

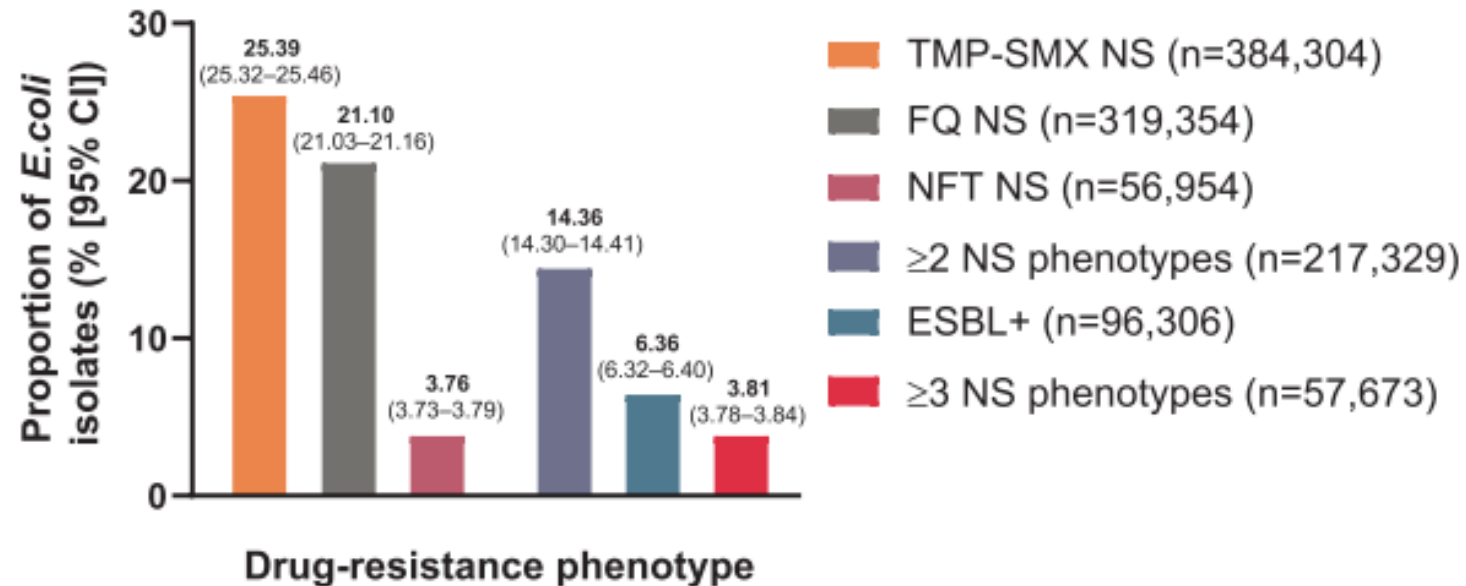
New (old) Drugs for UTI

PIVMECILLINAM

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Resistance is Common and Rising

- Urine cultures from women in US outpatient facilities
- 1.5 million *E.coli* isolates



New Drug Check-List

- Spectrum
- Indications & Evidence
- Resistance
- Safety, side-effects
- Practical aspects
- Role

New (to us) antibiotic: Pivmecillinam

- Available in Europe and Canada for decades
- Semi-synthetic penicillin
- PO only

Pivmecillinam - Spectrum

- Enterobacterales
 - including some ESBL (CTX-M) and AmpC
- *Staph saprophyticus*

