

Efficacy and Pharmacokinetics of LPCN 1021, a Novel Oral Testosterone Replacement Therapy, in Hypogonadal Men: Study of Androgen Replacement (SOAR)

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Disclosures

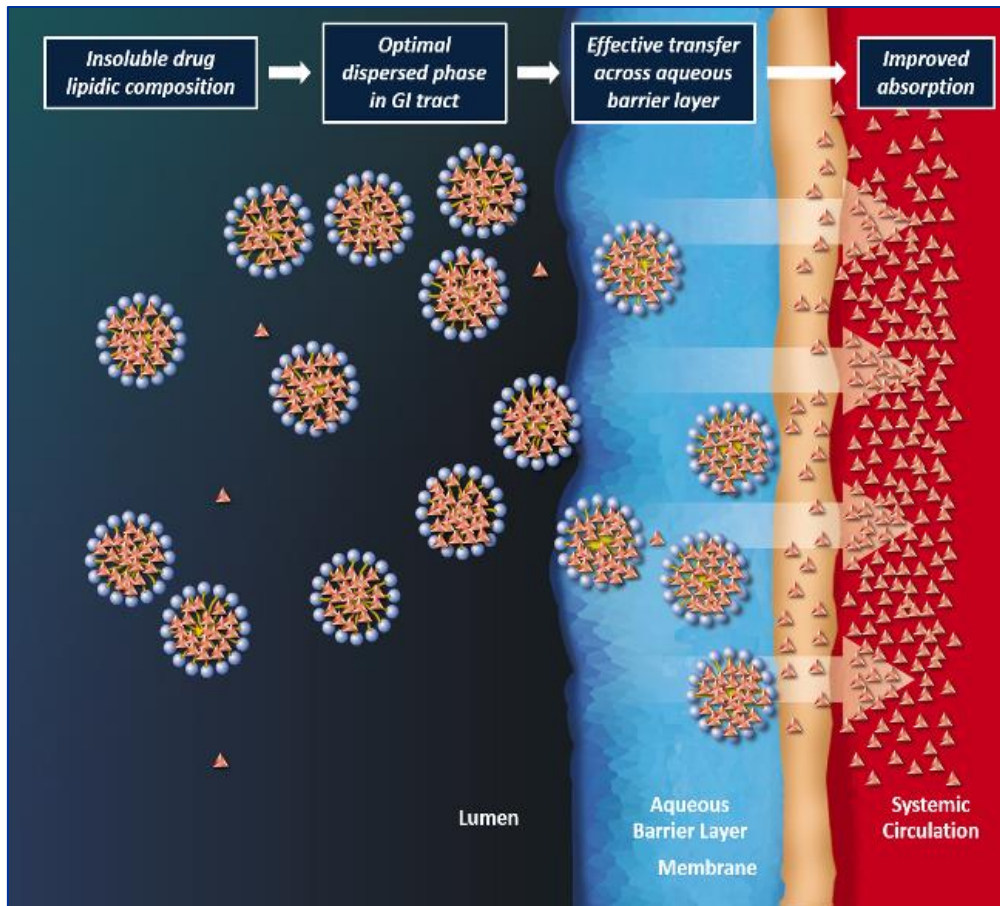
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Objectives

- To understand the key efficacy outcomes from an interim analysis of the SOAR Phase 3 study of LPCN 1021, including:
 - Percent of subjects with an average 24-hour serum testosterone concentration ($C_{\text{avg},24\text{h}}$) within the normal range after 13 weeks of treatment
 - Additional pharmacokinetic information
 - Frequency of dose adjustments

LPCN 1021



- LPCN 1021 is a novel oral testosterone undecanoate formulation that may avoid some of the undesirable attributes of non-oral testosterone formulations
- Utilizes a novel lipidic (lipid-like) oral delivery technology allowing twice-daily dosing leading to:
 - Improved solubilization
 - High drug-loading capacity
 - Improved bioavailability
 - Faster and more consistent absorption, leading to reduced variability

