

PSC Partners Seeking a Cure

Improving Outcomes for PSC Patients: Global PSC Efforts, Natural History Cohorts & Data Sharing

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Disclosures

I have no financial interests to disclose.





WHY? Outlook for a Person with PSC is DIRE

- Survival: average 21.3 years to TX or death¹
- Cancer: cholangiocarcinoma², gallbladder, colon cancer
 - Relative CCA risk ~ 10-1000
 - Lifetime CCA risk ~ 9–20%
- No treatment
- Comorbidities: IBD + others
- Symptoms
- Rare - PSC is not NASH
- No noninvasive validated biomarkers accepted as surrogate endpoints, YET
 - Biopsy hit or miss => need more reliable surrogate endpoints
- Heterogeneous

1. Boonstra, K., Weersma, R.K., van Erpecum, K.J., Rauws, E.A., Spanier, B.M., Poen, A.C., van Nieuwkerk, K.M., Drenth, J.P., Witteman, B.J., Tuynman, H.A., Naber, A.H., Kingma, P.J., van Buuren, H.R., van Hoek, B., Vleggaar, F.P., van Geloven, N., Beuers, U., Ponsioen, C.Y. and (2013), Population-based epidemiology, malignancy risk, and outcome of primary sclerosing cholangitis. *Hepatology*, 58: 2045-2055. <https://doi.org/10.1002/hep.26565>
2. Song J, Li Y, Bowlus CL, Yang G, Leung PSC, Gershwin ME. Cholangiocarcinoma in Patients with Primary Sclerosing Cholangitis (PSC): a Comprehensive Review. *Clin Rev Allergy Immunol*. 2020 Feb;58(1):134-149. doi: 10.1007/s12016-019-08764-7. PMID: 31463807



Unique Advantage of PSC Patient Organizations

Patient organizations *uniquely* have contact with thousands

- IRB approved and monitored Patient Registry (> 2,200 participants)
- Support and educational programming
- Our communities experience too much disability and death

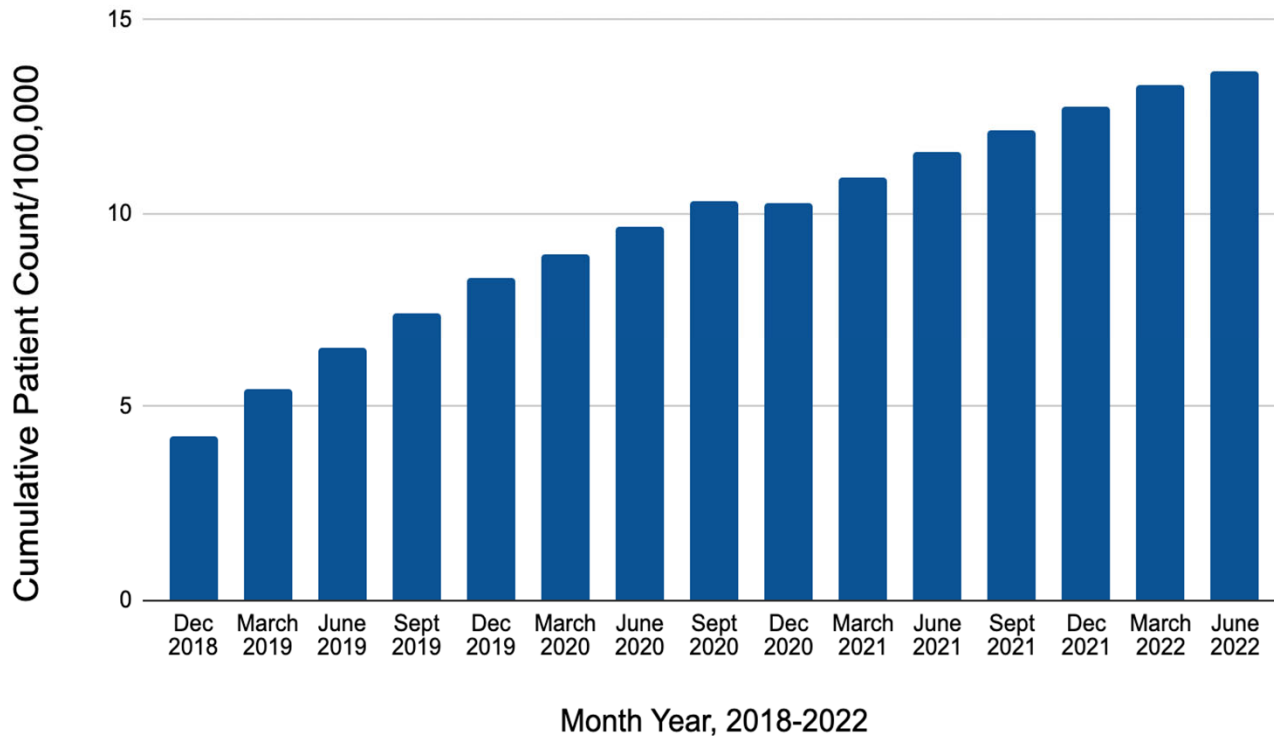
Externally-led Patient Focused Drug Development Meeting (2020), PFDD

