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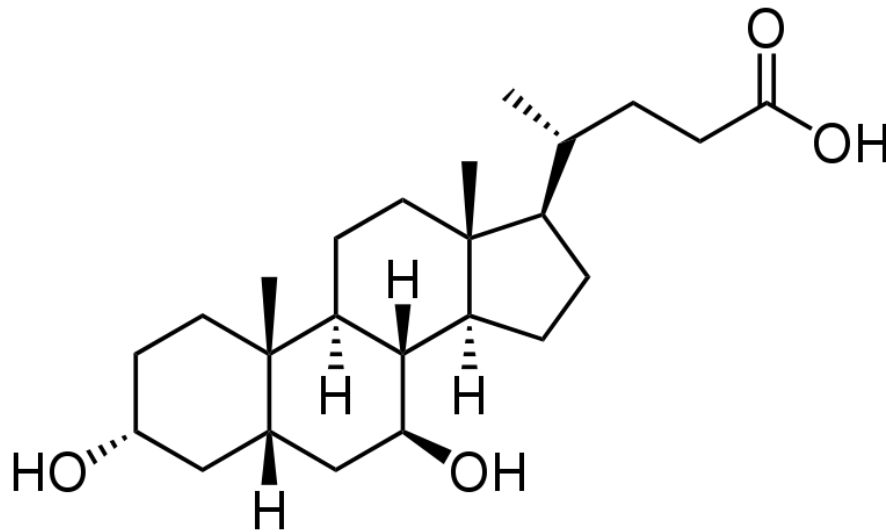
# **Treatment with Ursodeoxycholic Acid in PSC: What do we learn from the Scandinavian Urso Study?**

