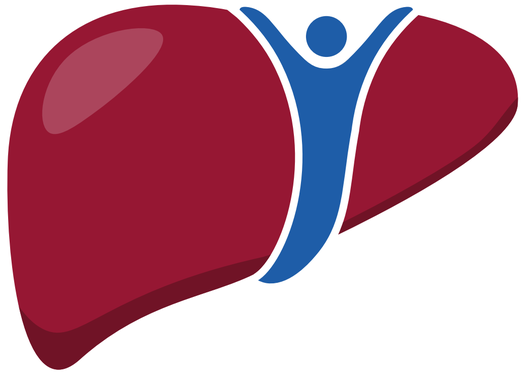


Improving **PBC** outcomes by prioritizing patients' needs

Trial summaries from the AASLD Liver Meeting 2024

Springer Healthcare IME

Fibrate-OCA (Fi-OCA) – A global snapshot of PBC practice around the globe

Abstract: 724 | Vincenzo Ronca[1], Antonio De Vincentis[2], Francesca Terracciani[2] *et al*

Improving **PBC** outcomes by prioritizing patients' needs

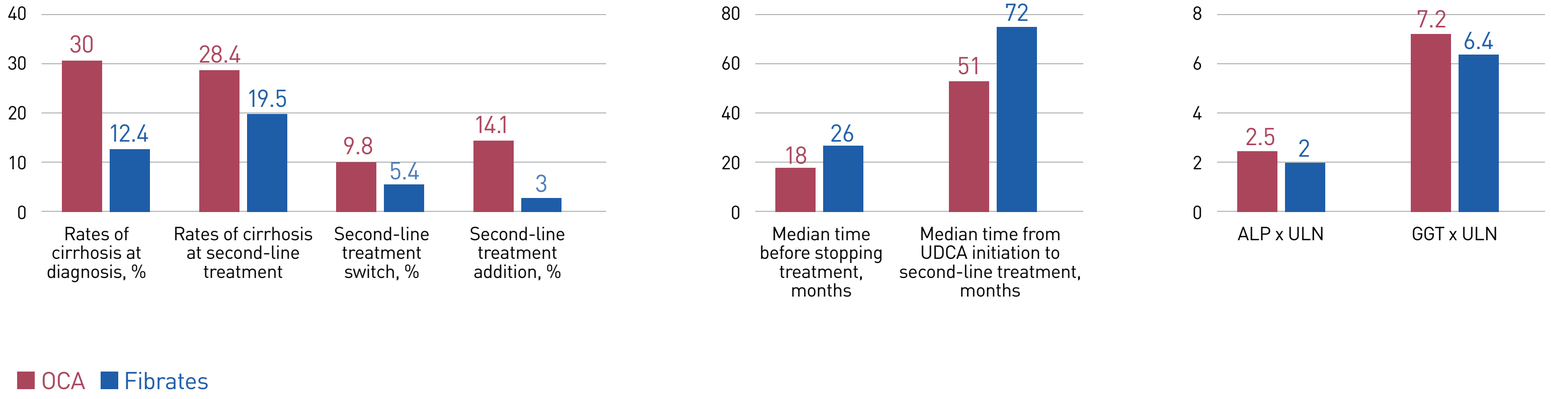
PARTICIPANTS

1825
Adults with PBC who are **intolerant to UDCA**

- **938** Patients treated with **second-line OCA** for at least 12 months
- **887** Patients treated with **second-line fibrates** (bezafibrate or fenofibrate) for at least 12 months

Locations:
40 liver centres across Europe, Canada, USA, Argentina, Israel, and Japan

RESULTS: *Significant treatment differences at baseline*



Treatment trajectory by the end of follow-up:

- **550 on OCA**
  510 started on OCA; 40 switched from fibrates.
- **713 on fibrates**
  632 started on fibrates; 81 switched from OCA.
- **141 on double treatment**
  12 started on double treatment; 105 OCA patients added a fibrate; 24 of fibrate patients added OCA.
- **289 stopped treatment**
  151 on OCA, 131 on fibrates.

CONCLUSIONS

Researchers quoted...

> The high rate of treatment changes and discontinuation highlights a suboptimal treatment allocation. A more granular definition of the international cohorts could increase details on patients' trajectories allowing the derivation of treatment allocation tools.

