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# ASCO GI FOLLOW-UP & PLANS FORWARD

JANUARY 23, 2023

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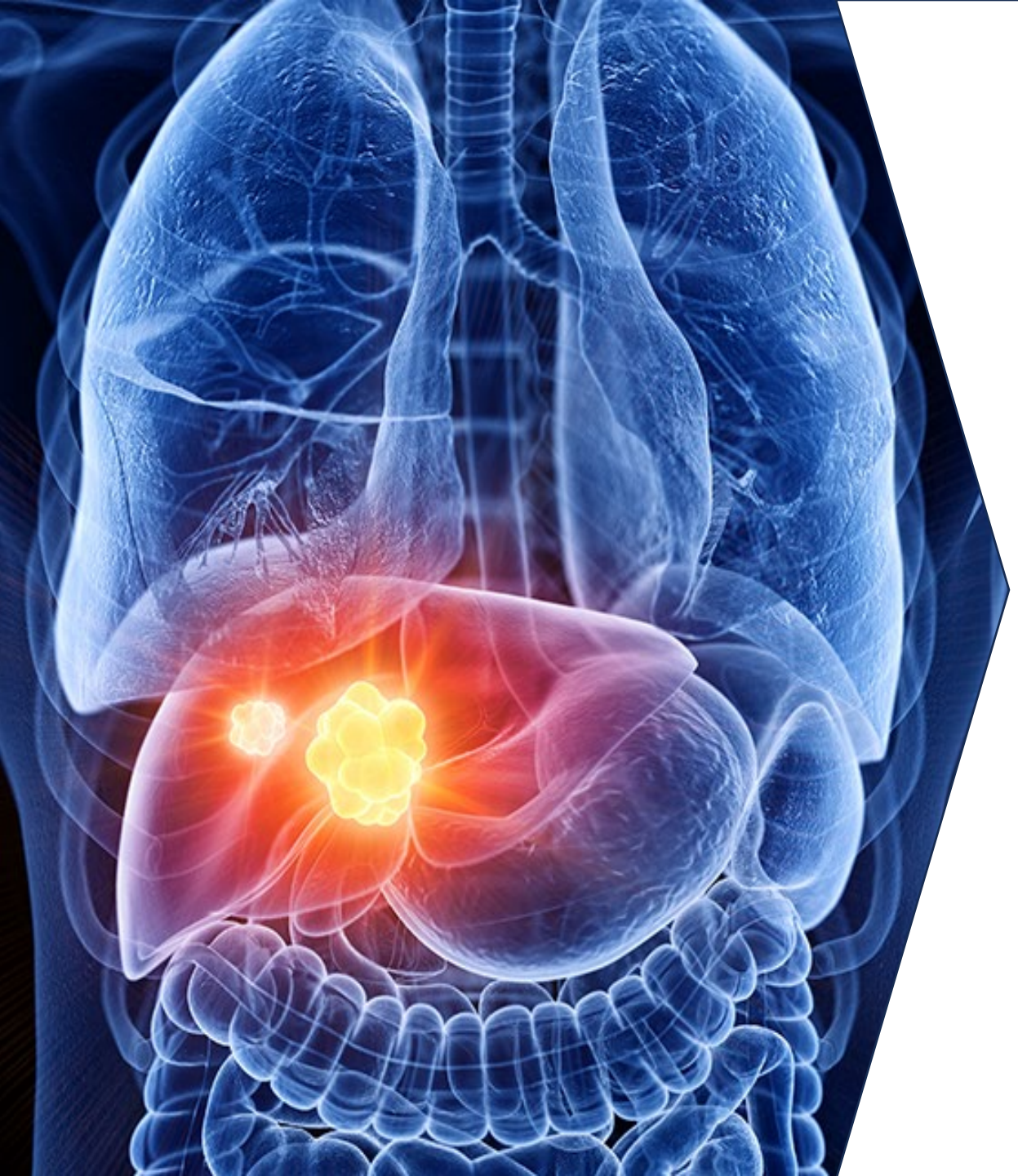

- ASCO GI Take-aways
- Fostrox + Lenvima® update from ASCO presentation
- Fostrox plans moving forward

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# Medivir at ASCO GI

- First data presentation for fostrox + Lenvima combination
- Global expert engagement and advise regarding fostrox development
- Insight sessions with Scientific Advisory Council & potential investigators in upcoming phase 2b study



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# ASCO GI take-aways & implications for fostrox

1. While there has been substantial development in 1L advanced HCC, 2L patient population is not in focus
2. Mainly 1L data (different IO combinations) together with new regimens in earlier stage HCC at congress, limited 2L data confirming previous efficacy benchmarks
3. Continued lack of development from other companies in 2L
    1. The planned fostrox + Lenvima study fills a clear research gap 2L
    2. Positive response on fostrox mechanism, data & and study design plan forward



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ASCO® Gastrointestinal Cancers Symposium

# 476P First safety and efficacy data from phase Ib/IIa study of fostroxacitabine bralpamide (fostrox, MIV-818) in combination with lenvatinib in patients with hepatocellular carcinoma (HCC)

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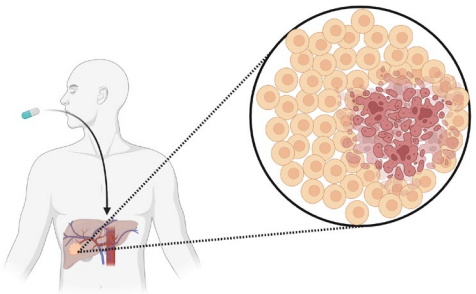
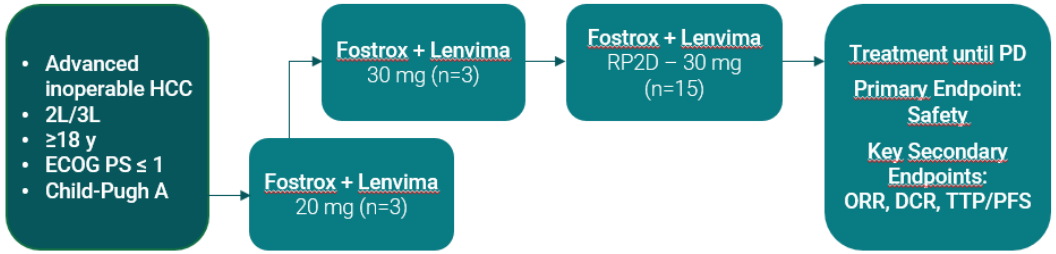
**Dr Maria Reig, Head of the Barcelona Clinic Liver Cancer at IDIBAPs and Liver Oncology Unit at Hospital Clinic of Barcelona and CIBEREHD, Spain**

