
Osilodrostat therapy improves physical features associated with hypercortisolism in patients with Cushing's disease: Findings from the Phase III LINC 3 study

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Disclosures

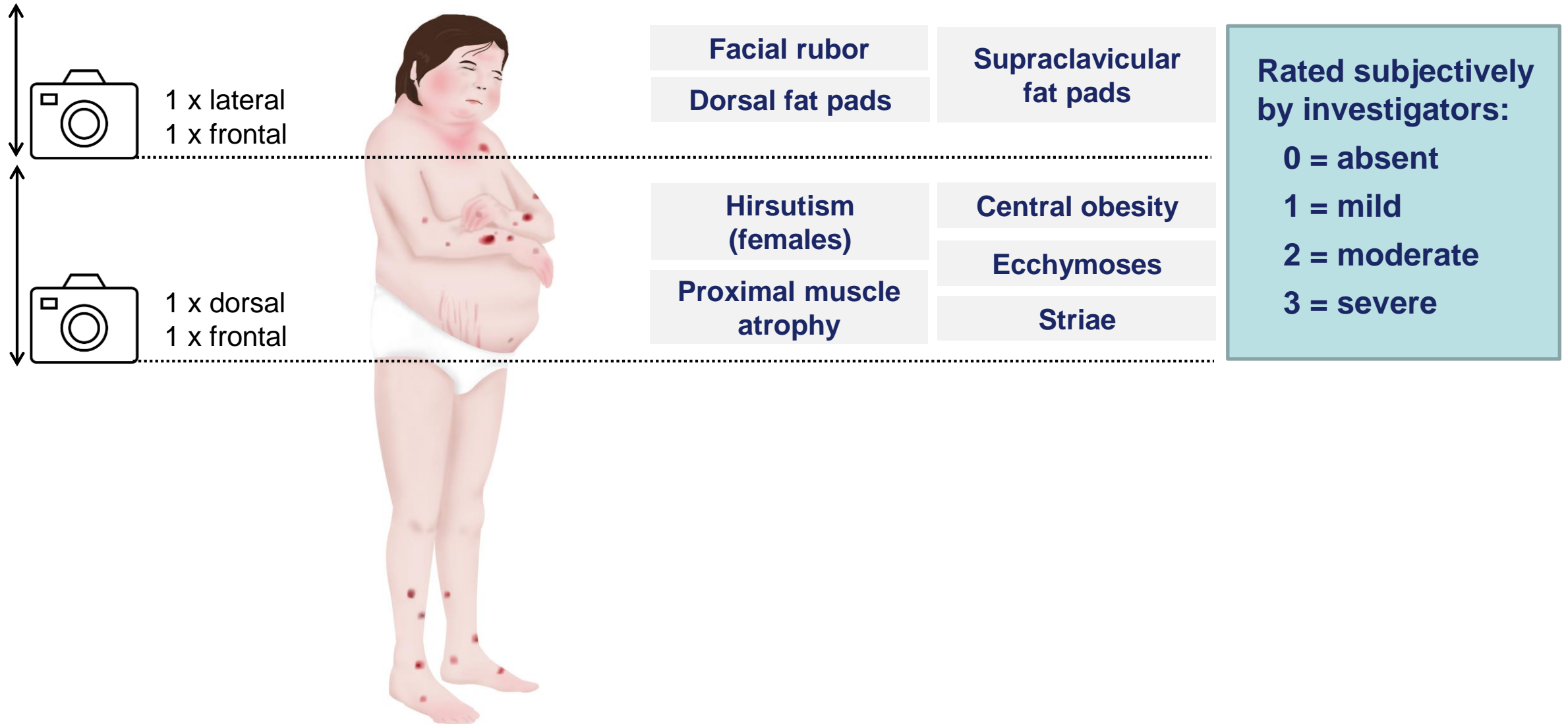
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Background

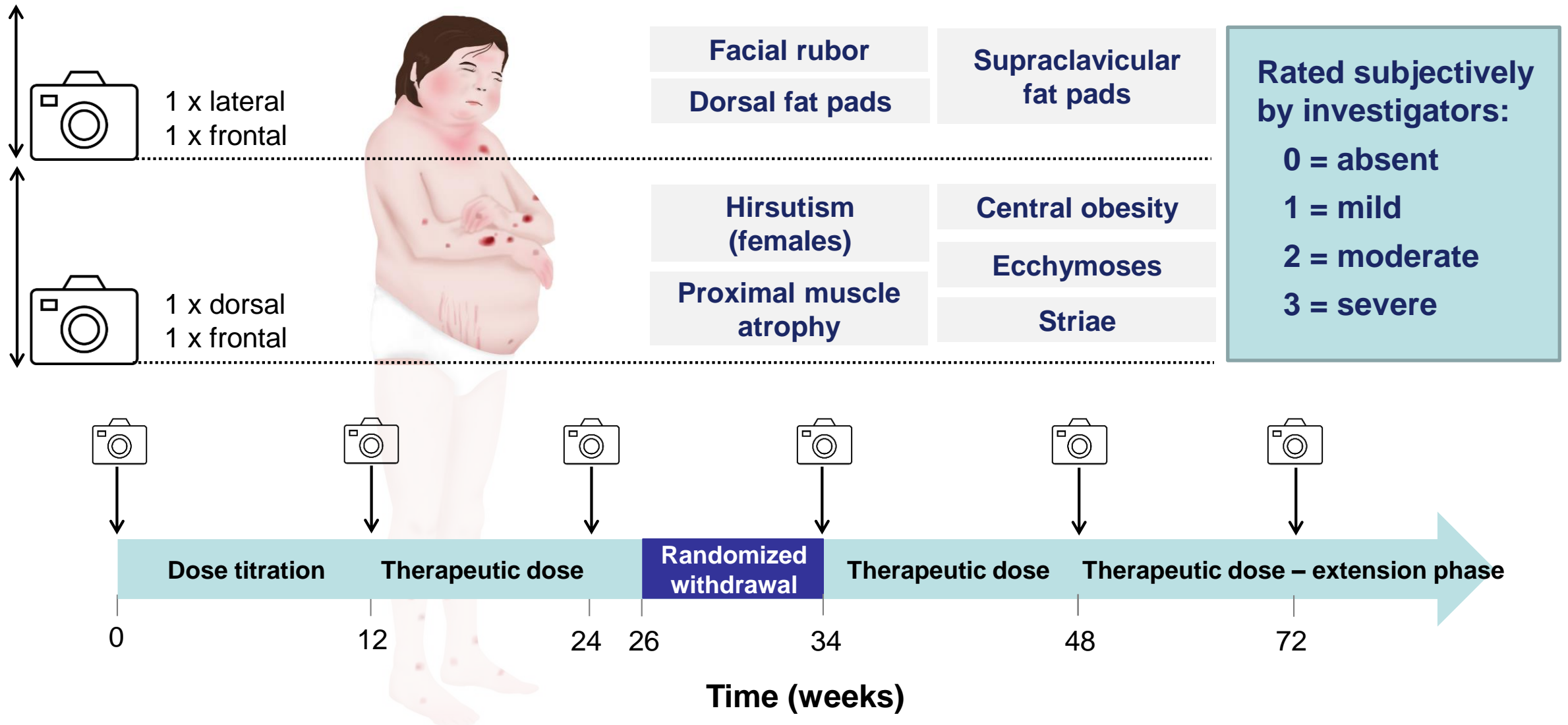
- Patients with Cushing's syndrome experience multiple physical features resulting from chronic hypercortisolism^{1,2}
 - Improving physical manifestations of hypercortisolism is an important treatment goal
- Osilodrostat, a potent oral inhibitor of 11 β -hydroxylase, is approved in the USA for treating patients with Cushing's disease when surgery is not an option or has not been curative³
 - Also approved in the EU, Switzerland and Japan for treating endogenous Cushing's syndrome⁴
- In the LINC 3 study, osilodrostat rapidly normalised and sustained control of mUFC in most patients with Cushing's disease over a median treatment period of 130 weeks⁵