Key Inclusion Criteria

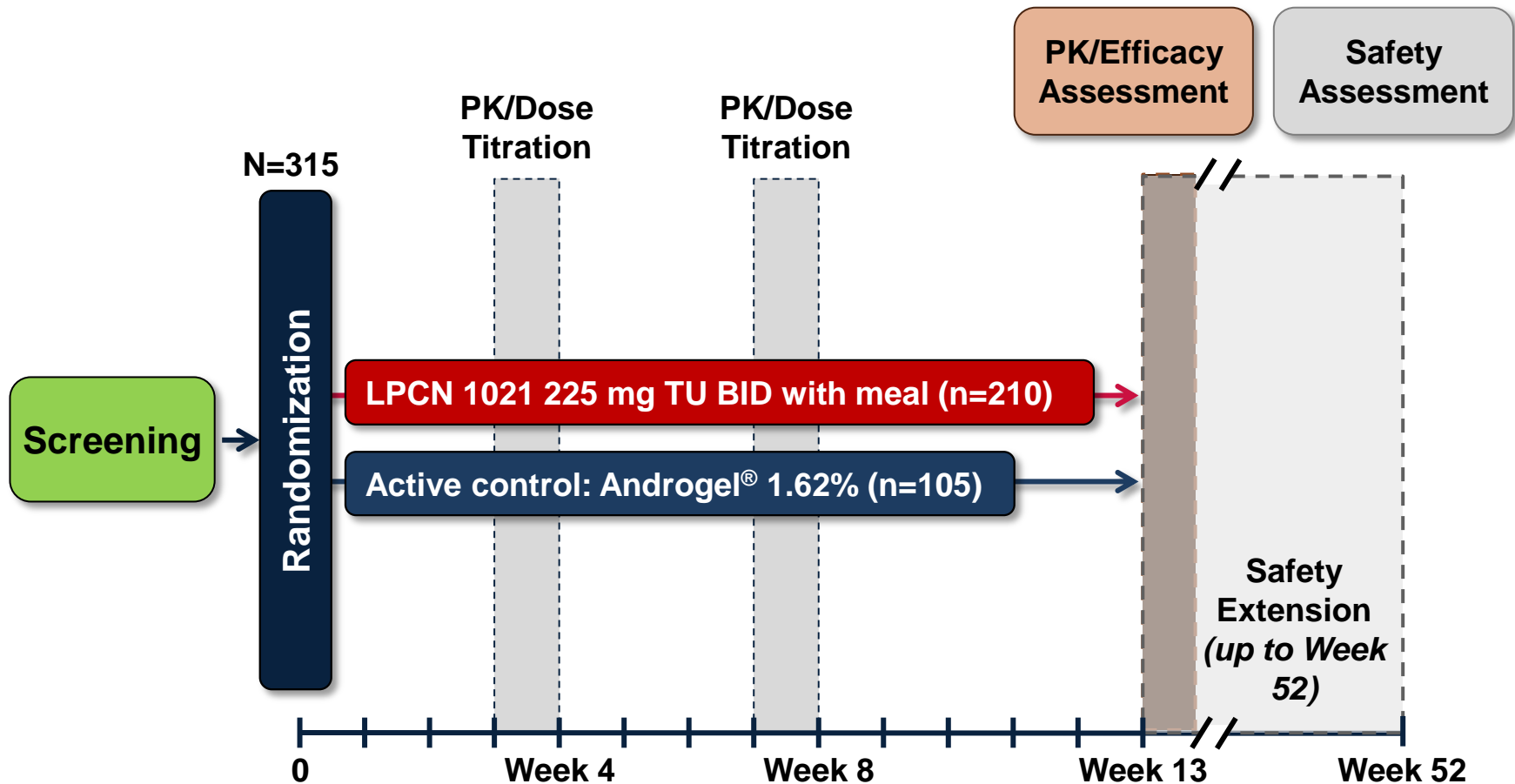
- Male 18-80 years of age with documented onset of hypogonadism prior to age 65
- Documented diagnosis of primary hypogonadism (congenital or acquired) or hypogonadotropic hypogonadism (congenital or acquired)
- Serum T <300 ng/dL based on 2 blood samples, taken approximately same time of day on 2 different days (between 6 and 10 a.m.)
- Naïve to androgen replacement or has discontinued current treatment and completed a washout of prior androgen therapy
 - Washout: 12 weeks following intramuscular androgens, 4 weeks following topical/buccal, 3 weeks following oral; or investigator discretion

Key Exclusion Criteria

- Abnormal prostate exam or I-PSS score >19 points
- Body mass index (BMI) ≥ 38 kg/m²
- Clinically significant abnormal laboratory value
- Concurrent medications that could affect PK measurements or patient health
- Partner who is concurrently pregnant or planning to become pregnant

SOAR Study Design

Open-label, randomized, active-controlled study of LPCN 1021 in 18-80 year-old hypogonadal men (T <300 ng/dL on 2 separate days)



