Biomarkers: Where do we go from here?

Brian I. Rini, MD

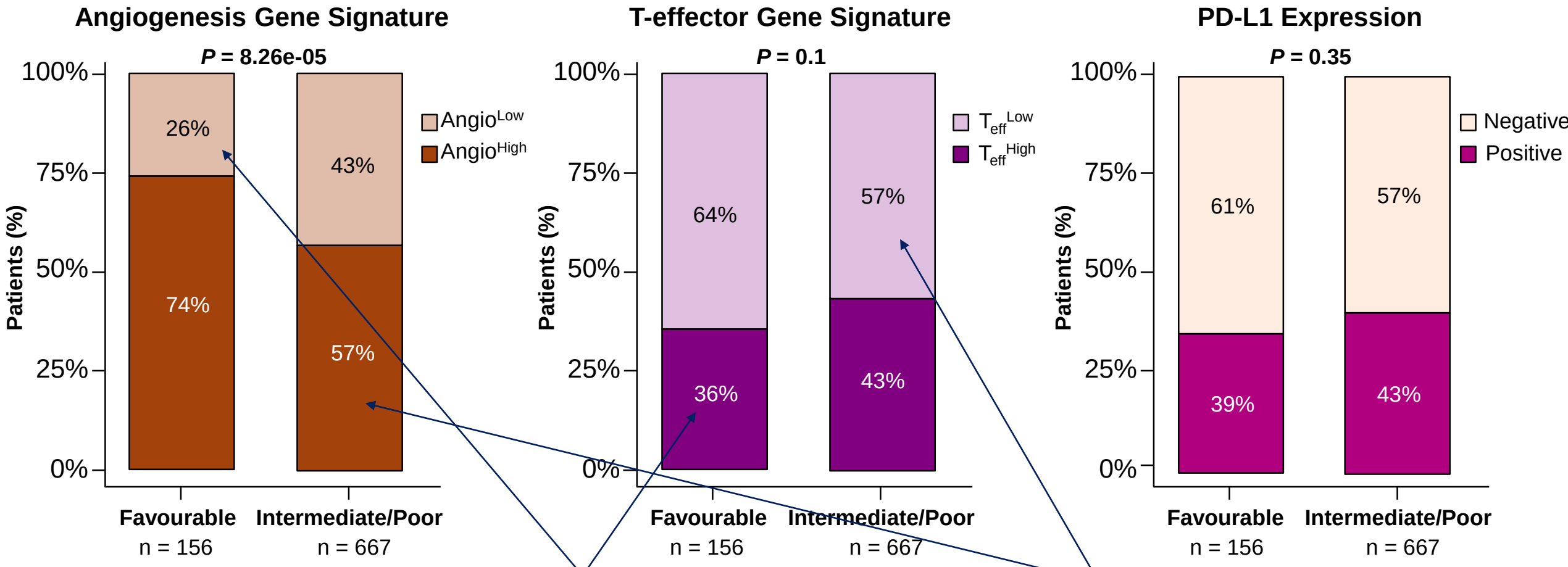
The Issue

- BOTH IO/IO and IO/VEGF are active regimens for front-line mRCC.
  - Both can produce durable disease control
  - Both have subpopulations that benefit more (or less/not at all)
  - Toxicity is not inconsequential with either, and can be life-threatening

- It is likely that across patients, or within a given patient, that VEGF-responsive, PD-1 responsive and CTLA-4-responsive subpopulations exist.

- One approach is to give all mechanisms to all patients, the other is to biologically (or clinically) define patient subsets to maximize benefit risk and give as little therapy as possible not as much as possible.

