ANV419, an IL-2R-βγ targeted antibody-IL-2 fusion protein, induces selective effector cell proliferation in patients with progressed cancer

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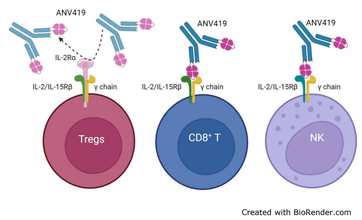
Background

- Developing a safe and effective non alpha IL-2R agonist to selectively stimulate immune effector cells remains an important therapeutic goal for the treatment of patients with cancer
- ANV419 is a fusion protein of an anti-IL-2 antibody and hIL-2 with selective signaling through the IL-2Rβγ, thus limiting the side effects of activating the IL-2Rα/β/γ (Fig. 1)
- In pre-clinical models, ANV419 has shown high effector selectivity and a favorable safety profile and the FIH phase I/II dose finding study is ongoing (ANV419-001; NCT04855929, Sponsored by ANAVEON AG)

Fig. 1 Cell activation by ANV419



ANV419 Clinical Programs and Patient Characteristics

Cut-off date August 16th

Phase I Study Population and Objectives

Inclusion Criteria
- Adults aged ≥ 18 years
- Advanced solid tumors with evidence of progressive disease as within last 3 months
- Relapsed/refractory advanced solid tumor, progressing after at least one line of treatment for advanced or metastatic disease
- ECOG PS 0-1

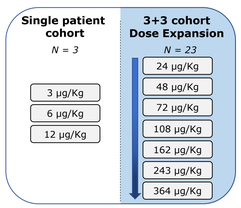
Primary objectives
- Safety and tolerability of ANV419
- Maximum Tolerated Dose (MTD) and Recommended Phase 2 Dose (RP2D) of ANV419

Secondary objectives (main)
- Objective Response Rate (RECIST v1.1)
- Pharmacokinetics of ANV419
- Pharmacodynamic markers of immune cell activation: immunophenotyping and ki67 proliferation

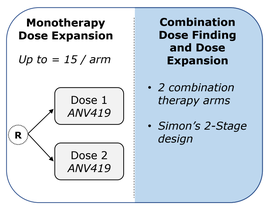
Table. 1 Phase I Patient Characteristics

Demographics/Performance Status	TOTAL n=26 (%)
Age (mean; yrs)	61
Male	17 (65%)
Female	9 (35%)
ECOG PS 0	13 (50%)
ECOG PS 1	13 (50%)
Primary cancer diagnosis	
Cutaneous Melanoma	4 (15%)
Non cutaneous melanoma (uveal, mucosal)	5 (19%)
Oesophageal adenocarcinoma	1 (4%)
Colorectal adenocarcinoma	3 (11%)
Hepatocellular carcinoma	1 (4%)
Renal carcinoma	3 (11%)
Pancreatic adenocarcinoma	2 (8%)
Adenoid cystic carcinoma maxillary sinus	2 (8%)
Acinar cell carcinoma of parotid gland	1 (4%)
Non-small cell lung cancer	3 (11%)
Cancer of Unknown Primary	1 (4%)
Number of lines of prior systemic therapy	
Lines of prior systemic therapy, range	1-8
Prior use of immunotherapy	21(81%)
Prior use of targeted therapy	14 (54%)
Prior use of chemotherapy	13 (50%)

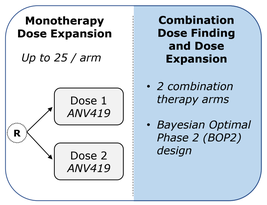
ANV419-001



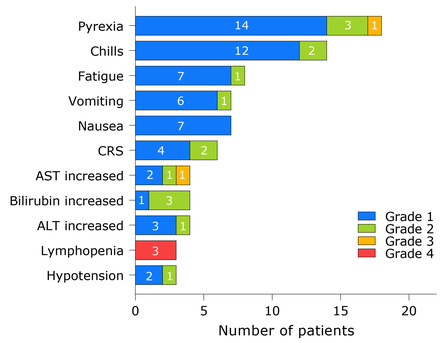
ANV419-101 (Melanoma)



