BERLIN 2025 ESMO congress

Efficacy of Cabozantinib Plus Nivolumab in Cluster 1/2 Metastatic Clear Cell Renal Cell Carcinoma

Results from OPTIC RCC, a phase II trial of a novel RNAseq-based biomarker

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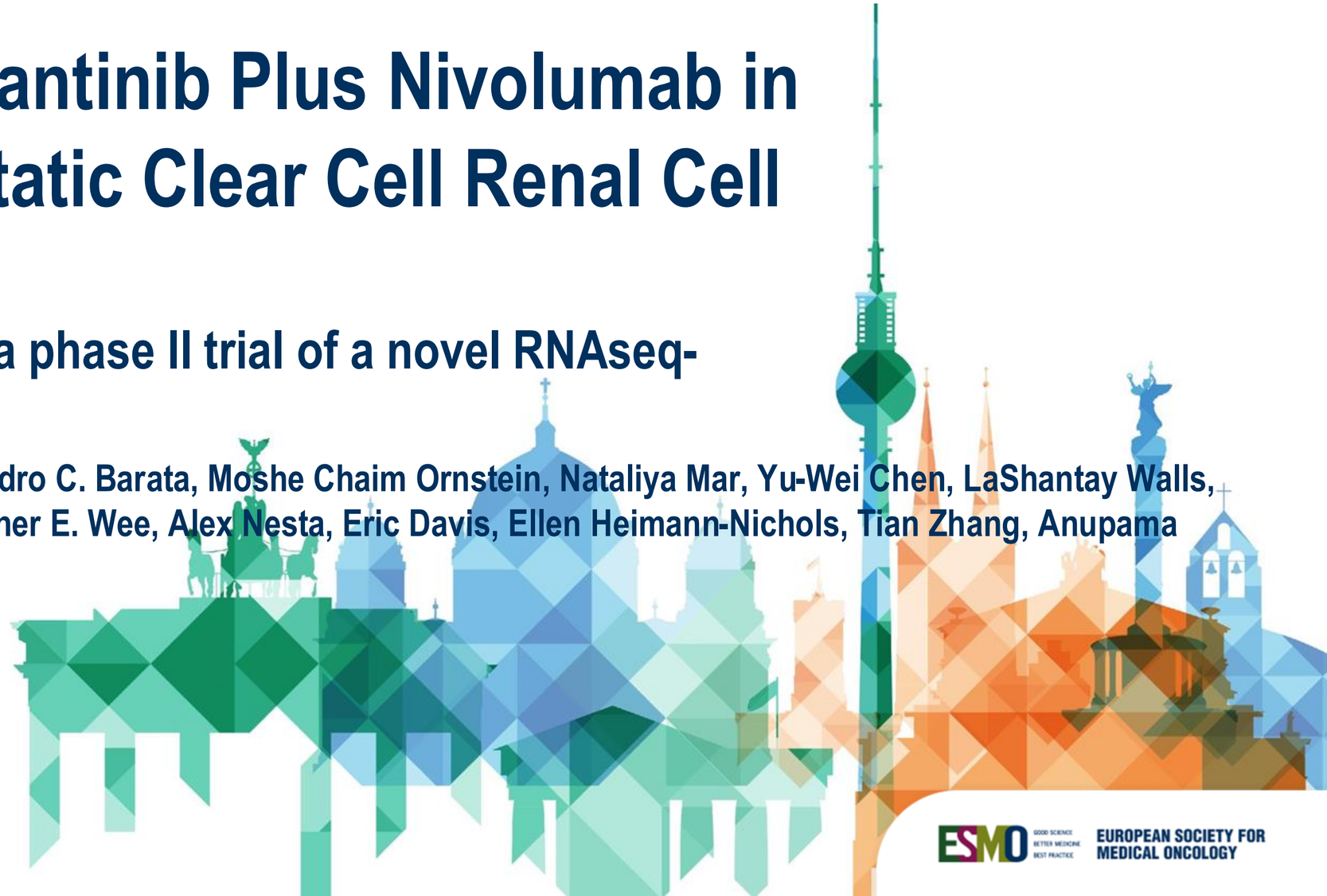
17 October 2025



ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE EUROPEAN SOCIETY FOR MEDICAL ONCOLOGY

Declaration of Interests

- Invited speaker: Tempus
- Institutional research funding: BMS
- Ad board: Merck, Eisai, Exelixis

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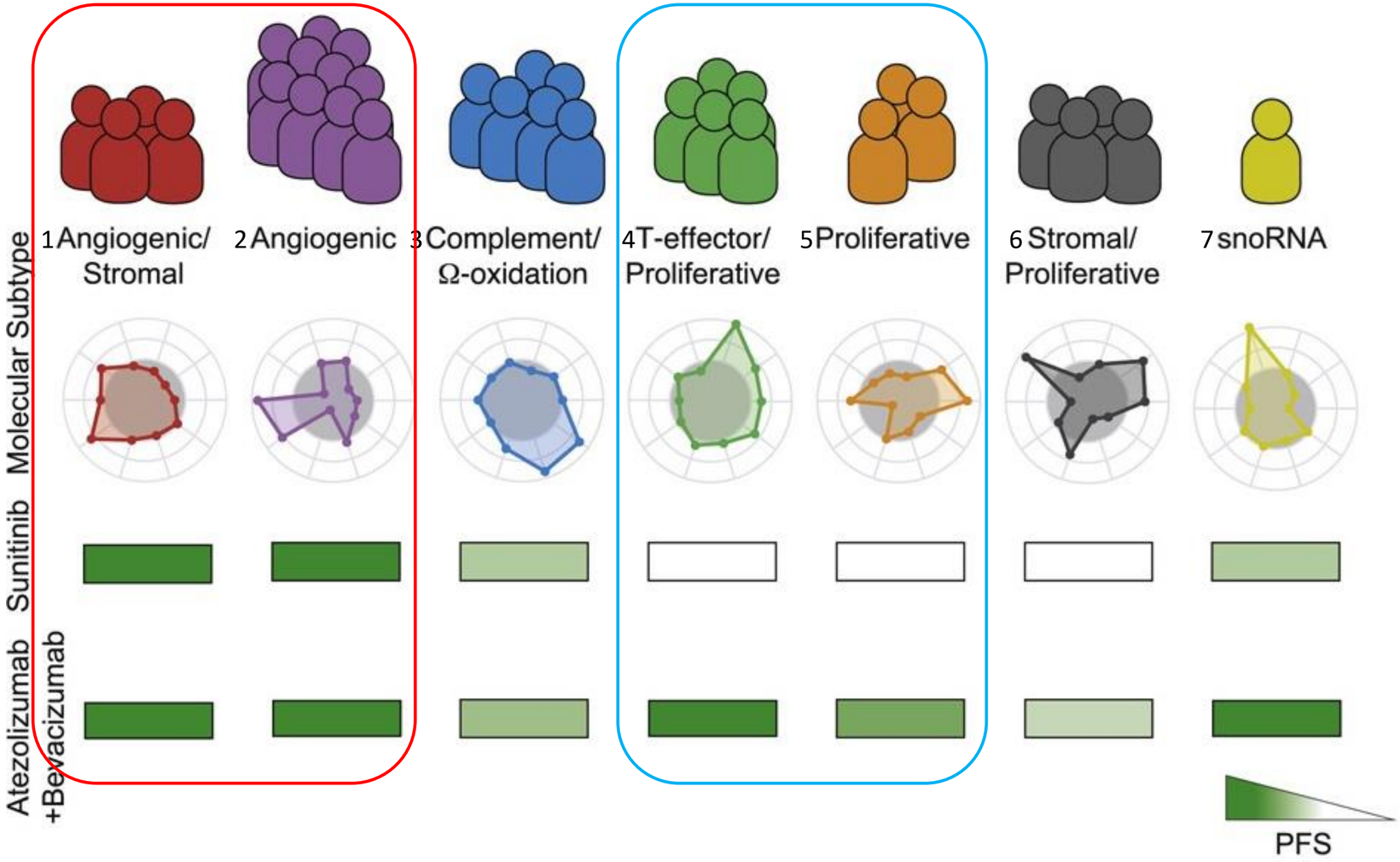
IMmotion 151 RNAseq-Defined Clusters



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Motzer et al., Cancer Cell 2020.

