FIRST-IN-HUMAN TRIAL OF THE TEAD INHIBITOR ODM-212 (TEADES) IN EPITHELIOID HEMANGIOENDOTHELIOMA (EHE)

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BACKGROUND

- The **Hippo pathway** is implicated in multiple human cancers including mesothelioma and epithelioid hemangioendothelioma (EHE).[1-3]
- When Hippo signalling is inactive, Yes-associated protein 1 (**YAP1**) and WW-domain-containing transcription regulator 1 (**TAZ**) locate to the nucleus, activating TEA domain family member (TEAD) transcription factors (**TEAD1-4**) to impact transcription and key oncogenic cellular processes.[1-3]
- **ODM-212 is a small molecule oral pan-TEAD inhibitor** with antitumour activity in vitro and in vivo in solid tumours.
- **Top-line-results on Phase I were presented in ASCO 2026, and ODM-212 was well tolerated, no dose limiting toxicities (DLTs)** were observed in dose escalation phase, maximal tolerated dose **(MTD) was not reached**.[4]

STUDY DESIGN

- TEADES is a Phase I/II multi-site, open-label, first-in-human trial with two parts (dose escalation and dose expansion) with ODM-212 (NCT06725758).
- Phase I of the study enrolled subjects ≥18 years of age with various types of advanced or metastatic solid tumours known to harbour mutations affecting or interacting with the Hippo pathway, or where Hippo pathway has been indicated to be involved in tumour growth, such as mesothelioma and EHE.
- The primary objectives for Phase I were safety, tolerability and PK, and for Phase II to define the optimal dose for further clinical development.
- The patients were in need for systemic therapy for their cancer, and had exhausted all approved treatment options per inclusion criteria.
- In the latter part of the trial, ECOG 0-2 was allowed for EHE patients for inclusion of serosal patients.

Table 1. Patient characteristics

Patient characteristic	EHE patients (N=43)	All Subjects (N=203)
Mean age, years (range)	53.6 (25-76)	61.4 (18-87)
Race, n (%)		
White / Not reported	24 (55.8) / 14 (32.6)	146 (71.9) / 41 (20.2)
Black or African American	3 (7.0)	3 (1.5)
Other / Asian	1 (2.3) / 1 (2.3)	3 (1.5) / 10 (4.9)
ECOG PS, n (%)		
0 / 1 / 2	28 (65.1) / 15 (34.9) / 0	82 (40.4) / 121 (59.6) / 0

Table 2. Previous treatments in EHE

Most common previous treatments for EHE Patients (%)	Part 1 (N=19)	Part 2 (N=24)
Any previous cancer treatment	68.4	41.7
mTOR inhibitors	21.1	25.0
Sirolimus	21.1	20.8
Everolimus	0	8.3
Other protein kinase inhibitors	42.1	20.8
Pazopanib	36.8	20.8
Sunitinib	15.3	0
Anthracyclines and related substances	15.8	0

Fig. 1. Study design for Phase I/II trial TEADES

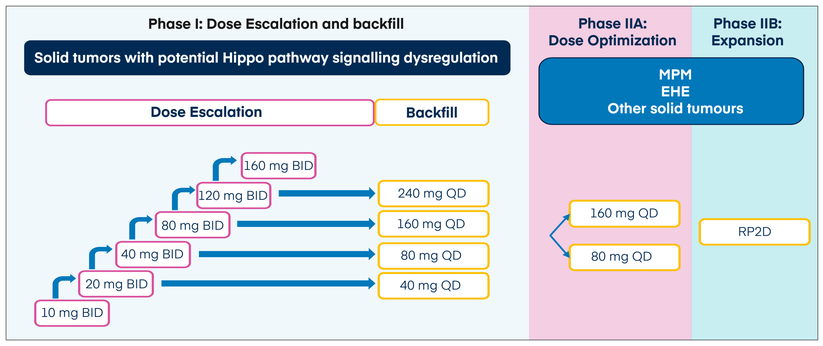
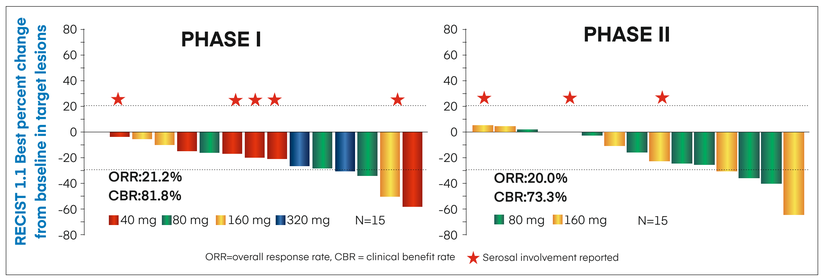


