# ACTHAR gel for Idiopathic Membranous Nephropathy

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# Methods:
# Study Population 1

- Adults > 18 years
- Biopsy proven idiopathic membranous nephropathy, less than 36 months prior
- < 30% glomerulosclerosis or IFTA
- At least 3 months of RAS blockade, BP < 130/75
- UProt:UCr ratio of $\geq$ 4; GFR $\geq$ 40

# Methods
# study population 2

Exclusions

- Active infections,
- Secondary membranous (hepatitis, SLE, malignancy)
- Type 1 or 2 diabetes
- H/0 acute thrombosis
- Pregnancy or nursing

# Methods
# study population 3

- Treatment Naive OR
- Documented resistance to immunosuppression routines used in iMN (calcineurin inhibitors + steroids or cytotoxic agent + steroid)
- But eligible if
  - H/o partial response to above regimens OR
  - Significant side effects to above regimens

# Design

- Phase 1b/2 dose finding
- Non blinded
- Randomized to two different doses of ACTHAR gel, 40 units or 80 units (I.e. No placebo - both groups with active drug)
- Drug given at day 0, 14 then every week till day 28 then twice a week till day 91 (week 12)

# Co-interventions

- For BP control: at discretion of treating nephrologist;
  - Patients already on single or dual RAS Blockade
    - CCB: only nonDHP agents allowed
- 10 mg atorvastatin if severe hyperlipidemia and dose titration up per KDIGO GL
- Salt restriction (2-3 g/day) and dietary protein target of 0.8 g/kg/day - counselling

# Results: baseline

- n of 20
- Age 51 +/- 15 years; 63% men (?13 of 20)
- 19 were on RAAS blockade prior, one did not tolerate (hypotension)
- Median disease latency 14 months
- 13 patients treatment naive

# Table 1: baseline

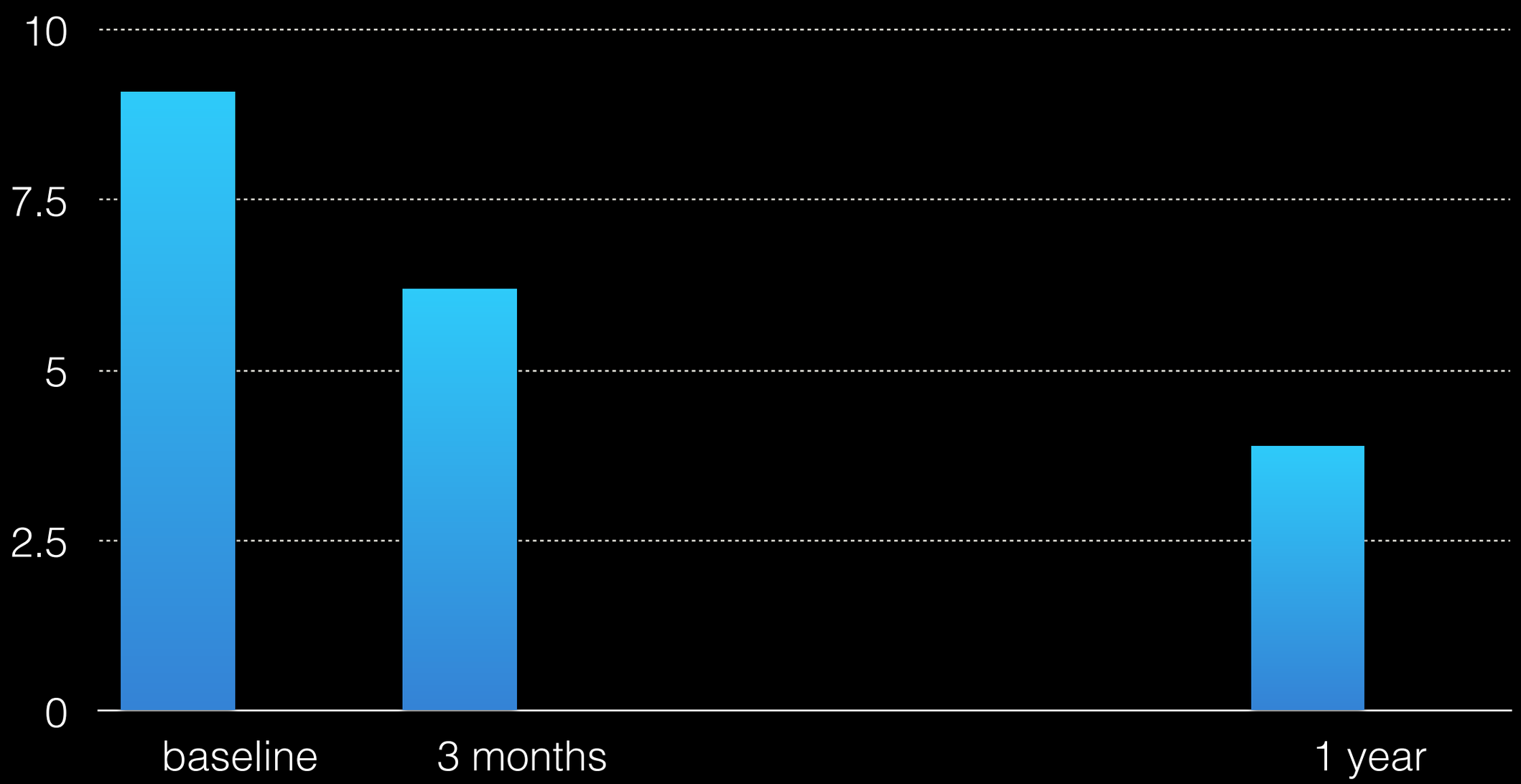
**Table 1.**

Baseline and follow-up variables in

| | Baseline |
|---|---|
| Systolic BP (mmHg) | 121 ± 16 |
| Diastolic BP (mmHg) | 72 ± 8 |
| Proteinuria (g/day) | 9068 ± 3384 |
| eGFR (mL/min) | 77 ± 30 |
| Albumin (mg/dL) | 2.72 ± 0.83 |
| Cholesterol (mg/dL) | 306 ± 133 |
| LDL (mg/dL) | 182 ± 85 |
| HDL (mg/dL) | 67 ± 29 |
| Trigycerides (mg/dL) | 225 ± 190 |

