

# AURELIO-04: A PHASE 2, OPEN-LABEL, SINGLE-ARM, MULTICENTER STUDY TO DETERMINE THE EFFICACY AND SAFETY OF SOT101 IN COMBINATION WITH PEMBROLIZUMAB IN PATIENTS WITH SELECTED ADVANCED SOLID TUMORS

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**Background** SOT101 (INN: nanrilkefusp alfa), a fusion protein of IL-15 and the IL-15 receptor  $\alpha$  sushi+ domain, was investigated in AURELIO-03 (NCT04234113), a phase 1 dose-escalation study, as monotherapy and in combination with pembrolizumab. In that trial, combination had a favorable safety profile and MTD was not reached up to the recommended phase 2 dose (RP2D) for monotherapy. Maximum activation of natural killer cells was observed already at low dose levels, maximum CD8<sup>+</sup> T cell activation was reached from 9 to 12  $\mu$ g/kg, no relevant effect on T regulatory cells was observed. Therefore, 12  $\mu$ g/kg SOT101 was selected as combination RP2D. Encouraging efficacy signals were observed, even in immune checkpoint inhibitor (CPI)-relapsed patients. For combination therapy, the majority of patients had clinical benefit.<sup>1,2</sup> Study AURELIO-04 (NCT05256381) aims to further evaluate the efficacy of SOT101 in combination with pembrolizumab in selected solid tumor indications.

**Methods** AURELIO-04 is a phase 2 single-arm study in:

- Non-small cell lung cancer after a CPI and/or platinum regimen, with no EGFR or ALK aberration
- Unresectable or metastatic MSI-H/dMMR colorectal cancer
- First-line cutaneous squamous cell carcinoma not curable by surgery or radiation and second-line after a CPI regimen
- Hepatocellular carcinoma after a CPI regimen
- Metastatic castrate-resistant prostate cancer (mCRPC) after docetaxel
- Ovarian cancer after a platinum regimen

Main inclusion criteria are measurable disease as per RECIST 1.1, accessible tumor tissue, ECOG PS 0-1, adequate organ function, no prior IL-2 or IL-15 therapy. For mCRPC, a defined number of patients with non-measurable disease is allowed.

Patients will receive 12  $\mu$ g/kg SOT101 s.c. on days 1, 2, 8, and 9 in combination with 200 mg pembrolizumab i.v. on day 1 every 3 weeks until disease progression or unacceptable toxicity.

Primary endpoint is overall response rate (ORR) per RECIST 1.1. Key secondary endpoints include efficacy

parameters such as progression-free survival, frequency and severity of treatment-emergent adverse events, pharmacokinetics (PK) including population PK, pharmacodynamics, and immunogenicity parameters.

Approximately 55 patients per indication will be enrolled. No formal testing of statistical hypotheses is planned, analyses will be descriptive. Considering benchmark ORRs, a futility analysis is planned for each indication separately. Exploratory analyses include immune and molecular biomarkers.

Recruitment started in June 2022.

## REFERENCES

1. Champiat S, Marabelle A, Galvao V, *et al.* SOT101, an IL-2/IL-15 R $\beta$ γ superagonist, in combination with pembrolizumab in patients with advanced solid tumors: Interim safety and efficacy results from the AURELIO-03 dose escalation trial. Presented at: American Association for Cancer Research Annual Meeting 2022; April 8-13, 2022; New Orleans, LA.
2. Garraida E, Naing A, Galvao V, *et al.* Interim safety and efficacy results from AURELIO-03, a phase 1 dose escalation study of the IL-2/IL-15R  $\beta$ γ receptor superagonist SOT101 as a single agent and in combination with pembrolizumab in patients with advanced solid tumors. Presented at: American Society of Clinical Oncology Annual Meeting 2022; June 3-7, 2022; Chicago, IL.

**Ethics Approval** The study was approved by Advarra Institutional Review Board approval number Pro00062123. Participants give informed consent before taking part

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