

## Health Technology Briefing November 2021

### Nivolumab with docetaxel for advanced castration-resistant prostate cancer

Company/Developer

Bristol Myers Squibb

New Active Substance

Significant Licence Extension (SLE)

NIHRIO ID: 28409

NICE ID: 10433

UKPS ID: 656449

#### Licensing and Market Availability Plans

Currently in phase III clinical trials

#### Summary

Nivolumab in addition to docetaxel is in clinical development for the treatment of adult males with advanced, castration-resistant prostate cancer. Prostate cancer is a common cancer caused by the growth of a tumour on the prostate gland. Advanced prostate cancer is a form of prostate cancer where the tumours have spread to other areas of the body. Castration-resistant prostate cancer refers to tumours that are still able to grow despite the levels of testosterone in the body being very low. The aim of treatment for advanced prostate cancer is to control the progression of the cancer, relieve symptoms and maintain the patient's quality of life.

Nivolumab is a type of protein (monoclonal antibody) administered by intravenous (IV) infusion to increase the ability of the immune system to kill cancer cells. Docetaxel is currently used in the treatment of prostate cancer as standard-of-care. The addition of nivolumab to docetaxel has previously shown good clinical results and could offer improved treatment outcomes to these patients. If licensed, nivolumab in addition to docetaxel would provide a new treatment option for advanced castration-resistant prostate cancer patients.

### Proposed Indication

Treatment of adult males with advanced castration-resistant prostate cancer who are chemotherapy-naïve and have received 1 or 2 prior second generation hormonal therapies<sup>1</sup>

### Technology

#### Description

Nivolumab (Opdivo) is a human immunoglobulin G4 (IgG4) monoclonal antibody (HuMAb), which binds to the programmed death-1 (PD-1) receptor and blocks its interaction with PD-L1 and PD-L2. The PD-1 receptor is a negative regulator of T-cell activity that has been shown to be involved in the control of T-cell immune responses. Engagement of PD-1 with ligands PD-L1 and PD-L2, which are expressed in antigen presenting cells and may be expressed by tumours or other cells in the tumour microenvironment, results in inhibition of T-cell proliferation and cytokine secretion. Nivolumab potentiates T-cell responses, including anti-tumour responses, through blockade of PD-1 binding to PD-L1 and PD-L2 ligands.<sup>2</sup>

Nivolumab in addition to docetaxel is in clinical development for the treatment of adult males with advanced castration-resistant prostate cancer. In the phase III clinical trial (CheckMate 7DX, NCT04100018), participants will receive nivolumab in addition to docetaxel and prednisone, at an unspecified dose and schedule.<sup>1</sup>

#### Key Innovation

NICE currently recommend docetaxel as a monotherapy for the treatment of adult males with advanced castration-resistant prostate cancer. NICE do not currently recommend the use of any PD-1 inhibitors in the treatment of prostate cancer.<sup>3</sup> While the antitumour activity of PD-1 inhibition alone is limited in prostate cancer, combining nivolumab immunotherapy with the current standard of care docetaxel, may improve treatment outcomes for patients. This combination has shown clinical activity in the CheckMate 9KD (NCT03338790) clinical trial.<sup>4</sup>

If licensed, nivolumab in addition to docetaxel could provide an additional treatment option for adult male patients with advanced castration-resistant prostate cancer.

#### Regulatory & Development Status

Nivolumab in addition to docetaxel does not currently have a Marketing Authorisation in the UK for any indication.<sup>2</sup>

Nivolumab as a monotherapy or in combination with various other medicinal products has a Marketing Authorisation in the UK for the following indications:<sup>2</sup>

- Melanoma
- Non-small cell lung cancer (NSCLC)
- Malignant pleural mesothelioma (MPM)
- Renal cell carcinoma (RCC)
- Classical Hodgkin lymphoma (cHL)
- Squamous cell cancer of the head and neck (SCCHN)
- Urothelial carcinoma
- Colorectal cancer (CRC)
- Oesophageal squamous cell carcinoma (OSCC)
- Oesophageal or gastro-oesophageal junction cancer (OC or GEJC)

