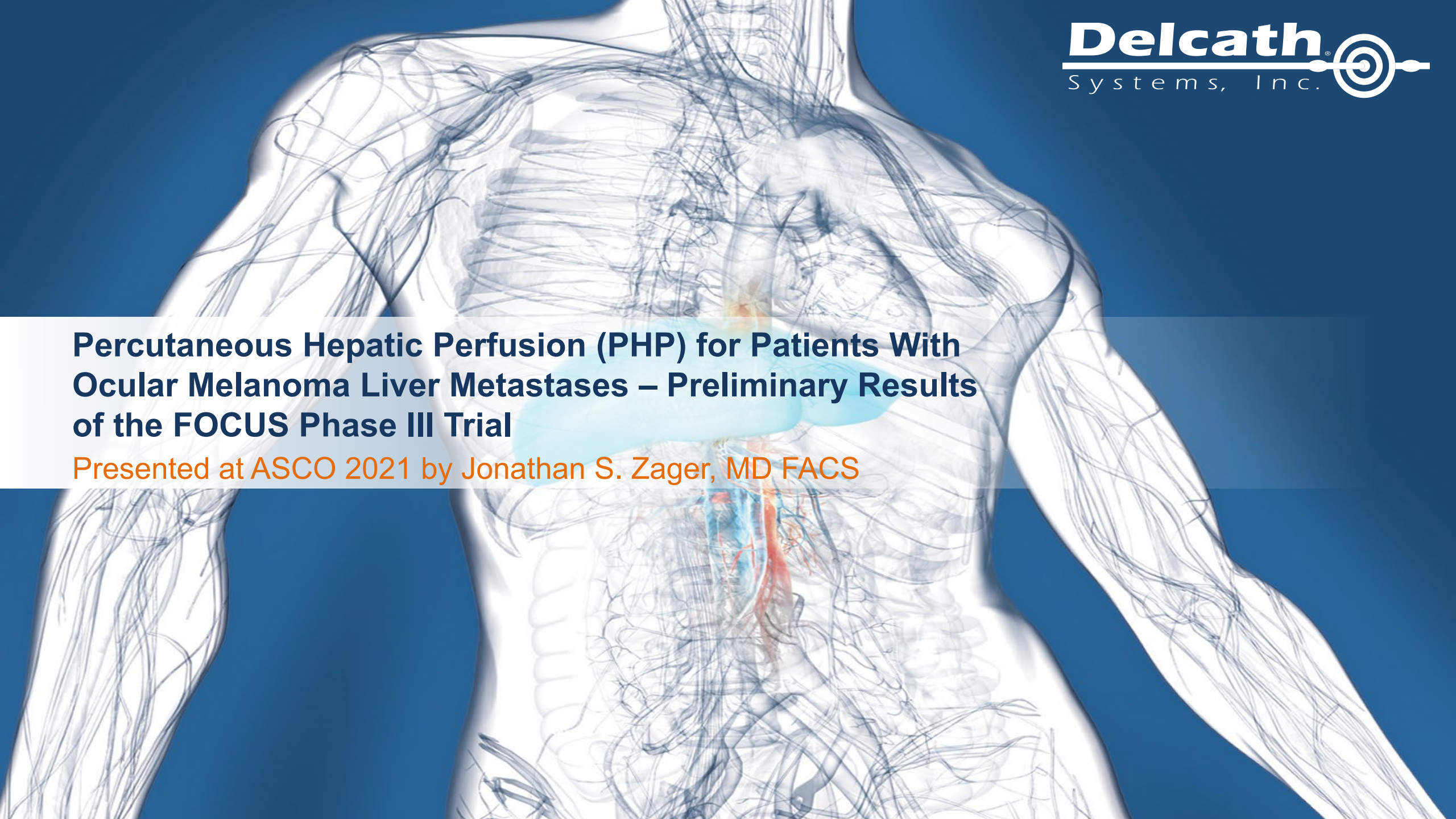

# Percutaneous Hepatic Perfusion (PHP) for Patients With Ocular Melanoma Liver Metastases – Preliminary Results of the FOCUS Phase III Trial

Presented at ASCO 2021 by Jonathan S. Zager, MD FACS

## Authors:

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# Ocular Melanoma

- Accounts for <5% of all melanoma cases[1]
- Approximately 3400 new cases in the USA each year[2]
- 2nd most common type of melanoma
- There are two major subtypes of ocular melanoma:
  - Uveal melanoma (85-90% of OM Cases[1])
    - Arises from the iris, choroid, or ciliary body
  - Conjunctival melanoma
    - Arises from the conjunctiva
    - ~50% of uveal melanoma patients eventually develop metastasis[1]
- Liver is the most common site and dominant of distant metastasis (up to 95% of cases) [1]