OPtimal Treatment by Invoking biologic Clusters in Renal Cell Carcinoma (OPTIC RCC)

Key Eligibility Criteria

- ECOG 0 or 1
- Metastatic clear cell RCC without prior systemic therapy in any setting
- Available tumor tissue for RNA-sequencing/cluster prediction

Simon's Minimax Two-Stage Design

Clusters 1/2 → **Nivolumab/Cabozantinib (N=26)**

- H_0: ORR ≤ 55%
- H_A: ORR > 55%
- Primary Endpoint: ORR>75%

Stage I (N=12) ≥7/12 responders → **Stage II (N=14)** ≥18/26

Clusters 4/5 → **Ipilimumab/Nivolumab (N=28)**

- H_0: ORR ≤ 40%
- H_A: ORR > 60%
- Primary Endpoint: ORR> 60%

Stage I (N=16) ≥7/16 responders → **Stage II (N=12)** ≥15/28

Remains open to accrual

Clusters 3/6/7 → Excluded from trial

Excluded from trial

Rini Haake Beckermann Reddy

Scott Haake, MD, PhD

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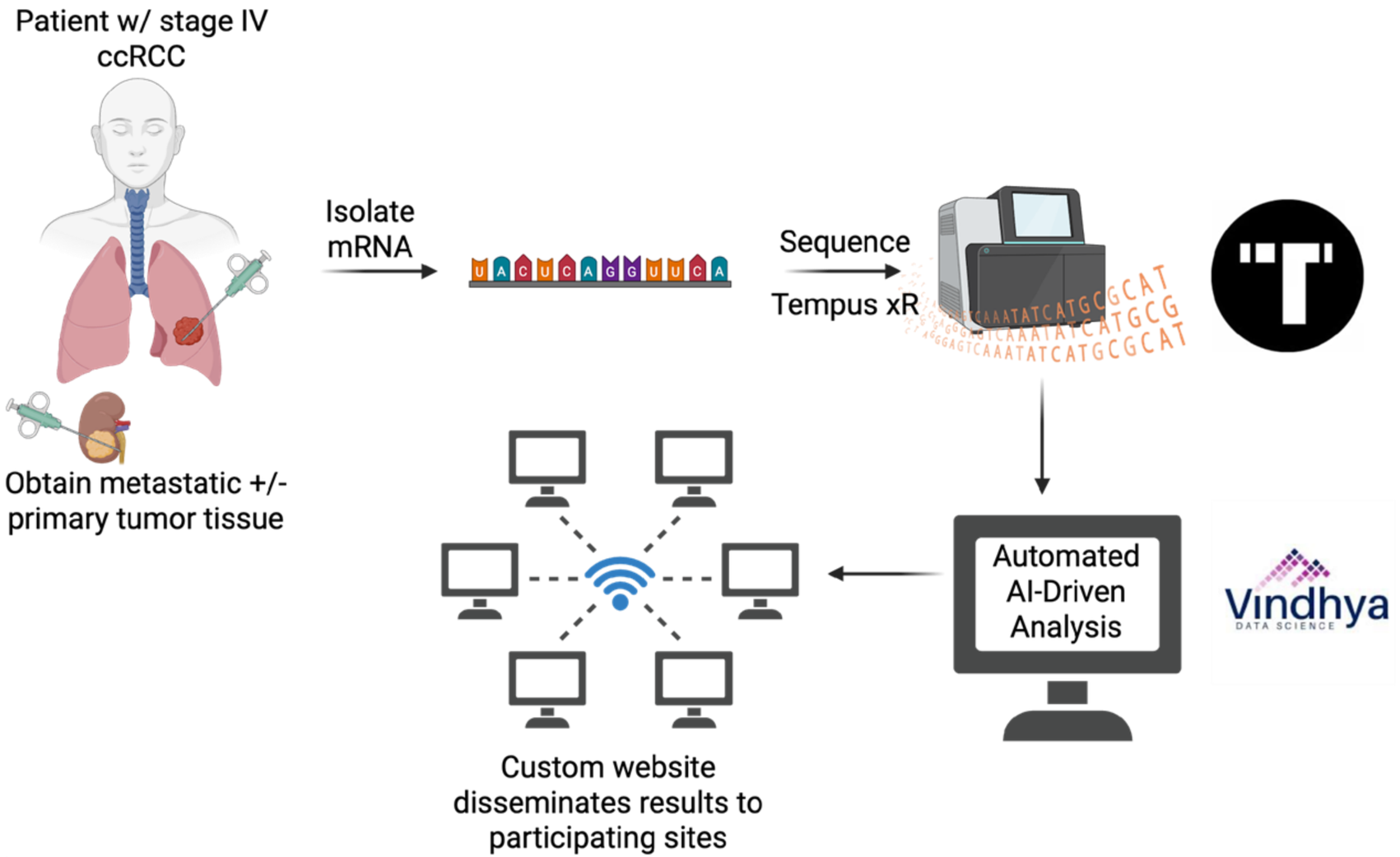
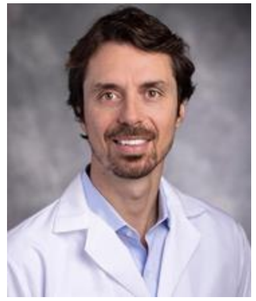
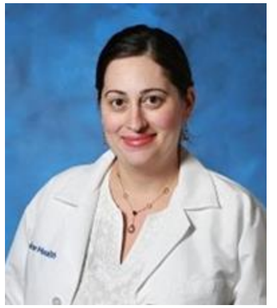
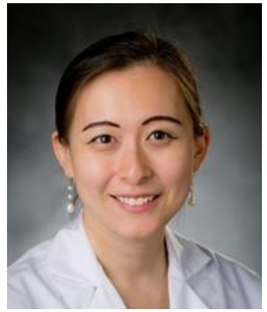
OPtimal Treatment by Invoking biologic Clusters in Renal Cell Carcinoma (OPTIC RCC)




