PSA levels were 1 to 2 ng/ml or 2 ng/ml and over respectively ([Akin-Akintayo et al. 2017](#)).

The evidence reports that Axumin use frequently results in major changes to patients' management plans compared with standard imaging (abdominopelvic CT, MRI or bone scans), particularly in the extent of planned salvage radiotherapy and the volumes targeted for radiotherapy. However, it is not certain from the available evidence that changes in management lead to improved outcomes for patients. This is an uncertainty common to all imaging modalities used to locate areas of prostate cancer recurrence. Also, with the exception of the FALCON study, all available evidence on changes to clinical management plans come from studies involving US centres, which may not reflect NHS practice. Longer-term studies or patient registries would be needed to assess the effect of Axumin-guided therapy on clinical outcomes such as earlier detection of recurrence, subsequent treatment and progression-free survival. Understanding the performance of Axumin PET/CT in different populations, such as in people grouped by previous treatment, Gleason score and PSA doubling times, may provide information that could help inform

the selection of patients for scanning.

In addition to the studies summarised in the table 1, 4 single-centre prospective studies ([Nanni et al. 2013](#); [Nanni et al. 2014](#); [Nanni et al. 2015](#); [Nanni et al. 2016](#)), and a case-series involving 10 patients ([Calais et al. 2018](#)) have compared the diagnostic performance of Axumin to ^{11}C -choline and prostate-specific membrane antigen (^{68}Ga -PSMA) respectively. Overall, data from these studies suggest that Axumin may be superior to ^{11}C -choline but inferior to ^{68}Ga -PSMA in detecting prostate cancer recurrence. No head-to-head data comparing Axumin with ^{18}F choline were identified.

Table 1 Summary of selected studies

| Andriole et al. (2019) | |
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| Study size, design and location | Prospective, open-label, multicentre, interventional LOCATE study looking at whether ^{18}F -fluciclovine-PET/CT testing changes clinical management in 213 men who had had curative-intent treatment but who were suspected as having recurrence based on rising PSA levels. The study was carried out across 17 US centres. |
| Intervention and comparator(s) | Intervention: ^{18}F -fluciclovine-PET/CT. No comparator. |
| Key outcomes | ^{18}F -fluciclovine-PET/CT detected 1 or more sites of recurrence in 57% of men with BCR. Overall, 59% (126/213) of patients had a change in management; 78% (98/126) of these were 'major' changes. The most frequent major changes were from salvage or non-curative systematic therapy to watchful waiting (25%), from non-curative systematic therapy to salvage therapy (24%) and from salvage therapy to non-curative systemic therapy (9%). At 6 months, 63% of patients had treatment that was concurrent with post-scan plans, a clinically important difference was found for 37%. |
| Strengths and limitations | Study included a relatively large number of patients across 15 centres, reducing bias and increasing generalisability. The study included a 6-month follow-up. It included US centres only, so results may not be generalisable to a UK NHS setting. Imaging results were not routinely confirmed with histological findings. The study was sponsored by the company. |
| Teoh et al. (2018) | |

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| Study size, design and location | Prospective, open-label, multicentre, interventional FALCON study involving 85 men being considered for curative-intent salvage therapy after initial radical therapy (pre-planned interim analysis of the first 85 patients). The study was carried out across 6 UK centres. |
| Intervention and comparator(s) | Intervention: ¹⁸ F-fluciclovine PET/CT. No comparator. |
| Key outcomes | Most of the men in this pre-planned interim analysis had previously had radical prostatectomy (65.9%), with 27 men having had salvage radiotherapy (± other therapy). After ¹⁸ F-fluciclovine PET/CT imaging, 61.2% of those imaged had a change in management, suggesting ¹⁸ F-fluciclovine PET/CT has an effect on clinical decisions for men with a first BCR of prostate cancer after curative-intent primary therapy. Recruitment was subsequently stopped as the pre-specified cut-off for efficacy (>45 treatment changes) was met. |
| Strengths and limitations | This was a multicentre study involving 6 UK sites, so results are likely to be generalisable to NHS practice. It was a planned interim analysis of the first 85 men published as a conference abstract only, so full study details and patient demographics were not available. Study was sponsored by the company. |
| <u>Bach-Gansmo et al. (2017)</u> | |
| Study size, design and location | Multicentre, retrospective, observational BED-001 study involving 596 patients who had ¹⁸ F-fluciclovine PET/CT at 4 centres (1 in US, 1 in Italy and 2 in Norway). |
| Intervention and comparator(s) | Intervention: ¹⁸ F-fluciclovine PET/CT. No comparator. |