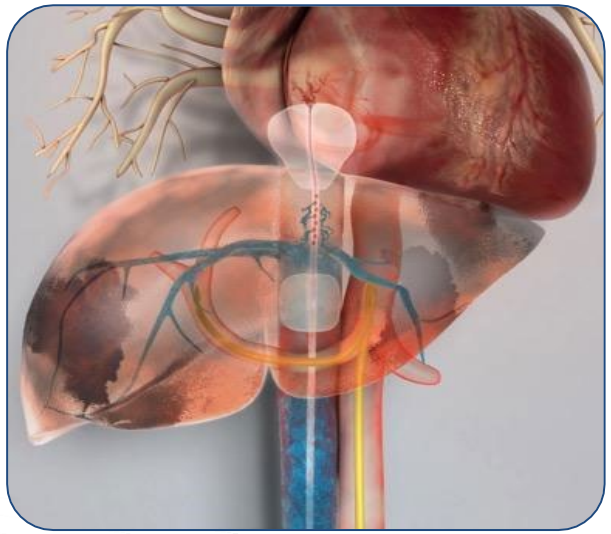

1. Jovanovic P, Mihajlovic M, Djordjevic-Jocic J, Vlajkovic S, Cekic S, Stefanovic V. Ocular melanoma: an overview of the current status. Int J Clin Exp Pathol. 2013 Jun 15;6(7):1230-44.
2. Cancer.net Editorial Board (2020) Eye Cancer - Statistics. In: Cancer.Net. https://www.cancer.net/cancer-types/eye-cancer/statistics. Accessed 26 April 2021.

# PHP: Liver-Focused Disease Control

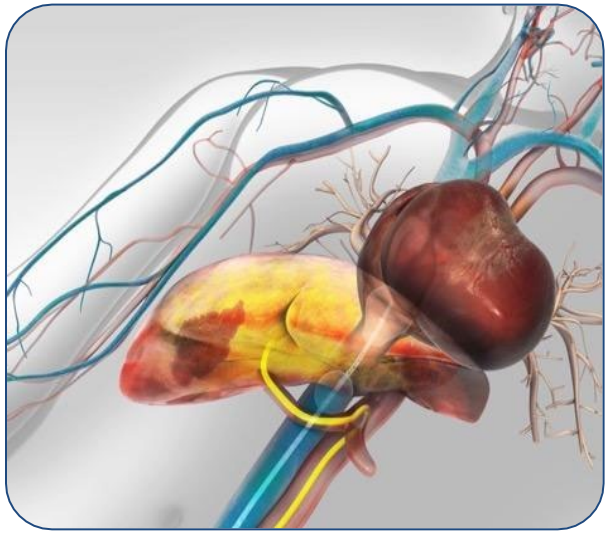
- Percutaneous Hepatic Perfusion (PHP) **uniquely treats the entire liver**

- This therapy **isolates** the liver circulation, delivers a **high concentration of chemotherapy** (melphalan), and then **filters most of the chemotherapy out** of the blood prior to returning it to the patient

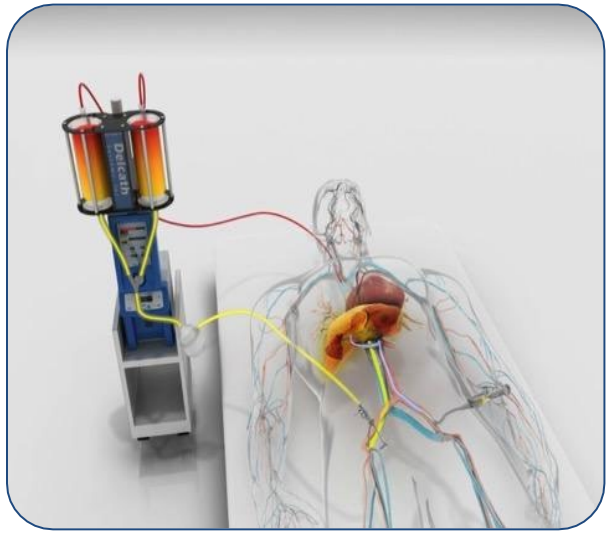
**Liver Isolated Via Double Balloon Catheter In IVC**