Here, we describe improvements in physical features of Cushing's disease during long-term treatment with osilodrostat to control hypercortisolism

Assessment of physical manifestations of hypercortisolism during the Phase III LINC 3 study



Assessment of physical manifestations of hypercortisolism during the Phase III LINC 3 study



Patient demographics and baseline characteristics

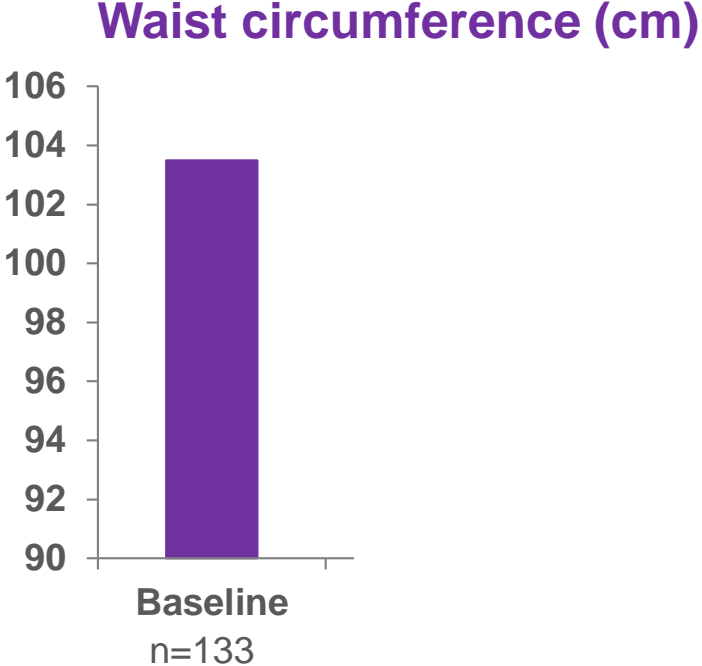
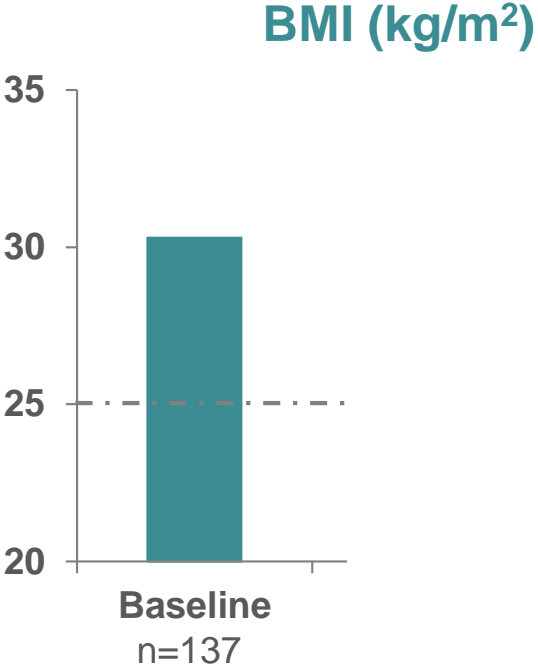
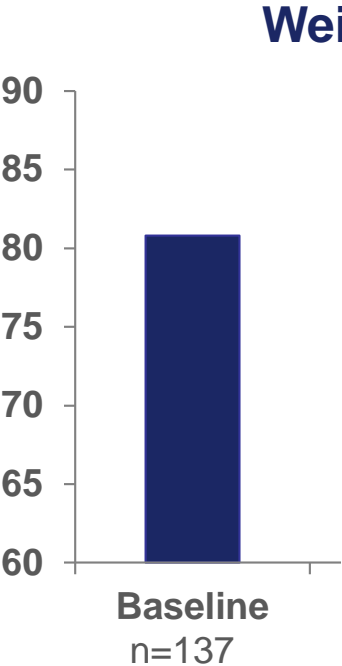
	LINC 3 (N=137)
Median age, years (min–max)	40.0 (19.0–70.0)
Female, %	77.4
Median time since diagnosis, months (IQR)	47.2 (19.0–88.3)
Previous pituitary surgery, %	87.6
Previous pituitary irradiation, %	16.1
mUFC, x ULN*	
Median (IQR)	3.5 (2.3–6.7)
Mean (SD)	7.3 (11.5)

ULN for mUFC = 50 µg/24h (138 nmol/24 h).

