Kidney Cancer Research Summit KCRS21

Overcoming Kidney Cancer Resistance to Immune Checkpoint Inhibitors

Initiating PI: Kiyoshi Ariizumi, PhD, Dermatology

Partnering PI: Hans Hammers MD, PhD, Internal Medicine

UT Southwestern Medical Center at Dallas TX

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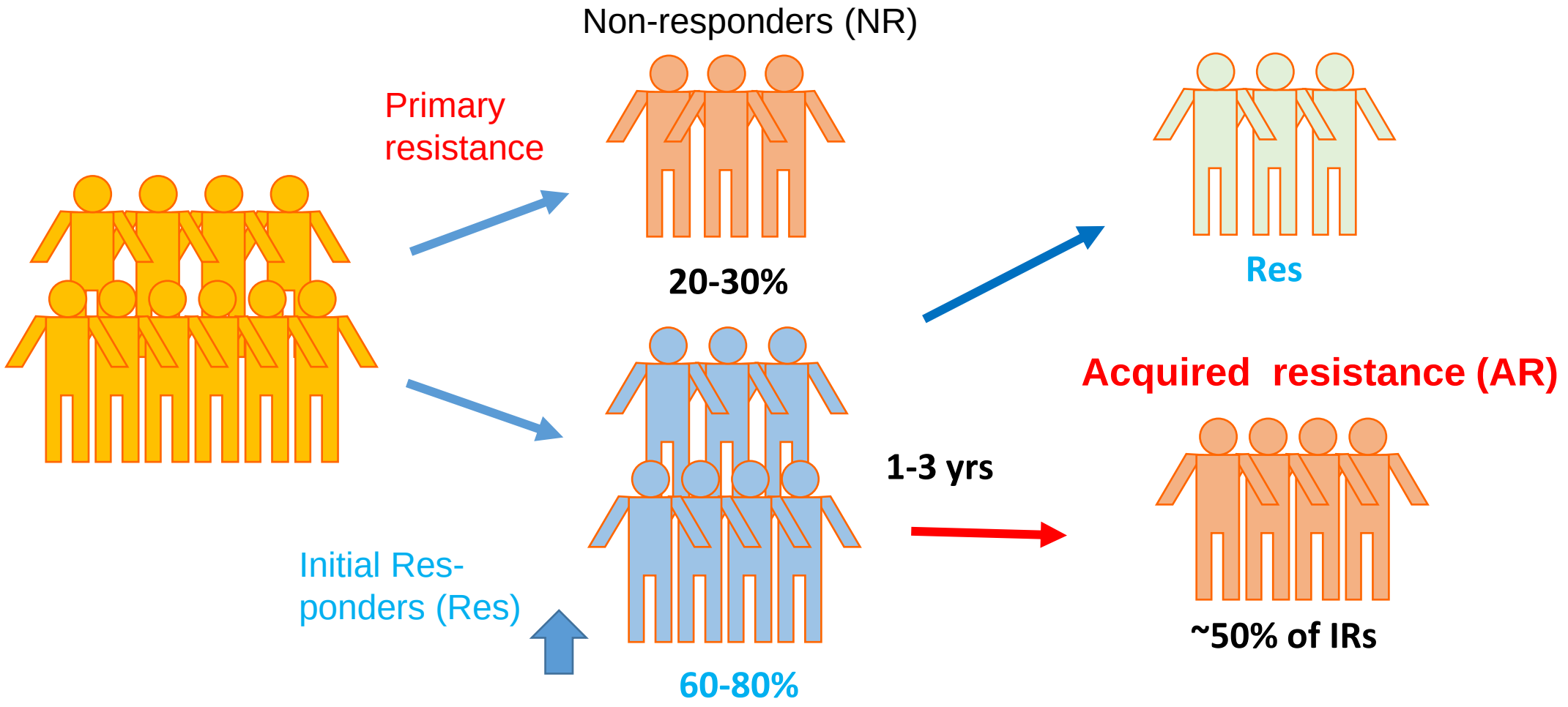
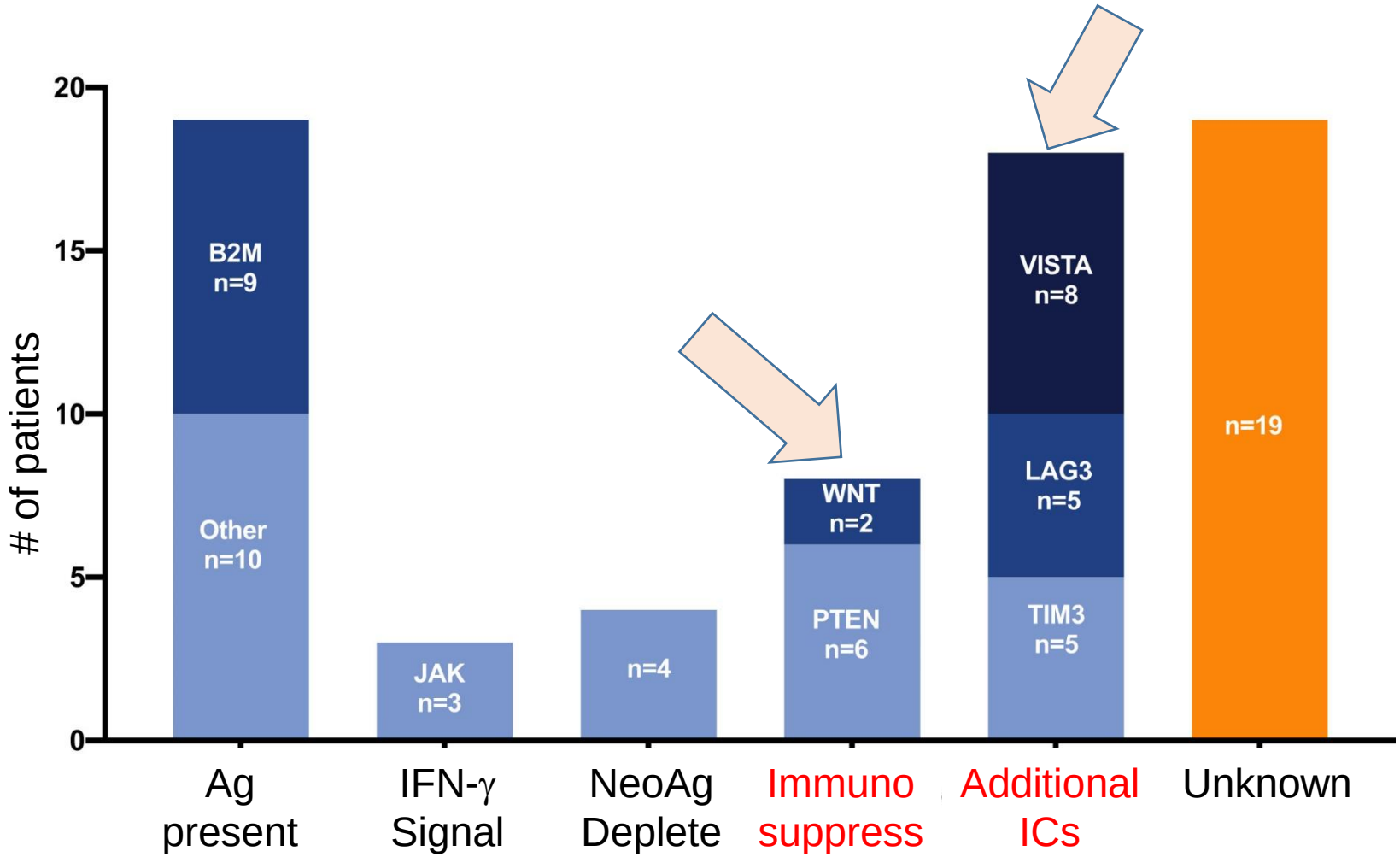
Resistance of RCC to ICI