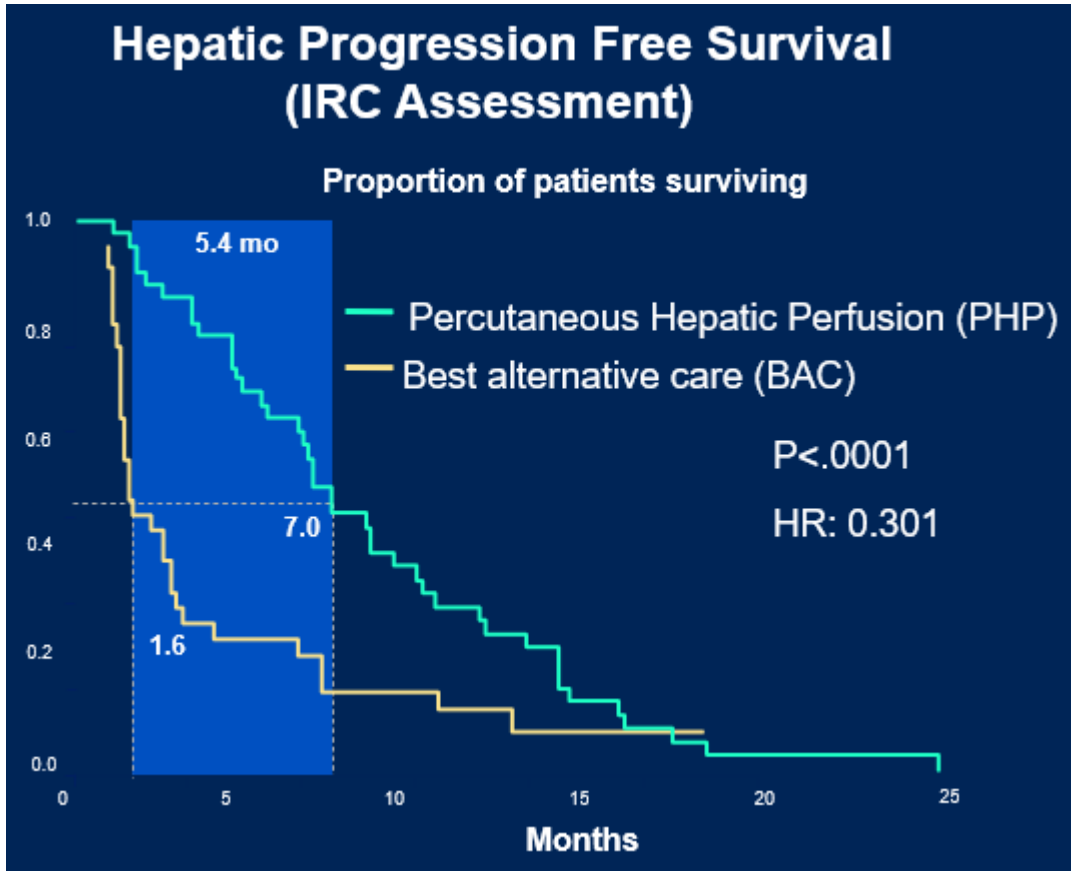
**Melphalan Infused Directly Into Liver Via Catheter In Hepatic Artery**