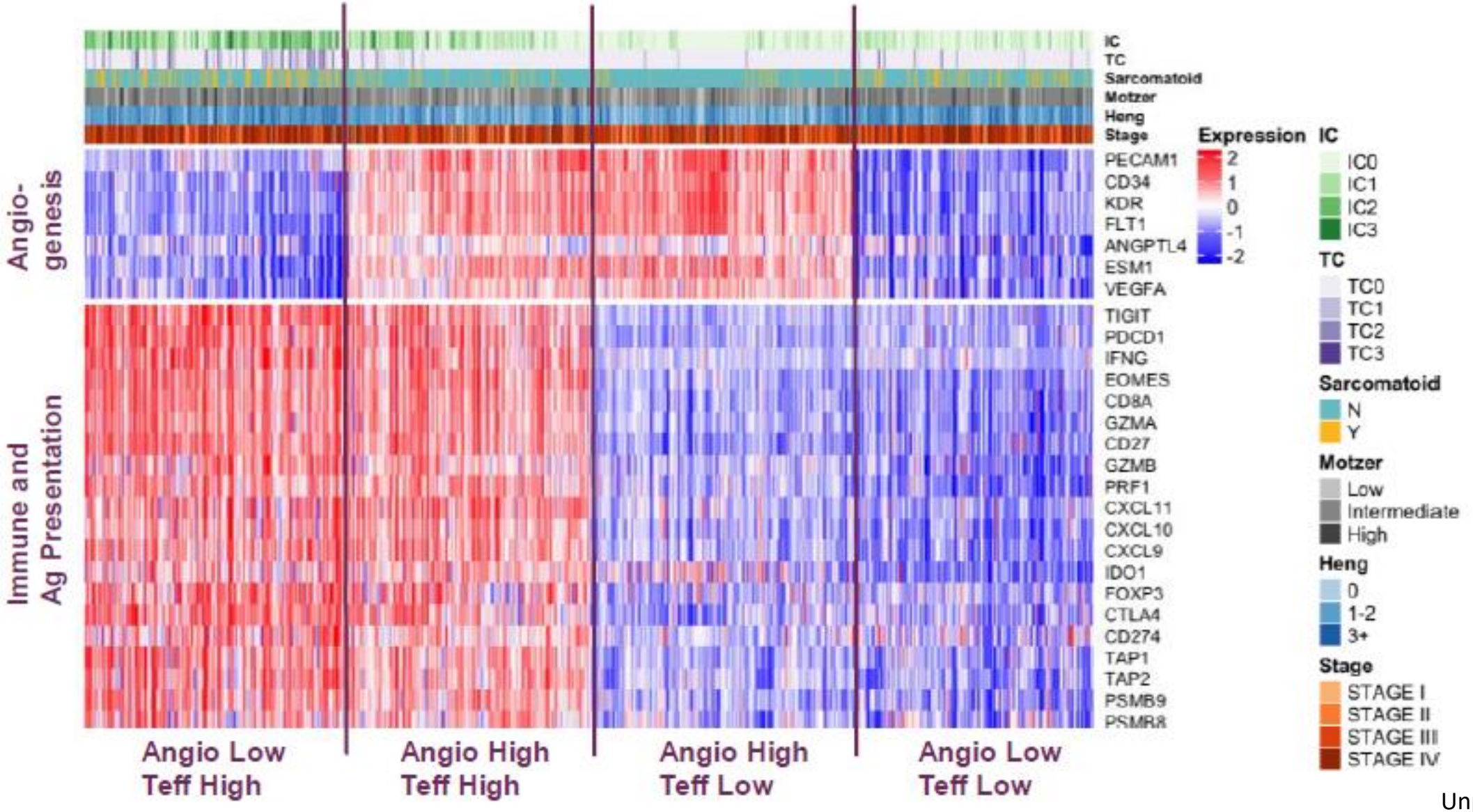
VEGF and PD1/CTLA-4 axis are both important in RCC biology



A significant proportion of favorable risk patients are Angio low and Teff high and likely to 'need' IO therapy

A significant proportion of int/poor risk patients are Angio high and Teff low and likely to 'need' VEGF therapy

