

# Small molecule in combination with Immune Checkpoint therapies

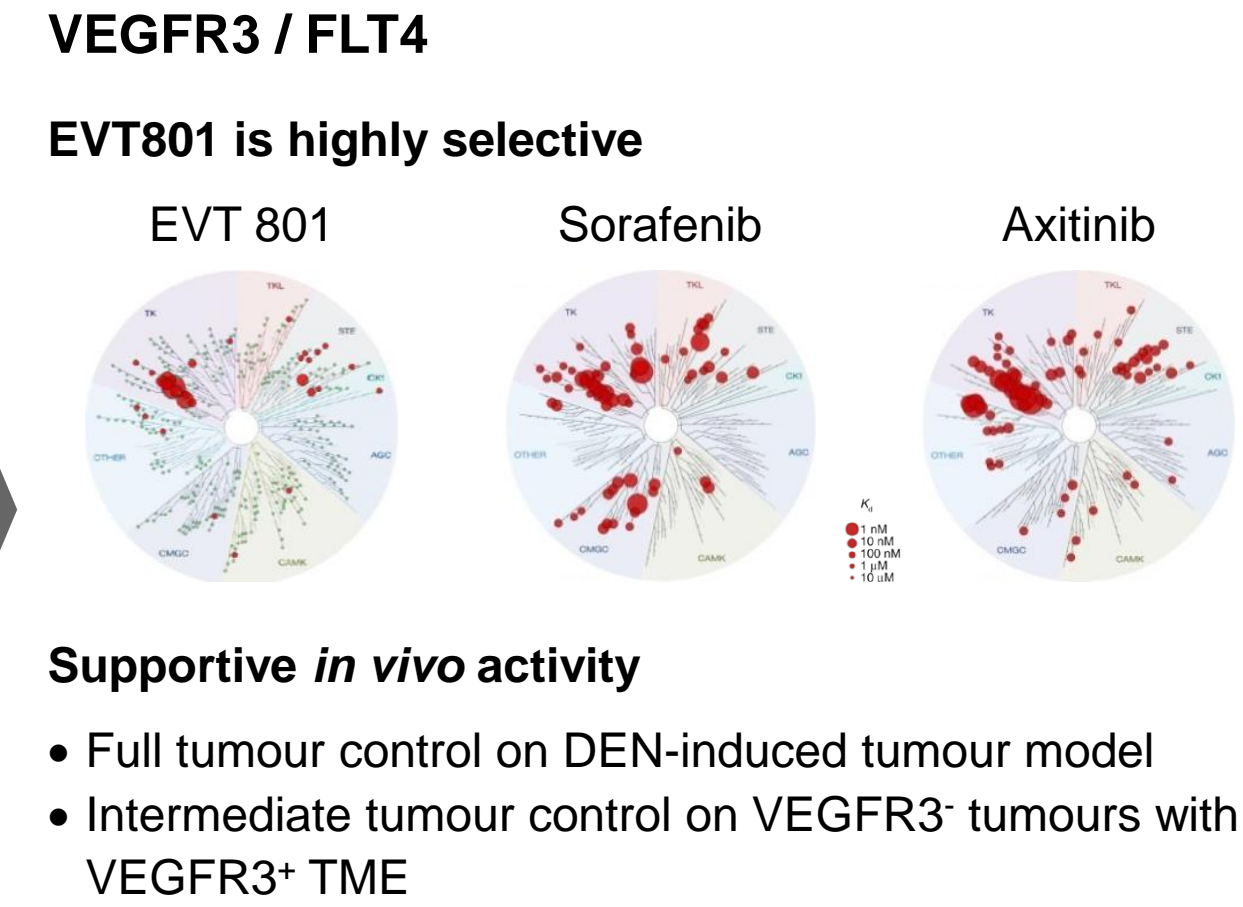
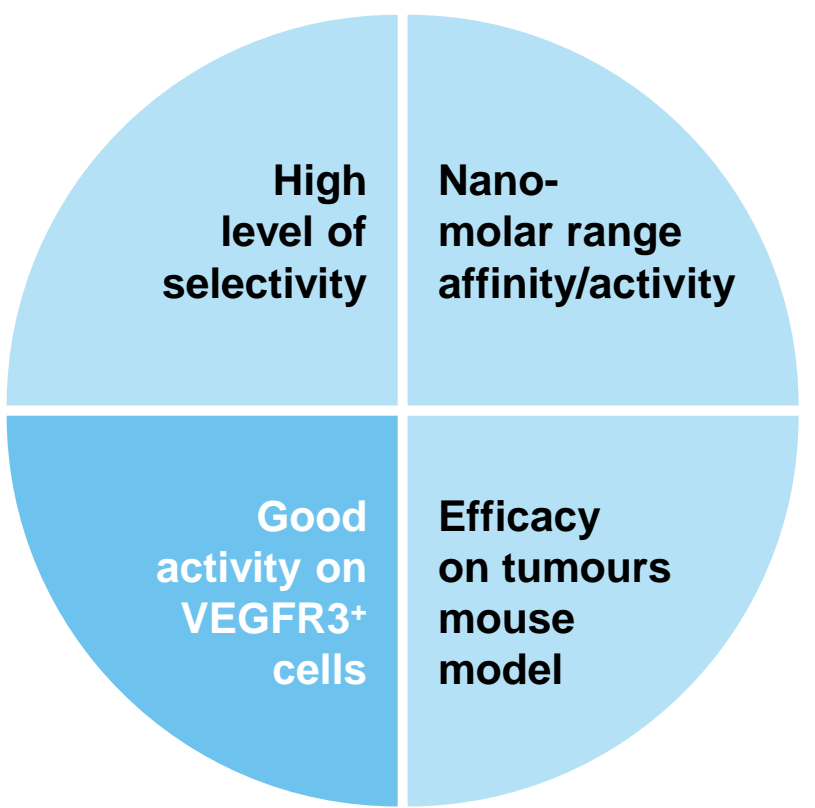
## Positive immunomodulation by specific VEGFR3 inhibition

