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Health Technology Briefing
June 2025

Tiragolumab with bevacizumab and atezolizumab for previously untreated advanced hepatocellular carcinoma

Company/Developer	Roche Products Ltd.

☒ New Active Substance ☐ Significant Licence Extension (SLE)

NIHRIO ID: 37483	NICE ID: Not Available	UKPS ID: 673729

Licensing and Market Availability Plans

Currently in phase III clinical development.

Summary

Tiragolumab in combination with bevacizumab and atezolizumab is being developed as a first-line treatment for adults with an advanced stage of liver cancer called hepatocellular carcinoma (HCC). HCC is the most common type of primary liver cancer and often develops in people with liver cirrhosis. It is usually diagnosed at an advanced stage, when curative treatments are limited. Symptoms may include weight loss, tiredness, abdominal pain or swelling, yellowing of the skin or eyes (jaundice), and nausea. There is a need for more effective treatment options, particularly for patients who do not respond to currently available immunotherapies that target the PD-1/PD-L1 pathway (proteins which play a crucial role in regulating the immune system).

Tiragolumab is a type of immunotherapy known as a monoclonal antibody that is given by intravenous (into the vein) infusion every three weeks. It works by blocking a protein called TIGIT, which helps cancer cells avoid being attacked by the immune system. By stopping TIGIT from binding to its target, tiragolumab may help restore the immune system's ability to fight the cancer. This new approach may enhance the effectiveness of existing immunotherapies like atezolizumab in combination with bevacizumab, especially in patients who previously did not benefit from them. If approved, tiragolumab in combination with atezolizumab and bevacizumab could offer a new first-line treatment option for people with advanced HCC.

Proposed Indication

This briefing reflects the evidence available at the time of writing and a limited literature search. It is not intended to be a definitive statement on the safety, efficacy or effectiveness of the health technology covered and should not be used for commercial purposes or commissioning without additional information. A version of the briefing was sent to the company for a factual accuracy check. The company was available to comment.

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Treatment of untreated locally advanced or metastatic hepatocellular carcinoma (HCC).[1]

Technology

Description

Tiragolumab (RG-6058, MTIG7192A) is a fully human monoclonal antibody IgG1/kappa with an intact fragment crystallisable Fc region targeting T-cell immunoreceptor with Ig and immunoreceptor tyrosine based inhibitory motif (TIGIT) which is expressed on natural killer cells and T cells. TIGIT strongly correlates with PD-1 and inhibits immune cell activity by binding to the receptor/poliovirus receptor ligand on tumour and antigen-presenting cells.[2,3] This can lead to suppression of T-cell proliferation and activation which can allow tumour cell evasion from the immune system.[2] Tiragolumab can prevent TIGIT from binding to its ligand, and therefore restore the antitumor response and could complement the activity of anti–PD-L1/PD-1 antibodies.[2]

Tiragolumab in combination with bevacizumab and atezolizumab is currently in phase III clinical development for patients with unresectable, locally advanced or metastatic HCC. In a phase III clinical trial (NCT05904886), tiragolumab is administered intravenously at a fixed dose of 600 mg on day 1 of each 21-day cycle.[1]

Key Innovation

There is an unmet need for effective immunotherapy options for patients with unresectable, locally advanced or metastatic HCC, particularly for those who do not respond to current checkpoint inhibitors. Existing therapies targeting the PD-1/PD-L1 axis have limited efficacy in a significant subset of patients, highlighting a need for novel immunomodulatory strategies.[4,5] Myeloid and T regulatory cells are key immunosuppressive cell types within the hepatic tumour microenvironment associated with clinical resistance to atezolizumab and bevacizumab therapy for HCC and overall poor prognosis. Therapeutic targeting of TIGIT with tiragolumab, which is highly expressed in these cells, may overcome the immunosuppressive environment and improve clinical benefit, a hypothesis supported by positive efficacy signals in the Phase Ib/II MORPHEUS-Liver study.[6] In addition, preclinical data suggested that anti-TIGIT plus anti–PD-L1 agents synergistically improve tumour control and prolong survival compared with either antibody alone.[2]

If licensed, tiragolumab in combination with bevacizumab and atezolizumab could provide an additional treatment option for patients with unresectable locally advanced or metastatic HCC.