Ornstein (CCF)


Barata (UH)


Mar (UCI)


Zhang (UTSW)

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CONSORT diagram & cluster distribution

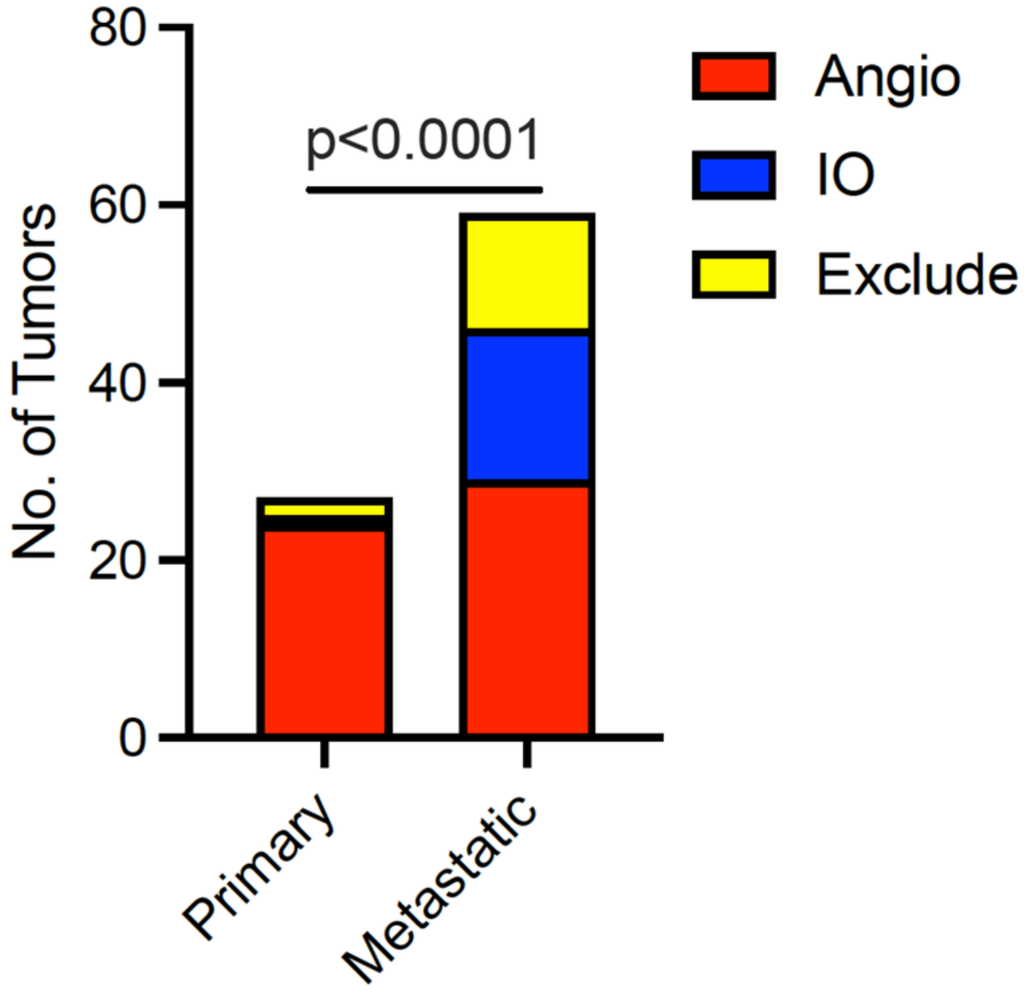
101: signed screening consent

13: Cluster IO (ipi/nivo)
14: Cluster exclude (excluded from study)
7: Cluster assigned, observed off systemic therapy
2: Pending RNAseq results
1: Cluster angio, pending start of treatment

23: Failed QC
5: Met exclusion criteria

1: Died during screening
6: Withdrew consent
2: Insurance denied

27: Cluster angio (cabo/nivo)



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Patient Characteristics

Characteristic (n=27)	
Age (year) – median (range)	68 (52-86)
Gender – M:F (%)	56:44
Race – White:Black:Asian (%)	89:7:4
ECOG performance status – 0:1 (%)	70:30
IMDC prognostic risk score – Favorable:Intermediate:Poor (%)	41:52:7
Source of RNA – Primary:Metastatic (%)	22:78
Sarcomatoid histology– no. (%)	0 (0)
Nephrectomy – no. (%)	22 (81)
No. metastatic sites – median (range)	2 (1-5)
Most common sites of metastasis – no. (%)	
Lung	18 (67)
Pancreas	8 (30)
Adrenal	7 (26)
Lymph Node	7 (26)
CNS	5 (19)
Liver	4 (15)
Soft Tissue	5 (19)
Bone	2 (7)
Other (peritoneum, cervix, spleen, thyroid)	5 (19)

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Objective Response

	Cluster 1/2 (n=25)*
Objective response – no. (%)	18 (72)
Best overall response – no. (%)	
Complete response	2 (8)
Partial response	16 (64)
Stable disease	8 (32)
Progressive disease	0 (0)
Patients with tumor shrinkage – no. (%)	25 (100)
% tumor shrinkage – median (range)	42 (5-100)

* 2 patients recently enrolled without a post-baseline scan to date

- Median follow-up: 11.1 months (range 0.9 – 31.5); 17 of 27 patients remain on study

