

Two-part, First-in-Human Trial Evaluating a PVRIGxPD-L1 Bispecific Antibody in Participants with Selected Advanced Solid Tumours

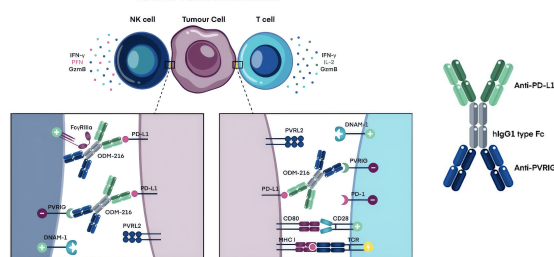
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INTRODUCTION

- ODM-216 is a novel tetravalent anti-human PVRIGxPD-L1 bispecific IgG1 antibody engineered to bind PVRIG and PD-L1 with high affinity.
- The bispecific antibody is expected to enhance immune cell recruitment and activation in the tumour microenvironment due to the coordinated interruption of 2 inhibitory checkpoint pathways:
 - PD-L1 interacts with PD-1 on T-cells to inhibit activation and proliferation of T-cells.
 - PVRIG binds to its ligand PVR2 (CD112) on tumour cells and antigen-presenting cells to suppress T-cell and natural killer (NK) cell function within the tumour microenvironment.^{1,2}
- Preclinical models demonstrate that simultaneous blockade of PVRIG and PD-L1 provides improved tumour growth control relative to blocking either PD-L1 or PVRIG alone.
- A repeat-dose toxicity study in cynomolgus monkeys demonstrated that ODM-216 was tolerated at all dose levels tested, with no dose-limiting toxicities observed.

Tumour Microenvironment

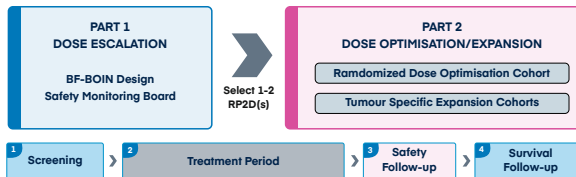


ELIGIBILITY CRITERIA

- At least 18 years old
- ECOG 0 or 1 performance status
- Confirmed advanced solid malignancy refractory to or intolerant to established standard of care therapies.
- Progressed on or after at least one and no more than 3 prior lines of therapy and have documented disease progression during or after the most recent anticancer treatment
- Tumour tissue is available by archival sample taken in the past 6 months or willingness to undergo fresh biopsy
- Measurable disease per RECIST v. 1.1
- Adequate organ function
- No history of autoimmune disease that has required treatment in the past 2 years. Hormone replacement therapy (e.g., thyroxine, insulin, or physiological corticosteroid) is allowed
- No history of immunodeficiency or chronic systemic steroid therapy
- No brain metastases unless asymptomatic and stable for at least 3 months prior to enrolment
- No significant cardiovascular disease
- No current or prior non-infectious pneumonitis that required steroids
- No active hepatitis B or hepatitis C or uncontrolled HIV infection

STUDY DESIGN

SCHEMA



Key: RP2D = recommended Part 2 dose; OBD = optimal biological dose; BF-BOIN = Bayesian optimal interval design with backfill.

- BiCIDES is an open-label, multi-site, first-in-human trial of ODM-216 (NCT07805252).
- Part 1 dose-escalation uses a backfilling Bayesian optimal interval (BF-BOIN) model-assisted design to collect safety, PK, pharmacodynamic (PD), and preliminary efficacy data across a range of dose levels.
- Part 2 includes a randomised dose optimisation cohort and single arm expansion cohorts to evaluate preliminary efficacy and optimal dose regimens in specific tumour types.
- Participants may receive ODM-216 until completion of a maximum of 2 years of treatment, disease progression, death, intolerable toxicity or any other discontinuation criterion is met.
- Safety is closely monitored with at least weekly clinic visits during cycles 1-2 and then once per cycle thereafter.
- Tumour imaging assessments occur every 6 weeks for 48 weeks and then every 12 weeks until disease progression according to RECIST version 1.1.

OBJECTIVES/ENDPOINTS

OBJECTIVE	ENDPOINT
PART 1 DOSE ESCALATION	
PRIMARY	
• To evaluate safety and tolerability • To identify recommended doses for evaluation in Part 2	• Incidence of DLT, TEAEs, treatment-related adverse events, dose modifications, and clinical laboratory/diagnostic abnormalities
SECONDARY	
• To characterise PK • To evaluate immunogenicity • To evaluate preliminary efficacy	• Single and multidose PK parameters • Number and rates of participants with ADA • ORR, DOR, TTR, DCR, PFS
PART 2 DOSE OPTIMISATION/EXPANSION	
PRIMARY	
• To evaluate anti-tumour effects in specific tumour types • To select or confirm an optimal biological dose	• ORR according to RECIST v. 1.1
SECONDARY	
• To evaluate safety and tolerability • To evaluate efficacy parameters in specific tumour types	• Incidence of DLTs, TEAEs, treatment-related adverse events, and clinical laboratory abnormalities • DOR, TTR, DCR, PFS, overall survival

DCR= Disease Control Rate; DLT= Dose-Limiting Toxicity; DOR= Duration Of Response; ORR= Objective Response Rate; PK= Pharmacokinetics; PFS= Progression-Free Survival; TEAEs= Treatment-Related Adverse Events; TTR= Time To Response.

PARTICIPATING SITES

- Spain: 7 sites activated and recruiting in Barcelona, Logroño, Madrid and Pamplona
- United Kingdom: sites pending activation in Glasgow, Leicester, Oxford, and London (Sutton)



SITES OPEN FOR ENROLLMENT

START Barcelona - HM Nau Delfos
Clínica Universidad de Navarra, Madrid and Pamplona
START Madrid - CIOCC - Universitario HM Sanchinarro

START Madrid - Universitario Fundación Jiménez Díaz
START Rioja - Universitario San Pedro, Logroño
NEXT Oncology - Universitario Quirónsalud Puzuela, Madrid

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- We thank all investigators and clinical site staff for their dedication, collaboration, and contributions to this study.

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Declaration of Interests:

- Research support to institution: PharmaMar, Boehringer-Ingelheim, Servier
- Advisory boards/consulting: AstraZeneca (unpaid)
- Travel, accommodation or meeting expenses: Roche
- Leadership roles in sponsored trials: Orion Therapeutics

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