Phase I dose escalation study in patients with advanced solid tumors with ANV419, a novel fusion protein selective for IL-2Rβ/γ

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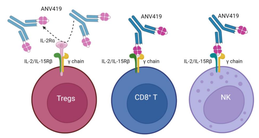
ANV419, a selective IL-2R-βγ, antibody-IL-2 fusion protein

Cell activation by ANV419



- 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
- In pre-clinical models, ANV419 has shown high effector selectivity and a favorable safety profile
- FIH phase I dose finding study is ongoing (ANV419-001; NCT04855929, Sponsored by ANAVEON AG)

ANV419-001 Study

Cut-off date Sept 20th

ANV419-001

Eligibility
- ≥ 18 years old
- Advanced solid tumors with disease progression within last 3 months
- ECOG PS 0-1

ANV419 administered as 15 min intravenous infusion Q2W

3 µg/Kg (n=1)
6 µg/Kg (n=1)
12 µg/Kg (n=1)
24 µg/Kg (n=4)
48 µg/Kg (n=3)
72 µg/Kg (n=3)
108 µg/Kg (n=6)
162 µg/Kg (n=3)
243 µg/Kg (n=4)
364 µg/Kg (n=3)

→ RP2D

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

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

Patient Demographic

Demographics/Performance Status	TOTAL n=29(N)
Age (mean; yrs)	61
Male	17 (59%)
Female	12 (41%)
ECOG PS 0	16 (55%)
ECOG PS 1	13 (45%)
Primary cancer diagnosis	
Cutaneous Melanoma	4 (14%)
Non cutaneous melanoma (uveal, mucosal)	5 (17%)
Oesophageal adenocarcinoma	1 (3%)
Colorectal adenocarcinoma	5 (17%)
Hepatocellular carcinoma	1 (3%)
Renal carcinoma	3 (10%)
Pancreatic adenocarcinoma	2 (7%)
Adenoid cystic carcinoma maxillary sinus	2 (7%)
Acinar cell carcinoma of parotid gland	1 (3%)
NSCLC	3 (10%)
CUP	1 (3%)
Number of lines of prior systemic therapy	
Lines of prior systemic therapy, range	1-8
Lines of prior systemic therapy, median	3.5
Prior use of immunotherapy	22(76%)
Prior use of targeted therapy	15 (52%)
Prior use of chemotherapy	16 (55%)

Upcoming studies

ANV419-101 Melanoma

Eligibility
- ≥ 18 years old
- unresectable and metastatic cutaneous melanoma following at least one line of standard of care
- ECOG PS 0-1

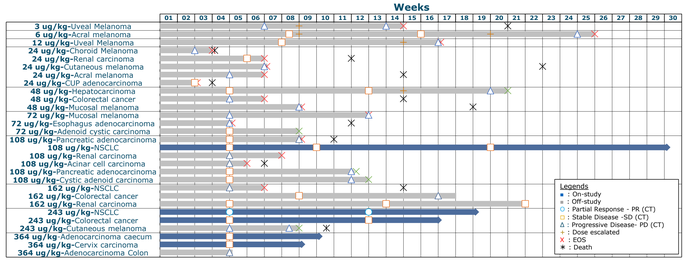
→ Dose 1 ANV419
→ Dose 2 ANV419

ANV419-101 study will be conducted in 3 parts: Monotherapy Dose Expansion, Combination Dose Finding and Dose expansion

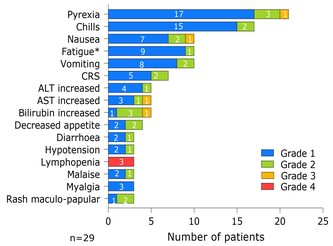
ANV419-102 Multiple Myeloma

- Patients with relapsed or refractory multiple myeloma (MM) who have received 2 or more lines of previous therapy
- ANV419-102 study will be conducted in 2 parts: Monotherapy followed by a combination therapy

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



Safety: Drug Related AEs reported in at least 10% of Patients (CTCAE v5.0)

