



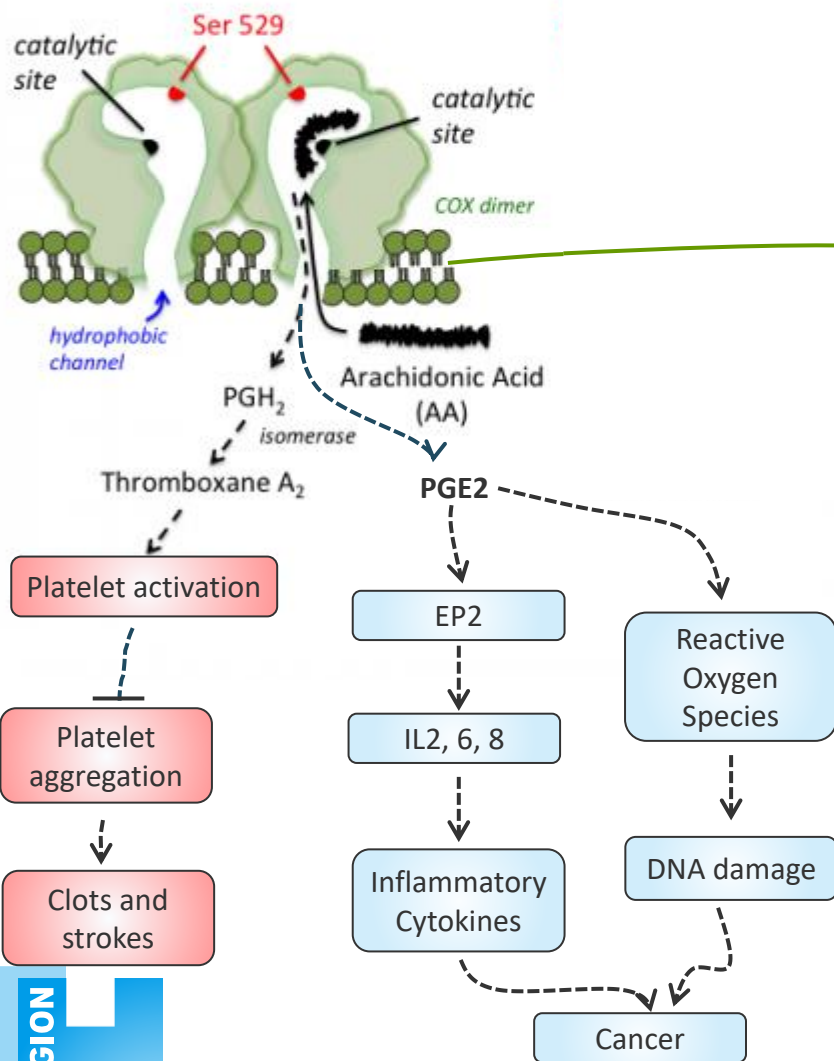
# Aspirin (ASA) and Mesalamine (5-ASA) in colorectal cancer prevention

Lars Joachim Lindberg and Christina Therkildsen  
Invitation to a new international clinical trial