# Background

- Fostrox is a liver targeted, oral prodrug of troxacitabine that achieves 100-fold higher liver exposure versus IV troxacitabine
- Clinical development in combination with lenvatinib in advanced HCC progressed on prior treatment (NCT03781934)



# Phase Ib/IIa study




| Patient Characteristics | N = 20 |
|---|---|
| Mean age (range) | 63 y (42 - 82) |
| Gender, Female / Male (%) | 25 / 75 |
| ECOG PS 0/1 (%) | 70 / 30 |
| Child-Pugh A (%) | 100 |
| Viral/Non-viral (%) | 75* / 25 |
| Extra hepatic lesion Y/N (%) | 70 / 30 |
| Region, Asia / Europe (%) | 65 / 35 |
| Prior treatment lines; 2L/3L (%) | 85 /15 |
| Prior atezo/bev 1L (%) | 85 |
| Prior local therapy (TACE, RFA etc) | 65 |
| PD on prior treatment (%) | 100 |
| Starting dose fostrox, 20mg / 30mg (%) | 15 / 85 |

*HepB-80% and HepC-20%

**Dosing:** Fostrox: oral, QD for 5 days/21 days cycle, Lenvatinib: oral, 8 or 12 mg QD according to weight
**Enrollment:** 15 sites in the UK, Spain and South Korea
**Imaging assessment:** every 6 weeks with CT and MRI

**Abbreviations:** Heptatocellular carcinoma (HCC), recommended phase II dose (RP2D), progressive disease (PD), overall response rate (ORR), disease control rate (DCR), time to progression (TTP), progression free survival (PFS), Eastern Cooperative Oncology Group Performance Status (ECOG PS), Trans arterial chemoembolisation (TACE), radio frequency ablation (RFA),

# Fostrox + lenvatinib was tolerable with no new unexpected safety events

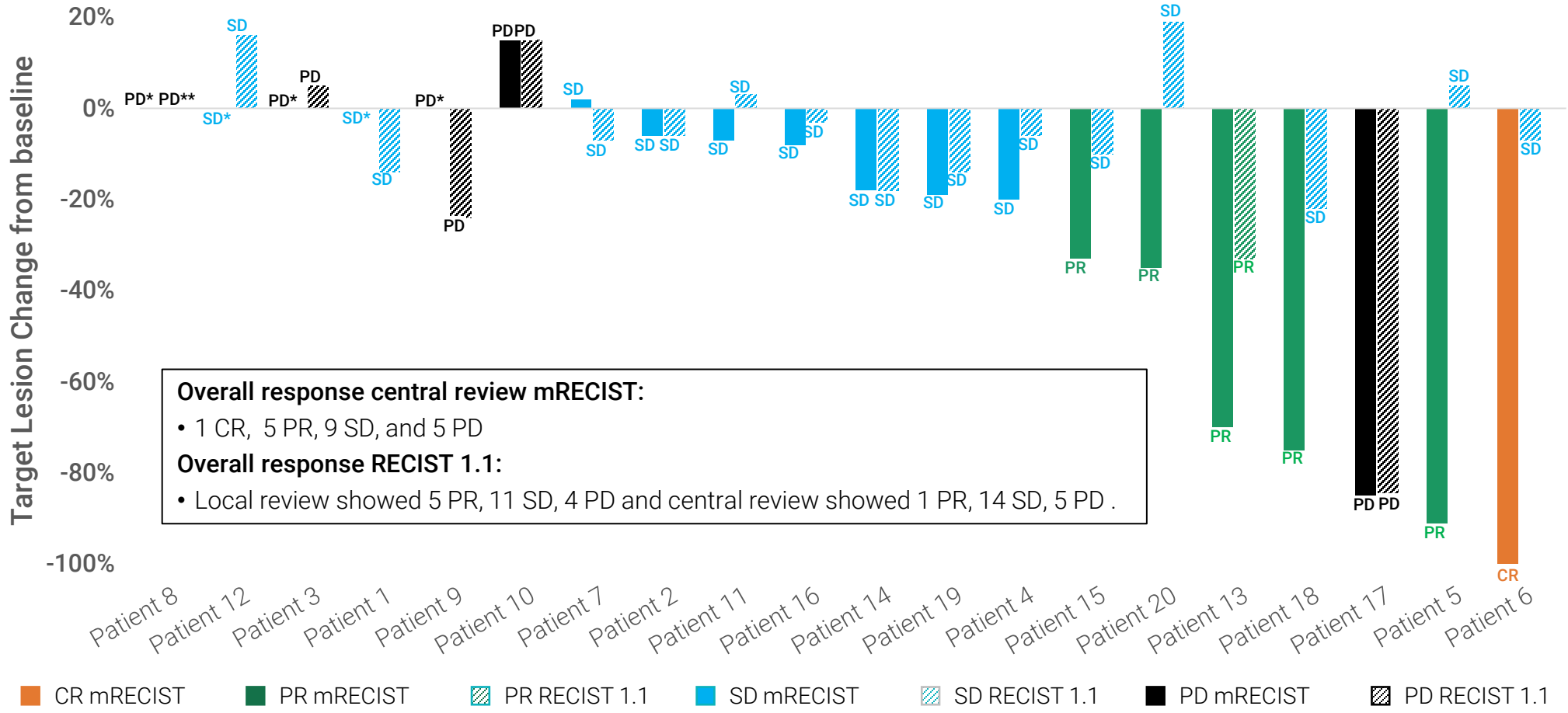
- Fostrox treatment emergent adverse events (TEAE) were typically transient and manageable haematological events
- 30% dose reduced and 5% discontinued due to fostrox adverse events
- Lenvatinib related adverse event and dose modifications (55% of the patients) were in line with expectations for monotherapy use
- No Grade 5 AE was observed