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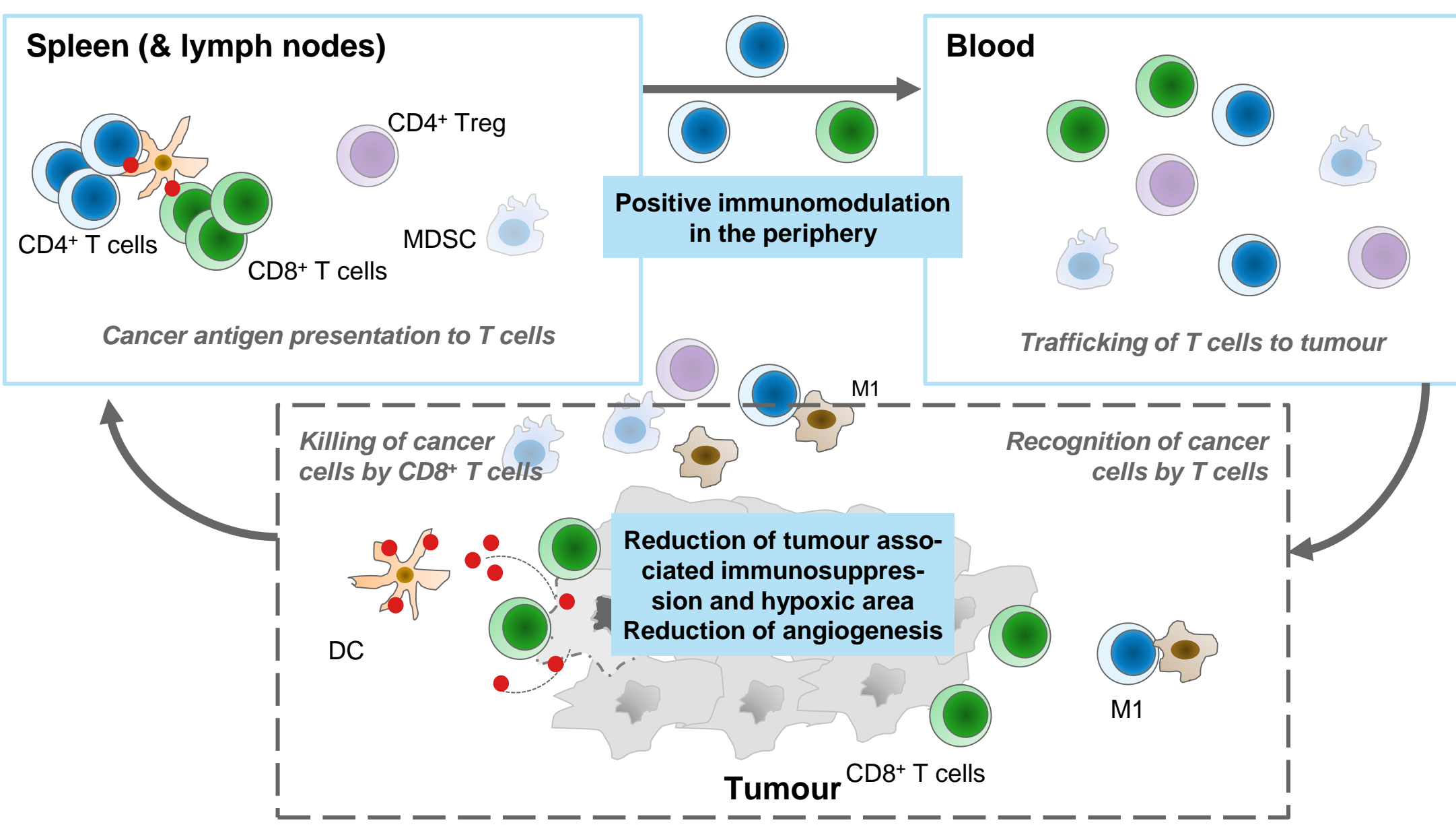
<b>Drug concept</b>	Develop a small molecule for cancer immunotherapy that targets immunosuppressive cell trafficking to increase ICT response rate
<b>Target class</b>	EVT801 is a specific inhibitor of the tyrosine kinase VEGFR3
<b>Project status</b>	Drug candidate / 1 year from phase I
<b>Targeted indication</b>	Combination with immune checkpoint therapies for non-responder patients
<b>Administration</b>	Oral administration