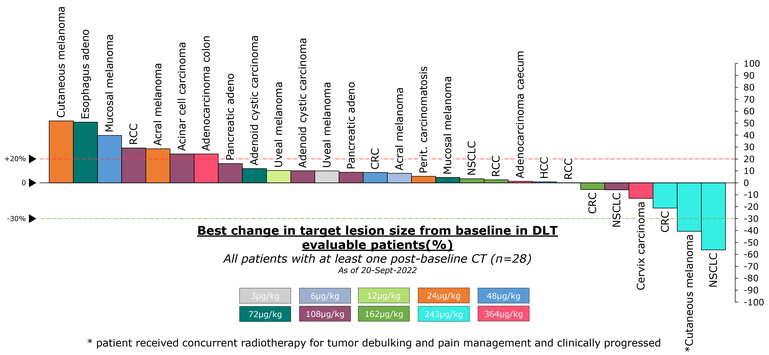


- ANV419 generally well tolerated, no DLTs up to and including 243µg/kg dose
- All drug related events were reversible and responsive to standard supportive therapy
- 8 drug related SAEs were reported in 5 patients (5 CRS G1, nausea G3, Fever G1, creatinine increase G3)
- At 364µg/kg (recruitment ongoing) one patient experienced two DLTs of G3 mucositis and G3 bullous erythema
- 2/29 (7%) patients reduced dose due to AE
- Transient and self-limiting lymphopenia with no clinical sequelae was observed in all patients, usually considered non clinically significant
- CRS consisted of fever with nausea or hypotension and resolved with anti-pyretic treatment, intravenous fluids and/or steroid treatment

* fatigue also includes the reported term 'asthenia'

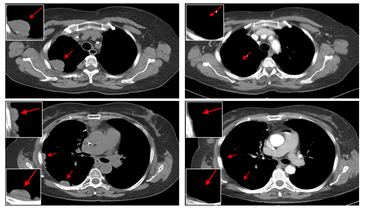
Best Tumor Change from Baseline

- 55% of patients (n=16) achieved at least disease stabilization (15 SD and 1 PR)
- At ANV419 doses ≥108 µg/kg, 66% of patients achieved at least disease stabilization (9 SD and 1 PR)



* patient received concurrent radiotherapy for tumor debulking and pain management and clinically progressed

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



Background:

Previous smoker; NSCLC (adenocarcinoma) pleuro-pulmonary, mediastinal and adrenal metastases; PD-L1-ve, KRAS, STK11 +ve; baseline LDH 1102 U/L; baseline target SLD 89mm

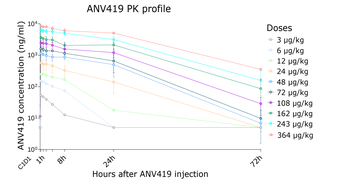
Treatment history:
- Feb 21: Surgical lobectomy, mediastinal lymphadenectomy
- Nov 21: Relapse, metastases in pleura and lymph nodes
- Jan 22: PR after 4 cycles carboplatin, pemetrexed, pembrolizumab
- April 22: Progression pleural (from 18 to 36mm) and mediastinal lymph node metastases with new adrenal 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
- At cycle 8, LDH value reduced 77% (249U/L) compared to the initial value

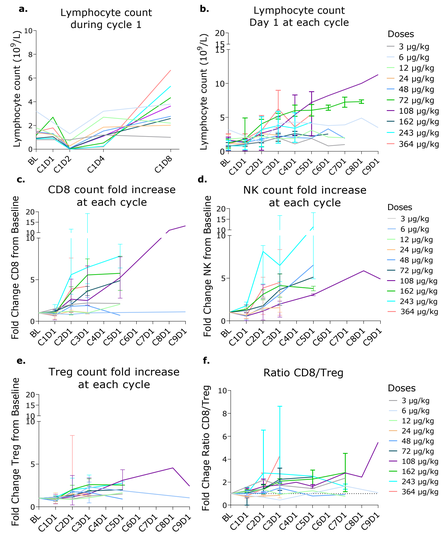
Pharmacokinetic & Pharmacodynamic

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 cycles
- At low doses PK is impacted by target dependent disposition, which is overcome at higher doses. This is reflected in the increase of half-life from 3.6 hours at 3µg/kg up to 28 hours at high doses of ANV419



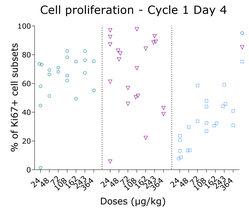
ANV419 induces over time a dose dependent lymphocyte expansion



- 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 the lymphopenia described after administration of multiple doses of IL-2 (high dose IL-2)
- ANV419 induces a higher fold increase of CD8+ (c.) and NK (d.) cells than of Treg (e.) over multiple cycle
- Ratio CD8/Treg in peripheral blood increase over ANV419 treatment (f.)

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 has been generally well tolerated across cycles, dose escalation is ongoing at 364µg/kg
- No patients discontinued study due to drug related AEs
- ANV419 induces a selective and dose dependent proliferation of CD8+ T and NK cells, but a lower increase of proliferating Tregs
- At doses of ≥ 108µg/kg, 66% of patients achieved at least disease stabilization (9 SD and 1 PR)
- Based on these encouraging data, ANV419 will be studied in melanoma and in multiple myeloma
- Visit poster 1099 with the preclinical data supporting ANV419 combination studies

Acknowledgments

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