

What did we learn from trials that failed?

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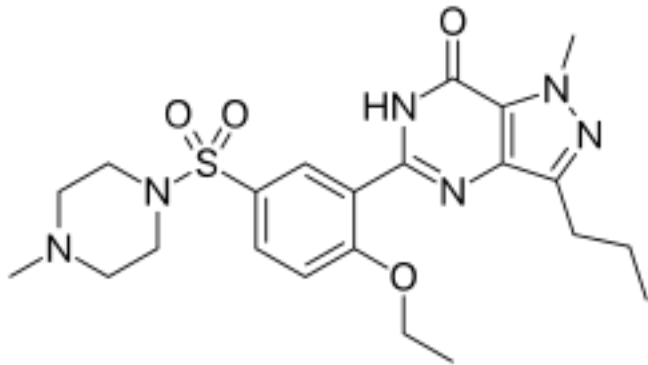


Conflicts of interest

Type of affiliation / financial interest	Name of commercial company
Research funding, speaker and advisory honoraria	Astellas
Research funding, speaker and advisory honoraria	AstraZeneca
Speaker and advisory honoraria, travel support	Bayer
Speaker and advisory honoraria, travel support	BMS
Research funding	Exelixis
Speaker and advisory honoraria, travel support	Ipsen
Speaker and advisory honoraria, travel support	Janssen
Speaker and advisory honoraria, travel support	Merck Serono
Speaker and advisory honoraria, travel support	MSD
Research funding, speaker and advisory honoraria	Novartis / AAA
Research funding, speaker and advisory honoraria	Pfizer
Research funding, speaker and advisory honoraria	Roche
Advisory honoraria	Seagen

