Percutaneous Hepatic Perfusion (PHP) for Patients With Ocular Melanoma Liver Metastases – FOCUS Trial Results

Jonathan S. Zager, MD, FACS
FOCUS Trial Global Lead Investigator
Chief Academic Officer, Director of Regional Therapies, and Senior Member, Departments of Cutaneous Oncology and Sarcoma, Moffitt Cancer Center;
Chair, Department of Oncologic Sciences and Professor of Surgery,
USF, Morsani School of Medicine, Tampa, FL

Delcath

Methods

- 301: Eligible patients with hepatic-dominant ocular melanoma were randomized 1:1 to receive PHP or BAC (investigator's choice of TACE, pembrolizumab, ipilimumab, or dacarbazine)
- 301A: All eligible patients received PHP
- PHP patients could receive up to 6 PHP treatments
- PHP was repeated every 6-8 weeks
- Melphalan dosed at 3.0 mg/kg ideal body weight (IBW)
- Patients with hepatic or extra-hepatic progressive disease (PD) were discontinued from study treatment and all patients are followed until death
- Patients were imaged every 12 (±2) weeks
- The primary endpoint, ORR (per RECIST 1.1) was assessed by Independent Review Committee

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FOCUS Trial Results - Enrollment

	Enrolled	Treated
Total	144	123
PHP Arm	102	91
Best Alternative Care (BAC) Arm	42	32
Dacarbazine	1	0
Ipilimumab	7	1
Pembrolizumab	8	6
Transarterial Chemoembolization (TACE)	26	25

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FOCUS Trial Results - Demographics

	PHP Arm (n=102)	BAC Arm (n=42)
Age at Baseline (years)		
Mean	58.1	61.7
Median	62.0	62.0
Min, Max	20.0, 79.0	31.0, 82.0
Gender		
Male	52 (51.0%)	17 (40.5%)
Female	50 (49.0%)	25 (59.5%)
Time since diagnosis of liver metastases (months)		
Median	5.65	2.53
Min, Max	0.2, 109.3	0.4, 26.0

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FOCUS Trial Results – Cycle Information

# Cycles	Patients (n=91)
1 Cycle Only	7 (7.7%)
2 Cycles Only	18 (19.8%)
3 Cycles Only	11 (12.1%)
4 Cycles Only	15 (16.5%)
5 Cycles Only	5 (5.5%)
6 Cycles Only	35 (38.5%)

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FOCUS Trial – Safety Comparison with Previous Trials

Category	FOCUS Trial* (N=91)	Pooled Analysis of Prior Studies (N=121)
Patients who Withdrew due to an AE or SAE	20 (22%)	46 (38%)
Patients who Required a Dose Reduction	12 (13.2%)	27 (22.3%)
Average Number of Cycles	4.1	2.8

*90% of Data Monitored

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Hematological Toxicities - Comparison with Previous Trials

Grade 3 or higher Adverse Events	Focus Trial * (n=91)	Hughes 2016 (n=70)
Anemia	27 (29.7%)	44 (62.9%)
Thrombocytopenia	24 (26.4%)	56 (80.0%)
Neutropenia	18 (19.8%)	60 (85.7%)

*90% of Data Monitored

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FOCUS Trial Analysis: Prespecified Endpoint Met

Intent to Treat:

Primary Effectiveness Endpoint[19]	PHP (N=91 treated + 11 untreated)	95% CI*
Objective Response Rate	**31.4%**	**[22.55 - 41.31]**

*A meta-analysis of checkpoint inhibitors (476 patients,16 publications) calculated a 95% Confidence Interval for ORR of 3.6% - 8.3%

Lower bound 22.55% far exceeds 8.3% upper bound prespecified threshold.