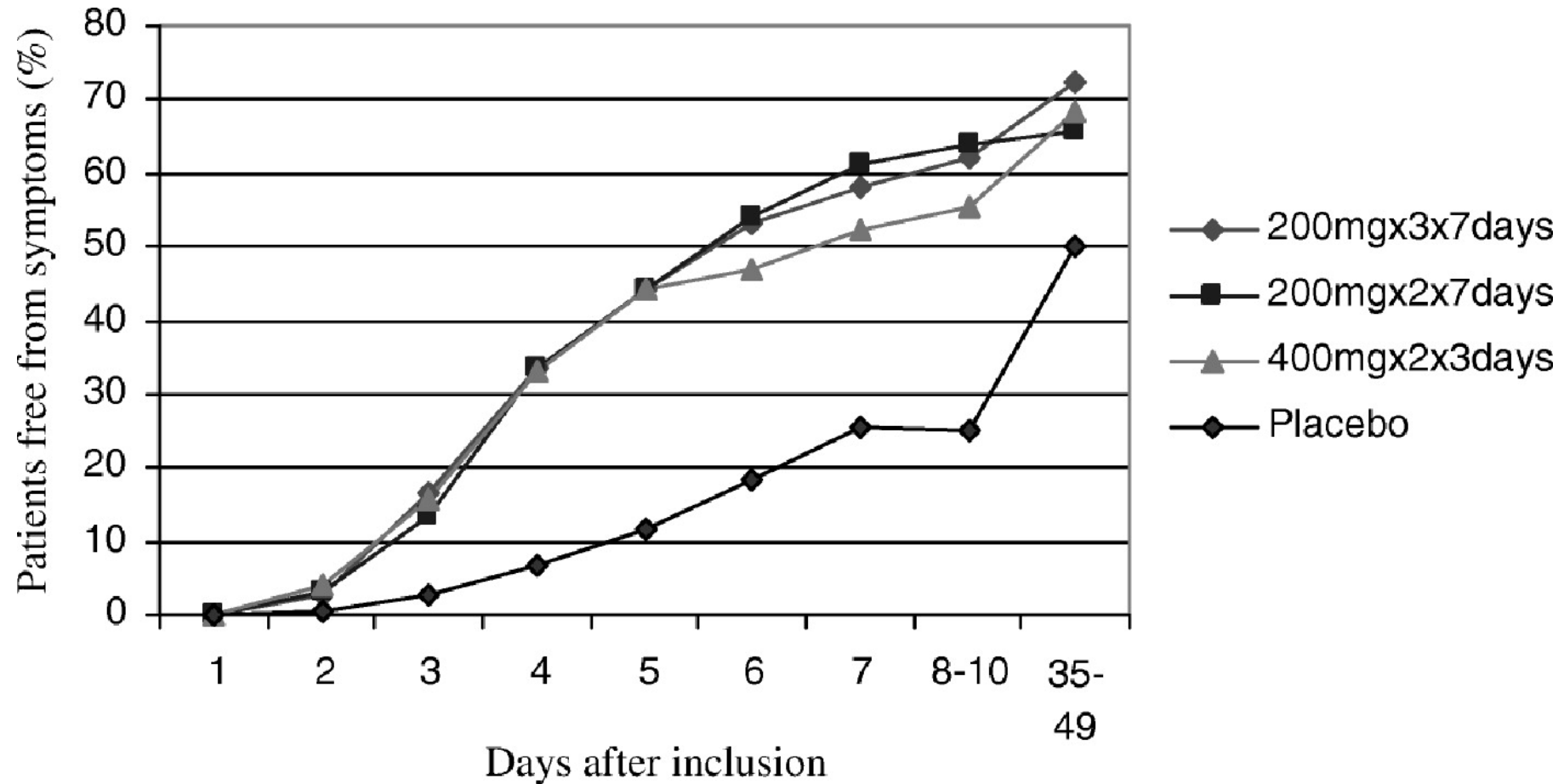
Pivmecillinam – Indications & Evidence

- FDA approval April 2024
 - uUTI in adult women caused by *E.coli*, *Proteus mirailis*, *Staph saprophyticus*
 - 185 mg PO TID x 3-7 days
- Evidence:
 - Of 14 studies, 3 RCTs were reanalyzed for the FDA approval
 - Non-pregnant, adult women, uUTI
 - Inclusion: 2 symptoms + pyuria
 - >86% had monomicrobial GNR infection
 - Endpoints: composite clinical + micro, clinical, micro ITT

Table 3. Reanalysis of 3 Primary Studies at Test of Cure Visit (Microbiological Intention-to-Treat Analysis Set)

End Point	Response at Test of Cure Visit	Ferry et al [13]		Menday [14]		Vik et al [15]		
		Pivmecillinam Hydrochloride 200 mg tid for 7 d (N = 137)	Placebo (N = 134)	Pivmecillinam Hydrochloride 200 mg tid for 3 d (N = 127)	Cephalexin 250 mg qid for 7 d (N = 132)	Pivmecillinam Hydrochloride 200 mg tid for 3 d (N = 105)	Ibuprofen 600 mg tid for 3 d (N = 119)	
Improved + TOC (d7-15)	Overall response	Success, ^a n (%)	85 (62.0)	14 (10.4)	91 (71.7)	100 (75.8)	69 (65.7)	26 (21.8)
	Difference		51.6	...	-4.1	...	43.9	...
	95% CI for the difference		41.2-62.0	...	-15.6 to 7.4	...	31.2-56.5	...
	Failure, n (%)		45 (32.8)	110 (82.1)	29 (22.8)	24 (18.2)	35 (33.3)	91 (76.5)
	Indeterminate, n (%)		7 (5.1)	10 (7.5)	7 (5.5)	8 (6.1)	1 (1.0)	2 (1.7)
Clinical response	Success, n (%)		87 (63.5)	31 (23.1)	105 (82.7)	112 (84.8)	81 (77.1)	45 (37.8)
	Difference		40.4	...	-2.2	...	39.3	...
	95% CI for the difference		28.9-51.9	...	-11.9 to 7.6	...	26.6-52.1	...
	Failure, n (%)		43 (31.4)	93 (69.4)	20 (15.7)	12 (9.1)	16 (15.2)	65 (54.6)
	Indeterminate, n (%)		7 (5.1)	10 (7.5)	2 (1.6)	8 (6.1)	8 (7.6)	9 (7.6)

Eradication of Sx



Pivmecillinam - Resistance

- US susceptibility is 95%
- Global resistance exists, though low 4-6%
- Minimal cross-resistance with other β -lactams

Pivmecillinam – Safety & Side-effects

- Most frequent side-effects
 - Nausea (2%)
- Contraindicated with severe cutaneous reactions to other β -lactam drugs, carnitine deficiency, porphyria

Pivmecillinam – Practical aspects

- Still quite new in US
 - don't know which pharmacies stock it or cost
- Efficacy against ESBL is largely in vitro with limited clinical data, but looks promising
 - Some studies used higher dose (400mg TID)
- Susceptibility testing difficult, no test available
- Norwegian guidelines rec for pyelonephritis

New UTI drugs - role

	Spectrum	Indication & Evidence	Resistance	Safety & side-effects	Practical aspects	Role	Upper Tract Infections
Gepotidacin	Common UTI pathogens	uUTI	Rare No cross	Well tolerated QTc prolong	?	Cystitis if other PO not possible, ESBL	?
Pivmecillinam	Common UTI pathogens	uUTI	Rare, despite long use	Well tolerated	?	Cystitis is other PO not possible, ESBL	Some say so