

Kompetenzzentrum Galaktosämie

Aktuelle Forschungsergebnisse zur Galaktosetoleranz

Peter Schadewaldt

- **Grundlagen der Galaktosämie**
- **Galaktosetoleranz bei Galaktosämie**

Die Duarte D2-Varianten

Studie: Galaktosebelastung

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Der Leloir-Stoffwechselweg

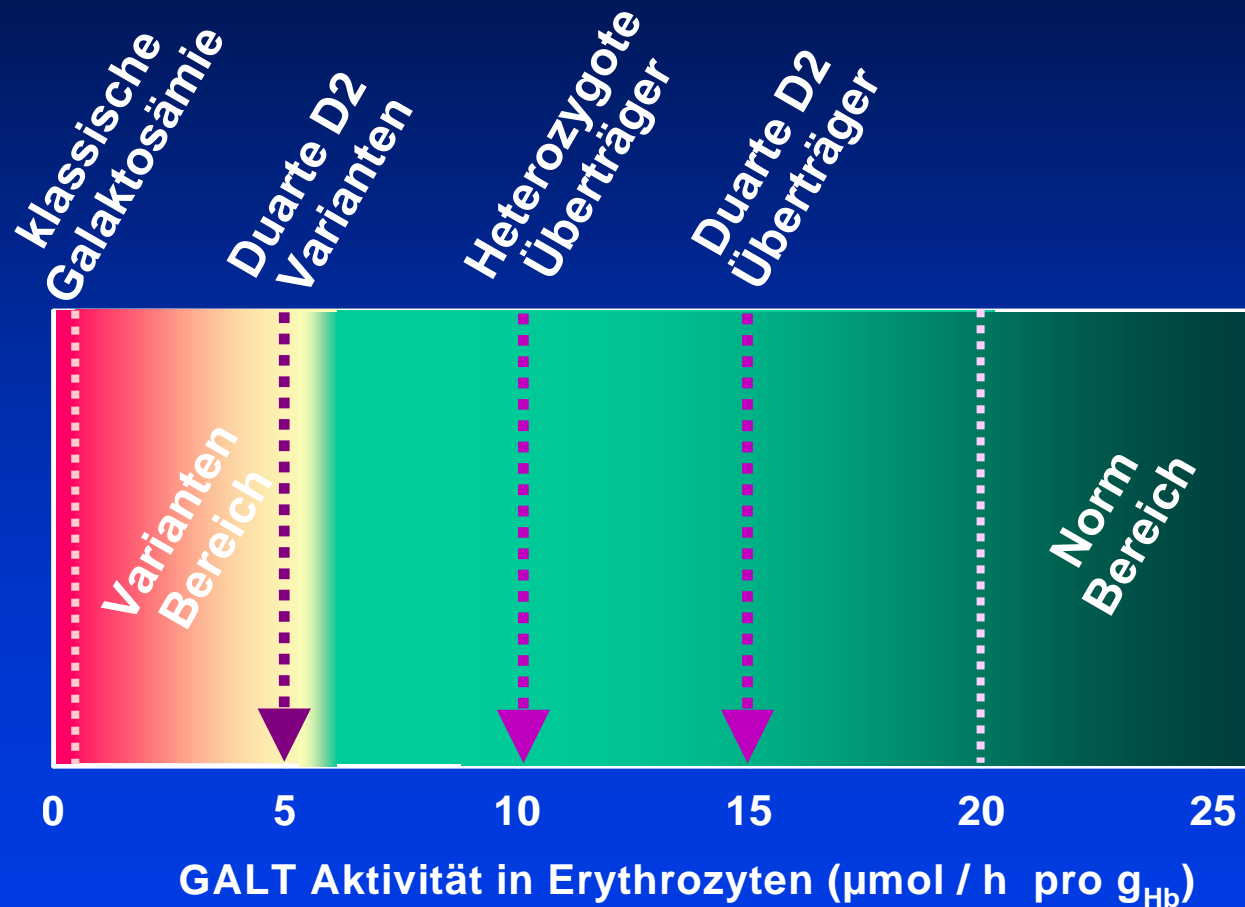


Ursachen der klass. Galaktosämie



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Verschiedene Formen des ‚GALT-Mangels‘



Charakteristische Stoffwechselfparameter (Erwachsene)

- **klassische Galaktosämie** (Diätbehandlung)

GALT $< 0.4 \mu\text{mol/h/g}_{\text{Hb}}$, Gal-1-P $> 2 \text{ mg/dL}_{\text{Ery}}$,
Galaktitol $> 100 \mu\text{mol/mmol}_{\text{Crea}}$