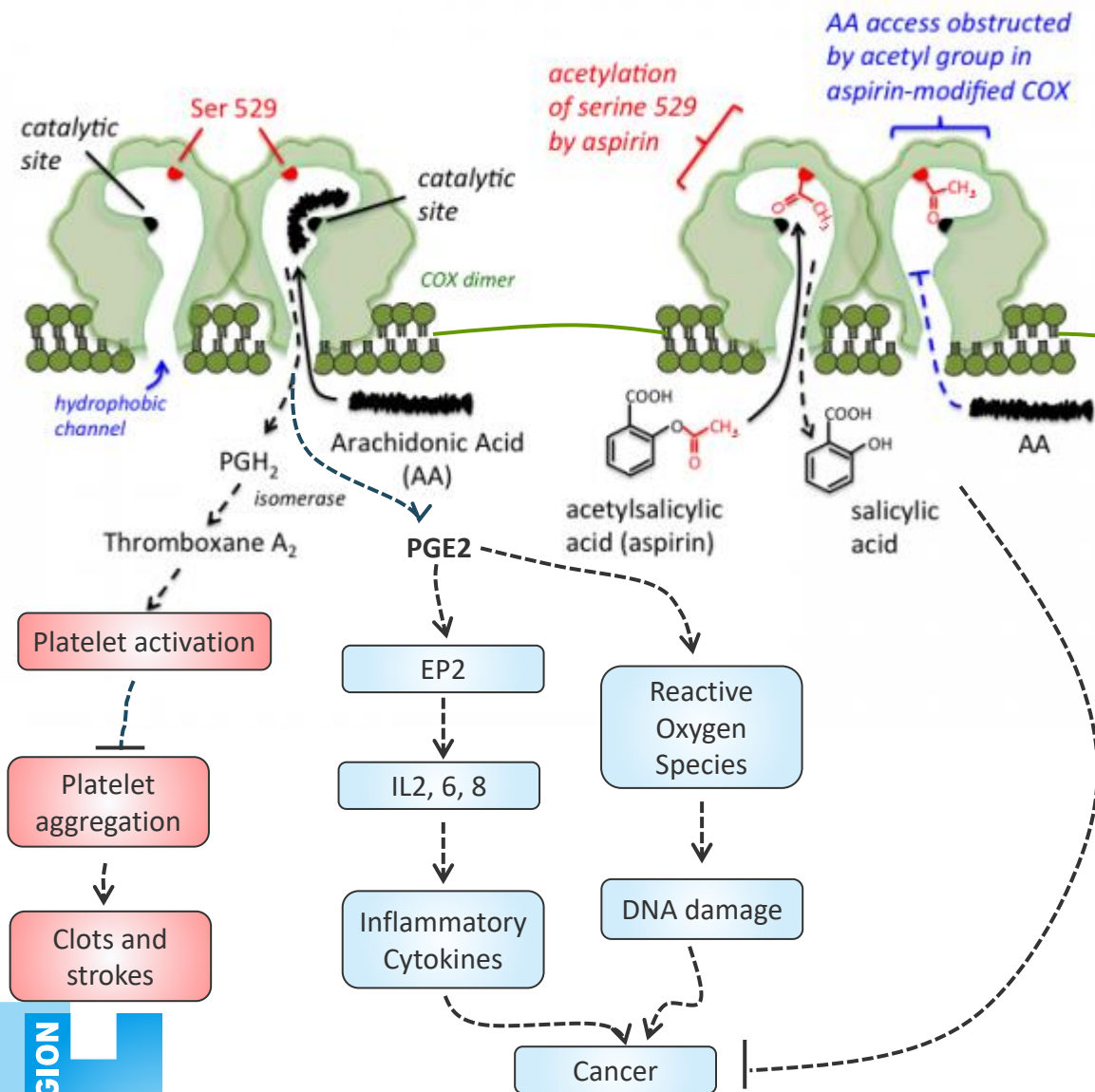
## Aspirin (ASA)

- Aspirin – old anticoagulant drug used to prevent cardiovascular diseases
- In the 80'ies a reduction in colorectal cancer was first associated with Aspirin intake
- Colorectal Adenoma/Carcinoma Prevention Programme (CAPP) 1 focused on cancer prevention in FAP families – weak results
- CAPP2 was focused on Lynch syndrome – positive results after 5 years