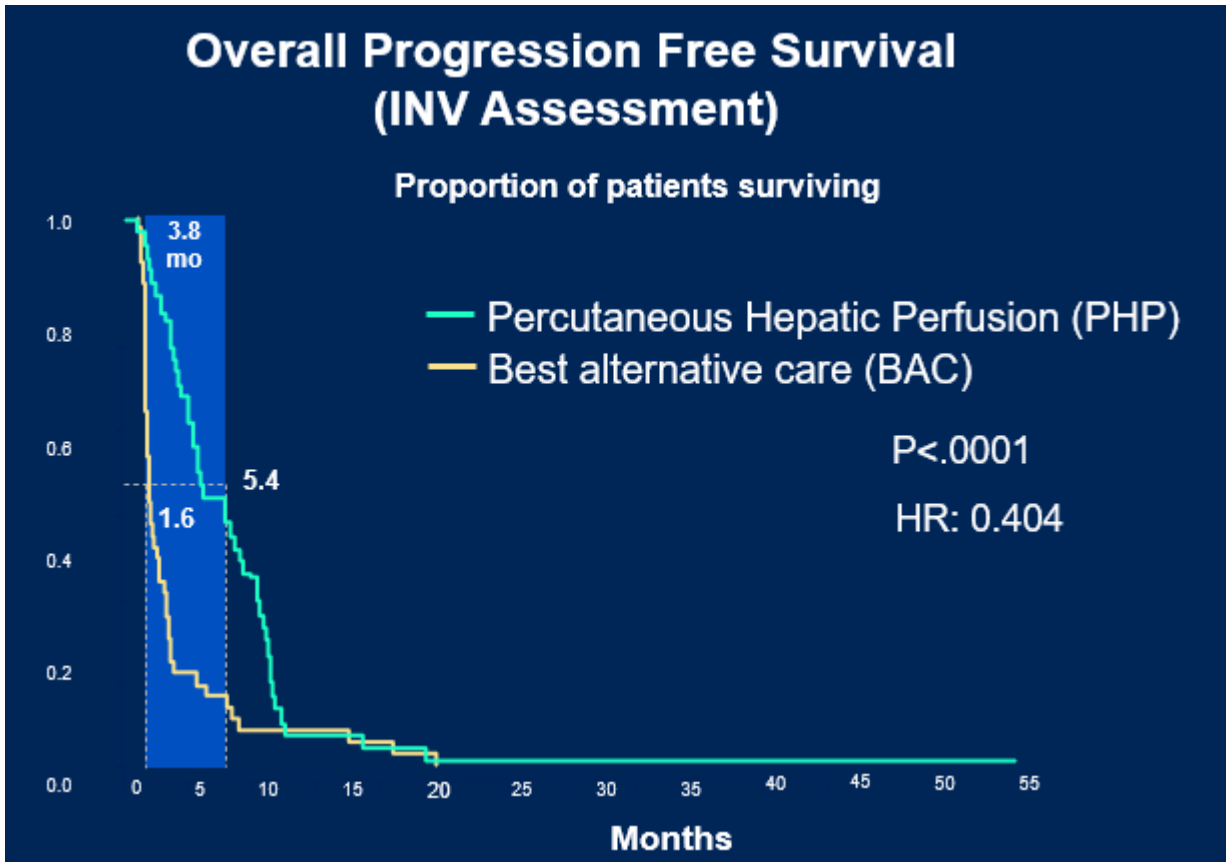


**Blood Exiting The Liver Filtered By Proprietary Extra-corporeal Filters**



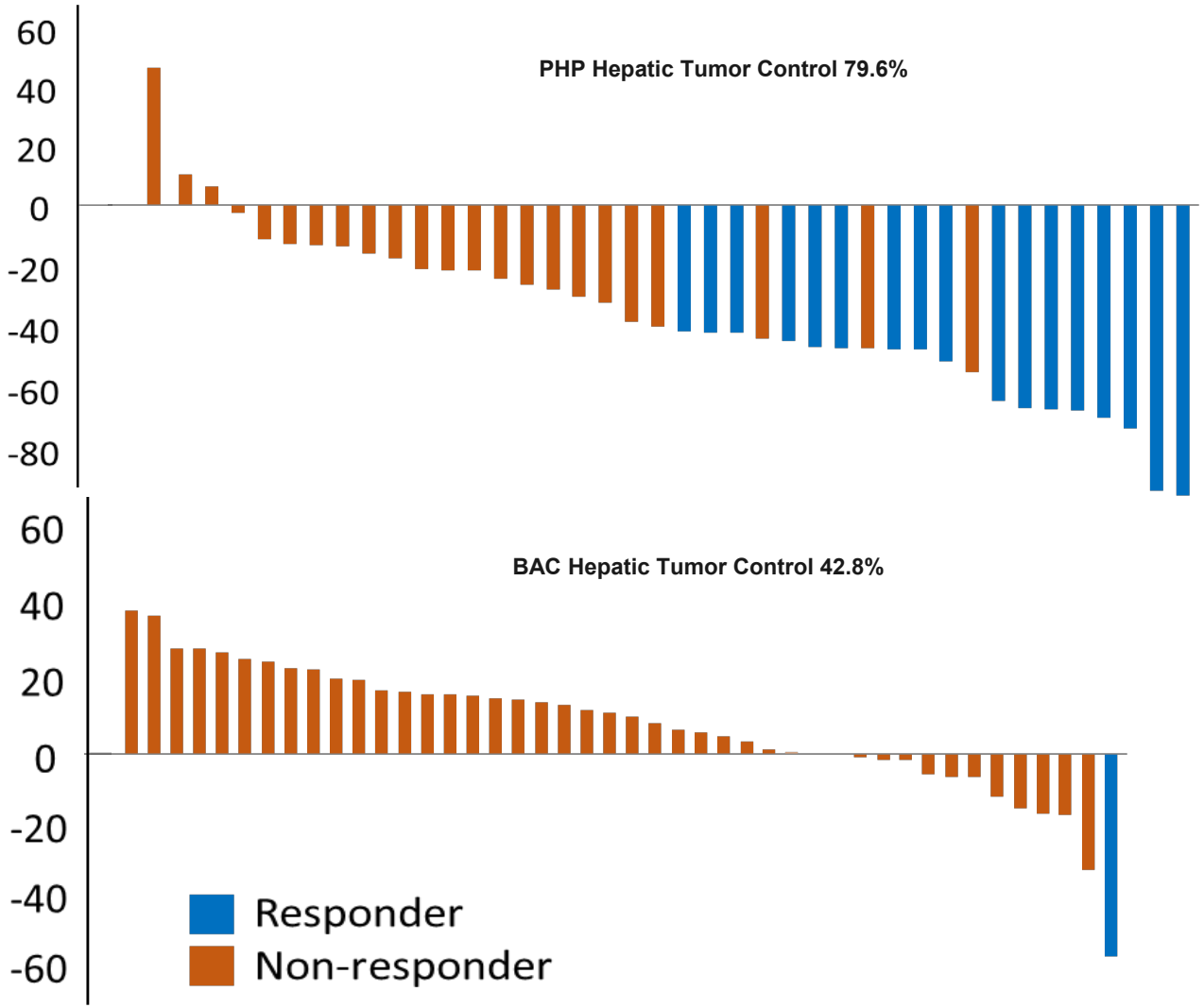
# PHP – Previous Phase III Trial Results (2012) – PFS