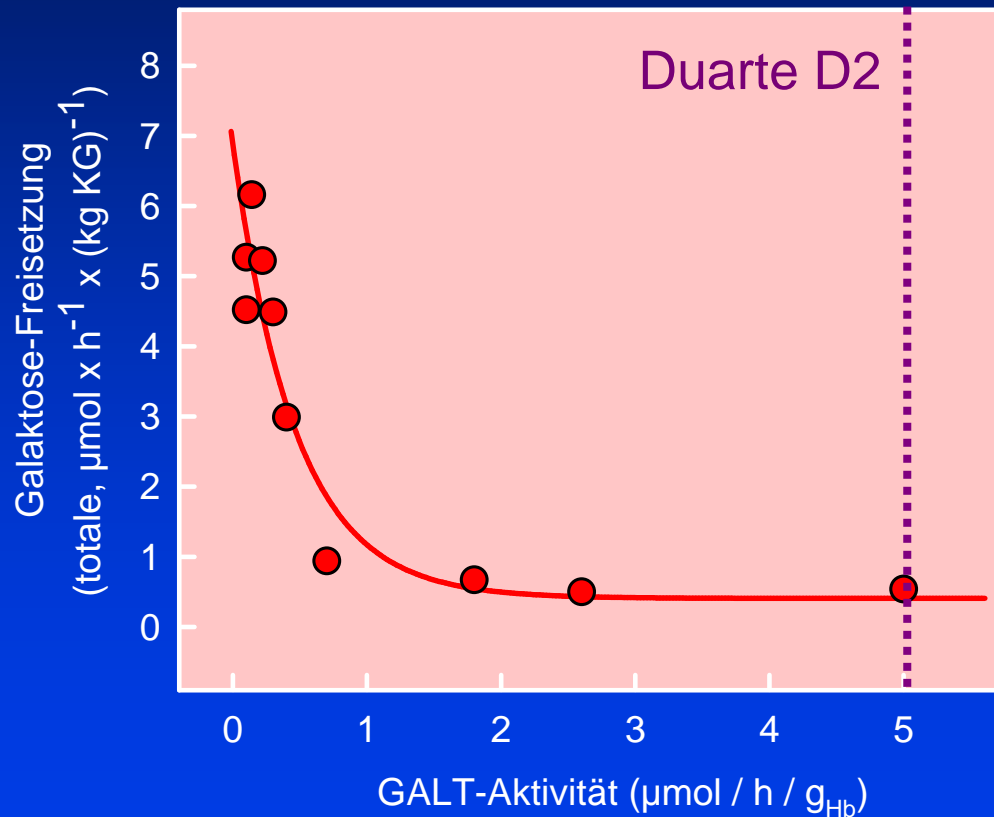
- **Variante** (\pm Laktoserestriktion)

GALT > 0.4 bis $> 4.0 \mu\text{mol/h/g}_{\text{Hb}}$, Gal-1-P $< 2 \text{ mg/dL}_{\text{Ery}}$,
Galaktitol $< 100 \mu\text{mol/mmol}_{\text{Crea}}$

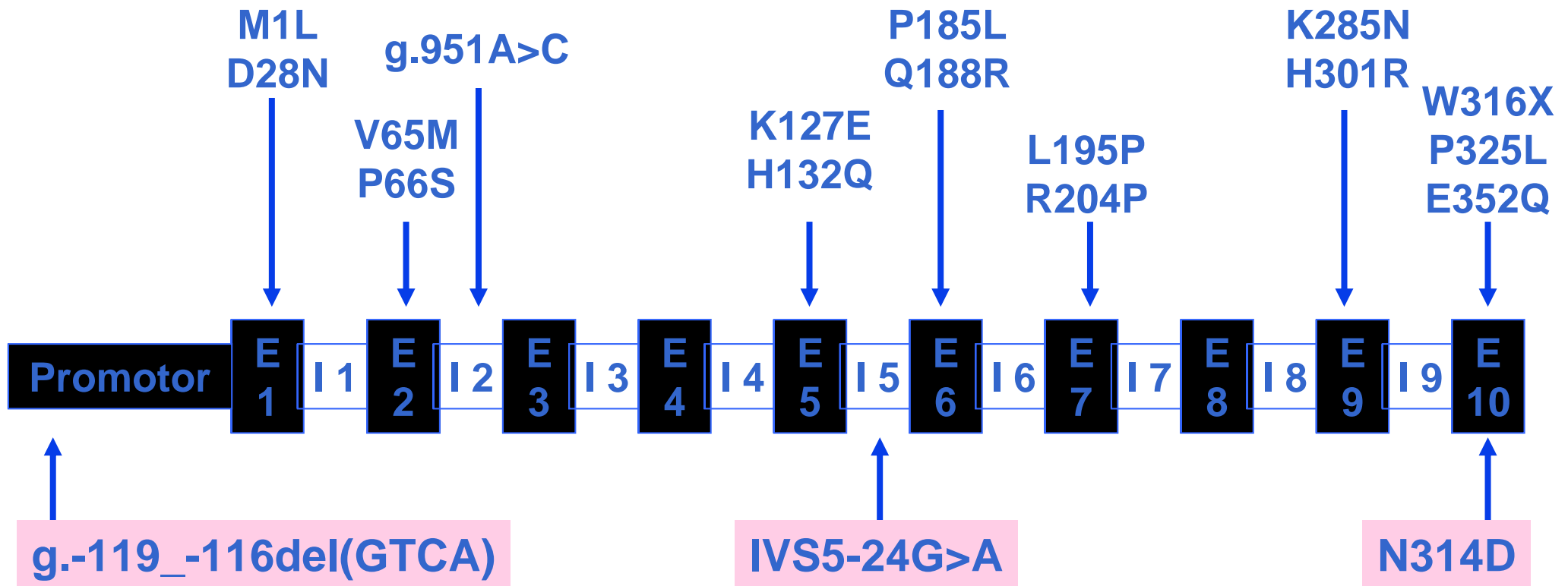
- **Duarte D2** (keine Einschränkung)

GALT $4-6 \mu\text{mol/h/g}_{\text{Hb}}$, Gal-1-P $< 0.3 \text{ mg/dL}_{\text{Ery}}$,
Galaktitol $> 10 \mu\text{mol/mmol}_{\text{Crea}}$