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# NOTHING TO DISCLOSE

# Ursodeoxycholic acid (UDCA)



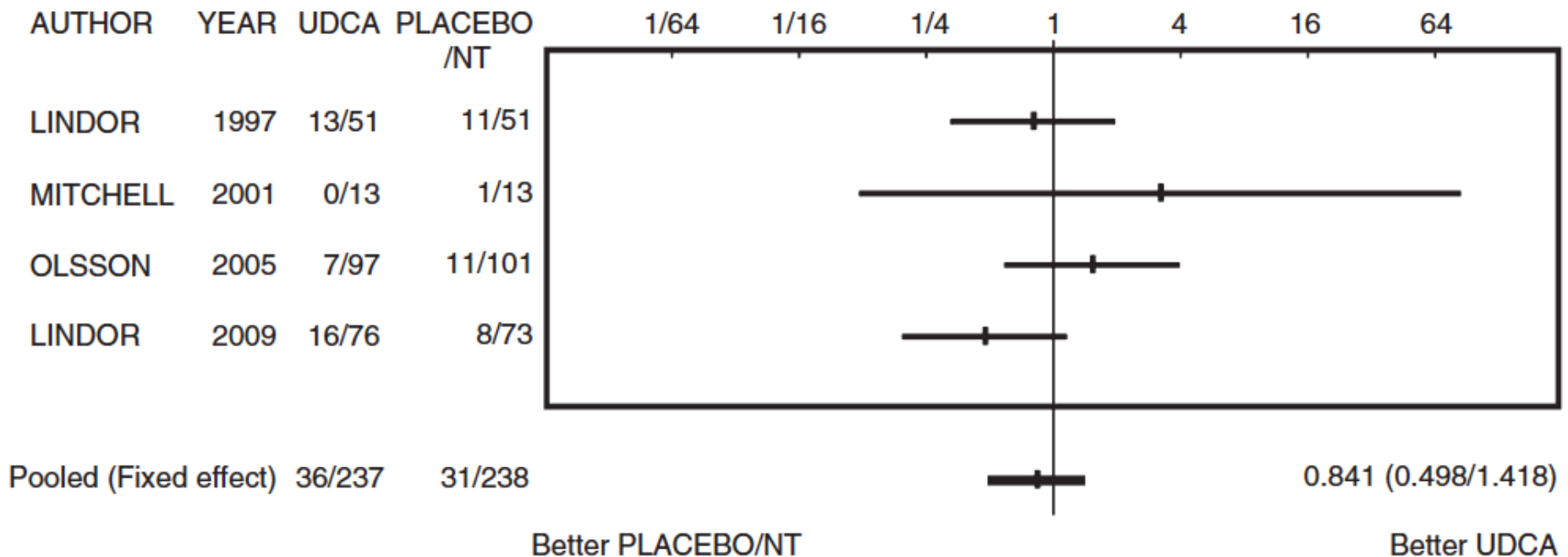
# Effects of UDCA in PSC

## Different doses and follow-up times

<b>Study</b>	<b>Duration</b>	<b>n</b>	<b>Dose mg/kg/day</b>	<b>Effect</b>
<b>Lindor et al, 1997</b>	<b>2 yrs</b>	<b>105</b>	<b>10-15</b>	<b>Improved biochemistry</b>
<b>Mitchell et al, 2001</b>	<b>2 yrs</b>	<b>26</b>	<b>20</b>	<b>Improved biochemistry</b>
<b>Olsson et al, 2005</b>	<b>5 yrs</b>	<b>198</b>	<b>17-23</b>	<b>No significant changes</b>
<b>Lindor et al, 2009</b>	<b>3 yrs</b>	<b>150</b>	<b>28-30</b>	<b>Increased risk for adverse outcomes</b>

