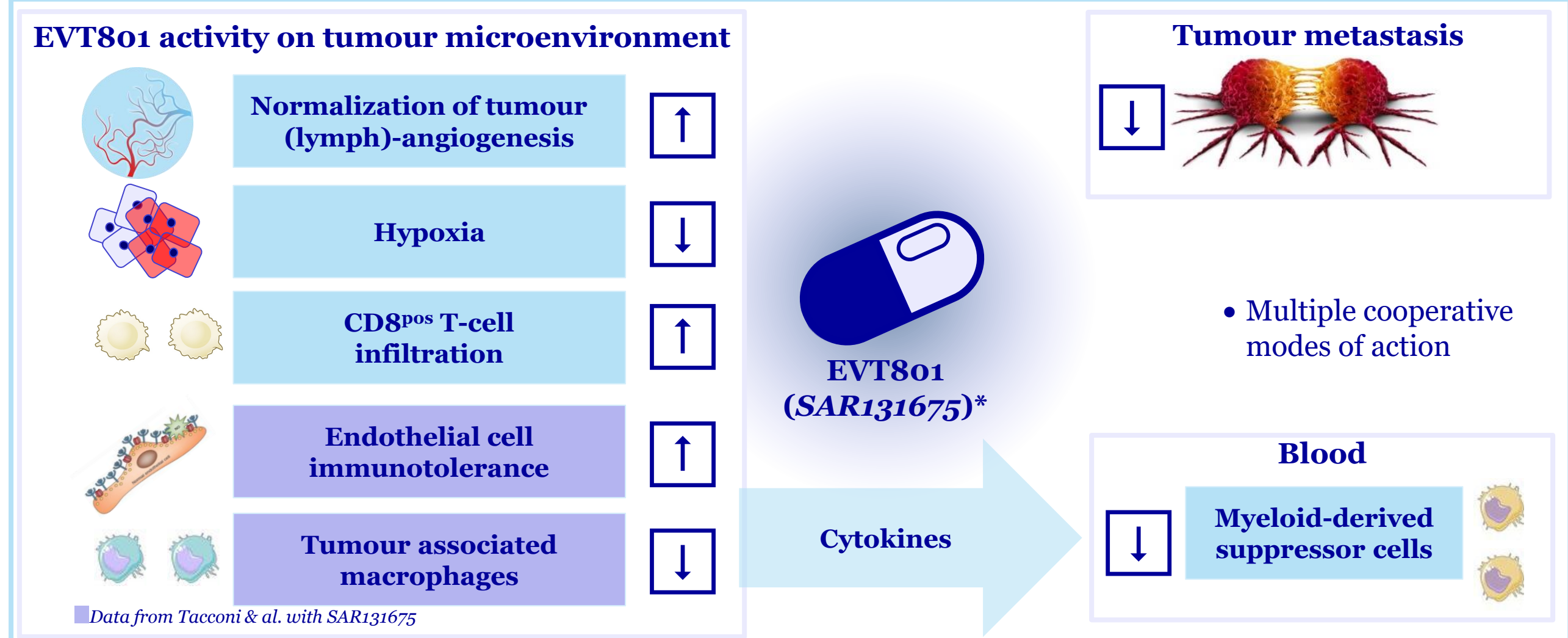


Carlos Gomez-Roca<sup>1</sup>, Philippe Cassier<sup>2</sup>, Philippe Rochaix<sup>1</sup>, Jean-Pierre Delord<sup>1</sup>, Lise Davenne<sup>3</sup>, Pierre-Benoit Ancy<sup>3</sup>, Oona Delpuech<sup>3</sup>, Vincent Piras<sup>3</sup>, Michael Paillasse<sup>3</sup>, John Friend<sup>4</sup>, Michael Fitzgerald<sup>4</sup> & Pierre Fons<sup>3\*</sup>  
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**FPN: 137P**

