Health Technology Briefing
June 2024

Vimseltinib for treating Tenosynovial Giant Cell Tumour

Company/Developer	Deciphera Pharmaceuticals LLC

☒ New Active Substance ☐ Significant Licence Extension (SLE)

NIHRIO ID: 13781	NICE ID: Not Available	UKPS ID: Not Available

Licensing and Market Availability Plans

In phase III clinical development.

Summary

Vimseltinib is in development to treat tenosynovial giant cell tumour (TGCT) in adults. TGCTs are rare but non-cancerous tumours that develop in tissues around joints. TGCTs can be diffuse, meaning the tumour affects most of a large joint (e.g., knee), or localised, meaning the tumour is limited to a specific area of the joint (normally smaller joints such as toes). Symptoms may vary depending on the location of the TGCT but commonly include pain, swelling, and limited movement in affected joints. Surgery is often the primary treatment, but sometimes the tumours can come back, especially in larger joints like the knees. If not treated properly, they can lead to joint damage and the joint may require amputation. Patients who aren't eligible for surgery currently have no treatment options.

Vimseltinib is an oral drug that targets a specific protein involved in tumour growth called colony-stimulating factor 1 receptor (CSF1R). By binding to this protein, vimseltinib is believed to prevent the growth of the tumour. Vimseltinib is highly selective for CSF1R which limits the side effects of the drug. If licensed, vimseltinib could provide the first treatment option for patients with TGCT, where surgery is not an option.

Proposed Indication

Treatment of adults with tenosynovial giant cell tumour (TGCTs) where surgical removal of the tumour is not an option.[1]

Technology

Description

Vimseltinib (DCC-3014) is a potent and highly selective switch-control kinase inhibitor of colony-stimulating factor 1 receptor (CSF1R), whereby it binds to the switch-pocket region.[2,3] In TGCT the CSF1 gene is aberrantly expressed, with high levels of this driving the expansion of the tumour mass.[4] Vimseltinib binding to CSF1R receptors reduces the effect of CSF1, reducing tumour growth and symptoms of the disease.[5,6]

Vimseltinib is in clinical development for the treatment of TGCT in adult patients where surgical removal of the tumour is not an option. In the phase III clinical trial (MOTION, NCT05059262) participants are orally administered 30 mg of vimseltinib twice a week for 24 weeks, in part one, followed by 30 mg twice a week in part 2, which is the long term, open label treatment phase.[1]

Key Innovation

Vimseltinib's unique switch-control design provides high selectivity for CSF1R, meaning that it has minimal effect on closely related kinases such as KIT (receptor tyrosine kinase), PDGFRA (platelet derived growth factor receptor alpha), PDGFRB (platelet derived growth factor receptor beta) and FLT3 (FMS-like tyrosine kinase 3). In a preclinical study, vimseltinib was >500-fold more selective for CSF1R than KIT, PDGFRA, PDGFRB and FLT3.[3] Binding to these closely related kinases can limit CSF1R suppression due to off-target activity and the associated adverse events such as hair colour changes.[3,7]

Currently, surgery is the main treatment option for patients with TGCT, but these tumours frequently reoccur which can result in damage and degeneration in the affected joint and surrounding tissues, which can cause significant disability.[2] For patients not amenable to resection there are currently no NICE recommended treatment options for TGCT. If licenced vimseltinib will provide the first treatment option for patients with unresectable TGCT.

Regulatory & Development Status

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

Vimseltinib is not in phase II or III clinical development for any other indication.

Vimseltinib has been designated an orphan drug in the European Union in 2019 for the treatment of TGCT.[5]

Patient Group

Disease Area and Clinical Need

TGCTs are a group of rare, benign tumours that involve the synovium, bursae, and tendon sheath. Synovium is the thin layer of tissue or membrane that covers the inner surface of the joint spaces and the bursae and tendon sheaths. These tumours cause the affected synovium, bursae or tendon sheaths to thicken and overgrow. Symptoms can include pain, swelling, tenderness and limitation of movement of the joint. In localised TGCT, smaller joints tend to be affected, such as digits and parts of the foot. In diffuse TGCT, large joints tend to be involved, most commonly the knee. Recurrence is common particularly in diffuse TGCT which was previously known as pigmented villonodular synovitis. If untreated or if the tumour continually recurs, they can result in damage and degeneration of the affected joint and surrounding tissues or

structures. Sometimes, they can cause significant disability and in rare cases, amputation is warranted. TGCT is believed to arise due to a randomly occurring chromosomal abnormality within some of the cells in the TGCT tumour but there are no environmental, genetic, occupational, lifestyle, demographic or regional risk factors that have been conclusively shown to be involved with the development of these tumours. TGCT mainly affect individuals between 25-50 years of age.[8]