| Treatment Emergent Adverse Events (TEAE) * | TEAE any grade No of pts (%) | TEAE Grade ≥ 3 No of pts (%) |
|---|---|---|
| **Any TEAE** | **20 (100)** | **14 (70)** |
| Thrombocytopenia | 13 (65) | 6 (30) |
| Hypothyroidism | 11 (55) | |
| Neutropenia (no febrile) | 10 (50) | 8 (40) |
| Diarrhoea | 9 (45) | |
| Hand-foot syndrome | 9 (45) | 1 (5) |
| Leukocyte decrease | 8 (40) | 2 (10) |
| Anaemia | 7 (35) | 2 (10) |
| Asthenia | 7 (35) | 3 (15) |
| Decreased appetite | 7 (35) | |
| Fatigue | 7 (35) | |
| Nausea | 6 (30) | |
| Cough | 5 (25) | |
| Hypertension (worsening) | 5 (25) | 1 (5) |
| Proteinuria | 5 (25) | 1 (5) |
| Pruritus | 4 (20) | |

*CTCAE, v5, data cut-off Sept 2023

# Promising best/overall response

## Central review – best response RECIST 1.1 and mRECIST




**Overall response central review mRECIST:**

- 1 CR, 5 PR, 9 SD, and 5 PD

**Overall response RECIST 1.1:**

- Local review showed 5 PR, 11 SD, 4 PD and central review showed 1 PR, 14 SD, 5 PD .



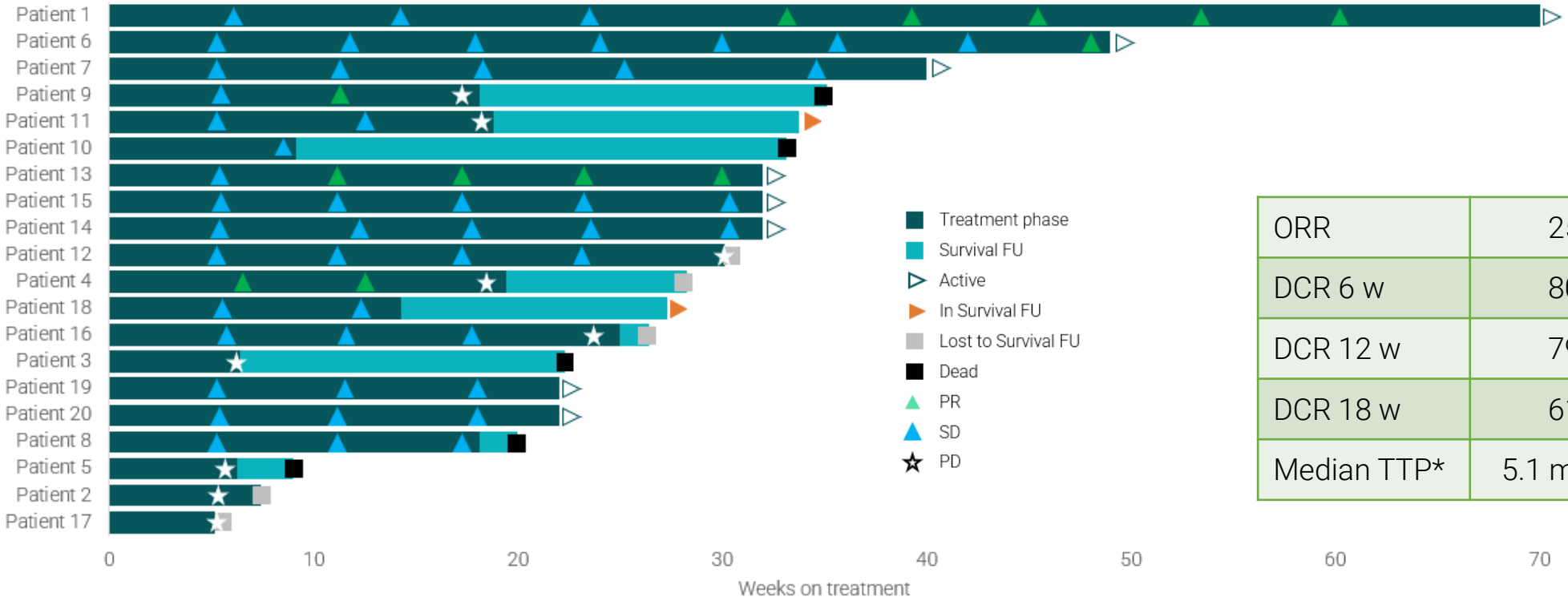
Data cut-off Sept 2023

*patients lacking contrast enhancement in arterial phase and could not be evaluated with mRECIST where 3 had PD in NTL.

**patient number 8 had no measurable TL with central RECIST 1.1

# First efficacy data showed encouraging clinical benefit

## Local review, disease control & time to progression RECIST 1.1




| | |
|---|---|
| ORR | 25% |
| DCR 6 w | 80% |
| DCR 12 w | 79% |
| DCR 18 w | 61% |
| Median TTP* | 5.1 months |

*Data cut-off Jan 2, 2024
20 patients included >12 w follow-up

Abbreviations: complete response (CR), partial response (PR), stable disease (SD), progressive disease (PD), follow-up (FU), disease control rate (DCR)

# Conclusion

- Fostrox + lenvatinib in 2L/3L showed an acceptable safety and tolerability profile with encouraging efficacy outcome in HCC patients, progressed on predominantly atezolizumab/bevacizumab in 1L
- Disease control rate was high and durable with 61% still having clinical benefit at 18 weeks (local review RECIST 1.1)
- Based on these results, a randomized phase IIb study is planned to further evaluate the clinical benefit of fostrox 30 mg in addition to lenvatinib standard dose in 2L HCC patients progressed on IO combinations in 1L