Biomarker subgroups from IMmotion 151



Unpublished data

KidneyCAN

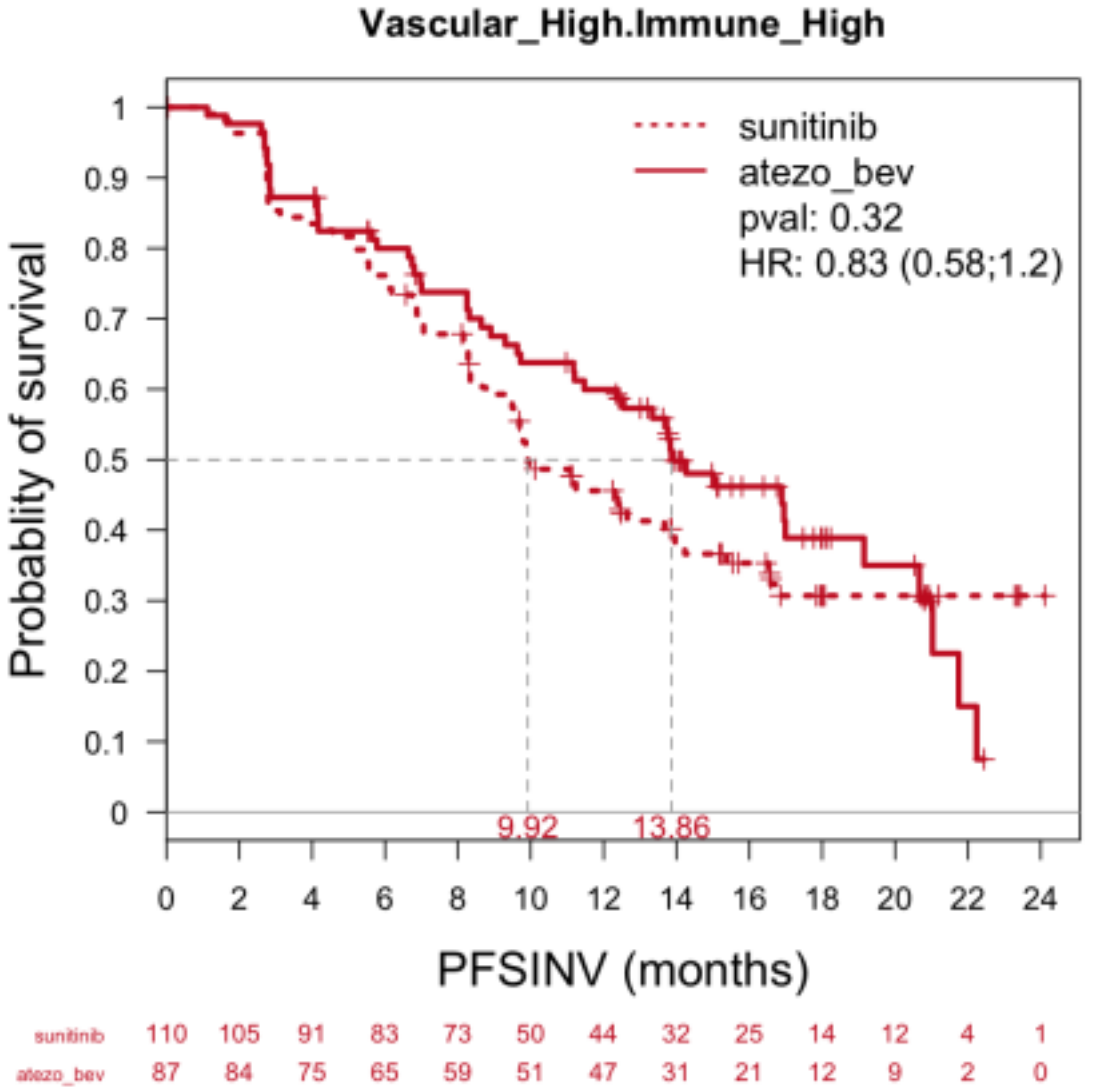
A biomarker-based approach

Angio high / Teff high → VEGF + IO