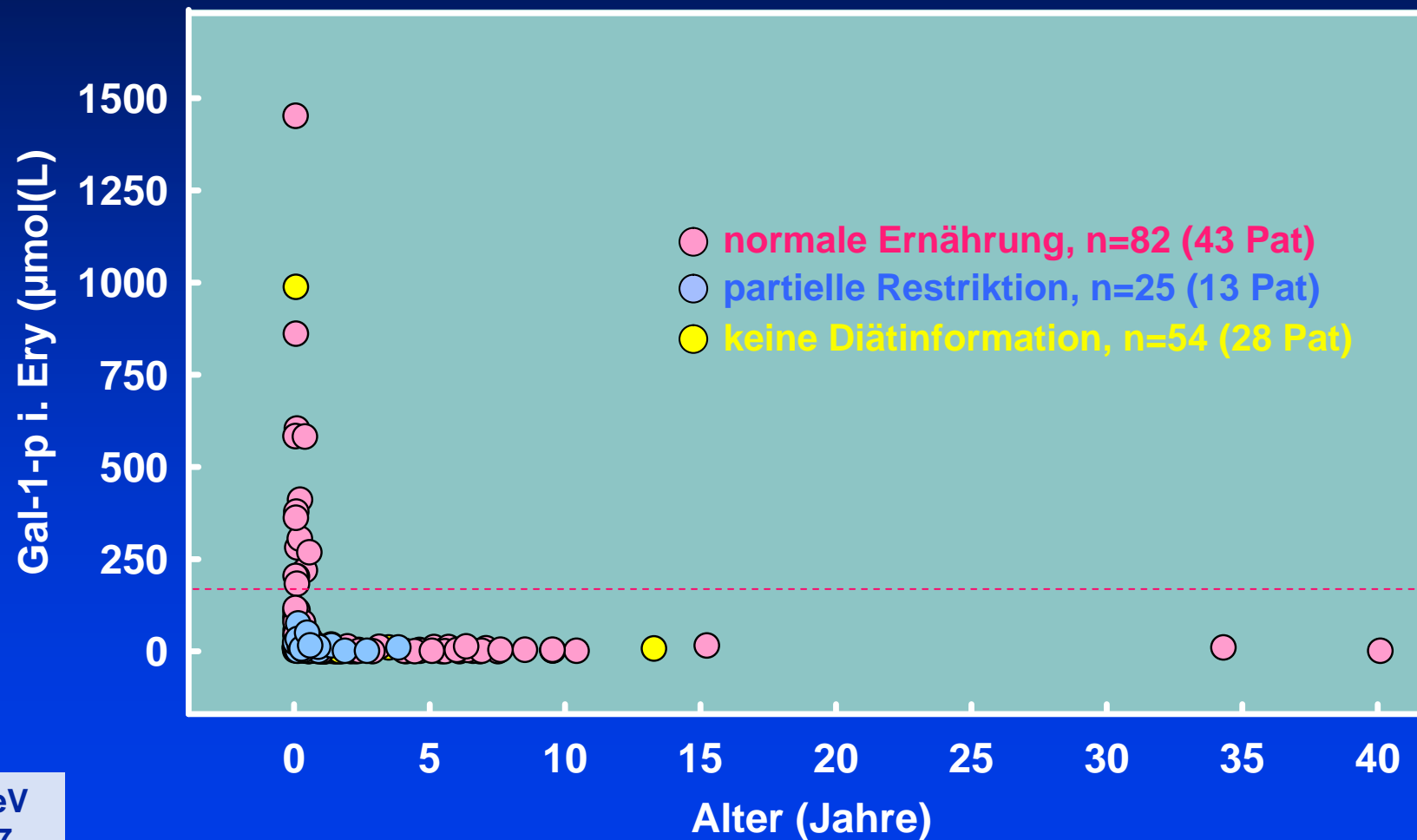
Endogene Galaktosefreisetzung *in vivo* versus residuale GALT-Aktivität *in vitro*