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FOCUS Trial – ORR and DCR

Intent to Treat:

Efficacy Endpoint	PHP (N=102)	BAC (N=42)	P-Value*
Objective Response Rate - Primary	**32 (31.4%)**	**4 (9.5%)**	0.0059
95% CI	[22.55 - 41.31]	[2.66 - 22.62]	
Disease Control Rate	**67 (65.7%)**	**12 (28.6%)**	<0.0001
95% CI	[55.63 - 74.81]	[15.72 - 44.58]	

Modified Intent to Treat**:

Efficacy Endpoint	PHP (N=91)	BAC (N=32)	P-Value*
Objective Response Rate	**32 (35.2%)**	**4 (12.5%)**	0.0154
95% CI	[25.44 - 45.88]	[3.51 - 28.99]	
Disease Control Rate	**67 (73.6%)**	**12 (37.5%)**	0.0002
95% CI	[63.35 - 82.31]	[21.10 - 56.31]	

*Chi-square
** mITT Population – any patient who received at least one study treatment

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FOCUS Trial – Duration of Response

	mITT Population	
	PHP (N=91)	BAC (N=32)
Duration of Response (DOR, median)	14 months	NC
95% CI	[8.54 - NC]	[6.93 - NC]
Patients with Confirmed CR or PR	32 (7 CR's, 25 PR's)	4 (All PR's
Patients with Subsequent PD	14 (43.7%)	1 (25.0%)
Censored	18 (56.3%)	3 (75.0%)

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FOCUS Trial – Progression-Free Survival

Secondary Endpoint		PHP (N=91)	BAC (N=32)	P-Value
Median Progression-Free Survival		**9.03 mos.**	**3.12 mos.**	0.0007
	95% CI	[6.34 - 11.56]	[2.89 - 5.65]	
PFS Status	Events	64 (70.3%)	25 (78.1%)	
	Censored	27 (29.7%)	7 (21.9%)	
Hazard Ratio Estimate		0.39		0.0002
	95% CI	[0.237 - 0.643]		

- Treated patients only, per the protocol untreated patients were not followed

Data continues to mature; patients will continue to be followed for approximately 18 months.

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Focus Trial Results – 12 Month Survival – Post Hoc Analysis

Intent to Treat:

Secondary Endpoint	PHP (N=102)	BAC (N=42)
% Surviving at 12 months	68%	36%
Hazard Ratio*	0.42	
95% CI	0.20 - 0.88	
p-value	0.0215	

Modified Intent to Treat**:

Secondary Endpoint	PHP (N=91)	BAC (N=32)
% Surviving at 12 months	75%	47%
Hazard Ratio*	0.37	
95% CI	0.17 - 0.79	
p-value	0.010	

* Log Rank Test
** mITT Population – any patient who received at least one study treatment

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Focus Trial Results – Overall Survival

Intent to Treat:

Secondary Endpoint		PHP (N=102)	BAC (N=42)	P-Value*
Overall Survival (OS, Median)		**19.25 mos.**	**14.06 mos.**	0.2021
	95% CI	[16.30 - 24.35]	[9.99 - 19.78]	
OS Status	Events	66 (64.7%)	23 (54.8%)	
	Censored	36 (35.3%)	19 (45.2%)	
Hazard Ratio Estimate		0.739		0.2308
	95% CI	[0.451 - 1.212]		

Modified Intent to Treat**:

Secondary Endpoint		PHP (N=91)	BAC (N=32)	P-Value*
Overall Survival (OS, Median)		**20.53 mos.**	**14.06 mos.**	0.1626
	95% CI	[16.59 – 24.35]	[9.99 - 19.78]	
OS Status	Events	64 (70.3%)	23 (71.9%)	
	Censored	27 (29.7%)	9 (28.1%)	
Hazard Ratio Estimate		0.708		0.1725
	95% CI	[0.431 - 1.163]		

*Chi-square
** mITT Population – any patient who received at least one study treatment

Data continues to mature; patients will continue to be followed for approximately 18 months.