Nivolumab in addition to docetaxel and various other medicinal products is in phase III clinical development for NSCLC.<sup>5</sup> Nivolumab as a monotherapy and in addition to various other medicinal products is being developed for numerous cancer indications in phase II and phase III clinical trials.<sup>6</sup>

## Patient Group

### Disease Area and Clinical Need

Prostate cancer is a malignant tumour of the prostate gland. It is often slow growing and unlikely to cause pain, although some may be aggressive in growth. Symptoms of prostate cancer can include lower back or bone pain, lethargy, erectile dysfunction, haematuria, anorexia/weight loss and various lower urinary tract symptoms. 95% of prostate tumours are adenocarcinomas (cancers of glandular cells). The factors that can increase a person's risk of prostate cancer include increasing age, black ethnicity, a family history of prostate cancer and being overweight/obese.<sup>7</sup> Advanced prostate cancer is a form of prostate cancer where the cancer has spread to other areas of the body or to the bones. It may also be known as metastatic prostate cancer.<sup>8</sup> Castration-resistant prostate cancer refers to tumours that are still able to grow despite the levels of testosterone in the body being very low. Often, early stage tumours would require a normal level of testosterone to continue growth.<sup>9</sup>

There are approximately 42,500 men diagnosed with prostate cancer every year and at any one time, there may be around 346,000 men living with prostate cancer in England and Wales. There are also approximately 9,600 deaths from prostate cancer in England and Wales each year.<sup>10</sup> In England in 2020-21 there were 55,799 hospital admissions and 60,023 finished consultant episodes (FCE) for malignant neoplasm of prostate (ICD-10 C61).<sup>11</sup> Between 2013-17, around 87% of men diagnosed with prostate cancer will survive for five years following diagnosis.<sup>12</sup>

### Recommended Treatment Options

NICE recommend the following treatment options for advanced, castration-resistant prostate cancer:<sup>3,13</sup>

- Abiraterone in combination with prednisone or prednisolone in people who have no or mild symptoms after androgen deprivation therapy (ADT) has failed, and before chemotherapy is indicated
- Enzalutamide in people who have no or mild symptoms after ADT has failed and before chemotherapy is indicated
- A corticosteroid such as dexamethasone as third-line hormonal therapy after ADT and anti-androgen therapy
- Docetaxel chemotherapy to people with a Karnofsky performance-status score of 60% or more
- Cabazitaxel in combination with prednisone or prednisolone in people whose disease has progressed during or after docetaxel chemotherapy
- Enzalutamide in people whose disease has progressed during or after docetaxel-containing chemotherapy

## Clinical Trial Information

Trial

CheckMate7DX, [NCT04100018](#), [EudraCT2020-002030-36](#); CA209-7DX; A Phase 3, Randomised, Double-Blind Study of Nivolumab or Placebo in

	<p>Combination With Docetaxel, in Men With Metastatic Castration-resistant Prostate Cancer  <b>Phase III</b> - recruiting  <b>Location(s)</b>: 9 EU countries, UK, USA, Canada and other countries  <b>Primary completion date</b>: April 2023</p>
<b>Trial Design</b>	Randomised, parallel assignment, quadruple-blinded
<b>Population</b>	N=984 (planned); males aged 18 years and older; Subjects with histologically confirmed adenocarcinoma of the prostate without small cell features and with current evidence of metastatic disease
<b>Intervention(s)</b>	Nivolumab + prednisone + docetaxel at an unspecified dose and schedule
<b>Comparator(s)</b>	Placebo + prednisone + docetaxel at an unspecified dose and schedule
<b>Outcome(s)</b>	<p>Primary outcome measures:</p> <ul style="list-style-type: none"> <li>• Radiographic progressive free survival (rPFS) assessed by Blinded Independent Central Review (BICR) per Prostate Cancer Working Group (PCWG3) [Time Frame: From the date of randomisation to the first date of document progression or death due to any cause, whichever occurs first, approximately 25 months]</li> <li>• Overall survival (OS) [Time frame: From the date of randomisation to the date of death from any cause, approximately 38 months. For participants who are alive, their survival time will be censored at the last date that they were known to be alive]</li> </ul> <p>See trial record for a full list of other outcomes</p>
<b>Results (efficacy)</b>	-
<b>Results (safety)</b>	-