### Drug candidate profile

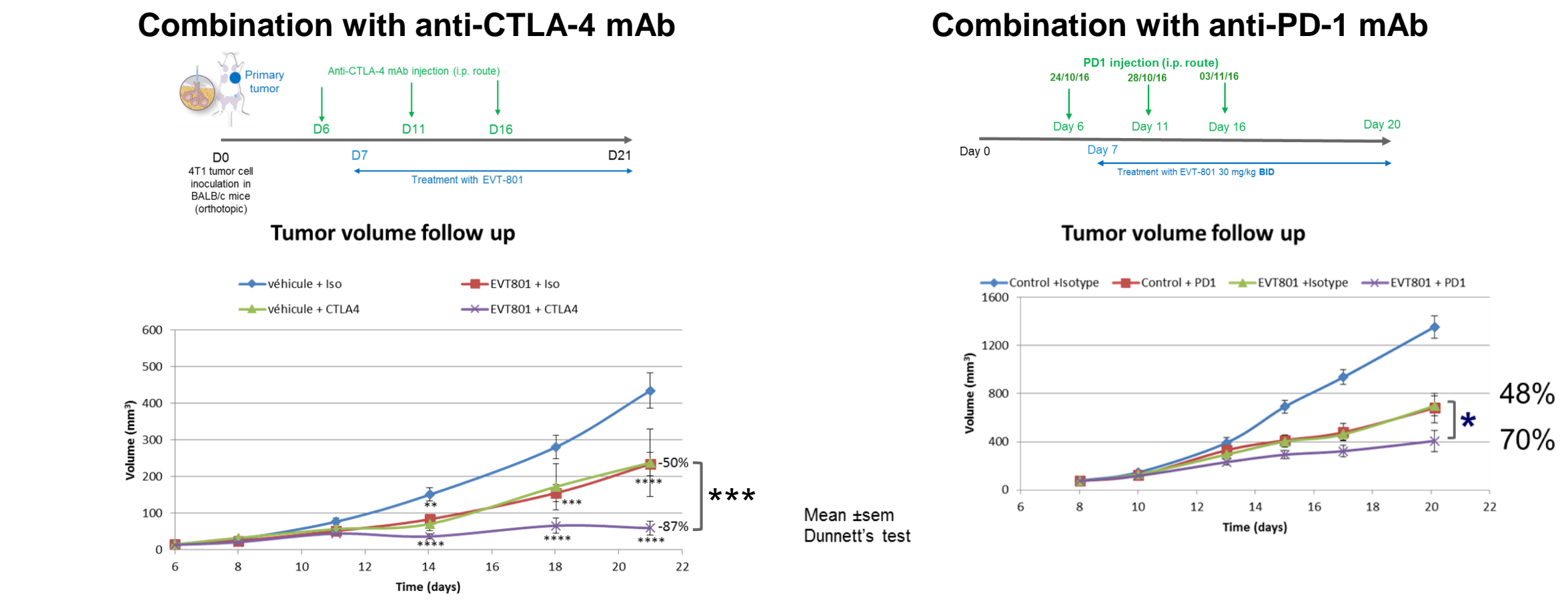


### Immuno-modulatory effects that we are seeking:

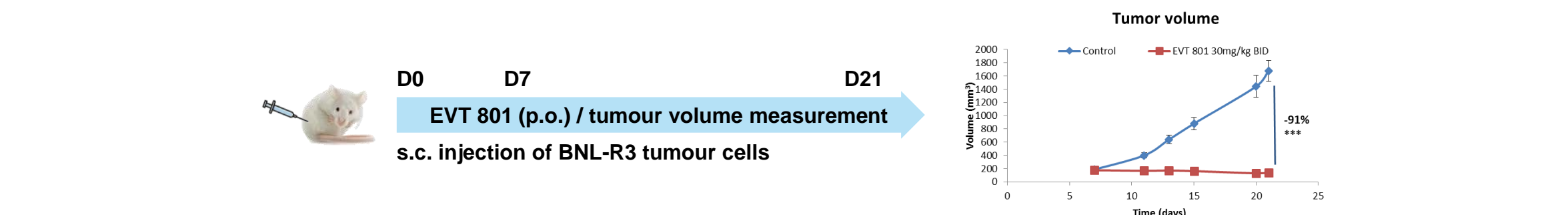
