OMNIA-1, a Phase I/II study of ANV419, an IL- 2R-βγ targeted antibody-IL-2 fusion protein, as monotherapy or in combination with anti-PD-1 or anti-CTLA-4 antibodies, in patients with advanced melanoma

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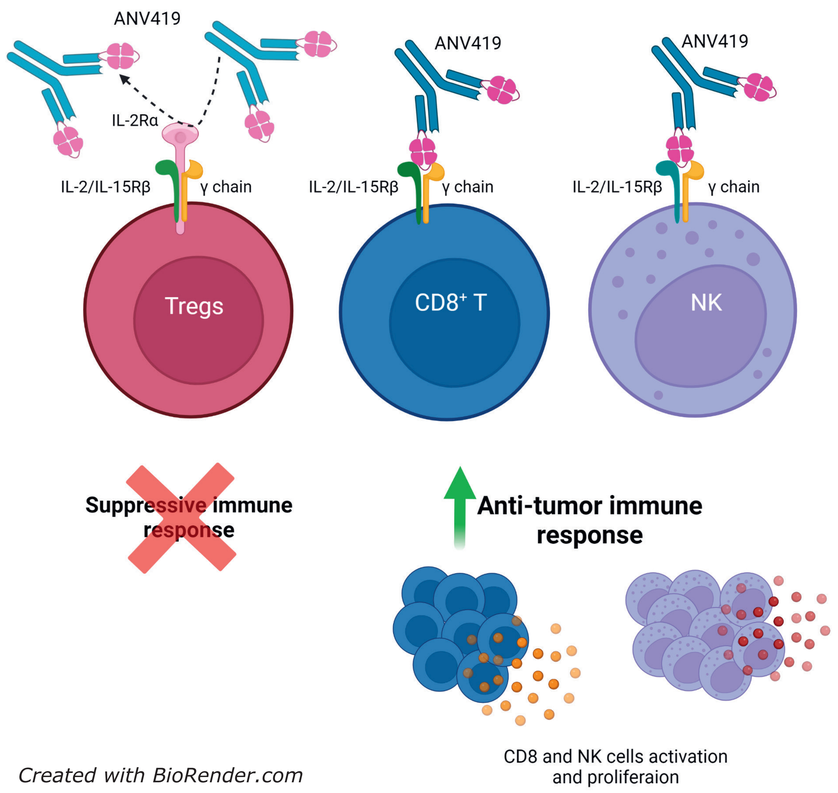
Background

- Significant advancements, including development of immune checkpoint inhibitors and targeted therapies have transformed outcomes for patients with unresectable or metastatic melanoma
- Patients who do not respond or who progress while receiving these regimens have limited options
- Recombinant IL-2 (aldesleukin) has demonstrated single agent anti-tumor efficacy and durable responses in approximately 10% of patients and is approved for the treatment of metastatic melanoma, but its use is limited due to safety/efficacy concerns, and logistic constraints[1]
- ANV419 is a fusion protein of IL-2 and anti-IL-2 monoclonal antibody ANV419, designed to selectively activate cytotoxic T cells and NK cells and avoid a suppressive tumor response while minimizing toxicities

Figure 1.



- Data from ANV419-001 first-in-human study (NCT04855929) demonstrate that ANV419 preferentially stimulates cytotoxic $CD8^+$ T and natural killer (NK) cells over immunosuppressive regulatory T cells and confirms that ANV419 can be delivered at high molar equivalent of IL-2
- The geometric mean half-life at the RP2D of 243 µg/kg of ANV419 Q2W is approximately 12 hours
- The safety profile of ANV419 is characterized by pyrexia/chills, nausea/vomiting, LFT elevations, lymphopenia, and low grade CRS
- Based on these data, ANV419 is being further explored as monotherapy and in combination with checkpoint inhibitors in patients with unresectable or metastatic melanoma (OMNIA-1), and multiple myeloma (OMNIA-2)
  - OMNIA-1 (ANV419-101), ClinicalTrials identifier NCT05578872
  - OMNIA-2 (ANV419-102), ClinicalTrials identifier NCT05641324 (see Trial in Progress TPS8068)

Thank you to all sites and patients in this study

Reference
Buchbinder et al. Journal for ImmunoTherapy of Cancer, (2019) 7:49

Research Sponsor: ANAVEON AG, Basel, Switzerland
ClinicalTrials.gov Identifier: NCT05578872