Angio high / Teff low → VEGF monotherapy or VEGF + IO

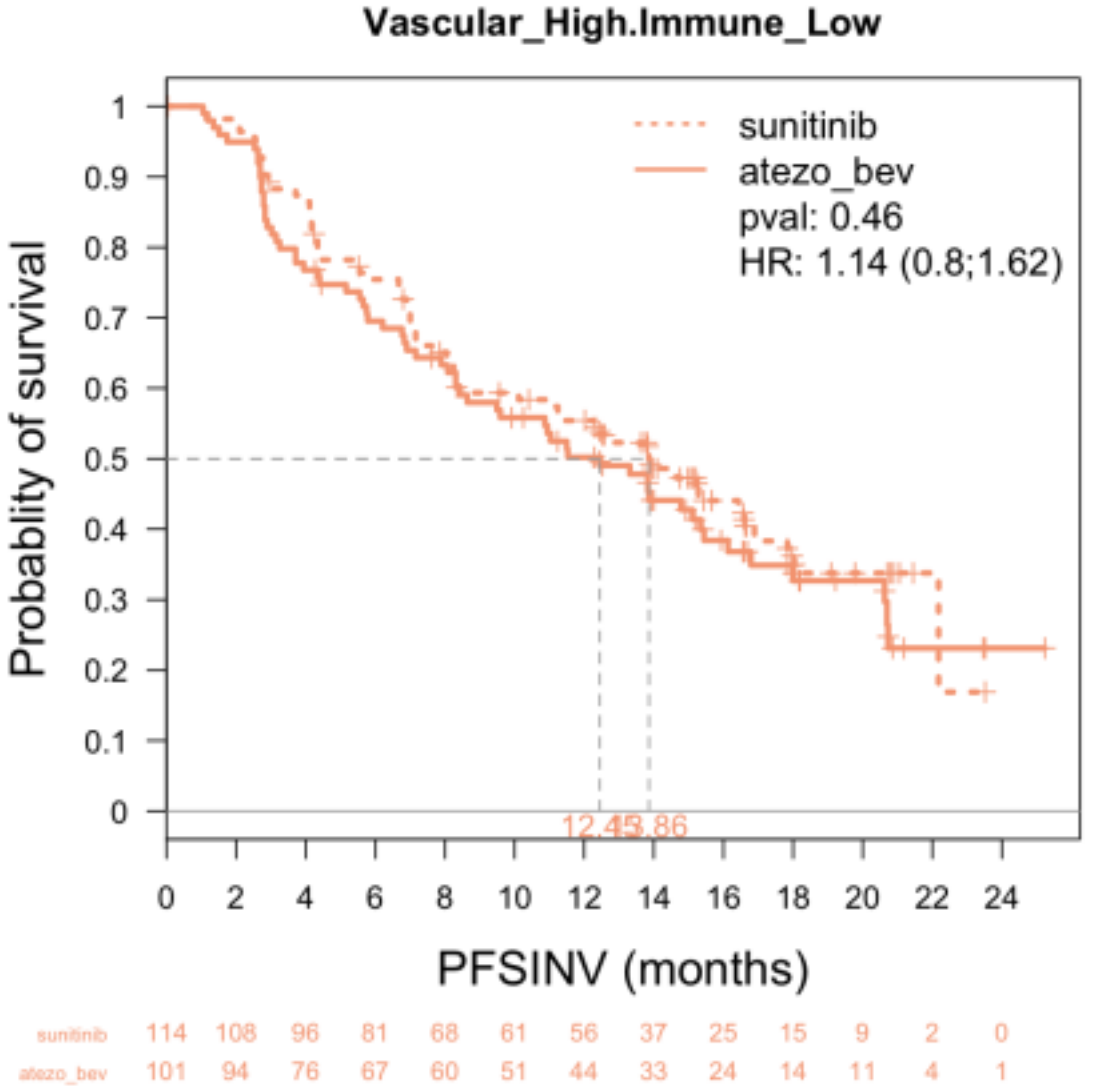
Angio low/ Teff high → IO monotherapy or IO + IO