## After aspirin



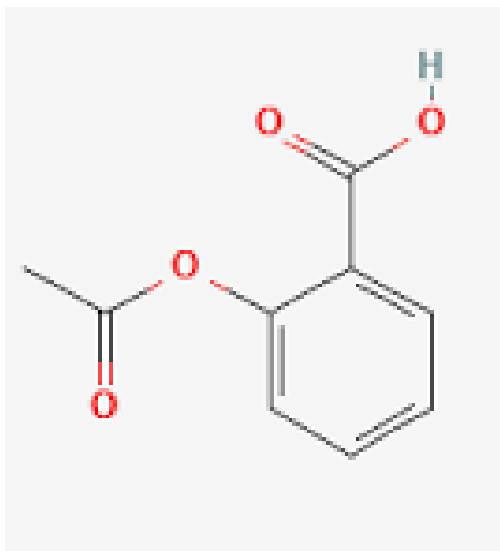


## Mesalamine (5-ASA)

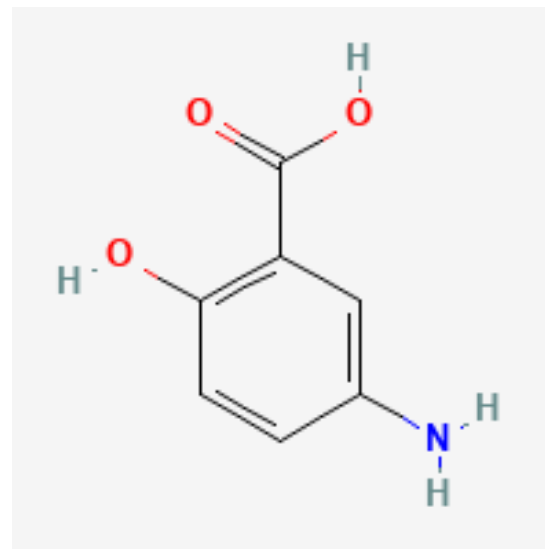
- Mesalamine is used to treat mild to moderate ulcerative colitis.
- Anti-inflammatory
- In 2007, Mesalamine was associated with colorectal cancer reduction in patients with ulcerative colitis



## Aspirin vs Mesalamine



Aspirin



Mesalamine





## Mesalamin side effects - frequent

- Gas, constipation, stomach pain, diarrhea, nausea, vomiting
- Dizziness
- Cold symptoms, sneezing and sore throat
- Back pain
- Headache
- Rash or abnormal liver tests



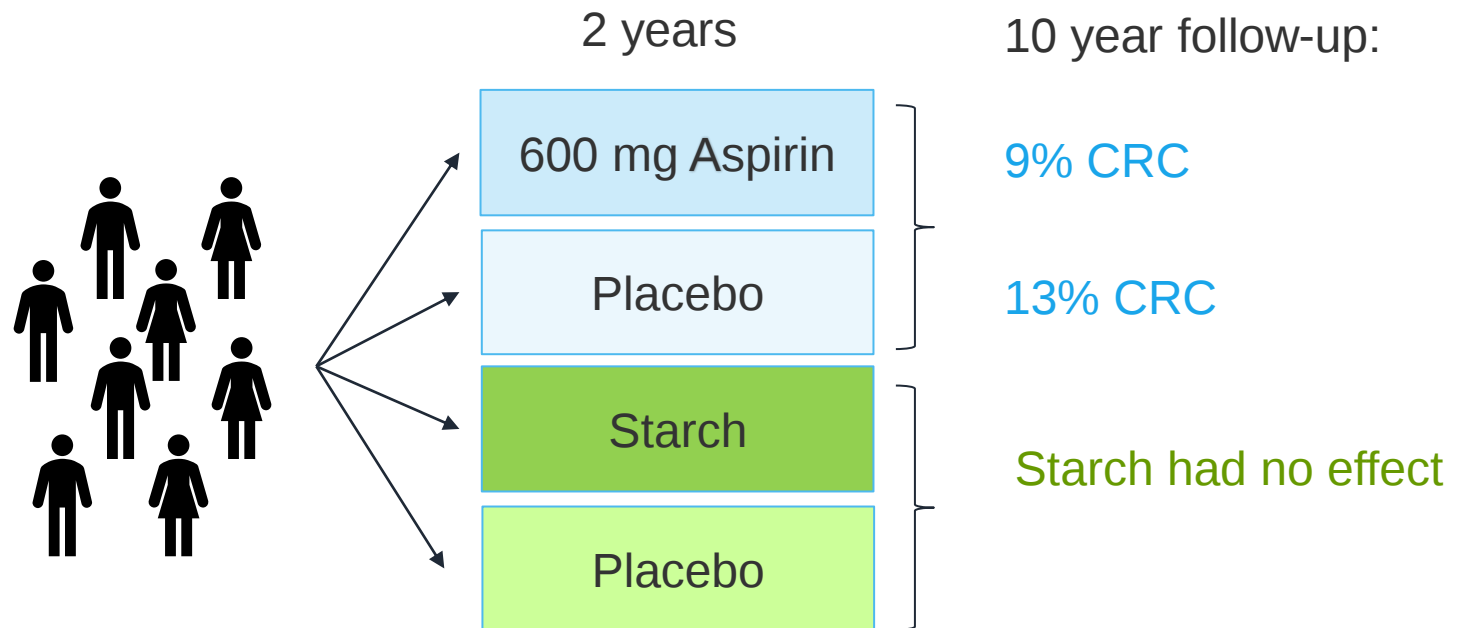
## Mesalamin sideeffect - serious

- Breathing difficulties, swelling in the face, lips, tongue or throat
- Strong stomach pain, stomach cramps, bloody diarrhea
- Fever, shivers, headache, mouth ulcers, sore throat, cough, dizziness, generally feeling sick
- Rash, itch, eye redness, easy bruising and bleeding, yellow eyes
- Bloody stool, coughing blood, vomit looks like coffee grounds
- Low number of white blood cells, signs on kidney stones (strong pain from side or back), frequent urination, bad urine smell, dark urine, kidney problems, swelling, weight increase, liver problems, loss of appetite, fatigue