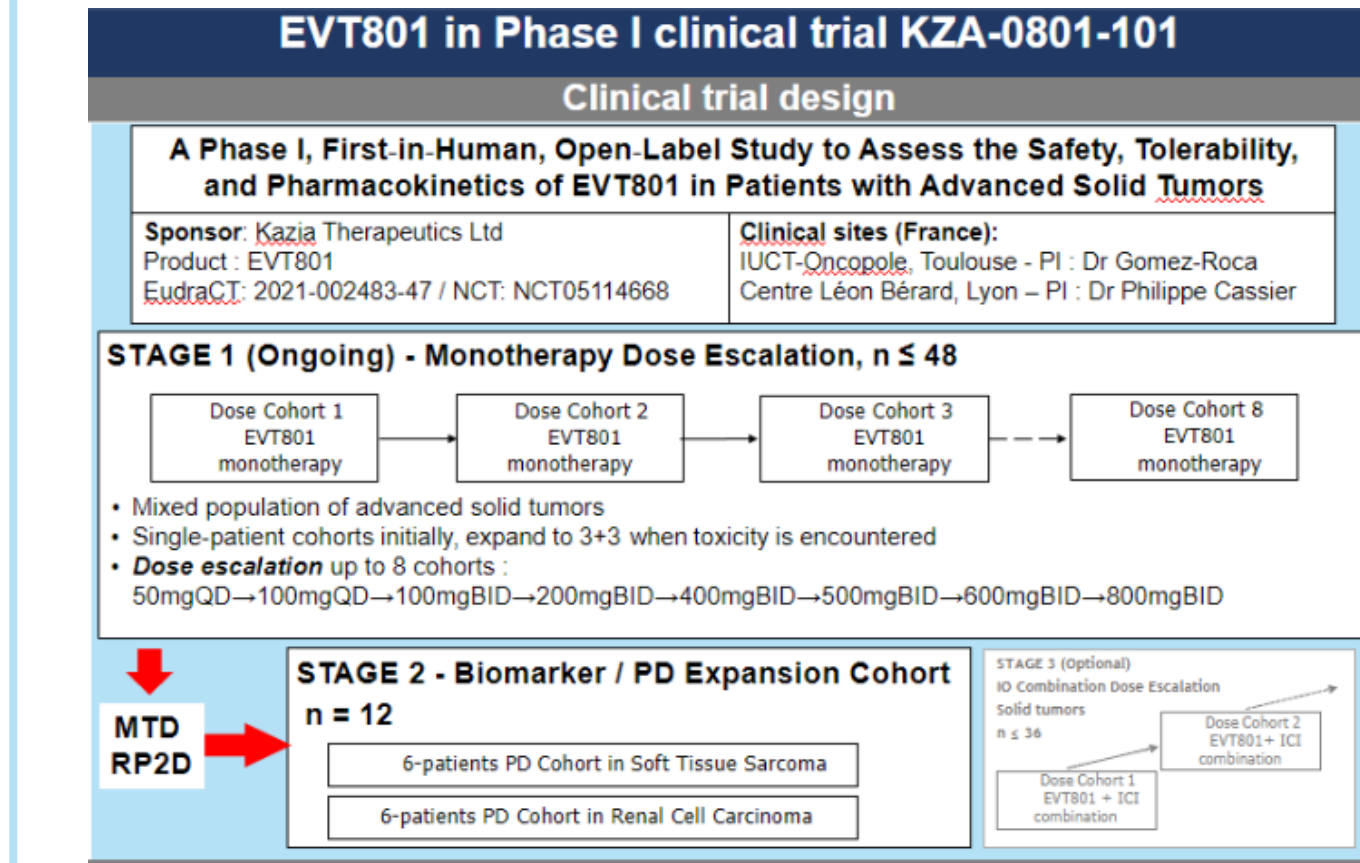
## EVT801: A differentiating anti-tumour approach

Targeting tumour angiogenesis with the selective VEGFR-3 inhibitor EVT801 in combination with cancer immunotherapy  
*Cancer Research Communications* (2022) 2 (11): 1504–1519.



**EVT801 MoA hypothesis:** EVT801 would induce VEGFR3<sup>POS</sup> tumour blood vessels normalization, reducing hypoxia and improving CD8<sup>POS</sup> T-cells infiltration

## EVT801 in Phase I clinical trial KZA-0801-101



**Approvals from regulatory bodies obtained in September 2021**

- First-Patient-In in Oct 2021
- 2 clinical sites in France (Toulouse IUCT and Lyon CLB)

**To date 26 patients included in stage I**

- 20 patients treated
- 5 cohorts (doses) reached up to 400 BID

**NCT05114668**

## EVT801 Biomarkers strategy

**Patient characterization based on VEGFR-3/CAIX/CD8 expression on archival tissues and/or biopsies**

- VEGFR-3 protein signature by histology
- VEGFR-3/CAIX/CD8/CD31/PD-L1

**VEGFR-3 & Resistance to PD-1 mAb mRNA signatures on archival tissues and/or biopsies:**

- VEGFR-3 mRNA signature by Fluidigm
- PD-1 mAb resistance mRNA signature

**Safety biomarkers to control hypertension:**

- Blood pressure measurement to control that EVT801 does not induce hypertension (as demonstrated in preclinical model)