Angio low/ Teff low → Something else



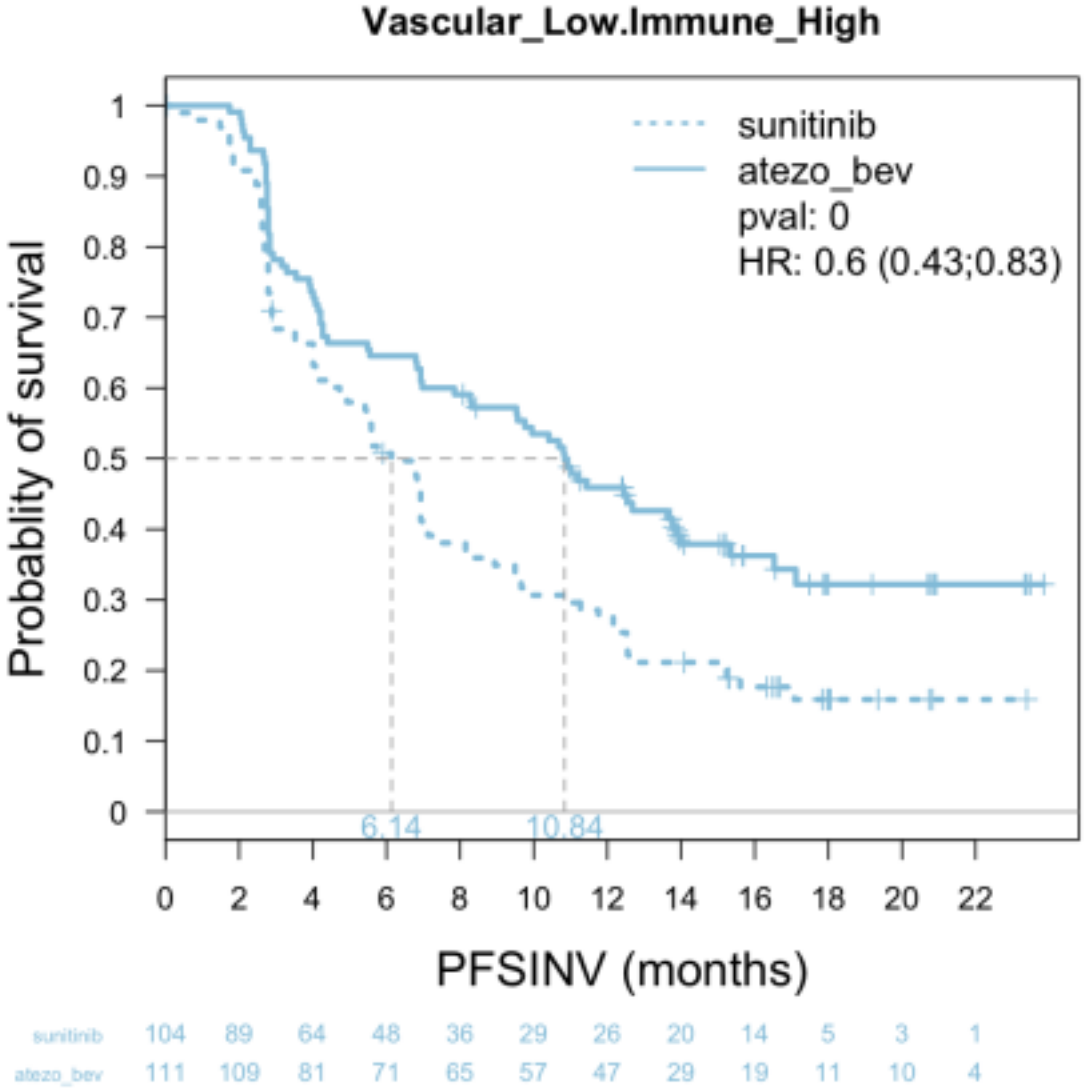
A biomarker-based approach

Angio high / Teff high	→	VEGF + IO
Angio high / Teff low	→	VEGF monotherapy or VEGF + IO
Angio low/ Teff high	→	IO monotherapy or IO + IO
Angio low/ Teff low	→	Something else