# Improved clinical benefit with maturing data and patients staying longer on treatment

| RECIST 1.1 | **Interim data #1**<br>**2023-10-05**<br>**n=18** | **ASCO GI**<br>**2024-01-17**<br>**n=20** |
|---|---|---|
| ORR | 17% | 25% |
| DCR 12 weeks | 72% | 79% |
| Median TTP | 4.5 months | 5.1 months* |

*Data cut-off Jan 2, 2024



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# What Happens at Progression? Sequential Therapy Recommendations for Advanced HCC

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Phase I Program Director
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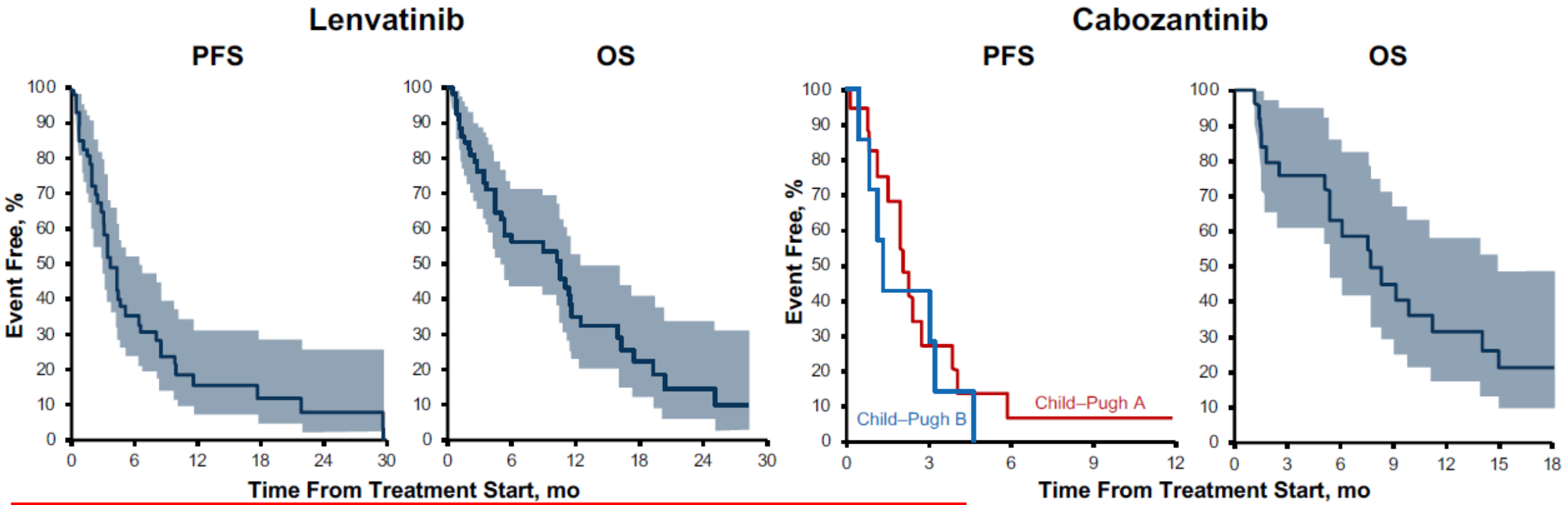
Los Angeles, California

PeerView
Live

# How Do We Sequence Following Immunotherapy?[1-3]

**Currently, there is no strong evidence to identify optimal post-IO options**



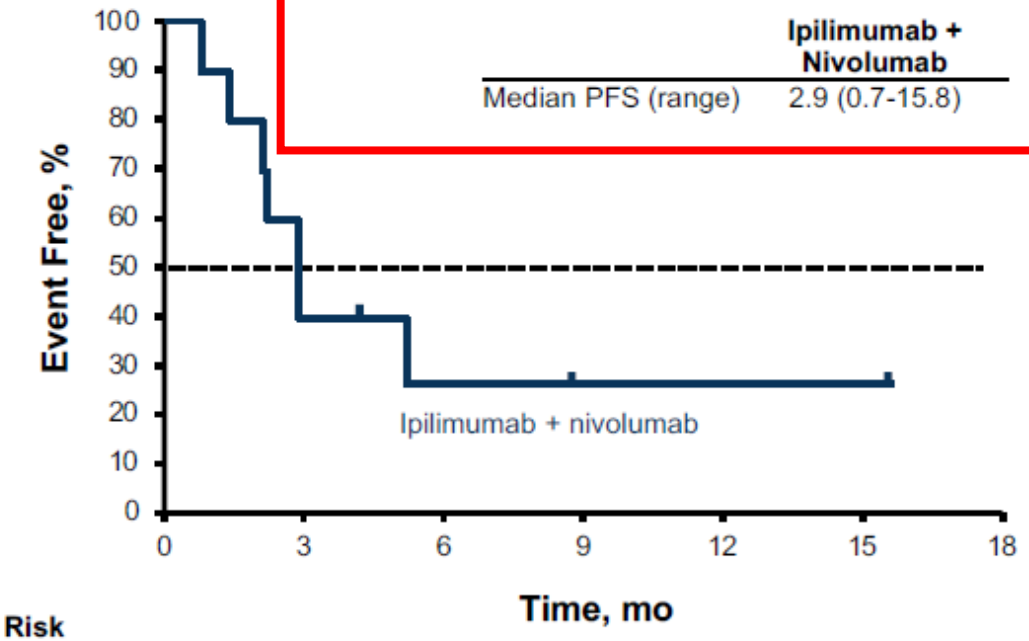

- Lenvatinib demonstrated a PFS of 3.7 mo; mOS of 12.8 mo (n = 53)
- Cabozantinib demonstrated a PFS of 2.1 mo; mOS of 7.7 mo (n = 26)
- Other studies are currently underway to evaluate other 2L options post atezo/bev (eg, regorafenib[3])

1. Gile J et al. ASCO GI 2023. Abstract 507. 2. Palmer M et al. ASCO GI 2023. Abstract 559. 3. Cheon J et al. ASCO GI 2023. Abstract TPS634.