Patient Disposition

Status	LPCN 1021 n (%)	Androgel 1.62% n (%)	Overall n (%)
Subjects Enrolled			326
Subjects Randomized	210	105	315
Subjects in Safety Set	210 (100)	105 (100)	315 (100)
Subjects in Full Analysis Set	192 (91.4)	0	192 (61.0)
Subjects in Efficacy Population	152 (72.4)	0	152 (48.3)

Patient Demographics

- Baseline demographics were similar between groups

Parameter	LPCN 1021 (n=210)	Androgel 1.62% (n=105)	Overall (N=315)
Mean age, yrs (SD)	52.6 (10.24)	54.2 (9.40)	53.1 (9.99)
<65 years, n (%)	190 (90.5)	96 (91.4)	286 (90.8)
≥65 years, n (%)	20 (9.5)	9 (8.6)	29 (9.2)
Race, n (%)			
Black or African American	32 (15.2)	10 (9.5)	42 (13.3)
White	172 (81.9)	92 (87.6)	264 (83.8)
Other	6 (2.9)	3 (2.9)	9 (2.9)
Mean wt, kg (SD)	97.1 (14.96)	99.2 (14.78)	97.8 (14.91)
Mean BMI, kg/m² (SD)	30.8 (3.88)	31.0 (3.9)	30.9 (3.87)

LPCN 1021 Dosing

- The starting dose of LPCN 1021 was 225 mg TU BID taken with a standard meal
- The dose could be titrated up to 300 mg BID (eg, if T $C_{avg,24h}$ was <300 ng/dL) or down to 150 mg BID (eg, if T C_{max} was >1500 ng/dL and/or $C_{avg,24h} >1140$ ng/dL) at weeks 4 and 8

Primary Outcome

- Percentage of subjects with serum total T $C_{avg,24h}$ within the normal range of 300-1140 ng/dL
 - The % of subjects with $C_{avg,24h}$ within the normal range should be $\geq 75\%$ and the lower bound 95% CI $\geq 65\%$
 - Efficacy was assessed on week 13 based on T $C_{avg,24h}$ from serum samples collected over 24 hours for T assayed using LC-MS/MS
 - Analysis was conducted using the Efficacy Population Set (subjects with ≥ 1 PK profile and no major protocol deviations; n=152 LPCN 1021)