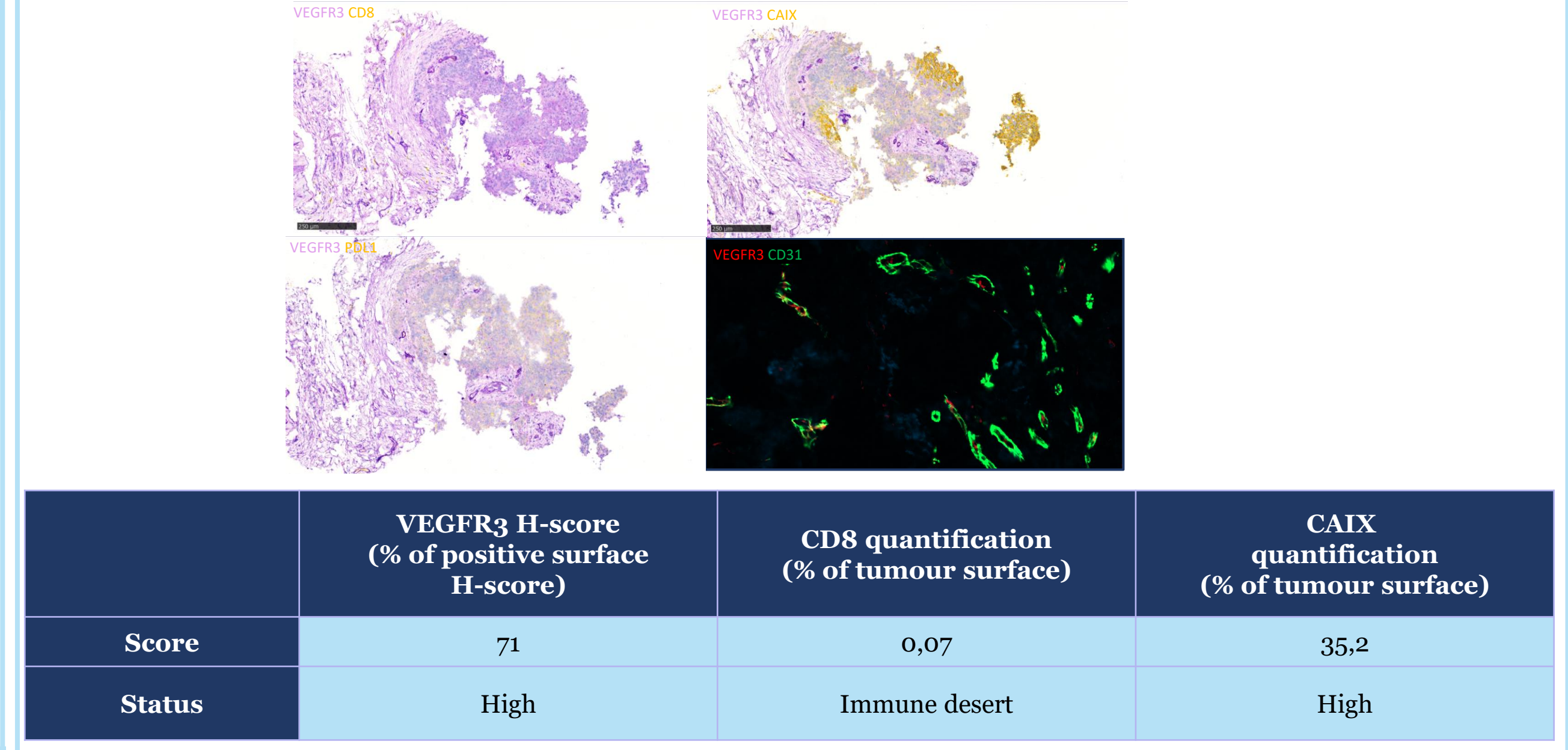
**Circulating endpoint biomarkers:**

- Immunomonitoring based on CD8<sup>POS</sup> T-cells / MDSC ratio
- Proteins signature based on chemokines involved in inflammation & angiogenesis

