



European  
Crohn's and Colitis  
Organisation

# **Thiopurine and allopurinol combination therapy**

*and the risk of adverse outcomes and step-up medical therapy in  
Inflammatory Bowel Disease patients:*

*A nationwide Danish cohort study*

*Copenhagen, March 07 2019*

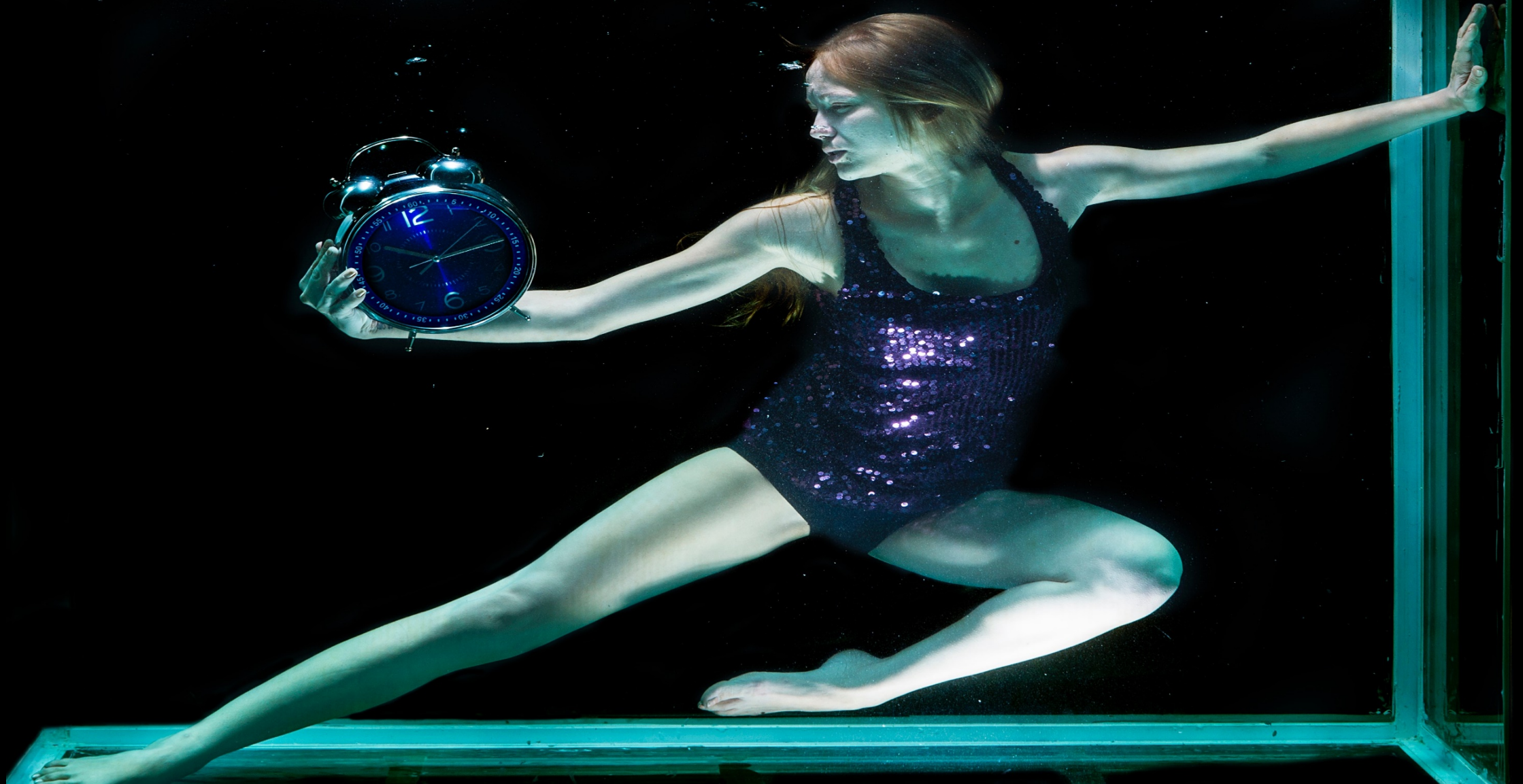
## Disclosures

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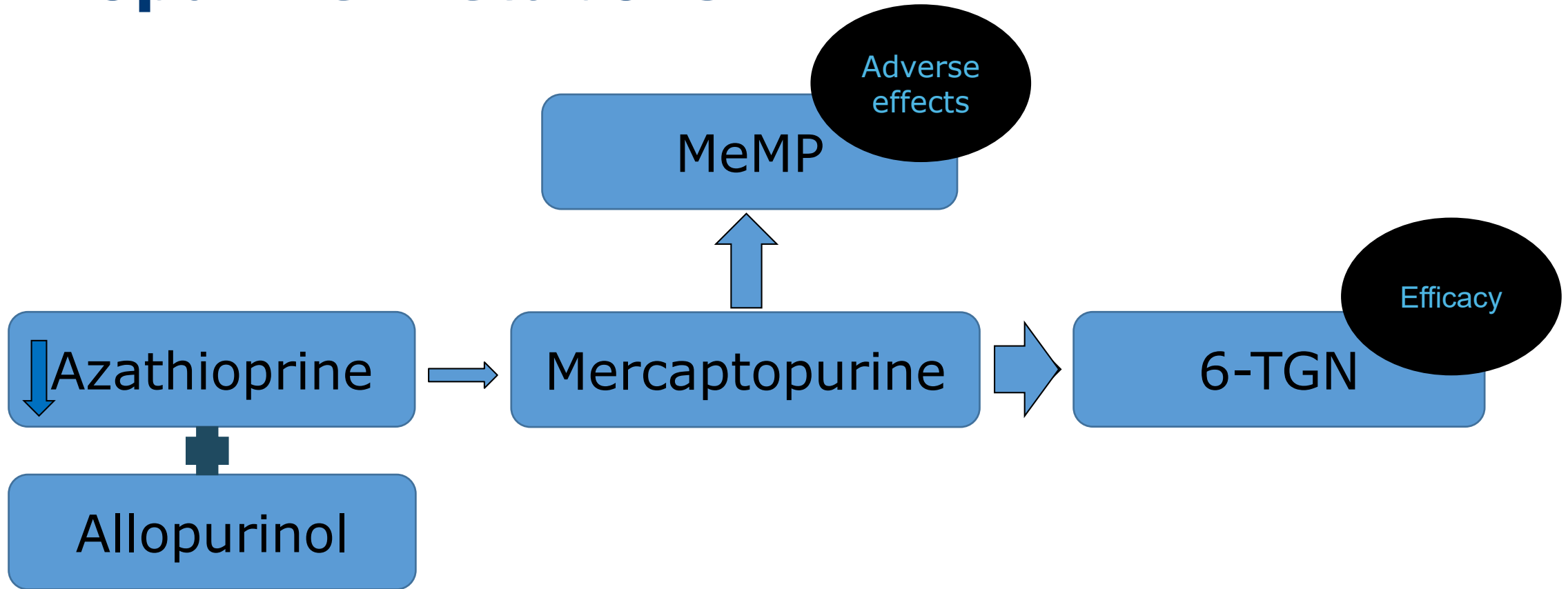
## Acknowledgements

- K. H. Allin; J. Burisch; C. B. Jensen; S. Hansen; L. L. Gluud; K. Theede; M. Kiszka-Kanowitz; A. Mertz Nielsen; T. Jess

***Louise - Crohn's disease, 18 years old  
Aims for professional dancing career  
50 % risk of surgery in 10 years***



# Thiopurine metabolism



## Background

- Moreau AC, Paul S, Del Tedesco E, et al. Association Between 6-Thioguanine Nucleotides Levels and Clinical Remission in Inflammatory Disease. *Inflamm Bowel Dis.* 2014;20(3):464-471.
- Kiszka-Kanowitz M, Theede K, Mertz-Nielsen A. Randomized clinical trial: a pilot study comparing efficacy of low-dose azathioprine and allopurinol to azathioprine on clinical outcomes in inflammatory bowel disease. *Scand J Gastroenterol.* 2016;51(12):1470-1475.