Duarte D2-Genotyp



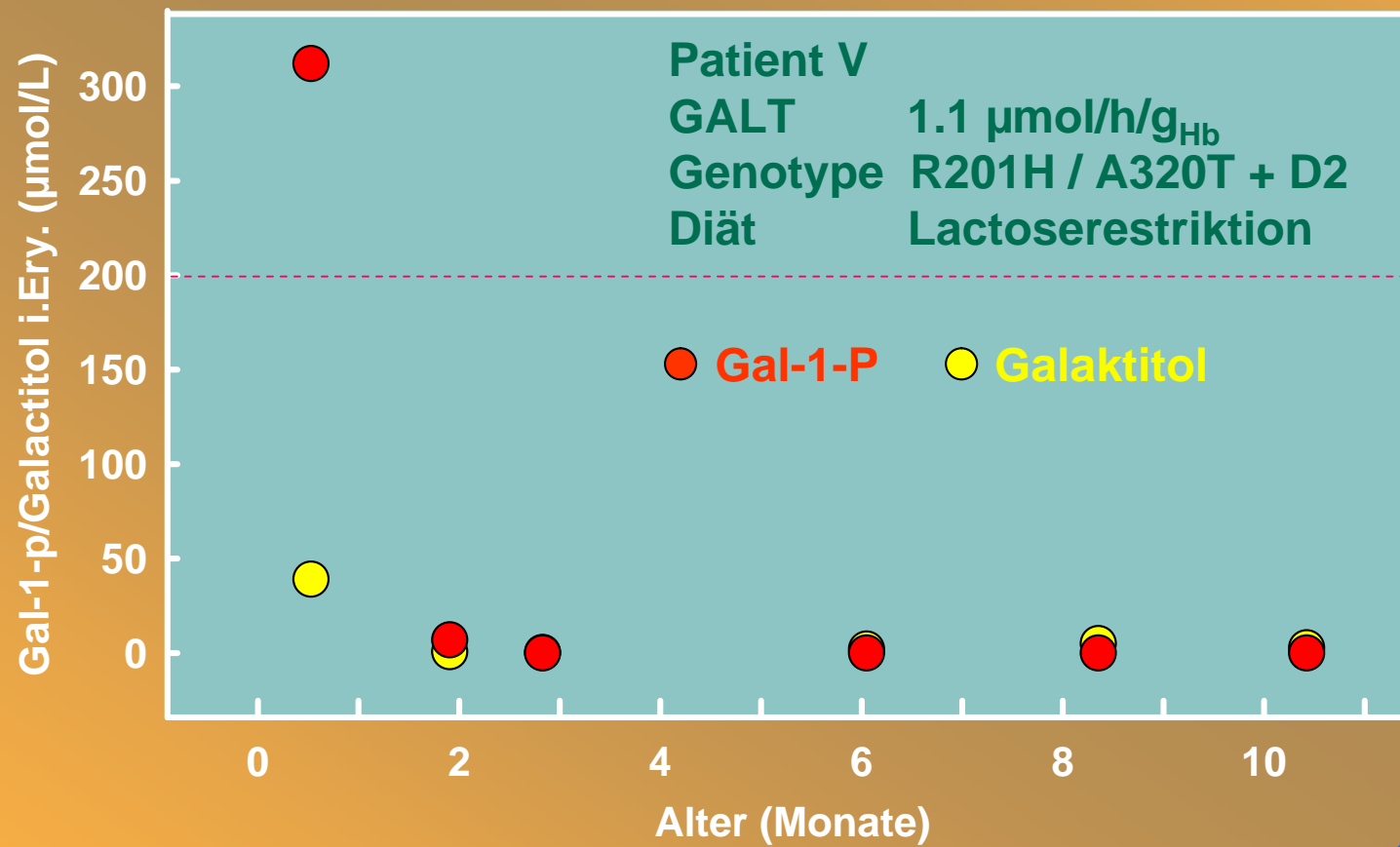
Gal-1-P bei Duarte D2



Schlussfolgerungen

Liegt die Restaktivität der GALT
i. Ery über ca. 20% der Norm
wie z.B. bei Duarte D2-Varianten
sind keinerlei diätetische
Einschränkungen erforderlich

Variante Galaktosämie



- Grundlagen der Galaktosämie
- **Galaktosetoleranz bei Galaktosämie**

Die Duarte D2-Varianten

Studie: Galaktosebelastung

Sporadische Berichte über unbehandelte Galaktosämie

CASE REPORT

Case report

A woman with untreated galactosaemia

Philip J Lee, Margaret Lilburn, Udo Wendel, Peter Schadewaldt

A 38-year-old Caucasian female presented in July, 2002, after her new-born niece was diagnosed with classical galactosaemia; an autosomal recessive trait caused by the absence of the enzyme galactose-1-phosphate uridylyltransferase (GALT). As an infant, our patient had also been diagnosed with galactosaemia, after she developed anorexia and jaundice at 6 days of age. She was prescribed a galactose-free diet and her symptoms resolved. She had a mild speech delay, but all other developmental milestones were normal. At the age of 2 years, her diet was relaxed and galactose restriction was discontinued altogether at 3 years of age. She attended school, obtained continuous full-time clerical work, and lives independently. She had primary amenorrhoea, and started hormone replacement therapy at 15 years of age, but has not had other medical complaints.

On examination, we found no signs of liver disease or cataracts. Full secondary sexual characteristics were present. There was a fine resting tremor, but deep tendon

	Patient result	Reference range
Metabolite		
Red cell galactose-1-phosphate ($\mu\text{mol/L}_{\text{RBC}}$)	124	<190*
Plasma galactose ($\mu\text{mol/l}$)	3.1	<0.3
Plasma galactitol ($\mu\text{mol/l}$)	11.5	<0.3
Urinary galactose ($\mu\text{mol/kg body wt/hr}$)	0.09	<0.05
Urinary galactitol ($\mu\text{mol/kg body wt/hr}$)	1.07	<0.05
Galactose production ($\mu\text{mol/kg body wt/hr}$)	2.39	<0.3

*Treated galactosaemics

Biochemical measures of galactosaemia

The patient reported here had an outcome no worse than that seen in many treated individuals. She has classical galactosaemia; biochemically, enzymatically and genetically and her endogenous galactose production does not differ from treated patients. Despite absence of dietary galactose restriction for 35 years, her medical problems are limited to ovarian failure, and a low IQ.

