Health Technology Briefing
November 2021

Atezolizumab for adjuvant treatment of squamous cell carcinoma of the head and neck

Company/Developer	Roche Products Ltd

☐ New Active Substance ☒ Significant Licence Extension (SLE)

NIHRIO ID: 23970	NICE ID: 10487	UKPS ID: 656161

Licensing and Market Availability Plans

Currently in phase III clinical trial.

Summary

Atezolizumab is in clinical development for the adjuvant treatment of high-risk locally advanced squamous cell carcinoma of the head and neck (SCCHN), for patients who have received definitive local therapy. SSCHN is the most common type of head and neck cancer and it develops from the mucosal epithelium in the oral cavity, pharynx and larynx. Symptoms differentiate depending on the region and aetiology of the tumour but includes pain and difficulty with chewing, breathing and speaking. After definitive local therapy, patients are monitored for local reoccurrence and distant metastases as locally advanced SCCHN is associated with a high risk for local recurrence and distant metastases. As of yet, there are no adjuvant treatments indicated for SSCHN.

Atezolizumab is administered via intravenous (IV) infusion. Atezolizumab is a type of protein called an antibody, which can bind to a protein called programmed death-ligand 1 (PD-L1) to prevent it from interacting with its target (PD-1). Thus, helping immune cells kill cancer cells and is used to treat many different types of cancer that express PD-L1. Atezolizumab is already approved for use in different types of cancers and has shown promising clinical benefit in SCCHN from earlier phase I studies. If licensed, atezolizumab will provide a novel adjuvant treatment option for SCCHN patient after definitive local therapy.

Proposed Indication

Adjuvant therapy of patients who have received definitive local therapy for high-risk locally advanced squamous cell carcinoma of the head and neck (SCCHN).[1]

Technology

Description

Atezolizumab is an Fc-engineered, humanised immunoglobulin G1 (IgG1) monoclonal antibody that directly binds to programmed death-ligand 1 (PD-L1) and provides a dual blockade of the PD-1 and B7.1 receptors, releasing PD-L1/PD-1 mediated inhibition of the immune response, including reactivating the antitumour immune response without inducing antibody-dependent cellular cytotoxicity. Atezolizumab spares the PD-L2/PD-1 interaction allowing PD-L2/PD-1 mediated inhibitory signals to persist.[2,3] PD-L1 may be expressed on tumour cells and/or tumour-infiltrating immune cells, and can contribute to the inhibition of the antitumour immune response in the tumour microenvironment. Binding of PD-L1 to the PD-1 and B7.1 receptors found on T-cells and antigen presenting cells suppresses cytotoxic T-cell activity, T-cell proliferation and cytokine production.[2]

Atezolizumab is in clinical development as an adjuvant treatment after definitive local therapy in patients with high-risk, locally advanced SCCHN.[1] In the clinical trial NCT03452137, patients will be administered 1200mg atezolizumab as an IV infusion on day 1 of each 21-day cycle for 16 cycles or 1 year (whichever occurs first).[1]

Key Innovation

Locally advanced SCCHN is associated with a high risk for local recurrence and distant metastases. Current treatment options include a combination of surgery, radiation therapy and chemotherapy to optimize the chances for long-term disease control and improved survival. As standard of care, patients are monitored after definitive local therapy for local recurrence and/or distant metastases. No effective systemic adjuvant treatment has been identified. Results from a phase I trial (NCT01375842) suggested that atezolizumab offers promising clinical benefit in SCCHN.[4,5]

Regulatory & Development Status

Atezolizumab is currently licensed (as monotherapy or in combination) for the following indications:[2]

- Locally advanced or metastatic urothelial carcinoma
- Locally advanced or metastatic non-small cell lung cancer
- Extensive stage small cell lung cancer
- Unresectable locally advance or metastatic triple negative breast cancer
- Advanced or unresectable hepatocellular carcinoma

Atezolizumab is currently in phase II and III development in combination, and as a monotherapy for several lines of treatment and cancers including NSCLC, bladder cancer, melanoma and cervical cancer.[6]

Patient Group

Disease Area and Clinical Need

Squamous cell carcinoma of the head and neck (SCCHN) develop from the mucosal epithelium in the oral cavity, pharynx and larynx and are the most common malignancies that arise in the head and neck. The burden of SCCHNs varies across countries/regions and has generally been correlated with exposure to tobacco-derived carcinogens, excessive alcohol consumption, or both. Increasingly, tumours that arise in

the oropharynx are linked to prior infection with oncogenic strains of human papillomavirus (HPV), primarily HPV-16, and, to a lesser extent, HPV-18 and other strains. The classic presenting symptoms of SCCHN depends on both the anatomical site of the primary tumour and the aetiology of the tumour but can include pain with chewing or dysarthria, dysphagia, odynophagia, otalgia and dyspnoea.[7]