Study Design

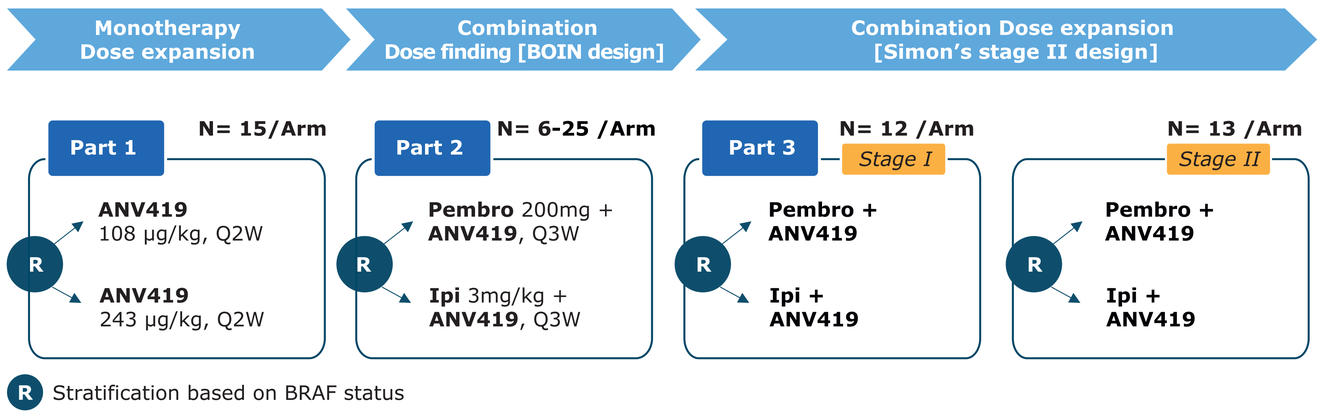
OMNIA-1 is an open label, randomized, parallel arm, Phase 1/2 adaptive study to evaluate the efficacy and safety of ANV419 as a monotherapy and in combination with pembrolizumab or ipilimumab in patients with previously treated unresectable or metastatic melanoma. There will be up to 3 separate parts in this study:

Part 1: Monotherapy dose expansion (N= 30)
- Patients are randomized to receive ANV419 108 µg/kg or 243 µg/kg every 2 weeks
- If Part 1 is successful, part 2 will be opened

Part 2: Combination dose finding (N= 50)
- Patients will be randomized to receive ANV419 in combination with pembrolizumab or ipilimumab every 3 weeks using the approved doses of pembrolizumab and ipilimumab
- Dose escalation will be guided by BOIN using a DLT observation period of 3 weeks

Part 3: Combination dose expansion (N= 50)
- Part 3 will evaluate the safety and efficacy of ANV419 in combination with pembrolizumab or ipilimumab using a Simon 2-stage design

Duration of treatment
- ANV419 +/- pembrolizumab: up to 12 months in absence of progression/unacceptable toxicity
- ANV419 + ipilimumab up to 4 cycles, followed by ANV419 monotherapy (Q3W) up to 12 months in absence of progression/unacceptable toxicity



Key eligibility criteria*

- ≥ 18 years of age
- Histologically confirmed Stage 3 (unresectable) or Stage 4 (metastatic) cutaneous melanoma (uveal/ocular and mucosal excluded)
- Progressed on or following at least 1 line of standard of care immunotherapy
- Patients with BRAF mutant disease must have received prior BRAF/MEK inhibitors
- If CNS involvement, no active disease and no carcinomatous meningitis
- Measurable disease per RECIST criteria
- ECOG performance status of 0 or 1

**As per protocol V.3, other criteria also apply*

Study objectives and endpoints

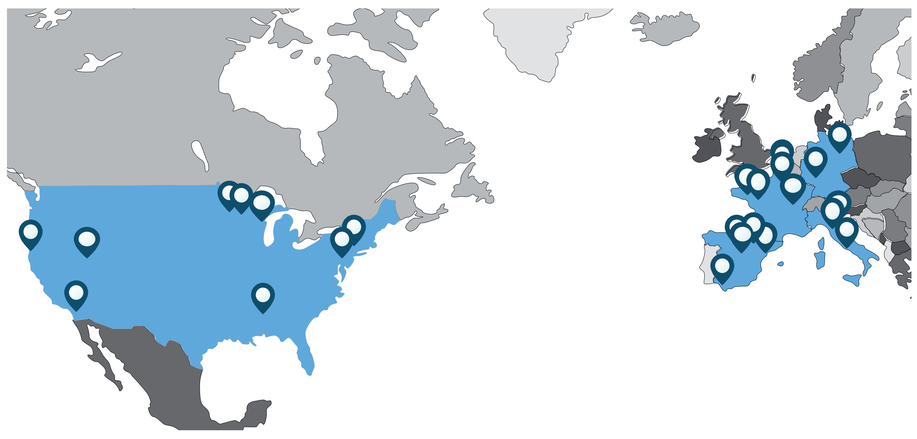
Objective
To assess the efficacy and safety of ANV419 single agent or in combination with pembrolizumab or ipilimumab in patients with unresectable or metastatic cutaneous melanoma

Primary Endpoints
- Objective Response Rate of ANV419 single agent (Part 1) and in combination (Part 3) by RECIST 1.1
- Safety/tolerability and RP2D determination of ANV419 in combination (Part 2)

Secondary Endpoints
- DOR, DCR, PFS and OS
- Pharmacokinetics (PK) and Pharmacodynamics (PD)
- Immunogenicity
- QoL

Exploratory Endpoints
- Changes in tumor microenvironment before and after ANV419

Participating countries



Part 1 ongoing in the USA, France, Spain, Germany and Italy

First patient dosed in Dec 2022

Preliminary monotherapy efficacy expected by Q1/2024

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