Galaktose-Belastung bei Galaktosämie

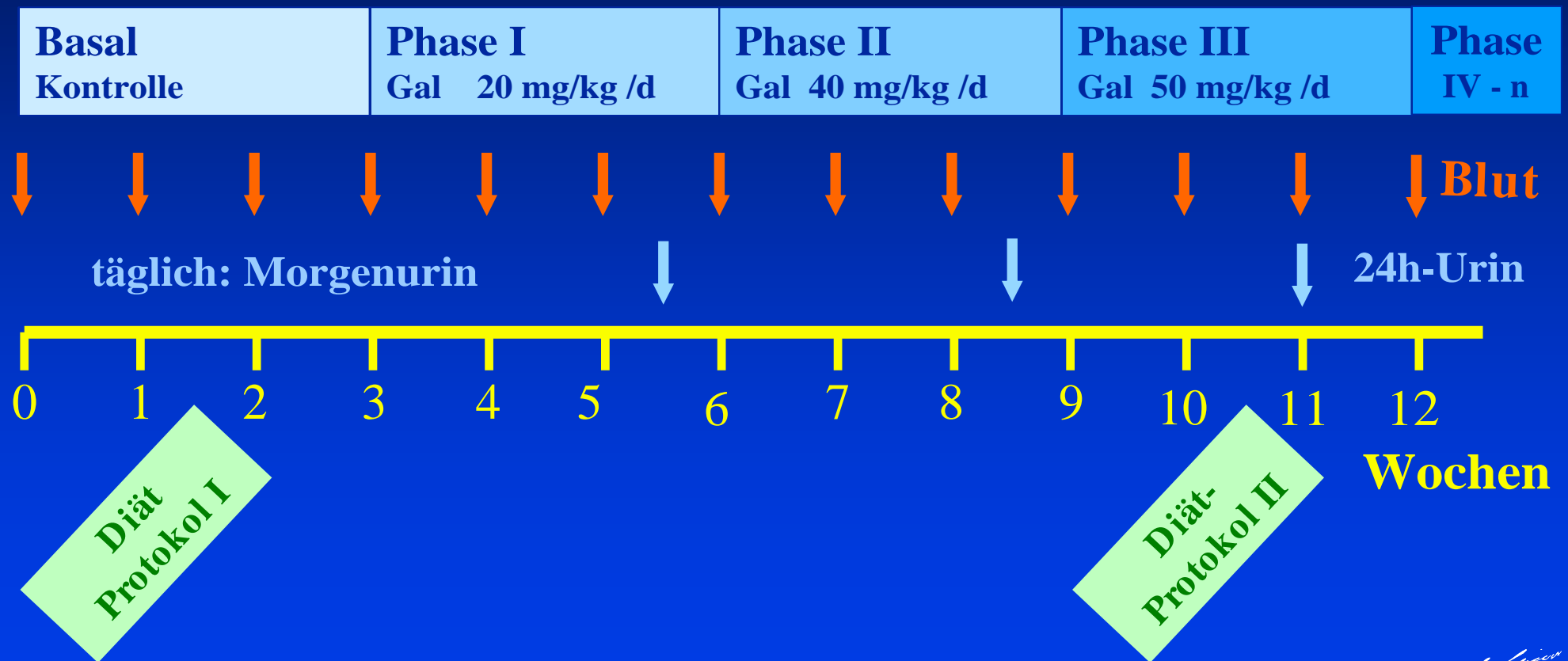
Wirkung auf Gal-1-P in Ery's

Patient UW

Galaktose-Belastung (mg/kg/d)



Ermittlung der Galaktose-Toleranz in vivo: Skizze der Fortsetzungsstudie



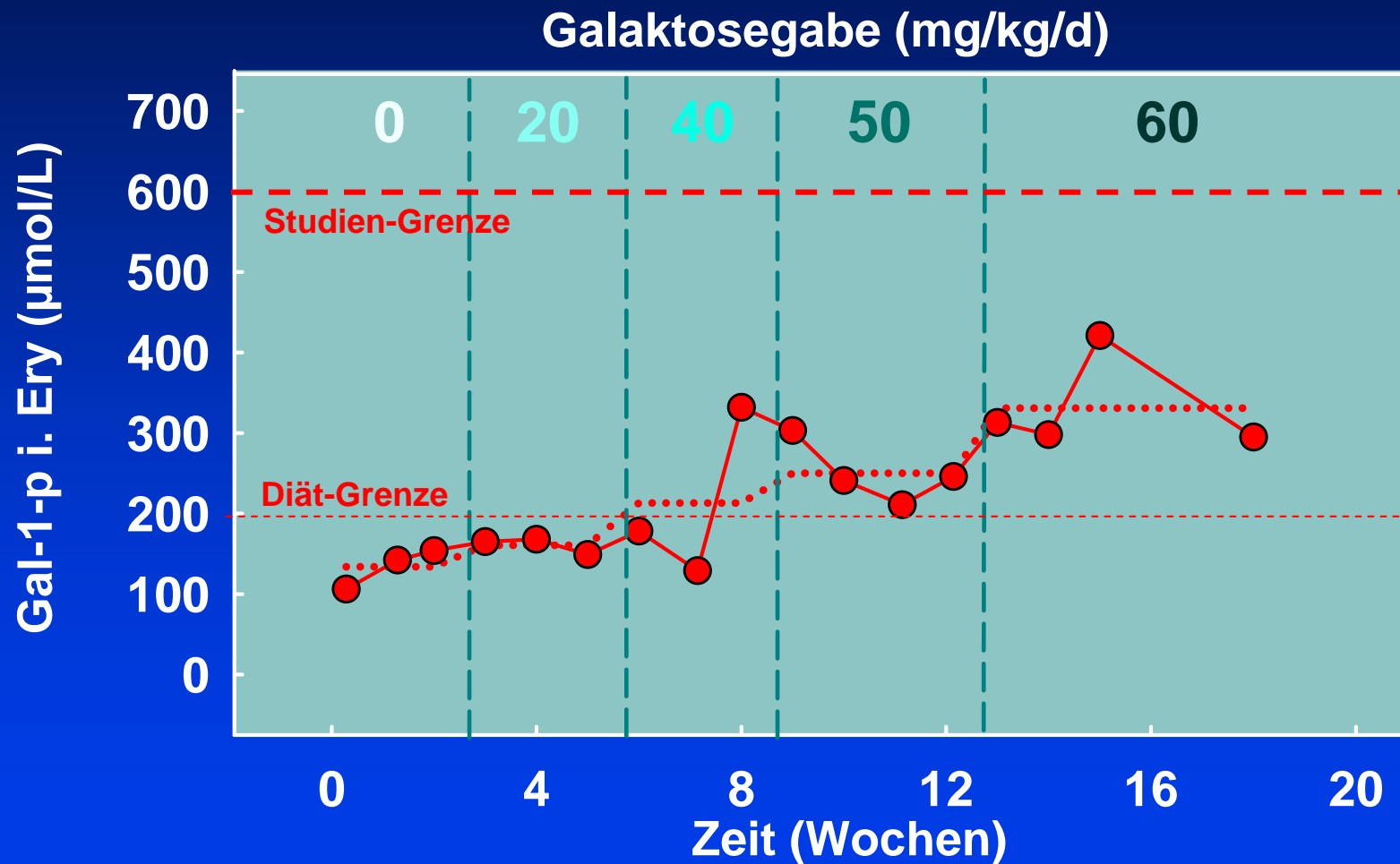
Patient der Pilotstudie

- männlich, geboren 1971
- Landschaftspfleger
- GALT < 2% der Norm
- Genotyp Q188R/ K285N