Head and neck cancer is the 8th most common cancer in the UK, accounting for 3% of all new cancer cases. There are around 12,400 new head and neck cancer cases in the UK every year.[8] About 90% of head and neck cancers are squamous cell carcinomas. Applying this statistic to the Cancer Research UK (CRUK) statistic above, this would mean that approximately 11,160 people would be diagnosed with SSCHN in the UK annually.[8,9]

Recommended Treatment Options

NICE recommends the following treatment options for locally advanced SCCHN after local therapy:[10]

- Cetuximab in combination with radiotherapy is recommended as a treatment option only for patients with locally advanced SCCHN

NICE currently does not have any published guidance for the adjuvant treatment of high-risk SCCHN following definitive local therapy.

Clinical Trial Information

Trial	NCT03452137, 2017-003302-40; A Phase III, Multicenter, Randomized, Double-Blind, Placebo-Controlled Study of Atezolizumab (Anti-Pd-L1 Antibody) as Adjuvant Therapy After Definitive Local Therapy in Patients With High-Risk Locally Advanced Squamous Cell Carcinoma of the Head and Neck **Phase III** - Recruiting **Location(s):** 9 countries in EU, UK, USA, Canada and other countries **Primary completion date:** October 2022
Trial Design	Randomised, parallel assignment, quadruple-blinded
Population	N = 400; participants with SCCHN who have completed definitive local therapy; have an absence of metastatic disease; stable anticoagulant regimen for patients receiving therapeutic anticoagulation; confirmed response of Complete Response (CR), Partial Response (PR), or Stable Disease (SD) to definitive local therapy documented by CT with contrast or MRI with contract to head and neck region done >= 8 weeks after completion of definitive local therapy and within 28 days prior to initiation of study drug; 18 years and older.
Intervention(s)	Atezolizumab will be administered as an IV infusion at a fixed dose on day 1 of each 21-day cycle for 16 cycles or 1 year (whichever occurs first).
Comparator(s)	Matched placebo
Outcome(s)	• Investigator-assessed Event Free Survival (EFS): [Time frame: Randomization to the first documented disease recurrence, or disease progression (per Response Evaluation Criteria In Solid Tumors (RECIST v1.1)), or death from any cause, whichever occurs first, through the end of study (approximately 54 months)]

	• Overall Survival (OS) after randomization: [Time frame: Randomization to death from any cause, through the end of study (approximately 54 months)] See trial record for full list of other outcomes.
Results (efficacy)	-
Results (safety)	-

Estimated Cost

The list price of atezolizumab is £3807.69 per 1200mg/20mL concentrate for solution for infusion vial and £2,665.38 per 840mg/14ml concentrate for solution for infusion vial.[11]

Relevant Guidance

NICE Guidance

- NICE technology appraisal guidance. Cetuximab for the treatment of locally advanced squamous cell cancer of the head and neck (TA145). June 2008.
- NICE guideline. Cancer of the upper aerodigestive tract: assessment and management in people aged 16 and over (NG36). June 2018.
- NICE quality standard. Head and neck cancer (QS146). March 2017.

NHS England (Policy/Commissioning) Guidance

- NHS England. 2013/14 NHS Standard Contract for Cancer: Head and Neck (Adult). B16/S/a
- NHS England. 2013/14 NHS Standard Contract for Cancer: Chemotherapy (Adult). B15/S/a.
- NHS England. 2013/14 NHS Standard Contract for Cancer: Chemotherapy (Children, Teenagers and Young Adults). B12/S/b.
- NHS England. 2013/14 NHS Standard Contract for Cancer: Radiotherapy (All Ages). B01/S/a.

Other Guidance

- Spanish society of medical oncology (SEOM). SEOM clinical guidelines for the treatment of head and neck cancer. 2021.[12]
- European Society for medical oncology (ESMO). Squamous cell carcinoma of the oral cavity, larynx, oropharynx and hypopharynx: EHNS–ESMO–ESTRO Clinical Practice Guidelines for diagnosis, treatment and follow-up. 2020.[13]
- The Journal of Laryngology & Otology. Head and Neck Cancer: United Kingdom National Multidisciplinary Guidelines. May 2016.[14]

Additional Information

References

1 ClinicalTrials.gov. *A Study of Atezolizumab (Anti-Pd-L1 Antibody) as Adjuvant Therapy After Definitive Local Therapy in Patients With High-Risk Locally Advanced Squamous Cell Carcinoma of the Head and Neck. Trial ID: NCT03452137*. 2018. Available from: https://clinicaltrials.gov/ct2/show/NCT03452137 [Accessed 29th October 2021].