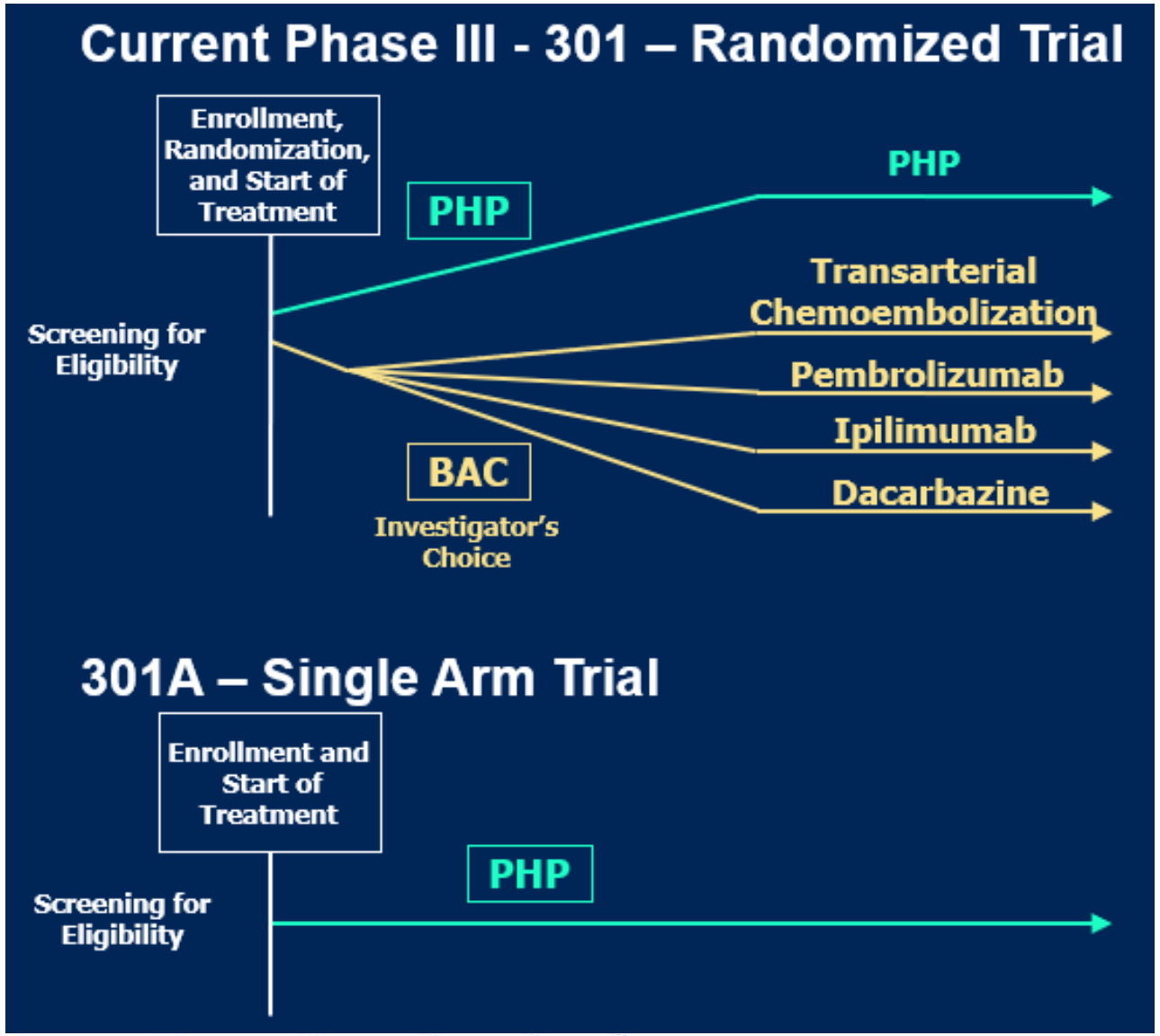




**57.1% of the subjects in the BAC arm were able to crossover to the PHP arm. Due to this crossover design of the study, the overall survival benefit was confounded.**

# PHP – Previous Phase III Trial Results - Responses




| Cohort | hOR | ORR |
|---|---|---|
| PHP (n = 44) | 36.4% | 27.3% |
| BAC (n = 49) | 2.0% | 4.1% |
| p value | <0.001 | =0.003 |




- Focus trial began as randomized trial PHP : BAC
- BAC arm was Investigator's choice of 1 of 4 treatment options
- Due to slow enrollment and patient reluctance to receive BAC treatment, trial was amended to single arm after discussion with FDA
- Current trial's primary endpoint is ORR per RECIST 1.1 based on Independent Review Committee

# 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

# Focus Trial Results – Enrollment & Inclusion in Preliminary Analysis

- Criteria for Preliminary Analysis: At least 2 evaluable response timepoints received prior to 3-12-2021 unless the subject had PD at the first evaluable timepoint or had no scans acquired (and none that will be acquired in the future) after the first evaluable timepoint

| | Enrolled | Treated | Preliminary Analysis |
|---|---|---|---|
| Total | 144 | 123 | 108 |
| Melphalan/HDS Arm | 102 | 91 | 79 |
| Best Alternative Care (BAC) Arm | 42 | 32 | 29 |
| Dacarbazine | 1 | 0 | 0 |
| Ipilimumab | 7 | 1 | 0 |
| Pembrolizumab | 8 | 6 | 6 |
| Transarterial Chemoembolization (TACE) | 26 | 25 | 23 |

# Focus Trial Results – Demographics (Efficacy Analysis Population)

| | Melphalan/HDS Arm (n=102) | BAC Arm (n=42) | Total (n=144) |
|---|---|---|---|
| Age at Baseline (years) | | | |
| Mean | 57.10 | 60.17 | 57.92 |
| Median | 61.0 | 61.0 | 61.0 |
| Min, Max | 20.0, 78.0 | 31.0, 82.0 | 20.0, 82.0 |
| Gender | | | |
| Male | 39 (50.6%) | 13 (44.8%) | 52 (48.2%) |
| Female | 40 (49.4%) | 16 (55.2%) | 56 (51.9%) |
| Time since diagnosis of liver metastases (months) | | | |
| Median | 5.29 | 2.53 | 4.57 |
| Min, Max | 0.2, 109.3 | 0.4, 26.0 | 0.2, 109.3 |