## CAPP2

- 1999 – 2005, 861 participants, 19 countries, incl. Denmark





## Challenges in CAPP2

- High Aspirin dosage (600 mg daily)
  - CAPP3 is initiated to test dose-respose
- A lot of side effect in individuals +65 years
- The time of treatment and length of preventive effect is unknown
- CAPP3 initiated in 2014-2024 – without Denmark



# The MESA-CAPP study

Study design and feasibility

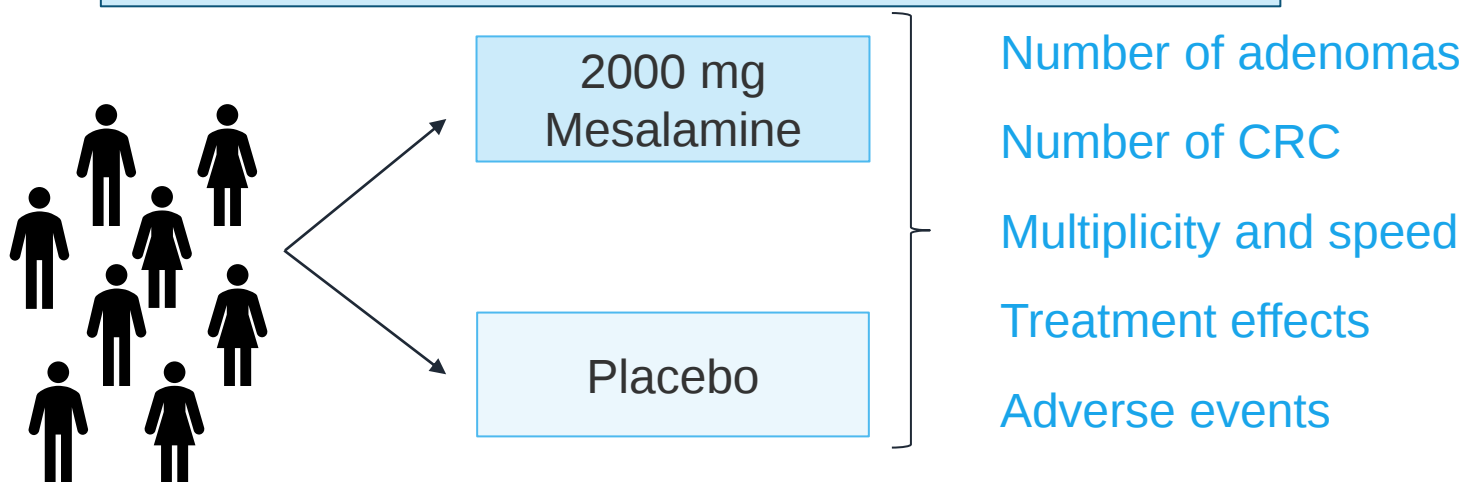


## MesaCAPP – like CAPP2

- 2022 – 2042, 260 participants, 6 countries, incl. Denmark

**Expected to find a 50% reduction in  
the development of adenoma/CRC**

Follow-up:



<https://clinicaltrials.gov/ct2/show/NCT04920149>



## Principal investigator and funding

- Ann-Sofie Backman, PhD and MD
- Karolinska Institute, Stockholm, Sweden
- Funding from the Swedish Research Council
- Sponsored by Ferring, which is packing the drug and placebo
- Co-authorships given for at least 5 participants
- Approximately 6000 DKK per patient included