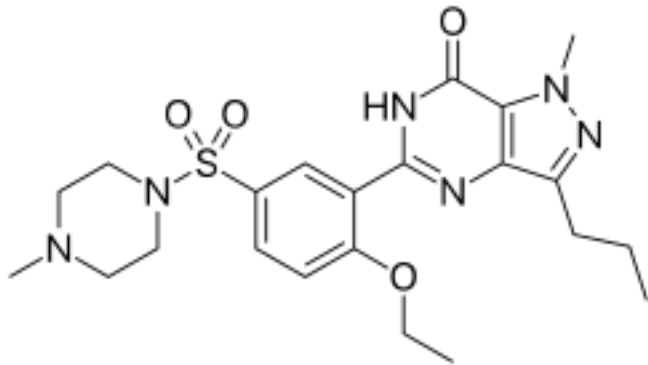
A history of failure

UK-92480 – a PDE5 inhibitor

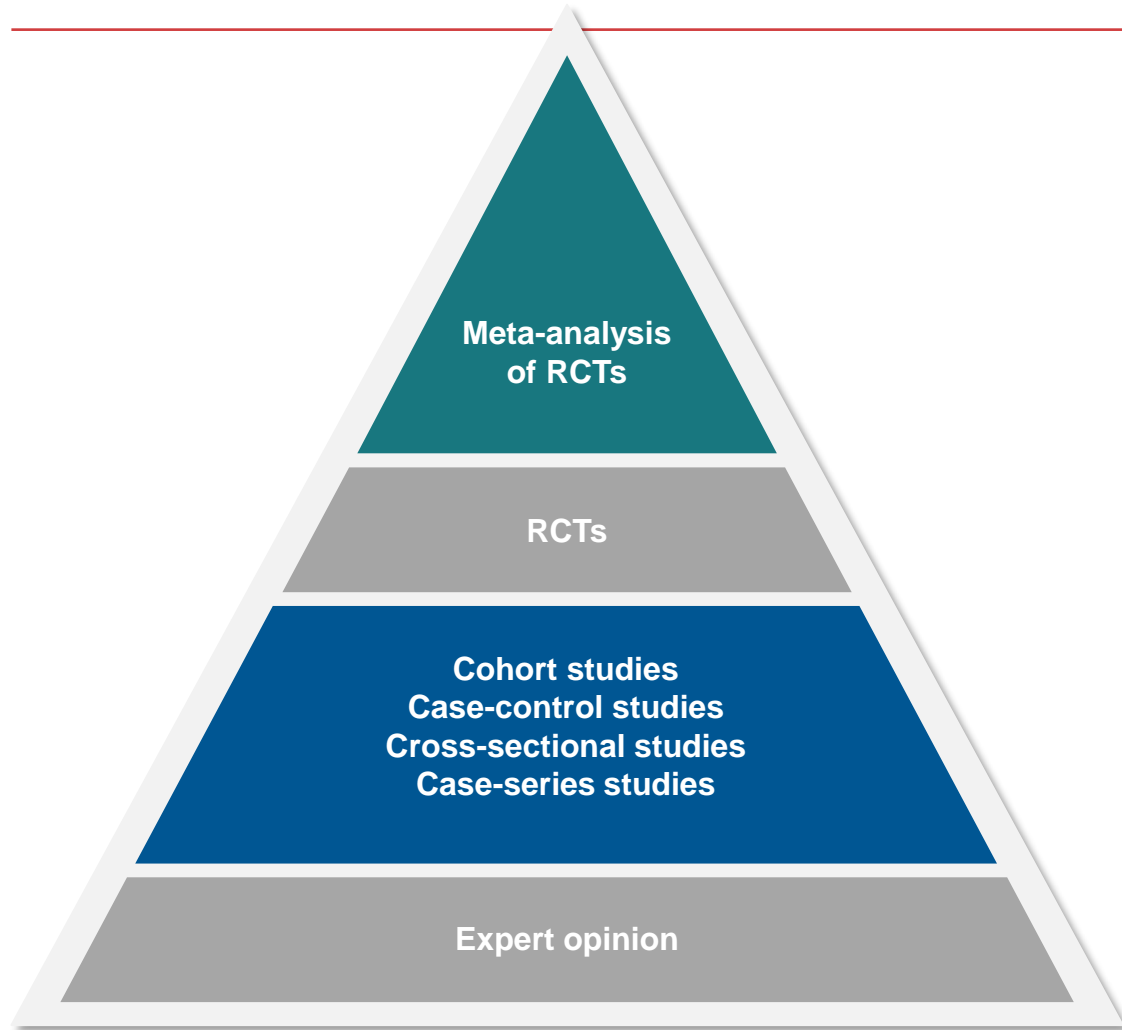


A history of failure