Only minority (<30%) achieve durable response

Data from Jenkins et. al., BJC, 2018

Reported mechanisms of acquired resistance to ICIs



AJ Schoenfeld et. al., Cancer Cell, 2020

DC-HIL immune checkpoint differs from other ICs

Properties	**CTLA-4**	**PD-1**	**DC-HIL**
Tumor expression	Many cancers	Many cancers	Some of melanoma, lung and kidney cancer
Host expression	Activated T cells Treg	Activated T cells Treg IFNg-non-lymphoid cells	Activated T cells IL1β/IFNg-myeloid cells MDSC
Ligand	CD80, CD86	PD-L1 and PDL2	Rare heparan sulfate glycans
Function	Immune suppression	Immune suppression	Immune suppression Angiogenesis
Target tumors	Solid cancers, lymphomas	Solid cancers, lymphomas	Solid cancers

DC-HIL is a regulator of immune-vascular system.

Animal studies demonstrated that:

DC-HIL is a resistance mechanism for ICI treatment.

Hypothesis:

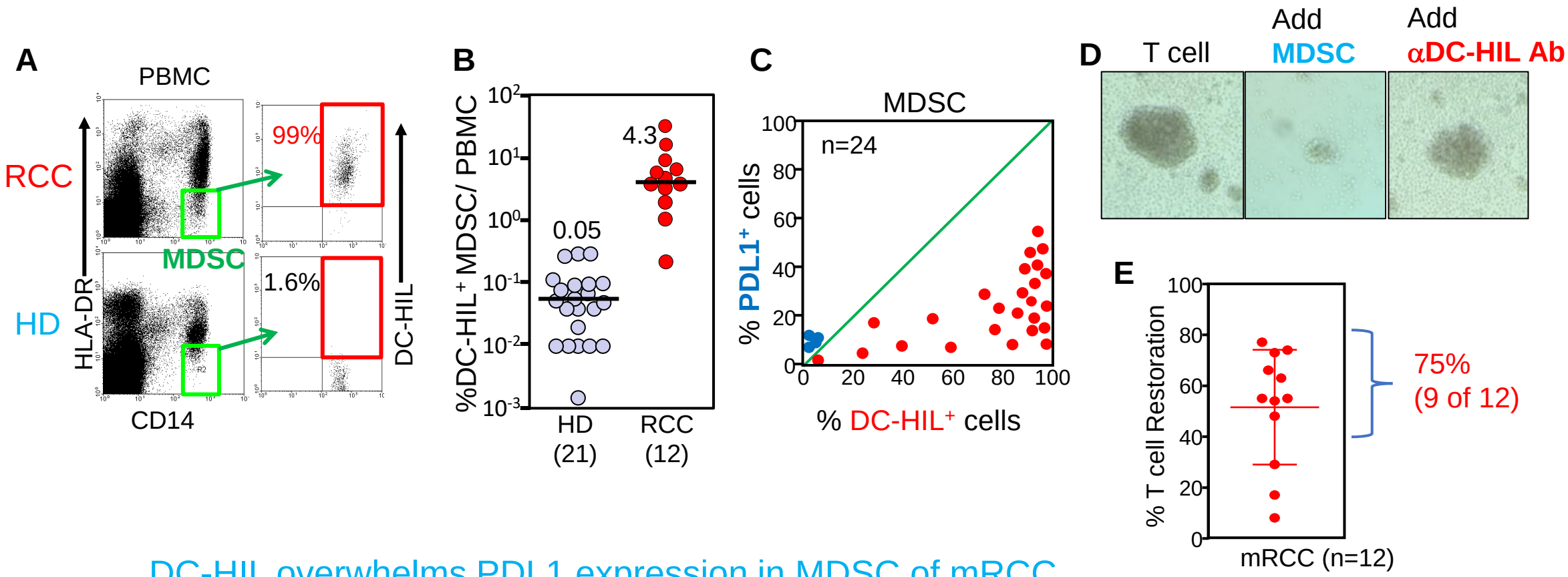
DC-HIL expression is a biomarker for predicting RCC response to ICI treatment

Objectives are:

- To evaluate the predictive value of DC-HIL expression for KC resistance to ICI;
- To determine the efficacy of DC-HIL inhibitors to treat KC in mice.