Abbreviations ALP: alkaline phosphatase; GGT: gamma-glutamyl transferase; OCA: obeticholic acid; PBC: primary biliary cholangitis; UDCA: ursodeoxycholic acid; ULN: upper limit of normal

[1]Humanitas University; Milan, Italy; [2]University Campus Bio-Medico of Rome, Italy

Springer Healthcare IME

Long-term efficacy and safety of open-label seladelpar treatment in patients with primary biliary cholangitis: Pooled interim results for up to 3 years from the ASSURE study

Abstract: 5044 | Eric Lawitz[1], Palak Trivedi[2], Kris Kowdley[3] *et al*

Improving **PBC** outcomes by prioritizing patients' needs

PARTICIPANTS

337 Adults with PBC taking seladelpar 10 mg/day for between 12 and 30 months, with 124 (37%) having ≥24 months of exposure

At baseline:

- Mean ALP was 287.5 U/L
- Mean TB was 0.75 mg/dL
- 16% of patients had cirrhosis
- Mean pruritus NRS was 6.3

RESULTS

Primary efficacy endpoints

Rate	12 months	24 months	30 months
Rate of composite biochemical response*, %	73	73	81
ALP normalization, %	38	38	41
ALT normalization, %	61	66	90

*Biochemical response: ALP <1.67 X ULN plus ≥15% reduction from baseline and TB level ≤ULN

- Mean 3.3-point reduction (improvement) in pruritus NRS at 6 months among 99 patients with moderate-to-severe pruritus (NRS ≥4) at baseline.

Primary safety endpoints

Rate	12 months	24 months	30 months
Exposure-adjusted AEs per 100 patient–years, %	85.8	70.0	63.0
Grade ≥3 AEs, %	9.6	8.4	8.4

- Most AEs of grade 1 or 2 in severity.
- COVID-19, pruritus and nausea were the most common AEs (6.8 and 5.2%, respectively).
- Rates of exposure-adjusted liver, muscle, and renal-related AEs remained stable or decreased over the 3 years of seladelpar treatment.

CONCLUSIONS

Researchers quoted...

> Seladelpar continues to appear safe and well tolerated, showing no new safety signals or changes in the frequency of adverse events after up to 3 years of exposure.

Abbreviations AE: adverse event; ALP: alkaline phosphatase; ALT: alanine aminotransferase; NRS: numerical rating scale; PBC; primary biliary cholangitis ULN: upper limit of normal; TB: total bilirubin

[1]University of Texas Health San Antonio, TX, USA; [2]University of Birmingham, UK [3]Liver Institute Northwest, Seattle, WA, USA

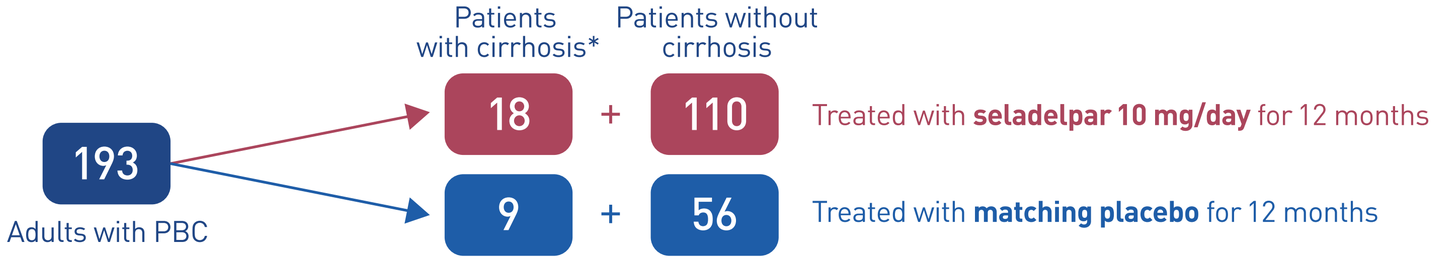
Springer Healthcare IME

Efficacy and safety of seladelpar in patients with primary biliary cholangitis and compensated cirrhosis in the phase 3 placebo-controlled RESPONSE trial

Abstract: 700 | Alejandra Villamil[1], Ziad Younes[2], Christopher Bowlus[3] *et al*

