

Panel Challenge Question

What role can prior evidence about HTE play in confirmatory trial design and analysis?

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A cautionary tale



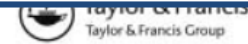
Region	Gender	rhC1INH		Saline		p-value
		N (censored)	Median (95% CI)	N (censored)	Median (95% CI)	
USA	Female	11 (3)	151 (32, -)	14 (5)	90 (35, -)	0.5552
USA	Male	11 (3)	45 (30, -)	2 (1)	- (60, -)	0.5045
ROW	Female	17 (1)	90 (60, 150)	5 (1)	152 (105, 334)	0.1990
ROW	Male	5 (1)	91 (45, 210)	10 (7)	- (44, -)	0.0065
USA		22 (6)	98 (32, 240)	16 (6)	90 (35, -)	0.9842
ROW		22 (2)	90 (61, 120)	15 (8)	334 (120, -)	0.0011
Female		28 (4)	113 (61, 151)	19 (6)	105 (50, 334)	0.8139
Male		16 (4)	75 (30, 210)	12 (8)	480 (60, -)	0.0140

Source: Statistical review of RUCONEST, 5/16/2014;

<https://www.fda.gov/BiologicsBloodVaccines/BloodBloodProducts/ApprovedProducts/LicensedProductsBLAs/FractionatedPlasmaProducts/ucm405629.htm>

Another cautionary tale

Nicotine & Tobacco Research Volume 7, Number 1 (February 2005) 119–127



Nicotine patch and lozenge are effective for women

Nicotine & Tobacco Research Volume 7, Number 6 (December 2005) 915–916



Letter

Comment on Shiffman and colleagues, “Nicotine patch and lozenge are effective for women”

Nicotine & Tobacco Research Volume 10, Number 7 (July 2008) 1245–1251

healthcare

Sex differences in long-term smoking cessation rates due to nicotine patch

Planning ahead



- Stratification
- Pre-planned subgroup analyses
 - Default choice should probably be some kind of shrinkage estimate
- In presence of unusually strong prior evidence, consider
 - Adaptive dose selection by subgroup
 - Subgroup-specific interim decision-making
 - Stratified benefit-risk assessments