Fig. 2 Tumour reductions with ODM-212 observed in EHE across Phase I and early Phase II



ORR = (CR + PR), CBR = best response of CR and/or PR and/or at least 8 weeks of SD by RECIST v. 1.1

Fig. 3 Durability of response observed in Phase I, with most patients ongoing in Phase I and II

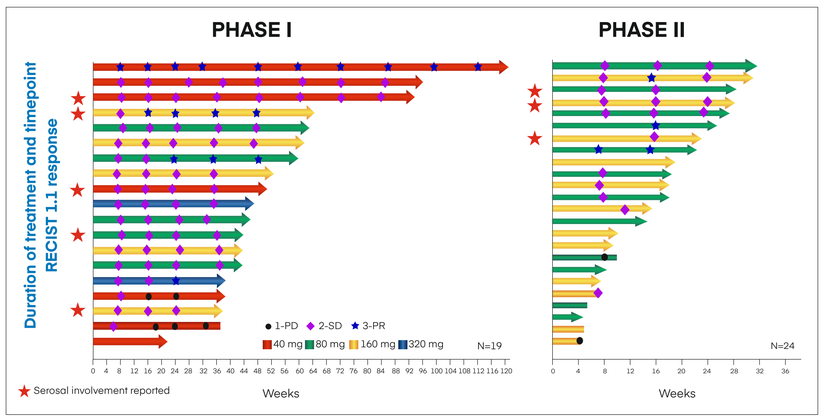


Fig. 4 Durable reductions in target lesions observed with ODM-212 in EHE

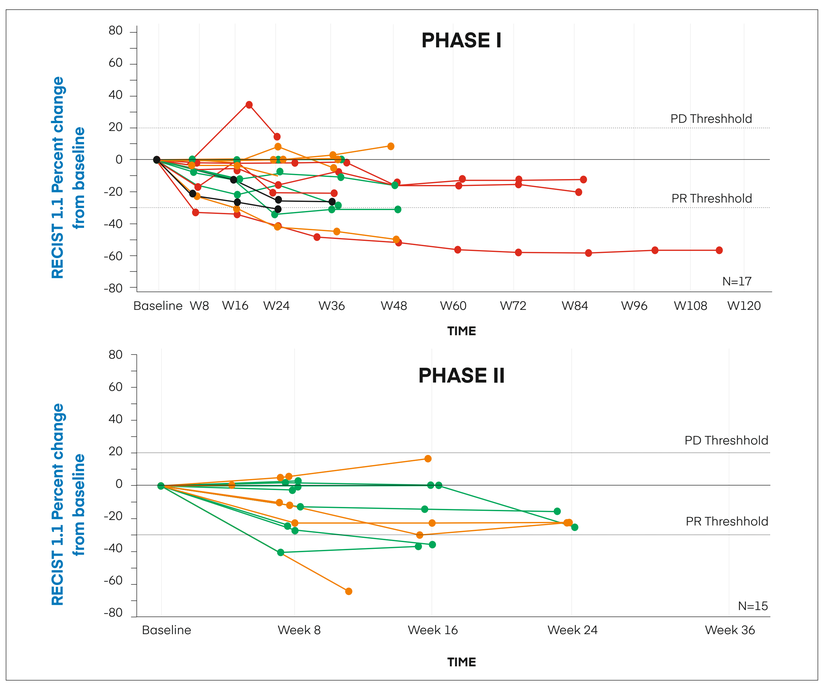


Table 3. Safety and tolerability

Adverse events observed in total ≥10% of subjects in total population by study Phase			
TRAEs[1] %	**Phase 1 (N=91)**	**Phase 2 (N=112)**	**Total (N=203)**
Proteinuria	30.8	18.8	24.1
Lipase increased	16.5	17.0	16.7
Amylase increased	12.1	19.6	16.3
Oedema peripheral	14.3	12.5	13.3
Nausea	12.1	11.6	11.8
Grade ≥3 TRAEs %			
	31.9	32.1	32.0
TEAEs[2] %			
Proteinuria	31.9	19.6	25.1
Lipase increased	24.2	19.6	21.7
Amylase increased	16.5	23.2	20.2
Oedema peripheral	19.8	19.6	19.7
Nausea	22.0	16.1	18.7
Anaemia	14.3	18.8	16.7
Fatigue	23.1	11.6	16.7
Aspartate aminotransferase increased	15.4	15.2	15.3
Dyspnoea	17.6	12.5	14.8
Alanine aminotransferase increased	13.2	11.6	12.3
Grade ≥3 TEAEs %			
	7.7	7.1	7.4
SAEs[3] %			
	25.3	32.1	29.1

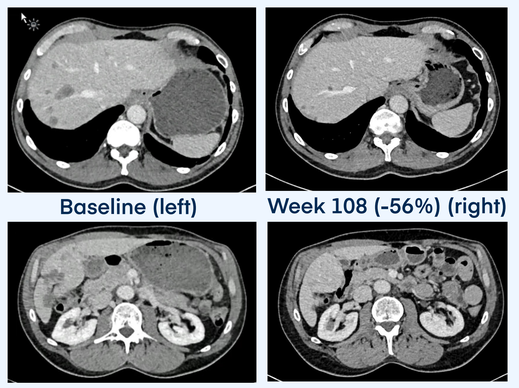
TRAE=Treatment related adverse event, TEAE=treatment emergent adverse event, SAE = serious adverse event. The safety profile in EHE subjects was similar to the total population.