### Estimated Cost

Nivolumab is already marketed in the UK for various indications; a 100mg/10ml vial costs £1097.00, a 240mg/ml vial costs £2633.00 and a 40mg/ml vial costs £439.00.<sup>14</sup>

### Relevant Guidance

#### NICE Guidance

- NICE technology appraisal. Nivolumab in combination for treating hormone-relapsed metastatic prostate cancer before chemotherapy (GID-TA10490). Expected publication date TBC.
- NICE technology appraisal. Abiraterone for treating metastatic hormone-relapsed prostate cancer before chemotherapy is indicated (TA387). July 2016.
- NICE technology appraisal. Enzalutamide for treating metastatic hormone-relapsed prostate cancer before chemotherapy is indicated (TA377). January 2016.

- NICE technology appraisal. Docetaxel for the treatment of hormone-refractory metastatic prostate cancer (TA101). June 2006.
- NICE guideline. Prostate cancer: diagnosis and management (NG131). May 2019.
- NICE quality standard. Prostate cancer (QS91). May 2019.

#### NHS England (Policy/Commissioning) Guidance

- NHS England. 2013/14 NHS Standard Contract for Cancer: Specialised Kidney, Bladder and Prostate Cancer Services (Adult). B14/S/a.

#### Other Guidance

- Gonzalez Del Abla A, Mendez-Vidal MJ, Vazquez S, Castro E, Climent MA et al. SEOM clinical guidelines for the treatment of advanced prostate cancer (2020). May 2021.<sup>15</sup>
- Cornford P, van den Bergh RCN, Briers E, van den Broeck T, Cumberbatch MG et al. EAU-EANM-ESTRO-ESUR-SIOG Guidelines on Prostate Cancer. Part II -2020 Update: Treatment of Relapsing and Metastatic Prostate Cancer. February 2021.<sup>16</sup>
- European Association of Urology. Oncology Guidelines: Prostate Cancer. 2021.<sup>17</sup>
- ESMO Guidelines Committee. Prostate cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow up. June 2020.<sup>18</sup>

### Additional Information

### References

- 1 Clinicaltrials.gov. *A Study of Nivolumab or Placebo in Combination With Docetaxel in Men With Advanced Castration-resistant Prostate Cancer (CheckMate 7DX)*. Trial ID: NCT04100018. 2019. Status: Recruiting. Available from: <https://clinicaltrials.gov/ct2/show/NCT04100018> [Accessed 11 October 2021].
- 2 Electronic Medicines Compendium (emc). *OPDIVO 10mg/mL concentrate for solution for infusion*. 2021. Available from: <https://www.medicines.org.uk/emc/product/6888> [Accessed 11 October 2021].
- 3 National Institute for Health and Care Excellence. *NICE Pathways: Treating hormone-relapsed metastatic prostate cancer*. 2021. Available from: <https://pathways.nice.org.uk/pathways/prostate-cancer#path=view%3A/pathways/prostate-cancer/treating-hormone-relapsed-metastatic-prostate-cancer.xml&content=view-node%3Anodes-docetaxel> [Accessed 11 October 2021].
- 4 Fizazi K, Gonzalez Mella P, Castellano D, Minatta JN, Rezazadeh Kalebasty A, Shaffer D, et al. LBA52 - Efficacy and safety of nivolumab in combination with docetaxel in men with metastatic castration-resistant prostate cancer in CheckMate 9KD. *Annals of Oncology*. 2019 2019/10/01/;30:v885-v6. Available from: <https://doi.org/10.1093/annonc/mdz394.045>.
- 5 Clinicaltrials.gov. *Nivolumab AND docetaxel - Phase III clinical trials*. 2021. Available from: <https://clinicaltrials.gov/ct2/results?cond=&term=Nivolumab+AND+docetaxel&spons=Bristol+Myers+Squibb&cntry=&state=&city=&dist=&Search=Search&recrs=a&recrs=b&recrs=d&recrs=e&recrs=f&phase=2> [Accessed 12 October 2021].
- 6 clinicaltrials.gov. *Nivolumab - Phase 2 and 3 clinical trials*. 2021. Available from: <https://clinicaltrials.gov/ct2/results?cond=&term=Nivolumab&type=&rslt=&recrs=b&recrs=>