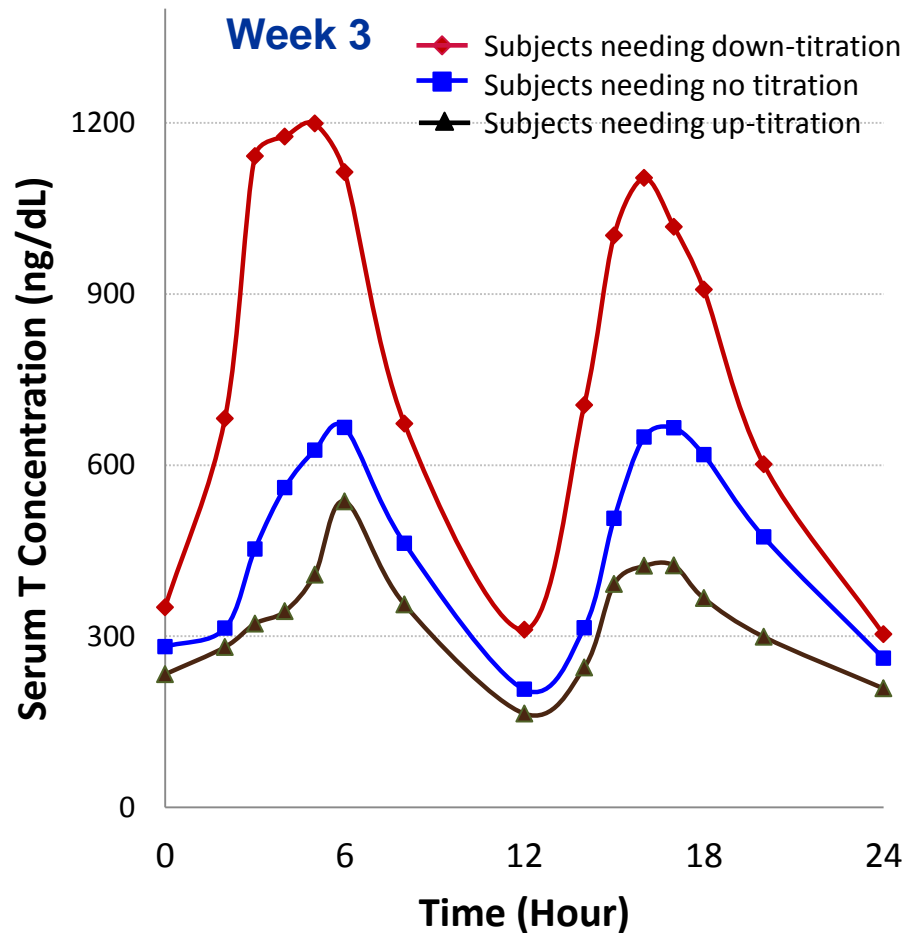
Primary Outcome

- LPCN 1021 reliably restored and maintained T levels in the eugonadal range (300-1140 ng/dL) in 88% of hypogonadal men (lower bound 95% CI=81.9%)

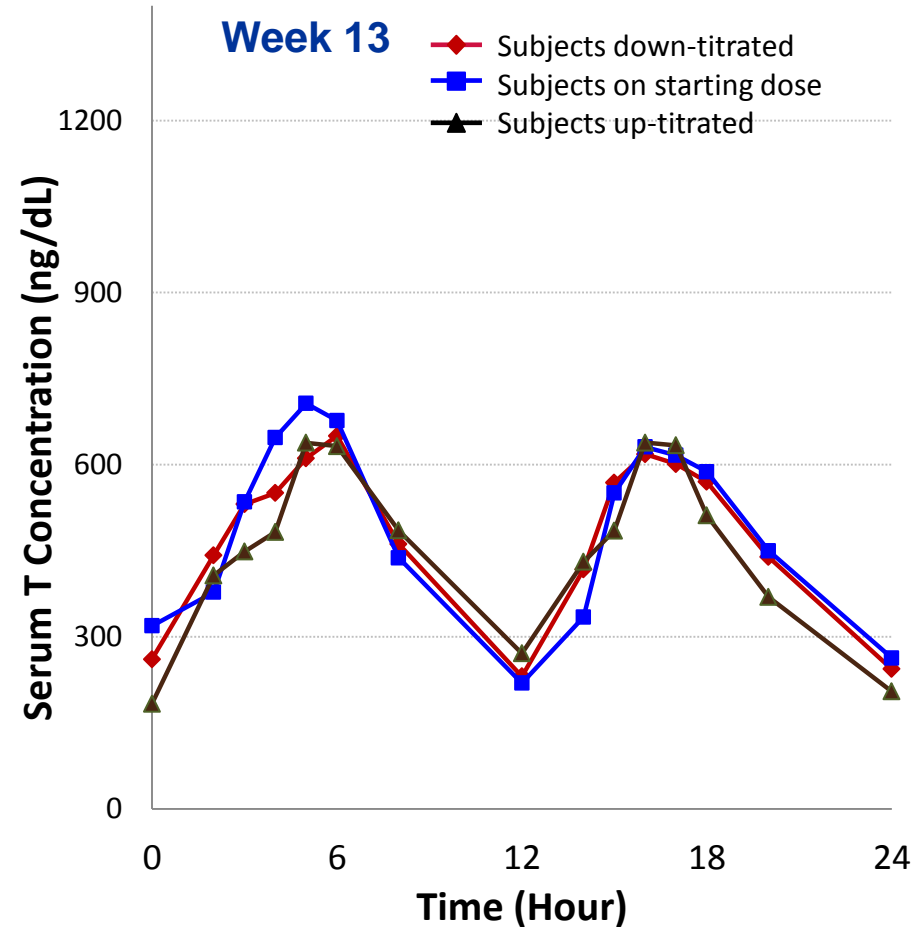
	Frequency, n (%) (n=152)	95% CI
C_{avg,24h} within 300-1140 ng/dL	134 (88.2)	81.93, 92.83
<i>Additional Outcomes</i>		
C_{avg,24h} below 300 ng/dL	17 (11.2)	
C_{avg,24h} above 1140 ng/dL	1 (0.7)	

Converging Titration Regimen

Pre-titration Profile (all subjects at 225 mg)