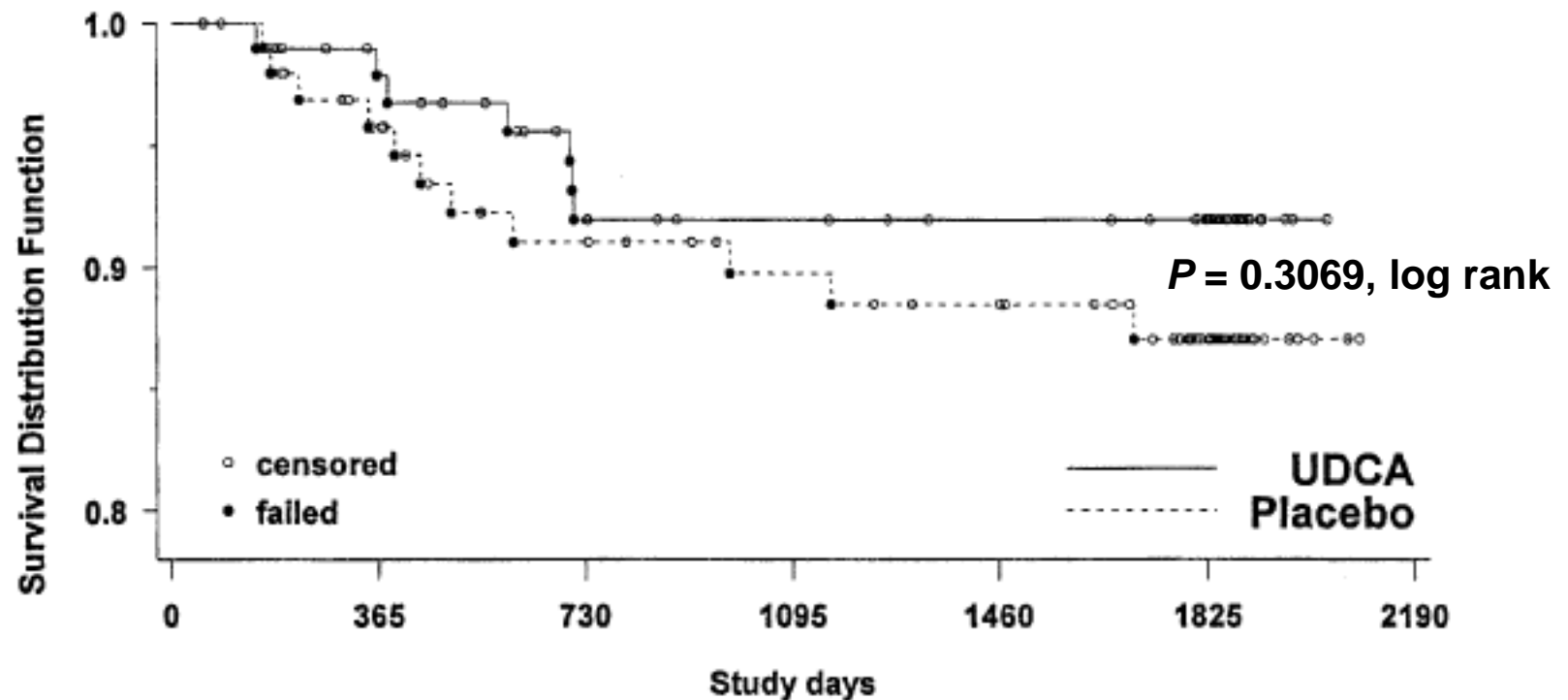
# Meta-analysis: UDCA in PSC

## Effects on overall mortality or OLT



*Triantos et al. Aliment Pharmacol Ther 2011*

# The Scandinavian UDCA for PSC trial (17-23 mg/kg)



*Olsson et al. Gastroenterology 2005*

# Biochemical response and survival in PBC

- In PBC a biochemical response to UDCA has been associated with a better long-term outcome  
*(Pares 2006, Corpechot 2008, 2011, Kuiper 2009, Kumagi 2010)*
- Biochemical response: reduction in alkaline phosphatase (ALP)  $\geq 40\%$  or normal levels after 1 year of treatment  
*(Pares 2006 – "Barcelona Criteria")*



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# **A Reduction in Alkaline Phosphatase is Associated with Better Prognosis in Primary Sclerosing Cholangitis**

## **A 14-Year Follow-up of the Scandinavian Ursodeoxycholic Acid Trial**

**Reference: Lina Lindström<sup>1</sup>, Rolf Hultcrantz<sup>1</sup>, Kirsten M Boberg<sup>2</sup>, Ingalill Friis-Liby<sup>3</sup>,  
Annika Bergquist<sup>1</sup> . Association between Reduced levels of Alkaline Phosphatase and  
Survival Times of Patients With Primary Sclerosing Cholangitis *Clin Gastroenterol Hepatol.***

**2013**

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## We wanted to

- Study the long-term survival in PSC patients treated with a moderate dose of UDCA (17-23 mg/kg/day)
- To investigate if response to UDCA (improved of alkaline phosphatase levels) influenced prognosis

# HOW DID WE DO OUR STUDY?

# Methods

- Multicentre study
  - Sweden, Norway, Denmark
  - PSC patients from 39 hospitals
- Follow-up until 2010 (n=198)
  - Collected data on treatment with UDCA after end of initial study, liver transplantation, cholangiocarcinoma and death
- Biochemical response
  - Reduction in ALP with  $\geq 40\%$  or normal levels after 1 year of treatment