ANV419-102 (Multiple Myeloma)

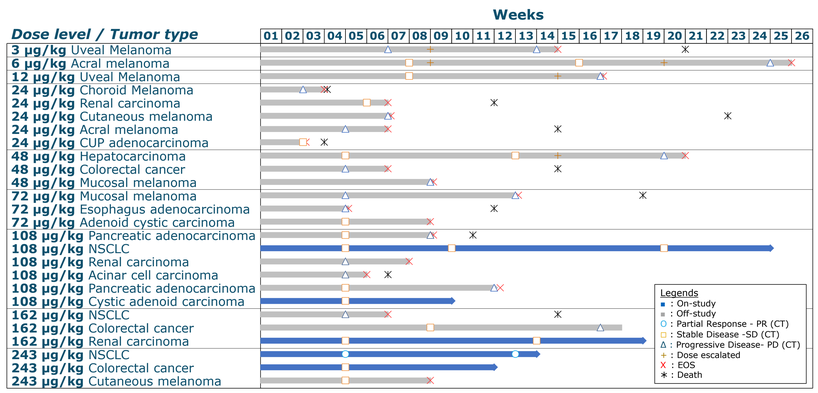


Safety: Drug Related AEs reported in at least 10% of Patients



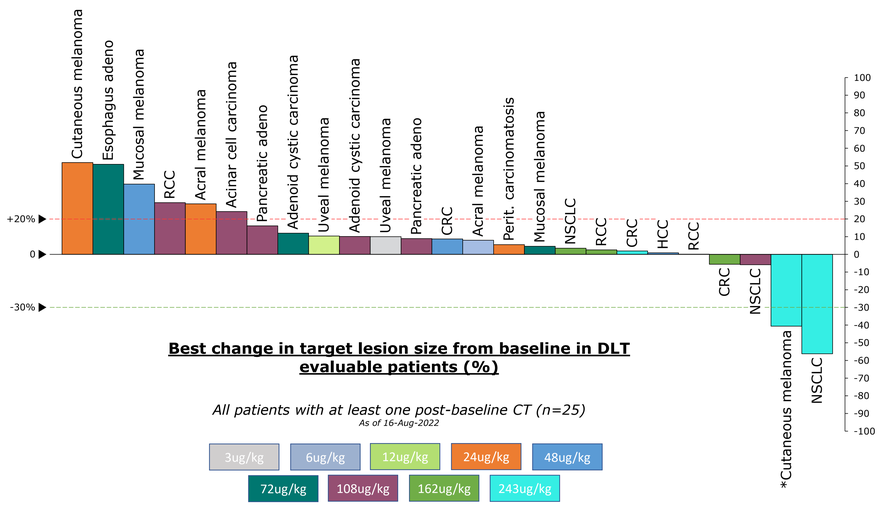
- ANV419 generally well tolerated, no dose-limiting toxicities (DLTs) up to and including 243 µg/kg
- No patients discontinued due to AEs
- Transient and self-limiting lymphopenia in all patients, usually considered non-clinically significant
- All drug related events reversible and responsive to supportive care therapy
- Cytokine release syndrome (CRS) resolved with standard anti-pyretic treatment, intravenous fluid or steroids
- AEs that were reported in less than 10% of patients were G1 and G2 only (not shown)

Exposure: On-study Patients' Duration & Responses by RECIST v1.1



Best Tumor Change from Baseline

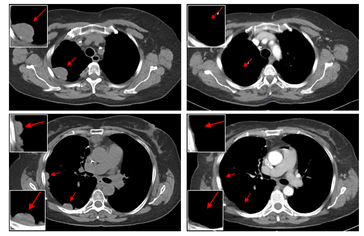
Overall, 58% of patients (n=14) achieved at least disease stabilization (13 SD and 1 PR)
At ANV419 doses ≥108 µg/kg, 75% of patients achieved at least disease stabilization (8 SD and 1 PR)



* Patient experienced clinical progression and had also received radiotherapy while ANV419 therapy for tumor debulking to manage pain

