

Asp-PSC

Effect of Aspirin on Reducing Cancer & Mortality in Primary Sclerosing Cholangitis (Phase III Randomised, Clinical Trial)

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on behalf of the Asp-PSC Clinical Trial Team



IBD Investigators Day

Monday 29th January 2024

bsg BRITISH SOCIETY OF
GASTROENTEROLOGY
Sandy Park, Exeter

Asp-PSC: Aspirin in PSC INVESTIGATOR TEAM

Clinician Scientists

- Shahid A Khan (PI - Chair Cholangiocarcinoma-UK [BASL-SIG])
- Simon Rushbrook (Co-PI [UK-PSC])
- Palak Trivedi (UK-PSC)
- Hassan Malik (Chair of The British Association of Surgical Oncology, BASO)
- Ruth Langley (Co-Chair, UK Therapeutic Cancer Prevention Network Group, UKTCPN)
- Catherine Williamson (Obstetric Medicine)
- Nick Powell (Gastroneterology, Imperial College London)

Patient and Public Involvement and Engagement (PPIE)

- Martine Walmsley (Chair, PSC-Support)
- Maxine Tapp (Programme Development Officer, PSC Support)
- Helen Morement (Founder & CEO of AMMF, The UK's Cholangiocarcinoma Charity)

Statistician (Kings Clinical Trials Unit)

Francesca Fiorentino

PREVENTION
IS BETTER THAN
CURE!



Why this study is needed

- PSC patients are at **high risk of liver failure and cancer: liver, biliary tract/cholangiocarcinoma, colorectal**
- No cure except liver transplant if cirrhosis and liver failure occur
- Cancer is usually a contraindication to transplant
- No screening or preventive mechanism known to reduce liver/biliary tract cancer risk

Summary of studies reporting statistically significant protective effects of Aspirin against cancers PSC-IBD patients are at high risk of

Evidence of Aspirin Users Potential Protection against HPB and CRC Cancers

1. Choi et al. 2016: **OR 0.29 - 0.35** for all CCA subtypes (50% reduction in PSC associated CCA)

2. Simon et al 2020: **HR 0.57** for HCC

3. Lapumnuaypol et al. 2019: **OR 0.56** for CCA (Meta-analysis)

4, Xiong et al. 2018: **iCCA OR 0.33** for iCCA; **OR=0.56** for eCCA (Meta-analysis)

5. Bosetti et al. 2020: **RR 0.62** for HPB cancers

6. Garcia Rodriguez et al. 2017: **RR 0.53** for Dukes Stage A CRC

7. Burn et al 2020: CAPP-2 Randomised Controlled Trial: **HR 0.63** for CRC in Lynch syndrome

Post-diagnosis aspirin use associated with decreased biliary tract cancer-specific mortality