# WHAT DID WE FIND? RESULTS

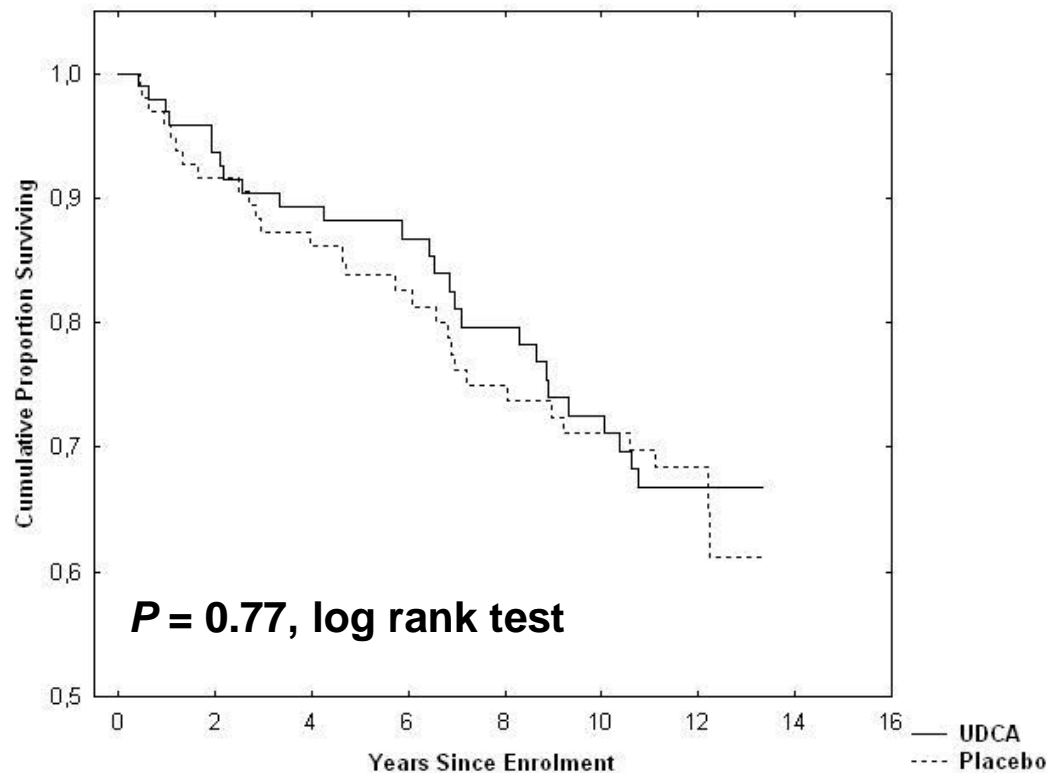
## Clinical characteristics at baseline

<b>Variable</b>	<b>UDCA (n=97)</b>	<b>Placebo (n=101)</b>
<b>Male sex</b> n (%)	71 (73)	69 (68)
<b>IBD</b> n (%)	80 (82)	85 (84)
<b>Mean age at enrolment (SD)</b> yrs (SD)	44 (13)	43 (11)
<b>Duration of PSC at enrolment</b> yrs (SD)	6 (6)	6 (5)
<b>No symptoms at enrolment</b> n (%)	45 (46)	51 (50)
<b>Mean ALP at enrolment</b> IU/L (SD), normal range (44-147)	296 (239)	314 (286)

## Extended follow-up 14 yrs after randomization

- 28 / 198 patients lost to follow-up  
(19 UDCA / 9 placebo)
- 55 / 170 ( 32% ) patients were transplanted or diagnosed with cancer or dead.