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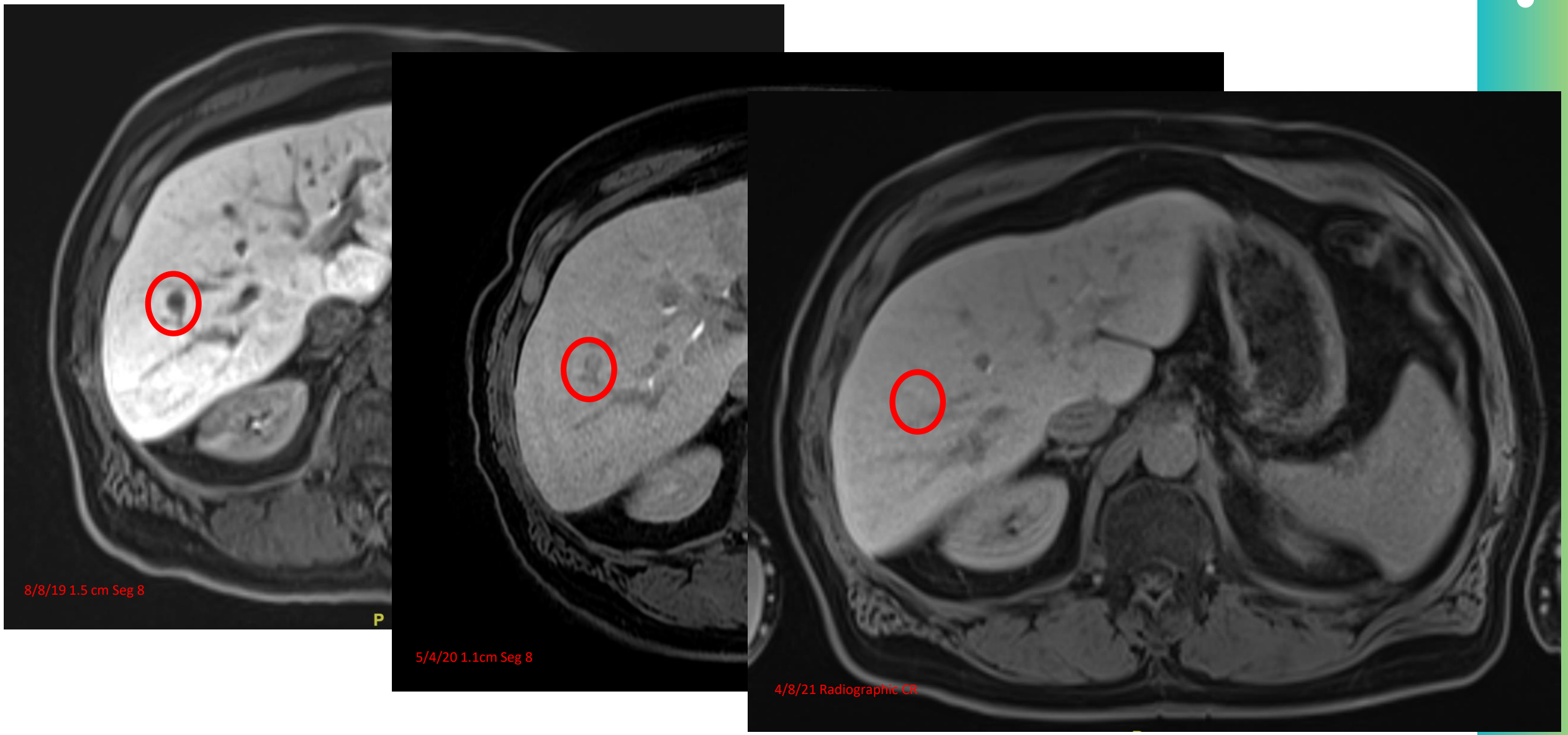
