

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

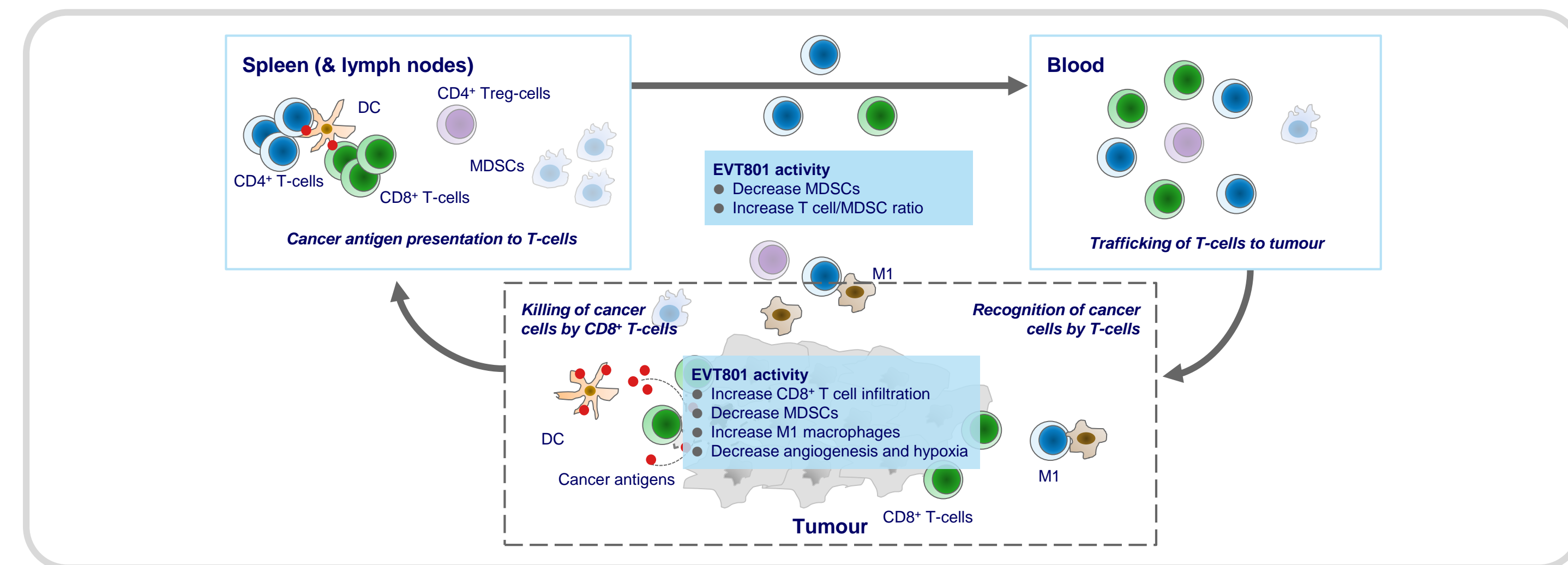
## Selective inhibitor of VEGFR3 for patients resistant to immune checkpoint inhibitors: Clinical translation activities

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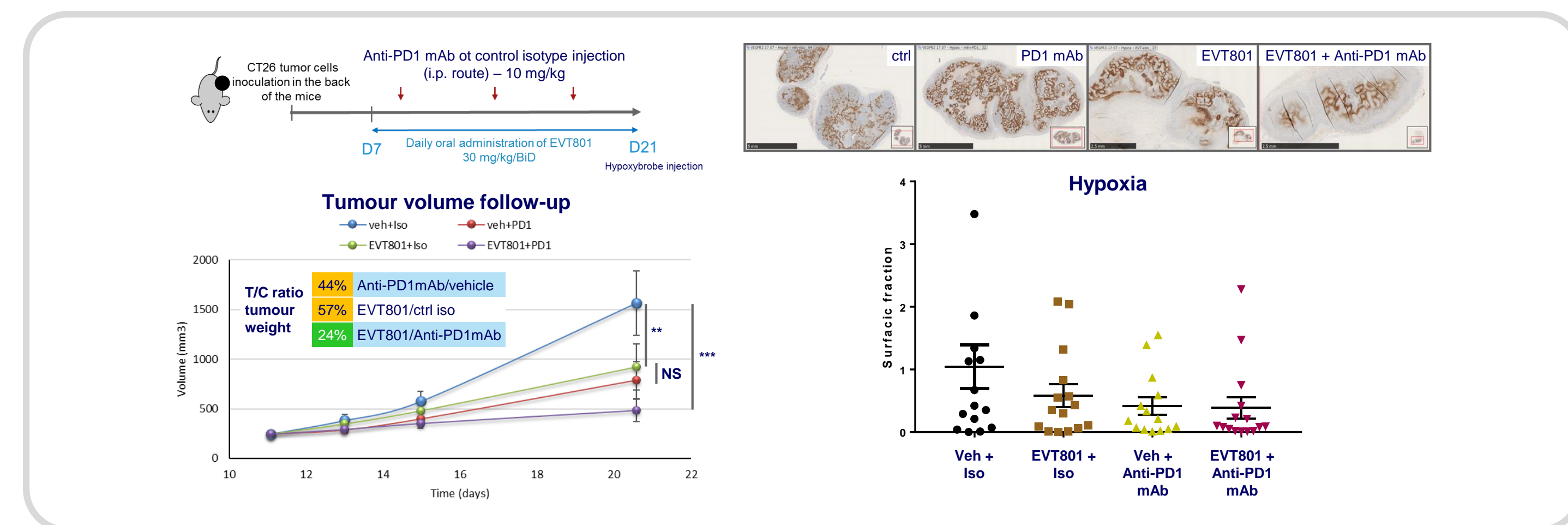
### Overview