Expression and function of DC-HIL and PDL1 in blood MDSC of mRCC

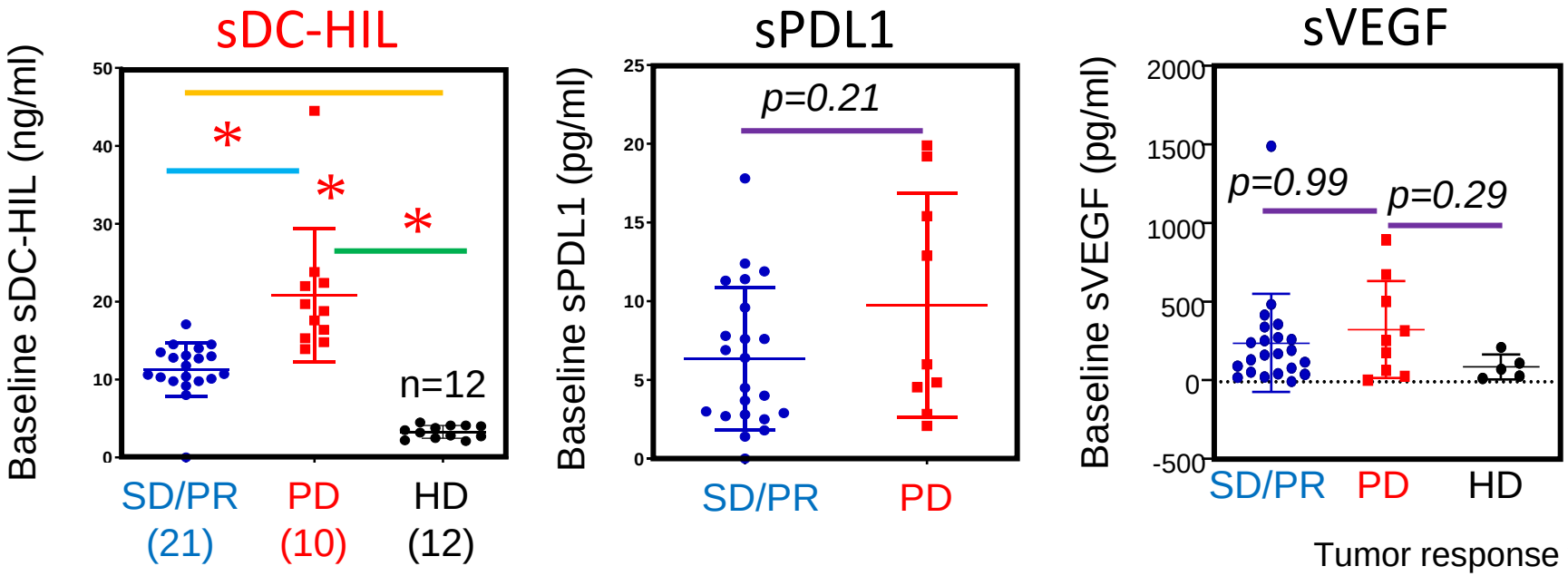
MDSCs, the strong immune regulator



DC-HIL overwhelms PDL1 expression in MDSC of mRCC

Blood markers in responders vs. non-responders to ICI

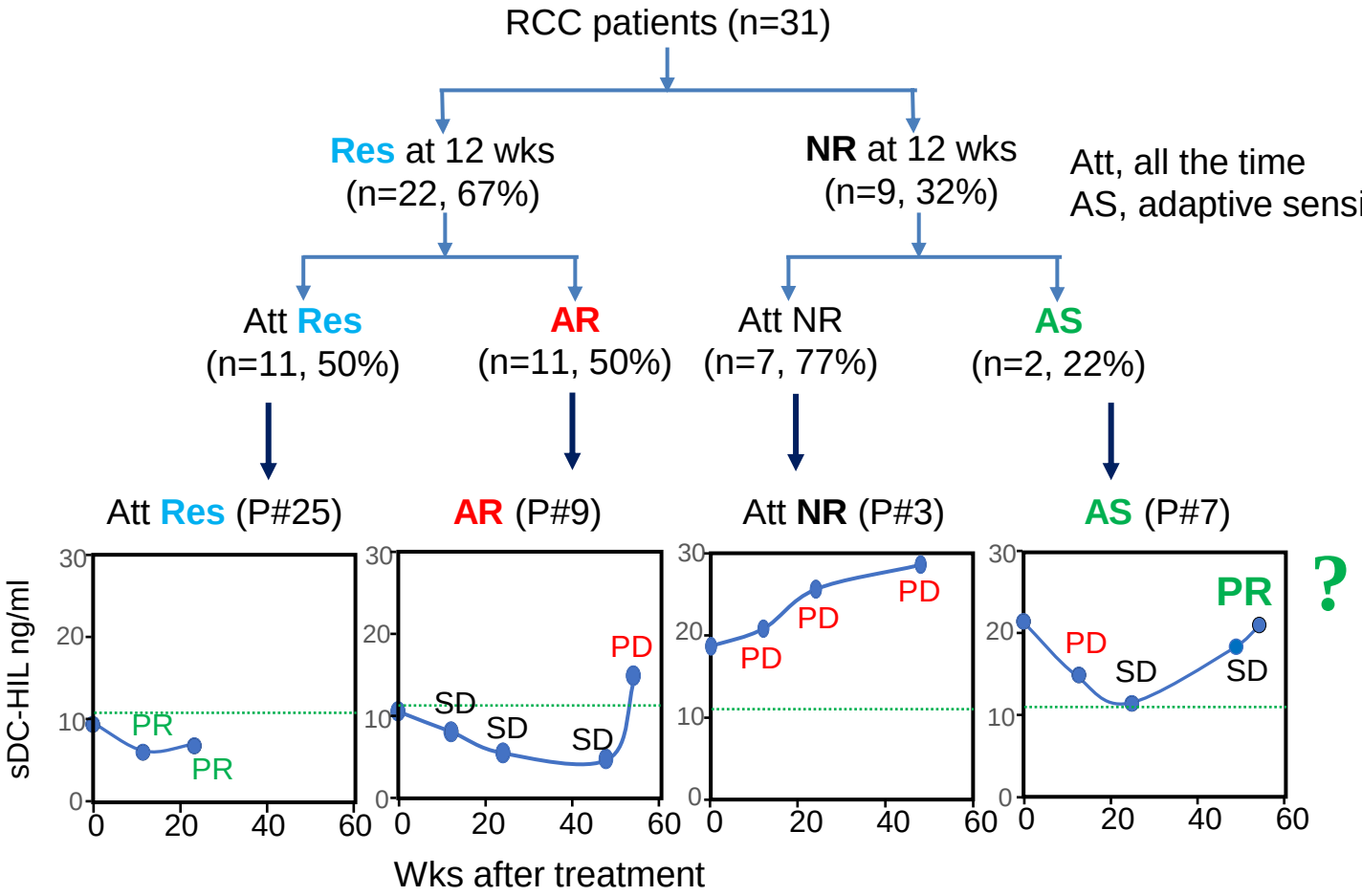
