MADRID 2026 ESMO congress

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Primary analysis of TANGENT: A phase 3 randomised trial evaluating the safety and efficacy of emactuzumab in patients with tenosynovial giant cell tumours

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Background

Tenosynovial giant cell tumours (TGCTs) are rare, chronic inflammatory and locally aggressive mesenchymal tumours, often debilitating and resulting in decreased function and range of motion (ROM), pain, stiffness, and joint degeneration. Treatments include surgery or oral colony-stimulating factor 1 receptor (CSF-1R) inhibitors, and tyrosine kinase inhibitors require chronic administration. Emactuzumab (EMAC) is a novel, intravenous monoclonal antibody in development that inhibits CSF-1R and requires only short-course therapy for TGCT. We present the primary analysis of the phase 3 TANGENT trial.

Methods

TANGENT (NCT05417789) is a randomised, double-blind, global, placebo-controlled, phase 3 trial evaluating the efficacy and safety of EMAC in TGCT. Pts were randomised 2:1 to 1000 mg of EMAC or placebo (PBO) every 2 weeks (wk), for 5 doses. The primary objective was to estimate the treatment effect of EMAC by overall response rate (ORR) at 6 months (mo). The primary endpoint was ORR by RECIST v1.1 and an associated key secondary endpoint was ORR by tumour volume score (TVS). Key secondary functional endpoints at 6 mo included changes from baseline in PROMIS-PF TGCT, passive ROM, Worst Pain, Worst Stiffness, and EQ-5D-5L VAS.

Results

136 pts were treated (EMAC n=91; PBO n=45). Primary and key secondary endpoints were highly statistically significant vs PBO (Table). Safety was consistent with phase 1 data and CSF-1R inhibitors.Table: LBA89

TANGENT primary and key secondary endpoints

Endpoint	Responders PBO	EMAC	Difference (95% CI; *P* value)
ORR RECIST v1.1	2.2%	29.7%	27.8 (16.2, 38.5; *P*<0.001)
ORR TVS	6.7%	53.8%	47.8 (33.7, 59.4; *P*<0.001)
	LS mean change from baseline PBO	Difference (95% CI; *P* value)	EMAC
PROMIS-PF	-1.3	4.3	5.6 (3.3, 7.9; *P*<0.001)
Passive ROM	2.12	9.93	7.81 (3.17, 12.45; *P*<0.001)
Worst stiffness	-0.3	-2.4	-2.1 (-3.0, -1.3; *P*<0.001)
Worst pain	-0.4	-2.5	-2.2 (-3.0, -1.4; *P*<0.001)
EQ-5D-5L VAS	-0.4	2.0	2.4 (-4.2, 9.1; *P*=0.238)

Conclusions

EMAC, the only short-course treatment in development for TGCT (5 infusions over 8 wks), demonstrated robust evidence of efficacy, radiographically and functionally, and manageable safety in pts with TGCT. EMAC may offer a potent treatment alternative for TGCT.

Clinical trial identification

NCT05417789.

Editorial acknowledgement

Medical editorial support was provided by Laura Rolfs, PhD of AOIC, LLC and was funded by SynOx Therapeutics Ltd.

Legal entity responsible for the study

SynOx Therapeutics Ltd.

Funding

SynOx Therapeutics Ltd.