- 6 hours of programming
- Voice of the Patient Report links.pscpartners.org/PFDD



US Use of PSC ICD-10 K83.01 Code

Unique Patients with K83.01 Billing Code



- Data source: Komodo Health Prism
- ~ 324M US patient universe
- PSC prevalence estimates range [0,31.7] per 100,000 from 2021 meta-analysis: 15 studies across 3 continents -
- US prevalence estimates range [0,13.6] per 100,000



Mehta, TI, Weissman, S, Fung, BM, Sotiriadis, J, Lindor, KD, Tabibian, JH. Global incidence, prevalence and features of primary sclerosing cholangitis: A systematic review and meta-analysis. *Liver Int.* 2021; 41: 2418– 2426. <https://doi.org/10.1111/liv.15007>

PSC Partners Organization Update

- Patient education and support programs
- Seed grants for promising & novel PSC research (5.5M)
- New
 - Chan Zuckerberg Initiative *Rare As One*
 - 3 fulltime science staff
 - Diversity equity and inclusion committee
 - International Collaborative Research Network
 - Convenings
 - Patient-prioritized research agenda
 - Strategic research plan



Sponsored Patient-Partnered Research

1. PROM - Patient Reported Outcome Measures
2. WIND natural history study initiative



PSC Partners WIND Initiative

- Clinician-reported natural history data + PROMs
- PSC Partners sponsored launch
 - US & Canada PSC community donations
- Min five-years prospective data
- International sites
- Central database
- 21 CFR part 11



Aims

1. **BIOMARKERS:** Development of a large biomarker dataset with the aim of identifying associations with endpoints of interest, including cirrhosis, hepatic decompensation, MELD score, liver transplant and death
2. **PROMs:** Capture of prospective symptoms, quality of life (QoL), and other direct patient experiences to evaluate how these experiences change over time and are associated with clinical markers and disease progression
3. **RWD:** Data collection to enable an appropriate synthetic comparator cohort to be built to replace the placebo arm for the confirmatory outcomes trial portion of the Accelerated Approval pathway



Potential of WIND to support drug development

1. To contribute to a placebo arm of a confirmatory trial for accelerated approval pathway
 2. To establish key liver related event rates for an outcomes trial for full approval
 3. Incidence/prevalence of key clinical symptoms to support symptom-based drug approvals
- Will seek appropriate guidance from the FDA through the Critical Path Innovation Meeting (CPIM)
 - Seeking feedback now!



Why PSC Partners?

- Sole focus on PSC - we cannot wait.
- Incredible partners
 - Financial
 - Patient group mentorship
 - Advisors
 - Working group
 - Regional leads:
 - US: Chris Bowlus, Cynthia Levy
 - Canada: Gideon Hirschfield
 - Europe: Christoph Schramm
 - Biostat: Bettina Hansen
 - Central Data Coordination Center



Status as of Nov 2022

- Working group met through spring 2022
- Regional leads + biostat meeting monthly for protocol drafting
- Negotiation and contracting with SDCC
- Ethics, governance, data sharing agreements
- Contracting with individual sites



Looking Forward for PSC Partners

- Ongoing programs: support, education, seed grants
- NEW
 - DEI
 - 2 large sponsored projects: WIND & PROM
 - ICRNetwork & Strategic Research Plan
- **What is next?**
 - RDCA-DAP?
 - Placebo trial data?
 - Platform trials?
 - PROM implementation?
 - Growing global patient collaboration?