BP, blood pressure; NS is not sign

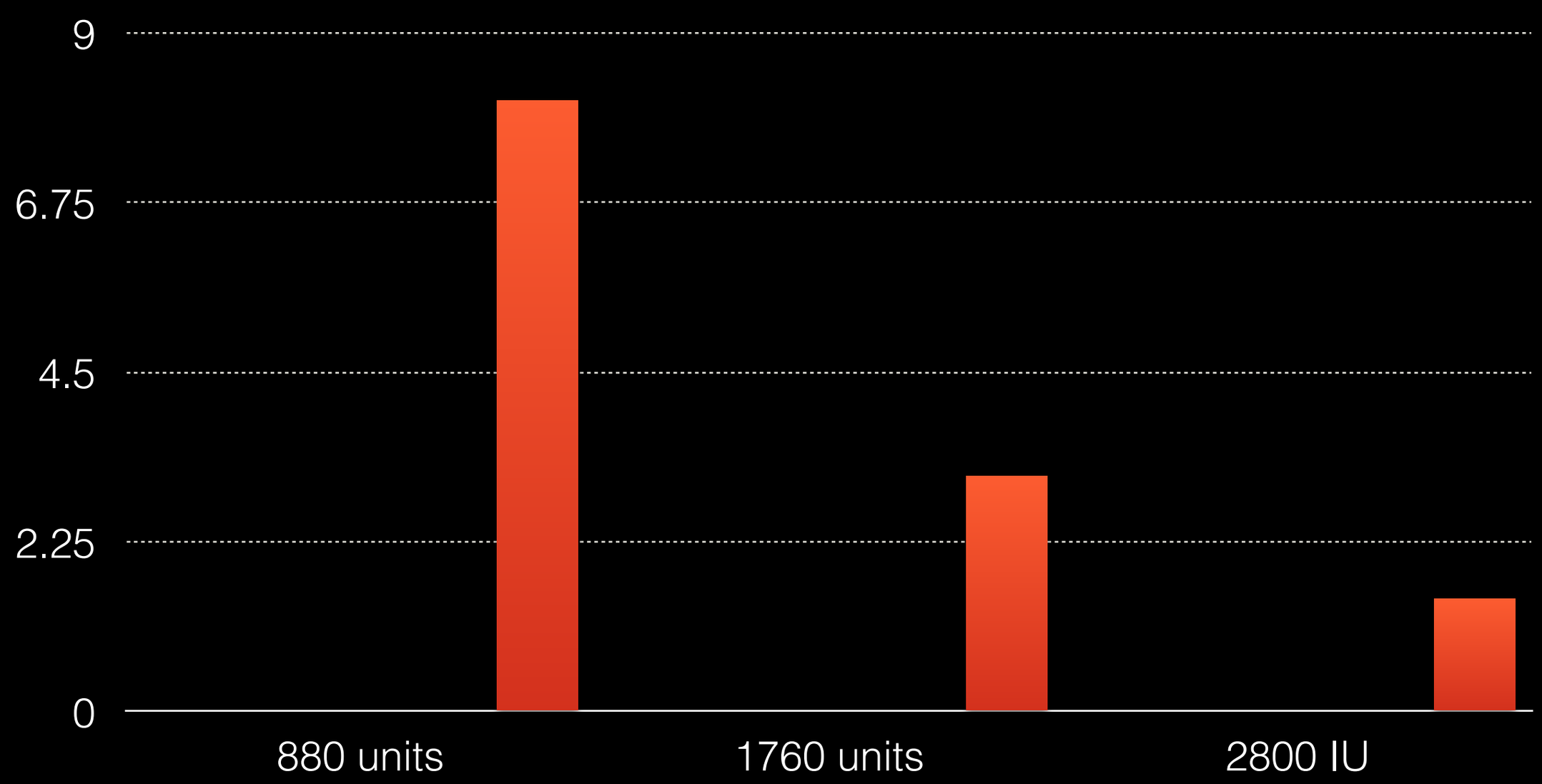
# Results: overall proteinuria



# Actual therapy

- 11 received 80 units per dose (total 1760 units)
- 9 were started on 40 units
  - None responded by 12 weeks
  - 5/9 were given *additional* 12 weeks of 80 units twice a week (2800 units total)

# Results: final proteinuria by dose received



# Adverse effects of ACTHAR

- None required discontinuation for side effects
- 3 had Cushingoid appearance
- Acne, bloating,bronzing in 2-3 patients each
- Psychological effects in six patients
- Transient insomnia in six patients
- Blood sugar increase (to > than 130) in six, transient in 5, one required dietary intervention for sustained hyperglycemia

# Anti-PLA2R assay

- Western blot using human glomerular extract and recombinant PLa2R
- Baseline assay standardized to compare subsequent intra-patient comparisons

# PLA2R results

- 15/20 had detectable levels
- 3 patients cleared completely
- 4 patients had reduction in levels.
- Strong correlation between levels of antiPLa2 and proteinuria