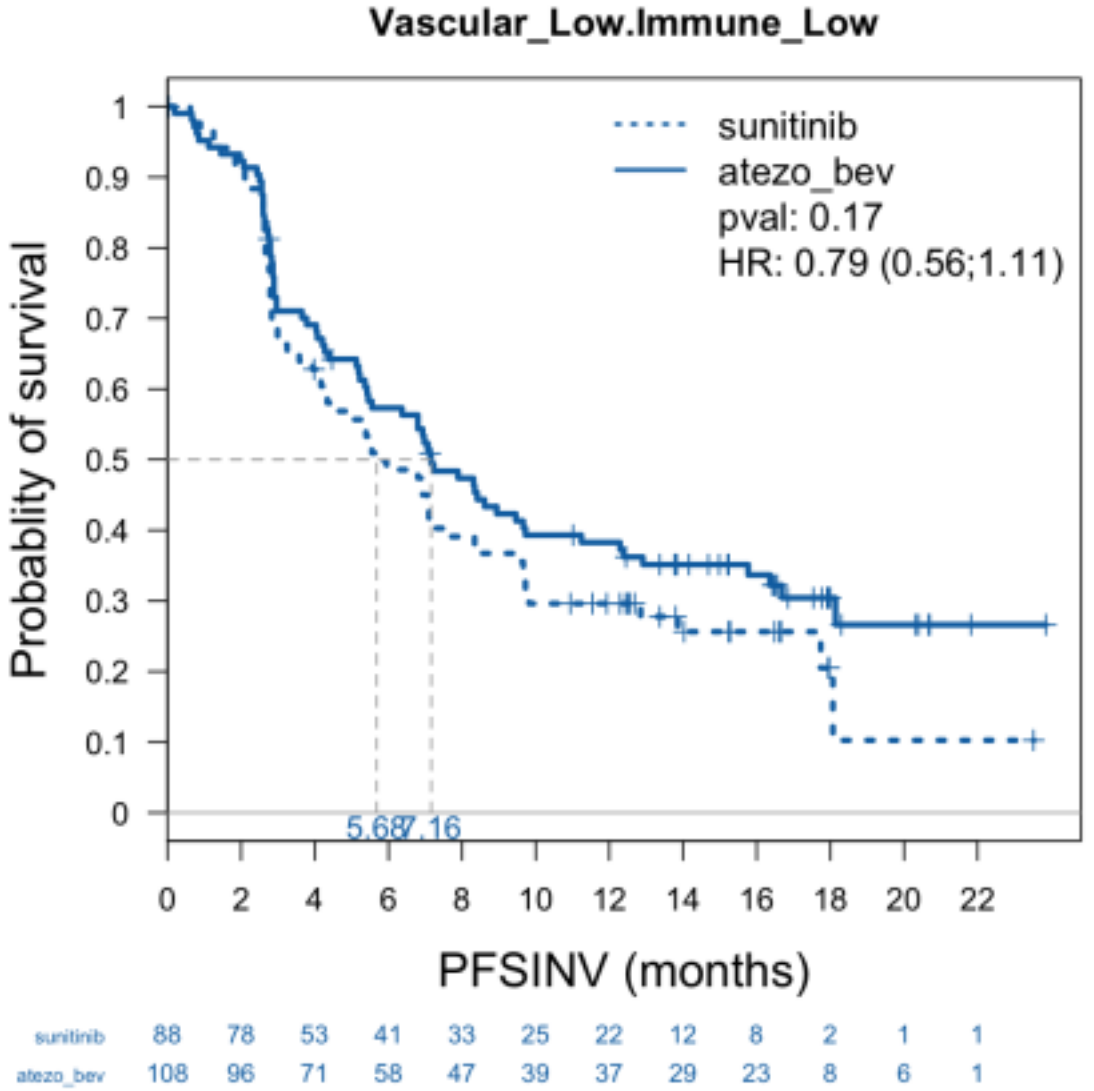
A biomarker-based approach

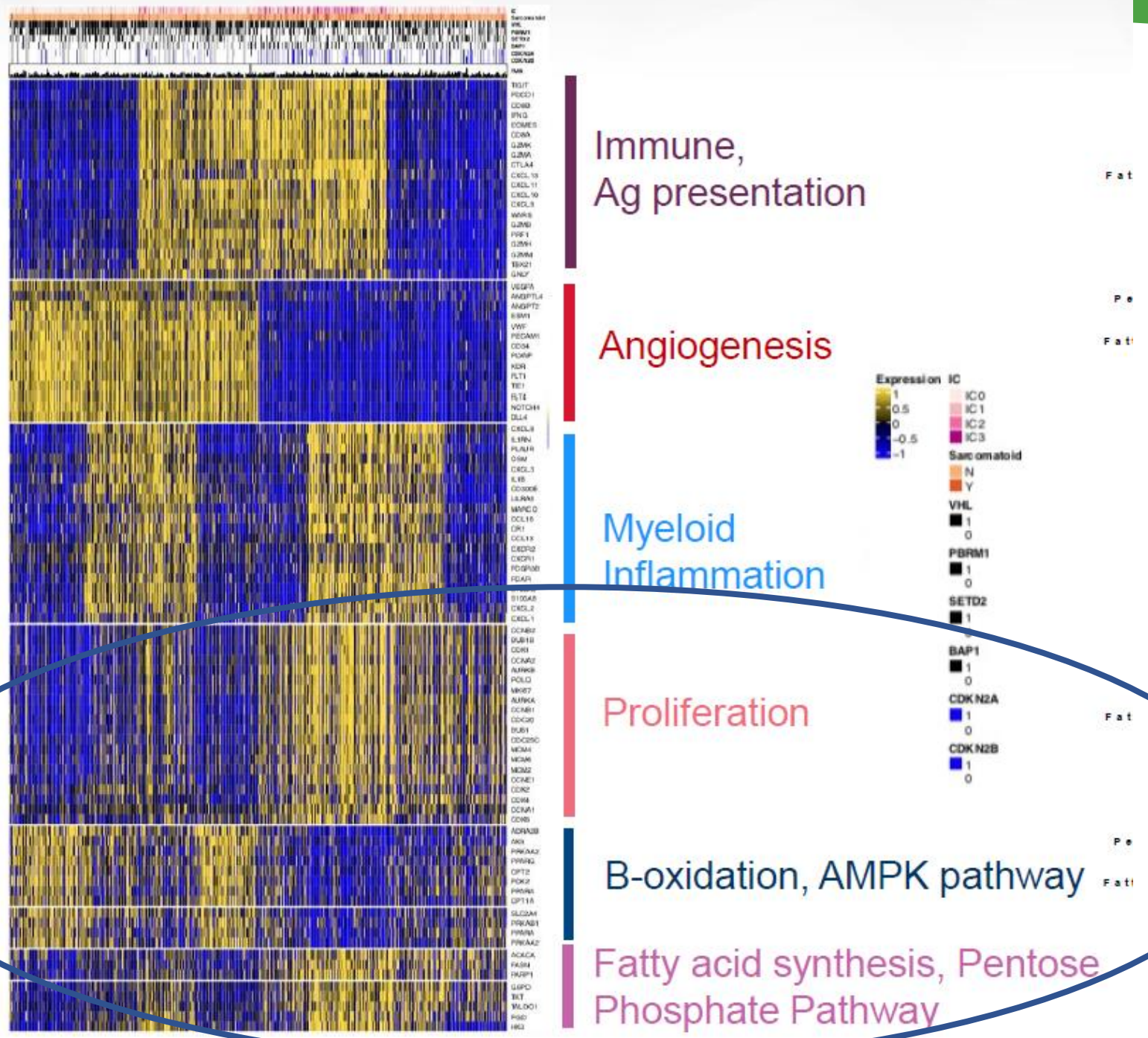
Angio high / Teff high	→	VEGF + IO
Angio high / Teff low	→	VEGF monotherapy or VEGF + IO
Angio low/ Teff high	→	IO monotherapy or IO + IO
Angio low/ Teff low	→	Something else