Regulatory & Development Status

Tiragolumab does not currently have marketing authorisation in the EU/UK for any indication.

Atezolizumab has EU/UK authorisation as a monotherapy for the following indications:[7]

- Urothelial carcinoma
- Advanced NSCLC
- Early-stage non-small cell lung cancer (NSCLC)

Atezolizumab is currently marketed in the EU/UK in combination with other technologies for the following indications:[7]

- Advanced NSCLC
- Small cell lung cancer
- Triple negative breast cancer

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- HCC

Bevacizumab is currently marketed in the EU/UK in combination with other technologies for the following indications:[8]

- Metastatic carcinoma of the colon or rectum
- Metastatic breast cancer
- Metastatic or recurrent NSCLC
- Metastatic or recurrent non-squamous NSCLC
- Metastatic renal cell cancer
- Advanced epithelial ovarian, fallopian tube, or primary peritoneal cancer
- Platinum-sensitive epithelial ovarian, fallopian tube or primary peritoneal cancer
- Platinum-resistant epithelial ovarian, fallopian tube or primary peritoneal cancer
- Metastatic cervical cancer
- Hepatocellular carcinoma[7]

Tiragolumab is also in phase II and/or III clinical development in combination with other technologies for, but not limited to, the following indications:[9]

- Oesophageal squamous cell carcinoma
- NSCLC
- Solid tumours
- Cervical cancer
- Small cell lung carcinoma
- Squamous cell carcinoma of the head and neck

Patient Group

Disease Area and Clinical Need

HCC is the most common type of primary liver cancer.[10] It develops from the main liver cells known as hepatocytes. The major risk factor for HCC is liver cirrhosis, which is scarring of the liver due to previous damage, although not all patients will have cirrhosis prior to developing HCC.[11,12] Other risk factors include smoking, obesity, hepatitis B or C and non-alcoholic fatty liver disease.[11] In the UK, around 1 in 10 cases are caused by drinking alcohol.[13] There is also evidence that the incidence and mortality of HCC are increasing and disproportionally affecting marginalised groups.[14] Symptoms of liver cancer often do not appear until the cancer is at an advanced stage, with the majority of patients (80%) not diagnosed until an advanced stage of the HCC when it is usually not amenable to surgery (i.e. unresectable). Symptoms include, unintentional weight loss, loss of appetite, feeling nauseous, pain or swelling in the abdomen, jaundice, itchy skin and feeling very tired or weak.[10]

Approximately 3,600 people are diagnosed with HCC each year in the UK. While HCC is the third most common cancer worldwide, it remains relatively rare in the UK. Approximately 1 in 10 (8.0%) people diagnosed with liver cancer in England survive their disease for ten years or more. Additionally, liver cancer five-year survival in England is higher in males than females. Around a third (34.3%) of people in England diagnosed with liver cancer aged 15-44 survive their disease for five years or more, compared with around 5 in 100 (6.0%) people diagnosed aged 75-99.[15] In England in 2023-2024, there were 11,151 finished consultant episodes (FCE) and 7,961 finished admission episodes (FAEs) for malignant neoplasm of liver and intrahepatic bile ducts (ICD-10 code C22.0) which resulted in 23,366 FCE bed days and 3,871 day cases.[16]

Recommended Treatment Options

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NICE recommends the following treatment options as first-line for patients with advanced HCC:[17-19]