*Baseline mUFC calculated from two or three 24-hour urine samples

IQR, interquartile range; SD, standard deviation; ULN, upper limit of normal

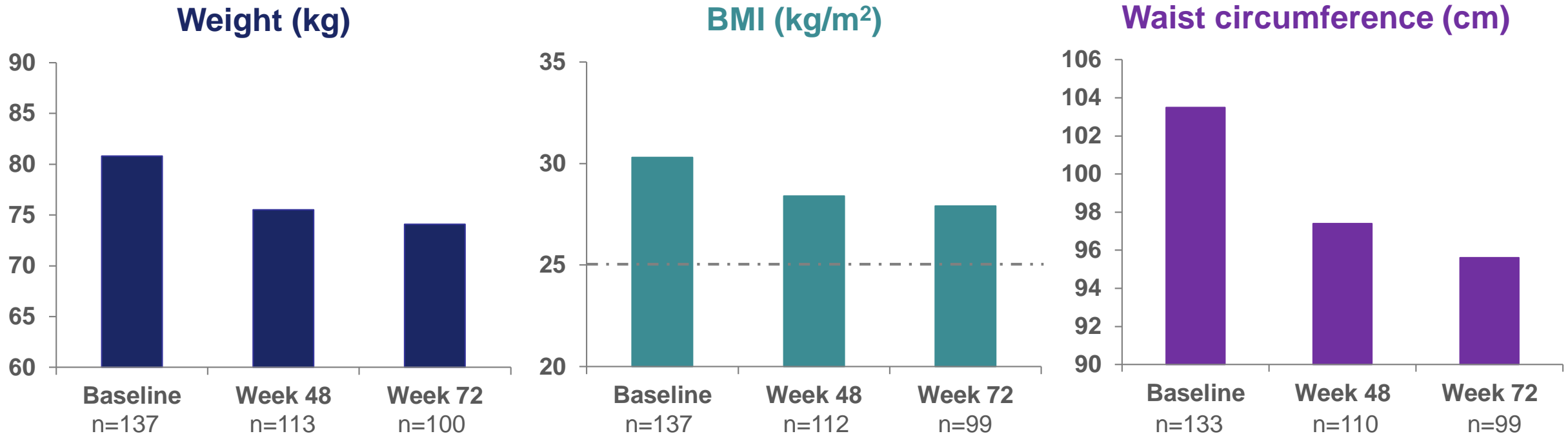
Mean body weight, BMI and waist circumference



Dotted line indicates upper limit of BMI for healthy adult weight (healthy weight 18.5–24.9, overweight 25.0–29.9, obese ≥30.0 kg/m²)

BMI, body mass index

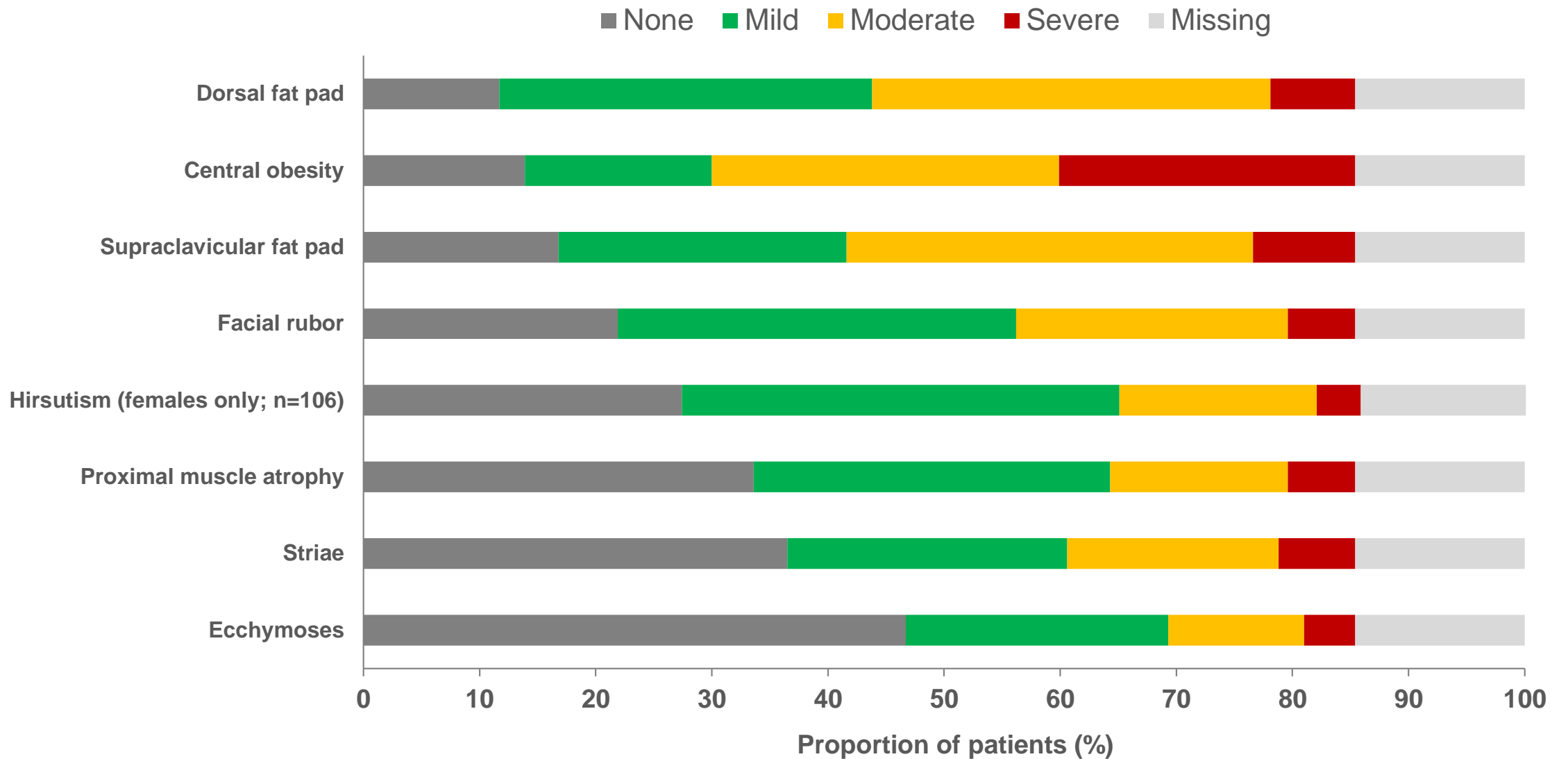
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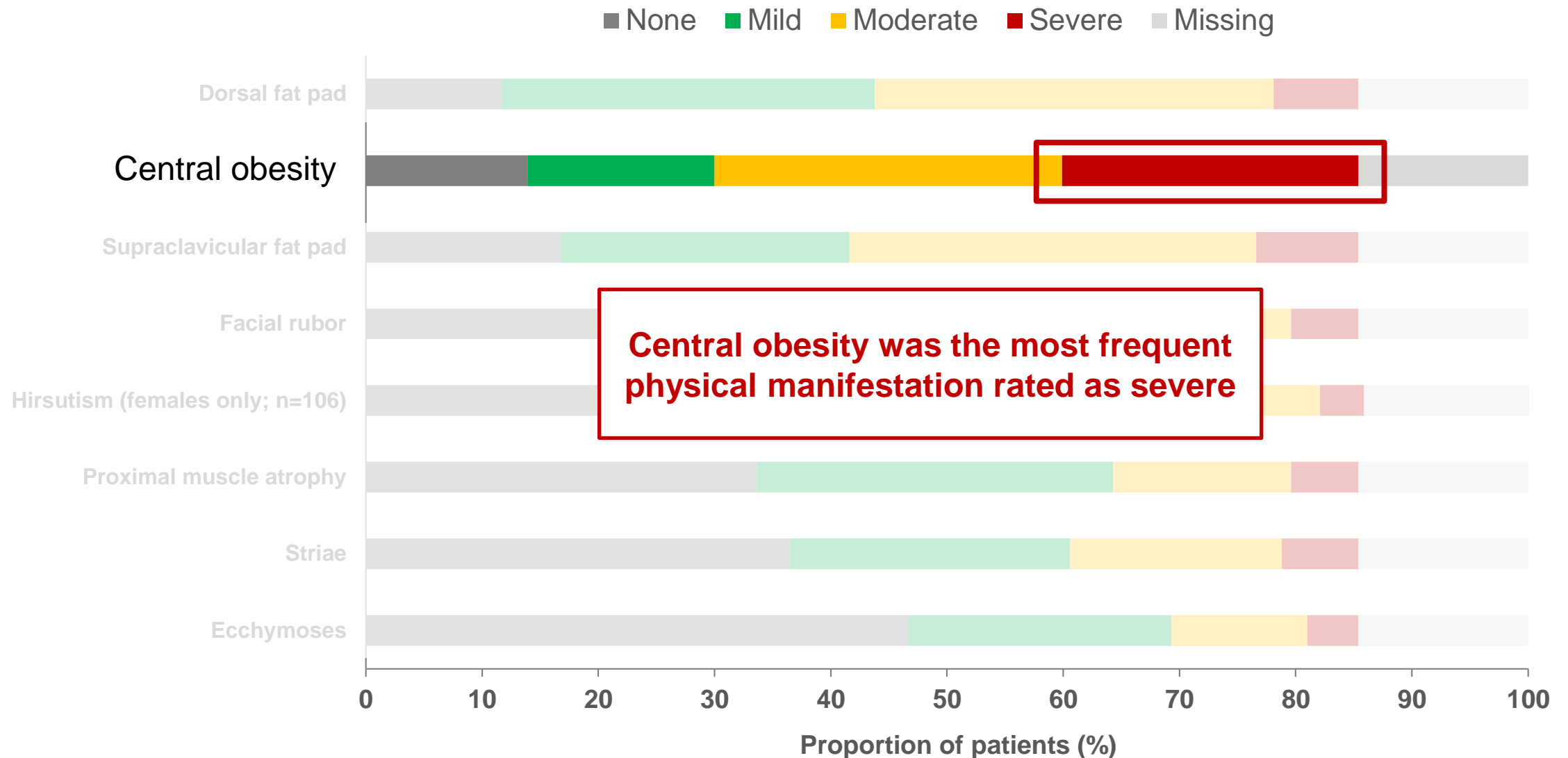
BMI, body mass index