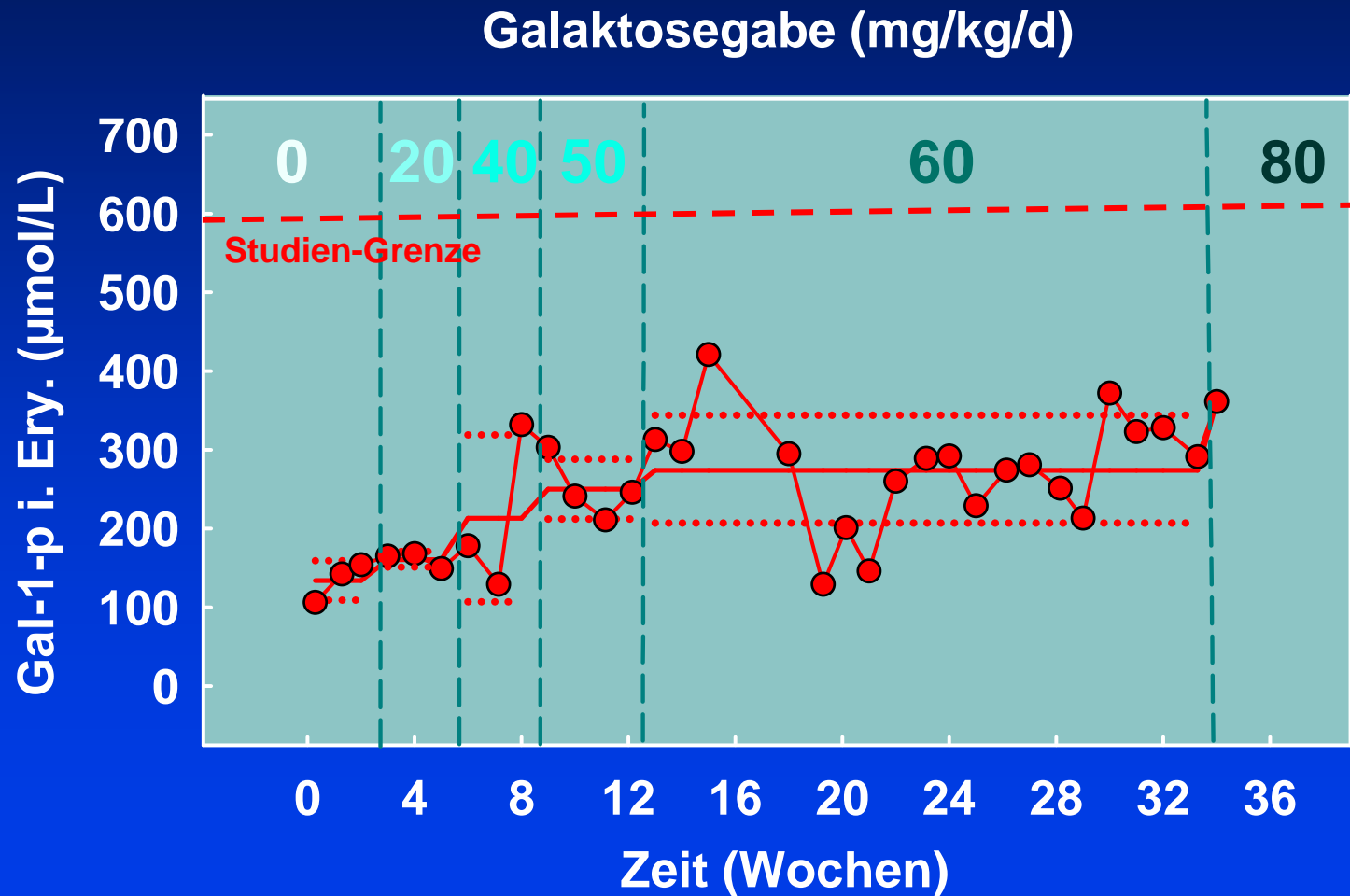
Abbruchkriterien

- **dauerhafter Anstieg
der Leberwerte**
- **Gal-1-P i.Ery.
mehrfach > 15 mg/ dL**