<b>Drug concept</b>	● Develop a small molecule for cancer immunotherapy that targets immunosuppressive cell trafficking to increase ICT response rate
<b>Target class</b>	● EVT801 is a selective inhibitor of the VEGFR3 tyrosine kinase
<b>Project status</b>	● EVT801 is currently in late preclinical development and is anticipated to be Phase 1 ready in Q3 2018
<b>Targeted indication</b>	● Combination with immune checkpoint therapies for non-responder patients with VEGFR3 <sup>+</sup> microenvironment
<b>Gateway indication</b>	● Solid tumours with VEGFR3 <sup>+</sup> microenvironment and/or Kaposi's sarcoma as orphan disease
<b>Administration</b>	● Oral administration
<b>Biomarkers</b>	● Patient stratification: VEGFR3 expression on TME & circulating MDSCs quantification ● PD biomarker: ERK/AKT phosphorylation & gene signature ● Biomarker of activity: Gene signature & circulating immune-cells quantification

### EVT801 MoA in immuno-oncology

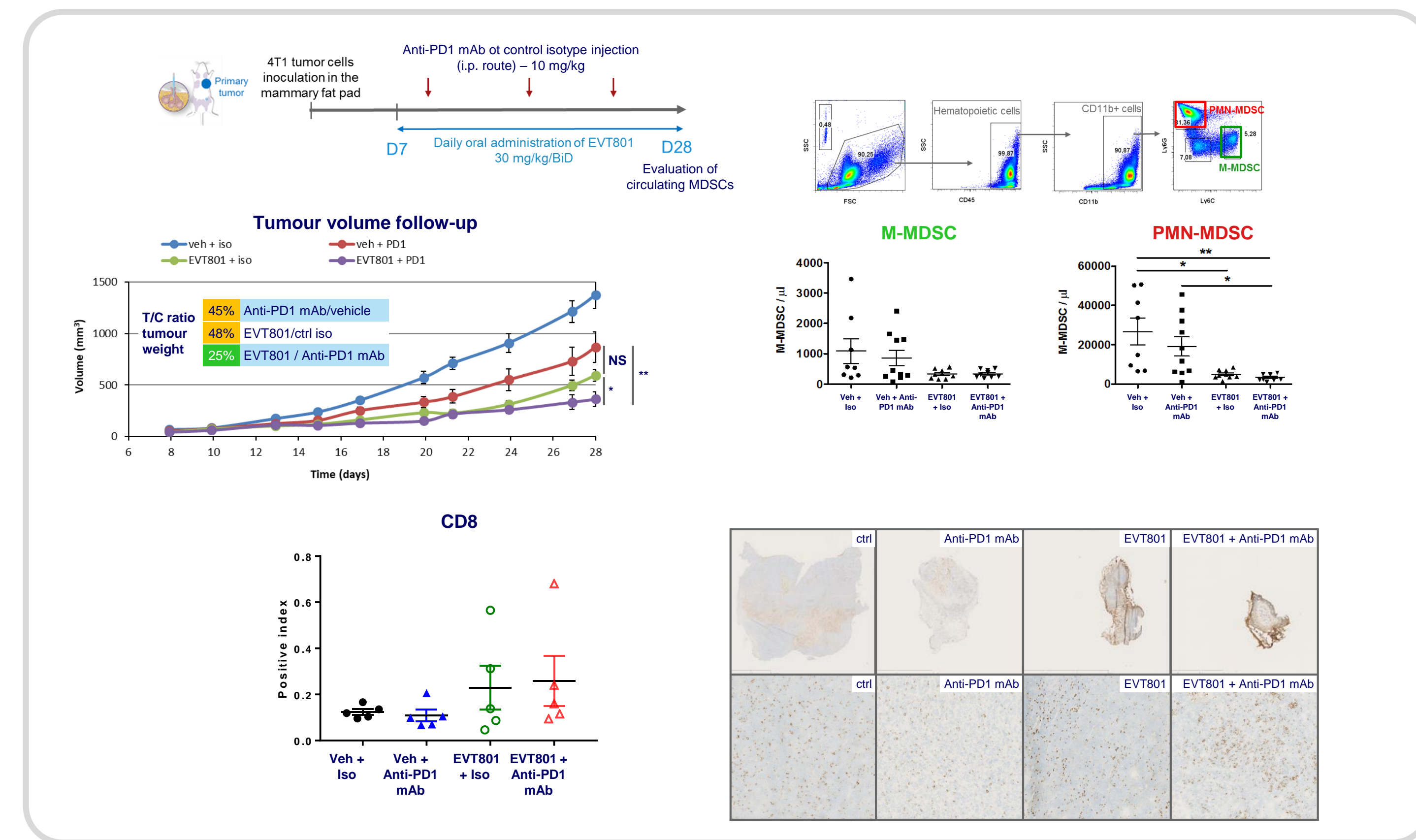


### EVT801 and combination with anti-PD1 mAb: Acting on hypoxia to control tumour outgrowth

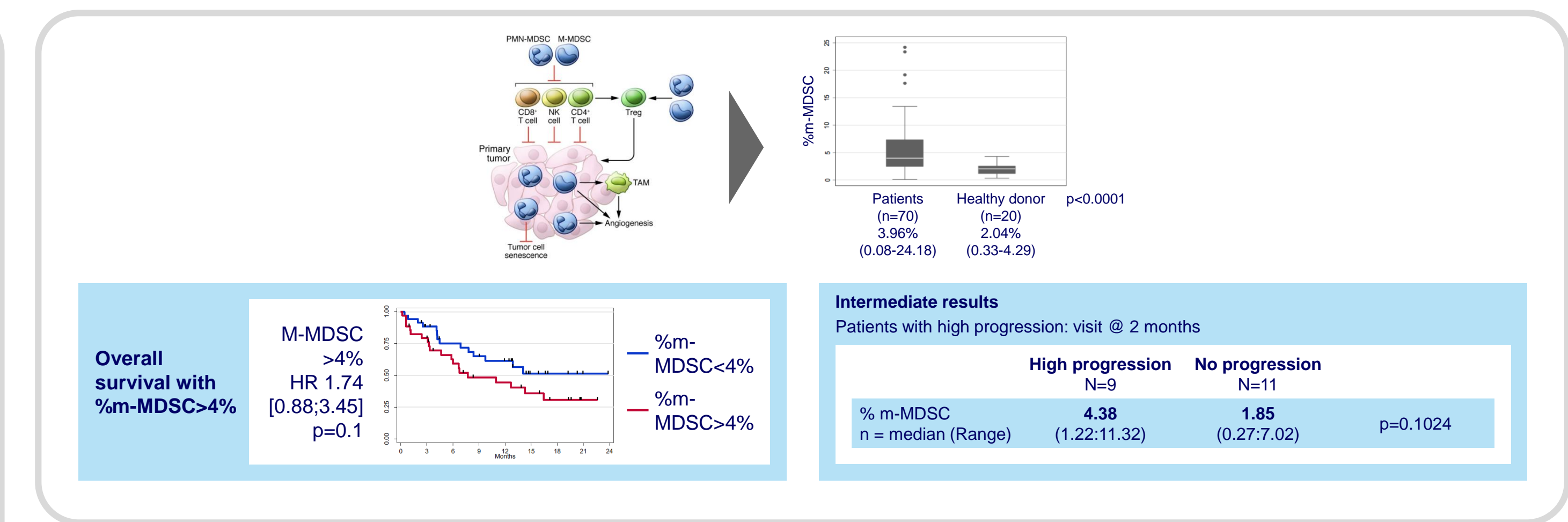


**The CT26 mouse model is a model with heterogeneity, highly dependent on hypoxia and with low MDSC frequency**  
 ● Combination of EVT801 and anti-PD1 mAb results in a strong therapeutic activity  
 ● Treatment with EVT801 is associated with a decrease of hypoxia

### EVT801: Decreasing circulating MDSCs and increasing CD8<sup>+</sup> T-cell tumour infiltration to generate anti-tumour immunity



