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.

PHARMACOKINETIC PARAMETERS

Maximum concentration (Cmax) = 92.0 µg/mL
Volume of distribution (Vd) = 135.1 mL/kg
Clearance (Cl) = 1.075 mL/kg/h
Half-life (t1/2) = 88.91 h = 3.7 days

• 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.

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 Vd was increased maybe due to NS-related edema; Cmax was lower, Cl was increased and t1/2 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.