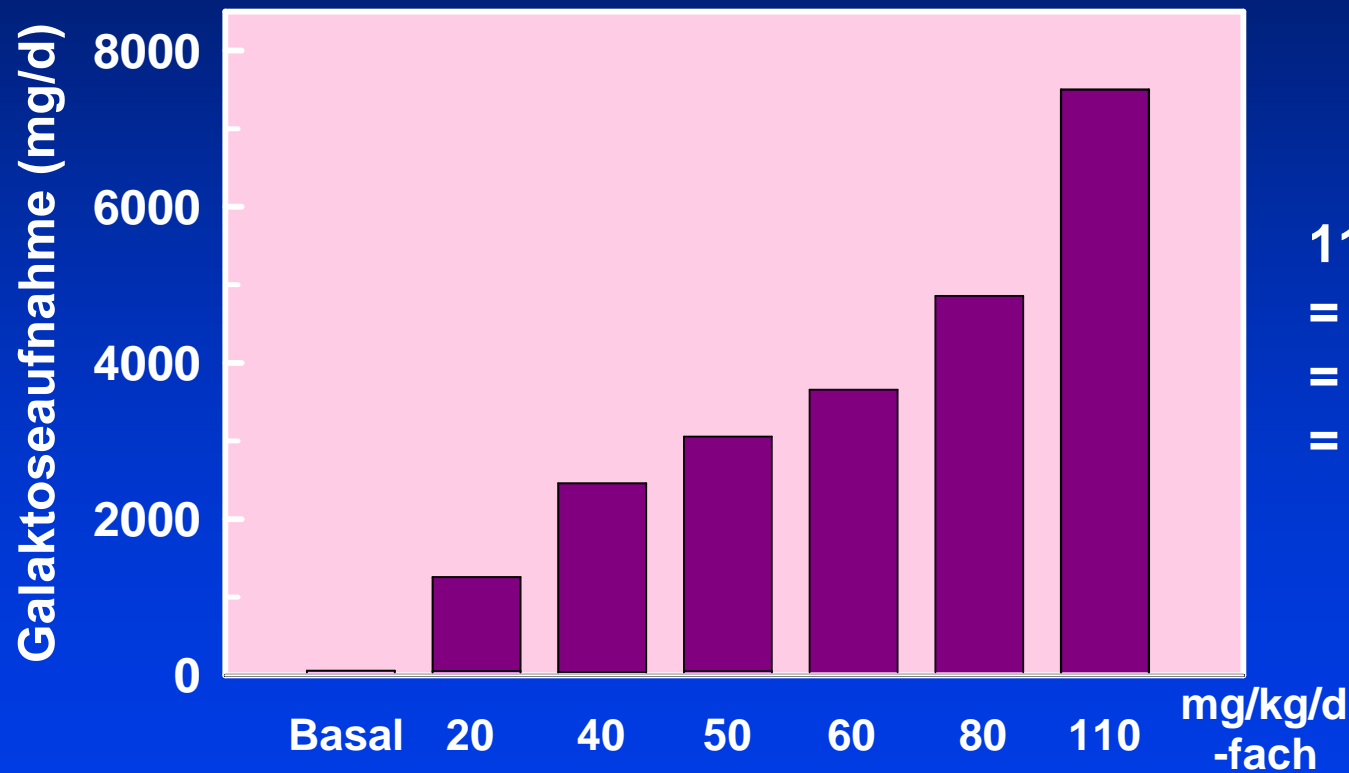
Wirkung der Galaktose-Belastung auf Gal-1-P i. Ery.



Wirkung der Galaktose-Belastung auf Gal-1-P i. Ery.