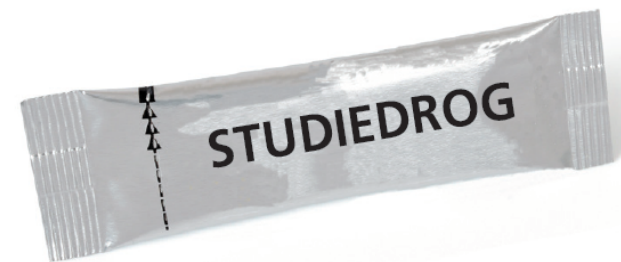
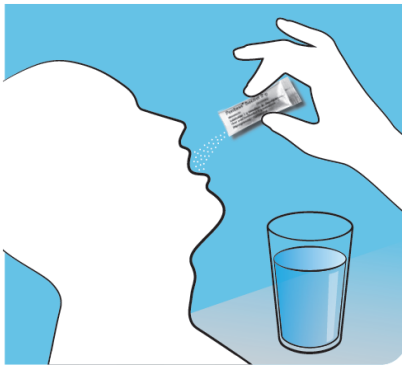
## Study design

- Daily treatment with Mesalamine/placebo for 2 years
- Routine colonoscopy at entry and after 2 years
- Blood sample, physical examination, organ control (before inclusion, at 3 months, 1 year and 2 year)
- Follow up telephone interview at 4 years
- Follow up with no patient contact for 14 years



## Dosage and intake

- Mesalamine/placebo will be given as one bag of granulate to be digested each morning
- The granulate will slowly release the active Mesalamine after digestion





## Patient inclusion proces

- Patients can be identified through the HNPCC register or at Clinical Departments
- Patients invited when they receive their regular colonoscopic invitation
- Questionnaire and consent at colonoscopy date
- Blood samples and physical examination
- Colonoscopy and evaluation of findings
- Cancer/polyp-free Lynch syndrome carriers with normal liver and kidney function will be randomized from Sweden