* *p<0.004*



Tumor response was evaluated at 12 weks-follow up

Baseline sDC-HIL may be a useful marker for predicting ICI response

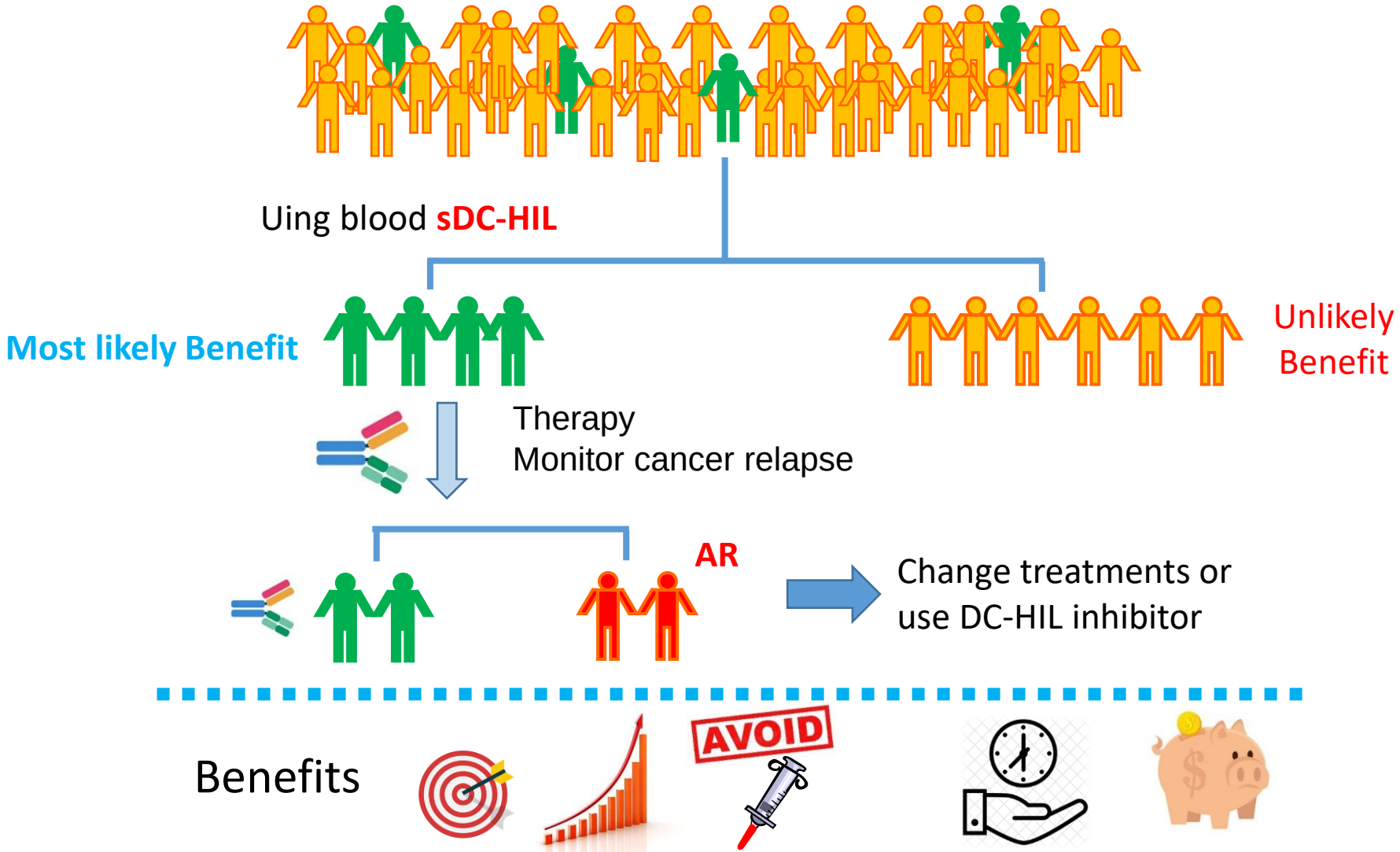
Correlation of tumor response and changes in blood sDC-HIL



11.3 ng/ml SD/PR median

sDC-HIL may be a useful marker for acquired resistance

Hope: Precision ICI Cancer Therapy



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UT Oncologists:

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Biostatisian:

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MD Student:

Vinita Popat