# Potential Use for Nivolumab + Ipilimumab Is Effective in the Post-ICI Setting[1]

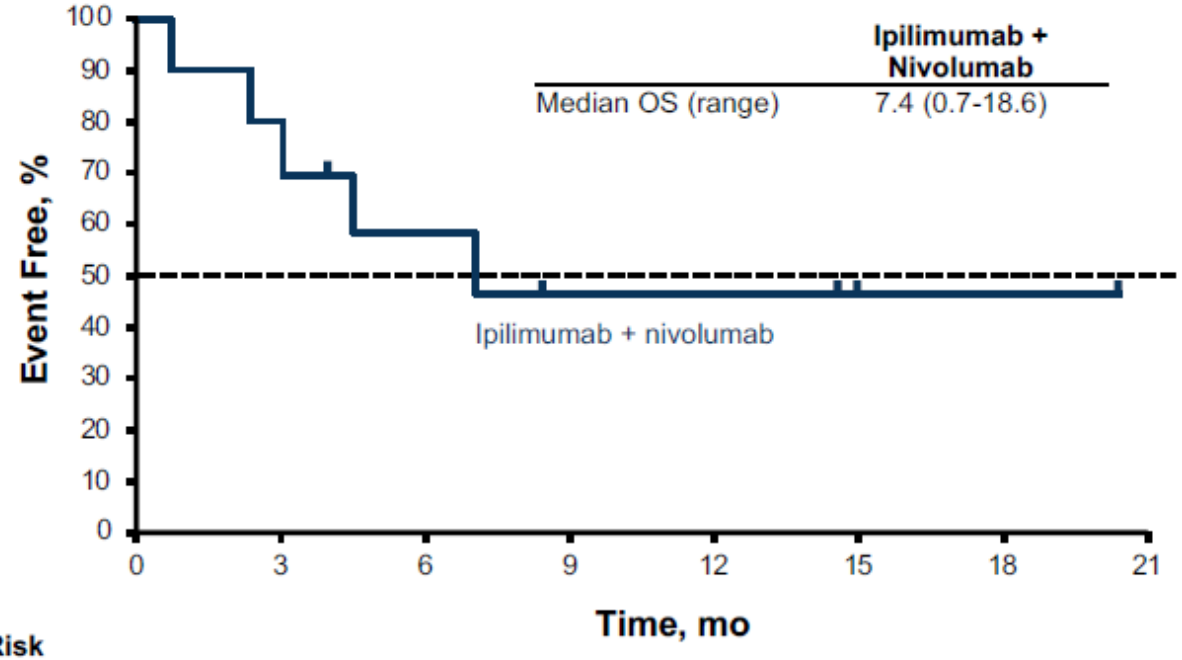
## A Multicenter Retrospective Study of Ipi + Nivo After Failure of 1L Atezo/Bev[a]

### Progression-Free Survival




| No. at Risk | | | | | | | |
|---|---|---|---|---|---|---|---|
| Ipilimumab + nivolumab | 10 | 4 | 2 | 1 | 1 | 1 | 0 |

### Overall Survival




| No. at Risk | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Ipilimumab + nivolumab | 10 | 8 | 5 | 3 | 3 | 3 | 1 | 1 |

[a] Kaplan-Meier analyses of patients with advanced HCC with ipilimumab and nivolumab after the failure of prior PD-1/PD-L1 inhibitor-based combination therapy.

1. Roessler D et al. 2022. *J Cancer Res Clin Oncol*.

# Take-Homes for Selection of 2L HCC Therapy

| Patient With Advanced HCC | Options for 2L Therapy | Supporting Evidence |
|---|---|---|
| 1L therapy with atezo + bev, durva + treme, or single-agent durva | • TKI<br>• Combination IO | Currently no strong evidence for selecting post-immunotherapy options |
| 1L therapy with sorafenib or lenvatinib | • Cabozantinib or regorafenib<br>• Single-agent antiangiogenic therapy<br>• Combination IO<br>• Single-agent IO | • CELESTIAL, RESORCE<br>• REACH-2<br>• CheckMate -040<br>• KEYNOTE-224 |

# Fostrox + Lenvima compares favourably with benchmarks

| RECIST 1.1 | Previous 2nd line studies[1] | 2nd line Lenvima[2] (n=12) | Fostrox + Lenvima[3] (n=20) |
|---|---|---|---|
| ORR | ~10% | 8-17% | **25%** |
| DCR | ~60% | 58%* | **79%*** |
| Median PFS/TTP | ~3.5 months | 2.8-4.1 months | **5.1 months*** |

*DCR at 12 weeks

[1]Data from previous 2L phase 3 HCC studies with Stivarga, Cyramza & Cabometyx
[2]Kobayashi et al., Clinical Cancer Research, Oct 5, 2023 online
[3]Preliminary results from Investigator review (All 21 patients data cut-off January 22, 2024)