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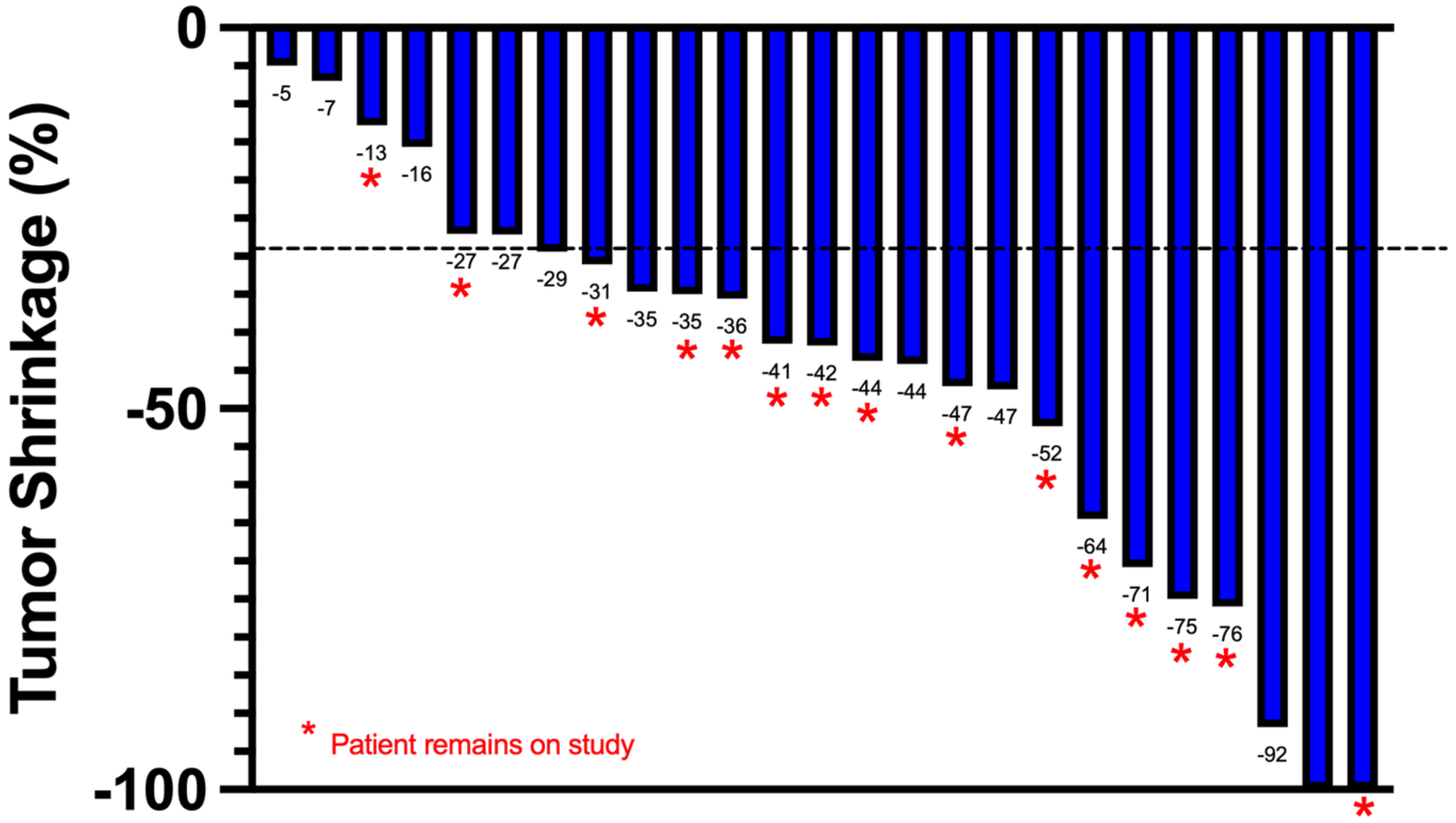
Depth of response