**) Related SAEs reported by the DCO: colitis, headache, pancreatitis, sepsis, and toxic skin eruption. Events colitis and sepsis occurred in a same patient, and were re-assessed as not related after the DCO.*

Fig.5. EHE patient case

- Male 59 years old.
- Diagnosed with EHE in March 2021.
- WWTR1-CAMTA1 fusion.
- Lesions in liver, lung and bone.
- 1st line treatment liposomal doxorubicin resulted into SD -27%, but followed by PD in liver lesions.
- Enrolled into TEADES Phase I trial with 40mg ODM-212 daily dose in June 24.
- Week 8 imaging showed PR -32%, and the response is still ongoing with -56% at week 108.

CT showed ongoing tumour shrinkage in liver lesions at week 108



Baseline (left) | Week 108 (-56%) (right)

The patient images are published with the patient's consent.

CONCLUSION

- ODM-212 has shown promising early efficacy in EHE, an ultra-rare sarcoma with no approved treatment options.[5]
- Efficacy has been observed also in patients with serosal involvement, a population with worsened prognosis.[5]
- Durable, deepening responses have been observed in EHE.
- ODM-212 has been well tolerated in TEADES Phase I/II.
- The data supports continuing development of ODM-212 in EHE.

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* Data cut-off 3 Sep 2026

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ODM-212 is an investigational agent and has not been approved by any regulatory authority. Its safety and efficacy have not been established.

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