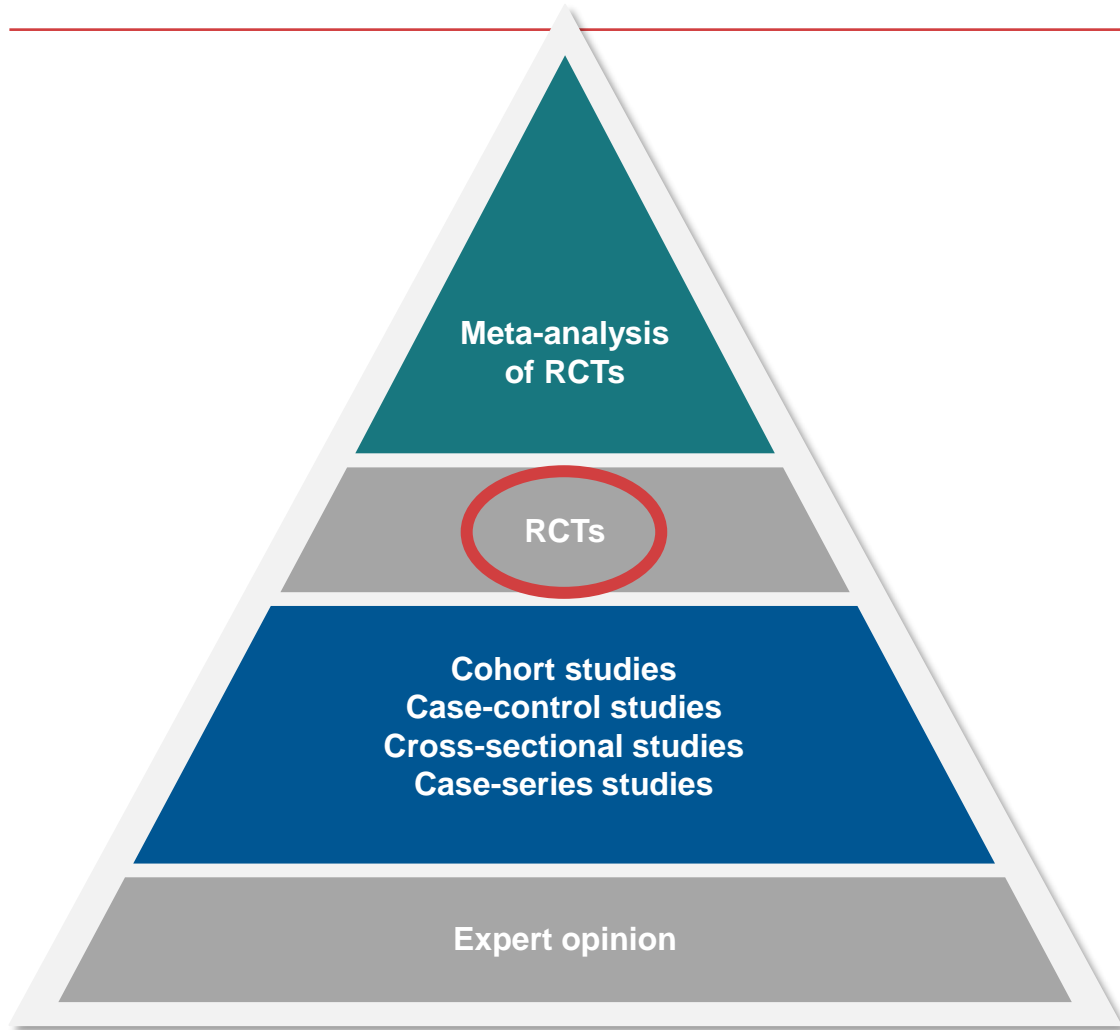
UK-92480 – a PDE5 inhibitor



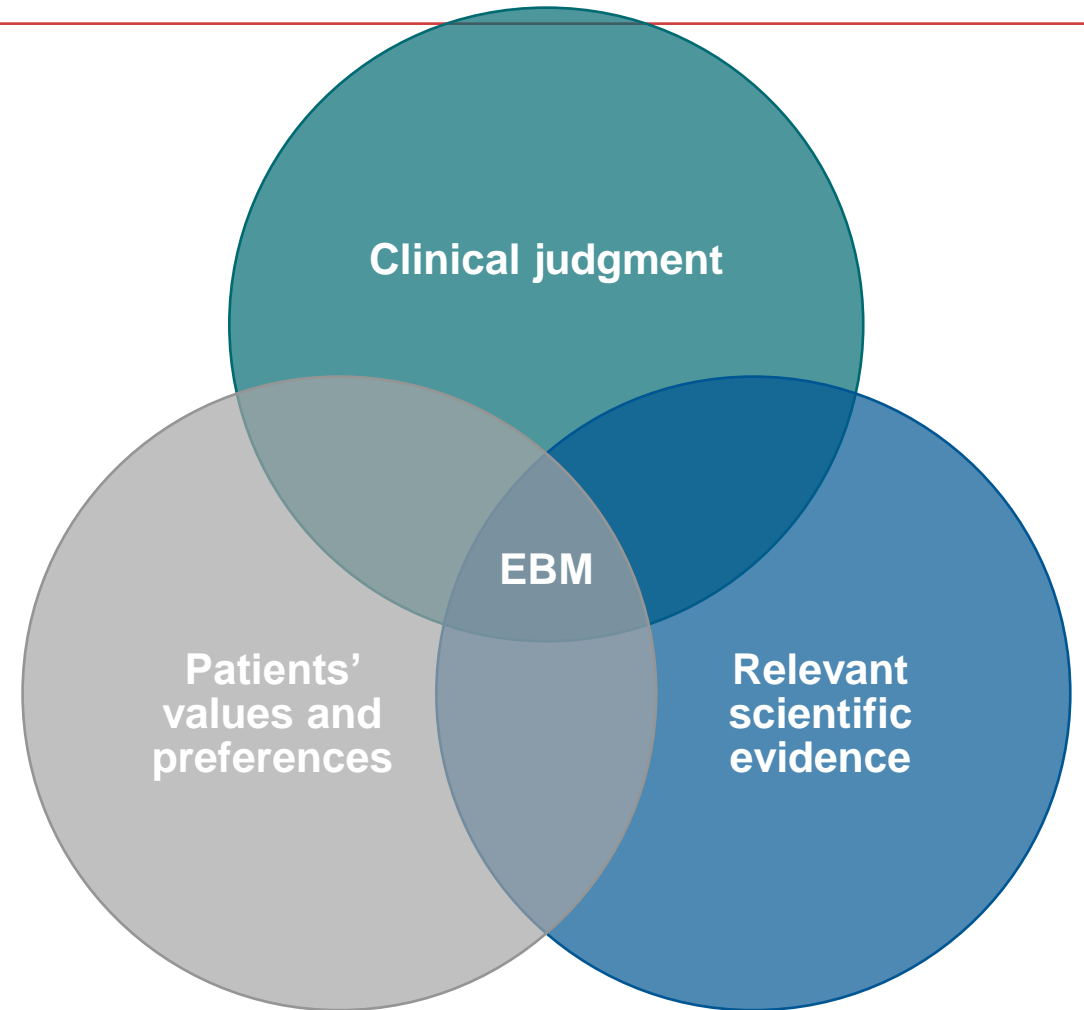
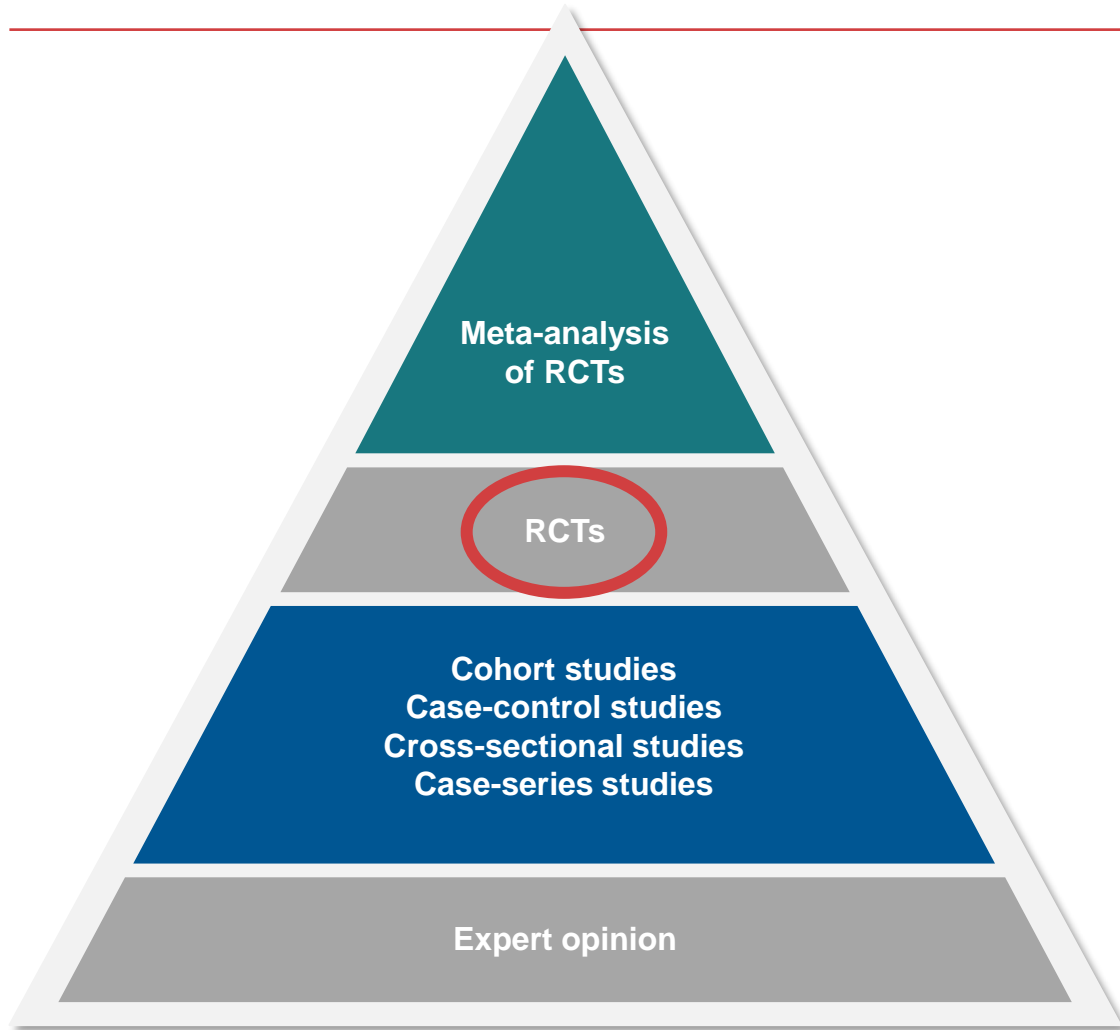
Why do we do trials?