A biomarker-based approach

Angio high / Teff high	→	VEGF + IO
Angio high / Teff low	→	VEGF monotherapy or VEGF + IO
Angio low/ Teff high	→	IO monotherapy or IO + IO
Angio low/ Teff low	→	Something else

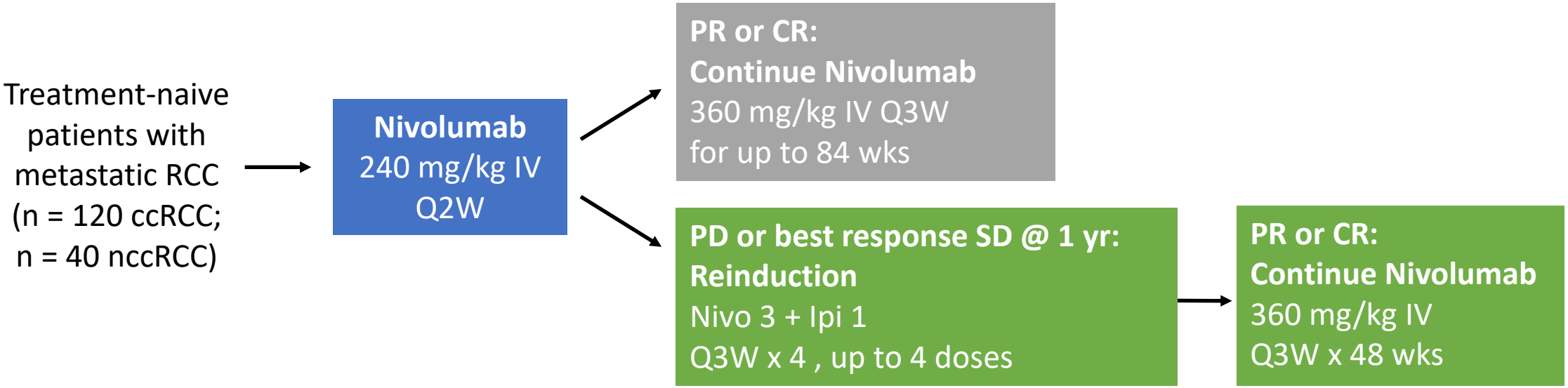




Unpublished data

KidneyCAN

Clinical selection of patients: HCRN GU 26: Trial Schema



Extensive biomarker studies to be done in collaboration with the DFHCC Kidney Cancer SPORE Investigators
DOD Translational Partnership Grant (Atkins, Wu)

Atkins, Hammers co-leaders

12 institutions

NCT03117309

Conclusions

- A ‘real’ biomarker allows for selection for or against a particular drug/regimen based on efficacy and/or toxicity
  - None yet exist in RCC

- We need to discuss whether clinical or biomarker selection trials are better suited to produce meaningful results.