Improving **PBC** outcomes by prioritizing patients' needs

PARTICIPANTS



RESULTS

Change in ALP at 12 months

	Mean ALP level at baseline	Seladelpar 10 mg	Placebo
Patients with cirrhosis,U/L	345.8	−121.4#	23.2
Patients without cirrhosis, U/L	309.2	−134.8##	−18.0

Change in GGT at 12 months

	Mean GGT level at baseline	Seladelpar 10 mg	Placebo
Patients with cirrhosis, U/L	241.2–461.9	−76.1	10.3
Patients without cirrhosis, U/L	259.5–273.6	−112.4	−23.4##

Change in TB at 12 months

	Mean TB level at baseline	Seladelpar 10 mg	Placebo
Patients with cirrhosis, mg/dL	0.97	0.17	0.43
Patients without cirrhosis, mg/dL	0.72	−0.05	−0.02

- Sustained reductions in ALP, GGT, and ALT with seladelpar in patients with and without cirrhosis.
- TB and liver elasticity remained stable with seladelpar in patients with versus without cirrhosis.

Safety

- The AE profile and elevation of liver enzymes in patients taking seladelpar were similar to those of patients taking placebo, irrespective of cirrhosis.

#p<0.05; ##p<0.0001

CONCLUSIONS

Researchers quoted...

> In patients with PBC and cirrhosis, seladelpar decreased cholestatic and liver injury markers compared with placebo, similar to effects seen in patients without cirrhosis in the RESPONSE trial.

Abbreviations AE: adverse event; ALP: alkaline phosphatase; GGT: gamma glutamyl transferase; PBC: primary biliary cholangitis; TB: total bilirubin

[1]Hospital Italiano de Buenos Aires, Argentina; Switzerland; [2]Gastro One, Germantown, TN, USA; [3]University of California, Davis, Sacramento, CA, USA

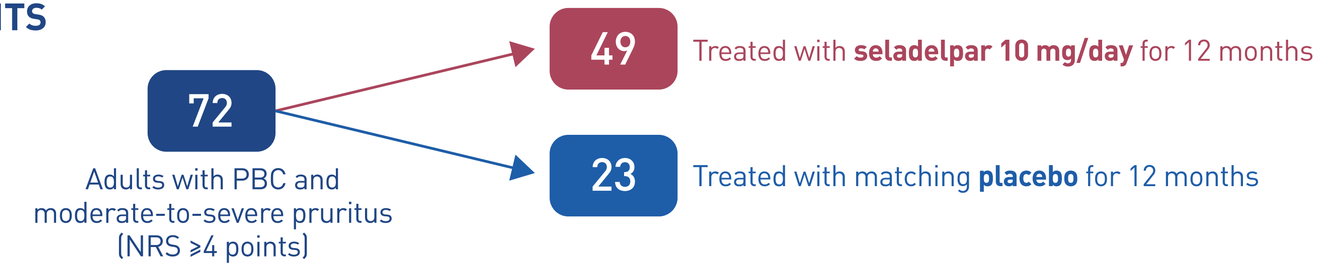
Springer Healthcare IME

Attenuation, near resolution, and prevention of pruritus in patients with primary biliary cholangitis treated with seladelpar: A secondary analysis of patterns of pruritus change in the RESPONSE trial

Abstract: 703 | Andreas Kremer[1], Cynthia Levy[2], Marlyn Mayo[3] *et al*

Improving **PBC** outcomes by prioritizing patients' needs

PARTICIPANTS



RESULTS

Pruritus NRS response rates at 12 months

	Seladelpar 10 mg	Placebo
Patients with a ≥3-point decline in pruritus NRS, %	46.9	21.7
Patients with a ≥4-point decline in pruritus NRS, %	30.6	8.7

Rates of pruritus near resolution (NRS ≤1) at 12 months

	Seladelpar 10 mg	Placebo
Patients with baseline NRS ≥4, %	26.5	0.0
Patients with baseline NRS ≥7, %	18.8	0.0

*NRS: 0-10-point scale, where 0=no itch and 10=worst possible itch

- Seladelpar reduced itch to mild levels.
- Seladelpar led to near resolution of itch in nearly one in five patients with severe pruritus (NRS ≥7) at baseline and improved sleep disturbance and fatigue on the PBC-40.
- Seladelpar reduced itch to clinically nonsignificant levels in 40% of patients with clinically significant pruritus (PBC-40 itch domain ≥7) at baseline, with reductions in sleep disturbance and fatigue.
- Among patients without itch at baseline, none of those treated with seladelpar had developed de novo itch at 12 months versus 27% of those treated with placebo.