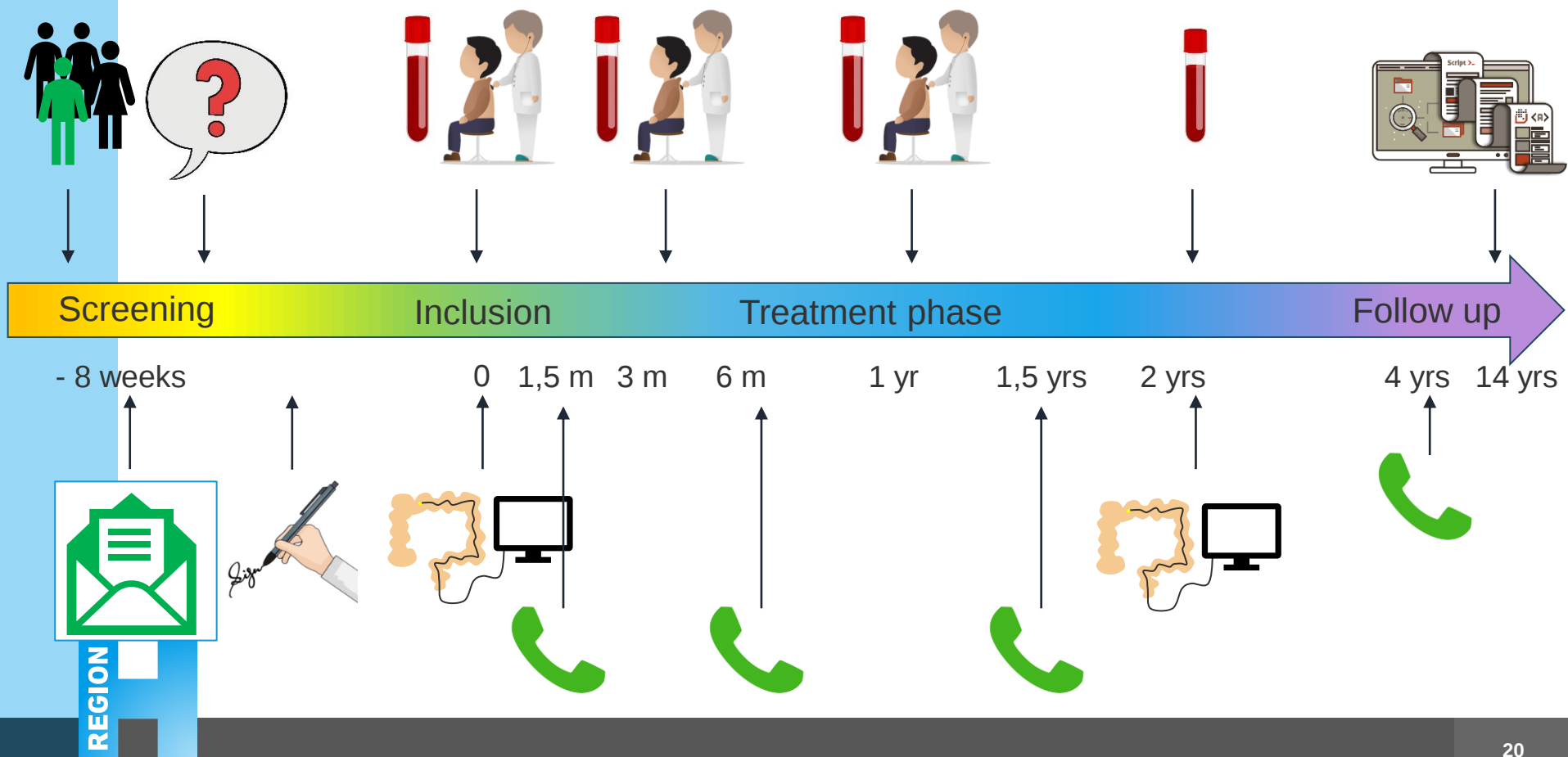


## Inclusion criteria

- Above 30 years
- Men and women
- Women who have been post-menopausal more than 1 year or women of child-bearing potential using highly efficient method of contraception (<1% failure rate)
- Negative pregnancy test for women with child-bearing potential
- Lynch syndrome carriers (of pathogenic MMR variants)
- Proven tumor and polyp free at colonoscopy
- Signed informed consent (understands and speak Danish)