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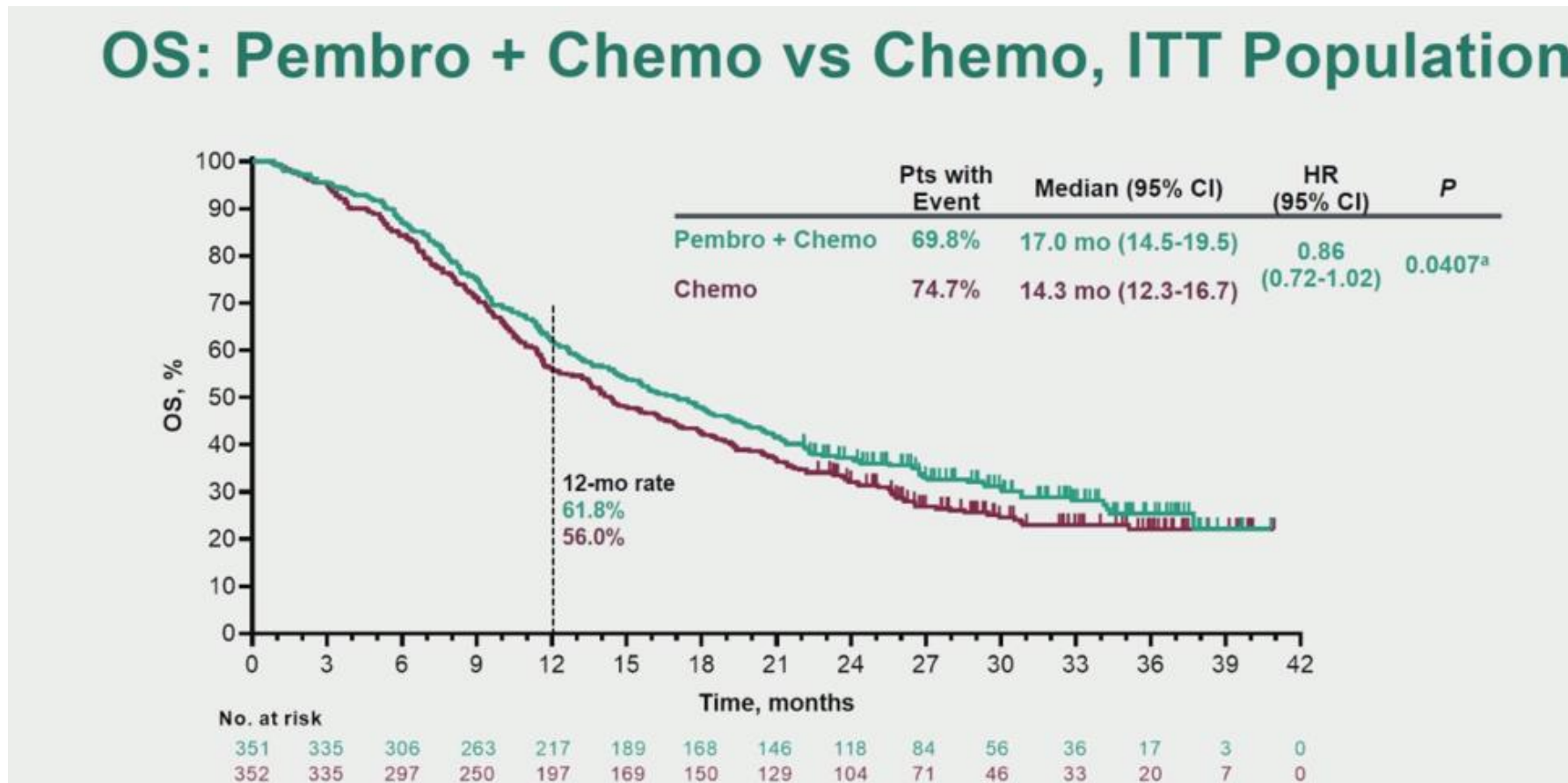
"Failure is success in progress."

— Albert Einstein



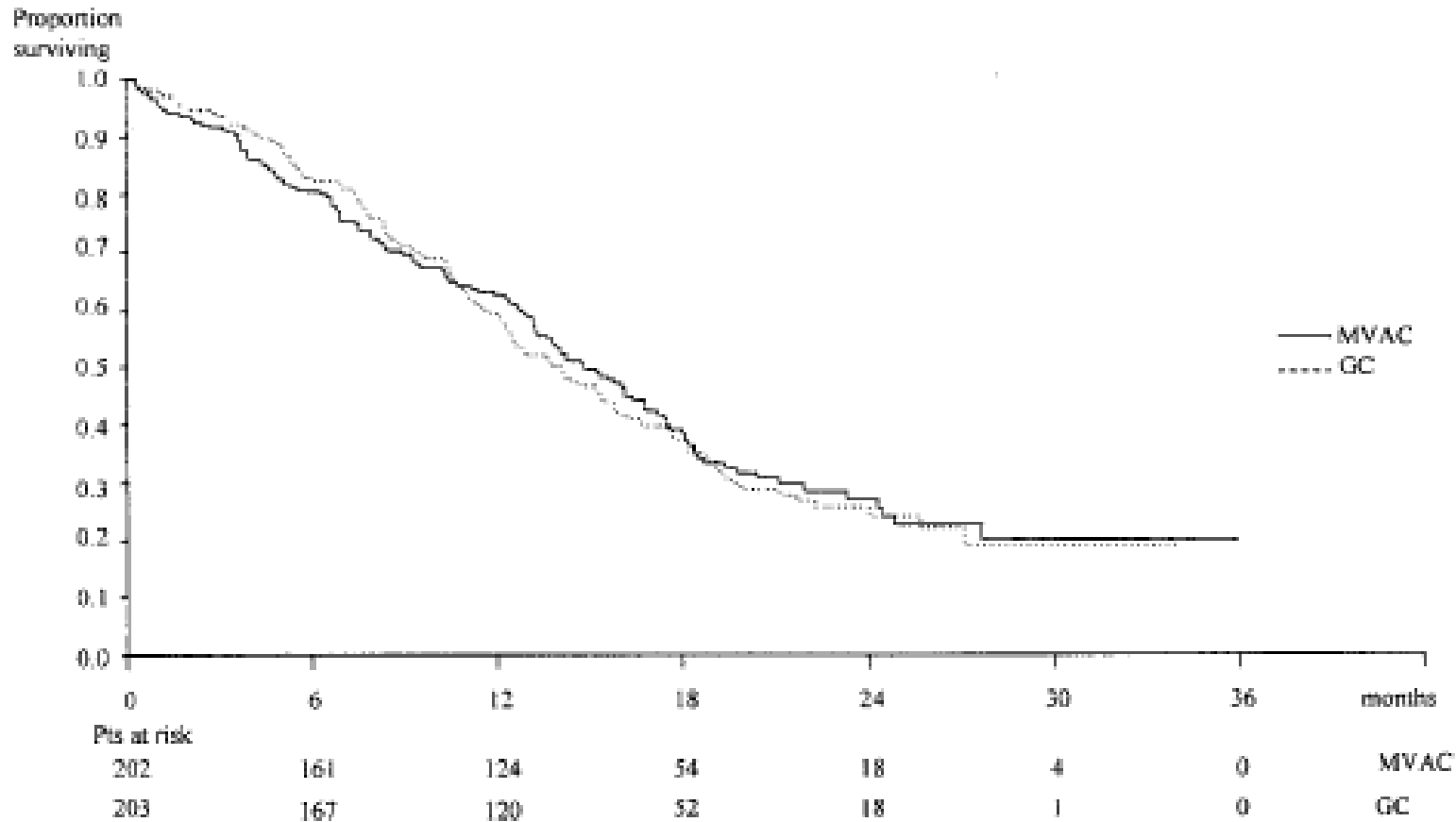
What is failure in a clinical trial?