Optimal potential to synergize with immune check point inhibitors



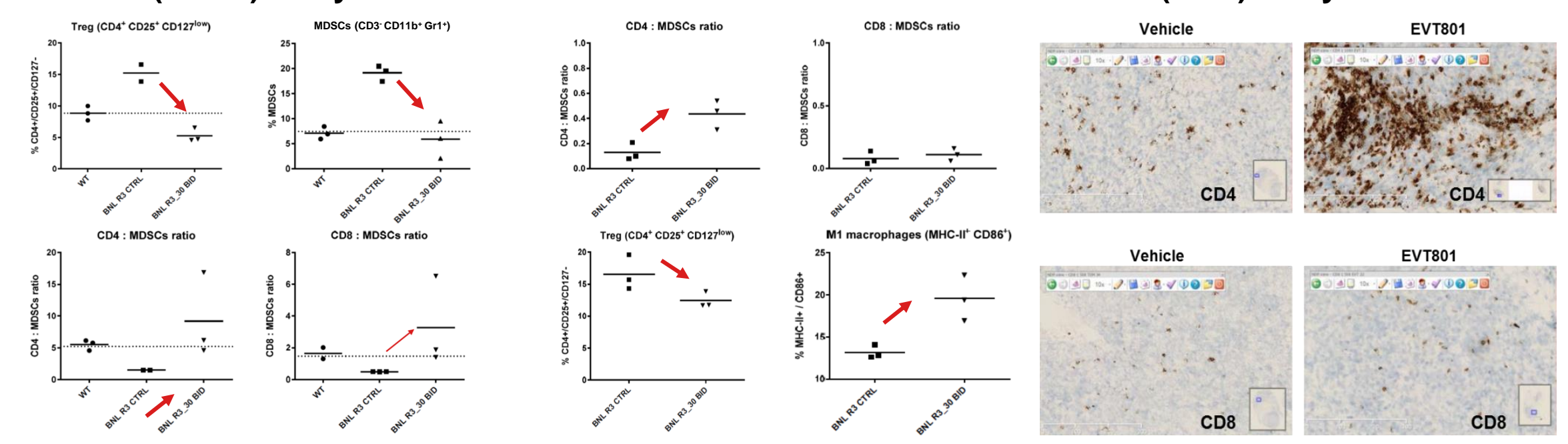
### Increased efficacy of combinations with ICTs