# Focus Trial Results – Objective Response Rate

| | Preliminary Analysis Population | | ITT Preliminary Analysis Population | |
|---|---|---|---|---|
| | PHP (N=79) | BAC (N=29) | PHP (N=89) | BAC (N=39) |
| Objective Response Rate | 26 (32.9%) | 4 (13.8%) | 26 (29.2%) | 4 (10.3%) |
| 95% CI | [22.75-40.40] | [3.89-31.66] | [20.05-39.81] | [2.87-24.22] |
| *p*-value (Chi-square) | 0.0493 | | 0.0198 | |

# Focus Trial Results – Objective Response Rate - Detail

| | Preliminary Analysis Population | | ITT Preliminary Analysis Population | |
|---|---|---|---|---|
| | PHP (N=79) | BAC (N=29) | PHP (N=89) | BAC (N=39) |
| Complete Response (CR) | 6 (7.6%) | 0 | 6 (6.7%) | 0 |
| Partial Response (PR) | 20 (25.3%) | 4 (13.8%) | 20 (22.5%) | 4 (10.3%) |
| Stable Disease (SD) | 30 (38.0%) | 8 (27.6%) | 30 (33.7%) | 8 (20.5%) |
| Progressive Disease (PD) | 22 (27.9%) | 16 (55.2%) | 22 (24.7%) | 16 (41.0%) |
| Not Evaluable (NE) | 1 (1.3%) | 1 (3.5%) | 11 (12.4%) | 11 (28.2%) |

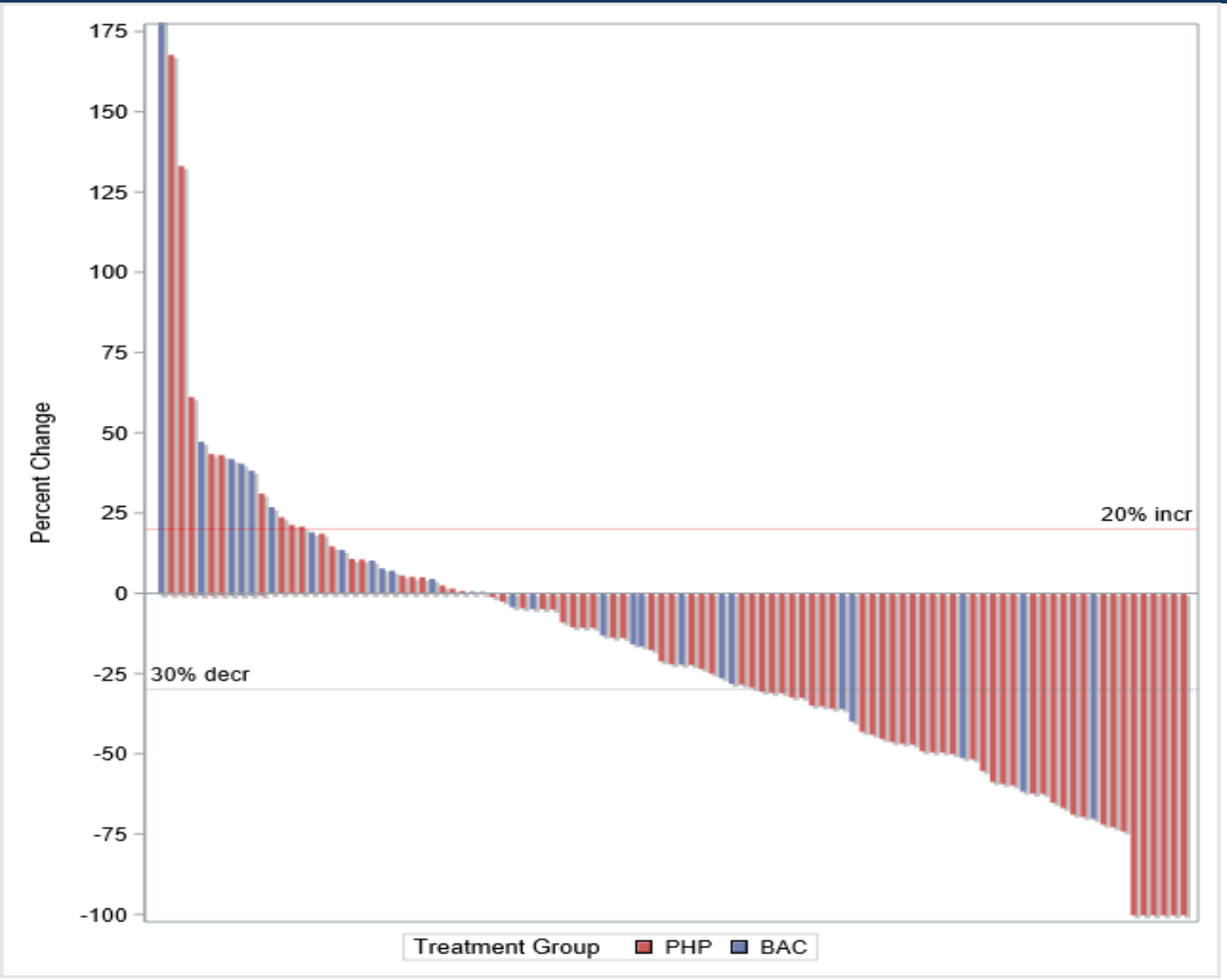
# Focus Trial Results – Disease Control Rate

| | Preliminary Analysis Population | | ITT Preliminary Analysis Population | |
|---|---|---|---|---|
| | PHP (N=79) | BAC (N=29) | PHP (N=89) | BAC (N=39) |
| Disease Control Rate | 56 (71%) | 11 (38%) | 56 (63%) | 11 (28%) |
| 95% CI | [59.58-80.57] | [20.69-57.74] | [52.03-72.93] | [15.00-44.87] |
| *p*-value (Chi-square) | 0.002 | | <0.0003 | |