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| Key outcomes | At a subject level, ¹⁸ F-fluciclovine PET/CT showed a detection rate of 67.7% (403/595 scans). At a regional level, positive findings were detected in the prostate/bed in 38.7% and in pelvic lymph nodes in 32.6% of scans. Metastatic involvement outside the lymph nodes was detected in 26.2% of scans. Subject level detection rate in those in the lowest quartile for baseline PSA (0.79 ng/ml or less) was 41.4%. The positive predictive value of ¹⁸ F-fluciclovine PET/CT for all sampled lesions was 62.2%, and was 92.3% and 71.8% for extraprostatic and prostate/bed involvement respectively. Treatment emergent adverse events were experienced by 5.4% of patients but none were considered adverse reactions to ¹⁸ F-fluciclovine. The safety profile was not noticeably altered after repeat administration. |
| Strengths and limitations | Study included a large number of people from 4 clinical centres. It involved non-UK centres only so results may not be transferable to NHS clinical practice. The retrospective nature of the study meant that the use of comparative imaging and biopsy technique were not standardised, information on change in treatment was not be systematically captured, and findings could not be confirmed by histology in all patients. Only adverse events occurring within the first 35 days after administration were determined from site records. |
| <u>Jani et al. (2017)</u> | |
| Study size, design and location | Prospective, single-centre randomised, controlled clinical trial involving 96 patients with rising levels of PSA after prostatectomy being considered for salvage radiotherapy. |
| Intervention and comparator(s) | Intervention: ¹⁸ F-fluciclovine PET/CT (n=49). Comparator: Radiation therapy based on conventional imaging (bone scan and abdominopelvic CT and/or MRI scan; n=47). |

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| Key outcomes | With the exception of PTV2, all post-registration volumes were statistically significantly larger than the corresponding pre-registration volumes, suggesting that, in most cases, including information from ¹⁸ F-fluciclovine PET/CT in the treatment planning process may lead to larger volumes targeted for salvage therapy. This was associated with higher doses of radiotherapy (40 Gy and 60 Gy) to the penile bulb (p=0.001 and p=0.002 respectively), but no statistically significant difference in rectal or bladder doses. Acute toxicity results were not statistically significantly different between the control and experimental arms and no acute grade 3, 4 or 5 toxicity was seen in the experimental arm, suggesting treatment to the modified clinical target is tolerable. |
| Strengths and limitations | Randomised trial with intention-to-treat design, helping to remove selection bias and avoid the effects of loss to follow-up. This was a planned analysis of secondary end points for the first 96 patients (accrual goal is 162), so the current follow-up only shows provider-reported acute toxicity outcomes; no information on disease-free survival or long-term toxicity can be determined. Single-centre study conducted in the US, results may not be generalisable to a UK NHS setting. Study was sponsored by the company. |
| <u>Akin-Akintayo et al. (2017)</u> | |
| Study size, design and location | Randomised, prospective, intention-to-treat clinical trial involving men with PSA failure after radical prostatectomy. 87 men were recruited and 44 were randomised to the intervention. |
| Intervention and comparator(s) | Intervention: ¹⁸ F-fluciclovine PET/CT. Comparator: standard care. |

