EXPAND-1, a Phase I/II study of ANV600, a PD-1 targeted IL-2Rβγ agonist, in monotherapy and in combination with pembrolizumab, in advanced solid tumors

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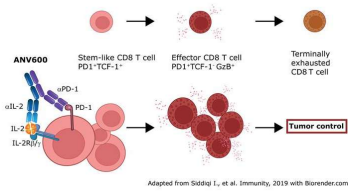
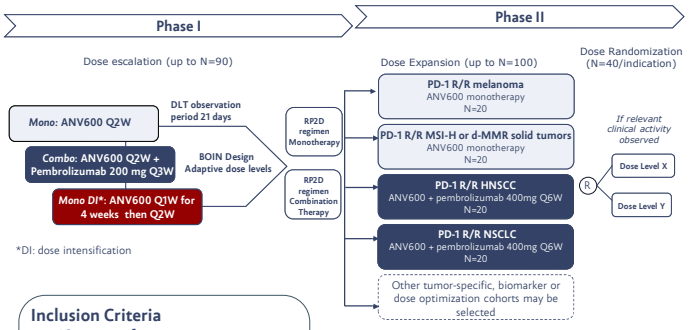
Background

ANV600 is a novel PD-1-targeted, IL-2Rβ/γ agonist, which binds, without blocking, a unique epitope distinct from pembrolizumab, or other PD-1 checkpoint inhibitors. It is designed to preferentially stimulate PD-1⁺ CD8⁺ T cells with a pre-exhausted, cytotoxic phenotype, aiming to activate tumor antigen-experienced T cells within the tumor microenvironment. This targeted approach may reduce IL-2 related toxicities and potentiate response in checkpoint-refractory tumors.

Figure 1: Cell activation by ANV600



EXPAND-1 clinical programs and patient characteristics



Inclusion Criteria

- ≥ 18 years of age
- ECOG PS 0 or 1
- Measurable disease per RECIST v1.1 criteria
- Adequate organ function
- No IL-2 or IL-2 analogues prior anti-cancer therapy within 18 months
- No known active central nervous system metastases and/or carcinomatous meningitis

Primary Endpoints:

Phase I:

To determine MTD and/or RP2D of ANV600 single agent and in combination with pembrolizumab

Phase II:

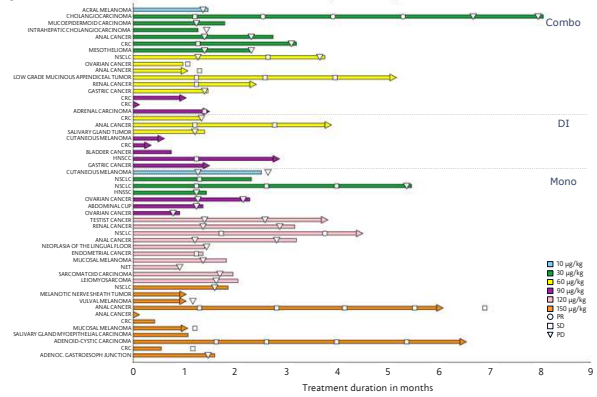
To assess the anti-tumor activity of ANV600 as single agent and in combination with pembrolizumab

Demographic /performance status	Total n=52 (%)
Age (mean; years)	60
Male	33
Female	19
ECOG PS 0	20
ECOG PS 1	32
Primary cancer diagnosis	
Colorectal Cancer (CRC)	7
Anal Cancer	6
Non-small Cell Lung Cancer (NSCLC)	5
Ovarian Cancer	3
Cutaneous Melanoma	2
Gastric Cancer	2
Head And Neck Squamous Cell Carcinoma (HNSCC)	2
Renal Cancer (RCC)	2
Mucosal Melanoma	2
Other	21
Prior line of therapy	
Lines of prior systemic therapy (range)	4 (1 - 16)

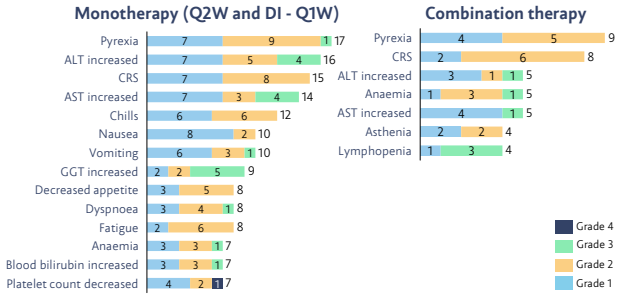
Results

EXPAND-1: Ongoing and completed dose escalation cohort status

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

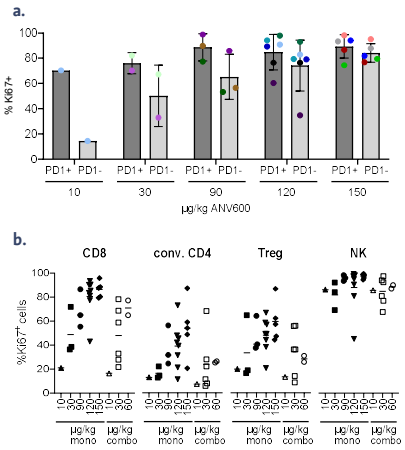


Safety: ANV600 related AEs reported in ≥ 20% of Patients (CTCAE v5.0)



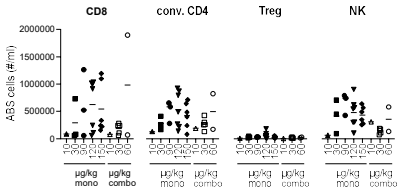
- ANV600 was generally well tolerated
- All drug-related events were reversible
- Eight patients received tocilizumab or corticosteroids for CRS management
- Three patients treated at 150 µg/kg in monotherapy had DLTs
- One patient treated at 60 µg/kg in combination therapy had a DLT (G2 immune-mediated myocarditis)
- Two G4 related AEs (lymphocyte count decrease and platelet count decrease)
- No capillary leak syndrome was observed

Pharmacodynamics: Percentage of proliferating immune cells in peripheral blood



Pharmacodynamic data at C1D4 demonstrate selective targeting of IL-2 to PD-1⁺ cells, confirmed by preferential induction of proliferating PD-1⁺ CD8⁺ over PD-1⁻ CD8⁺ T cells (Fig a., data from monotherapy cohort). ANV600 treatment results in higher proportions of proliferating CD8⁺ T cells and NK cells compared to Tregs, consistent with its IL-2Rβγ-selective mechanism of action (Fig b.).

Pharmacodynamics: Absolute count of immune cell subsets in peripheral blood



ANV600 treatment results in higher absolute numbers of CD8⁺ T cells than Tregs in peripheral blood at C1D8.

Conclusions

- In this first group of patients, ANV600 is well tolerated as monotherapy and in combination with pembrolizumab
- Symptoms related to CRS (mainly prolonged pyrexia and some tachycardia) and transient increase of liver transaminases were the most frequently reported AEs
- All drug-related events were reversible and responded to standard supportive therapy
- MTD and RP2D have not yet been determined
- PRs were reported for one patient treated with 120 µg/kg ANV600 monotherapy and one patient treated with 30 µg/kg ANV600/pembrolizumab combination
- Treatment with ANV600 resulted in a dose-dependent preferential stimulation of PD1⁺ CD8 T cells with higher absolute counts of CD8⁺ T cells and NK cells over regulatory T cells

Thank you to all sites and patients in the study!

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