Translation to the clinic of EVT801: A novel immune-oncology agent for expanding patient population responding to immune checkpoint therapies

Selective inhibitor of VEGFR3 for patients resistant to immune checkpoint inhibitors: Clinical translation activities

Olivier Bogen, Bertrand Bertrand, Julien Mazières, Dominique Cheng, Anne Gomez, Sarah Pradines, Pierre Fons,ธนาวัฒน์ทรัพย์กู์, Michael Fallerer, Anna Lenzmann, and Dominique Vallet

Circulating MEDSCs as stratification biomarker IMMUNOPREDICT Trial NCT02827344

Overview

**Drug concept**
- EVT801 is a novel immune-oncology agent for expanding patients population responding to immune checkpoint therapies
- EVT801 is a highly effective agent in preclinical models
- EVT801 has shown to increase T cell/MDSC ratio
- EVT801 is currently in late preclinical development and is anticipated to be Phase 1 ready in Q3 2018

**Target clsse**
- Solid tumours with VEGFR3 expression and/or microenvironment

**Project status**
- EVT801 is currently in late preclinical development and is anticipated to be Phase 1 ready in Q3 2018

**Targeted indication**
- Combination with immune checkpoint therapies for non-responder patients with VEGFDR/microenvironment

**Gateways indicator**
- Solid tumours with VEGFR3 microenvironment and/or microenvironment

**Administration**
- One administration

**Biomarkers**
- Patient stratification: VEGFR3 expression on TME & circulating MEDSCs quantification
- PD biomarker: ERK/AKT phosphorylation & gene signature
- Improvement of activity: Gene signature related to resistance to PD1/VEGFR3 signalling pathways

**Patient stratification**
- VEGFR3 expression on TME & circulating MEDSCs quantification
- Increase M1 macrophages
- No 2 Biopsies feasible
- Gene signature related to resistance to PD1/VEGFR3 signalling pathways

**Current ideas for clinical plan up to PoC**

**EVT801: Decreasing circulating MDSCs and Increasing CD8+ T-cell tumour infiltration to generate anti-tumour immunity**

- EVT801 MoA in immuno-oncology
- EVT801 and combination with anti-PD1 mAb: Acting on hypoxia to control tumour outgrowth

**Dedicated biomarker approach developed for EVT801**
- Patient stratification: VEGFR3 expression on tumour cells and in TME tumour microenvironment from biopsies
- High level of circulating MEDSCs
- Baseline circulating markers of suppressor cells and response to anti-PD1 mAbs in non-small cell lung cancer patients: Collaboration Oncopodect CRCT/Evotec (IMMUNOPREDICT trial NCT02827344)

**Biomarker of activity/resistance**
- Single agent: Gene signature related to resistance to PD1/VEGFR3 signalling pathways
- Combination with ICT (checkpoint Targeting Therapy): Quantiﬁcation of circulating immune cells and circulating MEDSCs
- Single agent and Combination with ICT: Development of specific labelling by ICT related to EVT801 MoA for co-treatment biopsies

We are actively looking for partners for clinical development

---

**EVT801: Decreasing circulating MDSCs and Increasing CD8+ T-cell tumour infiltration to generate anti-tumour immunity**

**Circulating MEDSCs as stratification biomarker**

**IMMUNOPREDICT Trial NCT02827344**

**Overview**

- **Drug concept**
  - EVT801 is a novel immune-oncology agent for expanding patients population responding to immune checkpoint therapies
  - EVT801 has shown to increase T cell/MDSC ratio
  - EVT801 is currently in late preclinical development and is anticipated to be Phase 1 ready in Q3 2018

- **Target class**
  - Solid tumours with VEGFR3 expression and/or microenvironment

- **Project status**
  - EVT801 is currently in late preclinical development and is anticipated to be Phase 1 ready in Q3 2018

- **Targeted indication**
  - Combination with immune checkpoint therapies for non-responder patients with VEGFDR/microenvironment

- **Gateways indicator**
  - Solid tumours with VEGFR3 microenvironment and/or microenvironment

- **Administration**
  - One administration

- **Biomarkers**
  - Patient stratification: VEGFR3 expression on TME & circulating MEDSCs quantification
  - PD biomarker: ERK/AKT phosphorylation & gene signature
  - Biomarker of activity: Gene signature related to resistance to PD1/VEGFR3 signalling pathways

- **Patient stratification**
  - VEGFR3 expression on TME & circulating MEDSCs quantification
  - Increase M1 macrophages
  - No 2 Biopsies feasible
  - Gene signature related to resistance to PD1/VEGFR3 signalling pathways

- **Current ideas for clinical plan up to PoC**

  - **EVT801: Decreasing circulating MDSCs and Increasing CD8+ T-cell tumour infiltration to generate anti-tumour immunity**
    - EVT801 MoA in immuno-oncology
    - EVT801 and combination with anti-PD1 mAb: Acting on hypoxia to control tumour outgrowth

  - **Dedicated biomarker approach developed for EVT801**
    - Patient stratification: VEGFR3 expression on tumour cells and in TME tumour microenvironment from biopsies
      - High level of circulating MEDSCs
      - Baseline circulating markers of suppressor cells and response to anti-PD1 mAbs in non-small cell lung cancer patients: Collaboration Oncopodect CRCT/Evotec (IMMUNOPREDICT trial NCT02827344)

    - **Biomarker of activity/resistance**
      - Single agent: Gene signature related to resistance to PD1/VEGFR3 signalling pathways
      - Combination with ICT (checkpoint Targeting Therapy): Quantiﬁcation of circulating immune cells and circulating MEDSCs
      - Single agent and Combination with ICT: Development of specific labelling by ICT related to EVT801 MoA for co-treatment biopsies

    - We are actively looking for partners for clinical development