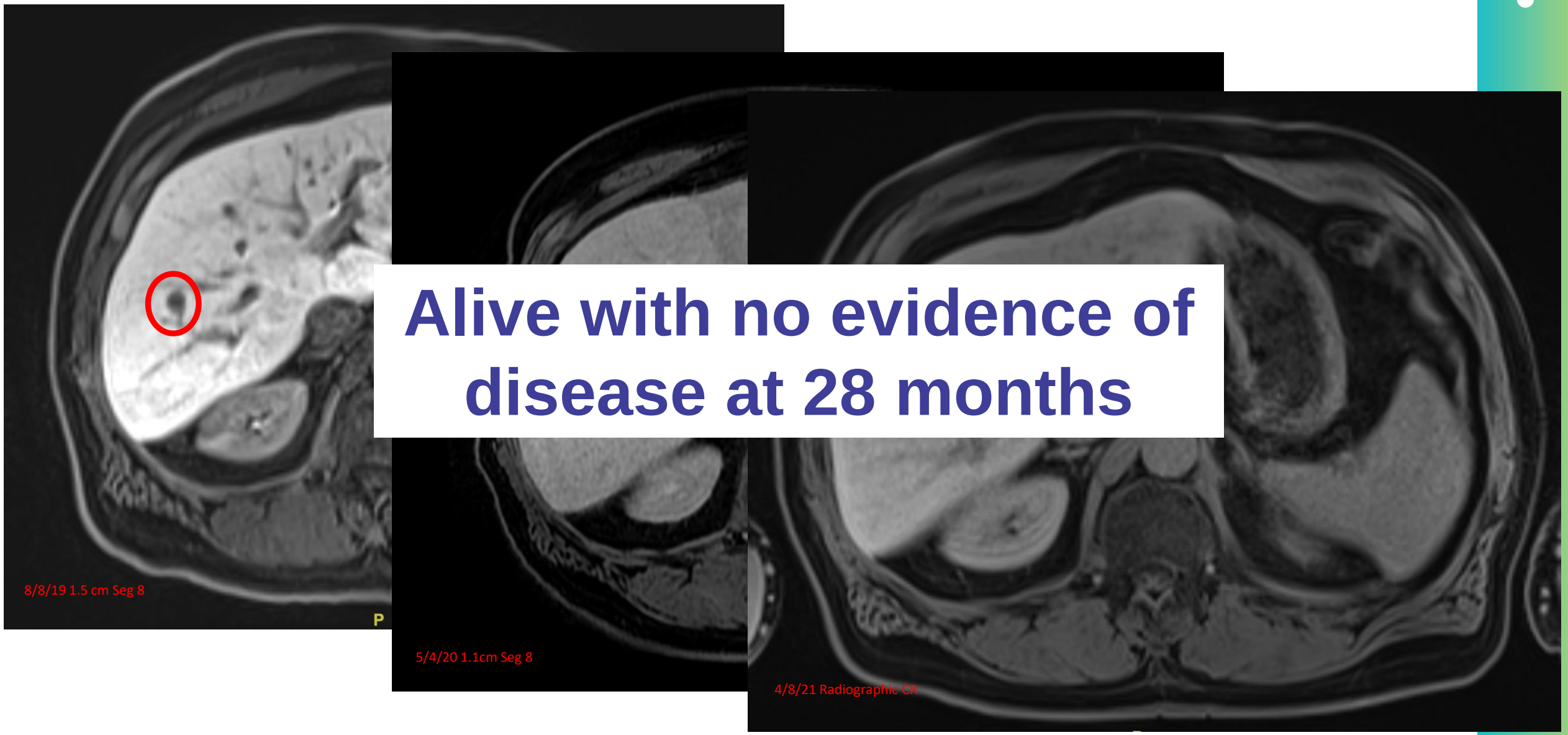
65 y/o Male-2 PHPs-Radiographic CR-20mos after 1st PHP