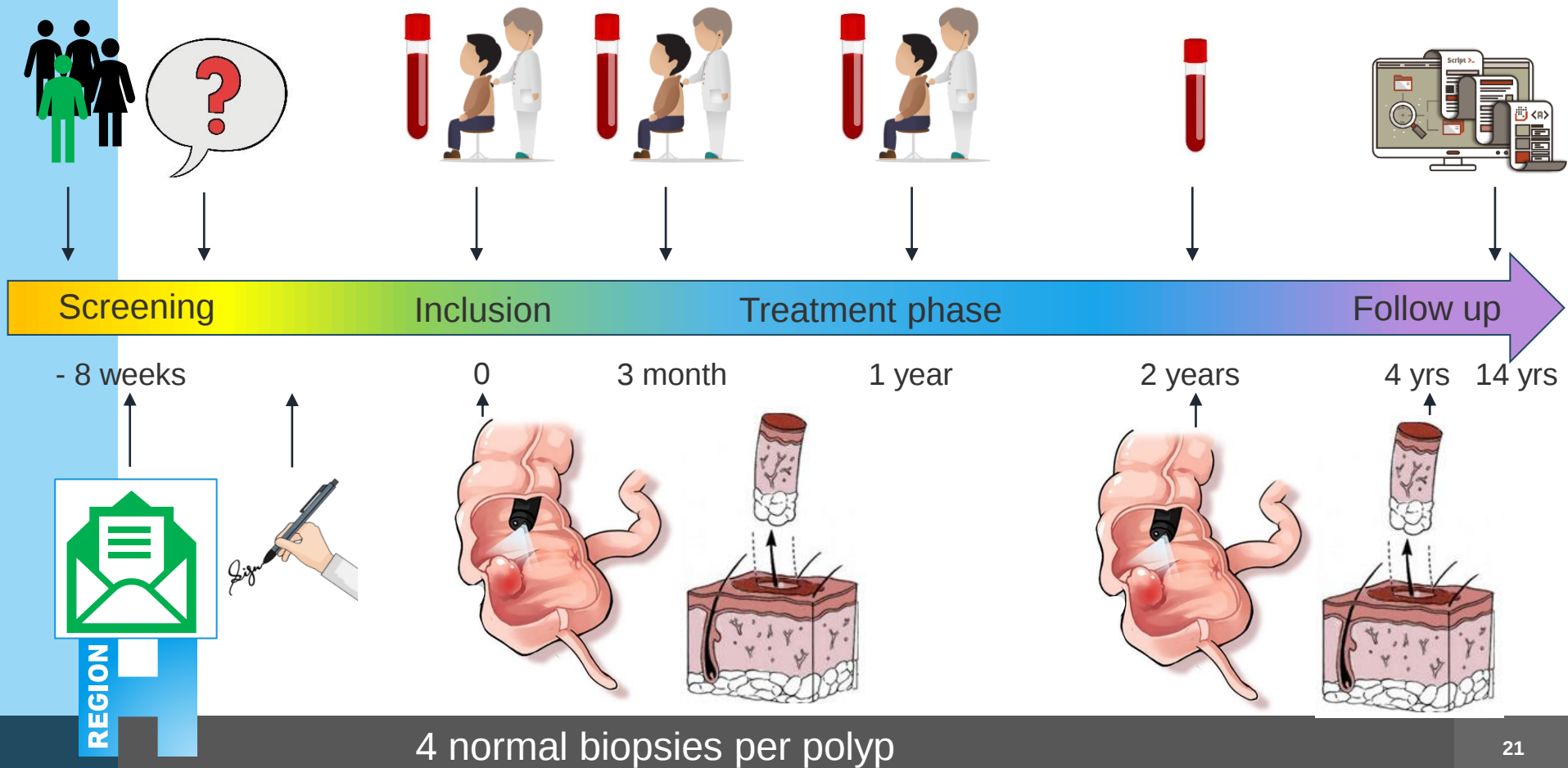


## Flow chart



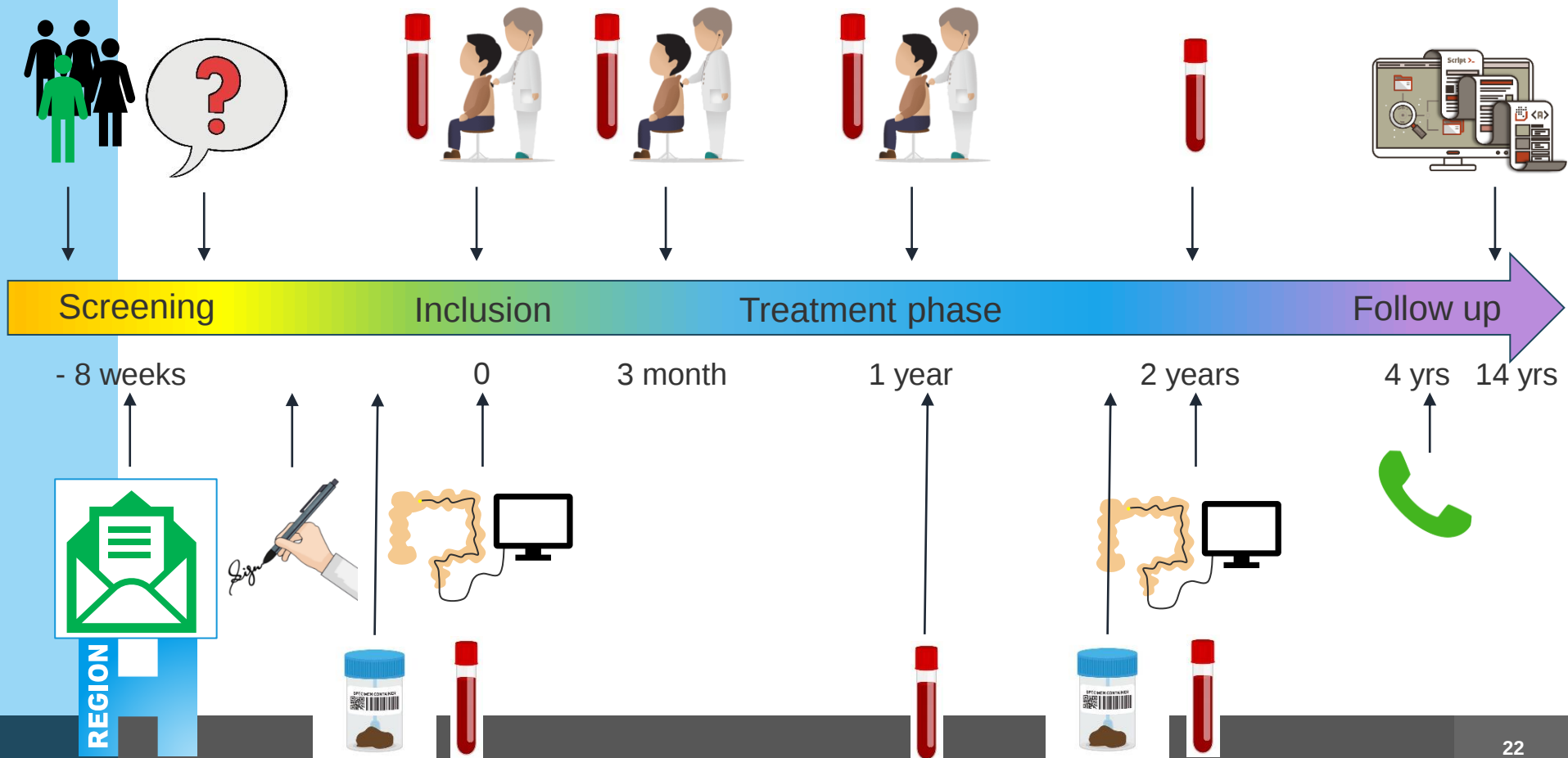


## Flow chart





## Flow chart – extra samples for research



# A daily diary needs to be filled out to note any side effects

Patient number:

Birth date:

| Day | Date | Drug intake?                                             | Time | Side effects or other drug intake                        | Comments |
|-----|------|----------------------------------------------------------|------|----------------------------------------------------------|----------|
| 1   |      | <input type="checkbox"/> Yes <input type="checkbox"/> No |      | Yes <input type="checkbox"/> No <input type="checkbox"/> |          |
| 2   |      | <input type="checkbox"/> Yes <input type="checkbox"/> No |      | Yes <input type="checkbox"/> No <input type="checkbox"/> |          |
| 3   |      | <input type="checkbox"/> Yes <input type="checkbox"/> No |      | Yes <input type="checkbox"/> No <input type="checkbox"/> |          |
| 4   |      | <input type="checkbox"/> Yes <input type="checkbox"/> No |      | Yes <input type="checkbox"/> No <input type="checkbox"/> |          |
| 5   |      | <input type="checkbox"/> Yes <input type="checkbox"/> No |      | Yes <input type="checkbox"/> No <input type="checkbox"/> |          |
| 6   |      | <input type="checkbox"/> Yes <input type="checkbox"/> No |      | Yes <input type="checkbox"/> No <input type="checkbox"/> |          |
| 7   |      | <input type="checkbox"/> Yes <input type="checkbox"/> No |      | Yes <input type="checkbox"/> No <input type="checkbox"/> |          |
| Day | Date | Drug intake?                                             | Time | Side effects or other drug intake                        | Comments |