- Practice affirmation: Keynote - 361



What is failure in a clinical trial?

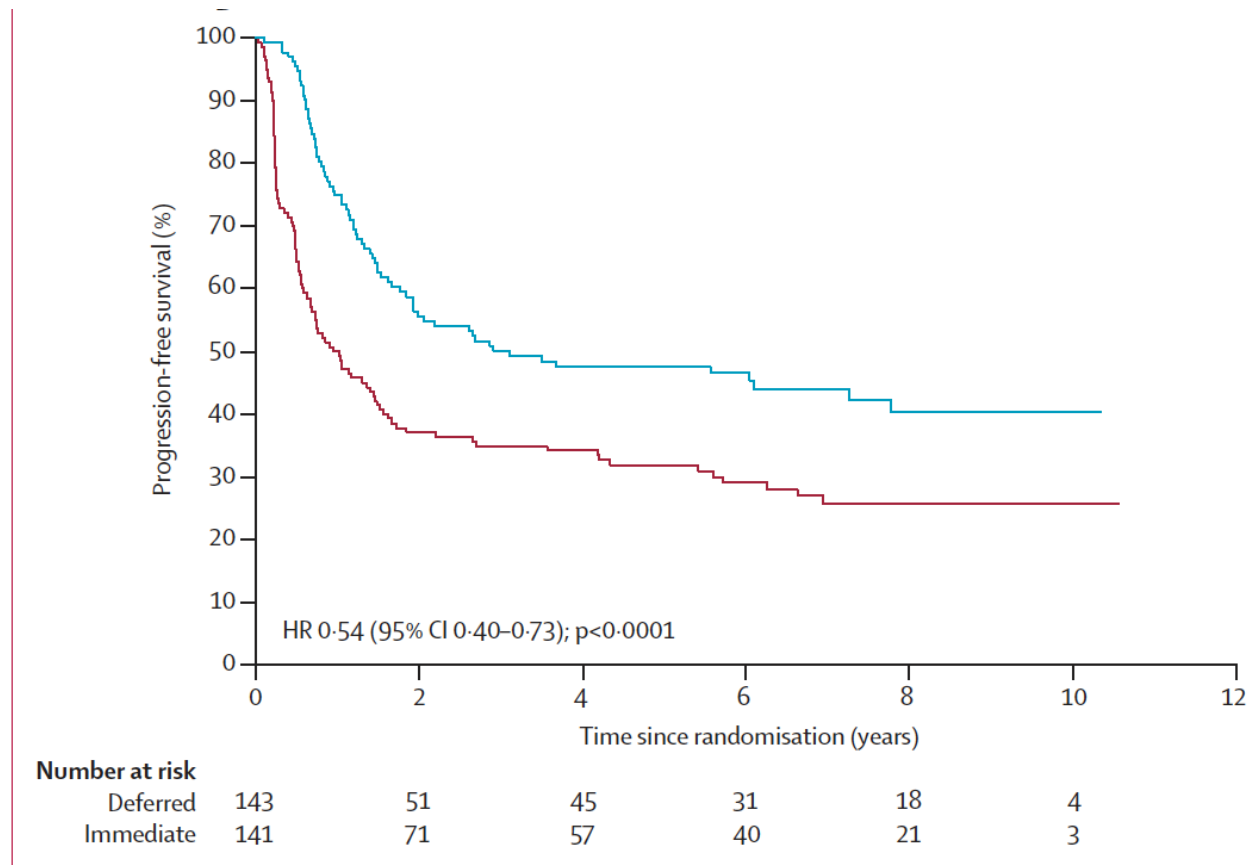
- Demonstrating that a treatment isn't safe / tolerable (with minimal harm done)



von der Maase et al. 2000

What is failure in a clinical trial?

- Failure to accrue



What is failure in a clinical trial?

- Failure of the system
 - Funding
 - Investigator failure
 - Failure of design

So what did we learn from the trials that failed in urothelial cancer?

