COMBINATION IMMUNE CHECKPOINT INHIBITION WITH LOCOREGIONAL THERAPIES IN HEPATOCELLULAR CARCINOMA

Authors R. WETZEL[1], C. MONGE[2], C. XIE[2], D. MABRY[2], L. AKOTH[2], B. REDD[3], E. LEVY[3], B. WOOD[3], TF GRETEN[2]

1 Hematology Oncology, Walter Reed National Military Medical Center

2 Gastrointestinal Malignancies Section, Thoracic and GI Oncology Branch, Center for Cancer Research, National Cancer Institute, National Institutes of Health

3 Radiology and Imaging Sciences, Center for Cancer Research, National Cancer Institute, National Institutes of Health

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INTRODUCTION

- Immune checkpoint inhibition has demonstrated compelling activity in hepatocellular carcinoma (HCC), particularly with augmentation of the immune response by ablative procedures to improve efficacy of single immune checkpoint inhibitors
- The impact of ablation modality (TACE vs RFA) in combination with dual immune checkpoint inhibitors with tremelimumab (anti-CTLA4) and durvalumab (anti-PD1) has not been previously described

AIM

Primary objective:

- 6-month progression free survival (PFS)

Secondary objectives:

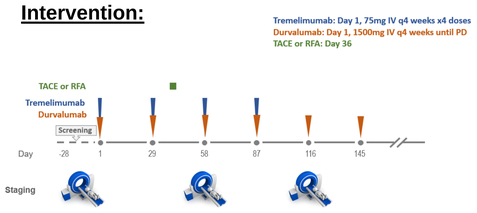
- safety and feasibility of this combination treatment

METHOD

Eligibility:

- Advanced or unresectable HCC; progressed on, refused, or been intolerant to sorafenib
- Disease technically amenable to TACE or RFA with at least two measurable lesions
- Child Pugh score of A/B7 if liver cirrhosis present, Barcelona Clinic Liver Cancer (BCLC) stage B or C, ECOG PS of 0 or 1

Intervention:



RESULTS

Table 1

Patient Characteristics	
Total patients	30
Median age	64 (range 19-81)
Locally advanced disease	57%
BCLC stage C	73%
Hepatitis C	53%
Hepatitis B	17%
Received prior sorafenib	30%
RFA patients and BCLC stage C	86%
TACE patients and BCLC stage C	71%
Treatment Allocation	
Received immunotherapy alone	9
Assigned to TACE or RFA	21
Underwent TACE with IT	7
Underwent RFA with IT	7

Table 2

Outcomes	Median OS (m)	Median PFS (m)
Combination Immunotherapy alone	19.2	4.9
Combination Immunotherapy and ablation (ITT)	13.6	4.4
TACE plus immunotherapy	20.5	7.4
RFA plus immunotherapy	16.5	4.3

Table 3

Grade 3-4 adverse events	
Lymphopenia	43%
Increased AST	43%
Increased amylase	33%
Anemia	30%

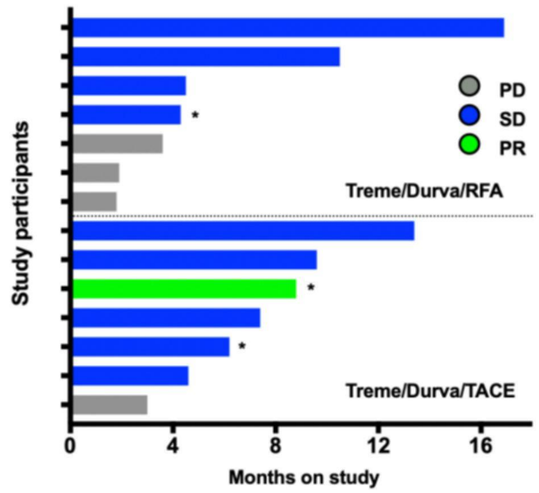


Figure 1 Efficacy data for study population
Swimmer's plot demonstrating progression free survival for patients undergoing tremelimumab and durvalumab with RFA or TACE. The asterisks indicate BCLC stage B; all other patients are BCLC stage C. PD= progressive disease, SD= stable disease, PR= partial response

CONCLUSIONS

- Combined checkpoint inhibition in combination with tumor ablative procedures is a safe and effective treatment strategy for patients with advanced HCC
- The addition of ablative therapies may improve patient outcomes
- Combined with immunotherapy may represent a therapeutic approach for patients with a contraindication to vascular endothelial growth factor (VEGF) inhibitors for patients with HCC
- Further studies are warranted to identify patient populations most likely to respond to these interventions

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ACKNOWLEDGEMENTS

Our patients, their families, and the entire staff at the National Institutes of Health

CONTACT INFORMATION

rebecca.a.wetzel2.mil@mail.mil; rebecca.wetzel@nih.gov

Rebecca Wetzel, DO

tim.greten@nih.gov

Tim Greten, MD