Based on a 2017 Dutch study, the global incidence has been estimated to be 43 cases of TGCT per one million people in the general population (comprising 39 cases of localised TGCT and four cases per million for diffuse TGCT respectively).[8] In England in 2022-2023, there were 320 finished consultant episodes (FCE) for TGCT (ICD-10 code: M12.2), with 318 hospital admissions resulting in 209 FCE bed days and 205 day cases.[9]

Recommended Treatment Options
There are currently no NICE recommended treatments for TGCT.

Clinical Trial Information

Trial	**MOTION; NCT05059262; EudraCT-2020-004883-25** ; A Phase 3, Randomized, Placebo-controlled, Double-blind Study of Vimseltinib to Assess the Efficacy and Safety in Patients With Tenosynovial Giant Cell Tumour **Phase III –** Active, not recruiting. **Location(s)**: 7 EU countries, USA, UK, Canada and other countries **Primary completion date:** August 2023
Trial Design	Randomised, parallel assignment, quadruple blinded, placebo-controlled
Population	N=120; Subjects with TGCT in which surgery is not an option; adults aged 18 years and over
Intervention(s)	Vimseltinib 30 mg oral tablets two times a week
Comparator(s)	Matched placebo
Outcome(s)	Primary outcome measure: - Objective Response Rate (ORR= complete response + partial response), assessed by central read using Response Evaluation Criteria in Solid Tumours (RECIST) Version 1.1 See trial record for full list of other outcomes.
Results (efficacy)	The study met its primary endpoint in the intent-to-treat (ITT) population demonstrating statistically significant and clinically meaningful improvement versus placebo in ORR at week 25 based on independent radiologic review per RECIST v1.1. In the ITT population, the ORR at week 25 was 40% (95% CI: 29%, 51%) for the vimseltinib arm and 0% (95% CI: 0%, 9%) for the placebo arm resulting in a response difference (vimseltinib versus placebo) of 40% (95% CI: 29%, 51%) ($p<0.0001$). In addition to meeting the primary endpoint, the study also achieved statistically significant and clinically meaningful improvements versus placebo in all key secondary endpoints assessed at week 25 including ORR per tumour volume score, active range of motion, physical function, stiffness, quality of life, and pain.

	In the ITT population, the ORR at week 25 based on independent radiologic review per tumour volume score was 67% (95% CI: 56%, 77%) for the vimseltinib arm and 0% (95% CI: 0%, 9%) for the placebo arm (p<0.0001). Treatment with vimseltinib also demonstrated an improvement in mean change from baseline in active range of motion at week 25 of 18.4% versus a 3.8% improvement for placebo (p=0.0077).[10]
Results (safety)	Vimseltinib was well-tolerated and the safety profile in the MOTION study was consistent with previously disclosed data. There was no evidence of cholestatic hepatotoxicity in patients treated with vimseltinib. Patients with treatment-emergent adverse events leading to treatment discontinuation was 6% in the vimseltinib arm.[10]

Estimated Cost

The cost of vimseltinib is not yet known.

Relevant Guidance

NICE Guidance

No relevant guidance identified.

NHS England (Policy/Commissioning) Guidance

No relevant guidance identified.

Other Guidance

- Multidisciplinary sarcoma experts in collaboration with patient representatives from the Sarcoma Patient Advocacy Global Network (SPAGN). Best clinical management of tenosynovial giant cell tumour (TGCT): A consensus paper from the community of experts. 2022.[11]
- Healey et al., Management of Tenosynovial Giant Cell Tumor: A Neoplastic and Inflammatory Disease. 2020.[12]

Additional Information

No information was received from Deciphera. Deciphera Pharmaceuticals LLC did not enter information about this technology onto the UK PharmaScan database; the primary source of information for UK horizon scanning organisations on new medicines in development. As a result, the NIHR Innovation Observatory has had to obtain data from other sources. UK PharmaScan is an essential tool to support effective NHS forward planning; allowing more effective decision making and faster uptake of innovative new medicines for patients who could benefit. We urge pharmaceutical companies to use UK PharmaScan so that we can be assured of up-to-date, accurate and comprehensive information on new medicines.

References

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NB: This briefing presents independent research funded by the National Institute for Health and Care Research (NIHR). The views expressed are those of the author and not necessarily those of the NHS, the NIHR or the Department of Health.