# Focus Trial Results – Progression-Free Survival

| | Preliminary Analysis Population | |
|---|---|---|
| | PHP (N=79) | BAC (N=29) |
| Progression-Free Survival (PFS, median) | 9.03 months | 3.06 months |
| 95% CI | [6.24-11.83] | [2.69-5.65] |
| *p*-value | 0.0004 | |
| PFS Status | | |
| Events | 50 (63.3%) | 22 (75.9%) |
| Censored | 29 (36.7%) | 7 (24.1%) |
| Hazard Ratio Estimate | 0.41 | |
| 95% CI | [0.246-0.686] | |
| *p*-value | 0.0007 | |

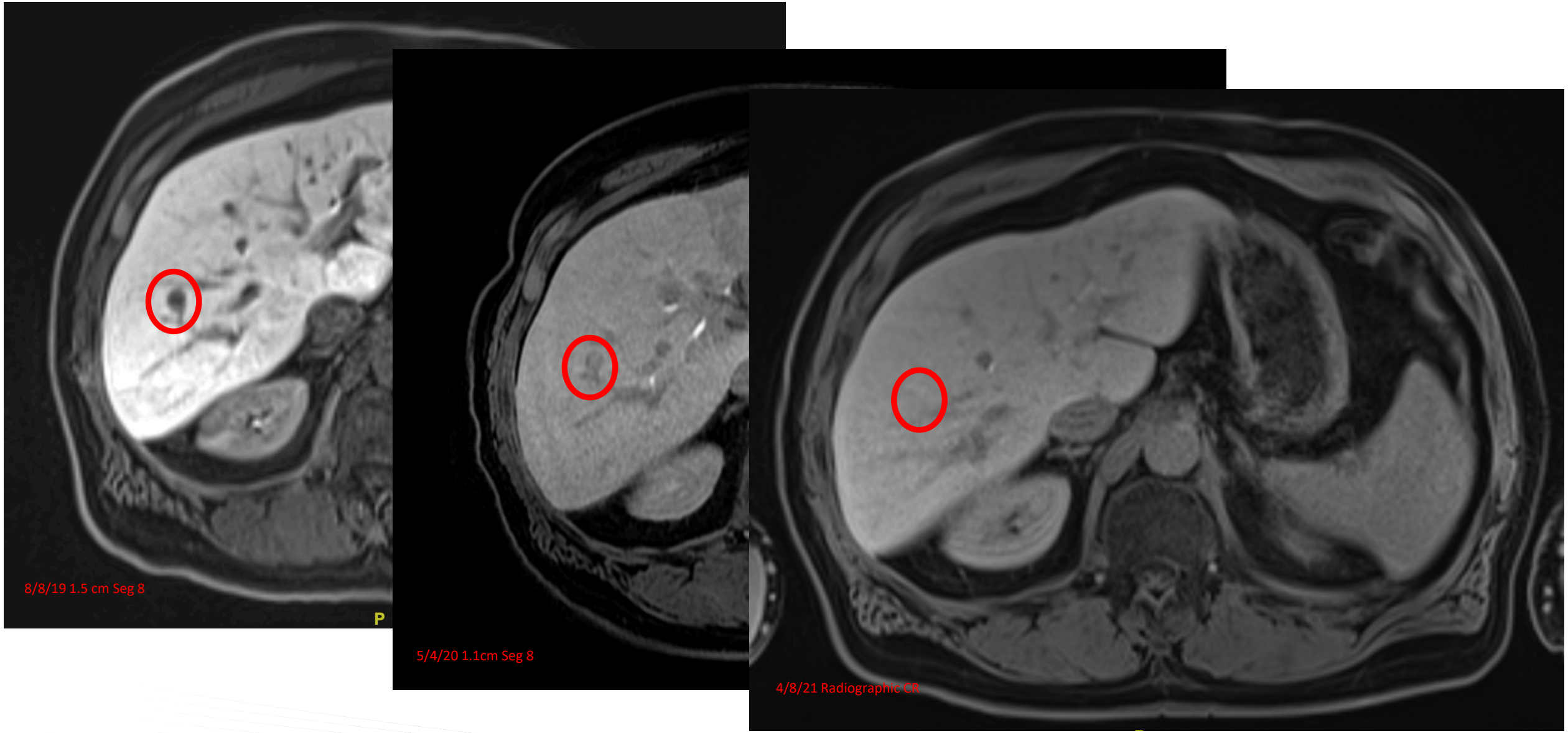
# Focus Trial Results – Best Overall Response (Single Time Point)