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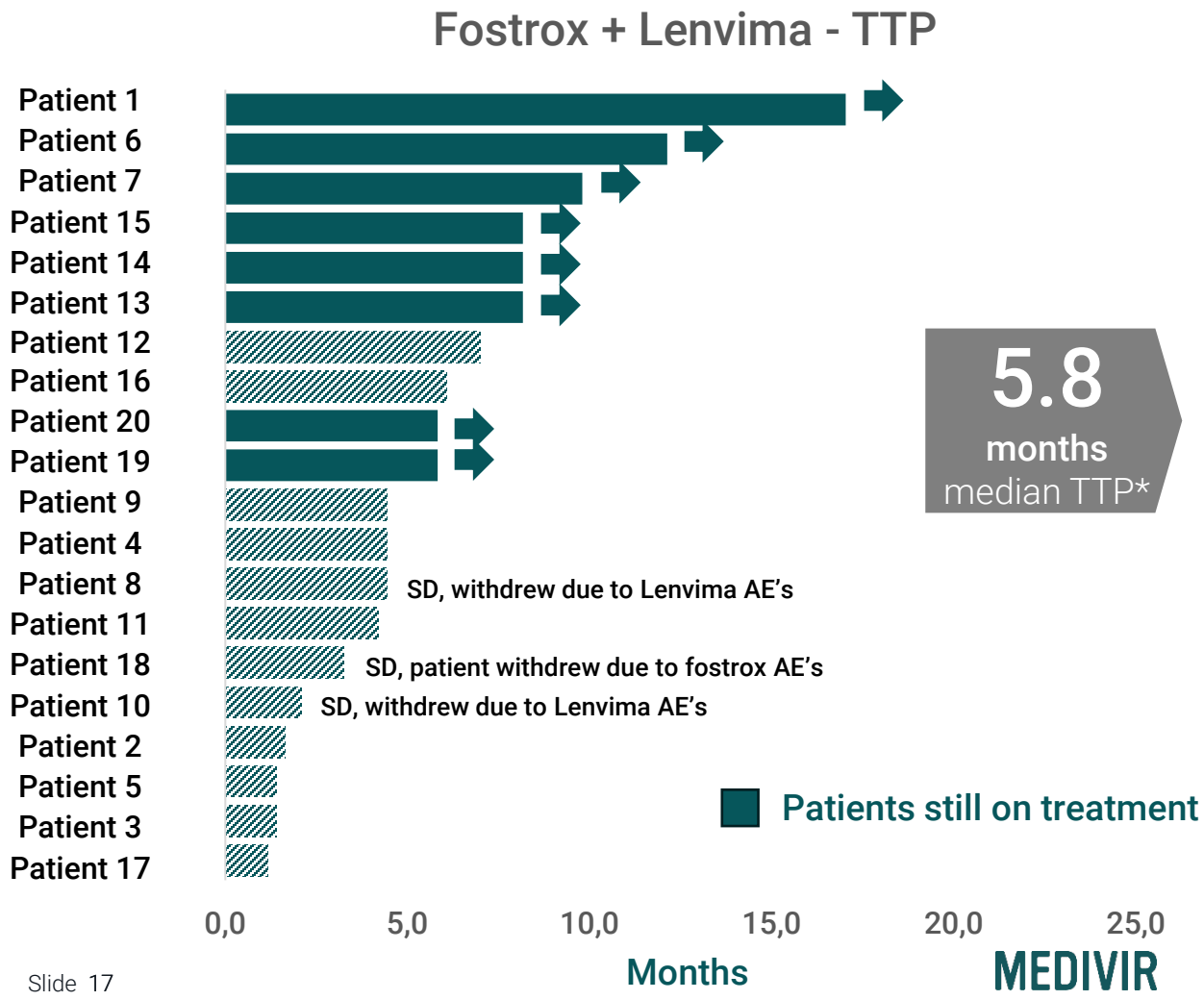
# Long duration of benefit seen in patients with limited effect on prior treatment, updated median TTP 5.8 months*






*TTP – Time to Progression, data cut-off January 22, 2024, >40% of patients still on treatment

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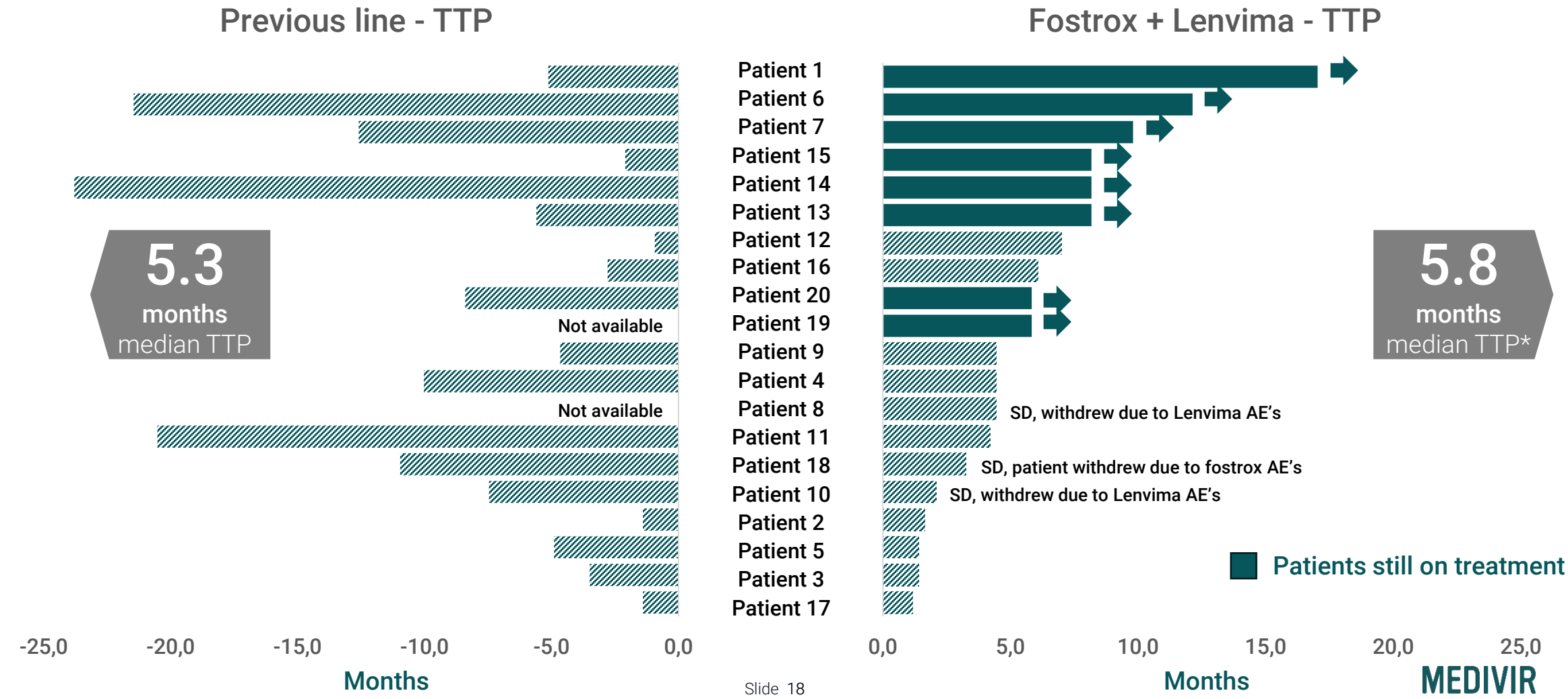