Physical manifestations of hypercortisolism at baseline (N=137)



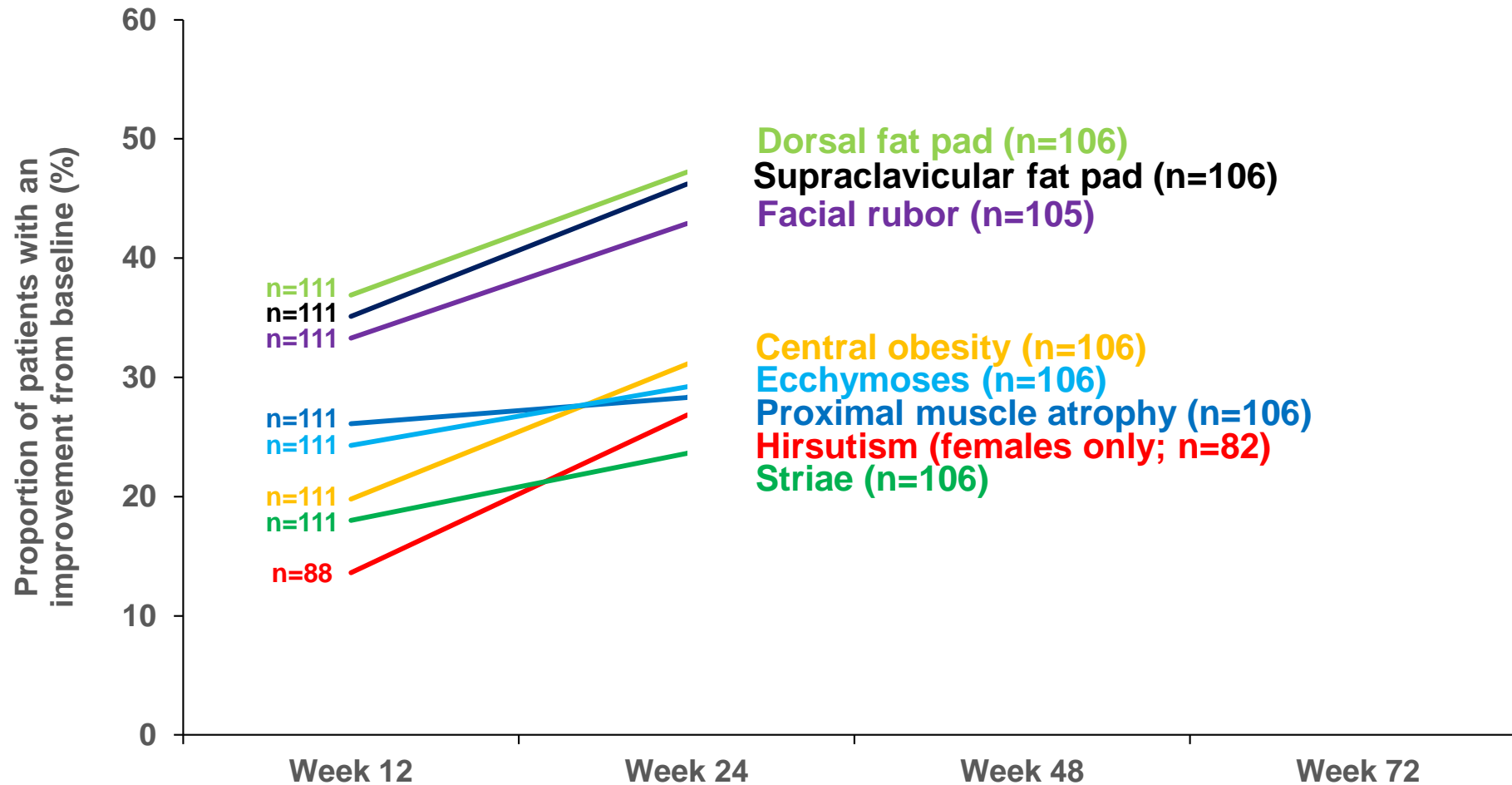
The denominator for the percentage is the number of patients in the full analysis set (n)