**Resting samples will include:**

- Frozen plasma
- Frozen whole blood
- Frozen PBMCs

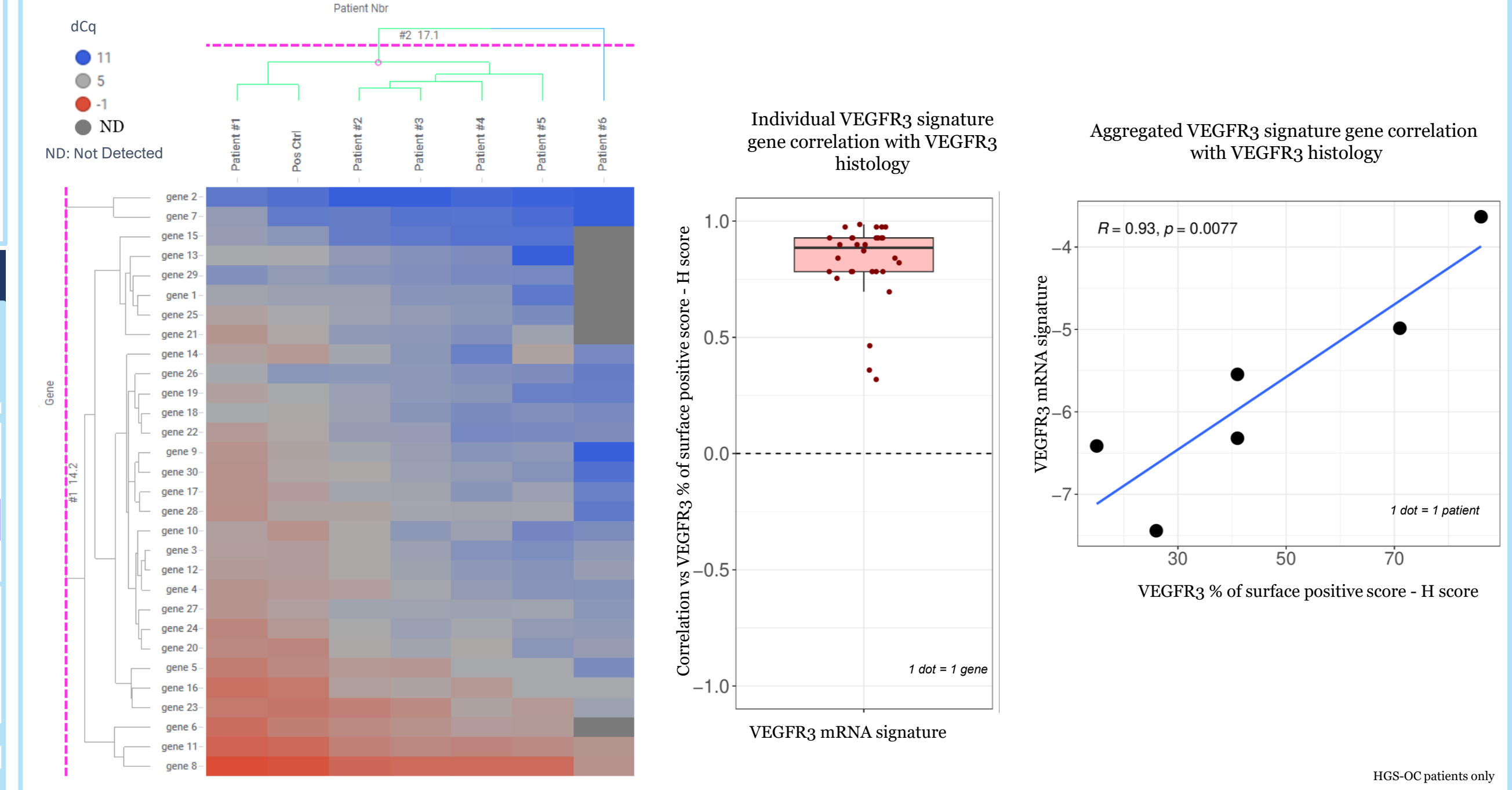
## Example of histology labelling on HGS-OC patient