Safety

- The percentage of patients with AEs was comparable for the seladelpar and placebo groups, regardless of baseline itch severity.
- There were no treatment-related serious AEs.

CONCLUSIONS

Researchers quoted...

> Seladelpar reduced pruritus severity in patients with PBC compared with placebo, leading to clinically meaningful declines in NRS.

Abbreviations AE: adverse event; NRS: numerical rating scale; PBC: primary biliary cholangitis; PBC-40 RO: reported outcome

[1]University of Zurich, Switzerland; [2]University of Miami School of Medicine, FL., USA; [3]University of Texas Southwest Medical Centre, Dallas, TX, USA

Springer Healthcare IME

Effect of obeticholic acid on inflammatory markers and fibrosis scores in POISE incomplete responders: A retrospective review of POISE, a phase 3 trial of obeticholic acid for the treatment of primary biliary cholangitis

Abstract: 949 | David Victor[1], Jing Li[2], Radhika Nair[2] et al*et al*

Improving **PBC** outcomes by prioritizing patients' needs

PARTICIPANTS

39 Patients with PBC who did not respond* to 12 months of OCA, at a dose of **10 mg/day**

38 Patients with PBC who did not respond* to 12 months of OCA, at a dose of **5 or 10 mg/day**

***Incomplete responders** did not achieve composite endpoint of ALP <1.67 x ULN with ⩾15% reduction from baseline and TB ⩽ULN at 12 months

RESULTS

Median percentage increase (improvement) from baseline

	Fibrosis growth factor 19 (FGF19)		C-reactive protein (CRP)		Immunoglobulin M (IgM)		Cleaved cytokeratine-18 (CK-18)		Fibrosis- (FIB-4)		Aspartate aminotransferase-to-platelet ratio index (APRI) score	
	OCA 5 or 10 mg, %	OCA 10 mg, %	OCA 5 or 10 mg, %	OCA 10 mg, %	OCA 5 or 10 mg, %	OCA 10 mg, %	OCA 5 or 10 mg, %	OCA 10 mg, %	OCA 5 or 10 mg, %	OCA 10 mg, %	OCA 5 or 10 mg, %	OCA 10 mg, %
6 months	67	86	2	29	9	18	30	36	2	5	13	20
OCA vs placebo	p<0.001	p<0.0001	NS	p<0.01	p<0.05	p<0.0001	p<0.05	p<0.01	NS	NS	p<0.05	p<0.01
12 months	52	94	31	32	13	318	26	37	15	8	27	27
OCA vs placebo	p<0.01	p<0.0001	p<0.05	p<0.05	p<0.01	p<0.0001	NS	p<0.001	p<0.05	NS	p<0.001	p<0.001

Significantly higher FGF19 levels versus placebo mean greater downregulation of bile acid production, which can prevent damage to small bile ducts.

Reductions in immune-mediated inflammatory markers, which can signal worsening disease

Reduced fibrosis scores

**placebo=66 incomplete responders after 12 months of OCA

CONCLUSIONS

Researchers quoted...

> These findings suggest that patients who do not achieve the composite endpoint for ALP and TB may still benefit from OCA in terms of lower inflammation and reduced fibrosis progression.

Abbreviations ALP: alkaline phosphatase; ALT: alanine transaminase; AST: aspartate transaminase; FGF19: fibroblast growth factor 19; NS: not significant; OCA: obeticholic acid; PBC: primary biliary cholangitis; TEAE: treatment-emergent adverse event; TB: total bilirubin; ULN; upper limit of normal

[1]Houston Methodist Hospital, TX, USA; [2]Intercept Pharmaceuticals, Morriston, NJ, USA

Springer Healthcare IME

Long-term efficacy and safety of elafibranor in primary biliary cholangitis: Interim results from the open-label extension of the ELATIVE® trial up to 3 years