# Endpoint-free survival at 14 years: Patients initially assigned to UDCA or placebo

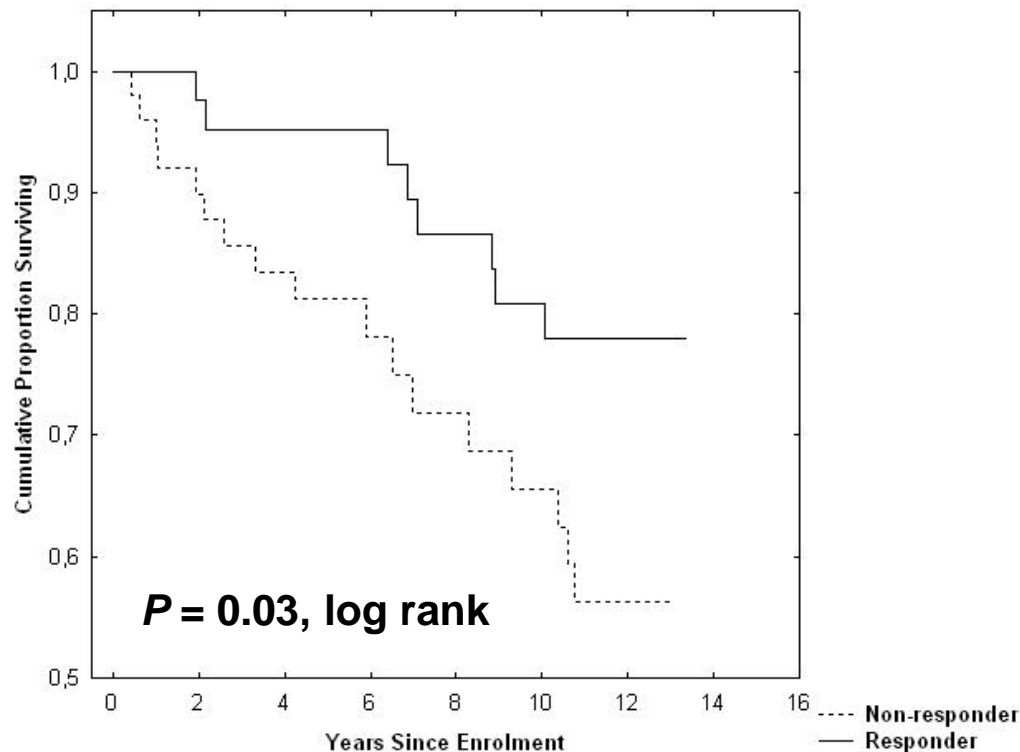


## UDCA treatment after the trial

- UDCA 55%
- Placebo 48%

UDCA	97	84	78	56	51	20
Placebo	101	84	72	59	56	19

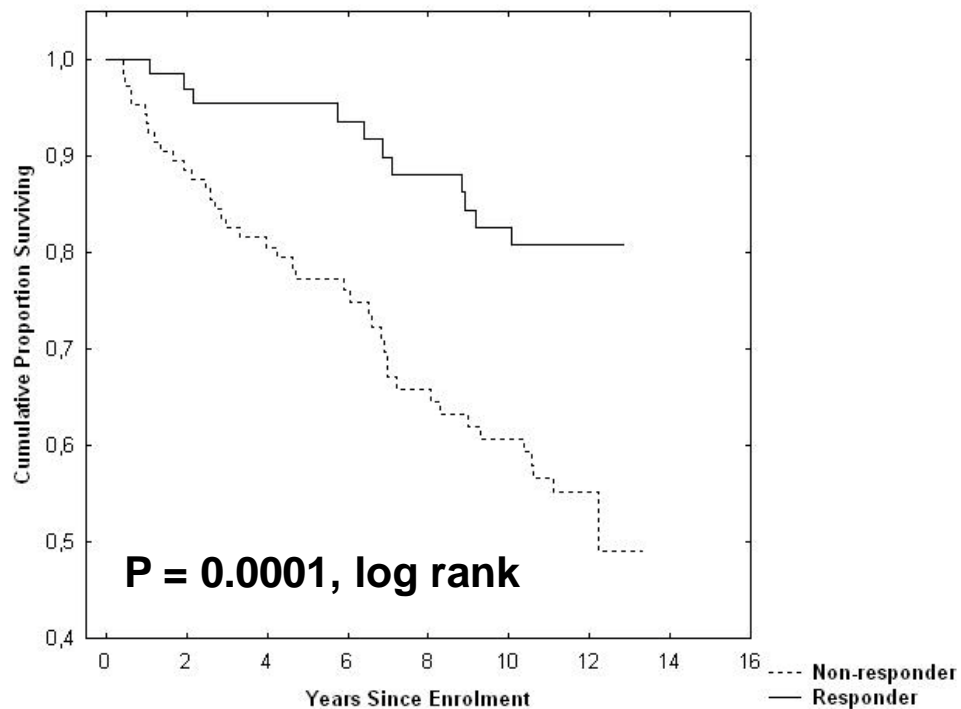
# Comparison of patients with or without biochemical response to UDCA



<b>Responders</b>	<b>43</b>	<b>40</b>	<b>34</b>	<b>24</b>	<b>23</b>
<b>Non responders</b>	<b>51</b>	<b>45</b>	<b>35</b>	<b>19</b>	<b>15</b>