Post-titration Profile



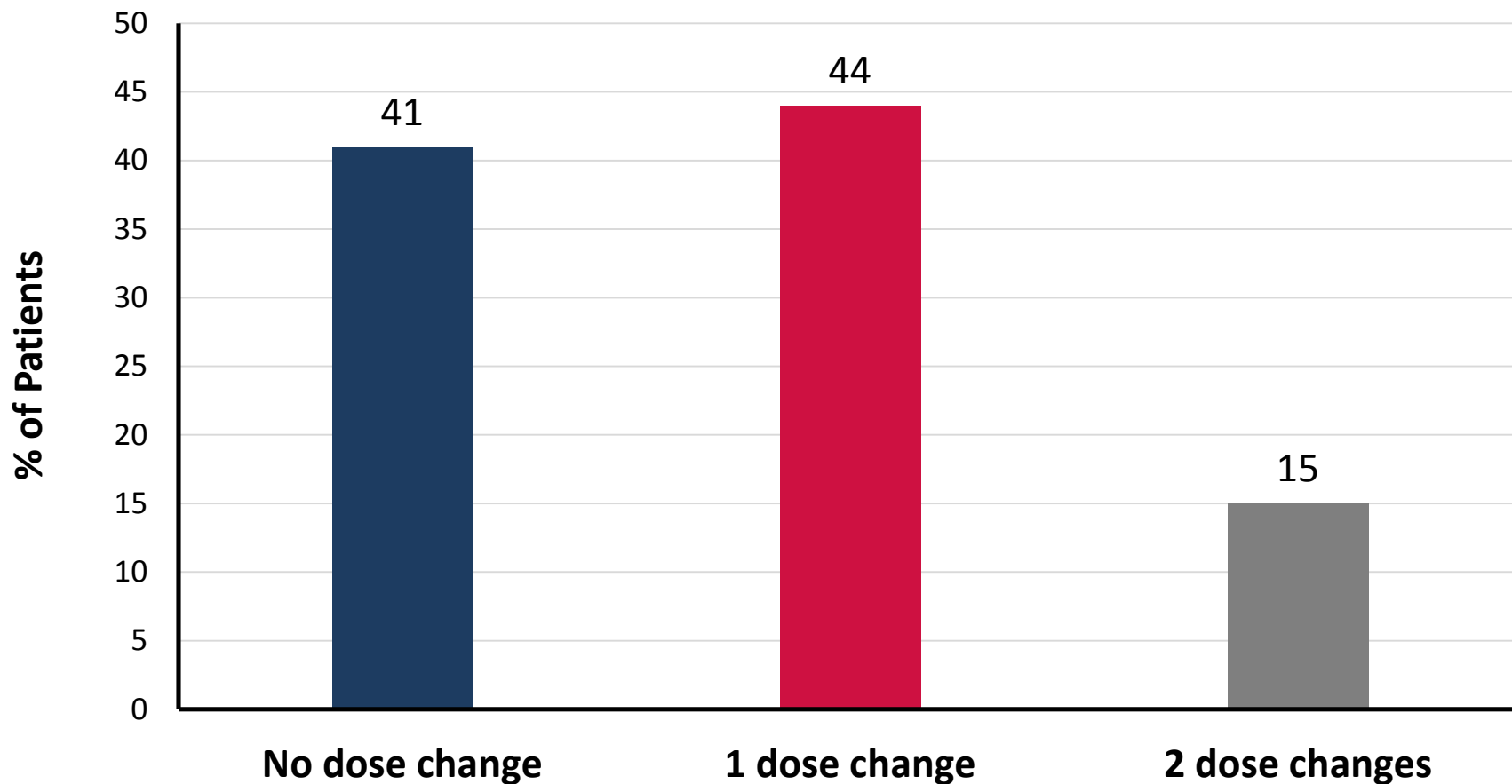
Pharmacokinetics of LPCN 1021

- In the Efficacy Population Set, mean T $C_{avg,24h}$ value was 447 ng/dL and overall variability was 37% (CV for $C_{avg,24h}$), consistent with other non-oral TRT therapies
- 82.9% of subjects had serum T C_{max} <1500 ng/dL, <5% had C_{max} 1800-2500 ng/dL, and only 2% (3 subjects) had serum T levels >2500 ng/dL (high serum T was sporadic, transient, and isolated, with no reported clinical adverse events)

	Efficacy Population Set (n=152)		Full Analysis Set (n=192)	
	$C_{avg,24h}$ ng/dL	C_{max} ng/dL	$C_{avg,24h}$ ng/dL	C_{max} ng/dL
Geometric mean	447	1128	479	1250
CV %	37	45	41	49