Physical manifestations of hypercortisolism at baseline (N=137)



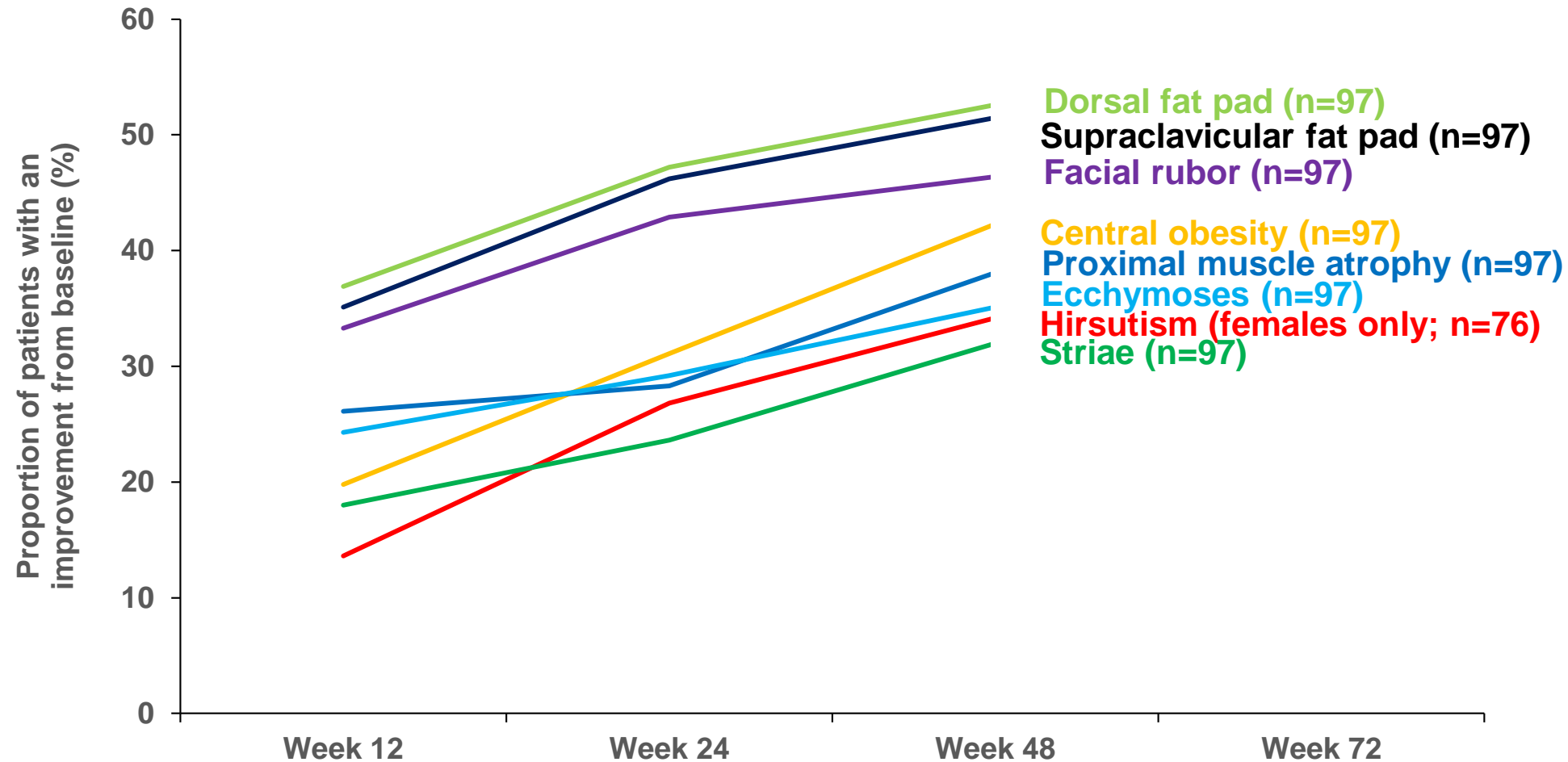
The denominator for the percentage is the number of patients in the full analysis set (n)

Improvements from baseline in physical manifestations of hypercortisolism over time