Abstract: 5041 | Kris Kowdley[1], Christopher Bowlus[2], Cynthia Levy[3] *et al*

Improving **PBC** outcomes by prioritizing patients' needs

PARTICIPANTS

108 Patients with PBC taking **continuous elafibranor 80 mg/day in DBP and OLE for 156 weeks**

45 Patients with PBC **crossing over from placebo in DBP to elafibranor in OLE for 52 weeks**

RESULTS

Primary endpoints

	Rate of biochemical response			Rate of ALP normalization			Serious TEAEs
	Baseline	Week 52	Week 156	Baseline	Week 52	Week 156	Week 52
Continuous elafibranor	57%	56%	85%	16%	13%	39%	7.5%
Placebo - elafibranor	0%	51%	N/A	0%	22%	N/A	13.3%

Biochemical response: ALP <1.67 X ULN plus ≥15% reduction from baseline and TB level <ULN
ALP normalization: ULN 104 U/L in women and 129 U/L in men

- 70% of biochemical responders at week 52 achieved biochemical response on at least one study visit between weeks 52 and 156.
- 37% of biochemical non-responders at week 52 achieved biochemical response on at least one study visit between weeks 52 and 156.
- No new safety signals identified.

CONCLUSIONS

Researchers quoted...

> In the ongoing ELATIVE® OLE, elafibranor led to sustained improvements in biomarkers of cholestasis and pruritus, and stabilization of surrogates for fibrosis, up to Week 156, and remained well tolerated. Patients crossing over from placebo had similar results at Week 52 to those who received elafibranor in the DBP.

Abbreviations ALP: alkaline phosphatase; DBP: double-blind phase; OLE: open-label extension; PBC: primary biliary cholangitis; TEAE: treatment-emergent adverse event; TB: total bilirubin; ULN; upper limit of normal

[1]Liver Institute Northwest, Seattle, WA, USA; [2]UC David School of Medicine, Sacramento, CA, USA; [3]University of Miami, FL, USA

Springer Healthcare IME

One-year treatment with elafibranor in the phase III ELATIVE® trial improves GLOBE and UK-PBC prognostic scores

Abstract: 2371 | Kris Kowdley[1], Christopher Bowlus[2], Mark Sonderup[3] *et al*

Improving **PBC** outcomes by prioritizing patients' needs

PARTICIPANTS

108 Patients with PBC taking **elafibranor** 80 mg/day for 52 weeks

53 Patients with PBC taking daily **placebo** for 52 weeks

RESULTS

Elafibranor group

	Baseline	Change at 52 weeks
GLOBE, mean	0.63	-0.36
UK-PBC, mean	0.74	-0.27

Placebo group

	Baseline	Change at 52 weeks
GLOBE, mean	0.73	0.13
UK-PBC, mean	0.80	0.05

GLOBE includes age, TB, ALP, albumin and platelet count
UK-PBC includesALP, AST or ALT, TB, albumin and platelet count

Median estimated transplant-free survival rates based on scores at week 52

	GLOBE scores		UK-PBC scores	
	Elafibranor, %	Placebo, %	Elafibranor, %	Placebo, %
10 years	94.1	92.6	98.2	97.4
15 years	89.7	87.2	96.7	95.1

- Greater improvements in GLOBE and UK-PBC scores with elafibranor than placebo from as early as week 4, driven by reduction in ALP.
- Improvements in all parameters (ALP, TB, AST, ALT, albumin, platelets) contributing to GLOBE and UK-PBC scores with elafibranor.

CONCLUSIONS

Researchers quoted...

> Based on GLOBE and UK-PBC scores, there were higher estimated transplant-free survival rates in patients who received elafibranor compared with placebo, including in those with advanced disease and biochemical non-response.

Abbreviations ALP: alkaline phosphatase; ALT: alanine transaminase; AST: aspartate transaminase; PBC: primary biliary cholangitis; TEAE: treatment-emergent adverse event; TB: total bilirubin; ULN; upper limit of normal

[1]Liver Institute Northwest, Seattle, WA, USA; [2]University of Texas Health, San Antonio, TX, USA; [3]University of Cape Town, South Africa

Springer Healthcare IME

Impact of elafibranor on fatigue in patients with primary biliary cholangitis: Interim results from the long-term open-label extension of the ELATIVE® trial

Abstract: 5042 | Mark Swain[1], David Jones[2], Cynthia Levy[3] *et al*

Improving **PBC** outcomes by prioritizing patients' needs

PARTICIPANTS

48 Patients with PBC taking elafibranor 80 mg/day in the DBL phase and OLE. Follow-up at 104 weeks

Primary endpoints:

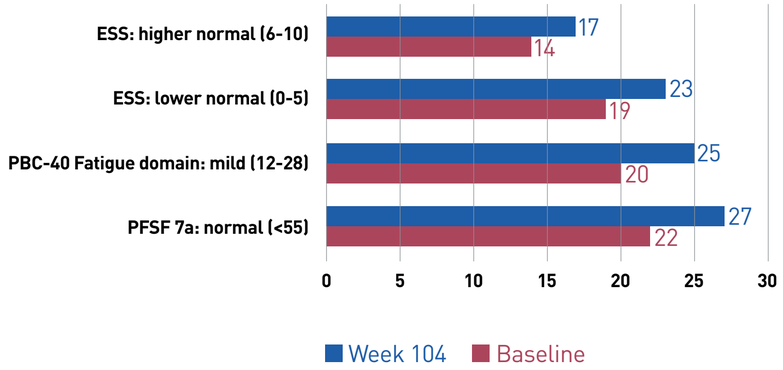
- Fatigue and sleep assessed using the Patient-Reported Outcomes Measurement Information System (PROMIS), Fatigue Short Form 7a (PFSF 7a), PBC-40 Fatigue domain, and Epworth Sleepiness Scale (ESS).

RESULTS

	Basline n (%)	Percentage of patients with at least MCID* improvement at week 104
PFSF 7a total score ≥60 points	18 (38%)	56%
PBC-40 Fatigue domain total score ≥29 points	24 (50%)	50%
ESS total score ≥10 points	16 (33%)	69%

***Minimal clinically important difference** (MCID) defined as decrease from baseline of ≥3 points for PFSF 7a, ≥5 points for PBC-40 Fatigue domain, and ≥2 points for ESS

- Mean reductions in total scores for each PRO at week 104.
- Improvement in percentage of patients reporting normal or mild fatigue/sleepiness at week 104.



CONCLUSIONS

Researchers quoted...

> Long-term treatment with elafibranor in the ongoing ELATIVE® OLE resulted in clinically meaningful improvements in fatigue and sleep in patients with PBC who had moderate-to-severe fatigue or excessive sleepiness at baseline.

Abbreviations DBP: double-blind phase; OLE: open-label extension; PBC: primary biliary cholangitis; PRO: patient-reported outcome

[1]University of Calgary, Alberta, ON, Canada; [2]Newcastle University, UK; [3]University of Miami, FL, USA

Springer Healthcare IME

Volixibat for cholestatic pruritus in primary biliary cholangitis: An adaptive, randomized, placebo-controlled phase 2b trial (Vantage): Interim results

Abstract: 5038 | Kris Kowdley[1] , Mitchell Schiffman[2], Debra Weinstein[3] *et al*

Improving **PBC** outcomes by prioritizing patients' needs

PARTICIPANTS

RESULTS

Significant reduction in primary endpoint at week 16

	Baseline Adult Itch-RO score*	Mean reduction (improvement) in Adult Itch-RO score from baseline	Difference vs placebo in favor of VLX	p-value
VLX 20 mg	6.8	3.7 points	2.4 points	0.0041
VLX 80 mg	6.3	3.8 points	2.6 points	0.0011
Placebo	6.2	1.3 points		

***Adult Itch-RO:** 0-10-point scale, where 0=no itch and 10=worst possible itch

- No new safety signals identified. TEAEs of grade 3 or above in 18.2% of patients in each dose group versus 6.3% of placebo-treated patients.
  - Mild diarrhea reported in 77% of pooled VLX patients leading to one treatment discontinuation.
- Significant improvements in some PBC-40 Domain scores with VLX versus placebo: itch, fatigue, cognitive, emotional.
- Numerically higher proportion of patients taking VLX than placebo achieved a serum bile acid response (≥50% reduction from baseline).

CONCLUSIONS

Researchers quoted...

> Given the similar results between volixibat doses, the 20 mg BID dose was selected for Part 2 of VANTAGE (continuing enrollment), constituting a new promising therapy to address important symptoms in PBC.

Abbreviations PBC: primary biliary cholangitis; PBC-40 RO: reported outcome; TEAE: treatment-emergent adverse event; VLX; volixibat

[1]Liver Institute Northwest, Seattle, WA, USA; [2]Bon Secours Mercy Health, Richmond, VA, USA; [3]Science 37, Culver City, CA, USA

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