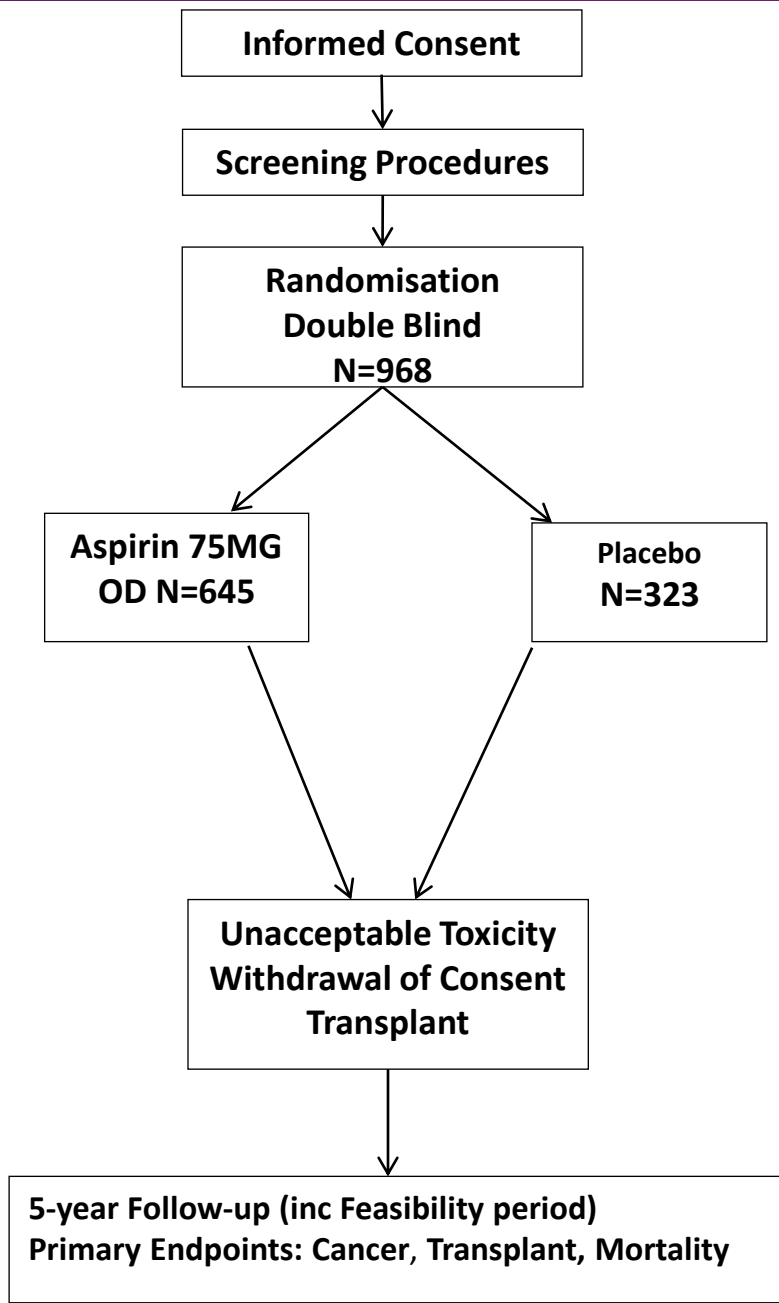
7. Liao et al. 2021: **HR 0.55**

8. Jackson et al. 2019: **HR 0.44 to 0.71** across all BTC sites

Biological Plausibility for how Aspirin May Modulate Carcinogenesis

- Inhibiting COX-2
 - Preventing platelet aggregation
 - Inhibiting activation of nuclear factor-kB
 - Modulating Wnt signalling via both COX-dependent and COX-independent pathways
 - Upregulating tumour suppressor genes
 - Stabilization of DNA mismatch-repair proteins (Shen et al 2020)
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- **Hypothesis:** Aspirin reduces the combined endpoint of PSC related cancers and PSC related morbidity and mortality
 - **Main Aim:** to investigate if daily low dose Aspirin improves PSC-related cancer free survival, overall survival, and time to liver decompensation and liver transplantation

Flow Chart: Asp-PSC



Stratified by:

- level of advanced liver fibrosis/cirrhosis
- time since PSC diagnosis (by time bands e.g., 1-3 years, 3-5 and > 5years from diagnosis)
- aminosalicylate use

(Secondary Endpoints:

Bleeding events, Liver decompensation, IBD Flares

Basic Inclusion/Exclusion Criteria

Inclusion Criteria

- PSC and IBD
- Age >18 years
- Able to give informed consent
- No previous cancer
- Not already on aspirin
- At least 12 months post diagnosis

Exclusion Criteria

- Previous PSC related cancer
- Already taking aspirin
- On Transplant waiting list
- Non-variceal gastrointestinal bleeding within 1 yr
- <12 months from PSC diagnosis
- Allergy to Aspirin

Asp-PSC Trial – funded by Cancer Research UK

Costed for and awarded **£5.3 million**, pending recruitment

Recruitment to start early 2024

We need 968 PSC-IBD patients

This will require a strong pan UK collaborative effort

Please start thinking about potential patients now!

Do you have any patients with PSC-IBD who

- are at least 12 months from diagnosis, and
- have not had cancer, colectomy or a transplant?

If so, please consider them for the

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Asp-PSC TRIAL
“Effect of Aspirin on
Reducing Cancer &
Improving Outcomes in
Primary Sclerosing
Cholangitis”

Design

- Investigator led
- Double-blind
- Randomised Controlled Trial
- Aspirin vs Placebo (2:1)
- For 5-years
- Multi-centre
- **968** patients needed

Primary Endpoints

1. **Cancer:** cholangiocarcinoma, gallbladder, hepatocellular, colorectal, pancreas
2. Listing for Liver **transplantation**
3. All-cause **mortality**