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| <p>Key outcomes</p> | <p>2 patients dropped out before PET/CT scanning.</p> <p>81.0% (34/42) of patients had a positive results on ¹⁸F-fluciclovine PET/CT. All 42 patients who had ¹⁸F-fluciclovine PET/CT were initially planned for radiotherapy. After ¹⁸F-fluciclovine PET/CT findings, radiotherapy decisions were changed in 40.5% patients (17/42). 4.8% (2/42) of patients had radiotherapy decisions withdrawn because of evidence of extra-pelvic disease. Of the remaining patients, 37.5% (15/40) had radiotherapy fields changed; with 73.3% (11/15) of these fields increased from prostate bed only to both prostate and pelvis, and 26.7% (4/15) reduced from both prostate bed and pelvis to the prostate bed only. Changes in radiotherapy field and overall radiotherapy decision were both statistically significant (p<0.001) with ¹⁸F-fluciclovine PET/CT, but change in the decision to offer radiotherapy or not was not statistically significant (p=0.15).</p> |
| <p>Strengths and limitations</p> | <p>This was a planned interim analysis of a secondary end point and the study had not reached final accrual goal (81 patients in each arm). Pre-fluciclovine radiotherapy decisions would have been influenced by a number of factors including patient history, pathology and PSA trajectory. However, several radiotherapy providers were used, meaning pre-fluciclovine decisions are likely to be representative of those made in clinical practice. Single-centre study conducted in the US, so results may not be generalisable to a UK NHS setting. The study centre was given cassettes of ¹⁸F-fluciclovine by the company.</p> |
| <p><u>Ren et al. (2016)</u></p> | |
| <p>Study size, design and location</p> | <p>Systematic review and meta-analysis of published data about the performance of ¹⁸F-fluciclovine PET/CT in the diagnosis of recurrent prostate cancer. 6 studies were included, involving a total of 251 patients with suspected prostate cancer recurrence.</p> |
| <p>Intervention and comparator(s)</p> | <p>Intervention: ¹⁸F-fluciclovine PET/CT.</p> <p>Comparators: ¹¹C-choline PET/CT, ¹¹¹In-capromab pendetide SPECT/CT, T2W MRI.</p> |
| <p>Key outcomes</p> | <p>¹⁸F-fluciclovine PET/CT had an 87% pooled sensitivity, and a 66% pooled specificity. On a per-patient-based analysis in detecting prostate cancer recurrence, ¹⁸F-fluciclovine PET/CT had an area under the receiver-operating characteristic curve of 0.93.</p> |

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| Strengths and limitations | Only 6 studies were included in this meta-analysis; none of which were randomised controlled trials and most included a relatively small number of patients. All included studies involved histology, follow-up methods or both, and the methodology of these studies were evaluated and rated by 3 independent reviewers. Included studies were statistically heterogeneous in their estimates of specificity, possibly because of differences in methodology between the studies (for example, prospective versus retrospective design). |
| Abbreviations: BCR, biochemical recurrence; PET, positron emission tomography; PSA, prostate-specific antigen; SPECT, single photon emission computed tomography; T2W, T2-weighted. | |

Recent and ongoing studies

- [Fluciclovine \(18F\) PET/CT in biochemicAL reCurrence Of Prostate caNcer \(FALCON\)](#). ClinicalTrials.gov identifier: NCT02578940. Status: Active, not recruiting, interim results published in abstract form. Indication: Cancer of the Prostate. Intervention: Fluciclovine 18 F (Axumin). Study start date: November 2015, estimated study completion date: 31 August 2018.

Specialist commentator comments

Comments on this technology were invited from clinical experts working in the field. The comments received are individual opinions and do not represent NICE's view.

Two out of 6 specialist commentators had used Axumin before in a research setting. Two further commentators said that they were familiar with the use of other positron emission tomography (PET) tracers for prostate cancer.

Level of innovation

One commentator noted that the level of innovation depends on what is considered standard care. Compared with bone scans, CT scans and pelvic MRI alone, the technology would be considered innovative. However, pelvic MRI with ¹⁸F-choline PET/CT has become standard care in their centre and, compared with this, Axumin would be considered an addition that may offer several benefits but would not be transformational. Two commentators agreed with this notion: 1 thought it was a minor variation on choline PET/CT, the other thought it was similar to existing PET tracers but the only 1 using an amino acid transport mechanism in prostate cancer. The remaining 3 commentators