| 8   |      | <input type="checkbox"/> Yes <input type="checkbox"/> No |      | Yes <input type="checkbox"/> No <input type="checkbox"/> |          |
| 9   |      | <input type="checkbox"/> Yes <input type="checkbox"/> No |      | Yes <input type="checkbox"/> No <input type="checkbox"/> |          |
| 10  |      | <input type="checkbox"/> Yes <input type="checkbox"/> No |      | Yes <input type="checkbox"/> No <input type="checkbox"/> |          |
| 11  |      | <input type="checkbox"/> Yes <input type="checkbox"/> No |      | Yes <input type="checkbox"/> No <input type="checkbox"/> |          |
| 12  |      | <input type="checkbox"/> Yes <input type="checkbox"/> No |      | Yes <input type="checkbox"/> No <input type="checkbox"/> |          |
| 13  |      | <input type="checkbox"/> Yes <input type="checkbox"/> No |      | Yes <input type="checkbox"/> No <input type="checkbox"/> |          |
| 14  |      | <input type="checkbox"/> Yes <input type="checkbox"/> No |      | Yes <input type="checkbox"/> No <input type="checkbox"/> |          |



## How to participate

- Submission of protocol to the Ethical Committee (HNPCC)
- State your interest to the HNPCC register
- DPA will be sent directly from Karolinska Institute
- Drugs will be sent directly from Ferring
- GCP monitorization (100 hours for free per region)
- Colonoscopies, physical examinations and blood samples are done as routine
- Reporting via electronic platform (e-CRF) directly to Karolinska Institute
- Provide 24 hour phone service for adverse events for 6 years/patient



## Danish contribution

- Hvidovre Hospital plans to begin recruitment i 2022
- Aalborg Hospital (Lone Sunde and Inge Bernstein)
- Aarhus Hospital (Charlotte Lautrup)
- If you wish to participate please send a mail to:  
[christina.therkildsen@regionh.dk](mailto:christina.therkildsen@regionh.dk)

End of presentation