### Circulating MDSCs as stratification biomarker IMMUNOPREDICT trial NCT02827344

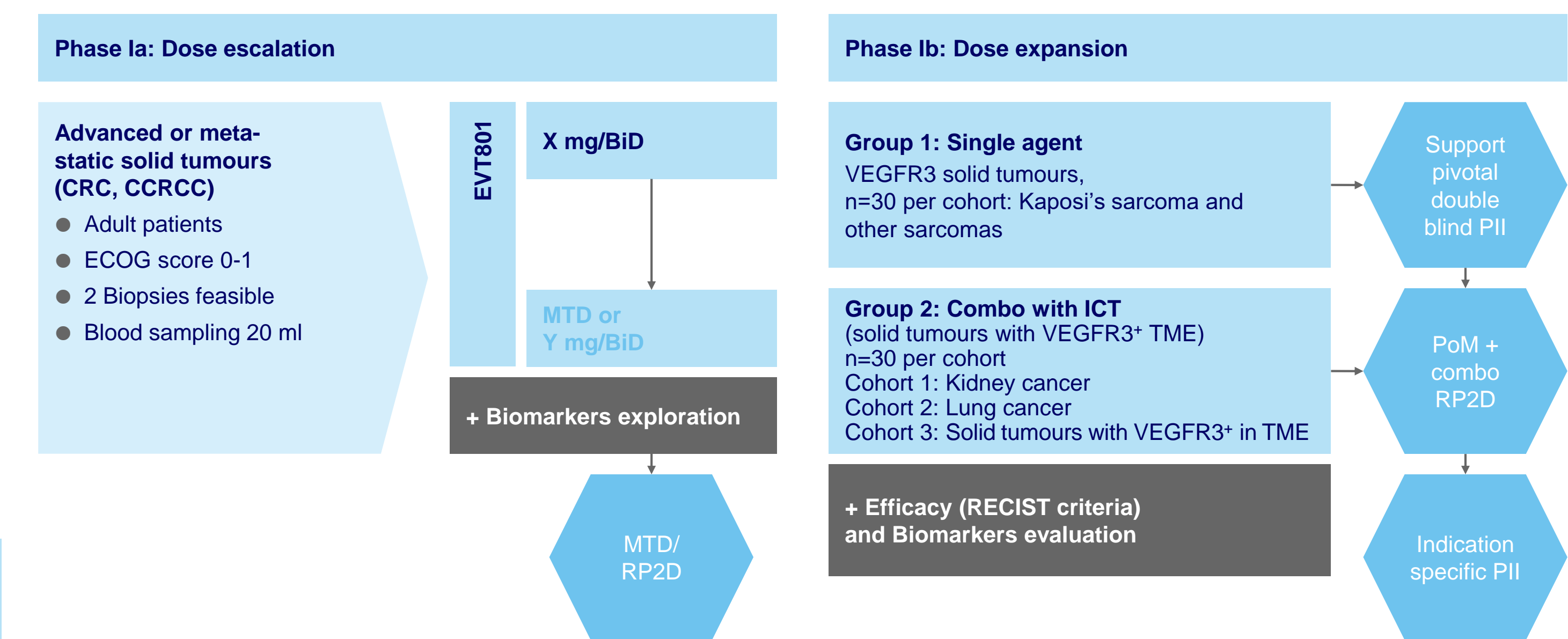


- Higher level of m-MDSCs in patients decrease Overall Survival
- Intermediate results seems to show that patients with high progression @ 2 months have a strong level of m-MDSCs and could be the population of interest for EVT801, especially if VEGFR3 is expressed in tumour and/or microenvironment

### VEGFR3 expression in tumour and microenvironment (in %)

Indication	HCC	HNSCC	NSCLC	Lung AC	Kaposi	CCRCC	Colon cancer
VEGFR3 expression in TME	30 to 100%	40%	100%	100%	100% on tumour cells	94%	30%
Access to patients eligible for Ph1a	No	Yes	+/-	+/-	Yes	Yes	Yes
Recommendation	Phase 2 combo	Ib combo	Ib combo	Ib combo	(1a) / 1b	(1a) / 1b	1a / 1b

### Current ideas for clinical plan up to PoC



### Dedicated biomarker approach developed for EVT801

- **Patient stratification**
  - VEGFR3 expression on tumour cells and in Tumour Microenvironment from biopsies
  - High level of circulating MDSCs
  - Baseline circulating myeloid-derived suppressor cells and response to anti-PD1 mAb in non-small cell lung cancer patients: Collaboration Oncopole/CRCT/Evotec (IMMUNOPREDICT trial NCT02827344)
- **Biomarker of activity/resistance**
  - **Single agent**
    - Gene signature related to resistance to PD1/VEGFR3 signalling pathways
    - Phosphorylation pathways: pERK and pAKT
  - **Combination with ICT (Immune Checkpoint Therapies)**
    - Quantification of circulating immune cells and circulating MDSCs
  - **Single agent and Combination with ICT**
    - Development of specific labelling by IHC related to EVT801 MoA for on-treatment biopsies

**We are actively looking for partners for clinical development**