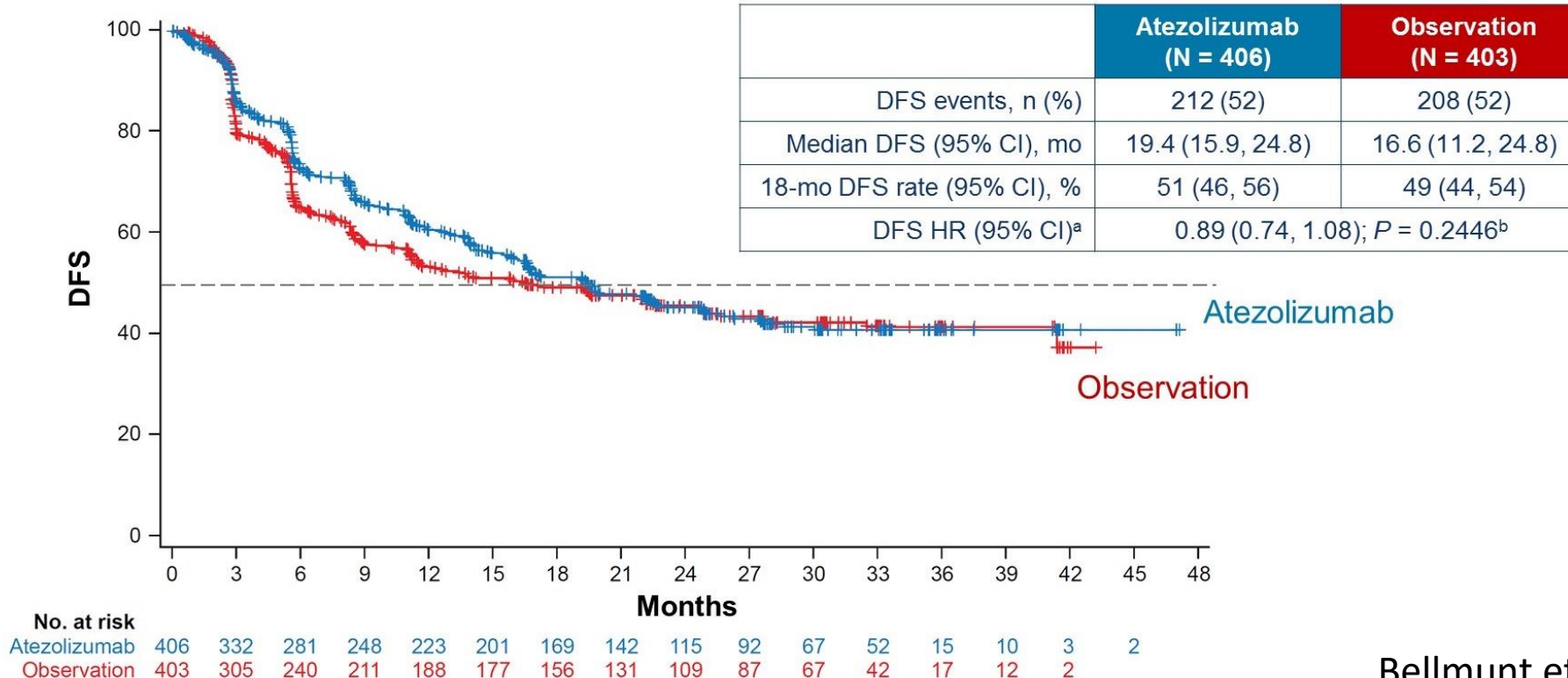


Exploratory data from one trial generate the next trial

ImVigor-010

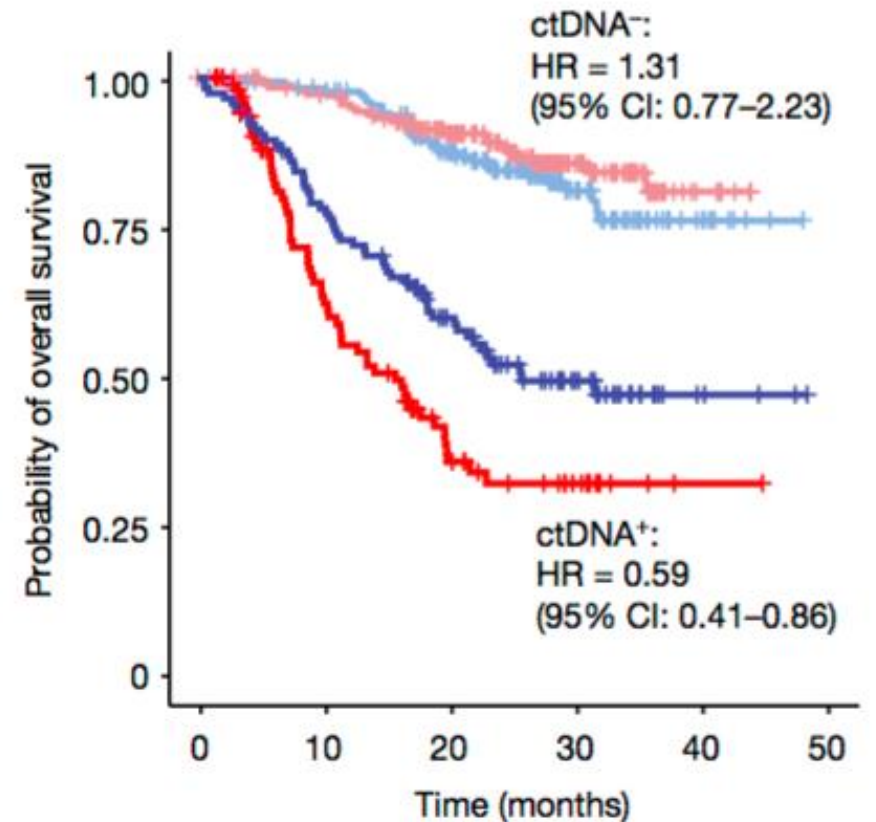
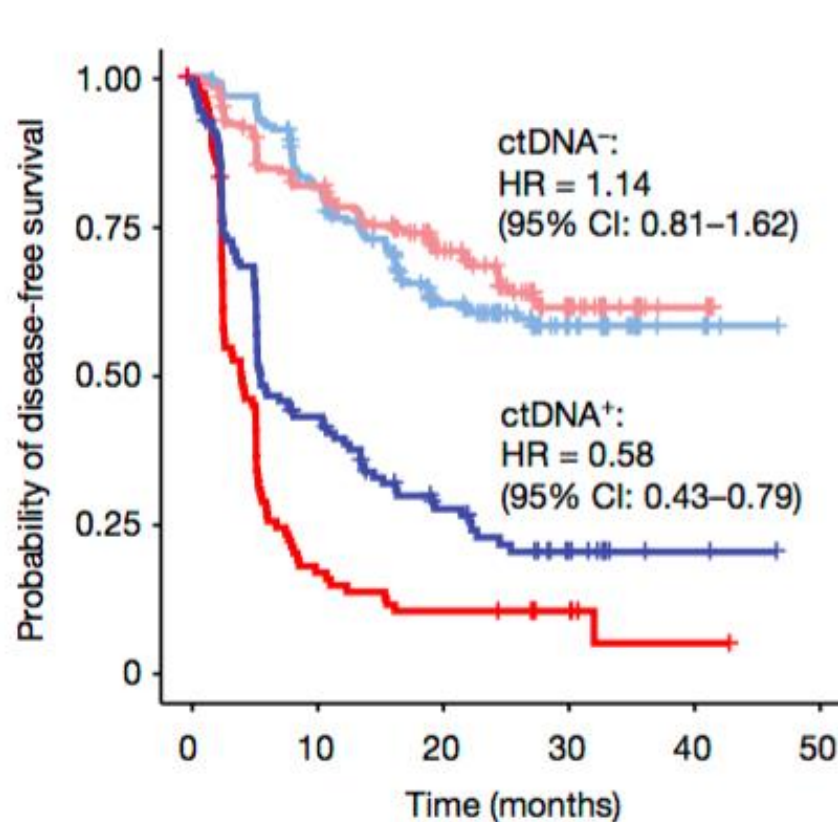
DFS in ITT Population