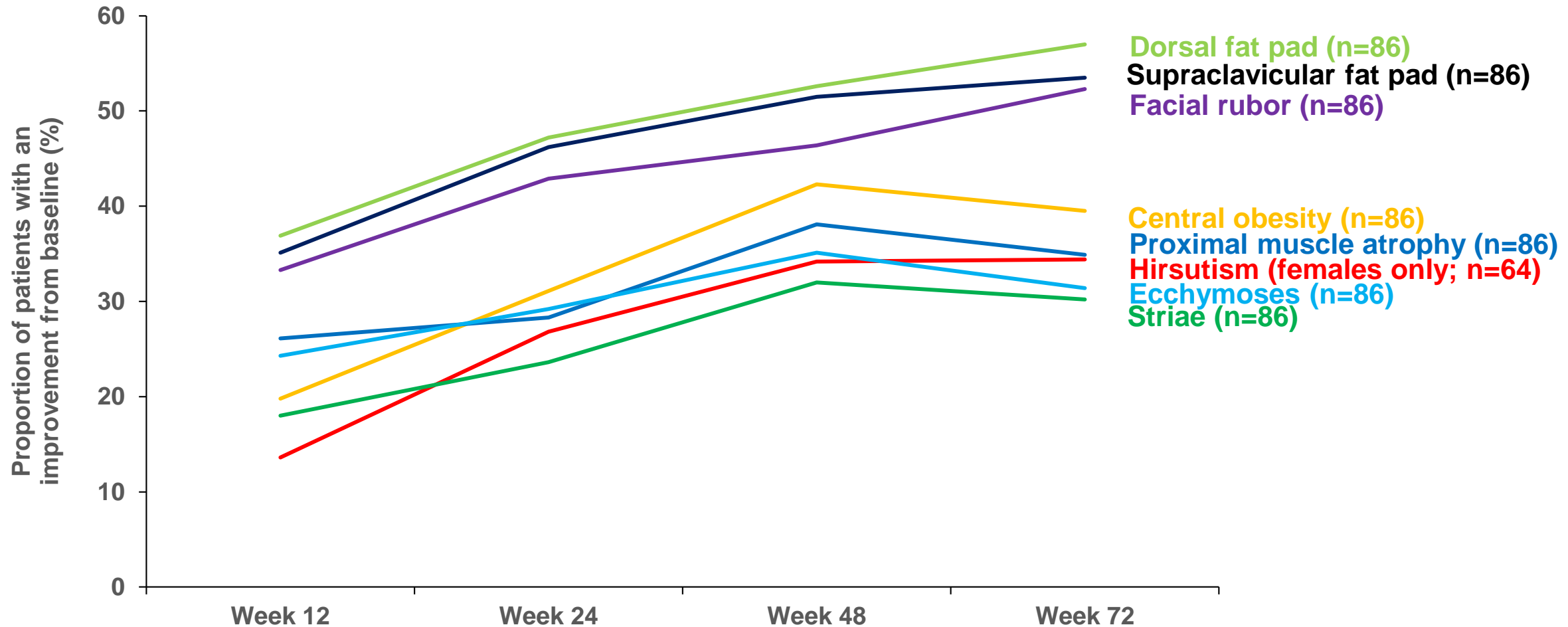
Improvement was defined as the symptom being less severe than at baseline. The denominator for the percentage is the number of patients in the full analysis set with data available at baseline and the given visit (n)

Improvements from baseline in physical manifestations of hypercortisolism over time



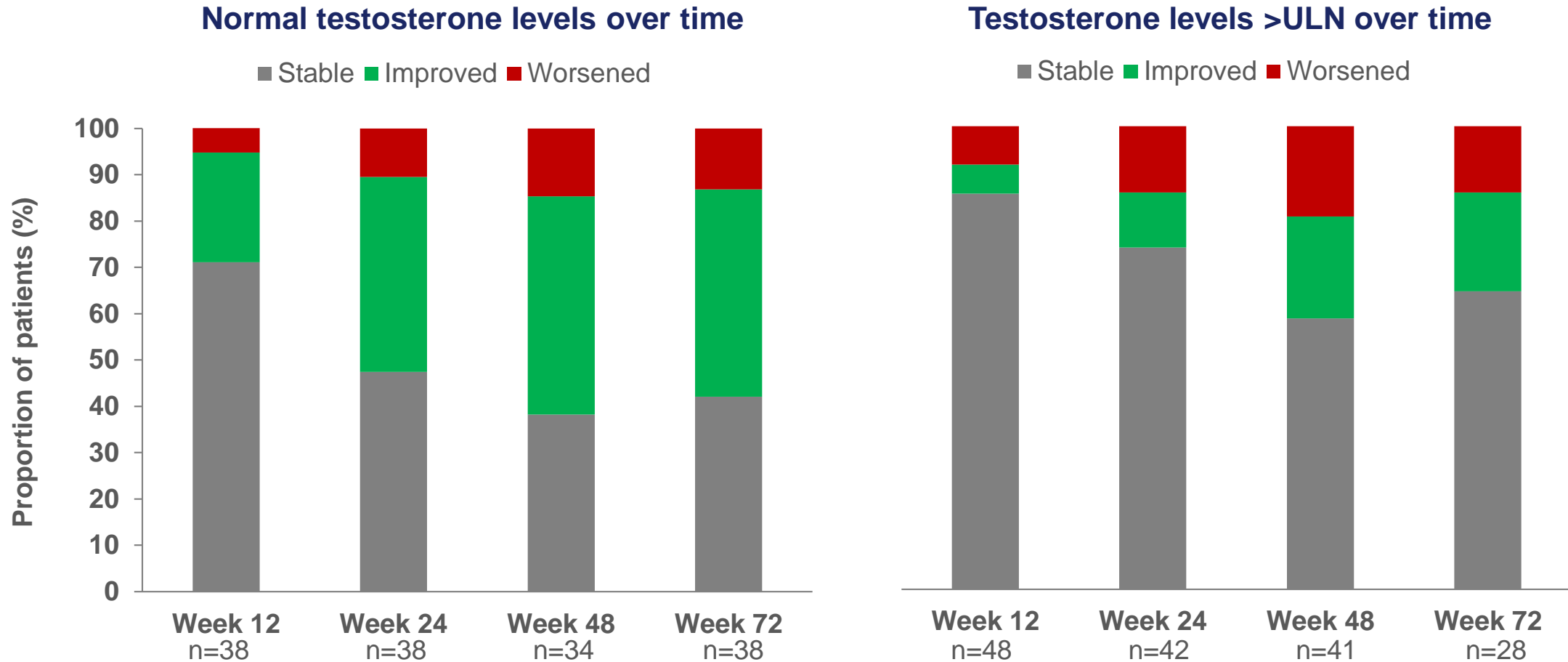
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Improvements from baseline in physical manifestations of hypercortisolism over time