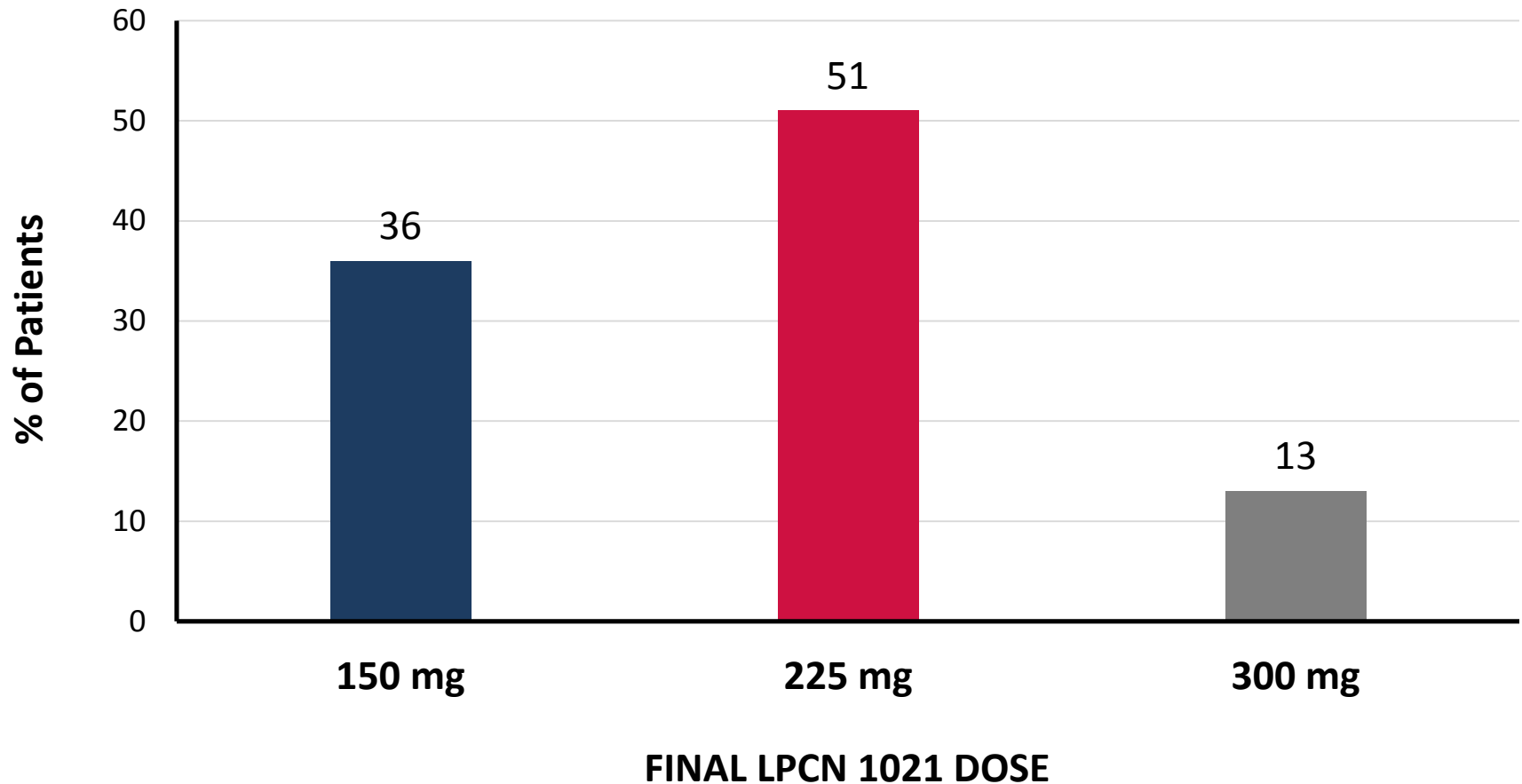
Dose Adjustments

■ 85% of patients required ≤ 1 dose adjustment



Final LPCN 1021 Dose Distribution

■ 51% of subjects had same final and starting doses



Serious Adverse Events (SAEs)

- As of January 31, 2015
 - No drug-related SAEs
 - No cardiac-related SAEs

Conclusions

- LPCN 1021 is an orally administered product for T replacement with acceptable C_{avg} levels, consistent with US FDA target guidelines
 - C_{max} levels were generally consistent with US FDA target guidelines
- LPCN 1021 may improve patient compliance as a generally safe, effective, and more convenient option compared to topical, transdermal, injectable, or implanted testosterone products