2 Electronic Medicines Compendium. *Tecentriq 1,200 mg concentrate for solution for infusion.* 2021. Available from: https://www.medicines.org.uk/emc/product/8442/smpc [Accessed 29th October 2021].

3 UK PharmaScan. *Technology Summary (656161)*. 2021. Available from: https://www.ukpharmascan.org.uk/HS/technology/656161 (login required). [Accessed 29th October 2021].

4 Wong DJ, Fayette J, Guo Y, Kowgier M, Cohen E, Nin RM, et al. Abstract CT123: IMvoke010: Randomized Phase III study of atezolizumab as adjuvant monotherapy after definitive therapy of squamous cell carcinoma of the head and neck (SCCHN). *Cancer Research*. 2019;79(13 Supplement):CT123. Available from: https://doi.org/10.1158/1538-7445.AM2019-CT123.

5 ClinicalTrials.gov. *A Study of Atezolizumab (an Engineered Anti-Programmed Death-Ligand 1 [PDL1] Antibody) to Evaluate Safety, Tolerability and Pharmacokinetics in Participants With Locally Advanced or Metastatic Solid Tumors. Trial ID: NCT01375842*. 2011. Available from: https://www.clinicaltrials.gov/ct2/show/NCT01375842 [Accessed 29th October 2021].

6 ClinicalTrials.gov. *Atezolizumab | Recruiting, Not yet recruiting, Active, not recruiting, Completed, Enrolling by invitation Studies | Phase 2, 3.* 2021. Available from: https://www.clinicaltrials.gov/ct2/results?term=Atezolizumab&recrs=b&recrs=a&recrs=f&recrs=d&recrs=e&age_v=&gndr=&type=&rslt=&phase=1&phase=2&Search=Apply [Accessed 4th November 2021].

7 Johnson DE, Burtness B, Leemans CR, Lui VWY, Bauman JE, Grandis JR. Head and neck squamous cell carcinoma. *Nature Reviews Disease Primers*. 2020 2020/11/26;6(1):92. Available from: https://doi.org/10.1038/s41572-020-00224-3.

8 Cancer Research UK. *Head and neck cancers statistics.* 2021. Available from: https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/head-and-neck-cancers#heading-Zero [Accessed 1st November 2021].

9 Macmillan Cancer Support. *The Rich Picture People with Cancer.* 2017. Available from: https://www.macmillan.org.uk/_images/head-neck-cancer_tcm9-282784.pdf [Accessed 1st November 2021].

10 National Institute of Clinical Excellence (NICE). *Treatment of upper aerodigestive tract cancer.* 2021. Available from: https://pathways.nice.org.uk/pathways/upper-aerodigestive-tract-cancer#path=view%3A/pathways/upper-aerodigestive-tract-cancer/treatment-of-upper-aerodigestive-tract-cancer.xml&content=view-node%3Anodes-drug-treatments-for-squamous-cell-carcinoma-of-the-head-and-neck [Accessed 2nd November 2021].

11 British National Formulary. *ATEZOLIZUMAB.* 2021. Available from: https://bnf.nice.org.uk/medicinal-forms/atezolizumab.html [Accessed 22nd November 2021].

12 Mesia R, Iglesias L, Lambea J, Martínez-Trufero J, Soria A, Taberna M, et al. SEOM clinical guidelines for the treatment of head and neck cancer (2020). *Clin Transl Oncol*. 2021 May;23(5):913-21. Available from: https://doi.org/10.1007/s12094-020-02533-1.

13 Machiels JP, René Leemans C, Golusinski W, Grau C, Licitra L, Gregoire V. Squamous cell carcinoma of the oral cavity, larynx, oropharynx and hypopharynx: EHNS–ESMO–ESTRO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Annals of Oncology.* 2020;31(11):1462-75. Available from: https://doi.org/10.1016/j.annonc.2020.07.011.

14 Roland VPaN. Head and Neck Cancer: United Kingdom National Multidisciplinary Guidelines *The Journal of Laryngology & Otology,*. 2016 May 2016;130(S2). Available from: https://www.cambridge.org/core/services/aop-file-manager/file/57fbbd73983d5b2b18ef2ac9/JLO-Head-and-Neck-Single-File.pdf.

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