

# RITUXIMAB PHARMACOKINETICS CHARACTERIZATION IN PLASMA AND URINE IN A PATIENT WITH NEPHROTIC SYNDROME (4CPS-062)

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## BACKGROUND AND IMPORTANCE

- **Rituximab** is a monoclonal antibody used to treat various conditions including glomerular diseases (GD) as an off-label indication.
- There is high variability in rituximab pharmacokinetics (PK) and it has scarcely being studied in case of nephrotic syndrome (NS).
- We report the PK analysis of rituximab in a case of GD and measure rituximab excretion in urine.



- **72 years old male** with hypertension, dislipemia, obesity (81kg).
- September 2020: a renal biopsy confirmed a diagnosis of **membranous nephropathy** with positive anti-PLA2R.
- Usual medication included magnesium, amlodipine and ezetimibe.

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- **Severe NS** (proteinuria:16g/24h, hypoalbuminemia:2.1g/ml, hypercholesterolemia:406mg/dl, creatinine 0.75mg/dl)
- According to recommendations, rituximab was prescribed and administered endovenously: 1g days 1 and 14.

- **Routine blood and 24h urine samples** were collected.
- Rituximab was measured in serum with **ELISA** kit: Lisa-Tracker®-Rituximab (Theradiag®).
- The quantitative determination of rituximab in urine was performed using in-house standards and urine samples diluted to 1/100 in Phosphate-Tween Buffer.
- Rituximab PK analysis was done using a monocompartmental model and non-linear regression (Winnolin®).
- By day 7 there were 93.2mg of rituximab in the body and 17.8mg were eliminated that day.
  - Considering a 1500ml/24h urine production:
    - > 3.18mg of rituximab were excreted at day 7
    - > 3.4% of rituximab in plasma was excreted by urine every 24h
    - > **urine excretion justified 17.9% of rituximab elimination.**



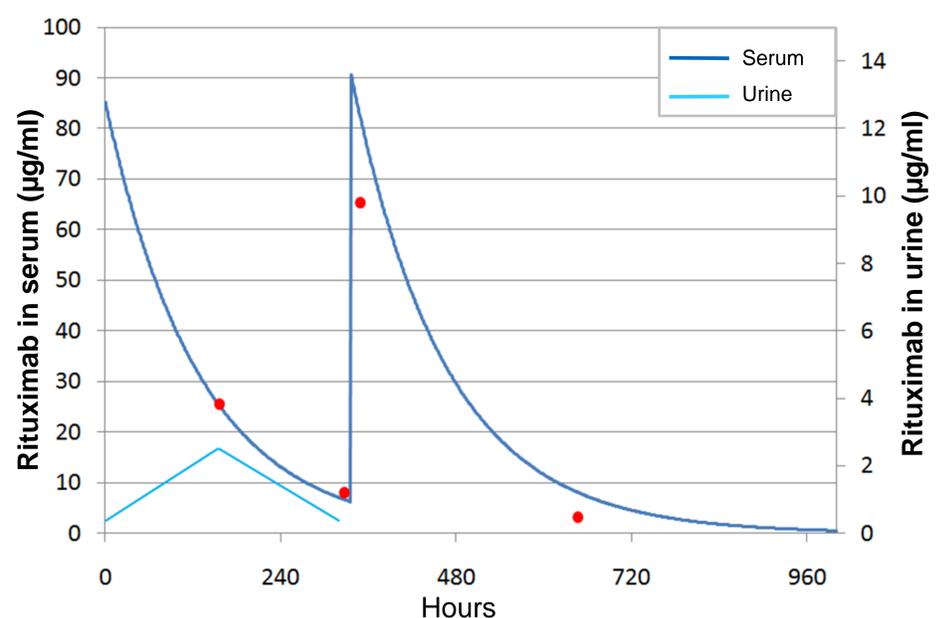
## PHARMACOKINETIC PARAMETERS

**Maximum concentration (C<sub>max</sub>)** = 92.0 µg/mL

**Volume of distribution (V<sub>d</sub>)** = 135.1 mL/kg

**Clearance (Cl)** = 1.075 mL/kg/h

**Half-life (t<sub>1/2</sub>)** = 88.91 h = 3.7 days



Day	Rituximab concentration (µg/mL)	
	Serum	Urine
0	0	0.1835
7	26.376	21.175
14 (pre-dose)	7.929	0.1794
14 (post-dose)	64.986	-
28	3.72	-

Ten months after rituximab administration the patient remains in **complete remission** (proteinuria:0.5g/24h, serum albumin:3.8g/ml, serum cholesterol:237mg/dl, creatinine 0.75mg/dl).

## CONCLUSIONS AND RELEVANCE

- Patient's rituximab V<sub>d</sub> was increased maybe due to NS-related edema; C<sub>max</sub> was lower, Cl was increased and t<sub>1/2</sub> was notably shorter than reported values, which can be justified by RTX elimination in urine.
- Rituximab PK's are altered in case of NS, leading to a reduced exposure.
- Rituximab may be aberrantly eliminated in urine in case of NS and its concentration can be measured with ELISA.