Omomyc: Bringing the first anti-Myc mini-protein into the clinic

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Myc is deregulated in most of human cancers and it has remained undruggable for a long time. Omomyc is a Myc dominant negative mini-protein that was designed more than 20 years ago. Since then, several groups have validated its mode of action and therapeutic effect in several preclinical models of cancers driven by various oncogenes [1]. The unexpected cell-penetrating properties and anti-tumour activity of the recombinant Omomyc mini-protein [2],[3], encouraged Peptomyc to push Omomyc towards the clinic. We recently published the PK analysis using a label-free MS approach to assess the structural integrity of Omomyc in preclinical tumour models, which demonstrated that not only the mini-protein reaches the tumour after 2 h following intravenous administration at tissue concentrations within the range of serum's, but also that the tumour concentrations are in fact higher than serum's, and persist there for at least 72 h [4].

Here, we present that the first-in-class direct MYC inhibitor OMO-103 shows excellent safety, target engagement and drug activity in a Phase I study [5]. The drug showed an excellent safety profile: the most common adverse events related to OMO-103 were mainly grade 1, infusion-related reactions consisting of chills, fever or nausea. 8 out of 12 patients with advanced solid tumours achieved stable disease (SD) and no anti-drug antibodies (ADAs) were detected. The PK analysis showed a plasma half-life of >40h and longer half-life in tissue. Regarding PD biomarkers, OMO-103 shuts down the Myc transcriptional signature in patient's tumour biopsies, supporting target engagement. Additionally, several soluble potential pharmacodynamic markers of response were also found modulated upon OMO-103 treatment.

In summary, OMO-103 is the first MYC inhibitor to successfully complete a Phase I clinical trial, demonstrating a favourable safety profile, with early signs of activity that merit further investigation.

[1] Massó-Vallés D., et al. *Cells.* **2020,** *9,* 883.
[2] Beaulieu M.-E., et al. *Sci. Transl. Med*. **2019**. *11* (484).
[3] Massó-Vallés D., et al. *Cancer Res. Commun*. **2022**, *2*,110–130.
[4] Beaulieu M.-E., et al. *Cancers*. **2023**, *15*, 826.
[5] Garralda E., et al. *Nat. Med.* In revision.