

First MYC inhibitor to demonstrate safety and anti-tumor activity in a phase I first-in-human clinical trial

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VHIO. Credit: VHIO

Directed by Laura Soucek, an ICREA Research Professor, Director of VHIO's Experimental Therapeutics Program and head of our Models of

Cancer Therapies Group, two decades of research aimed at combating resistance to therapy and cancer regression through inhibiting the MYC oncogene—found deregulated in most, if not all tumor types—has led to the in-house development of the Omomyc (OMO-103) therapeutic mini-protein by the VHIO and Catalan Institute of Research and Advanced Studies' (ICREA) spin-off company Peptomyc S.L., which Soucek co-founded in 2014 alongside Marie-Eve Beaulieu, Peptomyc's Chief Scientific Officer.

Having previously reported the preclinical efficacy and safety of this novel cell-penetrating mini-protein in mouse models, investigators of her Models of Cancer Therapies Group and the Peptomyc team worked in collaboration to successfully develop anti-MYC peptides for the treatment of several tumor types.

OMO-103 has since gained pace in becoming the first ever clinically viable and direct inhibitor of MYC thanks to its ability to enter cells and reach its target compartment, namely the nucleus. The successful intravenous systemic administration of this mighty mini-protein MYC inhibitor against various tumor types, led to the design of a first-in-human phase I clinical trial.

Bringing the first MYC inhibitor closer to the clinic

[Published](#) in the journal *Nature Medicine*, first findings of this phase I dose-escalation study in all-comers [solid tumors](#) demonstrate the excellent safety profile and early signs of anti-tumor clinical activity of OMO-103 in humans, supporting further studies evaluating its efficacy in specific indications, also in combination with standard of care.

Elena Garralda, Director of VHIO's Research Unit for Molecular Therapy of Cancer (UITM)—CaixaResearch and head of its Early Clinical Drug Development Group, along with the START early phase

clinical trial units at the Fundación Jiménez Díaz and HM CIOCC University Hospitals in Madrid, initiated this first-in-human dose escalation clinical trial in 2021. Enrolling a total of 22 patients, this study was designed to assess the safety, pharmacokinetics, and preliminary signs of clinical activity of OMO-103 in patients with advanced solid tumors.

The study participants had a wide range of metastatic solid tumors and had received between 2 and 12 previous lines of treatment, with no other therapeutic options available.

"The main aim of this study was to evaluate the safety of this novel MYC inhibitor. First results demonstrate a favorable safety profile, with only mild side effects including chills and nausea. We have now reported clinical benefits in patients, even at very low doses. In 8 of the 12 patients who underwent a CT scan at 9 weeks of treatment, we observed disease stabilization and halted tumor growth," says Emiliano Calvo, a Medical Oncologist at START-HM CIOCC and last author of this study along with corresponding author Soucek.

"In one patient with [pancreatic cancer](#) who received OMO-103 as fourth-line treatment and stayed in the study for more than six months, we observed an 8% tumor shrinkage and an 83% reduction of circulating tumor DNA. When evaluating the radiographic total burden of disease change, in collaboration with VHIO's Radiomics Group led by Raquel Perez-Lopez, this patient showed a 49% volume reduction, a notable result for advanced metastatic pancreatic cancer," observes co-first author Garralda.

"One patient with sarcoma, who showed a poor response to previous lines of treatment, remained stable for 8 months in this study. Also of note, a patient with a salivary gland tumor remained stable for 26 months, without any adverse events," she adds.

Identification of potential biomarkers

"Since this is the first time that our MYC inhibitor has been evaluated in humans, we aimed to demonstrate its efficacy in targeting MYC as well as identify possible biomarkers of response," explains Soucek, corresponding of this present study, who coordinated the comprehensive molecular characterization of OMO-103 along with Peptomyc's co-founder and first co-author Beaulieu.

The investigators analyzed the available tumor biopsies before and after treatment and confirmed that the transcriptional signature of MYC was modulated by OMO-103, demonstrating its anti-tumor activity. They identified a direct and specific correlation between MYC deactivation and clinical benefit in patients.

Soucek's teams have also identified two potential blood-based biomarkers that—upon validation—could be useful in the management of disease. They have detected a possible biomarker of pharmacodynamic activity that increases in blood when patients respond to treatment with OMO-103 and then decreases or disappears upon disease progression.

"Using non-invasive liquid biopsy, this marker could enable us to identify tumor progression earlier and help guide treatment decision making more rapidly. We have also identified a predictive biomarker that—through a simple blood test—could help us to predict those patients who could potentially derive benefit from treatment with OMO-103," observes Soucek.

Results of this first-in-human phase I clinical trial have led the initiation of a phase Ib clinical trial currently evaluating the activity of OMO-103 in combination with standard of care in patients with metastatic pancreatic cancer.

"Our goal is to continue investigating the anti-tumor activity of OMO-103, also in combination with other currently approved therapies, to assess its efficacy and potential cooperation with the standard of care in various tumor types," concludes Soucek.

More information: Elena Garralda et al, MYC targeting by OMO-103 in solid tumors: a phase 1 trial, *Nature Medicine* (2024). [DOI: 10.1038/s41591-024-02805-1](https://doi.org/10.1038/s41591-024-02805-1)

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