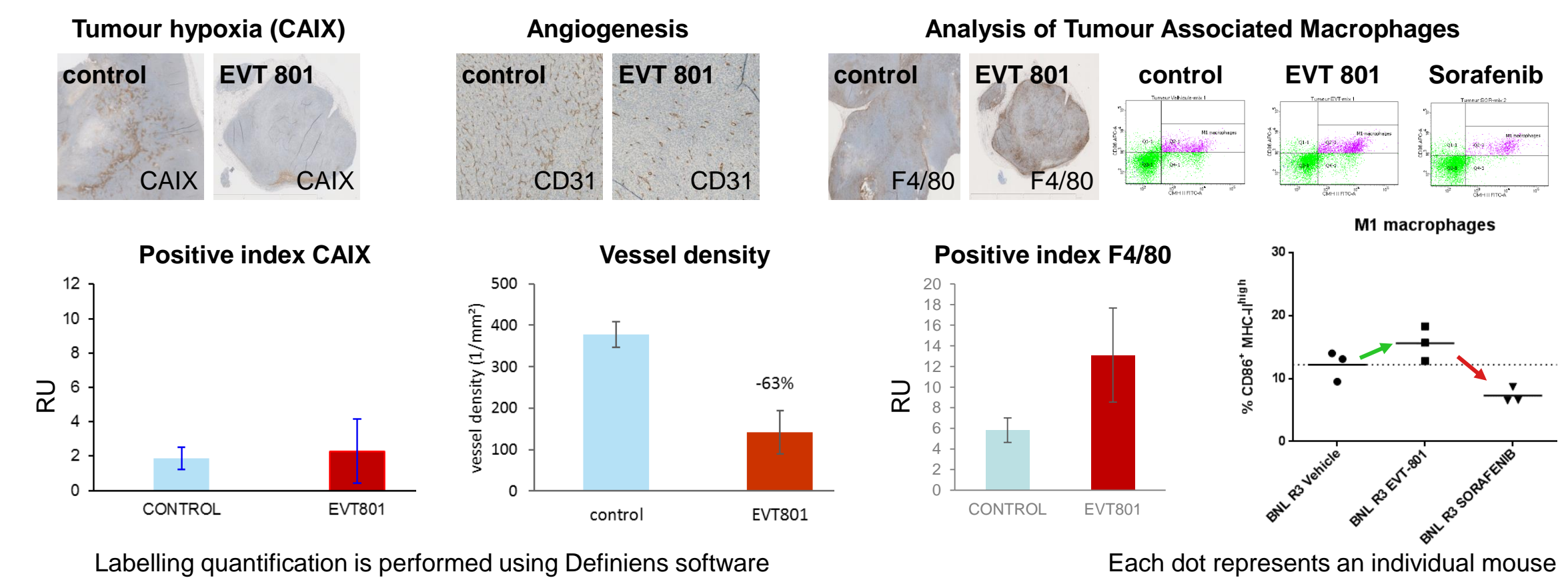
### Validation of EVT801 immuno-modulatory properties - activity on immune cells