Disclosure

H. Gelderblom: Financial Interests, Institutional, Local PI: Deciphera, Servier, Inhibrx Biosciences; Financial Interests, Institutional, Coordinating PI: Abbisko, Merck; Other, Other, Member Advies Commissie Pakket: Zorginstituut Nederland. E. Palmerini: Financial Interests, Institutional, Advisory Board: Daiichi Sankyo, Deciphera, EUSA Pharmaceuticals, SynOx, Ipsen, EMD Serono. M. van de Sande: Financial Interests, Institutional, Research Grant: Daiichi Sankyo, Implantcast, CarboFix; Financial Interests, Institutional, Advisory Board: Daiichi Sankyo, Implantcast, AmMax Bioio, Merck, Deciphera, Synox. J. Martin-Broto: Financial Interests, Personal, Advisory Board, Honoraria: PharmaMar, Bayer, Roche, Boehringer Ingelheim, Amgen; Financial Interests, Personal, Invited Speaker: PharmaMar; Financial Interests, Personal, Advisory Board, Speaker: Tecnofarma, Asofarma; Financial Interests, Personal, Advisory Board: Cogent Biosciences, GSK, Deciphera; Financial Interests, Personal, Other, Profits: Sarcoma Research Solutions SL; Financial Interests, Institutional, Coordinating PI: PharmaMar, Eisai, Novartis, Lixte, Karyopharm, Bayer, Pfizer, BMS, Lilly, Synox Therapeutics, ADC Therapeutics, Immunome.; Financial Interests, Institutional, Local PI: Blueprint, Deciphera, Amgen, Daiichi Sankyo, Adaptimmune, GSK, Ran Therapeutics, INHIBRX, Ayala Pharmaceuticals, Philogen, Cebiotex, PTC Therapeutics, Inc. and SpringWorks therapeutics, Boehringer Ingelheim, Abbisko, Biosplice; Non-Financial Interests, Leadership Role: Asociación Europea y Latinoamericana SELNET para la Investigación en Sarcomas. G. Tinoco: Financial Interests, Institutional, Advisory Board: Merck , Synox, Deciphera, Servier. S. Stacchiotti: Financial Interests, Personal, Advisory Board: Bayer, Daiichi Sankyo, Ikena, Pharma Essentia, Ipsen, GSK, Merck Serono, Parabilis, Deciphera, Orion, Agenus, Nec Immunoncology, Sun Pharmaceuticals; Financial Interests, Personal, Other, Travel Coverage to scientific conference: PharmaMar; Financial Interests, Personal, Advisory Board, Advisory board meetings: Boehringer; Financial Interests, Personal, Invited Speaker, Lectures: Gentili; Financial Interests, Personal, Advisory Board, Advisory board: Servier; Financial Interests, Personal, Invited Speaker: PeerView Institute; Financial Interests, Institutional, Local PI: Advenchen, Deciphera, Epizyme, Daiichi Sankyo, GSK, PharmaMar, SpringWorks, Inhibrix, Inhbrix; Financial Interests, Institutional, Coordinating PI: Bayer, Servier; Financial Interests, Institutional, Funding: Blueprint, Novartis; Financial Interests, Institutional, Other, Co-investigator in clinical study: Boehringer; Non-Financial Interests, Leadership Role, Past President: Connective Tissue Oncology Society; Non-Financial Interests, Advisory Role: Chordoma Foundation, Epithelioid Haemangiondothelioma Foundation, Desmoid Foundation, Epithelioid Hemangioendothelioma (EHE) Rare Cancer Charity (UK); Non-Financial Interests, Other, Vice Chair: EORTC soft tissue and bone sarcoma group; Non-Financial Interests, Leadership Role, President: Italian Sarcoma Group. H. Richardson: Financial Interests, Personal, Other, consultant: Synox Therapeutics. G. Layton: Financial Interests, Personal, Advisory Board, consultant: Synox Therapeutics. E. Seltzer: Financial Interests, Personal, Other, employee: Synox Therapeutics. M. Davies: Financial Interests, Personal, Other, employee: Synox Therapeutics. R. Coll: Financial Interests, Personal, Other, employee: Synox Therapeutics. J. Blay: Financial Interests, Institutional, Invited Speaker: MSD, MSD, PharmaMar; Financial Interests, Institutional, Advisory Board: Bayer, GSK, Roche, Daiichi Sankyo; Financial Interests, Personal, Advisory Board: Deciphera; Financial Interests, Institutional, Writing Engagement, coordination of book on rare cancers: PharmaMar; Financial Interests, Personal, Other, member of the supervisory board. No remunerations in 2021 and 2022.: Innate pharma; Financial Interests, Personal, Member of Board of Directors: Transgene; Financial Interests, Institutional, Funding: MSD, BMS, Deciphera; Financial Interests, Institutional, Research Grant: AstraZeneca, Roche, Bayer, GSK, Novartis, OSE pharma; Financial Interests, Coordinating PI, Coordinating PI for a RCT: SYNOX; Financial Interests, Institutional, Other, Support with drugs and research grant for a basket study: Daiichi Sankyo.

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