GLOBAL PSC AWARENESS DAY, October 29, 2022:
Strong together, and holding on to HOPE!



MAGTARMFÖRBUNDET

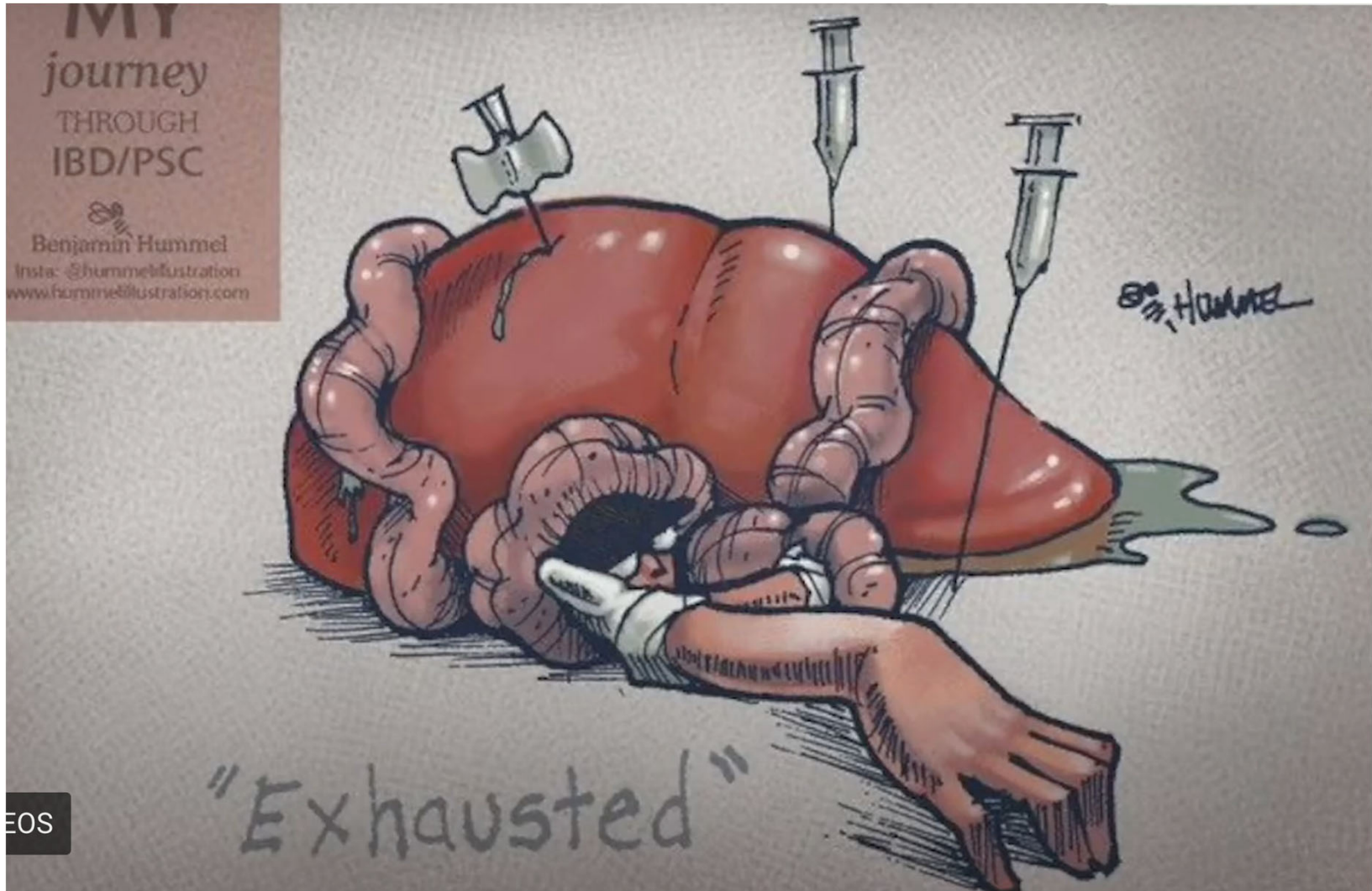


Held in collaboration with these international partners.

Follow PSC Partners' social media channels; Repost and use #PSCAware #PSCDay #RareLiverDiseases #LiverTwitter

Thank you to Sindee Weinbaum and ELPA for their leadership on Global PSC Awareness Day.





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Thank You

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