## Correlation analysis in ovarian cancer patients

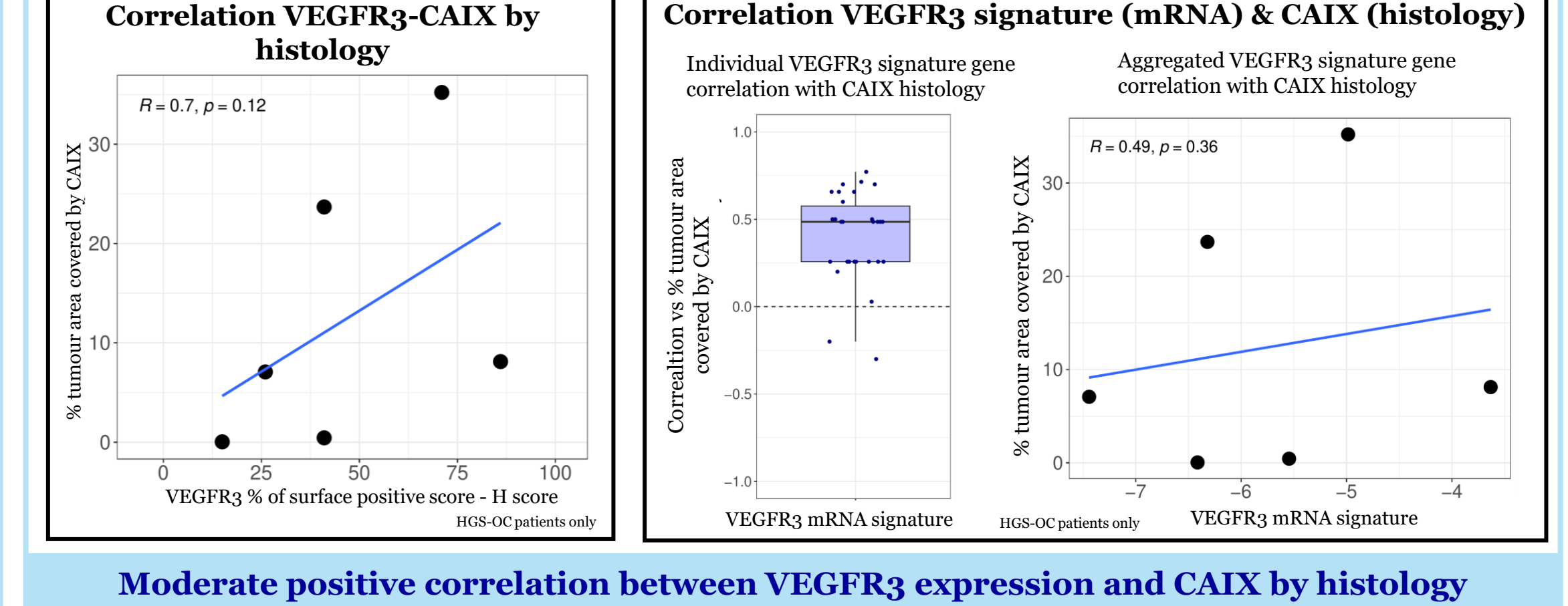
- Data analysis was performed on 6 patients with high grade serous ovarian cancer (HGS-OC) included into the clinical trial
- Hypotheses need to be confirmed with inclusion of new patients in different indications
- Bioinformatics team has designed signatures based on VEGFR3 associated genes and genes regulated differentially in resistant versus sensitive patients to PD1 mAb therapy
- Stage 2 will be pivotal to consolidate our hypotheses

## Correlation of VEGFR3 expression detected by histology & mRNA



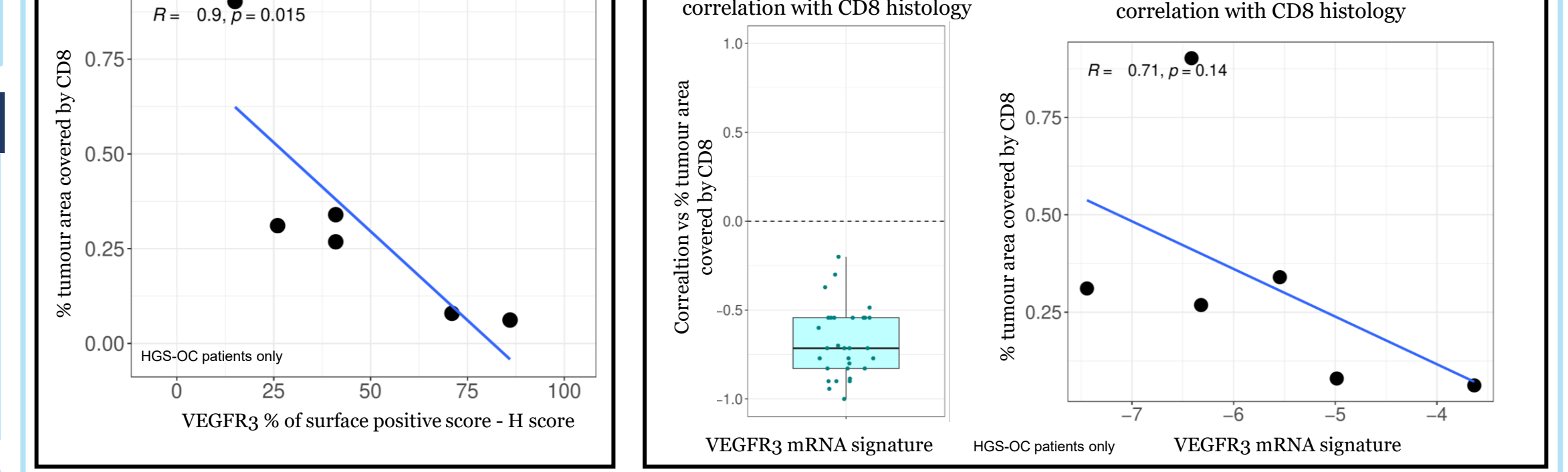
**Very strong correlation between VEGFR3 by histology and VEGFR3 mRNA signature allowing to compare mRNA signatures with other histology readouts**