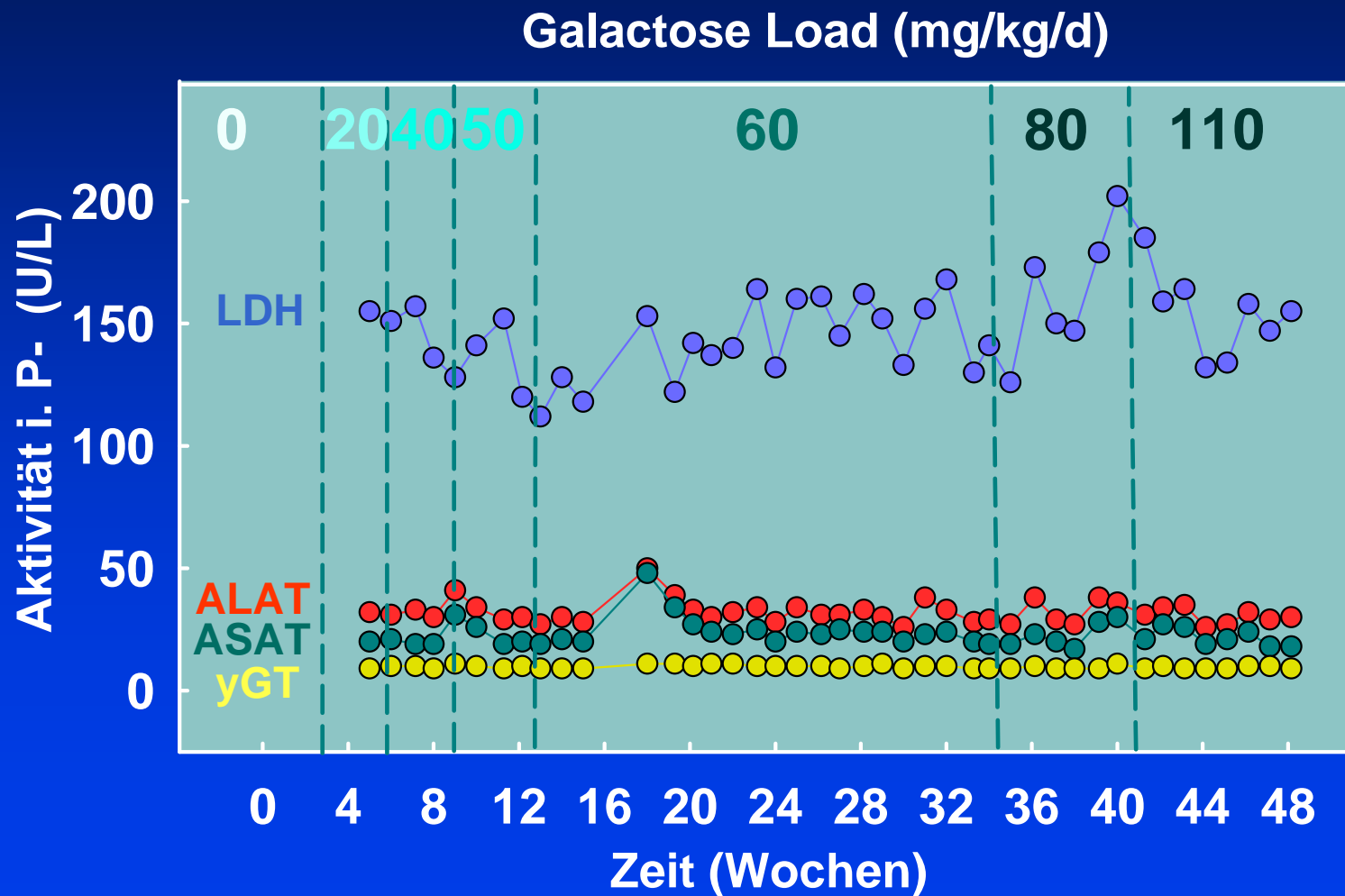


Regulär-diätetische Galaktosezufuhr und zusätzliche Galaktosegabe

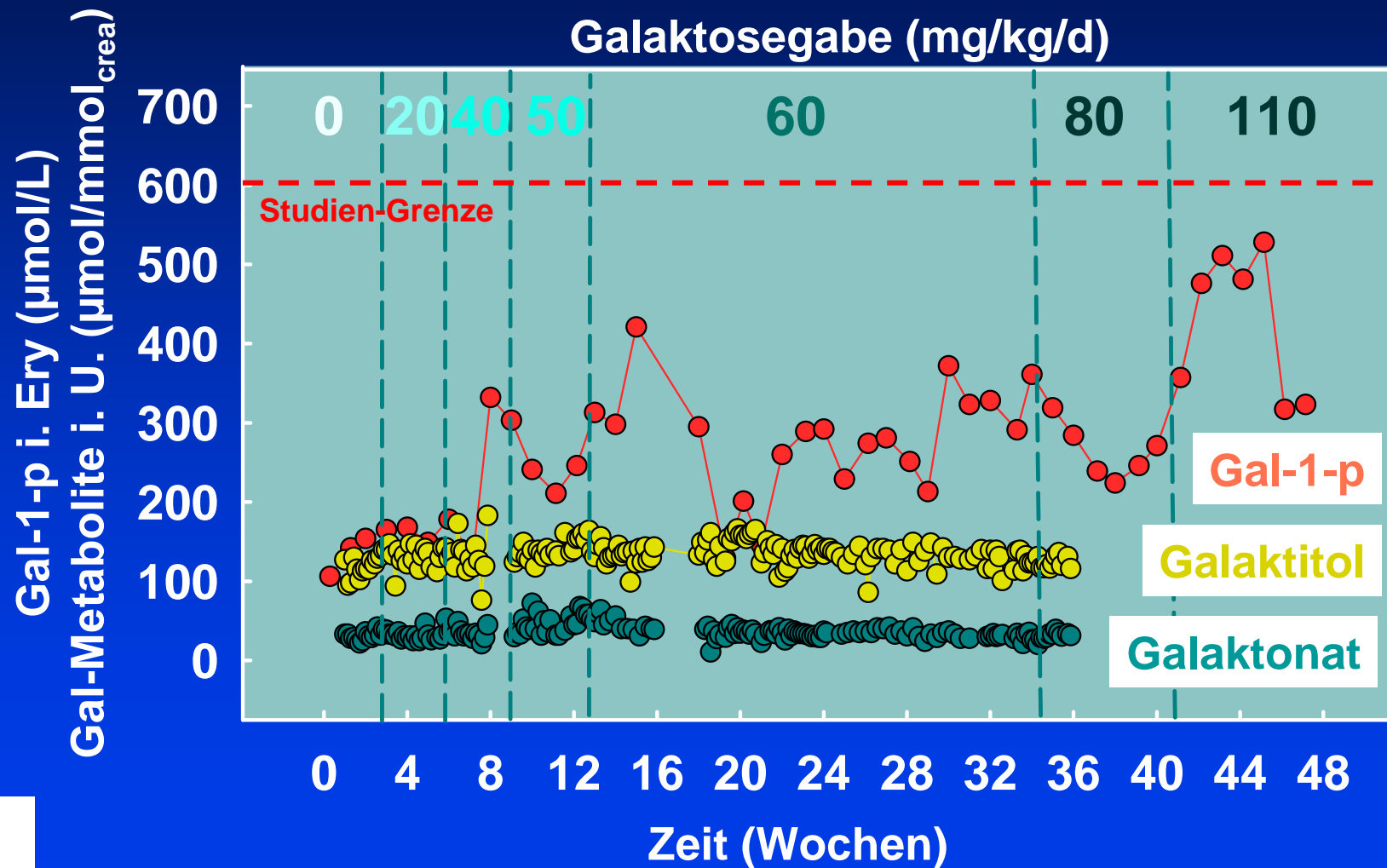


110 mg Gal/kg/d
= 7500 mg/d
= 15 mg Lactose/d
= 300 mL Milch/d

Wirkung der Galaktosegabe auf Leberenzyme im Blutplasma



Gal-1-P i.Ery. und Metabolitausscheidung während langfristiger Galaktosegabe



Offene Fragen

- **Grenze der Galaktosetoleranz ?**
- **Ist die Toleranz repräsentativ für erwachsene Patienten ?**
- **Wo liegt die Grenze bei Kindern ?**
- **Welche Toleranz haben Variante ?**

Danke !!

an alle

**Teilnehmer
und Beteiligte**