- Lenvatinib
- Sorafenib
- Atezolizumab with bevacizumab

Clinical Trial Information

Trial	**SKYSCRAPER-14;** NCT05904886, 2023-503422-39-00; A Phase III, randomized, double-blind, placebo-controlled study evaluating atezolizumab and bevacizumab, with or without tiragolumab, in patients with untreated locally advanced or metastatic hepatocellular carcinoma **Phase III** – Active, not recruiting **Location(s):** USA, UK, 6 EU countries and other countries **Primary completion date:** September 2026
Trial Design	Randomised, parallel assignment, quadruple-blind
Population	N=650 (estimated); subjects with untreated locally advanced or metastatic HCC; aged 18 years and older.
Intervention(s)	Intravenous (IV) atezolizumab (1200 mg) + IV bevacizumab (15 mg/kg) + IV tiragolumab (600 mg) on day 1 of each 21-day cycle. Administered every 3 weeks until unacceptable toxicity or loss of clinical benefit as determined by the investigator.
Comparator(s)	Intravenous (IV) atezolizumab (1200 mg) + IV bevacizumab (15 mg/kg) + placebo Administered every 3 weeks until unacceptable toxicity or loss of clinical benefit as determined by the investigator.
Outcome(s)	Primary outcome measures: • Investigator-assessed progression-free survival (PFS) according to response evaluation criteria in solid tumours (RECIST) v1.1 from randomisation to the first occurrence of disease progression or death from any cause, whichever occurs first (up to approximately 36 months). • Overall survival from randomization to death from any cause (up to approximately 36 months). See trial record for full list of all outcomes.
Results (efficacy)	-
Results (safety)	-

Estimated Cost

The cost of tiragolumab is not yet known.

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The NHS indicative price of 1 vial of atezolizumab is:[20]

- for 1200mg/20ml concentrate for solution for infusion vials £3,807.69
- for 840mg/14ml concentrate for solution for infusion vials £2,665.38.

The NHS indicative price of 1 vial of bevacizumab is:[21]

- for 100mg/4ml solution for infusion vials is £242.66.
- for 400mg/16ml solution for infusion vials is £924.40.

Relevant Guidance

NICE Guidance

- NICE technology appraisal in development. Durvalumab with bevacizumab and transarterial chemoembolisation for treating locally advanced hepatocellular carcinoma (ID3944). Expected publication date to be confirmed.
- NICE technology appraisal in development. Durvalumab with tremelimumab for untreated unresectable hepatocellular carcinoma (ID2725). Expected June 2025.
- NICE technology appraisal guidance. Atezolizumab with bevacizumab for treating advanced or unresectable hepatocellular carcinoma (TA666). December 2020.
- NICE technology appraisal guidance. Lenvatinib for untreated advanced hepatocellular carcinoma (TA551). December 2018.
- NICE technology appraisal guidance. Sorafenib for treating advanced hepatocellular carcinoma (TA474). September 2017.

NHS England (Policy/Commissioning) Guidance

- NHS Wales. 2021 NHS Standard Contract for Hepatobiliary and pancreas (adult). A02/S/a.
- NHS England. Clinical Commissioning Policy: Stereotactic ablative radiotherapy (SABR) for hepatocellular carcinoma (adults) (URN: 1913) [200206P]. March 2020.
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- NHS England. 2013/14 NHS Standard Contract for Hepatobiliary and pancreas (adult). A02/S/a.
- NHS England. 2013/14 NHS Standard Contract for Cancer: Radiotherapy (All Ages). B01/S/a.
- NHS England. 2013/14 NHS Standard Contract for Cancer: Chemotherapy (Adult). B15/S/a.

Other Guidance

- The European Society of Medical Oncology (ESMO). Hepatocellular carcinoma: ESMO Clinical Practice Guideline for diagnosis, treatment and follow-up. 2025.[22]
- The American Association for the Study of Liver Diseases (AASLD). Critical Update: AASLD Practice Guidance on prevention, diagnosis, and treatment of hepatocellular carcinoma. 2025.[23]
- British Society of Gastroenterology. British Society of Gastroenterology Best Practice Guidance: outpatient management of cirrhosis – part 3: special circumstances. 2023.[24]
- Barcelona Clinic Liver Cancer (BCLC) staging and treatment strategy in 2022[25]
- The European Association for the Study of the Liver (EASL). EASL Clinical Practice Guidelines: Management of hepatocellular carcinoma. 2018.[26]

Additional Information

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