## Correlation between VEGFR3 and CAIX expression

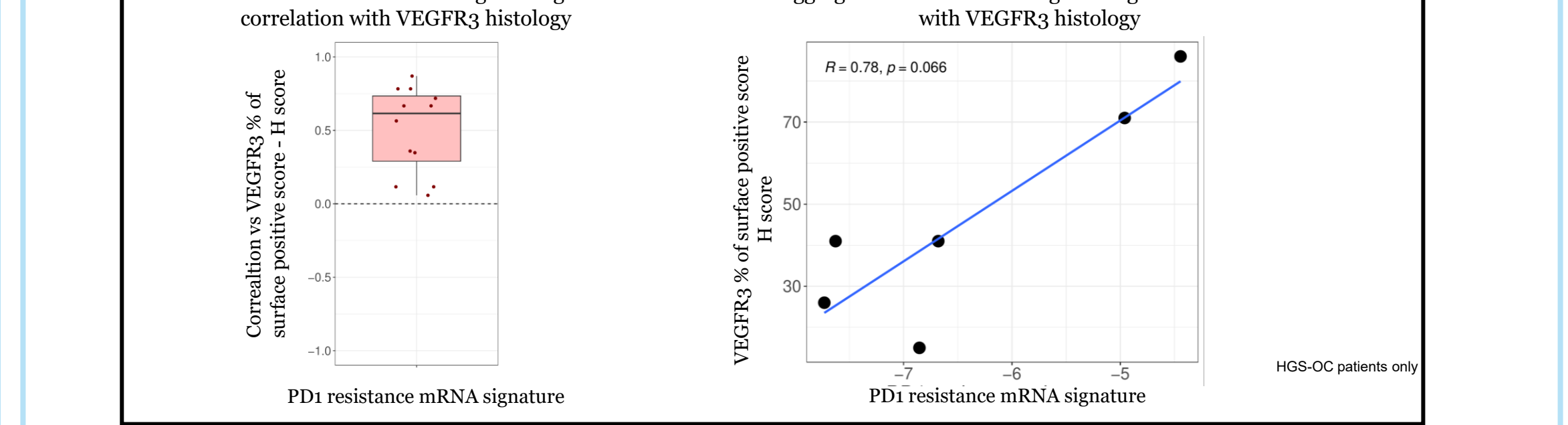


**Moderate positive correlation between VEGFR3 expression and CAIX by histology**

## Correlation between VEGFR3 and immune profile



## Correlation VEGFR3 (histology or mRNA signature) & PD1 mAb resistance signature



**High inverse correlation between VEGFR3 expression & CD8 expression and positive correlation between VEGFR3 expression & PD1 mAb resistance signature**

## Conclusion and next steps

- In HGS-OC patients enrolled, VEGFR3 expression tends to be positively correlated with hypoxia and PD1 resistance signature & negatively correlated with CD8<sup>POS</sup> T-cells infiltration.
- The correlations in HGS-OC patients are highly encouraging and informational while aligning with the EVT801 mechanism of action
- Patients with hypoxic HGS-OC tumour poorly infiltrated with CD8<sup>POS</sup> T-cells and with high VEGFR3 expression could benefit from EVT801 treatment