### Peripheral Immunomodulation (blood) – day 21

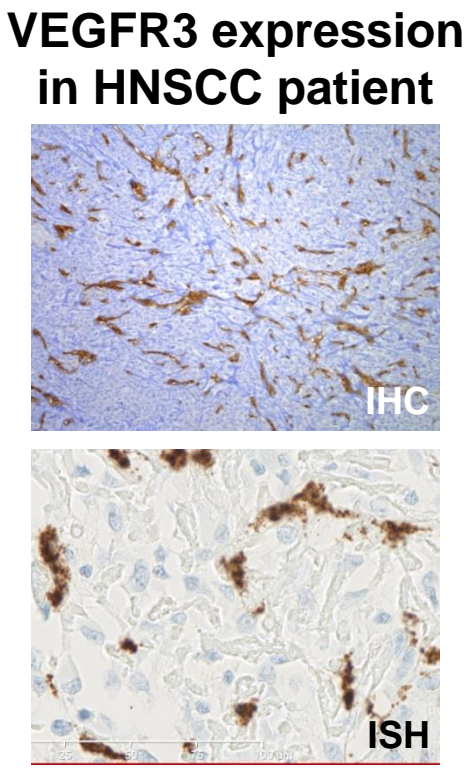


### Validation of EVT801 immuno-modulatory properties - activity on hypoxia and angiogenesis



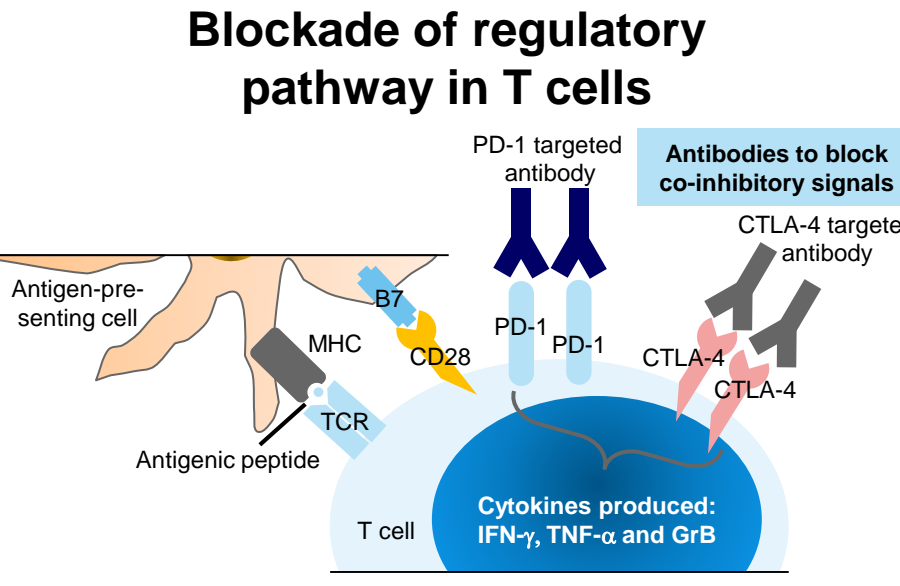
### Clinical Translation: biomarkers of stratification and activity

<b>Patient stratification</b>	VEGFR3 is expressed on 40-80% of the tumor microenvironment Specific cohorts are under investigation
<b>Biomarkers of activity in tumor</b>	Signaling pathway
<b>Biomarkers of activity in blood</b>	Collaboration with University Cancer institute of Toulouse for specific markers in patients receiving ICT



### Conclusion Sustained

- tumour blood vessel normalization**
- Decrease of tumour-associated immunosuppression**
  - Blood
    - Decrease of immunosuppressive cells: MDSCs
    - Increase of T cell: MDSCs ratio
  - Tumour
    - Increase of CD4+ TILs
    - Decrease of CD45+ PD-L1+ cells
    - Increase of M1 macrophages



Enhancement of antitumor immunity and activity on tumour microenvironment:  
**Potential to induce durable clinical responses**

- Efficacy**
  - Nanomolar activity on functional cellular assays
  - Strong anticancer effects in clinically relevant models
  - Greater efficacy expected in human (lower IC<sub>50</sub> and clearance)
- Selectivity**
  - ~10 fold less potent on VEGFR2 which is the only off-target
- MoA**
  - Long lasting anticancer effect
  - Sustained vessel normalization
  - Reduction of immunosuppression associated to tumour immunity
  - Sustained specific and memory T-cell responses without exhaustion
- First in Man Phase I clinical trial**
  - Expected in 2018

- Safety**
  - *In vitro* safety profile of EVT801 is compatible with progression into preclinical development
  - Therapeutic index above 10 according to rat DRF and monkey MTD
  - 4-week rat and monkey studies pending

**EVT801 has the potential to enlarge patient population sensitive to immune check point inhibitors**