Median follow up 21.9m



Bellmunt et al. *Lancet Oncol* 2021; 22: 525–37

Exploratory data from one trial generate the next trial

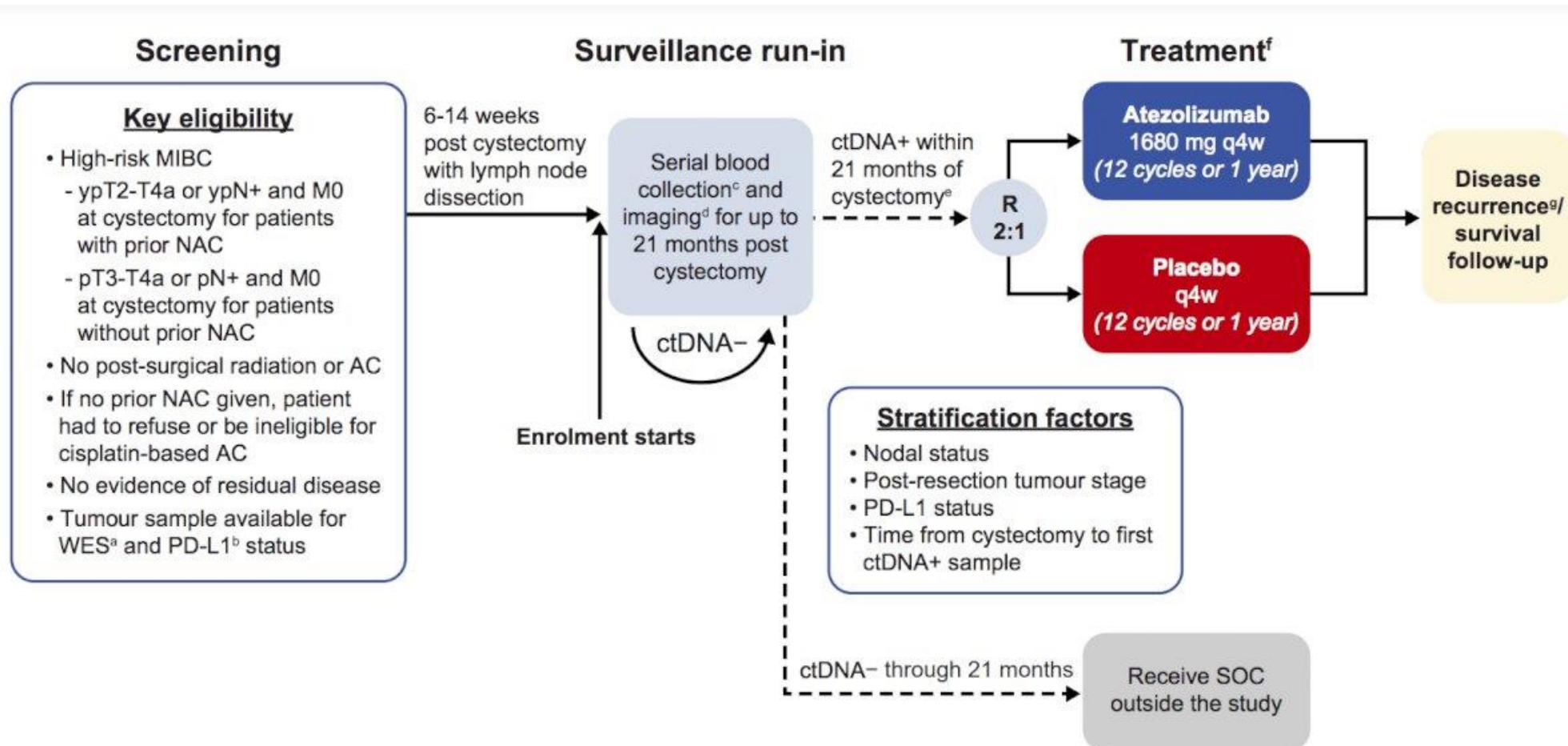


No. at risk		Time (months)					
		0	10	20	30	40	50
— Atezolizumab	ctDNA ⁻	184	144	85	44	5	0
		183	140	90	46	6	0
— Atezolizumab	ctDNA ⁺	116	48	25	13	2	0
		98	17	10	5	1	0

— Observation	ctDNA ⁻	184	174	129	57	10	0
		183	170	130	65	7	0
— Observation	ctDNA ⁺	116	88	55	25	4	0
		98	54	24	11	1	0

Exploratory data from one trial generate the next trial

ImVigor-011



"It is impossible to live without failing at something unless you live so cautiously that you might as well not have lived at all, in which case you have failed by default."