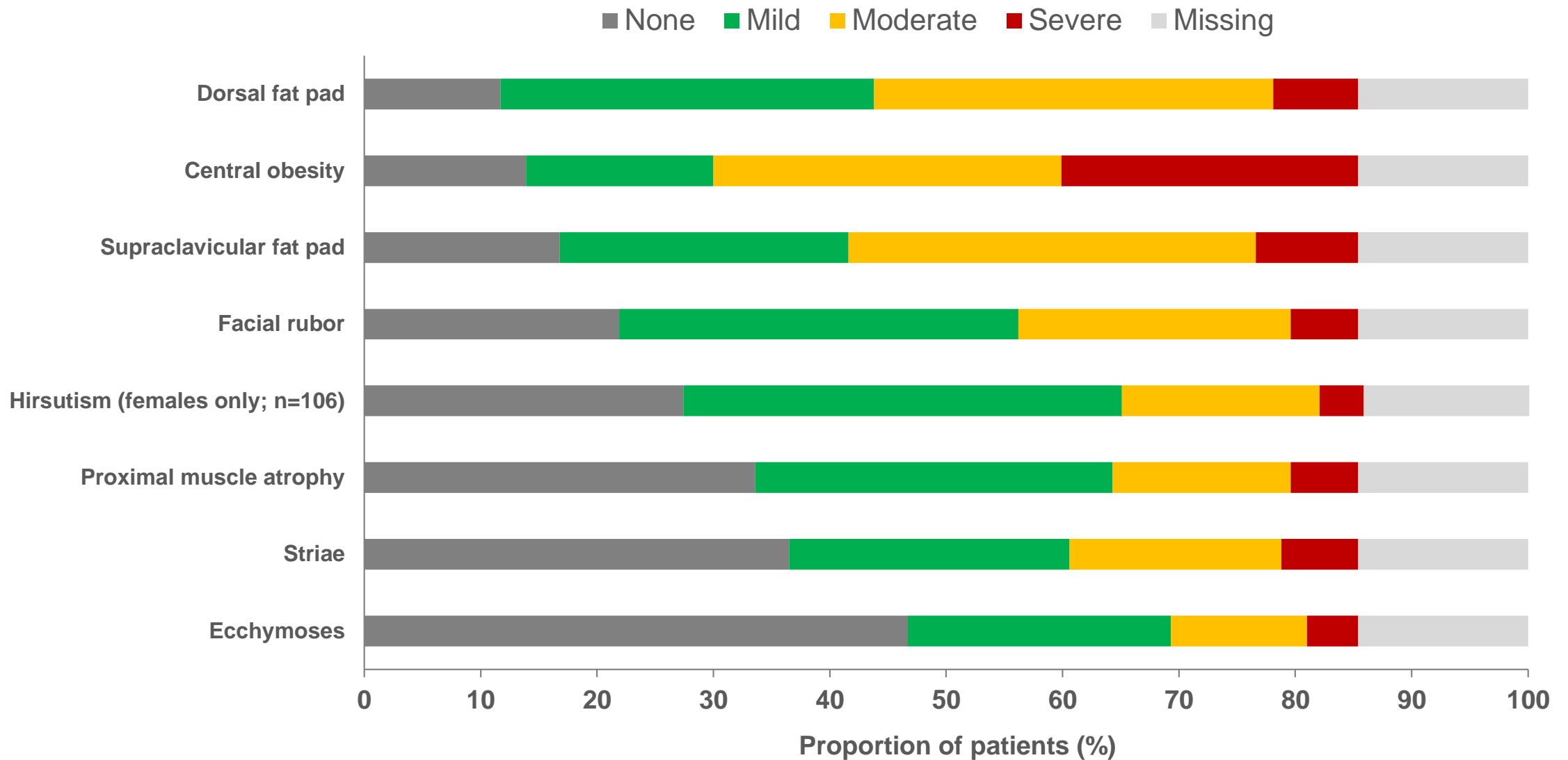
Improvement was defined as the symptom being less severe than at baseline. The denominator for the percentage is the number of patients in the full analysis set with data available at baseline and the given visit (n)

Improvements in hirsutism score in female patients by testosterone levels throughout the study



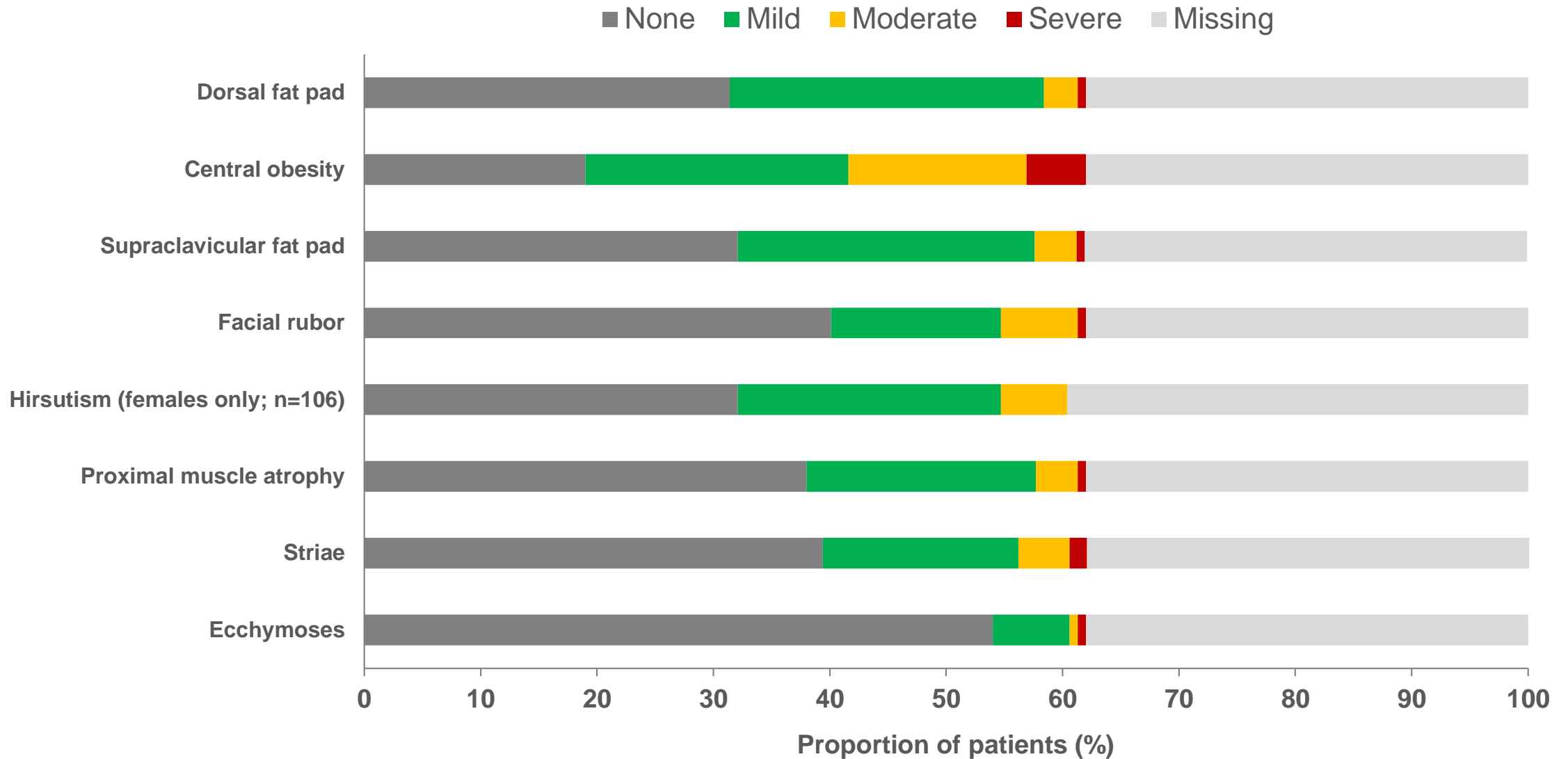
Hirsutism scores were stable or improved in most patients with either normal or above normal testosterone levels