# Aim





To compare patients with inflammatory bowel disease exposed to:

Thiopurine-allopurinol therapy vs. thiopurine monotherapy

on later need for surgery, hospitalization, biologics, and death.

Follow-up:  
24,714 person years

Primary outcome

-  IBD- related major surgery
-  IBD- related hospitalization
-  Biologics
-  Death

N=10,150  
Thiopurine

N=217  
Thiopurine  
Allopurinol



IBD-diagnosis

Timeline

1999

Exposure

Outcome

2014

Methods

Baseline description	Allopurinol	Monotherapy	p-value
<b>IBD-type</b>			0.002
Crohn's Disease (%)	88 (40.55)	5396 (53.16)	
Ulcerative Colitis (%)	129 (59.45)	4754 (46.84)	
<b>Sex</b>			<0.001
Women (%)	81 (37.33)	5171 (50.95)	
Men (%)	136 (62.67)	4979 (49.05)	
<b>Age at IBD-diagnosis</b>			<0.001
Mean (SD), years	41.47 (18.79)	36.18 (16.10)	
<b>Age (index)</b>			<0.001
Mean (SD), years	47.19 (18.95)	40.74 (16.49)	
<b>Duration of IBD</b>			<0.001
Mean (SD), years	5.68 (6.61)	4.51 (6.42)	
<b>Calendar year at medication initiation</b>			<0.001
1999-2003 (%)	26 (11.98)	3241 (32.01)	
2004-2008 (%)	32 (14.75)	2824 (27.82)	
2009-2014 (%)	159 (73.27)	4085 (40.25)	

Sparrow MP, Hande SA, Friedman S, et al. Allopurinol safely and effectively optimizes tioguanine metabolites in inflammatory bowel disease patients not responding to azathioprine and mercaptopurine. *Aliment Pharmacol Ther.* **2005**;22(5):441-446.

Outcomes	IRR in allopurinol vs. monotherapy					
	Crude			Adjusted		
	IRR	95%CI		IRR	95%CI	
<b>Composite outcome</b>	1.61	1.18	2.20	1.26	0.92	1.73
<b>Separate outcomes</b>						
Major surgery	1.32	0.76	2.28	1.31	0.76	2.27
Hospitalization	1.64	1.16	2.33	1.61	1.14	2.29
Biologics	1.39	0.88	2.18	0.74	0.47	1.16
Death	-	-	-	-	-	-

Stratification by calendar year						
1999-2003	3.70	1.92	7.13	4.88	2.53	9.45
2004-2008	1.90	1.02	3.54	2.19	1.17	4.09
2009-2014	0.73	0.48	1.30	0.80	0.52	1.23
Stratification by age						
≤40 years	0.79	0.37	1.65	0.46	0.22	2.98
>40 years	2.42	1.72	3.42	1.99	1.41	2.81

Adjusted for IBD-subtype, sex, age at treatment, calendar year, and age at IBD diagnosis

Composite outcome: IBD-related major surgery, IBD-related hospitalization, biological therapy, death



A silhouette of a person jumping joyfully against a sunset sky over a body of water. The sun is low on the horizon, creating a bright glow and reflecting on the water. The person's arms are raised, and their legs are bent in a classic jumping pose. The sky is a mix of orange, yellow, and blue. The water is calm, reflecting the sunset. In the background, there are silhouettes of buildings and trees along the shore.

Thank you

Conclusion