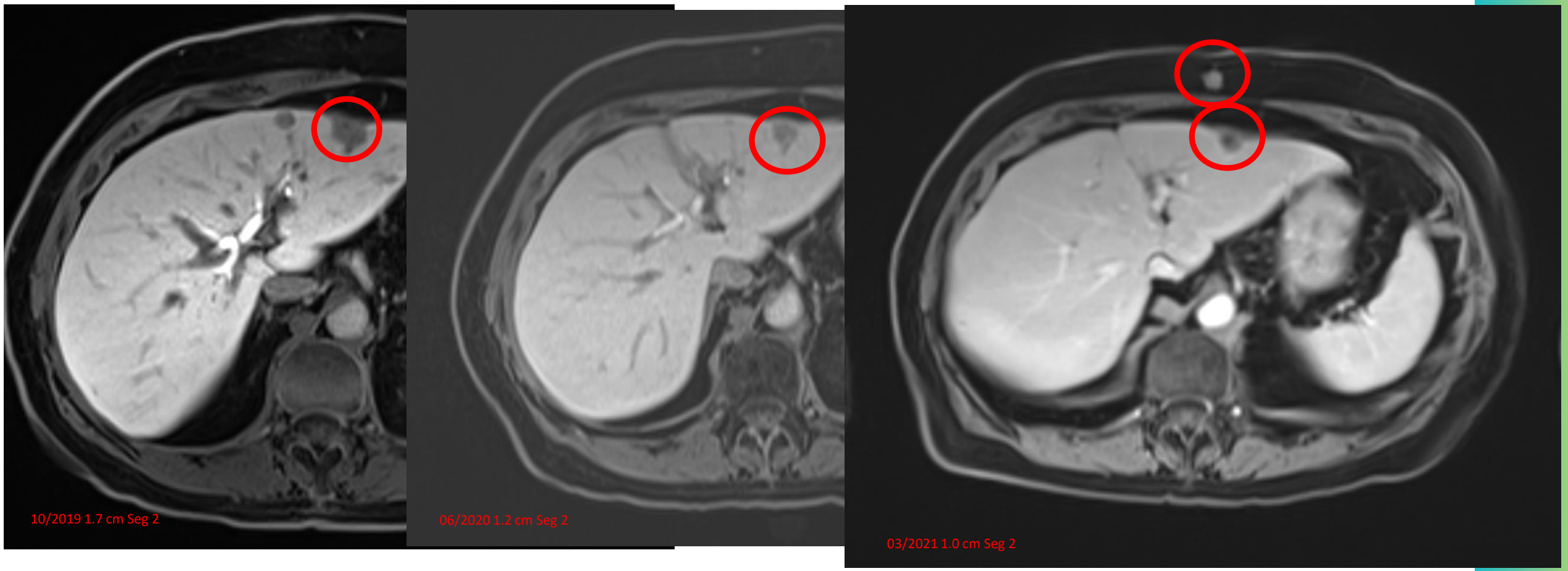


65 y/o Male-2 PHPs-Radiographic CR-20mos after 1st PHP



Alive with no evidence of disease at 28 months

73 y/o Female-6 PHPs-Radiographic hPR-20mos after 1st PHP



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Summary and Conclusions

- PHP has demonstrated a significant improvement over BAC treatments
- ORR was approximately 3 times better in PHP vs. BAC in both the ITT population (31.4% vs 9.5%) and the treated population (35.2% vs 12.5%)
- DCR was approximately doubled in favor of PHP vs. BAC in both the ITT population (65.7% vs 28.6%) and the treated population (73.6% vs 37.5%)
- PFS was nearly tripled in PHP vs BAC (9.03 mo vs 3.12 mo)

- Higher ORR and longer PFS seen in the FOCUS trial
- Although data continues to mature, meaningful advantage seen in OS
- 12-mo OS rate shows statistically significant advantage
- PHP is well-tolerated
- Most common adverse events are hematological
- These are manageable as an outpatient with observation in the majority of patients
- Data from this trial also shows an improvement over the previous phase III PHP study
- Lower toxicity observed, no treatment-related deaths

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