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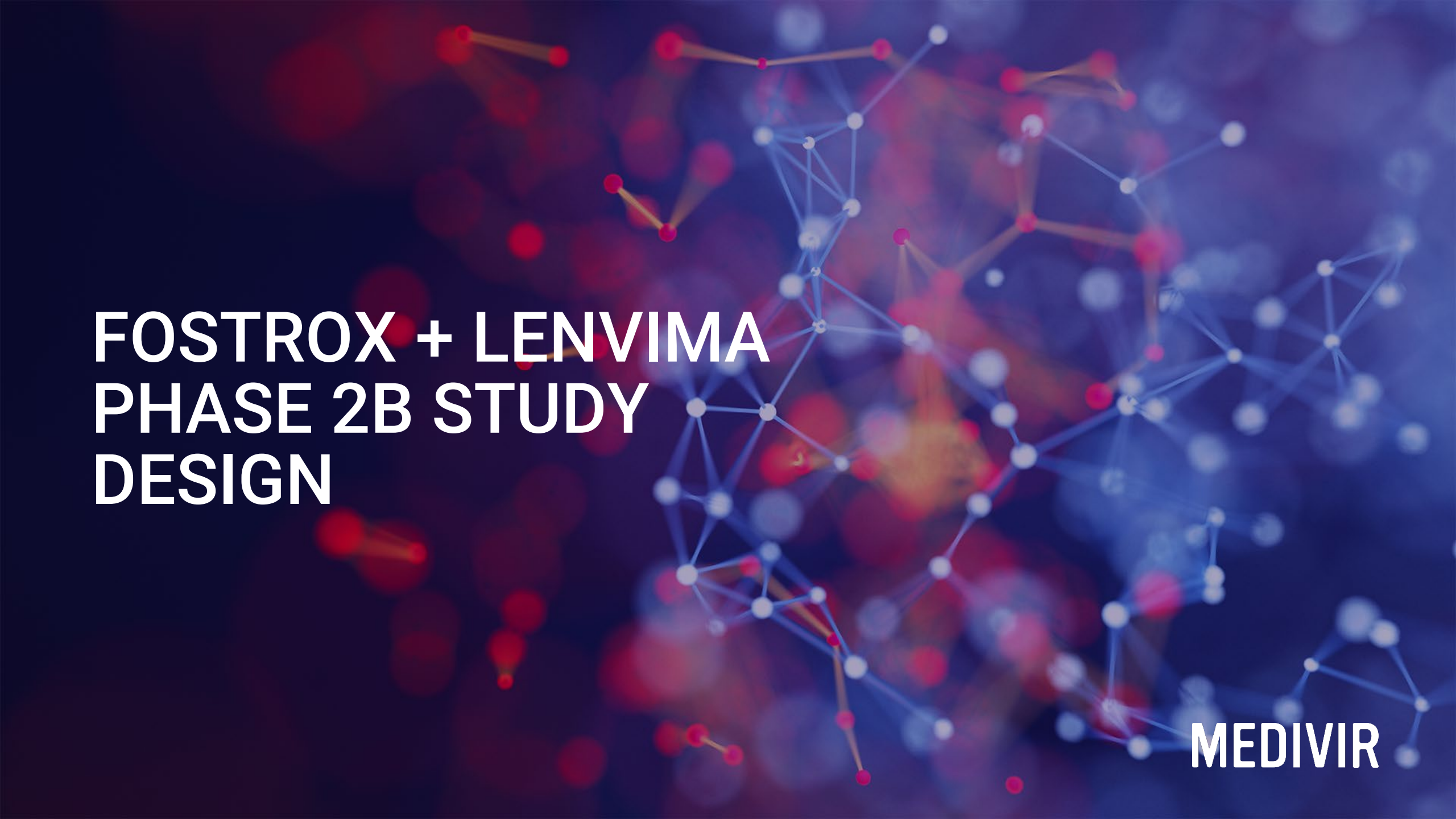
# FOSTROX + LENVIMA PHASE 2B STUDY DESIGN



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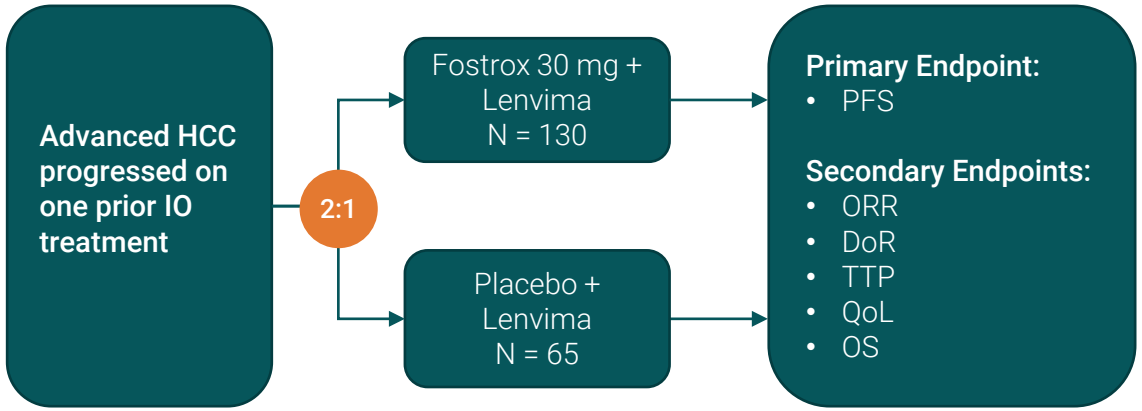
# Pivotal phase 2b; global HCC expert input at ASCO supports proposed study design ahead of FDA interactions