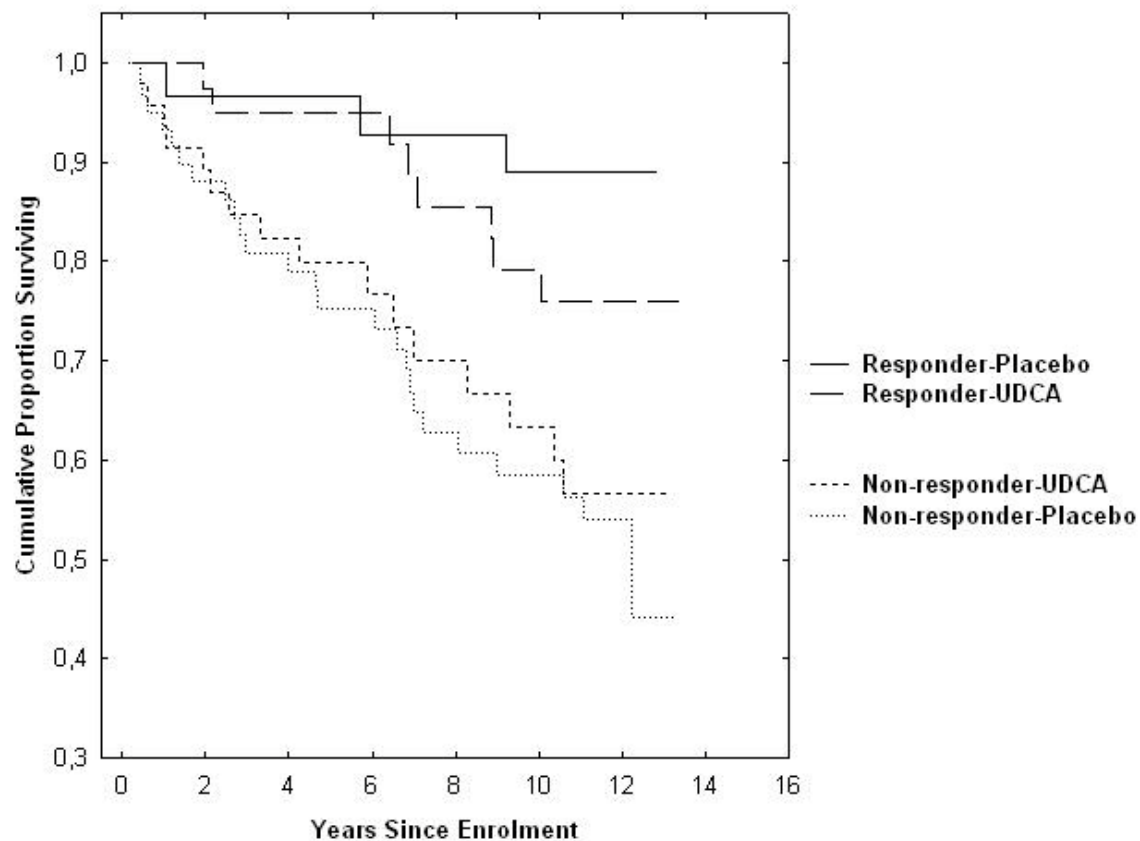


# Comparison of patients with or without biochemical response - regardless of treatment



<b>Responders</b>	<b>79</b>	<b>72</b>	<b>69</b>	<b>56</b>	<b>53</b>	<b>17</b>
<b>Non responders</b>	<b>116</b>	<b>93</b>	<b>78</b>	<b>56</b>	<b>52</b>	<b>21</b>

# Comparison of responders vs. non-responders



## What did we learn?

- Five years of treatment with UDCA in a moderate dose of 17-23 mg/kg does not improve the long-term survival in PSC
- ALP reduction, regardless of UDCA treatment is associated with better long-term prognosis

# Biochemical response and survival in PSC

- Improvement in ALP associated with better outcome  
*(Stanich 2011, Al Mamari 2013)*

## What did we learn?

- If UDCA leads to a reduced or even normalised ALP level treatment may be beneficial
- ALP is a suitable surrogate marker for disease progression and should be considered for further evaluation as a clinical endpoint in trials with PSC



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Thanks to

Patients

Co-investigators

PSC partners  
seeking a cure



SILK-Svensk Internmedicinsk Lever Klubb