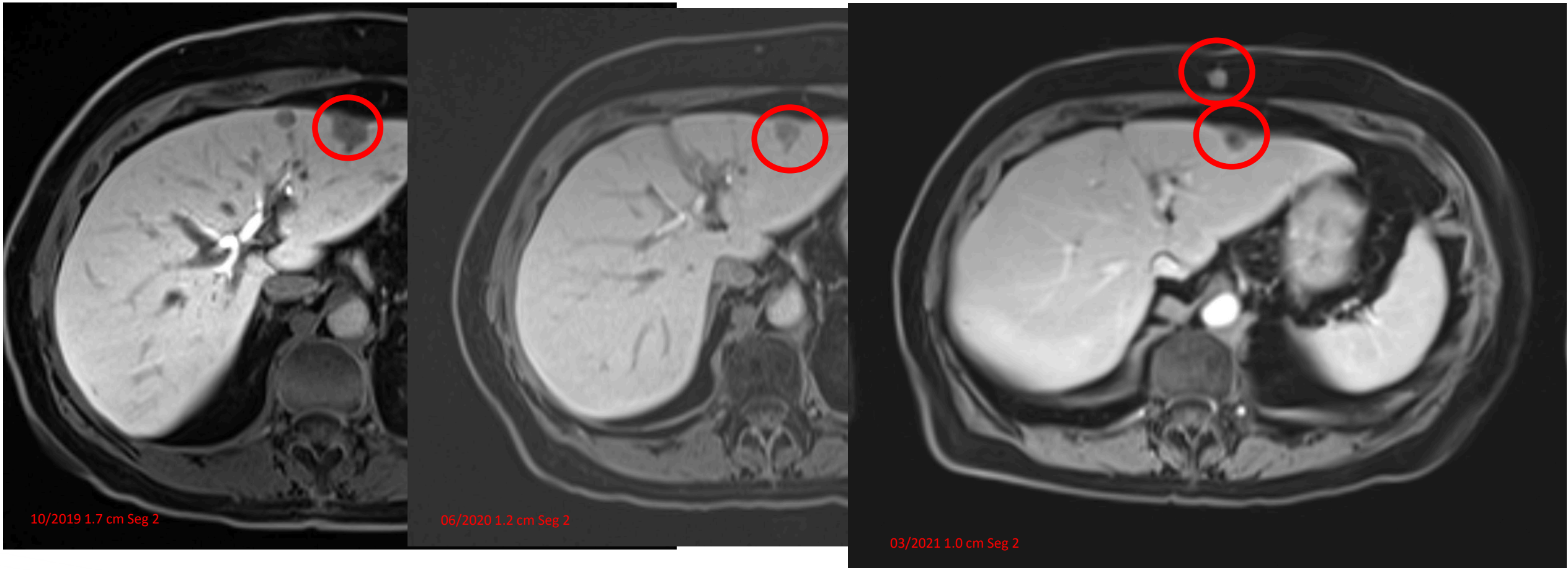

| Best Overall Response | Preliminary Analysis Population | |
|---|---|---|
| | PHP (N=79) | BAC (N=29) |
| Complete Response (CR) | 6 (7.6%) | 0 |
| Partial Response (PR) | 29 (36.7%) | 5 (17.2%) |
| Stable Disease (SD) | 21 (26.6%) | 7 (24.1%) |
| Progressive Disease (PD) | 22 (27.9%) | 16 (55.2%) |
| Not Evaluable (NE) | 1 (1.3%) | 1 (3.5%) |

Note: The efficacy analysis population includes two patients without post-baseline assessments and three patients with no evaluable post-baseline target lesion response assessments; these five patients (three PHP and two BAC) are omitted from the above graph.

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



# 73 y/o female, 6 PHPs, Radiographic hPR – 20 months after 1st PHP – new disease in SQ Tissues



# Serious TEAEs Occurring in >5% of PHP Patients

| Category | Focus Trial (n=94) |
|---|---|
| Bone Marrow Suppression* | 21 (22.3%) |
| Respiratory and Thoracic Disorders† | 6 (6.4%) |
| Cardiac Disorders‡ | 5 (5.3%) |

- * Most commonly thrombocytopenia (14.9%), neutropenia (10.9%), and leukopenia (4.2%)
- † Including hemothorax, pulmonary edema, and pleural effusion
- ‡ Including arrhythmias and cardiac arrest

# Summary and Conclusions

- PHP has demonstrated **a significant improvement** over BAC treatments
  - Preliminary ORR was nearly 3 times better in PHP vs. BAC in both treated **(32.9% vs 13.8%)** and preliminary ITT **(29.2% vs 10.3%)**
  - Preliminary DCR was approximately doubled in favor of PHP vs. BAC in both treated **(71% vs 38%)** and preliminary ITT **(63% vs 29%)**
  - Preliminary PFS was nearly tripled in PHP vs BAC **(9.03 mo vs 3.06 mo)**

- 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
  - Higher ORR and longer PFS seen in the FOCUS trial
  - Lower toxicity observed, no treatment-related deaths

# Thank You

| | |
|---|---|
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