## Phase 2b: randomized, double-blind study design



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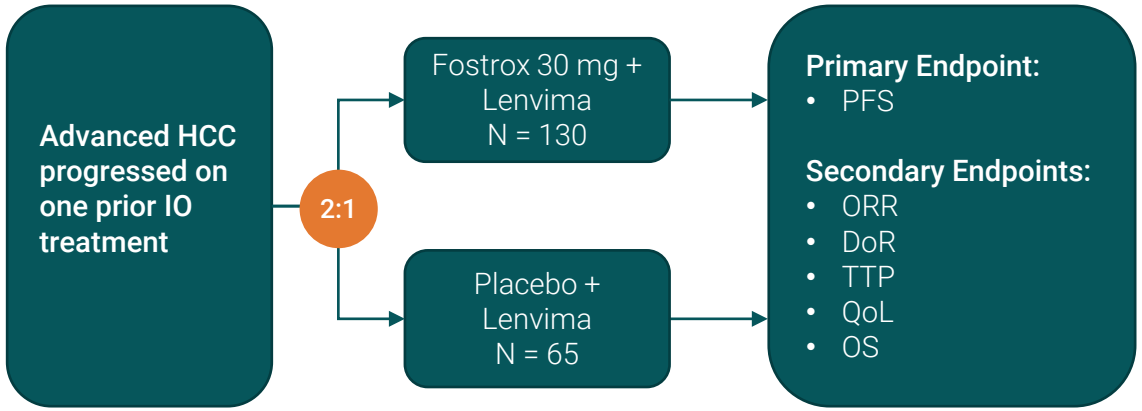
## Phase 2b: randomized, double-blind study design




### HCC experts feedback on study design

- ✓ No 2L data at progression on 1L IO; strong support for a randomized phase 2b study design
- ✓ Lenvima preferred 2L option, rational combination partner with fostrox
- ✓ Lenvima 2L monotherapy efficacy estimate; PFS/TTP ~4 months and ORR ~10%
- ✓ 2 months PFS benefit is clinically relevant
- ✓ Approriate study endpoints, to be confirmed in FDA interactions



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# Accelerating fostrox development

| | | |
|---|---|---|
| **CMC** | ▪ Updated commercial formulation for pivotal phase 2b study | ▪ Q4 ‘23 |
| | ▪ Process development suitable for commercial manufacture | ▪ Q4 ‘23 |
| | ▪ Manufacture of new GMP campaign for phase 2b | ▪ Initiated Q4 ‘23 |
| **Clinical** | ▪ Scientific Advisory Council study design | ▪ Jan ‘24 |
| | ▪ KOL/investigator outreach | ▪ ASCO GI & EASL |
| | ▪ CRO selection | ▪ Initiated Q4 ‘23 |
| **Regulatory** | ▪ FDA Type D meeting | ▪ Q4 ‘23 |
| | ▪ FDA Type C meeting | ▪ Initiated |
| | ▪ Open IND & apply for fast track designation | ▪ H1 ‘24 |



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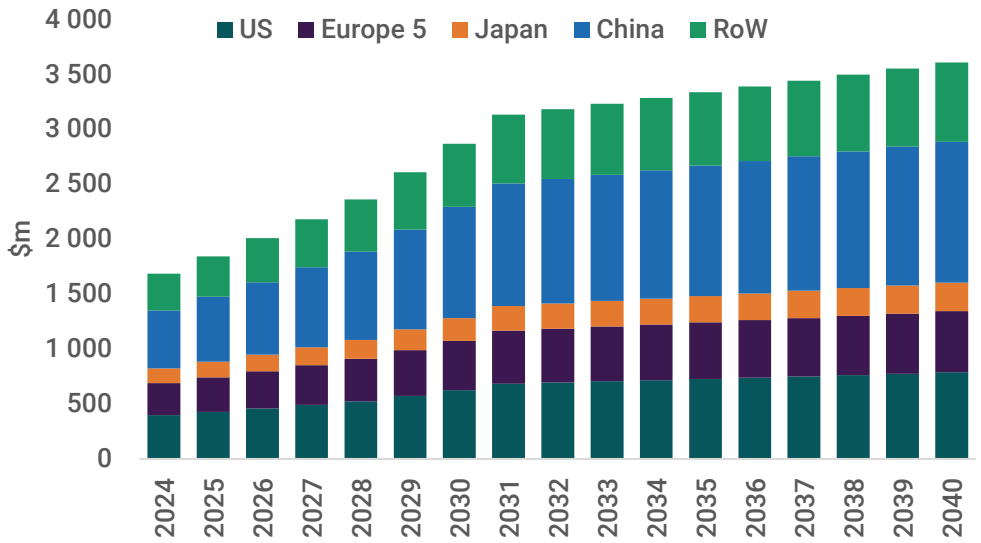
# ASCO GI interactions reinforces first-to-market opportunity for fostrox in 2nd line HCC market worth ~$2.5b by 2028

## Significant market growth* driven primarily by NASH/NAFLD induced HCC




## As medical treatments improve, 2nd line treatment duration will increase significantly*

| | |
|---|---|
| **2L treated patients 2028** | ▪ US: ~7.500 \| EU5: ~11.000 \| JP: 5.000 \| CN: ~38.000 |
| **2L treatment duration** | ▪ 2L patients assumed to be **treated for 7 months** on average |
| **Anticipated 2L competition 2028** | ▪ Base case – **no approved treatments post current 1L SoC** to compete with Fostrox + Lenvima |
| **Cost of therapy per month** | ▪ US - $10.000 \| EU - $5.000 \| JP - $5.000 \| CN - $3.000 |

*Source: GlobalData 2021 & internal analysis

**Strategic evolution – Earlier treatment lines in HCC provides additional market opportunity of >$5bn**



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# Fostrox – a smart chemotherapy with a unique, liver targeted & tumor selective treatment of HCC, potential for accelerated approval 27/28

- Fostrox + Lenvima clinical benefit improves as study matures and shows consistently improved efficacy compared with Lenvima alone
- Continued development for fostrox + Lenvima in 2nd line HCC with Accelerated Approval intent 2027/2028
- 2nd line HCC post Tecentriq® + Avastin® lacks approved treatments & is a market valued at ~$2.5bn annually



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