thought that Axumin was a novel concept on some level. PET/CT imaging using choline (^{18}F - or ^{11}C -labelled) and prostate-specific membrane antigen (^{68}Ga -PSMA) tracers were identified by commentators as competing technologies currently available to the NHS. Three of the commentators considered PSMA PET/CT to be superior to Axumin PET/CT in the detection of prostate cancer because of the higher sensitivity reported for the PSMA PET tracer. Minor advantages of Axumin over choline tracers were noted by 1 commentator. One commentator thought that, because of logistical challenges with PSMA PET/CT, Axumin may be a more versatile and straightforward tracer for routine use. Another commentator noted that, unlike most competing technologies, Axumin is a licensed product and it can be used in centres without a cyclotron, generator or radiopharmacy on site. In addition, early scanning after administration of Axumin has the potential to increase patient throughput.

Potential patient impact

More accurate and earlier detection of recurrent cancer compared with bone scans and pelvic MRI was identified as a key patient benefit by most commentators. Many added that this could potentially lead to earlier and more appropriate treatment strategies for individuals, and subsequently a greater chance of disease control. Two commentators noted that the use of Axumin may help treatment planning in radiotherapy, such as identifying the optimal radiation dose and treatment field. Others noted that the use of Axumin may help to avoid the need for repeat scans and, as such, result in fewer patient visits to the hospital or their specialist. The possibility of shorter examination times were noted by 1 commentator. According to 1 commentator, Axumin is unlikely to affect decisions on whether or not to offer pelvic radiotherapy given the recent practice-changing evidence from the STAMPEDE study ([Parker et al. 2018](#)). This supports prostate radiotherapy as a standard treatment option for men with low metastatic burden (based on bone, CT or MRI staging scan results). Overall, most of the commentators agreed that the technology has the potential to improve the current care pathway or clinical outcomes in some way. Most of the commentators identified people with rising prostate-specific antigen (PSA) levels after primary therapy (radical prostatectomy or radiotherapy) as the group of people who would benefit most from this technology. One commentator thought it would be particularly useful for people in whom conventional imaging had failed to locate the region of recurrence. Another commentator thought that other advanced prostate cancer states (such as high-risk, locally advanced prostate cancer; non-metastatic castrate-resistant prostate cancer, and oligometastatic hormone-sensitive and castrate-resistant prostate cancer) may also benefit although evidence to support this is lacking.

Potential system impact

Improved outcomes and better use of resources, such as a reduction in the number of additional

investigations needed, and unnecessary or inappropriate treatment, were identified as system benefits by commentators. Three commentators thought that Axumin would be an addition to standard imaging. Although, 2 of these specialists added it has the potential to replace CT and bone scans in centres where this is regarded as standard care. All other commentators thought that Axumin would be a replacement, in particular, for choline PET/CT tracers. Overall, most commentators thought that Axumin would cost more than bone scans, CT scans and pelvic MRI, more than or the same as choline PET/CT, and less than PSMA PET/CT. One commentator noted however, that the cost of PSMA PET/CT can vary and that, in their centre, PET/CT scans with Axumin cost more than those with PSMA PET tracers. Despite its initial upfront cost, some of the commentators thought it had the potential for long-term cost savings as it was shown to lead to earlier detection, and to reduce the number of repeat imaging and costs associated with unnecessary therapies. Two commentators thought that it was difficult to predict the cost impact without further economic evidence. All commentators agreed that implementing Axumin PET/CT would have minimal or no resource impact. A possible increase in workload or the number of radiographers and healthcare professionals working in PET/CT was mentioned by 1 specialist. According to specialists, no facility or infrastructure changes are needed to implement the technology because it can be used by any established PET/CT department. Four commentators noted that product-specific training for healthcare professionals would be needed for them to be able to do the scans and interpret results. None of the commentators were aware of any safety concerns or regulatory issues surrounding the technology.