[a&recrs=f&recrs=d&recrs=e&age\\_v=&gndr=&intr=&titles=&outc=&spons=Bristol+Myers+Sq  
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[Accessed 12 October 2021].

- 7 National Institute for Health and Care Excellence. *NICE Clinical Knowledge Summary: Prostate cancer* Last Update Date: June 2021. Available from: <https://cks.nice.org.uk/topics/prostate-cancer/> [Accessed 12 October 2021].
- 8 Cancer Research UK. *What is advanced prostate cancer?* 2021. Available from: <https://www.cancerresearchuk.org/about-cancer/prostate-cancer/advanced-cancer/about-advanced-cancer> [Accessed 12 October 2021].
- 9 National Cancer Institute. *NCI Dictionaries: castrate-resistant prostate cancer*. 2021. Available from: <https://www.cancer.gov/publications/dictionaries/cancer-terms/def/castrate-resistant-prostate-cancer> [Accessed 12 October 2021].
- 10 Prostate Cancer UK. *About prostate cancer*. 2019. Available from: <https://prostatecanceruk.org/prostate-information/about-prostate-cancer> [Accessed 12 October 2021].
- 11 Digital N. *Hospital Admitted Patient Care Activity 2020-21*. Available from: <https://digital.nhs.uk/data-and-information/publications/statistical/hospital-admitted-patient-care-activity/2020-21> [Downloaded 13 October 2021].
- 12 Cancer Research UK. *Prostate cancer statistics*. 2021. Available from: <https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/prostate-cancer#heading-Three> [Accessed 12 October 2021].
- 13 National Institute for Health and Care Excellence. *Prostate cancer: diagnosis and management (NG131)*. Last Update Date: Available from: <https://www.nice.org.uk/guidance/ng131> [Accessed 12 October 2021].
- 14 National Institute for Health and Care Excellence. *BNF: Nivolumab: Medicinal forms*. 2021. Available from: <https://bnf.nice.org.uk/medicinal-forms/nivolumab.html> [Accessed 13 October 2021].
- 15 González Del Alba A, Méndez-Vidal MJ, Vazquez S, Castro E, Climent MA, Gallardo E, et al. SEOM clinical guidelines for the treatment of advanced prostate cancer (2020). *Clin Transl Oncol*. 2021 May;23(5):969-79. Available from: <https://doi.org/10.1007/s12094-021-02561-5>.
- 16 Cornford P, van den Bergh RCN, Briers E, Van den Broeck T, Cumberbatch MG, De Santis M, et al. EAU-EANM-ESTRO-ESUR-SIOG Guidelines on Prostate Cancer. Part II-2020 Update: Treatment of Relapsing and Metastatic Prostate Cancer. *Eur Urol*. 2021 Feb;79(2):263-82. Available from: <https://doi.org/10.1016/j.eururo.2020.09.046>.
- 17 European Association of Urology. *Oncology Guidelines: Prostate Cancer* Last Update Date: Available from: <https://uroweb.org/guideline/prostate-cancer/> [Accessed 13 October 2021].
- 18 Parker C, Castro E, Fizazi K, Heidenreich A, Ost P, Procopio G, et al. Prostate cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Annals of Oncology*. 2020;31(9):1119-34. Available from: <https://doi.org/10.1016/j.annonc.2020.06.011>.

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