Evaluating zAvatar test-guided chemotherapy vs. standard of care in relapsed ovarian cancer and metastatic breast cancer: A multicenter randomized clinical trial (zAVATAR-FLUIDS).

Marcio Debiasi, Helena S. Gouveia, Filipa Ferreira da Silva, Marta Sofia Freitas Estrada, Bruna Costa, Raquel Mendes, Vanda Póvoa, Mariana Rebordão Pires, Rita Teixeira de Sousa, Catarina Abreu, Ana Maria Henriques Martins Carvalho Mourao, Gabriela Sousa, Teresa Carvalho Tavares, Ana Magalhães Ferreira, Ana Rita Lopes, Carolina Pereira, Diana Pessoa, Fatima Cardoso, Rita Ferreira da Fior; Breast Unit, Champalimaud Clinical Centre, Champalimaud Foundation, Lisboa, Portugal; Breast Unit, Champalimaud Foundation, Lisboa, Portugal; Gynecology Unit, Champalimaud Foundation, Lisboa, Portugal; Cancer Development and Innate Immune Evasion Lab, Champalimaud Research, Champalimaud Foundation, Lisboa, Portugal; Serviço de Oncologia Médica, Hospital de Santa Maria, ULS Santa Maria, Li, Portugal; Hospital de Santa Maria, Centro Hospitalar Universitário Lisboa Norte, Lisboa, Portugal; Oncology Division, Hospital de Santa Maria-Centro Hospitalar Universitário Lisboa Norte, Lisbon, Portugal; Serviço de Oncologia Médica, Hospital de São Francisco Xavier, ULS Lisboa Ocidental, Lisboa, Portugal; Instituto Português de Oncologia Francisco Gentil de Coimbra, Coimbra, Portugal; Instituto Português de Oncologia de Coimbra Francisco Gentil, Coimbra, Portugal; Instituto Português de Oncologia Francisco Gentil de Porto, Porto, Portugal; Instituto Português de Oncologia de Lisboa Francisco Gentil, Lisbon, Portugal; Instituto Português de Oncologia Francisco Gentil de Lisboa, Lisboa, Portugal; ABC Global Alliance, Lisbon, Portugal

Background: Relapsed ovarian cancer and metastatic breast cancer (MBC) present significant challenges due to tumor heterogeneity and limited treatment efficacy. Despite numerous recent achievements in personalized medicine, we still lack real-time molecular biomarkers to guide therapeutic decision-making, often resulting in multiple lines of trial-and-error chemotherapy (CT), which ultimately exposes patients to unnecessary toxicities. The zAvatar test – a patient-derived zebrafish xenograft model – has shown to accurately predict tumor response to treatment, providing a real-time and non-invasive means of guiding personalized therapy in advanced cancers (Fior R, et al, 10.1038/s41467-024-49051-0). This trial evaluates the clinical utility of zAvatar as a predictive tool to optimize therapeutic decisions for patients with relapsed ovarian cancer or MBC, presenting with malignant pleural effusion or ascites. **Methods:** In this multicenter, open-label, randomized clinical trial, patients with relapsed ovarian cancer or metastatic HER2-negative breast cancer, ECOG performance status 0-2, measurable disease by RECIST 1.1 and 2 or more equally effective CT options, who need drainage of ascites or pleural effusion, are randomized (1:1) into two groups: the control group will receive CT based on physicians´ choice, while the experimental group will receive treatment guided by the zAvatar-test results. Both groups will have zAvatars generated from tumor cells isolated from ascitic or pleural effusion fluids. The trial will include 276 patients (138 per cancer type). The study aims at determining whether zAvatar-guided decisions lead to improved progression-free survival (PFS) compared to standard of care, as primary endpoint. Recruitment started in January 2025, with an anticipated recruitment period of 3 years (2025–2028). The first patient is expected to be randomized in February 2025 and undergo zAvatar-test evaluations in centralized lab. This trial paves the way for an innovative approach for personalized medicine by validating the zAvatar test's ability to tailor treatment options in advanced cancers, which shall in the future bring into practice a real-time, patient-specific decision-making functional test. Clinical trial identification: EU-CTR n. 2023-509598-22. Legal sponsor: Champalimaud Clinical Centre, Lisbon, Portugal. Funding: Liga Portuguesa Contra Cancro. Protocol FC2024-001. Clinical trial information: 2023-509598-22. Research Sponsor: Liga Portuguesa Contra Cancro.