General comments

Most of the commentators noted that the technology was not widely or routinely used in across the NHS. Compared with standard PET/CT imaging, commentators identified no usability or practical issues with the technology. When used in a research setting, 1 of the commentators noted that Axumin was safe and easy to use. One commentator noted that a comparison with ^{11}C -choline is obsolete because this tracer has been replaced in most centres by ^{18}F -choline, which has a similar half-life to Axumin. Commentators confirmed that ^{18}F -, rather than ^{11}C -, choline PET/CT is considered the standard of care in the UK, and was said to be commissioned by the NHS for use in prostate cancer. The cost, NHS commissioning status and the lack of sufficient evidence to show superiority over existing choline and PSMA PET/CT tracers were identified by specialists as potential barriers to adoption for Axumin. One commentator felt that the relative diagnostic benefits of Axumin compared with PSMA are not compelling and if ^{18}F -labelled PSMA PET tracers become commercially available there may be less of a role for Axumin PET/CT in the management of prostate cancer. Data from a UK setting comparing the diagnostic accuracy and cost effectiveness of Axumin with that of PSMA and choline tracers were highlighted as future requirements by commentators. The need for data showing the long-term effects of the technology

on patient management and survival outcomes were also identified.

Patient organisation comments

A patient expert from Tackle Prostate Cancer commented that positron emission tomography (PET) scans are becoming more commonly used for detecting small, early, secondary tumours where prostate-specific antigen (PSA) levels are rising and no specific secondary tumours can be located with conventional imaging techniques (MRI/CT). As early detection is crucial to earlier treatment, they believe the technology could substantially change the treatment options for some patients by enabling the use of more targeted therapies, such as highly localised radiotherapy rather than systemic hormone therapy or radiotherapy with larger treatment fields. They thought that these changes could lead to improvements in physical, psychological and social wellbeing for patients. Tackle Prostate Cancer also commented that PET is not widely available throughout the UK, and this can lead to anxiety or distress for those patients who are unable to access the technology. They believed that if Axumin was proven to be as effective as other PET scan tracers with no additional adverse events, then it should be made available for use. They understood that it would only be available at specialist centres similar to other PET scan tracers for prostate cancer. If used as a primary investigation, Tackle Prostate Cancer believed that Axumin had the potential to reduce the time to diagnosis and remove the need for other scanning techniques that are currently used as first-line investigations after biochemical relapse. The cost of the tracer was listed by Tackle Prostate Cancer as a potential barrier to adoption in the UK. However, their patients would like all available and relevant techniques to be made available throughout the UK to appropriate people with prostate cancer. Tackle Prostate Cancer would be interested in seeing data evaluating the cost effectiveness of using Axumin as a first-line investigation instead of after a negative MRI or CT scan.

Specialist commentators

The following clinicians contributed to this briefing:

- Thomas Wagner, consultant in nuclear medicine, Royal Free London NHS Trust, did not declare any interests.

- Gary Cook, honorary consultant in nuclear medicine / professor of PET imaging, King's College London / Guy's & St Thomas' NHS Trust, was paid to provide a clinical assessment of ¹¹C-choline scans for a study sponsored by Blue Earth Diagnostics, provided consultancy services for NanoMab Technology Ltd, was an invited member of Prostate Cancer UK (PCUK) / NHS England Cancer Diagnostics Clinical Reference Group Joint meeting on new imaging methods for detecting disseminated disease (2018), contributed to Royal College of Radiologists / Royal College of Physicians guidelines on the clinical use of PET (2013 and 2016), his department was provided with a part-salary for a clinical research fellow by Thermognostics Ltd.
- Anwar R Padhani, professor of cancer imaging; consultant radiologist, lectured on Siemens Healthineers courses on the use of next generation imaging technologies for the assessment of advanced prostate cancer.
- Nagabhushan Seshadri, consultant in nuclear medicine, Royal Liverpool University Hospital, did not declare any interests.
- Roberto Alonzi, consultant in clinical oncology, Mount Vernon Cancer Centre, has taken part in the FALCON study evaluating the technology.
- Dr Radhakrishnan Jayan, consultant in radiology and nuclear medicine, Royal Liverpool University Hospital, did not declare any interests.

Representatives from the following patient organisations contributed to this briefing:

- Tackle Prostate Cancer

Development of this briefing

This briefing was developed by NICE. The [interim process and methods statement](#) sets out the process NICE uses to select topics, and how the briefings are developed, quality-assured and approved for publication.

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