Patient case: 63 yr female, NSCLC, PR with 56% Reduction Baseline Target SLD

11/May/22 ⟶ 08/August/22



Previous smoker; NSCLC (adenocarcinoma) pleuro-pulmonary, mediastinal and adrenal metastases; PD-L1 -ve, KRAS, STK11 +ve; baseline target SLD 89mm

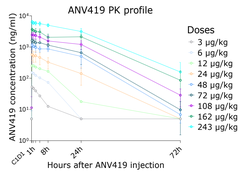
Treatment history:
Feb 21: Surgical lobectomy, mediastinal lymphadenectomy
Nov 21: Relapse, metastases in pleura and lymph nodes
Jan 22: PR after 4 cycles carboplatin, pemetrexed, pembrolizumab
April 22: Progression pleural (from 18 to 36mm) and mediastinal lymph node metastases with new adrenal lesions after 4 cycles of maintenance pemetrexed and pembrolizumab
May 22: Continued progression (from 43 to 46mm in mediastinal lymph nodes) prior to ANV419-001 study

On-study benefit:
PR after 2 cycles ANV419 (SLD reduced by 28mm, 31%) with deepening response of 56% reduction in target lesions, pleuro-pulmonary (from 42 to 12mm), mediastinal (from 32 to 23mm) and adrenal (from 15 to 4mm) metastases (SLD reduced by 50mm) at 3 months, and disappearance of adrenal non-target lesions

Pharmacokinetics & Pharmacodynamics

Serum C_{max} and half-life proportionally increase with ANV419 doses

ANV419 half-life increases up to 28 hours with increasing doses. Pharmacokinetic data show that ANV419 concentration is overall stable between cycle 1 and cycle 2

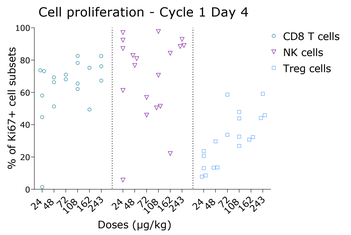


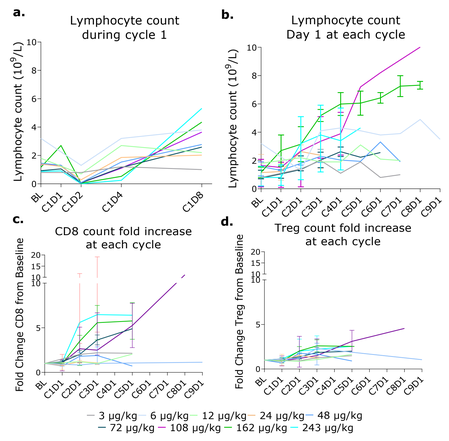
ANV419 induces over time a dose dependent increase lymphocyte expansion

ANV419 induces lymphopenia which persists up to 72hrs with higher doses (a.) with a more pronounced rebound and increased lymphocyte count at day 8 and subsequent cycles (b.); similar to that described with high dose of IL-2.
ANV419 induces a higher fold increase of CD8+ (c.) and NK cells than of Treg (d.) over multiple cycle. NK cell number and fold increase in line or exceeding increase of CD8+ T cells (not shown)

ANV419 selectively induces dose dependent proliferation of CD8+ T cells and NK cells but not Treg cells

Pharmacodynamic evaluation of ANV419 on day 4 post-dosing showed a selective and dose dependent proliferation of CD8+ T and NK cells, with a lower increase of proliferating Tregs. C2D4 values were comparable to C1D4 values at doses >108 µg/kg





Conclusions

- ANV419 was generally well tolerated across multiple cycles, with a manageable safety profile and no DLT up to and including 243 µg/kg
- No patients required ANV419 interruption or discontinuation due to AEs
- ANV419 induces a selective and dose dependent proliferation of CD8+ T and NK cells, but a lower increase of proliferating Tregs
- 58% of patients (n=14) achieved at least disease stabilization (SD or PR)
- These data support the further clinical evaluation of ANV419 as single agent and in combination, in patients with melanoma and multiple myeloma (studies ANV419-101 and ANV419-102)
- Visit poster 39P with the preclinical data supporting ANV419 combination studies

Acknowledgments

Thank you to the patients, their families and the sites for participation in this clinical study

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