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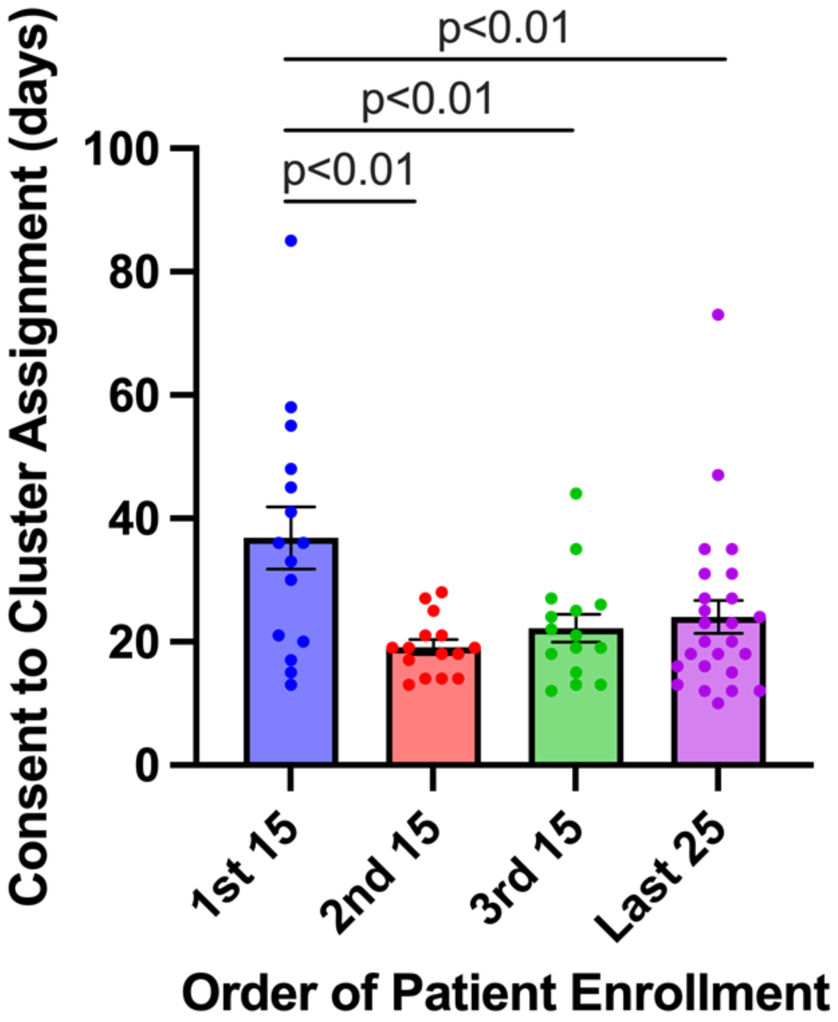
Consent-to-cluster turnaround time



Order of patient enrollment	Consent-to-cluster (months) – median (range)
1st 15	36 (13-85)
2nd 15	19 (13-28)
3rd 15	21 (12-44)
Last 25	20 (10-73)

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X genes are enriched in best responding tumors

- Analysis from Anupama comparing pre-treatment gene expression in tumors with >50% shrinkage versus tumors with <50% shrinkage

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Conclusions

- Prospective investigation of tissue-based RNAseq biomarkers to guide therapy is operationally feasible in a front-line metastatic ccRCC population
- Primary and metastatic tumors can exhibit different gene expression signatures, requiring metastatic tumor biopsies for a biomarker-driven study
- Selection of patients exhibiting an angiogenic gene expression signature enriches for clinical outcome to cabozantinib + nivolumab
  - High objective response rates, reduction of tumor burden in all patients and lack of primary progressive disease was observed.
- Time-to-event endpoints such as PFS and duration of response will require additional follow up

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Acknowledgements

Patients

OPTIC RCC Leadership:

- Brian Rini
- Katy Beckermann

Site PIs:

- Pedro Barata
- Moshe Ornstein
- Tian Zhang
- Nataliya Mar

Data Scientists:

- Anupama Reddy
- Alex Nesta

Tempus:

- LaShantay Walls
- Rebecca Ramenaden

Others:

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- Yu-Wei Chen
- W. Kimryn Rathmell
- Carmen Gray
- Jason Brown
- Christopher Wee
- Eric Davis

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Many, many others!!