Physical manifestations of hypercortisolism at baseline (N=137)



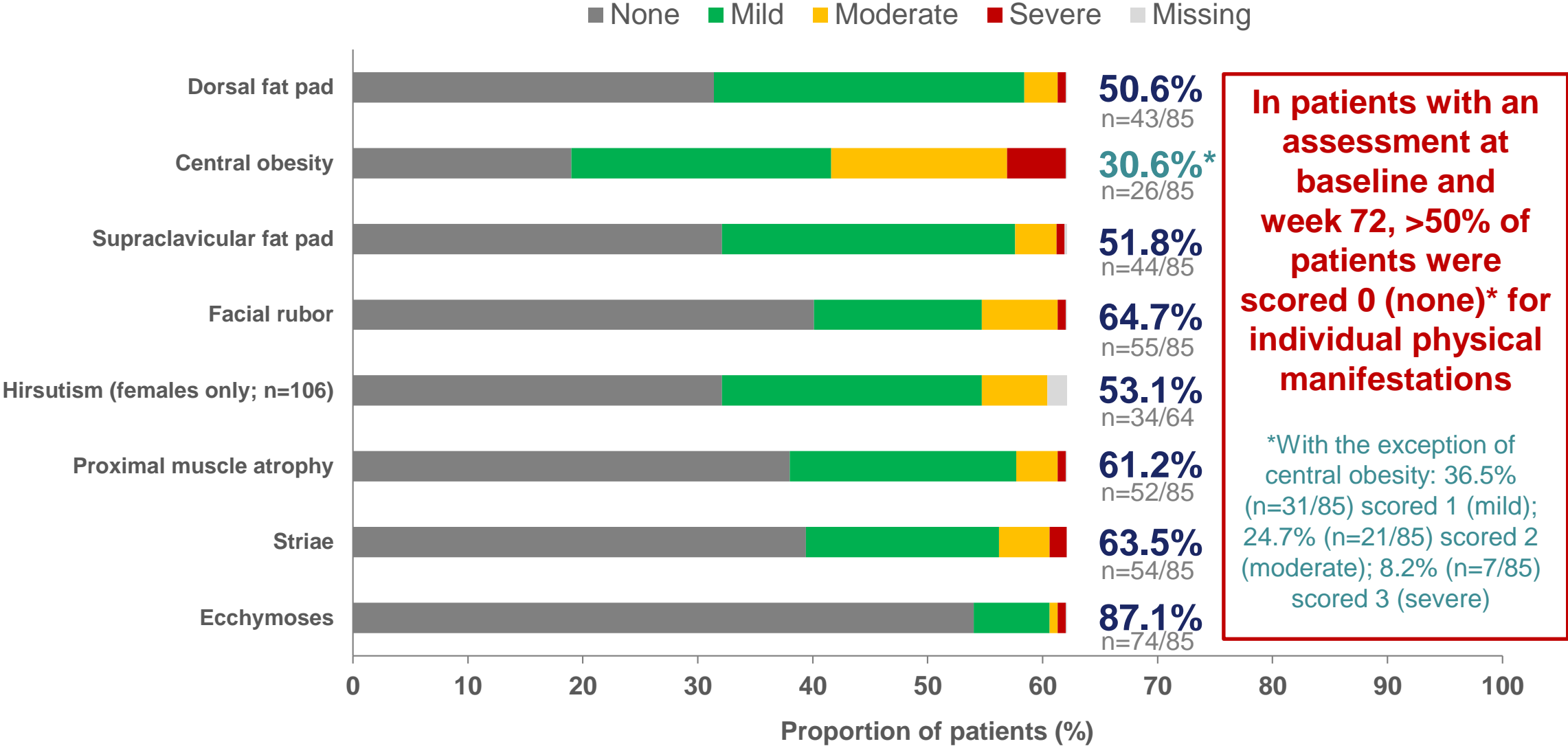
The denominator for the percentage is the number of patients in the full analysis set (n)

Physical manifestations of hypercortisolism at week 72



The denominator for the percentage is the number of patients in the full analysis set (n)

Physical manifestations of hypercortisolism at week 72



In patients with an assessment at baseline and week 72, >50% of patients were scored 0 (none)* for individual physical manifestations

*With the exception of central obesity: 36.5% (n=31/85) scored 1 (mild); 24.7% (n=21/85) scored 2 (moderate); 8.2% (n=7/85) scored 3 (severe)

The denominator for the percentage is the number of patients in the full analysis set with data available at baseline and the given visit (n)

Conclusions

- Most patients in LINC 3 were experiencing physical manifestations of hypercortisolism at baseline, most commonly related to accumulation of fat and central obesity
- During treatment with osilodrostat in the LINC 3 study:
 - There was an overall trend for reductions in mean body weight, BMI and waist circumference
 - The proportion of patients with an improvement from baseline in assessed physical manifestations increased from week 12 and was maintained until the end of the extension
 - Few physical manifestations were rated as worsening over time, including hirsutism in female patients
 - Most physical manifestations assessed were rated as absent by week 72 in ~50% of patients

Improvements in physical manifestations associated with hypercortisolism were observed soon after initiation of osilodrostat and were sustained throughout the study