— J.K. Rowling

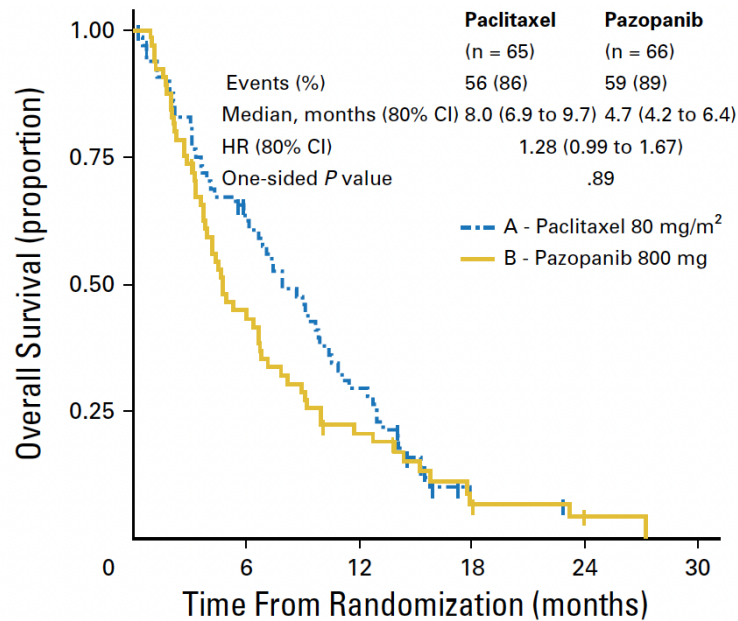


If you never fail, you're probably not trying hard enough

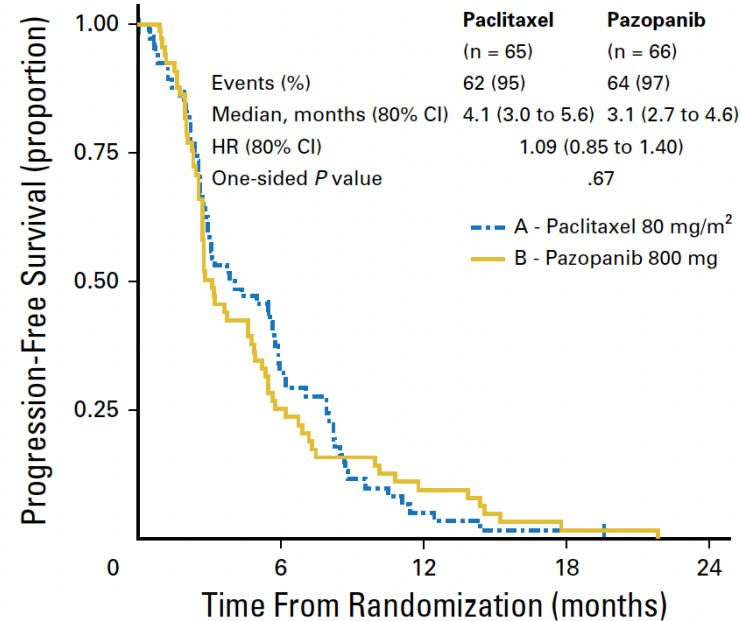
- BUT, we owe it to our patients to protect them from unwarranted risk of failure

If you never fail, you're probably not trying hard enough

- Randomised phase II



No. at risk:	0	3	6	9	12	15	18	21	24	27	30
A - Paclitaxel 80 mg/m ²	65	53	38	29	18	8	1	1	0	0	0
B - Pazopanib 800 mg	66	47	28	18	12	8	3	3	1	1	0



No. at risk:	0	3	6	9	12	15	18	21	24
A - Paclitaxel 80 mg/m ²	65	38	20	7	3	1	1	0	0
B - Pazopanib 800 mg	66	32	16	10	6	3	1	1	0

"It's fine to celebrate success but it is more important to heed the lessons of failure."

— Bill Gates



If we do fail, we should make sure we fail comprehensively,
so we don't have to try and fail again

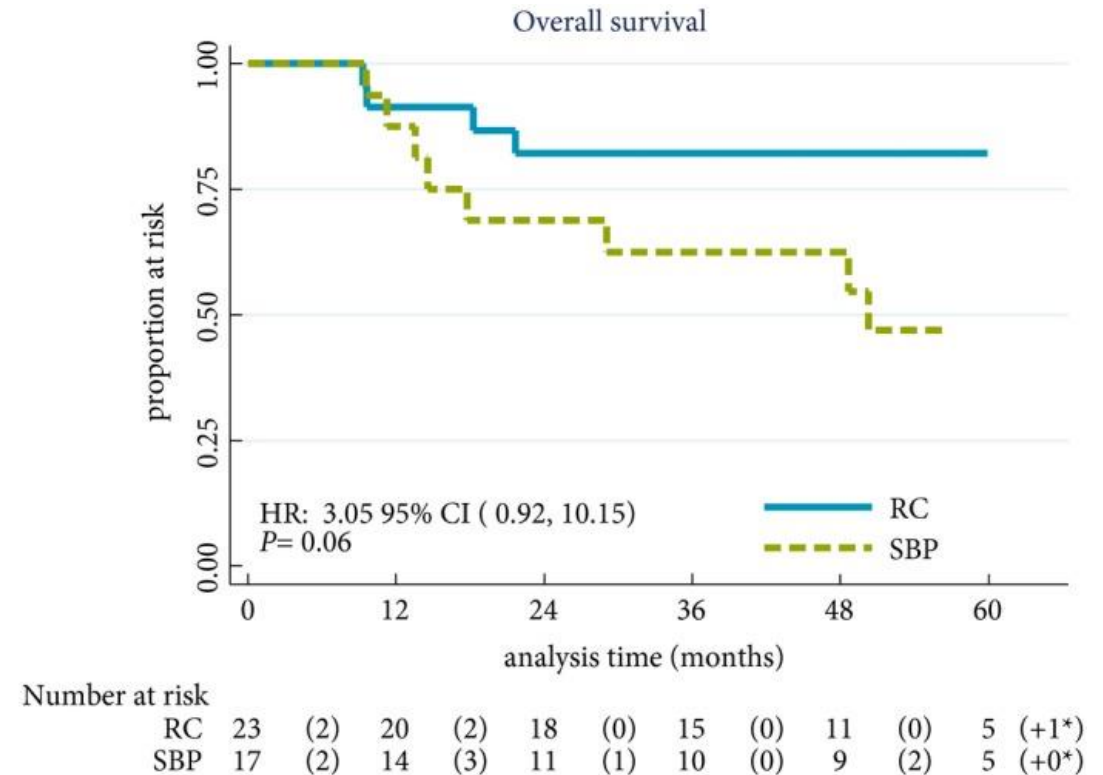
Which is best for MIBC: Cystectomy or radical radiotherapy?



If we do fail, we should make sure we fail comprehensively, so we don't have to try and fail again

Which is best for MIBC: Cystectomy or radical radiotherapy?

Non-inferiority trial
N=1015



Summary

- If we knew what we were doing, it wouldn't be research*
 - So failure is part of success
- Failed trials provide valuable data and tissue to generate new hypotheses
- We owe it to our patients to minimize exposure to failure
- We must only fail in the same way once

*Dr Albert Szent-Györgyi, 1959